External electrical and pharmacological cardioversion for atrial fibrillation, atrial flutter or atrial tachycardias

a network meta-analysis

RevMan: review – intervention; 566617061413585643 (version 2.4)
Status: UNPUBLISHED DRAFT

External electrical and pharmacological cardioversion for atrial fibrillation, atrial flutter or atrial tachycardias: a network meta-analysis

Table of contents

Editors: Cochrane Heart Group

Contact Person: Rui Providencia (r.providencia@ucl.ac.uk)

Barts Heart Centre, St Bartholomew's Hospital, Barts Health NHS Trust, London, UK

Kishore Kukendra-Rajah [1]Mahmood Ahmad [2]Mafalda Carrington [3]Adam Ioannou [4]Julie Taylor [5]

Yousuf Razvi [6]Nikolaos Papageorgiou [7]Gillian E Mead [8]Immaculate IF Nevis [9]Fabrizio D'Ascenzo [10]

Stephen B Wilton [11]Pier D Lambiase [12]Carlos A Morillo [13]Joey SW Kwong [14]Rui Providencia [7]

[1] Barts Health NHS Trust, London, UK

[2] Department of Cardiology, Royal Free Hospital, Royal Free London NHS Foundation Trust, London, UK

[3] Cardiology, Hospital do Espírito Santo de Evora, Évora, Portugal

[4] Royal Free London NHS Foundation Trust, London, UK

[5] Institute of Health Informatics Research, University College London, London, UK

[6] Department of Cardiology, Royal Free Hospital, London, UK

[7] Barts Heart Centre, St Bartholomew's Hospital, Barts Health NHS Trust, London, UK

[8] Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK

[9] Psychiatry, London Health Sciences, London, Canada

[10] Division of Cardiology, Department of Internal Medicine, University of Turin, Turin, Italy

[11] Libin Cardiovascular Institute, University of Calgary, Calgary, Canada

[12] Centre for Cardiology in the Young, The Heart Hospital, University College London Hospitals, London, UK

[13] Department of Cardiac Sciences, Cumming School of Medicine, Foothills Medical Centre, Calgary, Canada

[14] Global Health Nursing, Graduate School of Nursing Science, St. Luke's International University, Tokyo, Japan

Citation

Kukendra-Rajah K, Ahmad M, Carrington M, Ioannou A, Taylor J, Razvi Y, Papageorgiou N, Mead GE, Nevis IIF, D'Ascenzo F, Wilton SB, Lambiase PD, Morillo CA, Kwong JSW, Providencia R. External electrical and pharmacological cardioversion for atrial fibrillation, atrial flutter or atrial tachycardias: a network meta-analysis. Cochrane Database of Systematic Reviews TBD, Issue TBD. Art. No.: CD013255. DOI: 10.1002/14651858.CD013255.pub2.

Dates

Revision published: Issue TBD, TBD (TBD)

Version published (citation changed): Issue TBD, TBD (TBD)

Review first published: Issue TBD, TBD

Protocol first published: Issue 3, 2019

Abstract

Background

Atrial fibrillation (AF) is the most frequent sustained arrhythmia. Cardioversion is a rhythm control strategy to restore normal/sinus rhythm, and can be achieved through drugs (pharmacological) or a synchronized electric shock (electrical cardioversion).

Objectives

To assess the efficacy and safety of pharmacological and electrical cardioversion for AF.

Search methods

We searched CENTRAL, MEDLINE, Embase, Conference Proceedings Citation Index-Science (CPCI-S) and three trials registers (ClinicalTrials.gov, WHO ICTRP and ISRCTN) on 14 February 2023.

Selection criteria

We included randomised controlled trials (RCTs) at individual patient level. Patient populations were aged ≥18 years with AF of any type and duration, atrial flutter or other sustained related atrial arrhythmias, not occurring as a result of reversible causes.

Data collection and analysis

We used standard Cochrane methodology to collect data and performed a network meta-analysis using the standard frequentist graph-theoretical approach using the netmeta package in R. We used GRADE to assess the quality of the evidence which we presented in in our summary of findings with a judgement on certainty. We calculated differences using risk ratios (RR) and 95% confidence intervals (CI) as well as ranking treatments using a P-score. We assessed clinical and statistical heterogeneity and split the networks for the primary outcome and acute procedural success due to concerns about violating the transitivity assumption.

Main results

We included 112 RCTs (139 records), from which we pooled data from 15,968 patients. Average age was 47 to 72 years and proportion of male patients was 38%-92%.

79 trials were considered high risk of bias for at least one domain, 32 had no high risk of bias domains, but had at least one domain classified as uncertain risk, and one study was considered low risk for all domains.

For paroxysmal AF (35 trials), when compared to Placebo, AA/AP BTE incremental cardioversion (RR: 2.42; 95%CI 1.65 to 3.56), quinidine (RR: 2.23; 95%CI 1.49 to 3.34), ibutilide (RR: 2.00; 95%CI 1.28 to 3.12), propafenone (RR: 1.98; 95%CI 1.67 to 2.34), amiodarone (RR: 1.69; 95%CI 1.42 to 2.02), sotalol (RR: 1.58; 95%CI 1.08 to 2.31) and procainamide (RR: 1.49; 95%CI 1.13 to 1.97) likely result in a large increase in maintenance of sinus rhythm until hospital discharge or end of study follow-up (certainty of evidence: moderate). The effect size was larger for AA/AP incremental and was progressively smaller for the subsequent interventions. Despite low certainty of evidence Antazoline may result in a large increase (RR: 28.60; 95%CI 1.77 to 461.30) in this outcome. Similarly, low certainty evidence suggests a large increase on this outcome for flecainide (RR: 2.17; 95%CI 1.68 to 2.79), vernakalant (RR: 2.13; 95%CI 1.52 to 2.99), and magnesium (RR: 1.73; 95%CI 0.79 to 3.79) on this outcome.

For persistent AF (26 trials), one network was created for electrical cardioversion and showed that when compared to AP BTE incremental energy with patches, AP BTE maximum energy with patches (RR 1.35, 95%CI 1.17 to 1.55) likely results in large increase and Active compression AP BTE incremental energy with patches (RR: 1.14, 95%CI 1.00 to 1.131) likely results in an increase in maintenance of sinus rhythm at hospital discharge or end of study follow-up (certainty of evidence: high). Use of AP BTE incremental with paddles (RR: 1.03, 95%CI 0.98 to 1.09; certainty of evidence: low) may lead to a little increase, and AP MDS Incremental paddles (RR: 0.95, 95%CI 0.86 to 1.05; certainty of evidence: low) may lead to a little decrease in efficacy. On the other hand, AP MDS incremental energy using patches (RR: 0.78, 95%CI 0.70 to 0.87), AA RBW incremental energy with patches (RR: 0.76, 95%CI 0.66 to 0.88), AP RBW incremental energy with patches (RR: 0.76, 95%CI 0.68 to 0.86), AA MDS incremental energy with patches (RR: 0.76, 95%CI 0.67 to 0.86) and AA MDS incremental energy with paddles (RR: 0.68, 95%CI 0.53 to 0.83) probably result in a decrease on this outcome when compared to AP BTE incremental energy with patches (certainty of evidence: moderate). The network for pharmacological cardioversion showed that Bepridil (RR: 2.29, 95%CI 1.26 to 4.17) and Quindine (RR: 1.53, (95%CI 1.01 to 2.32) probably result in large increase in maintenance of sinus rhythm at hospital discharge or end of study follow-up when compared to amiodarone (certainty of evidence: moderate). Dofetilide (RR: 0.79, 95%CI 0.56 to 1.44), Sotalol (RR: 0.89, 95%CI 0.67 to 1.18), Propafenone (RR: 0.79, 95%CI 0.50 to 1.25) and Pilsicainide (RR: 0.39, 95%CI 0.02 to 7.01) may result in a reduction of this outcome when compared to amiodarone, but certainty of evidence is low

For atrial flutter (14 trials) a network could be created only for antiarrhythmic drugs. Using Placebo as the common comparator, ibutilide (RR: 21.45, 95%CI 4.41 to 104.37), propafenone (RR: 7.15, 95%CI 1.27 to 40.10), dofetilide (RR: 6.43, 95%CI 1.38 to 29.91), and sotalol (RR: 6.39, 95%CI 1.03 to 39.78) probably result in a large increase in maintenance of sinus rhythm at hospital discharge or end of study follow-up (certainty of evidence:

moderate), and procainamide (RR: 4.29, 95%CI 0.63 to 29.03), flecainide (RR 3.57, 95%CI 0.24 to 52.30) and vernakalant (RR: 1.18, 95%CI 0.05 to 27.37) may result in a large increase of maintenance of sinus rhythm at hospital discharge or end of study follow-up at (certainty of evidence: low) All tested electrical cardioversion strategies for atrial flutter had very high efficacy (97.9% to 100%).

Mortality (14 deaths) and Stroke or systemic embolism (3 events) at 30 days was extremely low.

Data on quality of life were scarce and of uncertain clinical significance. No information was available regarding heart failure readmissions. Data on duration of hospitalization was scarce, low quality, & could not be pooled.

Authors' conclusions

Despite the low quality of evidence, this systematic review provides important information on electrical and pharmacological strategies to help patients and physicians deal with AF and atrial flutter.

Assessing the patient comorbidity profile, antiarrhythmic drug onset of action & side effect profile vs. need for a physician with experience in sedation, or anaesthetics support, for electrical cardioversion are key aspects when choosing the cardioversion method.

Plain language summary

Electrical shocks (electrical cardioversion) and drugs (pharmacological cardioversion) for restoring normal rhythm in patients with Atrial fibrillation or Atrial Flutter

Key Messages

- Electrical cardioversion and drugs like vernakalant, flecainide, ibutilide, dofetilide, quinidine, propafenone, amiodarone, procainamide, bepridil, antazoline and sotalol can be used to restore the normal rhythm in patients with atrial fibrillation (AF) and atrial flutter. While electrical cardioversion is highly effective at dealing with all arrhythmias, efficacy of drugs varies, with some being only moderately effective or not working at all in persistent AF and atrial flutter.

- Electrical cardioversion seems to be a very safe option. Risk of severe complications with pharmacological cardioversion was low, but justifies additional precautions when drugs are used.

- We need further studies to find out if these treatment options also have a positive effect on quality of life, or if they lead to relevant differences in the duration of hospital stay.

What is atrial fibrillation?

AF is the most frequent abnormal heart rhythm seen in the world. Patients with this condition may feel their heart beating rapidly and irregularly. This can occur for separate brief or long episodes (paroxysmal AF) or it may become continuous (persistent AF). Atrial flutter is a similar arrhythmia than causes similar symptoms and can cause episodes of variable duration and also become continuous.

What is cardioversion?

Cardioversion is a treatment to restore the rhythm of the heart back to normal (sinus rhythm).

What did we want to find out?

We wanted to know if delivering a controlled electrical shock (i.e. electrical cardioversion) and drugs (i.e. pharmacological cardioversion) are effective and safe when restoring heart rhythm back to normal.

What did we do?

We searched for studies that investigated electrical and pharmacological cardioversion compared to each other or placebo (a medicine that looks like the real medicine but that has no active ingredient).

We compared and summarised the results of the studies and rated our trust in these results, based on factors such as study methods and sizes.

What did we find?

We found 112 studies. We were able to combine and analyse the results from 72 studies, with 15,968 participants. Thirty five included patients with paroxysmal AF, 26 studies patients with persistent AF, and 14 trials included patients with atrial flutter. The remaining included a mix of paroxysmal, persistent AF and atrial flutter. People in the studies were aged between 47 and 72 years.

Main results

For patients with paroxysmal AF, electrical cardioversion with biphasic incremental energy, fast acting drugs like intravenous vernakalant, flecainide, ibutilide and antazoline, and slower-acting and/or oral drugs as quinidine, propafenone, amiodarone and sotalol are effective at restoring sinus rhythm.

For patients with persistent AF electrical cardioversion with biphasic energy seems to be the most effective option, and Bepridil, Quinidine and Amiodarone tablets may also be effective in selected cases.

For patients with atrial flutter, electrical cardioversion followed by dofetilide are the most effective options.

Risk of death and stroke is very low for patients having cardioversion procedures.

Malignant arrhythmias (e.g. torsade de pointes, ventricular tachycardia or fibrillation) were observed for dofetilide, ibutilide, sotalol, quinidine and vernakalant, justifying the need for special care and closer monitoring when using these drugs. Duration of hospitalization data was available in 3 studies but not poolable as timings in these studies were defined differently. These studies suggest that duration of hospitlization may be lower with electrical cardioversion.

Heart failure was observed in a small number of patients treated with propafenone, flecainide, sotalol, amiodarone, vernakalant, and placebo, and was not observed in patients receiving electrical cardioversion, suggesting that the latter approach should be the preferred one if concerns exist regarding occurrence of this outcome.

Phlebitis (i.e. inflammation of the vein caused by using injectable drugs) occurred frequently in patients treated with amiodarone, and dysgeusia (i.e. impairment of the sense of taste) and sneezing occurred frequently in patients receiving vernakalant.

What are the limitations of the observed results?

We are sure or moderately sure on the results for the efficacy treatments available for persistent AF and atrial flutter. We are less sure on the results for some of the treatment options for paroxysmal AF.

Not enough data is available regarding quality of life, and data are scare regarding duration of hospital stay. Risk of stroke or dying was very low.

How up-to-date are the studies and information on this review?

The included studies and informatio is current to February 2023.

Background

Description of the condition

Atrial fibrillation (AF) is the most frequent arrhythmia seen in clinical practice, with a prevalence of 3% in recent community studies (Björck 2013; Haim 2015), and its prevalence is likely to rise in the next decades (Chugh 2014; Go 2011; Krijthe 2013; Lloyd-Jones 2004; Magnani 2011; Miyasaka 2006). This arrhythmia is associated with a high annual cost for healthcare systems (Maddox 2008), and is characterised by high clinical and biological heterogeneity, being responsible for causing a myriad of symptoms, like palpitations, shortness of breath, chest pain, syncope, among others (ESC Guidelines 2016). Unlike other arrhythmic disorders, AF is also associated with an increased risk of stroke and systemic embolism (Wolf 1978). Data from the Framingham study have shown that the presence of AF was an independent risk factor for death (odds ratio (OR) 1.9, 95% confidence interval (CI) 1.5 to 2.2 in females and OR 1.5, 95% CI 1.2 to 1.8 in men; Benjamin 1998).

Patients with AF episodes lasting more than seven days are usually described as having persistent AF. Paroxysmal AF is reserved for patients with episodes that self-terminate spontaneously or with intervention within 7 days of onset (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016; ESC Guidelines 2020). Patients who remain in AF and where a rate control strategy has been chosen, meaning that they will likely remain in AF for the rest of the time, are defined as having permanent AF. Those patients having an AF episode lasting for more than one year, but where rhythm control is still being pursued are defined as having long-standing persistent AF.

On a pathophysiological level, since the publication of the landmark paper by Haïssaguere and colleagues (Haïssaguerre 1998), the pulmonary veins are thought to be the initiators of paroxysms of AF and radiofrequency ablation as an effective way of treating this arrhythmia. It is thought that unlike paroxysmal AF where a predominance of local triggers/drivers, particularly from the pulmonary veins, is thought to occur, in persistent AF, re-entry substrates (initially functional and then structural) predominate following electrical and structural remodelling of the atria (Iwasaki 2011). This was supported by early reports of significantly improved efficacy of pulmonary vein isolation in paroxysmal AF compared with persistent AF (Oral 2002). However, pulmonary veins may also be responsible for starting approximately 50% of AF episodes in patients with persistent AF, as suggested by the results of the STAR-AF II trial (Verma 2015).

Postablation atrial tachycardias (or flutters) are thought to occur because of macro- or micro-reentrant circuits developing around areas of previous ablation where focal recovery has led to the development of reentrant-prone areas (Pappone 2012).

Unlike atrial fibrillation, typical atrial flutter occurs as a result of a macro-reentrant circuit in the right atrium with an isthmus in the cavotricuspid area (Feld 1992). Atrial flutter may coexist in 80% of patients with AF (Tunick 1992). Based on observational emergency department data, this atrial arrhythmia is more likely to respond to electrical cardioversion than to pharmacological cardioversion (Scheuermeyer 2011;Vaughan Williams 1984).

Description of the intervention

The treatment of AF currently consists of using anticoagulants for preventing stroke and systemic embolism and strategies aiming to control patients' symptoms (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016; NICE 2014). These strategies include two different approaches: rhythm control and rate control.

Rhythm control, which includes cardioversion (which can be electrical - i.e. direct-current cardioversion, or pharmacological - if antiarrhythmic agents are used), catheter ablation (usually pulmonary vein isolation) and antiarrhythmic agents, aims to restore the patient's rhythm back to normal (i.e. sinus rhythm), thus allowing the patient to recover atrial depolarisation and contraction, and atrioventricular synchrony. Hopefully this will increase the cardiac output, lead to a more controlled heart rate and resolve patients' symptoms. Unfortunately, these strategies under certain circumstances, like the presence of persistent AF, and structural heart disease, may be effective in less than 50% of patients, and sooner or later the rhythm will evolve to AF once again (Mont 2014; Verma 2015).

The other strategy, called rate control, consists of controlling the patient's ventricular rate, without making an attempt to interfere with the atrial arrhythmia. This seems to be the preferred alternative for asymptomatic patients, or those without a clear symptom-arrhythmia correlation, and for patients with low chances of remaining in sinus rhythm if the rhythm control strategy was used. Drugs (beta-blockers, calcium channel blockers, digoxin), or catheter ablation of the atrioventricular node and pacemaker implant can be used (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016).

The 'Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)' (Wyse 2002), and the 'Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study (RACE)' (Van Gelder 2002), were two landmark trials comparing rate versus rhythm control strategies and their impact on outcomes. The results showed there was no discernible difference between the two treatment strategies in terms of outcomes. Some of the suggested explanations for the results of the rhythm control strategy were the suboptimal use of anticoagulation, and possible toxicity induced by the used antiarrhythmic agents (Blackshear 2003).

A subanalysis of the AFFIRM trial suggested that being in sinus rhythm (independently of the treatment strategy) and receiving oral anticoagulation were associated with improved survival. Conversely, the use of antiarrhythmic agents was associated with increased mortality (Corley 2004). These data reinforce the main role of thromboembolic prophylaxis in AF patients and suggested that being in sinus rhythm should be pursued using a more effective approach, and with fewer adverse effects, than the antiarrhythmic agents used in this trial. However, inference about life-prolonging effects of being in sinus rhythm could be biased, because it may be assumed, that those in sinus rhythm were in a better general health condition than those in AF.

Subsequently, dronedarone an antiarrhythmic agent with a more favourable adverse effect profile (mainly on a thyroid and neurologic level) held some promise in the field. Despite being less effective than amiodarone (AF recurrence during a median of 7 months after successful cardioversion was 63.5% with dronedarone versus 42.0% with amiodarone; $P < 0.01$; Le Heuzey 2012), the results of dronedarone in the ATHENA trial (Hohnloser 2009), led to enthusiasm concerning this novel antiarrhythmic agent. This drug was associated with a reduction in the primary study endpoint of first hospitalisation due to cardiovascular effects or death (hazard ratio (HR) 0.76, 95% CI 0.69 to 0.84, $P < 0.001$), and it was also the first antiarrhythmic agent capable of reducing cardiovascular death (HR 0.71, 95% CI 0.51 to 0.98, $P = 0.03$) and stroke (HR 0.66, 95% CI 0.46 to 0.96, $P = 0.027$) (Connolly 2009). However, in the PALLAS trial, dronedarone used in patients with permanent AF increased rates of heart failure, stroke, and death from cardiovascular causes (Connolly 2011). These results led to recommendations by the Food and Drug Administration (FDA) and the National Institute for Health and Care Excellence (NICE) for the drug not to be to used in patients with permanent AF (FDA 2011; NICE 2013).

Recent data from a large nationwide registry suggest that the rhythm control strategy, through catheter ablation, may also be associated with lower mortality and stroke incidence (Friberg 2016). However, referral bias for ablation could explain such findings. For the population of AF patients with left ventricular ejection fraction < 35% in the 'Catheter Ablation versus Standard conventional Treatment in patients with LEft ventricular dysfunction and Atrial Fibrillation (CASTLE-AF)' trial, there was a reduction of all-cause mortality in patients treated with catheter ablation (HR 0.53, 95% CI 0.32 to 0.86, $P = 0.011$; Marrouche 2018). Among symptomatic AF patients aged ≥65 years or <65 years with ≥1 risk factors for stroke, the 'Catheter Ablation vs Anti-arrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA)', showed a reduction in all-cause mortality and cardiovascular hospitalization for those randomized to catheter ablation (51.7% vs. 58.1%; HR 0.83, 95% CI 0.74-0.93, $P = 0.001$) (Packer 2019). The recently published EAST-AFNET 4 trial showed that early rhythm control (treating patients who had AF for <1 year before enrolment) is superior to usual care (i.e. rate control) in improving cardiovascular outcomes (stroke and cardiovascular mortality) (EAST-AFNET 4).

In sum, a growing body of evidence is now providing support to rhythm control strategies, and their use is likely to increase further within the next few years.

How the intervention might work

A cardioversion is a procedure whereby a sustained abnormal rhythm is reverted back to sinus rhythm by means of a synchronised internal or external shock (electrical cardioversion) (Lown 1962; Lown 1963), or by the action of antiarrhythmic drugs (pharmacological cardioversion) (Gunton 1964; Wenckbach 1923).

In pharmacological cardioversion, antiarrhythmic drugs are used instead to terminate atrial activity in the atria by interfering with effective refractory periods of atrial myocytes and terminating the propagation of AF micro-reentrant wavelets and blocking atrial arrhythmia triggers (Boriani 2004; Knight 2015).

In an electrical cardioversion, a selected amount of electric current (usually in joules) over a predefined number of milliseconds at the optimal moment of the cardiac cycle is delivered by way of pads/patches (external cardioversion) or through an intravascular device (internal cardioversion) (Lévy 1992), halting the fibrillation activation fronts and allowing or giving rise to new wavefronts from the sinus node to resume and recover control (reversal of sinus rhythm) in case it works successfully (Cakulev 2010; Chen 1991; Knight 2015). Synchronisation with the R wave of the QRS complex is performed to prevent cardioversion-induced arrhythmias (e.g. ventricular fibrillation), which can occur if a shock is delivered to the vulnerable period of the T wave (R-on-T). Pads or patches can be positioned in anteroposterior or anterolateral positions (Kirchhof 2002). For electrical cardioversion, sedation is required, as the shock would be very painful for the patient if they were awake.

Cardioversion is usually performed under close monitoring in a hospital-based setting. This can occur in a cath lab, in an emergency department, or in an intensive care unit. Minimal requirements for procedural safety are electrocardiographic monitoring, regular measurement of blood pressure, and respiratory rate, and arterial oxygen saturation using a pulse oximeter. If the patient is unstable, with haemodynamic imbalance occurring as a result of the arrhythmia, it is performed urgently. However, more frequently, cardioversions are performed in stable patients on an elective basis (Knight 2017).

Possible complications include skin burn or skin irritation (for electrical cardioversion), muscle pain (for electrical cardioversion), sedation-related complications, proarrhythmia (unsynchronised cardioversion or drug-induced tachyarrhythmias), bradycardias (in case of severe sinus node disease), and postcardioversion cardiogenic shock or acute pulmonary oedema (as a result of postshock cardiac stunning) (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016; Knight 2015). Another possible complication is embolic stroke following the dislodgement of an intracardiac clot following cardioversion and/or the recovery of normal atrial contractility. For that reason, international guidelines have provided precise guidance on what precautions (anticoagulation and preprocedural transoesophageal echocardiogram) are required to prevent this complication (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016; 2023 ACC/AHA/ACCP/HRS Guideline).

Factors known to affect the success of cardioversion include AF episode duration and left atrial size. AF lasting for more than three years is more likely to recur (Resnekov 1968), and AF lasting for less than a month is more frequently associated with cardioversion success (Dalzell 1990). AF is more likely to recur in dilated left atria (Olshansky 2005). In recent-onset AF, faster-acting agents like ibutilide and vernakalant seem to be more effective than sotalol (Vos 1998), or amidoarone (Camm 2011), respectively.

Why it is important to do this review

AF is a highly prevalent heart condition (Go 2011; Magnani 2011), and is the most frequent cause of hospital admission because of arrhythmia (Bialy 1992). Cardioversions are performed very frequently all around the world to revert the rhythm back to sinus. Development of new antiarrhythmic agents (vernakalant, vanorexine, antazoline), and growing evidence in recent years that pursuing a rhythm control strategy may improve outcomes (Corley 2004; Friberg 2016; Hohnloser 2009; Marrouche 2018), supports the idea that besides having an effect on symptoms, interventions to restore the rhythm back to sinus-like cardioversion may have an impact on prognosis, and therefore the use of cardioversion and other rhythm control strategies is likely to increase even further. As there are several options for performing a cardioversion (pharmacological or electrical, and within pharmacological cardioversion there are several different drug options), it is important to clarify the efficacy of each of these techniques, and whether or not, one strategy shows better results, and therefore should be preferred.

In the clinical setting, the decision between using external electrical cardioversion and pharmacological cardioversion frequently depends on the clinician's preference and experience, internal protocols, and the availability of an anaesthetic support team to provide safe sedation when performing external electrical cardioversion. The International guidelines do not provide strong evidence or recommendations on which cardioversion strategy is more effective and should be preferred, except for the setting of haemodynamic instability, where electrical cardioversion is recommended (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016), the guidelines fail to provide a recommendation on which should be favoured, electrical or pharmacological cardioversion. According to the ESC, and AHA/ACC "Level of Evidence A" applies to a recommendation which evidence comes from "Data derived from multiple randomised clinical trials or meta-analyses", "Level of Evidence B" to "Data derived from a single randomized clinical trial or large non-randomized studies", and "Level of Evidence C" to "Consensus of opinion of the experts and/or small studies, retrospective studies, registries". Out of the eight recommendations in the American guidelines, three have level C evidence and three have level B evidence (ACC/AHA/HRS Guidelines 2014), while the ESC guidelines present six out of eight recommendations with level B evidence, suggesting that quality of evidence for cardioversion-related practice is low. Performing a systematic review addressing the topic allows for improvement of the level of evidence in future guidelines.

The previous reviews on electrical and pharmacological cardioversion of AF and flutter (Cordina 2005; Mead 2005), focused mainly on rhythm versus rate control strategy but did not focus on procedural data of cardioversion (efficacy, relapse rates, etc.), which means that this subject still needs to be covered in a Cochrane Review.

There are many different pharmacological approaches and different pad positions, wave forms and energies for electrical cardioversion, therefore an important question is not just which of pharmacological or electrical cardioversion approaches is superior with respect to efficacy or safety but what the differences are between individual treatement and also in which patient populations. Thus the question lends towards a network meta-analysis which should provide a synthesis of all available treatment data for this particular clinical problem.

Therefore the aim of this review will be to compare different pharmacological agents, electrical waveforms, pad positions and energy protocols as well as comparisons to placebo, to establish how well they achieve the main efficacy outcome of achieving sinus rhythm but also the risk of safety outcomes such as cerebrovascular events or cardiovascular mortality.

Objectives

To assess the efficacy and safety of different pharmacological and electrical cardioversion approaches for atrial fibrillation (AF) using a network meta-analysis.

We plan to rank treatmement according to: the primary efficacy outcome which is maintenance of sinus rhythm until hospital discharge or end of study follow-up. However we will also rank acute procedural success, 30-day mortality outcome, quality of life, duration of hospitalization, bradycardia, and ventricular tachycardia.

Methods

Criteria for considering studies for this review

Types of studies

We undertook this systematic review according to the recommendations stated in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We included randomised controlled trials (RCTs) at individual patient or cluster level which could be reported as full-text, published as abstract only, and unpublished data. We also allowed for inclusion of quasi-randomized controlled trials (RCTs where treatment allocation was obtained by alternation or other predictable methods) and cross-over trials. However, we did not include data from cross-over trials following the cross-over phase, as it is known that the different treatment alternatives can mutually affect each other, and could potentially contaminate the analysis (e.g. antiarrhythmic drugs in a patient with failed pharmacological cardioversion can remain in the bloodstream, and may increase the chances of success of a subsequent electrical cardioversion if performed shortly after).

Types of participants

All patients aged ≥ 18 years with AF of any type and duration, atrial flutter or other sustained related atrial arrhythmias, which did not occur as a result of cardiac surgery or other potentially reversible causes (i.e. sepsis, hyperthyroidism, trauma, critically ill in intensive care, etc.)

Types of interventions

The interventions were:

- External electrical cardioversion: all waveforms - biphasic truncated exponential (BTE) wave form, rectilinear biphasic (RB) waveform, pulsed biphasic (PB), monophasic damped sinewave (MDS); energy - fixed, incremental or maximum; patches or pads; positions - anteroposterior, or anterolateral/anteroapical.
- Pharmacological cardioversion (any approved anti arrhythmic drugs will be considered): vernakalant, dofetilide, ibutilide, propafenone, flecainide, amiodarone, sotalol, quinidine, procanimamide, magnesium, etc; antiarrhythmic drugs will be defined as any drugs utilized in routine clinical practice in at least one country with the goal of reverting AF back to sinus rhythm. Information for the same drug will be combined, irrespectively of duration and dose.
- Placebo

Networks of interventions will be built utilizing the different drugs, electrical cardioversion strategies, and placebo. Whenever possible (as allowed by trial data), drugs and electrical cardioversion strategies will be included on the same network.

Groups of patients being treated (intervention and placebo), need to be comparable with regard to cardiac disease (frequency, type and severity) and, mainly, the type and duration of AF. Also, groups ideally should receive similar treatment apart from the intervention being assessed i.e similar treatment regarding:

- Management, initiation, discontinuation, dose and surveillance of anticoagulation;
- Management and drugs used for hypertension and heart failure.

We excluded trials of internal cardioversion versus pharmacological cardioversion or internal cardioversion versus placebo. Reasons for excluding internal cardioversion included the need of having either an implantable cardioverter defibrillator or equivalent device, or an intravascular catheter with cardioverting capability. These occur in very specific scenarios such as patients with other arrhythmias, and also in specific patient populations such as those with heart failure, therefore it would introduce bias into this review.

Addressing the transitivity assumption is also important here as each intervention should be a potential treatment for patients in any trial in the network. In the context of cardioversion for AF it is unlikely that electrical or pharmacological approach would not be interchangeable, except in the context of internal cardioversion.

Types of outcome measures

Reporting one of more of the outcomes listed here in the trial is not an inclusion criterion for the review. Where a published report does not appear to report one of these outcomes, we will access the trial protocol and contact the trial authors to ascertain whether the outcomes were measured but not reported. We will include relevant trials in the review as part of the narrative which measured these outcomes but did not report the data at all, or not in a usable format.

Primary outcomes

- Maintenance of sinus rhythm until hospital discharge or end of study follow-up

Maintenance of sinus rhythm can be demonstrated through absence of symptoms and predischarge 12-lead electrocardiogram (ECG) in sinus rhythm, or through telemetry monitoring. Therefore, combination of information from these different sources is utilized to classify patients as being in sinus rhythm at discharge/end of follow-up, or being in AF (binary outcome).

Secondary outcomes

- Acute procedural success, defined as "restoration of sinus rhythm even if for only one beat" Antman EM 2012
- Stroke or systemic embolism occurring within the first 30 days following cardioversion, reported as a composite rather than individual outcomes as the 2 outcomes share the same mechanism;
- 30-day all-cause mortality
- 30-day cardiovascular mortality
- Duration of hospitalisation
- Quality of life, measured with any validated scale within the first year post cardioversion.
- Heart failure admission within the next month
- Development of ventricular arrhythmias following cardioversion while in hospital
- Development of bradyarrhythmias following cardioversion while in hospital
- Immediate (< 24 hours) procedure-related complications
- Complications deemed to be related to the procedure occurring within the first week.

Complications can be either rhythm-related as mentioned above, or skin burn or skin irritation, sedation-related complications, cardiogenic shock and acute pulmonary oedema.

Regarding the outcomes stroke and/or systemic embolism, or mortality (if stroke/embolic related), we excluded from analysis studies not following the current guidelines for thromboprophylaxis of thromboembolic events during cardioversion (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016;ESC Guidelines 2020). These recommendations state that: for AF of unknown duration or lasting ≥ 48 hours, patients require a preprocedural transoesophageal echocardiogram to exclude the presence of intracardiac clots or three weeks of effective anticoagulation. Following cardioversion, four weeks of anticoagulation will be required.

Search methods for identification of studies

Electronic searches

We searched the following sources, to identify relevant trials, on 14th February 2023:

1. Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (2023, Issue 2) (Cochrane 2022)
2. MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily and MEDLINE (Ovid, 1946 onwards)
3. Embase (Ovid, 1980 onwards)

4. Conference Proceedings Citation Index-Science (CPCI-S) on the Web of Science (Clarivate Analytics, 1990 onwards).

We adapted the search strategy for MEDLINE (Ovid) for use in the other databases (Appendix 1; Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7). We applied the Cochrane sensitivity and precision maximising RCT filter to MEDLINE (Ovid) and adaptations of it to the other databases (Lefebvre 2011), except CENTRAL. We did not impose restrictions with regard to language of publication or publication status.

We did not perform a separate search for adverse effects of electrical or pharmacological cardioversion used for the treatment of AF. We considered adverse effects described in included studies only.

Searching other resources

We searched three clinical trial registers on 14th February 2023: ClinicalTrials.gov (clinicaltrials.gov); the WHO ICTRP (who.int/ictrp/en); and the ISRCTN registry (ISRCTN), for ongoing or unpublished trials.

For identified studies with status of registration not present in any of the three aforementioned registries, we looked for additional evidence of registration in national trial registries, and clinical trial registries listed on the US Department of Health and Human Services website (HHS 2015).

We checked the reference lists of all included studies and any relevant systematic reviews identified. We also examined any relevant retraction statements and errata for included studies.

Data collection and analysis

Selection of studies

We obtained full-texts for all potentially eligible papers following assessment of the abstracts. Review authors (KK, RP, AI, MA and JT) independently assessed each paper. We used Covidence for accelerating the process of title and abstract screening.

Review authors (KK, RP, AI, MA, YR and JT) then independently assessed the full texts selected from the abstract screening in duplicate.

If we excluded a trial after analysis of its full paper, we added a record of the study and the reason for excluding it to a document. Differences between any two review authors in the selection process were resolved by discussion or by a third review author (RP) if agreement was not reached.

Data extraction and management

Review authors (KK, RP, AI, MA, JT, YR and MC) extracted data independently and in duplicate using a data collection form specifically developed for this task. When necessary, we contacted authors of primary studies for additional information. We checked the completed data forms for agreement and resolved any differences by discussion and consensus. When agreement was not reached, a third review author (RP) was contacted for a final decision.

In addition to data relating to the outcomes of the review, we collected information on the following.

1. Study methods and design (randomisation, allocation, concealment and blinding)
2. Information on the number of people eligible, N randomised, N completing treatment, N analysed, and N lost to follow-up (by treatment arm, and specifying reasons).
3. Baseline characteristics of patients: age, gender, BMI, episode/symptoms duration, prevalence and aetiology of heart disease, ECG data on left ventricular systolic and diastolic function and left atrial size, duration and type of AF, and used definitions for type of AF, presence of diabetes, hypertension, previous stroke, known coronary artery disease. The CHA2DS2VASc score is a marker of thromboembolic risk in AF patients, and is composed of the following risk factors: congestive heart failure, hypertension, age (over 65 years, or over 75 years), diabetes mellitus, stroke or transient ischaemic attack, and presence of vascular disease (Lip 2010).
4. Setting of cardioversion: emergency room/accident and emergency.
5. Details of treatment: method of cardioversion employed (direct-current cardioversion: energy, and waveform - mono or biphasic; pharmacological cardioversion: antiarrhythmic drugs and doses), information on preprocedural anticoagulation (duration - pre and postcardioversion, and type of anticoagulation and doses / international normalized ratio - INR - target), treatment used in control group and concomitant medication (beta-blockers, pretreatment with antiarrhythmic drugs in patients undergoing electrical cardioversion).
6. Follow-up: duration, patients lost to follow-up and withdrawals, method used for rhythm monitoring (implantable loop recorder, 24 hours, 48 hours, 7-day Holter or others).
7. Funding.
8. Information on published protocol/clinical trial register entry.
9. Planned outcomes, reported outcomes.

10. Trial authors' conflicts of interest.

One review author (MA) transferred data into the Review Manager file (RevMan 2014). We compared magnitude and direction of effects reported in the study with those in the review for confirming data accuracy (Higgins 2016).

Among all extracted variables, AF duration and type (paroxysmal or persistent) and body mass index (BMI) were considered as potential effect modifiers for the endpoints "Acute Procedural Success" and "Maintenance of sinus rhythm until hospital discharge or end of study follow-up". For that reason networks were split based on these to maintain the transitivity assumption within networks (i.e. all patients in the trials of a network should have similar population characteristics so that they could be randomised to any of the other treatments in the network).

These were the three different groupings utilized:

- studies with 100% patients with paroxysmal AF or AF < 48h (which also meets criteria for paroxysmal AF);

- studies with 100% patients with persistent AF

- studies with 100% patients with atrial flutter.

These 3 groups also have some pathophysiological support: paroxysmal AF being considered pulmonary vein-dependent in the majority of cases (Haïssaguerre 1998), persistent AF more frequently have extra-pulmonary vein triggers (Verma 2015) and atrial flutter having a cavotricuspid reentrant circuit (Feld 1992).

- studies with BMI < 30Kg/m2 (normal BMI or pre-obese individuals)

- studies with BMI ≥ 30Kg/m2 (obese individuals)

This division is based on the knowledge that electrical cardioversion may be less effective in obese patients (Voskoboinik 2018).

Assessment of risk of bias in included studies

We used the instructions given in the *Cochrane Handbook for Systematic Reviews of Interventions* in our evaluation of the methodology and the risk of bias of the included trials (Higgins 2011). Review authors (AI, KK, JT, MA, YR) independently assessed risk of bias for each included study. Disagreements were resolved by general consensus. We applied the Cochrane 'Risk of bias' tool by assessing the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias.

We judged each potential source of bias as 'high', 'low' or 'unclear' and report quote(s) from the study together with justification(s) for our judgement in the 'Risk of bias' table. We summarised the 'Risk of bias' judgements across different studies for each of the domains listed.

When considering the treatment effects, we took into account the risk of bias for the studies contributing to that outcome. We considered the implications of missing outcome data from individual participants per outcome, such as high dropout rates (for example, above 5 to 10%) or disparate attrition rates (for example, a difference of 10% or more between study arms).

We classified studies with low risk of bias in all domains as being at low risk. Studies with one or more "high risk" domains were considered at high risk of bias.

Furthermore, there were three endpoints where lack of blinding of patients and personnel was considered as not being a source of bias: "all-cause mortality", "stroke or systemic embolism occuring in the first 30 days following cardioversion" and "acute procedural success". This was based on the fact that these are not prone to bias or to depend on adjudication committee or subjects' opinion, and they all are based on objective events not subject to divergences in opinion: death, stroke or systemic embolism (which requires imaging confirmation) and confirming sinus rhythm on an electrocardiogram.

We contacted study authors in situations where we considered the risk unclear. When there is no clarification provided by the authors, we considered this high risk. We have discussed in the final review the limitations of the expected lack of 'blinding of participants and personnel' for conclusions (Hróbjartsson 2014; Pocock 2015).

Measures of treatment effect

Dichotomous outcomes

We used risk ratios (RRs) to calculate the likelihood of achieving sinus rhythm at discharge or the acute procedural success, as well as for other dichotomous events. RRs were presented alongside 95% confidence intervals (CIs).

Continuous outcomes

We aimed to use end values in preference to change in values/scores in our analyses, if these are both reported in the same study. When assessing continuous outcomes, the mean difference (MD) was used if studies reported the same scale to measure the outcome. When this was not possible, the standardized mean difference (SMD) was used. For studies where these data were not available, and only median and interquartile range are reported, we narratively described skewed data reported as medians and interquartile ranges.

Relative ranking

While performing the network meta-analysis we estimated the probabilities for each intervention of being at each possible rank. Then we obtained a treatment hierarchy using the probability of each intervention being the best treatment by using ranking of treatments (R (R 2017), metameta, command netrank (Rücker 2015)) based on P-scores, the frequentist analogue of the Surface Under the Cumulative RAnking curve (SUCRA) (Rücker 2015). P-score values quantify the intervention ranking, measuring the extent of certainty that a given intervention is better than another treatment, averaged over all competing treatments. Higher ranking treatments will present with larger P-score values.

We ranked the primary outcome, maintenance of sinus rhythm until end of inpatient study period, acute procedural success, and mortality or cardiovascular mortality within the first 30 days.

We will provide absolute risk reduction or difference and the respective 95% CIs.

Unit of analysis issues

All included trials were randomised at the individual participant level.

For studies with multiple-arm interventions and if more than two met the inclusion criteria, we combined them into electrical, pharmacological or placebo for the main analysis, and compared the three arms simultaneously; subsequently, for the specific intervention analysis (by antiarrhythmic type or electrical cardioversion strategy), we specified when multiple arms were present and compared the multiple treatment arms in a single analysis.

For studies where only a subset of participants was eligible (e.g. study population including a small group of participants with AF due to reversible causes), individual patient-data or sub-group analysis excluding non-eligible patients was requested to the authors. We did not identify any study where this scenario was applicable.

For cluster-randomized trials, we planned extracting the estimates of the observed effect measure (for example, risk ratio and confidence interval) accounting for the cluster design. These effect estimates and their standard errors would then be meta-analysed with those from the studies with a parallel design using the generic inverse-variance method (Higgins 2019). If the study had not accounted for clustering and had analysed the individual as the unit of analysis, we would extract the number of clusters, total number of participants, average size of each cluster, the outcome data and an estimate of the intracluster correlation coefficient obtained from similar studies (Higgins 2019). These cluster-RCTs would be excluded from our sensitivity analysis. We did not identify any cluster-randomized trials for the purpose of our review.

Dealing with missing data

We contacted investigators or study sponsors to obtain any missing data. We computed standard deviations (SDs) from other reported statistics whenever these were available.

We analysed the data on the basis of intention-to-treat. By default, we aimed to use available case analysis (missing patients will be considered as not to have experienced an event). Nevertheless, we also aimed to carry out the worst-case scenario intention-to-treat-analysis (all missing patients considered as having events) for the three outcomes of interest mentioned below, to test if any potential difference might have arisen due to losses to follow-up.

The outcomes of interest for these analyses were :

- maintenance of sinus rhythm until hospital discharge;
- stroke or systemic embolism occurring within the first 30 days following cardioversion; and
- 30-day all-cause mortality.

Whilst we did not have any missing data for maintenance of sinus rhythm until hospital discharge, for the outcomes of 30-day mortality and Stroke we found that the consistent lack of reporting of these outcomes meant that imputing data for worst or best case scenario for these outcomes would result in a very high degree of extrapolation making the conclusions unreliable.

Assessment of heterogeneity

Pair-wise meta-analysis

We measured the quantities of heterogeneity by the I^2 statistic (Higgins 2002; Higgins 2003). The importance of the observed value of I^2 depends on both magnitude and direction of effects and strength of evidence for heterogeneity, and uncertainty in the value of I^2 is substantial when the number of studies is small (Higgins

2011). We followed the recommendations for thresholds in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity; and
- 75% to 100%: may represent considerable heterogeneity.

Network meta-analysis

We compared potential effect modifiers (e.g. AF duration and type as described in the section "data extraction and management") using descriptive statistics to assess similarity of trials within and across comparisons. This allowed us to assess whether or not the 'transitivity assumption' is met (i.e., if there are no relevant differences across studies regarding factors that might alter treatment effects other than the intervention comparison being made). When the assumption is not respcted issues can occur as heterogeneity and inconsistency. As mentioned in the "Data extraction and management", we focused mainly on AF duration and type and BMI as potential effect modifiers for the efficacy endpoints, and pooled studies with similar populations as specified in that section.

To evaluate the presence of inconsistency in the entire network, we used the generalised heterogeneity statistic Q_{total} and the generalised I^2 statistic, as described in Schwarzer 2015. The R package netmeta provides a method for design-based decomposition of the generalised Q statistic into a sum of Q statistics between studies with the same design, and a Q statistic for assessing between design inconsistency (Higgins 2012, netmeta; R 2017; Jackson 2015).

In the instance of a high overall heterogeneity statistic, a new between design statistic (Q) can be calculated taking into account a full design by treatment interaction model assuming random effects by detaching the effects of individual designs that may contribute to the overall heterogeneity. If the resultant Q statistic still indicated significant heterogeneity then the network was determined to have high global heterogeneity/inconsistency (even when assuming random effects (Higgins 2012).

In order to assess local inconsistency (incoherence), we used the back calculation method available in the netmeta package in R to separate direct and indirect evidence as described in König 2013. This provides treatment effects for each comparison from direct and indirect estimates and provides a z and p-value for significance if disagreement, allowing us to assess the 'consistency assumption' (i.e., whether the effect estimates from indirect and direct evidence are in agreement).

Aside from statistical heterogeneity it is also important to consider clinical heterogeneity especially in the context of maintaining the transitivity assumption. We addressed this by reviewing individual study characteristics to indentify if there were clear differences in population attributes.

Assessment of reporting biases

We planned to assess publication bias and other reporting biases by visual inspection of funnel plots for primary outcomes if included at least 10 trials (Higgins 2011). However as there were no comparisons within which there were exceeded 10 trials, it was not possible to plot any funnel plots.

Data synthesis

Direct comparison

First, we will perform conventional pairwise meta-analyses for all outcomes and comparisons, provided that at least two studies are available; we will use statistical software, RevMan Web (RevMan Web 2023), provided by Cochrane, for these analyses.

We will use a random-effects model as the primary analysis for calculating RRs and MDs. The choice of the random-effects model allows accounting for between-study heterogeneity, and in case this is not present, results will be equal to those of the fixed-effect model. If the studies are found to be clinically very dissimilar, the pooled measure will be difficult to interpret and we may decide that we should avoid statistically combining them in a meta-analysis (Higgins 2011).

Network meta-analysis

Network meta-analysis combines direct evidence within trials and indirect evidence across trials (Mills 2012). This method synthesises information from a network of trials addressing the same question but involving different interventions.For a given comparison, for example, electrical cardioversion versus placebo, direct evidence is obtained from studies that compare these two treatments directly. In addition, indirect evidence for the electrical cardioversion versus placebo comparison can be obtained by synthesising studies comparing electrical cardioversion versus pharmacological cardioversion and placebo versus pharmacological cardioversion (Caldwell 2005; Higgins 1996). Network meta-analysis combines evidence into a single effect size, and under certain assumptions it can increase the precision in the estimates, while randomisation is respected. It is important that there are no major differences between the trials (clinical characteristics of the patients, settings, inclusion and exclusion criteria, study methods) making different comparisons other than the treatments being

compared. The main assumptions for this to occur are homogeneity, similarity, transitivity, and consistency. It is important that the results of trials on the same comparison are homogeneous, so they can be used for indirect comparisons. Even though it is of importance that trials are similar enough to be considered together, not only in design but also regarding effect modifiers, we do not require perfect homogeneity between studies to enable a useful analysis. In sum, we require a reasonable belief that heterogeneity between studies, and between studies and the target population, is not likely to materially affect the estimates and inference. AF duration may have an effecton the results of cardioversion. Therefore, AF duration should be similar among the two direct comparisons used for obtaining the indirect comparison. Finally, consistency can be assessed when direct and indirect data are available for a particular comparison of interventions. When consistency is present, the effect of a given treatment should be similar whether it is measured by direct or indirect comparison (Catala-Lopez 2014; Cipriani 2013).

Rücker has observed that graph theoretical models that have been used in electrical networks could also perform well in network meta-analysis (Rücker 2012). We performed network meta-analyses within a frequentist framework, assuming an equal heterogeneity parameter τ across all comparisons, and accounted for correlations induced by multiarm studies (Lu 2006; Salanti 2009). All analyses were done using the graph theoretical network meta-analysis method. We performed the analysis using R, version 3.4.2 (R 2017), netmeta package (netmeta); the codes and description of the methodology can be found in netmeta, Neupane 2014, and Schwarzer 2015.

We created a network plot, a visual representation of the different interventions being compared (i.e., the nodes) and the available direct comparisons in at least one trial (i.e., the lines). Each node was rendered as a circle with its own colour, and the lines were weighted according to the available evidence for that comparison, with more evidence translating into a thicker line. The network plot was obtained using the netgraph command. Participants were randomised to any intervention in the network/all eligible interventions were jointly randomisable.

We performed a network meta-analysis for specific treatment options (i.e. at least 2 studies for specific antiarrhythmic agents or cardioversion strategies). If there were trials with multiple arms we specified this within the netmeta command. This split the trial into comparisons correspodning to n! where n is the amount of arms originally in the trial.

We intended to undertake NMA for the following outcomes:

- maintenance of sinus rhythm until hospital discharge or end of study follow-up; acute procedural success; stroke or systemic embolism occurring within the first 30 days following cardioversion; 30-day all-cause mortality; 30-day cardiovascular mortality; duration of hospitalisation; & complications within the first week

As discussed in the "Measures of treatment effect" section, we will rank interventions using P-scores (Rücker 2015) for the endpoints maintenance of sinus rhythm until end of inpatient study period, acute procedural success, and mortality or cardiovascular mortality within the first 30 days.

Subgroup analysis and investigation of heterogeneity

We will investigate possible heterogeneity in the Network meta-analysis through subgroup analyses. These will be conducted for all endpoints where heterogeneity is considered of potential importance ($I^2 > 40\%$), and subgroups will include the following:

a) Type of AF or atrial arrhythmias

-non-valvular AF versus valvular AF

-patients with AF versus patients with atrial flutter

-patients with paroxysmal AF versus patients with persistent AF

b) Presence of previous catheter ablation procedure

-patients with previous ablation procedures

-ablation naïve patients

c) Concomitant clinical comorbidities

-patients with heart failure versus patients without heart failure

-patients with diabetes mellitus versus patients without diabetes mellitus

d) Route of Anti-arrhythmic Administration

-Oral

-Intravenous

e) Ongoing antiarrhythmic drug therapy*

-amiodarone

-vernakalant

-dronedarone

-azimilide

-flecainide

-dofetilide

-vanoxerine

-other antiarrhythmic drugs

f) Antiarrhythmic status precardioversion in patients undergoing electrical cardioversion

-no antiarrhythmics

-antiarrhythmics precardioversion

g) Antiarrhythmic status postcardioversion

-discontinued antiarrhythmic agents

-non-discontinued antiarrhythmics postcardioversion

h) Structural Heart Disease

-patients with structurally normal heart (lone atrial fibrillation)

-patients with structural changes (cardiomyopathy, valvular heart disease, etc.)

*We will pool data for all antiarrhythmic drugs and analyse it individually (for each specific drug).

We will conduct a significance test for assessing for differences between two or more subgroups (Borenstein 2008; Review Manager 2014).

Sensitivity analysis

We performed sensitivity analyses by selectively pooling:

- studies having the best methodological quality (low risk of bias);
- studies including the greatest number of patients (i.e. studies in the highest quartile of participants);
- trials with evidence of registration considered irrefutable* and with registration occurring before the start of study enrolment;
- and trials with evidence of registration considered irrefutable and with registration occurring at any time.
- RCTs only (excluding quasi-RCTs)

At least two studies fulfilling one of these pre-requisites were required for performing these four sensitivity analyses.

- A worst-case scenario to assess the effect of missing data (we will consider missing cases to have relapsed AF or developed the above mentioned outcomes)

The outcomes of interest for these analyses were:

- maintenance of sinus rhythm until hospital discharge;
- stroke or systemic embolism occurring within the first 30 days following cardioversion; and
- 30-day all-cause mortality.

*We will accept as irrefutable evidence the following sources.

1.Trial registration: for studies that began enrolment on or after 1 July 2008 based on World Health Organization (WHO) (Sim 2006; WHO 2006; WHO 2012) and the International Committee of Medical Journal Editors' recommendations (Laine 2007); we will search on ClinicalTrials.gov (clinicaltrials.gov), the WHO International Clinical Trials Registry Platform (ICTRP) (who.int/ictrp/en), and the ISRCTN registry (ISRCTN). For studies not identified in these databases, we will perform additional searches on national trial registries or other registries available on the US Department of Health and Human Services (HHS 2015).

2.Letters from ethics committees or trial authors confirming the study was approved by an ethics committee as a 'randomised trial'.

3.Evidence of trial registration in a different database provided by authors.

4.Publication of a peer reviewed protocol prior to the publication of the trial results.

We will contact authors for information on trial registration, and how this has been done (alternative trial registration database, etc).

Studies which began enrolment prior to the specified date, will have to address points 2, 3 or 4. Studies starting enrolment on or after 1 July 2008 will have to comply with points 1 and 2.

Summary of findings and assessment of the certainty of the evidence

We created 'Summary of findings' tables for the following outcomes:

1. Maintenance of sinus rhythm until hospital discharge or end of study follow-up;
2. Acute procedural success;
3. Stroke or systemic embolism occurring within the first 30 days following cardioversion;

4. 30-day all-cause mortality;
5. 30-day cardiovascular mortality; and
6. Duration of hospitalisation

We utilized the approach described by Yepes-Nuñez 2019 and created one table per outcome, illustrating the network(s) and representing each intervention/node with a different colour. The same colour for each intervention was utilized both in the network and on the table. Each table provided information on the PICO, setting, total studies, total participants, risk ratio (with 95%CI), anticipated absolute effects (with comparator, treatment and absolute risk difference and 95%CI), certainty of evidence, ranking and interpretation of findings as per Cochrane EPOC 2018.

We used the five Grading of Recommendations Assessment, Development and Evaluation (GRADE) considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the certainty of the body of evidence contributing with data to the meta-analyses of these selected outcomes. GRADE recommendations and methods as described by Puhan 2014 were applied. We presented justification to all downgrading decisions to the quality of studies utilizing using footnotes and comments for clarity of the manuscript readers where necessary. Judgements regarding quality of evidence were made by RP and MA working independently, with disagreements resolved by discussion or involving a third review author (KK).

For the outcomes the AF type was considered an effect modifier (i.e. "acute procedural success" & "maintenance of sinus rhythm until hospital discharge or end of study follow-up"), different networks were created for each of the following populations (as described in the section Data extraction and management):

- studies with 100% patients with paroxysmal AF or AF < 48h (which also meets criteria for being paroxysmal AF);

- studies with 100% patients with persistent AF

- studies with 100% patients with atrial flutter

Rating of evidence studies vs. placebo in the network meta-analysis was done using the GRADE Working Group's approach Puhan 2014, Brignardello-Petersen 2018.

Results

Description of studies

Results of the search

Our study selection process is illustrated in Figure 1. From the search that was conducted on 14 February 2023, 13551 records were identified. 299 more records were identified from other sources (e.g. clinical trial registries), and 2 more records after contact of clinical experts in the field. From a total of 13852 records, after removal of duplicates, 8240 records were screened. Upon first-level screening by reviewing titles and abstracts, we excluded 8019 clearly irrelevant records. Full-text reports and trial records of the remaining 221 were retrieved for further assessment. In the end, 112 studies (139 records) were selected for use in the review, with 72 used for the quantitative analysis (Figure 1).

Included studies

As described above we included data from 112 studies (139 records), all designated as randomized clinical trials, including 15,968 patients. No cluster randomized studies were included. Five studies had a quasirandomized design (Bertini 1990, Jakobsson 1990, Kühlkamp 1991, Romano 2001 & Vogziatis 2017).

Baseline Characteristics:

The baseline characteristics of the trials selected for the review are outline the additional tables. Table 1 outlines demographic data and co-morbidities, Table 2 outlines drugs prescribed and data from echocardiography. Table 3 details the AF type and follow-up duration. Average age across comparisons ranged from 47 to 72 years and the percentage of male patients had a large spread of 38% to 92%. The most commonly reported co-morbidities were hypertension with percentage range 3-80%, valvular heart disease with percentage 2-58%, and ischaemic heart disease with percentage range 0-49% (Table 1). The most commonly reported on drugs prescribed were beta-blockers, digoxin and calcium channel blockers with ranges; 0-83%; 0-100%; 0-100% respectively. Many trials reported on average left atrial diameter which ranged from 33-58 mm (Table 2). Braždžionytė 2006; Camm 2012; Channer 2004; Cybulski 2003; Khaykin 2003; Kirchhof 2005; Mattioli 1998; Mortensen 2007; Rajagopalan 2014; Reisinger 1998; Reisinger 2004; Risius 2009; Romano 2001; Schmidt 2019; Schmidt 2021; Siaplaouras 2004; Siaplaouras 2005; Singh 2005; Squara 2021; Stanaitienė 2008; Trendafilova 2021; Vogiatzis 2009; Voskoboinik 2018; Walsh 2005; provided detailed information on BMI. There were only a very few studies that actually published data on collected CHA_2DS_2-VASc score. Schmidt 2019 had 78% of patients with CHA_2DS_2-VASc $\geq$ 2 for the maximum fixed energy arm and had 72% for the low escalating arm. One other study gave the median CHA_2DS_2-VASc score which was 1.7 for vernakalant and 1.8 for ibutilide (Simon 2017). Schmidt 2021 had a mean CHA_2DS_2-VASc score of 2.6±1.7 in the anterior-lateral group vs. 2.5±1.5 in the anterior-posterior

group. Scheuermeyer 2019 included only patients with a $CHADS_2$ score of 0 or 1 (mean score was 0.4±0.6). Taha 2022 reported mean CHA_2DS_2-VASc score of 2.31±1.38 for amiodarone and 2.26±1.28 for propafenone.

Types of Arrhythmia in Studies:

Thirty five trials included only individuals with paroxysmal AF (Balla 2011; Baroffio 1995; Beatch 2016; Beatch 2017; Bellandi 1995; Bellone 2012; Bianconi 2000; Boriani 1997; Brodsky 1994; Camm 2011; Chiladakis 2001; Chu 2009; Cotter 1999; Cybulski 2003; Fresco 1996; Ganau 1998; Halinen 1995; Joseph 2000; Kochiadakis 1998a; Kochiadakis 2007; Kosior 2009; Kumagai 2000; Maciag 2017; Madrid 1993; Martínez-Marcos 2000; Negrini 1994; Noc 1990; Reisinger 2004; Romano 2001; Roy 2004; Scheuermeyer 2019; Taha 2022; Thomas 2004; Treglia 1994a; Xanthos 2007), whilst twenty-nine included only persistent AF patients (Alp 2000; Baroni 2011; Channer 2004; Falk 1997; Galperín 2001; Hohnloser 1995; Jakobsson 1990; Kanoupakis 2003; Khaykin 2003; Kirchhof 2005; Kochiadakis 1999; Kochiadakis 1999a; Kühlkamp 1991; Neumann 2004; Okishige 2000; Okishige 2006; Schmidt 2019; Siaplaouras 2004; Siaplaouras 2005; Singh 2005; Squara 2021; Stanaitienė 2008; Trendafilova 2021; Vijayalakshmi 2006; Vogiatzis 2009; Voskoboinik 2018; Yamase 2012; Yamashita 2009; Zehender 1994), and 4 assessed only atrial flutter patients (Camm 2012; Mortensen 2007; Risius 2009; Sun 2005). The remaining 44 trials included a mix of sustained atrial arrhythmias in different proportions, with Bianconi 2000 and Simon 2017 having approximately half persistent and half paroxysmal AF; Muñoz-Martínez 2010; Norgaard 1999, Rajagopalan 2014 & Ricard 2001 included mainly patients with persistent AF; Pratt 2010 had mainly paroxysmal AF patients, but also had a small share of persistent AF and atrial flutter; Reisinger 1998 & Roy 2008 also predominantly paroxysmal AF and a small share of persistent AF (no atrial flutter patients). Some trials did not provide a clear composition of sustained atrial arrhythmias based on the current paroxysmal/persistent classification (Blanc 1999; Bouida 2019; Davey 2005; Koster 2004; Mittal 2000; Nogic 2022; Norgaard 1999; Page 2002; Schmidt 2017; Vardas 2000; Walsh 2005; Yu 2013; Zhang 2005). Studies composed of patients with multiple types of atrial arrhythmias failed to provide outcomes for each arrhythmia type reported separately.

Khaykin 2003; Voskoboinik 2018; Rajagopalan 2014; were composed mainly or exclusively of patients with BMI ≥ 30Kg/m^2. These 3 trials were trials of persistent AF patients, assessing electrical cardioversion (Khaykin 2003; Voskoboinik 2018) or magnesium vs. placebo (Rajagopalan 2014), and, as such, were not included in the persistent AF network with the other trials of normal weight/pre-obese patients. A different network could not be formed including these 3 trials as there were not enough connection points.

Setting of Trials:

24 trials were set in accident and emergency departement (Azpitarte 1997; Balla 2011; Baroffio 1995; Bellone 2012; Bianconi 1998; Bouida 2019; Camm 2011; Chiladakis 2001; Cotter 1999; Davey 2005; Falk 1997; Ganau 1998; Joseph 2000; Kochiadakis 2007; Kosior 2009; Maciag 2017; Martínez-Marcos 2000; Negrini 1994; Nogic 2022; Reisinger 2004; Romano 2001; Scheuermeyer 2019; Simon 2017; Thomas 2004), and six trials were set in an acute cardiology department or ward (Bertini 1990; Cybulski 2003; Muñoz-Martínez 2010; Treglia 1994a; Trendafilova 2021; Xanthos 2007). A further 23 trials were set in elective admissions for cardioversion (Alp 2000; Botto 1999; Braždžionytė 2006; Halinen 1995; Jakobsson 1990; Khaykin 2003; Kirchhof 2005; Kochiadakis 1998; Koster 2004; Mittal 2000; Neumann 2004; Page 2002; Rajagopalan 2014; Roy 2008; Schmidt 2017; Schmidt 2019; Siaplaouras 2004; Siaplaouras 2005; Squara 2021; Vogiatzis 2009; Voskoboinik 2018; Walsh 2005; Zhang 2005) and there were 3 trials where there was a mix of patients in for elective procedure and attending the emergency department (Kochiadakis 1999; Kochiadakis 1999a; Vardas 2000). Ten trials were run in outpatients (Aliot 1996; Channer 2004; Galperín 2001; Kanoupakis 2003; Okishige 2000; Okishige 2006; Singh 2005; Vijayalakshmi 2006; Yamase 2012; Yamashita 2009). The setting of the study was not clearly described or included a combination of settings for the remaining trials (Table 3).

Comparisons:

Among the 112 studies included there were 2 in which electrical and pharmacological strategies were compared to each other (Bellone 2012; Scheuermeyer 2019). Thirteen more compared different waveforms and energies (Schmidt 2017; Schmidt 2019; Khaykin 2003; Kirchhof 2005; Koster 2004; Mortensen 2007; Mittal 2000; Neumann 2004; Page 2002; Ricard 2001; Siaplaouras 2004; Trendafilova 2021). There were 7 studies which compared different patch or paddle postitions (Alp 2000; Muñoz-Martínez 2010; Risius 2009; Siaplaouras 2005; Vogiatzis 2009; Walsh 2005; Schmidt 2021). Voskoboinik 2018 compared paddles vs patches for electrical cardioversion. Squara 2021 assessed the impact of active compression on defibrillation patches. 25 studies compared different pharmacological approaches only (Baroni 2011; Blanc 1999; Camm 2011; Halinen 1995; Kosior 2009; Kühlkamp 1991; Kumagai 2000; Madrid 1993; Martínez-Marcos 2000; Negrini 1994; Reisinger 1998; Reisinger 2004; Romano 2001; Simon 2017; Sun 2005; Suttorp 1990; Taha 2022; Treglia 1994a; Vogziatis 2017; Volgman 1998; Xanthos 2007; Yamase 2012; Yu 2013; Zehender 1994; Zhang 2005). 44 studies compared one or two pharmacological approaches to placebo (Abi Mansour 1998; Bouida 2019; Balla 2011; Baroffio 1995; Beatch 2016; Beatch 2017; Bellandi 1995; Bianconi 2000; Boriani 1997; Brodsky 1994; Camm 2012; Channer 2004; Chiladakis 2001; Chu 2009; Cotter 1999; Cybulski 2003; Davey 2005; Falk 1997; Fresco 1996; Galperín 2001; Ganau 1998; Joseph 2000; Kanoupakis 2003; Kochiadakis 1998; Kochiadakis 1998a; Kochiadakis 1999; Kochiadakis 1999a; Kochiadakis 2007; Lindeboom 2000; Maciag 2017; Nogic 2022; Norgaard 1999; Okishige 2000; Pratt 2010; Rajagopalan 2014; Roy 2004; Roy 2008; Singh 2000; Singh 2005; Stambler 1996; Suttorp 1989; Suttorp 1990; Vardas 2000; Vijayalakshmi 2006; Yamashita 2009).

Follow-up Duration:

Most trials (n=44) had 12h or less of follow-up (Abi Mansour 1998; Alp 2000; Baroffio 1995; Bellone 2012; Bouida 2019; Camm 2011; Chiladakis 2001; Chu 2009; Davey 2005; Falk 1997; Halinen 1995; Kirchhof 2005; Kochiadakis 1998; Koster 2004; Kumagai 2000; Lindeboom 2000; Maciag 2017; Madrid 1993; Martínez-Marcos 2000; Mittal 2000; Muñoz-Martínez 2010; Norgaard 1999;Noc 1990; Nogic 2022; Page 2002; Rajagopalan 2014; Reisinger 1998; Reisinger 2004; Ricard 2001; Scheuermeyer 2019; Schmidt 2017; Schmidt 2019; Schmidt 2021;Siaplaouras 2004; Siaplaouras 2005; Simon 2017; Squara 2021; Stambler 1996; Suttorp 1989; Suttorp 1990; Vogiatzis 2009; Voskoboinik 2018; Walsh 2005; Yu 2013). Twenty-five trials had 12 to 24h (Balla 2011; Baroni 2011; Beatch 2016; Beatch 2017; Bellandi 1995; Bianconi 2000; Boriani 1997; Camm 2012; Cotter 1999; Kochiadakis 1998a; Kochiadakis 1999; Kochiadakis 1999a; Kochiadakis 2007; Kosior 2009; Mortensen 2007; Negrini 1994; Pratt 2010; Risius 2009;Romano 2001; Roy 2008; Sun 2005; Taha 2022; Trendafilova 2021; Vardas 2000; Xanthos 2007) and 6 trials had 48 to 72h inpatient follow-up (Blanc 1999; Brodsky 1994; Joseph 2000; Treglia 1994a; Volgman 1998; Zhang 2005). Follow-up duration was not available for Khaykin 2003 & Neumann 2004, but was likely < 24h.

Thirty one trials also presented follow-up data post-discharge or post-randomization in outpatient clinic (Aliot 1996; Beatch 2017; Bellone 2012; Camm 2011; Camm 2012; Channer 2004; Cotter 1999; Galperín 2001; Hohnloser 1995; Kanoupakis 2003; Kim 2003; Kochiadakis 1999; Kochiadakis 1999a; Kühlkamp 1991; Nogic 2022; Okishige 2000; Okishige 2006; Pratt 2010; Roy 2004; Roy 2008; Scheuermeyer 2019; Singh 2000; Singh 2005; Stroobandt 1997; Vardas 2000; Vijayalakshmi 2006; Yamase 2012; Yamashita 2009; Zehender 1994). Twenty-five of these studies had follow-up data for at least 30 days (Aliot 1996; Beatch 2016; Beatch 2017; Bellone 2012; Camm 2011; Cotter 1999; Channer 2004; Galperín 2001; Hohnloser 1995; Kochiadakis 1998; Kochiadakis 1999; Kochiadakis 1999a; Kim 2003; Nogic 2022; Okishige 2000; Roy 2008; Scheuermeyer 2019; Singh 2000; Suttorp 1990; Vijayalakshmi 2006; Yamase 2012; Yamashita 2009; Zehender 1994;Vardas 2000, Zhang 2005).

Excluded studies

Sixty-three studies were excluded for the following reasons: 14 records were excluded due to wrong patient population, 33 due to wrong study design, 15 due to wrong comparator and 1 due to duplicate sample/population (Figure 1). A more detailed description of reasons for exclusion of studies is presented in Appendix 8.

One study compared early cardioversion to delayed cardioversion, and even though data was available separately for pharmacological approaches and electrical, as well as pooled together, the cardioversion method was not randomly assigned (Pluymaekers 2019). For this reason, we subsequently decided it was not for inclusion in any network-meta analyses or qualitative analysis and it was moved to excluded studies downgraded to wrong study design. Stiell 2020 compared electrical cardioversion to a combined approach, and whilst the the data for pharmacological outcomes prior to electrical cardioversion was available, only 30 minutes was allowed for the pharmacological approach to take effect. For some drugs, this may not be long enough for the drug to act. For that reason the decision was made to not include them in the network meta-analyses and to downgrade them to wrong study design.

38 records are awaiting clarification (Studies awaiting classification), with reasons summarized in Figure 1.

Risk of bias in included studies

The risk of bias across various domains for the studies assessed in our review are summarised in Figure 2.

Figure 3 demonstrates the proportion of bias risk across each domain assessed. Only one trial, Bouida 2019, had low risk of bias in all domains . Three further trials, Scheuermeyer 2019; Schmidt 2019 & Schmidt 2021, were classified as low risk of bias when assessing objective endpoints (acute procedural success, all-cause mortality and stroke or systemic embolism).

Seventy-nine trials were considered high risk of bias for at least one domain (Aliot 1996; Balla 2011; Baroffio 1995; Baroni 2011; Bellandi 1995; Bellone 2012; Bertini 1990; Bianconi 1998; Blanc 1999; Boriani 1997; Botto 1999; Braždžionytė 2006; Brodsky 1994; Camm 2011; Chiladakis 2001; Cotter 1999; Cybulski 2003; Davey 2005; Falk 1997; Fresco 1996; Halinen 1995; Hohnloser 1995; Jakobsson 1990; Joseph 2000; Kanoupakis 2003; Khaykin 2003; Kim 2003; Kirchhof 2005; Kochiadakis 1998; Kochiadakis 1998a; Kochiadakis 1999; Kochiadakis 1999a; Kochiadakis 2007; Kosior 2009; Koster 2004; Kühlkamp 1991; Kumagai 2000; Maciag 2017; Madrid 1993; Manegold 2007; Martínez-Marcos 2000; Mattioli 1998; Mittal 2000; Mortensen 2007; Muñoz-Martínez 2010; Negrini 1994; Neumann 2004; Noc 1990; Reisinger 1998; Reisinger 2004; Risius 2009; Romano 2001; Roy 2004; Satullo 1996a; Scheuermeyer 2019; Schmidt 2019; Schmidt 2021; Siaplaouras 2004; Siaplaouras 2005; Simon 2017; Singh 2005; Stanaitienė 2008; Suttorp 1989; Taha 2022; Thomas 2004; Treglia 1994a; Trendafilova 2021; Vardas 2000; Vijayalakshmi 2006; Vogiatzis 2009; Vogziatis 2017; Volgman 1998; Voskoboinik 2018; Walsh 2005; Xanthos 2007; Yamase 2012; Yu 2013; Zehender 1994; Zhang 2005), and 32 trials (Abi Mansour 1998; Alp 2000; Azpitarte 1997; Beatch 2016; Beatch 2017; Bianconi 2000; Camm 2012; Channer 2004; Chu 2009; Ellenbogen 1996; Fak 1997; Galperín 2001; Ganau 1998; Lindeboom 2000; Nogic 2022; Norgaard 1999; Okishige 2000; Okishige 2006; Page 2002; Pratt 2010; Rajagopalan 2014; Ricard 2001; Roy 2008; Schmidt 2017; Singh 2000; Squara 2021; Stambler 1996; Stroobandt 1997; Sun 2005; Suttorp 1990; Vos 1998; Yamashita 2009) despite not having any high risk domains, had at least one uncertain risk domain.

Allocation

There were greater than 50% of trials with unclear to high risk of bias in the selection bias domains (random sequence generation and allocation concealment).

With regards to "random sequence generation", only 13 trials were considered low risk (Alp 2000; Balla 2011; Bouida 2019;Maciag 2017; Manegold 2007; Negrini 1994; Scheuermeyer 2019; Schmidt 2017; Schmidt 2019; Schmidt 2021;Singh 2005; Squara 2021; Voskoboinik 2018). Eight trials were considered high risk (Bertini 1990; Davey 2005; Jakobsson 1990; Kirchhof 2005; Kühlkamp 1991; Romano 2001; Trendafilova 2021; Vogziatis 2017), and all remaining trials were considered uncertain risk, as no detailed information or not enough information was provided on the method for sequence generation.

The method for "allocation concealment" was not ellaborated sufficiently by most papers which were regarded as unclear risk. Ten trials were considered high risk for this domain. In Joseph 2000, the randomisation process was open for the first 85 patients until the investigators decided to keep the allocation concealed until inclusion and exclusion criteria were met, and therefore we determined this as high risk of bias. Kirchhof 2005 randomized patients in blocks of 100, with the first group assigned patches, and the second group of 100 assigned with paddles, which meant that at some point the study personnel would likely be able to predict the intervention to be assigned to the next patient and was considered high risk. Vogziatis 2017 was classified as high risk as treatment allocation was based on registry number (odd numbers - group A, and even numbers - group B). Walsh 2005 assigned the intervention based on a prepared schedule, which was based on the order of the patient's arrival on the ward on the day of the procedure and was classified as high risk. Bertini 1990; Jakobsson 1990 & Kühlkamp 1991, assigned patients to groups based on year or date of birth, whilst Romano 2001 & Trendafilova 2021 appeared to have used simple alternation, which makes these trials high risk for selection bias.

There were 16 trials (Beatch 2017; Bouida 2019; Channer 2004; Chu 2009; Cybulski 2003; Davey 2005; Manegold 2007; Muñoz-Martínez 2010; Negrini 1994; Nogic 2022; Scheuermeyer 2019; Schmidt 2019; Schmidt 2021; Simon 2017; Squara 2021; Sun 2005) with clear demonstration of allocation concealment.

Blinding

Acute procedural success, stroke or systemic embolism, and 30-day all-cause mortality

The reporting of blinding methods varied throughout most of the studies. For the endpoints acute procedural success, stroke or systemic embolism, and 30-day all-cause mortality, all studies were considered low risk of performance and detection bias, as these are objective endpoints.

All other outcomes

For the remaining endpoints, which included adverse reactions and maintenance of sinus rhythm later in the study, 24 trials were considered low risk for blinding of participants and personnel (Alp 2000; Azpitarte 1997; Beatch 2017; Bianconi 1998; Bianconi 2000; Bouida 2019; Camm 2011; Camm 2012; Channer 2004; Chu 2009; Davey 2005; Ellenbogen 1996; Maciag 2017; Nogic 2022; Norgaard 1999; Page 2002; Pratt 2010; Rajagopalan 2014; Roy 2004; Roy 2008; Squara 2021; Stambler 1996; Sun 2005; Yamashita 2009). Blinding of participants and personnel was domain with the highest number of trials (n=60) with high risk of bias in this domain (Aliot 1996; Balla 2011; Baroffio 1995; Baroni 2011; Bellandi 1995; Bellone 2012; Blanc 1999; Botto 1999; Bražd̄ionytė 2006; Cybulski 2003; Halinen 1995; Hohnloser 1995; Jakobsson 1990; Joseph 2000; Kanoupakis 2003; Khaykin 2003; Kim 2003; Kirchhof 2005; Kochiadakis 1998a; Kochiadakis 1999a; Kochiadakis 2007; Kosior 2009; Koster 2004; Kühlkamp 1991; Kumagai 2000; Madrid 1993; Manegold 2007; Martínez-Marcos 2000; Mattioli 1998; Mittal 2000; Mortensen 2007; Muñoz-Martínez 2010; Neumann 2004; Noc 1990; Reisinger 1998; Reisinger 2004; Risius 2009; Romano 2001; Satullo 1996a; Scheuermeyer 2019; Schmidt 2019; Schmidt 2021; Siaplaouras 2004; Siaplaouras 2005; Simon 2017; Simon 2017; Singh 2005; Stanaitienė 2008; Suttorp 1989; Taha 2022; Thomas 2004; Treglia 1994a; Trendafilova 2021; Vijayalakshmi 2006; Vogiatzis 2009; Vogziatis 2017; Volgman 1998; Voskoboinik 2018; Walsh 2005; Yamase 2012; Zehender 1994). The remaining trials did not provide enough evidence to determine if blinding of participants and personnel was done appropriately.

With regard to blinding of outcome assessment, 24 trials were considered low risk of bias (Alp 2000; Balla 2011; Beatch 2017; Blanc 1999; Bouida 2019; Camm 2011; Camm 2012; Chu 2009; Davey 2005; Koster 2004; Maciag 2017; Nogic 2022; Page 2002; Pratt 2010; Roy 2004; Roy 2008; Scheuermeyer 2019; Schmidt 2019;Singh 2005; Squara 2021; Stambler 1996; Sun 2005; Vos 1998; Yamashita 2009), 10 were considered high risk (Aliot 1996; Baroffio 1995; Baroni 2011; Bellone 2012; Bianconi 1998; Joseph 2000; Martínez-Marcos 2000; Simon 2017; Vijayalakshmi 2006; Yamase 2012), and all remaining, the majority (n=80), did not have enough information to demonstrate adequate blinding.

Incomplete outcome data

Attrition was assessed for outcomes assessed during the index admission or after discharge.

Outcomes assessed during index admission

There were 5 trials considered high risk for this domain (Davey 2005; Halinen 1995; Joseph 2000; Mittal 2000; Roy 2004). Davey 2005 7 to 8% had missing data regarding outcomes, Halinen 1995 had missing data for rhythm-related outcomes due to ambulatory electrocardiogram not being available for 10% in the Sotalol group and 7% in the Digoxin group. Patients were excluded due to protocol violations in Joseph 2000 and were unequally spread through the 3 intervention arms: 0% in the sotalol group, 2.5% in the amiodarone group and

10% in the digoxin group. In Mittal 2000 there is an 11 patient difference between treatment groups. Nine patients were excluded from the final analysis due to protocol violations. However, the difference in patient numbers accross the two treatment groups (77 vs 88 patients) makes us believe that these were unequally spread. Finally, in Roy 2004 30 to 40% of patients (those who did not respond to pharmacological cardioversion) receive electrical cardioversion, and therefore their data from most secondary endpoints is not presented/available. Falk 1997 was considered unclear risk due to some concerns with missing data: out of 3 patients with reported non-sustained ventricular tachycardia, electrocardiograms were only available for 1, suggesting potential issues with following study protocol for monitoring arrhythmias and record keeping for analysis by study investigators/adjudication committee. Vos 1998 was classified as unclear risk, as there was no clear mention of how many patients were reached on the 72h call or had a holter.

There were two studies which were terminated early due to safety (Schmidt 2017) and efficacy (Halinen 1995) issues.

Outcomes assessed after discharge

Most trials (n= 81) reported only on immediate outcomes and failed to assess outcomes after the initial hospital visit. Even though Bellone 2012 had no issues with outcomes assessed during the index admission, the authors reported very high number of patients lost during follow-up (data from tables shows that this ranged from 25% to 40%). Due to the aforementioned reason, Roy 2004 was also considered high risk for this domain.

The remaining 28 trials were considered low risk (Aliot 1996; Beatch 2017; Camm 2011; Camm 2012; Channer 2004; Cotter 1999; Galperín 2001; Hohnloser 1995; Kanoupakis 2003; Kim 2003; Kochiadakis 1999; Kochiadakis 1999a; Kühlkamp 1991; Nogic 2022; Okishige 2000; Okishige 2006; Pratt 2010; Roy 2008; Scheuermeyer 2019; Singh 2000; Singh 2005; Stroobandt 1997; Suttorp 1990; Vardas 2000; Vijayalakshmi 2006; Yamase 2012; Yamashita 2009; Zehender 1994).

Selective reporting

We looked for published study protocols as manuscripts or in clinicaltrials.gov, other trial repositories and when these were not available we contacted authors for a signed and dated copy of the protocol. We could find published protocols for only a minority of the trials (Beatch 2016; Beatch 2017; Bellone 2012; Bouida 2019; Camm 2011; Camm 2012; Maciag 2017; Nogic 2022; Pratt 2010; Rajagopalan 2014; Risius 2009; Roy 2008; Scheuermeyer 2019; Schmidt 2019; Schmidt 2021; Simon 2017; Trendafilova 2021; Voskoboinik 2018; Yamashita 2009) and we could confirm that these match the endpoints reported in the published manuscripts (i.e. low risk). However, some of these trials need to be highlighted as despite having the protocol made available on clinicaltrials.gov before publication of the study, this only became available during the enrolment period (Beatch 2016; Beatch 2017; Rajagopalan 2014), or sometimes after enrolment was finished (Bellone 2012; Camm 2012; Pratt 2010; Risius 2009). The remaining studies (Bouida 2019; Camm 2011; Maciag 2017; Nogic 2022; Scheuermeyer 2019; Schmidt 2019; Schmidt 2021; Simon 2017; Voskoboinik 2018; Yamashita 2009) all had the protocols published before enrolment.

Fourteen trials were considered high risk for this domain as pre-specified endpoints are not clearly or not entirely stated in the methods section of the paper or elsewhere (Chiladakis 2001; Falk 1997; Kochiadakis 1998; Kochiadakis 1998a; Kochiadakis 1999; Kochiadakis 1999a; Kochiadakis 2007; Neumann 2004; Roy 2004; Vardas 2000; Vogiatzis 2009; Vogziatis 2017; Xanthos 2007; Yu 2013).

Schmidt 2017 had the protocol available on clinicaltrials.gov with the outcomes available only after finishing enrolment. Furthermore, the published paper reported one additional endpoint which was not present in the published protocol and was therefore classified as unclear risk for this domain. All remaining trials mentioned the reported endpoints in their methods section. However, we could not access a copy of the protocol dated prior to study publication and therefore, these were considered unclear risk.

Other potential sources of bias

Twenty-five trials were considered high risk in the last domain (Baroffio 1995; Bellandi 1995; Bertini 1990; Boriani 1997; Braždžionytė 2006; Brodsky 1994; Camm 2011;Chiladakis 2001; Cotter 1999; Fresco 1996; Halinen 1995; Kochiadakis 1998a; Maciag 2017; Negrini 1994; Neumann 2004; Romano 2001; Satullo 1996a; Siaplaouras 2004; Siaplaouras 2005; Stanaitienė 2008; Suttorp 1989; Treglia 1994a; Yu 2013; Zehender 1994; Zhang 2005).

Reasons were: no proof of trial registration and failing to mention Ethics review or approval in the manuscript (Baroffio 1995; Bellandi 1995; Bertini 1990; Boriani 1997; Braždžionytė 2006; Brodsky 1994; Chiladakis 2001; Cotter 1999; Fresco 1996; Hohnloser 1995; Kochiadakis 1998a; Negrini 1994; Neumann 2004; Romano 2001; Satullo 1996a; Siaplaouras 2004; Siaplaouras 2005; Stanaitienė 2008; Suttorp 1989; Treglia 1994a; Zehender 1994), and not providing information of baseline variables in the different intervention groups (Yu 2013; Zhang 2005), potential issues with the randomization process (Baroffio 1995; Bellandi 1995; Fresco 1996; Negrini 1994; Romano 2001; Suttorp 1989), and lack of fairness in the comparisons (EMEA 2001) with timing for assessment of efficacy of endpoints favouring one of the drugs (i.e. vernakalant assessed on its peak efficacy vs. amiodarone before it achieves its peak cardioverting effect in Camm 2011, and in Maciag 2017 antazoline was assessed for fast cardioversion of paroxysmal AF, assessed within the first 90 min, and compared vs placebo, rather than an active comparator with similar fast acting profile -e.g. vernakalant or ibutilide). Whereas there were no baseline characteristics given for Zhang 2005 or explanation if there was any difference between them, in Yu 2013 the

authors stated there were no differences between groups and specified which baseline variables were compared (but failed to provide the values for the compared baseline characteristics).

Seven trials were considered low risk for the final domain (Bouida 2019; Nogic 2022; Scheuermeyer 2019; Schmidt 2019; Schmidt 2021; Voskoboinik 2018; Yamashita 2009).

The remaining 81 trials were considered unclear risk for multiple reasons: Six trials showed clear numerical but nonsignificant differences across treatment groups (Baroni 2011,Koster 2004; Norgaard 1999; Pratt 2010; Roy 2004; Simon 2017) suggesting potential issues with quality of randomization. No proof of trial registration was an issue for most trials (Abi Mansour 1998; Aliot 1996; Alp 2000; Azpitarte 1997; Balla 2011; Baroni 2011; Bianconi 1998; Bianconi 2000; Blanc 1999; Chu 2009; Cybulski 2003; Davey 2005; Ellenbogen 1996; Fak 1997; Falk 1997; Galperín 2001; Ganau 1998; Halinen 1995;Jakobsson 1990; Joseph 2000; Kanoupakis 2003; Khaykin 2003; Kim 2003; Kirchhof 2005; Kochiadakis 1998; Kochiadakis 1998a; Kochiadakis 1999; Kochiadakis 1999a; Kochiadakis 2007; Kosior 2009; Koster 2004; Kühlkamp 1991; Kumagai 2000; Lindeboom 2000; Madrid 1993; Manegold 2007; Martínez-Marcos 2000; Mattioli 1998; Mortensen 2007; Muñoz-Martínez 2010; Mittal 2000; Neumann 2004; Noc 1990; Norgaard 1999; Okishige 2000; Okishige 2006; Page 2002; Peuhkurinen 2000; Reisinger 1998; Reisinger 2004; Ricard 2001; Singh 2000; Singh 2005; Squara 2021; Stambler 1996; Stroobandt 1997; Sun 2005; Suttorp 1990; Taha 2022; Thomas 2004; Vardas 2000; Vijayalakshmi 2006; Vogiatzis 2009; Vogziatis 2017; Volgman 1998; Vos 1998; Walsh 2005; Xanthos 2007; Yamase 2012; Zhang 2005). Simon 2017 had evidence of trial registration and ethics review, but had potential issues with randomization. Trial registration only during or after enrolment was observed for 9 trials (Beatch 2016; Beatch 2017; Bellone 2012; Camm 2012; Pratt 2010; Rajagopalan 2014; Risius 2009; Roy 2008; Schmidt 2017; Trendafilova 2021). Finally, there 5 studies by the same author group with no mention to enrolment period (Kochiadakis 1998; Kochiadakis 1998a; Kochiadakis 1999; Kochiadakis 1999a; Kochiadakis 2007).

Most studies were not registered on a publicly available trial platform but mentioned some form of approval (e.g. by a local ethics committee or institutional review board; no letters provided on publication or via email). However, 20 trials (Baroffio 1995; Bellandi 1995; Bertini 1990; Boriani 1997; Braždžionytė 2006; Brodsky 1994; Chiladakis 2001; Cotter 1999; Fresco 1996; Hohnloser 1995; Kochiadakis 1998a; Negrini 1994; Neumann 2004, Romano 2001; Satullo 1996a; Siaplaouras 2004; Siaplaouras 2005; Suttorp 1989; Treglia 1994a; Zehender 1994) trials failed to mention if any approval for the study was obtained, mainly institutional review board or ethics committee.

We had planned to assess for publication bias using funnelplots, but were not able to do it as we could not identify 10 trials for any of the assessed comparisons.

Effects of interventions

Due to the lack of reporting of follow-up data in some studies and overall lack of follow-up post discharge in most of them, outcomes for stroke or systemic embolism in the first 30 days, duration of hospitalisation and 1 week complications were not analysed. Where data was reported on these outcomes it was mentioned in the narrative under results and shown in Supplementary Table 1. Due to discrepancy across studies in reporting for complications and definition of bradyarrhythmia or tachyarrhythmia (see Differences between protocol and review) leading to highly heterogeneous composite endpoints which could lead to issues when pooling or interpreting data, the decision was to describe results of trials in the results section only, without pooling them.

Heart failure admissions post discharge were also outcomes which were not routinely reported on and thus not commented on in the analysis.

Due to the small number of studies, and already high number of comparisons, we decided not to compare drug doses. Similarly we did not compare individual energies but did include the type of step up protocol.

There were not enough studies available at the end for each individual comparison to be able to be used in a standard direct frequentist meta-analysis.

Network graphs for each analysis are shown in Figure 4.

Primary Outcome

Maintenance of sinus rhythm until hospital discharge or end of study follow-up

AF type and duration was defined as a potential effect modifier for procedural success, and as such NMA including all trials on the same network was deemed not appropriate as it would violate the transitivity assumption. Therefore, separate analyses/networks of comparable populations (i.e. only patients with paroxysmal AF, only patients with persistent AF, and only patients with atrial flutter) were performed for "acute procedural success" and "Maintenance of sinus rhythm until hospital discharge or end of study follow-up".

There were only two studies comparing pharmacological and electrical cardioversion that could be used for the quantitative analysis (Bellone 2012 & Scheuermeyer 2019). All patients in Bellone 2012 & Scheuermeyer 2019 had <48hr of AF duration, contrasting with other studies looking at electrical cardioversion and including only patients with persistent AF, or with a mixture or paroxysmal and persistent AF patients. Therefore, as AF type/duration is an effect modifier, for mainting the transitivity assumption, we could only link electrical cardioversion to pharmacological cardioversion in the setting of paroxysmal AF (which also comprises AF < 48h). For the other trials, including only atrial flutter, and only persistent AF patients, electrical cardioversion and pharmacological cardioversion networks could not be linked.

Trials of Paroxysmal AF patients

Thirty-five trials included only individuals with paroxysmal AF (Balla 2011; Baroffio 1995; Beatch 2016; Beatch 2017; Bellandi 1995; Bellone 2012; Bianconi 1998; Boriani 1997; Brodsky 1994; Camm 2011; Chiladakis 2001; Chu 2009; Cotter 1999; Cybulski 2003; Fresco 1996; Ganau 1998; Halinen 1995; Joseph 2000; Kochiadakis 1998a; Kochiadakis 2007; Kosior 2009; Kumagai 2000; Maciag 2017; Madrid 1993; Martínez-Marcos 2000; Negrini 1994; Noc 1990; Reisinger 2004; Romano 2001; Roy 2004; Scheuermeyer 2019; Taha 2022; Treglia 1994a; Vogziatis 2017; Xanthos 2007).

The rate of paroxysmal patients meeting this endpoint across trials was available for 12 drugs, placebo and electrical cardioversion, with following ranges (Table 4): Amiodarone (5.2% at 90 min to 92% at 24h), Quinidine (35.7% at 3h to 86% at 12h and 91.4% at 24h), Propafenone (41.9% at 1h to 90.7% at 24h), Flecainide (56.4% at 90min to 90% at 12h), Sotalol (52% at 18h to 87.5% at 48h), Ibutilide (50% at 90min to 77% at 4h30), Vernakalant (36.1% at 60min, to 74.5% at 24h), Antazoline (72.7% at 90 min), Pilsicainide (72.5% at 2h), Procainamide (53.7% at 2h to 82.7% at 24h), Placebo (0% at 90min, to 22% at 6h and 64% at 24h), Magnesium (8.7% at 2h to 57% at 6h), Disopyramide (56.3% at 2h) and Biphasic incremental anteriorapical or anteroposterior (AA/AP) (88.4% to 89.3% with incremental up to 200J biphasic truncated exponential - BTE - from shock to up to 6h). Some of the drugs (e.g. Vernakalant, Ibutilide, Antazoline & Flecainide) cardioverted more than 50% in 90 or less minutes. Drugs like amiodarone, procainamide or sotalol cardioverted most patients but required 24h or longer.

Oral drugs were used in Balla 2011 (amiodarone, flecainide, propafenone & palcebo), Boriani 1997 (propafenone & placebo), Halinen 1995 (quinidine & sotalol), Kosior 2009 (quinidine & propafenone) and Taha 2022 (propafenone). Intravenous drugs were used in the 30 remaining trials.

The *network graph* is visible in panel A of Figure 4. The analysis was done assuming a random effects model and had a heterogeneity by I^2 of 76%. When assessing inconsistency via the node-splitting method, four comparisons had a signficant difference between direct and indirect evidence: Flecainide vs. Placebo (RR direct: 5.00, RR indirect: 1.98, p = 0.032) and Vernakalant vs. Placebo (RR direct: 1.43, RR indirect: 3.35, p = 0.014) in effect size point estimate (not direction of effect), and Amiodarone vs. Propafenone (RR direct: 0.99, RR indirect: 0.57, p = 0.002) and Amiodarone vs. Vernakalant (RR direct: 0.41, RR indirect: 1.15, p = 0.005), comparable effect of the two drugs vs. lower success rate with Amiodarone (Figure 5). These can result from the fact that results for this outcome were reported at different time points, and drug efficacy and time-dependancy varies across the different agents.

The forest plot of Figure 6 shows that, when compared to Placebo, AA/AP BTE incremental cardioversion (RR: 2.42; 95%CI 1.65 to 3.56), quinidine (RR: 2.23; 95%CI 1.49 to 3.34), ibutilide (RR: 2.00; 95%CI 1.28 to 3.12), propafenone (RR: 1.98; 95%CI 1.67 to 2.34), amiodarone (RR: 1.69; 95%CI 1.42 to 2.02), sotalol (RR: 1.58; 95%CI 1.08 to 2.31) and procainamide (RR: 1.49; 95%CI 1.13 to 1.97) likely result in a large increase in maintenance of sinus rhythm until hospital discharge or end of study follow-up (certainty of evidence: moderate), with effect size being larger for AA/AP incremental and being progressively smaller for the subsequent interventions (Figure 7). Despite low certainty of evidence Antazoline may result in a large increase (RR: 28.60; 95%CI 1.77 to 461.30) in maintenance of sinus rhythm until hospital discharge or end of study follow-up when compared to Placebo. Similarly, low certainty evidence suggests a large increase on this outcome for flecainide (RR: 2.17; 95%CI 1.68 to 2.79), vernakalant (RR: 2.13; 95%CI 1.52 to 2.99), and magnesium (RR: 1.73; 95%CI 0.79 to 3.79) on this outcome. Due to the absence of a common comparator, pilsicainide and disopyramide could not be linked to the network.

Pooling of direct data for *pairwise comparisons* with data available for ≥2 trials suggested that: Flecainide may be of little or no benefit when compared to Amiodarone (RR: 1.19, 95%CI 0.87 to 1.64; 180 participants, I^2 = 80%; 2 studies; Figure 8), Amiodarone and Propafenone probably result in large benefit vs. Placebo (RR: 1.68, 95%CI 1.33 to 2.11; 718 participants, I^2 = 71%, 7 studies; Figure 9 and RR: 2.27, 95%CI 1.68 to 3.06; 1182 participants, I^2 = 93%, 9 studies; Figure 10, respectively); Flecainide and Amiodarone may have comparable efficacy to propafenone, and hence their use produces little or no additional benefit (RR: 1.06, 95%CI 0.92 to 1.22; 482 participants, I^2 = 67%, 2 studies; Figure 11 and RR: 1.00, 95%CI 0.94 to 1.07; 772 participants, I^2 = 0%, 7 studies; Figure 12, respectively); similarly, Procainamide may have slightly lower or comparable efficacy to Amiodarone (RR: 0.89, 95%CI 0.67 to 1.17, 403 participants, I^2 = 87%, 2 studies; Figure 13); Vernakalant and Magnesium may lead to a large increase in maintenance of sinus rhythm until hospital discharge or end of study follow-up but the evidence is very uncertain (RR: 5.69, 95%CI 0.14 to 226.30; 364 participants, I^2 = 95%, 3 studies; Figure 14 and RR: 1.71, 95%CI 0.31 to 9.32; 112 participants, I^2 = 72%, 3 studies; Figure 15, respectively).

BTE incremental electrical cardioversion had superior efficacy to propafenone in Bellone 2012 (89.3% vs. 73.8%, p = 0.002) and procainamide in Scheuermeyer 2019 (88.4% vs. 53.7%, p = 0.001). Quinidine had higher efficacy than Sotalol (85.7% vs. 51.5%, p = 0.006; Halinen 1995) and was no different from Propafenone (92.1% vs. 90.7%, p = 0.82; Kosior 2009). In Joseph 2000, Sotalol was more effective than Placebo (87.5% vs. 58.3%, p = 0.008). In Kochiadakis 2007, Procainamide had a trend for lower efficacy than propafenone (68.5% vs. 80.2%, p = 0.08), and was comparable to placebo (68.5% vs. 61.1%, p = 0.30). Flecainide was more effective than Procainamide in Madrid 1993 (62.5% vs. 92.5%, p = 0.003). Ibutalide's efficacy was comparable to Flecainide in Reisinger 2004 (56.4% vs. 50%, p = 0.35) and Vernakalant in Vogziatis 2017 (52.8% vs. 52.4%, p = 0.97). In Kumagai 2000, it was uncertain whether Pilsicainide may lead to a small benefit over Disopyramide (72.5% vs. 56.25%, p = 0.17) (Table 5).

The league table for this comparison is presented in Table 6. This table provides the RR and 95%CI for all possible comparisons of included interventions in the analysis, either resulting from direct evidence (upper right triangle), or from network estimates. Values for each comparison can be found on the intersection of the horizontal and vertical lines arising from each intervention. The network estimates (bottom triangle) showed that placebo was likely less effective than all other treatment options, and possibly less effective than magnesium (RR: 0.58, 95%CI 0.26 to 1.26). Procainamide was likely to be less effective than Flecainide (RR: 0.75, 95%CI 0.58 to 0.98), Propafenone (RR: 0.69, 95%CI 0.52 to 0.92), Biphasic BTE electrical cardioversion (RR: 0.62, 95%CI 0.43 to 0.89) and Antazoline (RR: 0.05, 95%CI 0 to 0.85), and may be less effective than Vernakalant (RR: 0.70, 95%CI 0.47 to 1.05) and Quinidine (RR: 0.67, 95%CI 0.43 to 1.05). Sotalol was likely less effective than Antazoline (RR: 0.06, 95%CI 0 to 0.92) and may be less effective than biphasic BTE electrical cardioversion (RR: 0.65, 95%CI 0.39 to 1.09). Amiodarone is likely to be a little less effective than Propafenone (RR: 0.86, 95%CI 0.73 to 1.00), Flecainide (RR: 0.78, 95%CI 0.62 to 0.99), less effective than Antazoline (RR: 0.06, 95%CI 0 to 0.96), and may be less effective than Vernakalant (RR: 0.79, 95%CI 0.56 to 1.12), Quinidine (RR: 0.76, 95%CI 0.51 to 1.13), and Biphasic BTE electrical cardioversion (RR: 0.70, 95%CI 0.30 to 1.02). However, these figures need to be interpreted with caution taking into account the high heterogeneity of the network, and the inconsistency detected for some of the comparisons.

Trials of Persistent AF patients

Twenty-six trials included only patients with persistent AF (Alp 2000; Baroni 2011; Channer 2004; Galperín 2001; Kanoupakis 2003; Khaykin 2003; Kirchhof 2005; Kochiadakis 1999; Kochiadakis 1999a; Kühlkamp 1991; Muñoz-Martínez 2010; Neumann 2004; Okishige 2000; Schmidt 2019; Siaplaouras 2004; Siaplaouras 2005; Singh 2005; Squara 2021; Trendafilova 2021; Vijayalakshmi 2006; Vogiatzis 2009; Voskoboinik 2018; Yamase 2012; Yamashita 2009; Zehender 1994), or provided results for persistent AF patients in separate (Falk 1997).

Rate of persistent AF patients meeting this endpoint across trials was available for nine drugs, placebo and ten different electrical cardioversion approaches with following ranges (Table 4): Bepridil (52.5% to 85% at 3 months), Quinidine (25% at 3 days to 80% after 7 days), Amiodarone (6.25% at 4 weeks, to 47% at 30 days and 60% at 14 days), Cibenzoline (36.8% at 9 days), Propafenone (20% at 24h to 40.6% at 30 days), Flecainide (25% at 9 days), Dofetilide (21.3% at 6h), Pilsicainide (21.2% at 4 weeks), Sotalol (19.4% at 6 weeks to 24.2% at 28 days), and Placebo (0% at 6h and 6 weeks to 3.7% at 7 days). Electrical cardioversion studies follow-up was usually only a few hours only, and the following rates were observed: monophasic single-shock handheld AP paddles (18% to 34.5% with 360J), monophasic single-shock handheld AA paddles (60% with 360J), BTE maximum fixed AP patches (88% with 360J), monophasic incremental AP paddles (91.7% with 360J), monophasic incremental AP patches (73.7% with 360J to 96.8% with 360J), BTE active-compression AP patches (96.0% with 200J), Biphasic fixed AA patches (94.3% with 200J pulsed biphasic and 97.4% with 200J BTE), Incremental AA patches (62.5% to 96.9% with 200J BTE or 360J BTE, respectively, and 95.2% with 200J rectilinear biphasic waveform - RBW), Biphasic incremental AA patches (61% to 100% with 360J BTE, and 94.3% to 94.9% with 200J RBW), and BTE incremental AP handheld paddles (90% with 200J AA to 100% with 360J AP).

No trial of persistent AF patients compared drugs vs. electrical cardioversion, and hence two separate networks had to be created. The network graph for chemical cardioversion is demonstrated in panel B and electrical cardioversion in panel C Figure 4.

For the *electrical cardioversion network* different combinations of the following were compared: AA vs AP location, use of paddles or patches, presence of active compression, maximum vs incremental energy and energy waveforms (BTE, RBW or monophasic damped sine - MDS - waveform). The forest plot in Figure 16 uses AP BTE incremental patches as the comparator as this was one of the nodes with the most direct connections in the network. Heterogeneity by I^2 was 14% and when assessing inconsistency by the node splitting method there was no significant difference between direct and indirect estimates. When compared to AP BTE incremental energy with patches, AP BTE maximum energy with patches (RR 1.35, 95%CI 1.17 to 1.55) likely results in large increase and Active compression AP BTE incremental energy with patches (RR: 1.14, 95%CI 1.00 to 1.131) likely results in an increase in maintenance ofsinus rhythm at hospital discharge or end of study follow-up (certainty of evidence: high). Use of AP BTE incremental with paddles (RR: 1.03, 95%CI 0.98 to 1.09; certainty of evidence: low) may lead to a little increase, and AP MDS Incremental paddles (RR: 0.95, 95%CI 0.86 to 1.05; certainty of evidence: low) may lead to a little decrease in efficacy. On the other hand, AP MDS incremental energy using patches (RR: 0.78, 95%CI 0.70 to 0.87), AA RBW incremental energy with patches (RR: 0.76, 95%CI 0.66 to 0.88), AP RBW incremental energy with patches (RR: 0.76, 95%CI 0.68 to 0.86), AA MDS incremental energy with patches (RR: 0.76, 95%CI 0.67 to 0.86) and AA MDS incremental energy with paddles (RR: 0.68, 95%CI 0.53 to 0.83) probably result in a decrease in maintenance of sinus rhythm at hospital discharge or end of study follow-up when compared to AP BTE incremental energy with patches (certainty of evidence: moderate) (Figure 17).

We could not include Khaykin 2003 and Voskoboinik 2018 in the electrical cardioversion network due to the average BMI of the patient being high (all or most patients with BMI > 30Kg/m^2) as this is likely to skew the efficacy outcome. Alp 2000 could not be connected to other trials in the network.

Pooling of direct data for *pairwise comparisons* with data available for ≥2 trials suggested that AP BTE incremental is more effective than AP MDS incremental for achieving maintenance of sinus rhythm at hospital discharge or end of study follow-up (RR: 1.23, 95%CI 1.04 to 1.46; 319 participants, I^2 = 72%, 2 studies; Figure 18).

Kirchhof 2005 compared 4 different cardioversion strategies using AP positioning: BTE incremental paddles, BTE incremental patches, MDS incremental paddles and MDS incremental patches. Efficacy progressively descreased from the first to the last strategy (100%, 95.8%, 91.7% & 79.6%, respectively). When combining the two approaches, using paddles was more effective than using patches (96.2% vs. 87.6%, p = 0.04), and biphasic BTE was more effective than monophasic MDS (98.1% vs. 85.6%, p = 0.001). Data from Jakobsson 1990 suggested otherwise with AA paddles potentially seeming less effective than patches in the same location whilst MDS incremental energy (86.7% vs. 100%, p = 0.30). Squara 2021 compared active compression vs no compression using AP patches BTE using incremental energy, with the active compression approach being more successful (96% vs. 84%, p = 0.05). Schmidt 2019 compared AP BTE maximum energy (360J, 360J and 360J) vs. AP BTE incremental energy (125J, 150J and 200J, sequentially) and results favored the maximum energy approach as the most efficacious (88% vs. 66%, p < 0.001). Siaplaouras 2004 showed that AP BTE incremental energy with patches (120J, 150J, 200J & 200J) could obtain comparable efficacy to MDS utilizing lower energies (200J, 300J, 360J & 360J): 94.3% vs 96.8%, respectively, p = 0.31. Siaplaouras 2005 observed that efficacy results for AP vs. AA RBW incremental energy with patches were comparable: 95.0% vs 95.2%, p = 0.95. Vogiatzis 2009 reached a similar conclusion utilizing monophasic energy: AP vs AA patches using MDS incremental energy - 100% vs. 96.9%, p = 0.50 (Table 7).

The league table for this comparison is presented in Table 8. This ellucidates that AP BTE Maximum energy with patches is more effective than all other options, except for active compression AP BTE incremental with patches. Active compression AP BTE incremental with patches is more effective than all strategies except AP BTE maximum energy with patches, and AP BTE incremental energy with paddles. AP BTE incremental energy with paddles is more effective than AP MDS incremental energy with paddles or patches, AA and AP RBW incremental energy with patches, and AA MDS incremental energy with patches and paddles.

Voskoboinik 2018 compared of patches to paddles, in obese patients undergoing electrical cardioversion with Biphasic Truncated energy. Paddles were more effective and the authors suggested that patches may be inadequate in this patient population.

Figure 19 shows the forest-plot for the separate *network for persistent AF patients who were cardioverted with drugs* (panel C in Figure 4). Amiodarone was used as the comparator, and seven antiarrhythmic agents and placebo were included in the network. Heterogeneity by I^2 was 2% and when assessing inconsistency by the node splitting method there was no significant difference between direct and indirect estimates. The plot demonstrates that Bepridil (RR: 2.29, 95%CI 1.26 to 4.17) and Quindine (RR: 1.53, (95%CI 1.01 to 2.32) probably result in a large increase in sinus rhythm at in-patient discharge or longest available follow-up when compared to amiodarone (certainty of evidence: moderate). Dofetilide (RR: 0.79, 95%CI 0.56 to 1.44), Sotalol (RR: 0.89, 95%CI 0.67 to 1.18), Propafenone (RR: 0.79, 95%CI 0.50 to 1.25) and Pilsicainide (RR: 0.39, 95%CI 0.02 to 7.01) may result in a reduction in patients in sinus rhythm at in-patient discharge or longest available follow-up when compared to amiodarone, but certainty of evidence was low (Figure 20).

Oral drugs were used in Baroni 2011 (quinidine), Channer 2004, Galperín 2001 & Kanoupakis 2003 (amiodarone & placebo), Kühlkamp 1991(flecainide & cibenzoline), Okishige 2000 (pilsicainide & placebo), Singh 2005 & Vijayalakshmi 2006 (amiodarone, sotalol & placebo), Yamase 2012 (bepridil & amiodarone), Yamashita 2009 (bepridil & placebo) and Zehender 1994 (quinidine). Intravenous drugs were used in Baroni 2011 (propafenone & amiodarone), Falk 1997 (dofetilide & placebo), Kochiadakis 1999a (propafenone, amiodarone & placebo), Zehender 1994 (amiodarone).

Pooling of direct data for *pairwise comparisons* with data available for ≥2 trials suggested that Amiodarone and Sotalol were markedly more effective than placebo for sinus rhythm at in-patient discharge or longest available follow-up (RR: 20.81, 95%CI 7.89 to 54.88; 905 participants, I^2 = 8%, 6 studies; Figure 21, and RR: 26.38, 95%CI 5.14 to 135.38, 443 participants, I2 = 0%, 2 studies; Figure 22). Regarding this same endpoint, efficacy of Amiodarone seemed to be comparable to Propafenone (RR: 1.11, 95%CI 0.68 to 1.81; 126 participants, I^2 = 0%, 2 studies; Figure 23) and Sotalol (RR: 1.14, 95%I 0.86 to 1.52, 565 participants, I^2 = 0%, 2 studies; Figure 24), and may be comparable or possibly lower than Quinidine (RR: 0.57, 95%CI 0.27 to 1.19, 100 participants, I^2 = 65%, 2 studies; Figure 25).

In Yamase 2012, oral Bepridil and Amiodarone were compared and Bepridil seemed more efficacious (85% vs. 35%, p = 0.005). Bepridil was more effective than Placebo (52.5% vs. 3.4%, p = 0.006) in Yamashita 2009. Oral Pilsicainide was more effective than Placebo in Okishige 2000 for sinus rhythm at in-patient discharge or longest available follow-up. Flecainide was comparable to Cibenzoline for this outcome in Kühlkamp 1991 (25% vs. 36.8%, p = 0.51), but the two drugs could not be linked to the network due to the absence of a shared comparator. Propafenone, in Kochiadakis 1999a, and Dofetilide, in Falk 1997, both seemed more effective than Placebo (9.4% vs. 0%, p= 0.18, and 14.3% vs. 0%, p = 0.15, respectively) (Table 7).

The league table for this comparison is presented in Table 9. Bepridil and Quinidine may be more effective than Placebo (RR: 25, 95%CI 10 to 100, and RR: 16.67, 95%CI 7.14 to 50, respectively), Propafenone (RR: 2.86, 95%CI 1.35 to 6.25, and RR: 1.92, 95%CI 1.12 to 3.33, respectively), Sotalol (RR: 2.57, 95%CI 1.33 to 5, and RR: 1.72, 95%CI 1.05 to 3.33, respectively) and Amiodarone (RR: 2.27, 95%CI 1.25 to 4.17, and RR: 1.54, 95%CI 1.01 to 2.33, respectively). Amiodarone (RR: 11.11, 95%CI 5 to 25), Sotalol (RR: 10, 95%CI 4.17 to 25) and Propafenone (RR: 9.09, 95%CI 3.57 to 25) may be more effective than Placebo.

Trials of Atrial flutter patients

There were 14 trials where either only flutter patients were recruited or data for these patients was presented separately (Table 10). 4 assessed only atrial flutter patients (Camm 2012; Mortensen 2007; Risius 2009; Sun 2005) and 10 had data presented separately (Abi Mansour 1998; Falk 1997; Lindeboom 2000; Norgaard 1999; Stambler 1996; Schmidt 2017; Suttorp 1989; Suttorp 1990; Volgman 1998; Vos 1998).

The rate of atrial flutter patients meeting this endpoint across trials was available for 7 drugs, placebo and 3 different electrical cardioversion approaches with following ranges (Table 4 & Table 10): Ibutilide (56% at 1h to 90% at 90 min), Dofetilide (54.5% at 6h to 71.4% at 2h), Propafenone (30% at 90min to 40% at 1h), Flecainide (20% at 1h), Procainamide (15% at 1h), Sotalol (19.0% at 1h), Vernakalant (3% at 90min), Placebo (0% at 6h to 3.3% at 3h), Biphasic RBW incremental AP (97.9% with 200J to 100% with 200J), Biphasic RBW incremental AA (97.9% with 200J), Monophasic incremental AP (100% with 360J). Intravenous drugs were used in all trials.

Three of the trials were for electrical cardioversion therapies (Mortensen 2007; Risius 2009; Schmidt 2017). They compared AP monophasic damped sine waveform Incremental vs. AP rectilinear biphasic waveform (RBW) Incremental (Mortensen 2007), AP vs. AA RBW Incremental (Risius 2009) and AP biphasic trunkated exponential vs pulsed biphasic incremental (Schmidt 2017). All tested electrical cardioversion strategies had very high efficacy (97.9% to 100%).

The linked *network* (10 trials and 8 interventions) for the drug treatment comparisons and the forestplot are provided in Figure 4-Panel D, and Figure 26, respectively . Heterogeneity was very low (I^2=0%) and when assessing inconsistency by the node splitting method there was no significant difference between direct and indirect estimates. Using Placebo as the common comparator, ibutilide (RR: 21.45, 95%CI 4.41 to 104.37), propafenone (RR: 7.15, 95%CI 1.27 to 40.10), dofetilide (RR: 6.43, 95%CI 1.38 to 29.91), and sotalol (RR: 6.39, 95%CI 1.03 to 39.78) probably result in increased maintenance of sinus rhythm at hospital discharge or end of study follow-up (certainty of evidence: moderate), and procainamide (RR: 4.29, 95%CI 0.63 to 29.03), flecainide (RR: 3.57, 95%CI 0.24 to 52.30) and vernakalant (RR: 1.18, 95%CI 0.05 to 27.37) may result in increased maintenance of sinus rhythm at hospital discharge or end of study follow-up at (certainty of evidence: low) (Figure 27). Due to the lack of a common comparator, we could not link the electrical cardioversion strategies (all with very high efficacy as shown above) to this network.

Pooling of direct data for *pairwise comparisons* with data available for ≥2 trials suggested that: Dofetilide and Ibutilide probably result in large benefit at keeping patients in sinus rhythm until hospital discharge or end of study follow-up period when compared to Placebo (RR: 6.88, 95%CI 1.46 to 32.36; 43 patients, I^2 = 0%, 3 studies; Figure 28, and RR: 21.89, 95%CI 4.54 to 105.61; 178 patients, I^2 = 0%, 2 studies; Figure 29, respectively).

Sun 2005 demonstrated a superior efficacy of ibutilide over propafenone (90% vs. 30%; P <0.05). In Volgman 1998 ibutilide was more effective than procainamide (75.0% vs. 15.0%; P=0.003). In Vos 1998 ibutilide was more effective than sotalol (88.5% vs. 19.1%; P=0.0007). In Camm 2012 there was no difference between the efficacy of vernakalant and placebo (3% vs. 0%; P = 0.45). In Suttorp 1990 flecainide and propafenone had comparable efficacy (20% vs 40%; P=0.50). No successful cardioversions occurred in patients treated with flecainide or placebo in Suttorp 1989 (Table 10).

The league table (Table 11) suggested that Ibutilide might be more effective than Propafenone (RR: 3, 95%CI 1.52 to 5.88), Sotalol (RR: 3.33, 95%CI 1.35 to 8.33), Procainamide (RR: 5, 95%CI 1.69 to 14.29), and Placebo (RR: 20, 95%CI 4.35 to 100). Additionaly, Propafenone (RR: 7.14, 95%CI 1.28 to 50), Dofetilide (RR: 6.25, 95%CI 1.39 to 33.33) and Sotalol (RR: 6.25, 95%CI 1.03 to 33.33) seemed to be more effective than Placebo.

Secondary Outcomes

Acute Procedural Success

The analyses for this outcome were also split in paroxysmal & persistent AF, and atrial flutter as per previous reasoning. As before Khaykin 2003, Voskoboinik 2018 were not included on the persistent AF network due to high BMI (effect modifier). A separate network for persistent AF in patients with high BMI was not possible as these studies could not be linked: Khaykin 2003 compared monophasic vs. biphasic energy, Voskoboinik 2018 compared anteroapical vs. anteroposterior patch/pad location.

Trials of Paroxysmal AF patients

Acute procedural success for paroxysmal AF is represented in Figure 30 as a forest plot, the network is as it is for sinus rhythm at longest inpatient follow up or discharge (Figure 4, panel A). A random effects model was assumed and heterogeneity by I^2 was 81%. High global inconsistency was observed for this *network* (Figure 31).

Antazoline (RR: 28.60; 95%CI 1.69 to 484.43), flecainide (RR: 3.08; 95%CI 2.09 to 4.55), quinidine (RR: 1.99; 95%CI 0.99 to 3.98) and procainamide (RR: 1.63; 95%CI 1.08 to 2.45) when compared to placebo may result in increase of acute cardioversion to sinus rhythm but certainty of evidence is very low. For sotalol (RR: 1.35; 95%CI 0.75 to 2.44), and magnesium (RR: 1.46; 95%CI 0.70 to 3.03) there was uncertainty do the very low certainty of evidence on whether they result in increase in acute cardioversion or make no difference when compared to placebo. On the other hand, low certainty of evidence suggests that vernakalant (RR: 6.46; 95%CI 3.63 to 1.50), ibutilide (RR: 4.02; 95%CI 2.09 to 7.72), AP/AP BTE incremental cardioversion (RR: 2.83; 95%CI 1.59 to 5.01), propafenone (RR: 2.45; 95%CI 1.91 to 3.14), and amiodarone (RR: 1.50; 95%CI 1.14 to 1.97), may result in an increase (with effect size in descending order) when compared to placebo for acute conversion of paroxysmal AF (certainty of evidence: low; Figure 32).

Pooling of direct data for *pairwise comparisons* with data available for ≥2 trials suggested that: it was uncertain whether or not Flecainide leads to better acute procedural success than Amiodarone (RR: 2.22, 95%CI 0.27 to 14.91; 180 participants, I^2 = 97%, 2 studies; Figure 33). Similarly, it was uncertain whether or not Magnesium leads to a better acute procedural success than Placebo (RR: 1.29, 95%CI 0.45 to 3.73; 112 participants, I^2 = 64%, 3 studies; Figure 34), or if Procainamide leads to a better acute procedural success than Amiodarone (RR: 0.89, 95%CI 0.67 to 1.17; 403 participants, I^2 = 87%, 2 studies; Figure 35). On the other hand, Flecainide seemed more effective than Propafenone (RR: 1.28, 95%CI 1.02 to 1.59; 482 participants, I^2 = 55%, 3 studies; Figure 36), and Amiodarone (RR: 1.64, 95%CI 1.19 to 2.25; 718 participants, I^2 = 76%, 7 studies; Figure 37), Propafenone (RR: 2.35, 95%CI 1.68 to 3.27; 1182 participants, I^2 = 83%, 9 studies; Figure 38) and Vernakalant (RR: 8.20, 95%CI 2.06 to 32.71; 364 participants, I^2 = 60%, 3 studies; Figure 39) seemed more effective than Placebo for acute procedural success. Amiodarone seemed effective than Propafenone for acute cardioversion of paroxysmal AF (RR: 0.59, 95%CI 0.36 to 0.96; 772 participants, I^2 = 93%, 7 studies; Figure 40).

Results for comparisons with only one trial are presented in Table 5. Balla 2011, Beatch 2016, Beatch 2017, Boriani 1997, Camm 2011, Cotter 1999, Cybulski 2003, Fresco 1996, Halinen 1995, Kosior 2009, Martínez-Marcos 2000, Negrini 1994, Romano 2001, Roy 2004, Taha 2022 and Treglia 1994a reported different results for acute success and sinus rhythm at in-hospital discharge or longest available follow-up, either due to reporting of acute relapses or due to providing acute results before peak success for some of the slower acting drug agents.

When looking at the league table's estimates for the network (lower triangle in Table 12), Procainamide (RR: 0.06, 95%CI 0 to 0.99), Magnesium (RR: 0.05, 95%CI 0.00 to 0.95), Amiodarone (RR: 0.05, 95%CI 0 to 0.90), Sotalol (RR: 0.05, 95%CI 0 to 0.85), and Placebo (RR: 0.03, 95%CI 0 to 0.59) seemed less effective than Antazoline. Propafenone (RR: 0.38, 95%CI 0.21 to 0.69), Quinidine (RR: 0.31, 95%CI 0.13 to 0.74), Procainamide (RR: 0.25, 95%CI 0.13 to 0.49), Magnesium (RR: 0.23, 95%CI 0.09 to 0.57), Amiodarone (RR: 0.23, 95%CI 0.13 to 0.42), Sotalol (RR: 0.21, 95%CI 0.09 to 0.47), and Placebo (RR: 0.15, 95%CI 0.09 to 0.28) seemed less effective than Vernakalant. Procainamide (RR: 0.40, 95%CI 0.20 to 0.82), Magnesium (RR: 0.35, 95%CI 0.14 to 0.97), Amiodarone (RR: 0.37, 95%CI 0.19 to 0.72), Sotalol (RR: 0.34, 95%CI 0.14 to 0.79), and Placebo (RR: 0.25, 95%CI 0.13 to 0.48) seemed less effective than Ibutilide. Procainamide (RR: 0.53, 95%CI 0.34 to 0.82), Amiodarone (RR: 0.49, 95%CI 0.33 to 0.71), Sotalol (RR: 0.44, 95%CI 0.23 to 0.86), and Placebo (RR: 0.32, 95%CI 0.22 to 0.48), seemed more effective than Flecainide, and Magnesium (RR: 0.47, 95%CI 0.21 to 1.08) may be less effective than Flecainide. Procainamide (RR: 0.58, 95%CI 0.33 to 0.99), Amiodarone (RR: 0.53, 95%CI 0.30 to 0.94), and Placebo (RR: 0.35, 95%CI 0.20 to 0.63) seemed less effective than AA/AP BTE Incremental, and Sotalol (RR: 0.48, 95%CI 0.22 to 1.05) may be less effective than AA/AP BTE Incremental. Procainamide (RR: 0.66, 95%CI 0.45 to 0.98), Amiodarone (RR: 0.61, 95%CI 0.47 to 0.80), and Placebo (RR: 0.41, 95%CI 0.32 to 0.52), and Sotalol (RR: 0.55, 95%CI 0.30 to 1.01) may be less effective than Propafenone. Placebo may be less effective than Quinidine (RR: 0.50, 95%CI 0.25 to 1.01) and seemed less effective than Procainamide (RR: 0.61, 95%CI 0.41 to 0.93).

Trials of Persistent AF patients

The forest-plot for acute procedural success comparing persistent AF patients who had electrical cardioversion protocols is shown in Figure 41. As trials of electrical cardioversion had relatively short follow-up duration and did not provide info on early relapses before discharge from hospital, there were no differences between this analysis (Figure 42) and that of the one done for the outcome of maintenance of sinus rhythm until hospital discharge or end of study follow-up. Pooling of trial data from 2 trials suggested that AP BTE incremental is more effective than AP MDS incremental for acute procedural success (RR: 1.23, 95%CI 1.04 to 1.46; 319 participants, I^2 = 72%, 2 studies; Figure 43), similarly to what was observed for the endpoint sinus rhythm at inpatient discharge or longest available follow-up. The league table for acute procedural success of different electrical cardioversion strategies comparison is presented in Table 13.

Most chemical cardioversion studies of persistent AF patients used oral drugs and were run in the outpatient setting, looking at cardioversion success after ≥ 4 weeks, hence failing to provide information on acute results or timing of cardioversion (Channer 2004, Galperín 2001, Kanoupakis 2003, Kühlkamp 1991, Okishige 2000, Singh 2005, Vijayalakshmi 2006, Yamase 2012 & Yamashita 2009. The remaining trials (Baroni 2011, Baroni 2011, Falk 1997, Kochiadakis 1999a, & Zehender 1994), including at least part of patients treated with intravenous agents, showed that maximum efficacy of chemical cardioversion agents for persistent AF occurred over a matter of days/weeks, and hence the endpoint of acute procedural success does not seem to apply for this treatment option.

Trials of Atrial flutter patients

The acute procedural success results for atrial flutter patients treated with electrical cardioversion or drugs were similar as that for the previous endpoint, sinus rhythm at longest inpatient follow up period or discharge (Figure 44, Figure 45, Figure 46, Figure 47 & Table 14). This is due to short follow-up duration and no mention of early relapse in these trials.

Other Secondary Outcomes

The frequency of adverse events was collected across all studies Supplementary Table 1. However, high heterogeneity was observed across studies as not all outcomes were routinely reported (e.g. stroke and mortality were only reported on a minority of trials), and wide differences existed in the definition of outcomes (e.g. marked

differences in the definition of bradycardia and tachycardia outcomes). For that reason, most of the following outcomes will have a narrative description.

Stroke/ Systemic Embolism within 30 days

In total there were 3 recorded instances of ischaemic stroke occuring in the first 30 days that met our inclusion criteria for analysis. One event occurred in the first 24h on a patient assigned to digoxin (placebo) (Joseph 2000). A stroke was reported during the administration of intravenous amiodarone to a patient with AF thought to be of <24h duration (Martínez-Marcos 2000). A fatal stroke occurred on day 7 in a patient assigned to placebo and later prescribed with sotalol for cardioversion (Beatch 2016).

Despite these cases, the incidence of stroke in patients receiving antiarrhythmic drugs or placebo, and anticoagulated as per current guidelines (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016;ESC Guidelines 2020; 2023 ACC/AHA/ACCP/HRS Guideline) was extremely low (≤0.1%).

Three more strokes in the first 30 days were reported: all among ibutilide treated patients and occuring on day 2 (2 in Abi Mansour 1998 and 1 in Stambler 1996). These were not included in our analyses as these studies were conducted in the 90s and did not appear to routinely use any post-cardioversion anticoagulation regimen (i.e. patients not managed according to current guidelines for thromboprophylaxis of thromboembolic events during cardioversion - ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2016;ESC Guidelines 2020). The approach of recommending 4 weeks of anticoagulation post-cardioversion started being recommended in the mid to late 90s (Laupacis 1995), but only made it to guidelines a few years later.

Singh 2005 reports rates per 100 patient-years of follow-up for minor and major stroke with values from 0.68 to 2.03 for the three treatment arms (placebo, amiodarone and sotalol). However, no data are available for the number and timing of these events, namely whether any occurred during the first month post-randomization.

In Zhang 2005, a patient treated with propafenone developed ST-T segment changes and raised troponin after cardioversion, being diagnosed with myocardial infarction. It was not clear if this was a systemic embolic event, a type 2 myocardial infarction or an atherothrombotic event. Cotter 1999 described one patient with a "small myocardial infarction" in the group assigned to placebo.

Due to the low incidence of this adverse event it was not possible to do a meta-analysis to compare multiple therapies (Figure 48). Pooling of direct comparisons for Amiodarone vs. Placebo (Figure 49) and Vernakalant vs. Placebo (Figure 50) illustrates this matter. Similarly, sensitivity analyses for this endpoint were not possible.

30-day all-cause mortality

In total there were 14 instances of all cause mortality in the first 30 days post attempted cardioversion. Three cases occurred in patients randomized to placebo: one patient died with lung cancer (Vijayalakshmi 2006), one patient randomized to placebo (and subsequently cardioverted to sinus rhythm with sotalol) died of stroke on day 7 (Beatch 2016), and one patient died of respiratory failure 3.5h after receiving placebo (and being later electrically cardioverted from atrial flutter to sinus rhythm) (Stambler 1996).

One case of sudden death was observed 8h after electrical cardioversion (with biphasic truncated exponential waveform 200J AA patches) in a patient with severe mitral regurgitation and LV systolic dysfunction (Trendafilova 2021).

Nine mortality events were observed for patients randomized to treatment with antiarrhythmic agents. Vernakalant was associated with seven cases (Beatch 2016; Beatch 2017; Camm 2011; Pratt 2010; Roy 2008). In Roy 2008 there were 3 reported deaths in the 30 day folllow up period, all were patients who took vernakalant but none of the deaths were reported to be associated with the study drug. One patient had a ruptured aortic aneurysm during a gastroscopy the next day, one patient died of pneumonia and respiratory arrest 8 days later and one patient died from pulmonary oedema and congestive heart failure 26 days later. In Camm 2011 there was 1 death in the Vernakalant arm 24 hours after due to chronic obstructive pulmonary disease exacerbation and pulmonary embolism. In Pratt 2010 a patient with severe aortic stenosis and heart failure was enrolled despite some issues with haemodynamic instability prior to enrollment, they became hypotensive with the vernakalant infusion and developed ventricular fibrillation resulting in an unsuccessful resuscitation effort. Beatch 2016 reported one fatality case 29 days after treatment with vernakalant on a patient aged 77 who experienced cardiogenic shock shortly after the start of vernakalant infusion, and was then electrically cardioverted a few hours later. Multiple aggravating factors occurred afterwards, including rhabdomyolysis, electromechanical dissociation, gastritis, encephalopathy, coagulopathy, aspiration pneumonia, hepatic failure, acute renal failure, sepsis, anaemia, gastrointestinal haemorrhage, ischaemic colitis and hypovolemic shock. Study investigators classified this event not being drug-related. In Beatch 2017 one death was reported for vernakalant treated 82-year-old man. This patient had multiple comorbidities (history of abdominal aortic aneurysm, heart failure, idiopathic pulmonary fibrosis, rectal cancer, and pulmonary tuberculosis) and died at home sudden and unexpectedly whilst on his sleep on day 6. The cause of death was not ascertained (no autopsy was performed), but the death was considered no to be related to vernakalant (as the drug had been given 6 days before).

Singh 2000 described one death at D8 in a patient treated with Dofetilide. This was an unwitnessed event and was presumed to be a sudden cardiac death. One patient treated with Ibutilide in Abi Mansour 1998 died on day 9 with sepsis.

One studies (Hohnloser 1995) reported two cases of ventricular fibrillation with quinidine, but provided no information on whether the events were fatal. Also, Stroobandt 1997 reported one death due to ventricular

fibrillation in the setting of myocardial infarction in the placebo arm. However, this occurred during the 6 month follow-up period and no information is provided regarding timing (i.e. whether or not it occurred in the first month).

It was possible to link 5 interventions (amiodarone, ibutilide, sotalol, vernakalant and placebo) and 7 trials to perfom a network meta-analysis for 30-day all cause mortality Figure 51.

Trendafilova 2021 could not be linked to the network due to lack of a common comparator. Singh 2000 could not be linked to the network either as there was missing data (there were deaths occuring in the first year also for the placebo group and other doses of dofetilide, but no information on timing was provided, and hence we could not rule out if any of these occurred in the first month, and opted not to include this trial into the network).

Due to the low event rate (e.g. Figure 52, Figure 53 & Figure 54) and high imprecision it is not possible to conclude anything from it with any certainty (Figure 55). The network diagramme is represented in Figure 4 - panel E. The league table for this comparison presenting data for pairwise comparisons and the network meta-analysis is presented in Table 15. Similarly, the reduced total number of events and trials did not allow any meaningful subgroup or sensitivity analyses for this endpoint.

30-day cardiovascular mortality

Among the 14 deaths within the first 30 days post attempted cardioversion, 9 were likely of cardiovascular cause.

One of the 3 deaths in patients randomized to placebo was caused by stroke (Beatch 2016). The death reported among patients assigned to electrical cardioversion, was of likely sudden cardiac death (Trendafilova 2021).

Seven out of the 9 deaths among patients randomized to anti-arrhythmics were associated with cardiovascular causes or events: ruptured aortic aneurysm, pulmonary oedema/congestive heart failure (Roy 2008), pulmonary embolism (Camm 2011), severe aortic stenosis (Pratt 2010), cardiogenic shock (Beatch 2016) and potential sudden cardiac deaths in Beatch 2017 and Singh 2000. The first 6 of these deaths were in patients assigned to vernakalant, and the last was in a dofetilide treated patient.

It was possible to link 3 interventions (vernakalant, amiodarone & placebo) in 4 trials in the network meta-analysis for 30-daycardiovascular mortality (Figure 4 panel F). However, as for the previous endpoint, due to the low event number (e.g. Figure 56, Figure 57 & Figure 58) and high degree of imprecision we are not able to make any inferences (Figure 59 & Figure 60). The league table for this comparison is presented in Table 16.

Duration of hospitalisation

This finding was only reported in Bellone 2012, Halinen 1995 and Scheuermeyer 2019.

For Bellone 2012, the data was given as median and range of the time in the emergency room after cardioversion. This was 7h (2-23.3h) for propafenone and 3h (2-15h) for AP BTE Incremental.

Scheuermeyer 2019 compared biphasic cardioversion vs. intravenous procainamide in the Emergency Department setting in Canadian hospitals, and provided detail on different moments from registration to the Emergency Department to discharge: registration to physician assessment, physician assessment to randomization, randomization to cardioversion, and conversion to discharge. In this study, when cardioversion with the assigned method was not successful, cross-over was performed: procainamide infusion was started after the 3rd failed shock in 5 out of 43 (11.6%) patients of the electrical cardioversion group, and electrical cardioversion was performed in 19 out of 41 (46.3%) patients of the chemical cardioversion group, in media 110min after starting the procainamide infusion. Length of stay was shorter for patients assigned to electrical cardioversion first (registration to discharge: 3.5h, IQR 2.8-4.8 vs. 5.1h, IQR 3.5-6.3, P=0.005; randomization to discharge: 1.0h, IQR 0.8-2.7 vs. 3.1h, IQR 2.0-3.9, P<0.001). Even though these data suggest shorter duration of hospitalization for the electrical cardioversion group, no data are provided regarding length of stay for patients who did not require cross-over, and hence we are are unsure whether there are hospitalization duration differs when comparing patients with successful electrical cardioversion vs. patients with successful chemical cardioversion.

Halinen 1995 provided data as mean and standard deviation duration of hospital stay for cardioversion treatment, this was 20.3±13.8 hours for sotalol and 11.8±10.1 hours for quinidine. The Halinen 1995 data includes hospital treatment prior to cardioversion, therefore it is likely to be longer than the data given in Bellone 2012.

No data were pooled as Bellone 2012 and Halinen 1995, reported on different time intervals, and Scheuermeyer 2019 provided no results for patients with successful cardioversion with initially assigned intervention (Figure 61).

Quality of life, measured with any validated scale within the first year post cardioversion

Camm 2011 used the EQ-5D quality of life visual analog scale to assess change in quality of life from screening to hour 2 post-cardioversion of paroxysmal AF. Vernakalant was associated with a greater improvement in patient perception of state of health (mean adjusted increase from baseline 10.9 with vernakalant vs. 5.6 with amiodarone; P=0.0006).

Even though Beatch 2016 reports that vernakalant improves the "degree to which symptoms of AF impact on quality of life at 90min after drug exposure" when compared to placebo in patients with paroxysmal AF, the authors fail to provide information on the scale or method utilized to measure this outcome. A quality of life outcome, or an outcome phrased as above, is not mentioned in the protocol published in clinicaltrials.gov (NCT00989001). The clinicaltrials.gov protocol mentions the outcome "number of patients who report symptoms

at 90 minutes", which may be what the authors of Beatch 2016 mean when reporting the outcome "quality of life at 90min". However, it is uncertain to us, based on the provided information if this outcome can be included in our protocol definition of "quality of life, measured with any validated scale within the first year post cardioversion", as we are not sure if the authors are measuring quality of life, and there is no information on the utilized scale/instrument.

Yamashita 2009 assessed persistent quality of life of persistent AF patients treated with placebo vs bepridil at baseline, 4, 8 and 12-weeks, or at treatment discontinuation using the Japanase AF quality of life questionnaire (AFQLQ) and the Japanese version 2 of SF-36. No differences were observed for any of the 8 domains of SF-36 when comparing bepridil (100 or 200mg daily) vs. placebo. When assessing quality of life via the AFQLQ, bepridil 200mg daily performed better than placebo for variety and frequenty of symptoms, and for severity of symptoms (2 of the 3 domains). Patients receiving bepridil 200mg daily seemed to prevent better levels of the "severity of symptoms" domain when compared to those assigned to 100mg daily. Results for the AFQLQ score were presented on a graph, with no detail on the exact values and variance.

Singh 2005 reported on the change in quality of life measured with the SF-36 questionnaire between baseline and the end of the first year of follow-up. However, no comparisons were performed across the different treatment groups (sotalol, amiodarone and placebo). Presented values referred to patients remaining in sinus rhythm vs. those with persistent AF.

Due to utilization of different scales (EQ-5D, SF-36 & AFQLQ), uncertainty of the measured parameter or scale in one study (Beatch 2016), and no mention to the measured QOL levels for each treatment group in other studies (e.g. Singh 2005; Yamashita 2009) no pooling of data was possible.

Heart failure admission within the next month

None of the included trials reported on this outcome.

Development of ventricular arrhythmias following cardioversion while in hospital

Trials reported different types of ventricular arrhythmias, namely torsade de pointes (Bianconi 2000; Falk 1997; Hohnloser 1995; Kafkas 2007; Norgaard 1999; Pratt 2010; Reisinger 1998; Reisinger 2004; Roy 2008; Simon 2017; Stambler 1996, Singh 2000; Vogziatis 2017, Vos 1998), ventricular tachycardia (Abi Mansour 1998, Beatch 2016; Stambler 1996; Volgman 1998; Vos 1998), ventricular fibrillation (Hohnloser 1995; Pratt 2010; Roy 2004; Schmidt 2017; Singh 2000), or ventricular ectopy and/or non-sustained ventricular arrhythmias (Bianconi 2000; Blanc 1999; Camm 2011; Falk 1997; Halinen 1995; Pratt 2010; Roy 2004; Roy 2008; Schmidt 2017; Schmidt 2019; Simon 2017; Stambler 1996; Sun 2005; Volgman 1998; Vos 1998; Yu 2013).

Different definitions and cut-offs were utilized to define the composite ventricular arrhythmia endpoint, and therefore the data were not poolable.

Some drugs were associated with life-threatening ventricular arrhythmias. Dofetilide was associated with torsade de pointes in 4 trials (rate ranging from 0.8%, n=2 in Singh 2000, 3%, n=2 in Falk 1997 and Norgaard 1999, and 8.3%, n=4 in Bianconi 2000). The two patients with torsade de pointes in Singh 2000 degenerated into ventricular fibrillation. Ibutilide was associated with torsade de pointes in 3 trials (0.9%, n=1, in Reisinger 2004,and 7.1%, n=3, in Vogziatis 2017; In Simon 2017 the rate was 0%) and sustained polymorphic ventricular tachycardia in 4 trials (2.2%; n=5 in Abi Mansour 1998; 0.5%, n=1, in Vos 1998, 1.7%, n=3 in Stambler 1996 and 1.7%, n=1 in Volgman 1998). Abi Mansour 1998 also reported 1 event (0.5%) of sustained monomorphic ventricular tachycardia. Life-threatening ventricular arrhythmias were also observed for Vernakalant, with 0.8% of patients (n=1) having sustained ventricular tachycardia and 0.8% (n=1) ventricular fibrillation in Pratt 2010, 0.9% (n=1), and a rate of 3.1% (n=4) for ventricular tachycardia in Beatch 2016. One patient (1.9%) treated with sotalol in Reisinger 1998 developed torsade de pointes, and a patient in the placebo arm who had also received sotalol in Pratt 2010 experienced the same outcome. In Hohnloser 1995, three patients (12%) treated with quinidine experienced torsade de pointes and 1 patient (4%) developed monomorphic ventricular tachycardia. Of the three quinidine patients with torsade de pointes, 2 (8%) degenerated into ventricular fibrillation.

Non-sustained broad complex tachycardia was reported in 2 trials (Bianconi 2000; Falk 1997) with dofetilide at a rate of 4.2 to 4.9% (n=2 and n=3 respectively. Two vernakalant trials (Simon 2017; Vogziatis 2017) did not report ventricular arrhythmias. Ventricular fibrillation was observed in one additional vernakalant trial due to asynchronous shock delivered while cardioverting a patient after failure of vernakalant (Roy 2004). In Reisinger 2004 2 patients (1.9%) treated with ibutilide developed non-sustained ventricular tachycardia (morphology not specified). Seven patients (3.9%) treated with ibutilide developed non-sustained monomorphic ventricular tachycardia and 12 patients (6.7%) developed nonsustained polymorphic ventricular tachycardia in Stambler 1996. Non-sustained polymorphic VT with ibutilide was also reported in Abi Mansour 1998 at a rate of 4.1% (n=9) and 0.5% (n=1) in Vos 1998. In Volgman 1998 1 patient (1.7%) had non-sustained monomorphic ventricular tachycardia when treated with ibutilide. In Vos 1998 one patient (0.5%) treated with ibutilide developed nonsustained polymorphic ventricular tachycardia and 13 patients (6.2%) developed nonsustained monomorphic ventricular tachycardia. In Vos 1998, 4 patients (3.7%) treated with sotalol developed nonsustained monomorphic ventricular tachycardia.

There was a very low incidence of life-threatening ventricular arrhythmias in electrical cardioversion trials. The only occurence was in Schmidt 2017 where there were 1 patient developped ventricular fibrillation in the AP PB Incremental arm due to a malfunctioning device which was asynchronously shocking patients.

Development of bradyarrhythmias following cardioversion while in hospital

Included trials reported on different bradyarrhythmic events: pauses (Abi Mansour 1998; Azpitarte 1997; Beatch 2016; Bellandi 1995; Bertini 1990; Boriani 1997; Brodsky 1994; Camm 2011; Cybulski 2003; Negrini 1994; Reisinger 2004; Romano 2001; Schmidt 2017; Schmidt 2019; Treglia 1994a; Yu 2013; Zhang 2005), slow junctional rhythm (Bertini 1990; Boriani 1997; Martínez-Marcos 2000; Mattioli 1998; Romano 2001; Sun 2005; Treglia 1994a; Xanthos 2007; Vos 1998), atrioventricular block (Hohnloser 1995; Roy 2008; Schmidt 2019; Schmidt 2021; Stambler 1996; Trendafilova 2021; Vos 1998), sinus bradycardia, utilizing different cut-offs for definition of bradycardia, and other bradyarrhythmias were described in other studies (Abi Mansour 1998; Azpitarte 1997; Beatch 2016; Bellandi 1995; Boriani 1997; Bouida 2019; Camm 2011; Camm 2012; Cotter 1999; Cybulski 2003; Davey 2005;Ganau 1998; Hohnloser 1995; Joseph 2000; Kosior 2009; Mattioli 1998; Pratt 2010; Reisinger 1998; Reisinger 2004; Romano 2001; Roy 2004; Scheuermeyer 2019; Schmidt 2017; Schmidt 2019; Schmidt 2021; Simon 2017; Taha 2022; Thomas 2004; Treglia 1994a; Vos 1998; Xanthos 2007).

Pauses were reported in rare circumstances: one study reported this in vernakalant at a rate of 0.8% (n=1) (Beatch 2016), rates between 0.9 to 3.3% (n=1, n=2, and n = 1 respectively) were reported in patients treated with amiodarone (Camm 2011; Cybulski 2003; Negrini 1994), 2.0 to 7.0% (n=2 and n = 10 respectively) in patients on flecainide (Reisinger 2004; Romano 2001), 1.8 to 2.8% (n= 4 and n=3 respectively) in ibutilide treated patients (Abi Mansour 1998; Reisinger 2004). Six studies reported this complication with propafenone (3.4%; n=1 in Azpitarte 1997; 2.0%; n=2 in Bellandi 1995; 6.2%; n=1 in Bertini 1990; 0.8%; n=1 in Boriani 1997; 3.8%; n=4 in Zhang 2005; and 8.2%; n=4 in Yu 2013). Electrical cardioversion also associated with pauses: 3.1% (n=2) in AP BTE incremental, and 1.4% (n=1) in AP PB incremental (Schmidt 2017), and 1.4% (n=2) in AP BTE incremental (Schmidt 2019). This complication was reported also in 2.5% (n=3) patients receiving of placebo (Boriani 1997), suggesting that in some cases it can be observed as a result of underlying sinus node disease.

Slow junctional rhythm was reported in a few studies: ibutilide (1.9%; n=4 in Vos 1998), propafenone (6.2%; n=1 in Bertini 1990; 0.8%; n=1 in Boriani 1997; 2.6%; n=1 in Mattioli 1998; 1.2%; n=2 in Romano 2001; and 6%; n=3 in Martínez-Marcos 2000), flecainide (0.7%; n=1 in Romano 2001; 4%; n=2 in Martínez-Marcos 2000) and procainamide (11.5%; n=13 in Xanthos 2007).

Transient complete atrioventricular block was observed in 1 patient (0.4%) treated with vernakalant (Roy 2008), 1 patient (0.6%) treated with ibutilide (Stambler 1996) and 1 patient (0.9%) treated with sotalol (Vos 1998), 2nd or 3rd degree atriventricuclar block was observed in 2 patients (n=1.6%) receiving AP BTE maximum energy cardioversion (Schmidt 2019), transient 2nd degree Mobitz I was observed in 1 patient (4%) treated with sotalol (Hohnloser 1995), and advanced 2:1 atrioventricular block was found in 1 patient receiving AP BTE incremental energy cardioversion (Schmidt 2021).

Sinus bradycardia reporting was rare, 2 studies (Kosior 2009; Azpitarte 1997) reported events in propafenone treatment at rates between 2.2 to 2.3% (n=1 and n=1 respectively), one study reported an event with procainamide at a rate of 2.6% (Mattioli 1998), 2 studies (Joseph 2000; Hohnloser 1995) reported events with sotalol at rates between 5.0 to 32.0% (n=2 and n=8 respectively), with in 1 study with patients treated with vernakalant (Roy 2004) at a rate of 2.8% (n=1), and 2 studies (Cotter 1999; Camm 2011) reported on sinus bradycardia in patients treated with amiodarone at rates between 0.9 to 10% (n = 1 and n = 5 respectively). Further information on unspecfied aetiology bradycardia can be found in Supplementary Table 1.

Other Immediate procedure complications, or occuring within the first week

Five trials reported data on first week complications (Camm 2011; Kochiadakis 1999; Kochiadakis 1999a; Pratt 2010; Vardas 2000) and all other trials reported complications referred to the inpatient period.

Skin burns (blistering and necrosis) were reported in 2 patients (0.1% of all patients treated with electrical cardioversion and having this endpoint assessed) receiving AP MDS incremental cardioversion (Page 2002) and were not reported in any other trial looking at this endpoint (Mortensen 2007; Neumann 2004; Ricard 2001; Risius 2009; Schmidt 2017; Schmidt 2019; Schmidt 2021). Sedation-related complications were not reported in any of the included trials.

Acute heart failure was described in a few trials of pharmacological cardioversion. Left ventricular failure was reported in 2 patients (5.1%) treated with amiodarone and 6 patients (16.7%) treated with placebo by Joseph 2000. One patient (2%) in Martínez-Marcos 2000 and Reisinger 2004; treated with propafenone developped acute heart failure. One patient (1.9%) treated with Sotalol in Reisinger 1998 and one patient (1.0%) treated with flecainide in Reisinger 2004 had acute heart failure. Two patients (8%) treated with sotalol aggravated symptoms of congestive heart failure in Hohnloser 1995. In Roy 2008 and Beatch 2016 one patient (0.5% and 0.8%, respectively) with vernakalant had cardiogenic shock, and the same was observed for two patients (3.8%) treated with intravenous amiodarone in Thomas 2004. This endpoint was not reported in any trial of electrical cardioversion.

Frequent minor side effects were observed for some of the anti-arrhythmic agents: phlebitis (2.5%, n=1, in Joseph 2000; 11.5%, n=13, in Xanthos 2007; 16%, n=8, in Cotter 1999; 17%, n=17, in Vardas 2000; 18.5%, n=17, in Kochiadakis 2007; 35.3%, n=12, in Kochiadakis 1999; and 48%, n=11, in Treglia 1994a) and pain (6.8%, n=5, in Kafkas 2007) on the infusion site were reported for amiodarone, and dysgeusia (5.6%, n=3, in Vogziatis 2017; 6.1%, n=3, in Simon 2017; 6,9%, n=8, in Camm 2011; 14.8%, n= 19 in Beatch 2016; 21.4%, n=28, in Pratt 2010; 29.9%, n=66, in Roy 2008; and 38.5%, n=15, in Camm 2012) and sneezing (3.4%, n=4 in Camm 2011; 8.5%, n=11 in Beatch 2016; 12.2%, n=6, in Simon 2017; 16.3%, n=36, in Roy 2008; and 17.6%, n=23, in Pratt 2010) were described for vernakalant.

A more detailed description of the observed complications can be seen in Supplementary Table 1.

Sensitivity analyses

With regards to the pre-planned sensitivity analyses, these were possible only for the endpoint "maintenance of sinus rhythm until hospital discharge". As described in the "stroke or systemic embolism" and "30-day all-cause mortality" sections, sensitivity analyses for these endpoints were not considered feasible.

Maintenance of sinus rhythm until hospital discharge or end of study follow-up

As in previous sections, sensitivity analyses for this endpoint were by paroxysmal AF, persistent AF and atrial flutter.

Low Risk of Bias

There were only four studies with low risk of bias in all domains (or for all objective endpoints-related outcomes) (Bouida 2019; Scheuermeyer 2019; Schmidt 2019 & Schmidt 2021). However, no analyses were possible as these fell within different categories of AF duration, or there were no events or common comparators.

Irrefutable evidence of registration and occuring before enrolment

Paroxysmal AF

When assessing trials only with irrefutable evidece of registration prior to study participants enrolment, a network of four trials (Beatch 2016; Beatch 2017; Camm 2011 & Maciag 2017, as Scheuermeyer 2019 could not be linked due to the lack of a common comparator) was created. Four interventions (Antazoline, Vernakalant, Propafenone, Amiodarone) were compared to Placebo, but high heterogeneity (I^2 = 91%) and overlap of confidence intervals make any interpretations or further contribution to the main analysis difficult (Figure 62).

Persistent AF

Only two trials included only persistent AF (Schmidt 2019; Voskoboinik 2018), but we could not include Voskobonik 2018 due to the average BMI of enrolled patients > 30Kg/m^2, and hence no network as possible.

Atrial Flutter

No sensitivity analysis was possible due to the absence of trials meeting this criterion.

Irrefutable evidence of registration and occuring at anytime

Paroxysmal AF

When assessing trials only with irrefutable evidece of registration at any time. a network of seven trials (Beatch 2016; Beatch 2017; Bellone 2012; Camm 2011; Maciag 2017; Scheuermeyer 2019, Taha 2022) was created (Figure 63). Six interventions (Antazoline, Vernakalant, BTE incremental energy, Propafenone, Amiodarone and Procainamide) were compared to Placebo, but, once again, high heterogeneity (I^2 = 91%) and overlap of confidence intervals made any interpretation or further contribution to the main analysis impossible.

Persistent AF

There were three trials that Included only persistent AF patients or reported results separately (Kirchhof 2005; Schmidt 2019; Voskoboinik 2018). As for the previous sensitivity analysis of persistent AF patients, no network could be established.

Atrial Flutter

There were only 2 trials which included only patients with atrial flutter (Camm 2012; Risius 2009). These could not be compared as there were no linking treatments.

Highest Quartile of Participants

Paroxysmal AF

For studies with the highest quartile of participants from those included in first network (Figure 4 panel A) we included Bellone 2012; Boriani 1997; Romano 2001 . BTE incremental had the highest efficacy (RR: 2.49; 95%CI 1.88 to 3.29) followed by Propafenone (RR: 2.06; 95%CI 1.60 to 2.65) then Flecainide (RR: 2.01, 95%CI 1.54 to 2.61) and finally Placebo, which was the comparator (Figure 64). Q statistic was 0 due to the very low number of trials included.

Persistent AF

For persistent AF patients having electrical cardioversion the trials with the highest quartile of participants from the second network (Figure 4, panel B) were Schmidt 2019; Siaplaouras 2004. Due to the lack of a common comparator, we were not able to produce this analysis.

For the network of trials assessing chemical cardioversion, Singh 2005 alone included more than 25% of the participants.

Atrial Flutter

In the atrial flutter main network analysis, Stambler 1996 included > 25% of participants.

Excluding Quasi-Randomized Trials

Paroxysmal AF

After excluding quasi-randomized trial (Romano 2001 & Vogziatis 2017) the foresplot provides comparable estimates to the main anlysis for the primary endpoints of maintenance of sinus rhythm until hospital discharge or end of study follow-up (Figure 65).

Persistent AF

After excluding a quasi-randomized trial (Jakobsson 1990) the foresplot provides comparable estimates to the main anlysis for maintenance of sinus rhythm until hospital discharge or end of study follow-up (Figure 66).

No quasi-randomized trials were included in the chemical cardioversion entwork.

Atrial Flutter

No quasi-randomized trials were included in the atrial flutter network.

Subgroup analyses

Type of AF or Atrial Arrhythmias

Subgroup analyses by AF type for the primary endpoint were not done as this was already done in the previous sections to respect the transitivity assumption for efficacy endpoints.

Route of Anti-arrhythmic Administration

Subgroup analyses by AF type for the primary endpoint are presented below:

Paroxysmal AF

The subgroup analysis including trials with intravenous agents included 29 trials, with results presented in Figure 67. Twenty-nine trials were included in the analysis, which despite high heterogeneity (I^2 = 78%), suggested that all the utilized intravenous agents, except for magnesium, were largely more effective than Placebo: Antazoline (RR: 28.60, 95%CI 1.76 to 465.96), Flecainide (RR: 2.15, 95%CI 1.55 to 2.98), Vernakalant (RR: 2.15, 95%CI 2.00, 95%CI 1.48 to 3.12), Ibutilide (RR: 2.00, 95%CI 95%CI 1.21 to 3.29), Propafenone (RR: 1.93, 95%CI 1.57 to 2.37), Sotalol (RR: 1.67, 95%CI 1.03 to 2.70), Amiodarone (RR: 1.59, 95%CI 1.30 to 1.96) and Procainamide (1.44, 95%CI 1.05 to 1.97).

The subgroup analysis including trials with oral drugs were included 4 trials, assessing five drugs (Flecainide, Amiodarone, Quinidine, Propafenone and Sotalol). Flecainide (RR: 3.66, 95%CI 1.20 to 11.18), Amiodarone (RR: 3.56, 95%CI 1.16 to 10.88) and Propafenone (RR: 2.97, 95%CI 1.29 to 6.84) seemed largely more effective than Placebo, and despite uncertainty Quinidine may be more effective or no different than placebo (RR: 3.02, 95% 0.77 to 11.83) (Figure 68). On the other hand, we are uncertain whether oral Sotalol (RR: 1.81, 95%CI 0.31 to 10.70) is more effective than Placebo.

Due to the broad confidence intervals observed, namely for Antazoline, and the observed heterogeneity, we are uncertain about ranking the different agents and performing comparisons of antiarrhytmic intravenous and oral agents.

Persistent AF

The subgroup analysis including trials with intravenous agents included 3 trials and presented low heterogeneity (I^2 = 0%). Three drugs (amiodarone, Propafenone and Dofetilide) and Placebo where included in the plot (Figure 69), which had Amiodarone as the comparator, and showed that Placebo is less effective than Amiodarone (RR: 0.03, 95% 0 to 0.48).

The subgroup analysis including trials with oral agents included 8 trials. Bepridil, Amiodarone, Propafenone, Sotalol and Placebo were the assessed agents. Amidoarone was the comparator, and the plot showed that Bepridil (RR: 2.34, 95%CI 1.28 to 4.26) is likely more effective than Amiodarone, and Placebo seemed markedly less effective (RR: 0.09, 95%CI 0.04 to 0.22) (Figure 70).

Due to the broad and overlapping confidence intervals, we are uncertain about ranking the different agents and performing comparisons of antiarrhytmic intravenous and oral agents.

Atrial Flutter

All studies of antiarrhythmic drugs in atrial flutter patients used intravenous drugs.

Other Subgroup Analyses

The remaining planned subgroup analyses could not be performed as trials did not report subgroup outcomes to enable this or they were not excludable from the total network based on the whole patient population having one of the mentioned characteristics.

Discussion

Summary of main results

I. Maintenance of sinus rhythm until hospital discharge or end of study follow-up

II. Acute procedural success

Due to great overlap in data regarding these two endpoints as follow-up duration of trials is short, and only a small minority of trials reported relapses during admission or between cardioversion and the end of follow-up, discussion of these endpoints is done on the same section.

Electrical vs Pharmacological

Paroxysmal AF:

Biphasic incremental energy (89.3% with 200J at 6h), Flecainide (90% at 12h), Quinidine (91.4% at 24h), Amiodarone (92% at 24h), Propafenone (90.7% at 24h), Vernakalant (74.5% at 24h), Ibutilide (77% at 4h30), Sotalol (87.5% at 48h), Procainamide (82.7% at 24h), Antazoline (72.7% at 90 min), and Pilsicainide (72.5% at 2h) all had high efficacy at end of study follow-up. Follow-up for studies of electrical cardioversion was usually restricted to the inpatient period. It was possible to connect them through a network (Figure 4 - Panel A). When analyzing the comparisons (Figure 6), very high heterogeneity was noted (I^2=76%) and, due imprecision and overlap of broad confidence intervals, it was not possible to ascertain whether with certainty which strategies are more effective (Summary of Findings Table Figure 7). This was confirmed in the analysis of League Table 6 which showed no significant differences when comparing AP BTE incremental with the best performing phamarcological drug strategies. Data on Antazoline need to be interpreted with caution as they result from only one small study, and imprecision on the network is pronounced.

Analyses of the Network comparisons for the endpoint Acute success Table 12 and Figure 30 are similar to the previous outcome, except for one point: the league tables suggest that AP BTE incremental may be less effective than vernakalant. Taking into account the high global inconsistency and high heterogeneity of the network (I^2 = 81%), and the cardioversion efficacy rates for AP BTE incremental and Vernakalant presented in the paragraph above, which are higher for AP BTE incremental cardioversion, these data with very low certainty need to be interpreted with caution (Summary Findings Table Figure 32).

Persistent AF:

Comparison of the two strategies through the same network was not possible.

Electrical cardioversion had very high efficacy, namely when biphasic energy was utilized: BTE incremental AP handheld paddles (90% with 200J AA to 100% with 360J AP), Biphasic incremental AA patches (100% with 360J BTE, and 94.9% with 200J RBW), BTE active-compression AP patches (96.0% with 200J), Biphasic fixed AA patches (97.4% with 200J BTE), Incremental AA patches (96.9% with 360J BTE and 95.2% with 200J RBW), and BTE maximum fixed AP patches (88% with 360J). The rate of patients meeting these efficacy endpoints was lower in trials of pharmacological cardioversion, and antiarrhythmic agents took days to weeks to convert patients to sinus rhythm: Bepridil (82.5% at 3 months), Quinidine (80% at 7 days), Amiodarone (60% at 14 days), Propafenone (40.6% at 30 days), Cibenzoline (36.8% at 9 days), Flecainide (25% at 9 days), Dofetilide (21.3% at 6h), Pilsicainide (21.2% at 4 weeks), Sotalol (24.2% at 28 days), Dofetilide (21.3% at 6h), and Placebo (3.7% at 7 days).

Atrial flutter:

Comparison of the two strategies through the same network was not possible. Electrical cardioversion strategies had very high efficacy (97.9% to 100%), and among antiarrhythmic drugs only ibutilide (90% at 90 min) yielded comparable results. Dofetilide cadioverted 71.4% of patients, Propafenone only 40%. Flecainide (20% at 1h), Procainamide (15% at 1h) and Sotalol (19.0% at 1h) converted a minority of patients.

Phamacological vs Placebo

Paroxysmal AF:

In trials of paroxysmal AF patients cardioversion back to sinus rhythm was also observed even in the majority of patients treated with Magnesium (57% at 6h) and Placebo (64% at 24h).

We observed that antazoline, vernakalant, ibutilide, quinidine, flecainide, propafenone, amiodarone, sotalol and procainamide may result in a large increase in maintenance of sinus rhythm at hospital discharge or end of study follow-up when compared to placebo (Figure 6), but the certainty of evidence is low to moderate.

Persistent AF:

Unlike in paroxysmal AF, patients with persistent AF do not revert back to sinus rhythm when treated with placebo. Bepridil, Quinidine, Amiodarone, Sotalol and Propafenone are significantly more effective than placebo at restoring patients back to sinus rhythm (Table 9 & Figure 19). There is, however, uncertainty about the effect of Dofetilide and Pilsicainide (Summary of Findings Table Figure 20).

Atrial flutter:

Patients with atrial flutter very rarely reverted to sinus rhythm when assigned to the placebo arm. Ibutilide, Propafenone, Dofetilide and Sotalol are significantly better than placebo at converting atrial flutter patients to sinus rhythm (Figure 26; Figure 27). Vernakalant seems to be no better than placebo in this setting.

Electrical vs Placebo

There was no direct electrical vs placebo comparison in the meta-analysis, as none of the included studies performed a randomized comparison between the two strategies.

Paroxysmal AF

Inclusion of AP BTE Incremental in the network Figure 4, Figure 6 & Figure 30 allows us to compare this strategy vs. placebo. League Table 6 & Table 12 suggest that efficacy of placebo is approximately two thirds lower.

Persistent AF & Atrial Flutter

There was not network linking electrical cardioversion vs. placebo for any of these groups of patients. However, efficacy of placebo was 0% or nearly for trials of persistent AF and atrial flutter, whilst efficacy of electrical cardioversion strategies for persistent AF was 61 to 100% and for atrial flutter it was 97.9 to 100% (Table 4).

Electrical modalities

Comparison of different electrical cardioversion strategies was possible for trials of persistent AF patients (Figure 16 & Figure 41). What is clear from the electrical cardioversion comparison is that the maximum fixed energy AP BTE maximum shock with patches approach was superior to most other cardioversion strategies (Table 8 & Table 13). Active compression AP BTE incremental energy with patches and AP BPE incremental energy with paddles seemed like comparable high efficacy options (Summary of Findings Table Figure 17; Figure 42). One trial (Voskoboinik 2018) in obese patients (hence not included in the network) showed higher efficacy in the group treated with Paddles.

Pharmacological cardioversion options

Paroxysmal AF

Antazoline, Vernakalant, Flecainide, Quinidine, Ibutilide and Propafenone were the most effective drugs of the Network for this patient group for both endpoints (Figure 6, Table 6 & Table 12). However, it is important to highlight that the two network comparisons had very high heterogeneity. Unlike electrical cardioversion whose effect is immediate and depending on pressing a button. Pharmacological agents' onset of action varies with some of these agents (e.g. Vernakalant, Antazoline, Ibutilide and Flecainide) being fastar acting than other (e.g. Amiodarone or Sotalol). Importantly, data on Antazoline must be interpreted with caution as they result from a single small study and have high imprecision.

Persistent AF:

Quinidine seemed to be better than Propafenone and Amiodarone (Figure 19 & Table 9). Heterogeneity for this network was very low (I^2=2). Bepridil and Quinidine may be more effective than Propafenone, Sotalol and Amiodarone.

Atrial Flutter

Ibutilide may be more effective than Propafenone, Sotalol and Procainamide. It is uncertain whether Ibutilide is more effective than Dofetilide. Vernakalant was innefective in this patient population.

III. Stroke or Systemic Embolism within 30 days

There was not sufficient follow-up data extending to 30 days in all studies.

Out of all of the studies assessed there were only 3 reported strokes, one during administration of digoxin (placebo arm) (Joseph 2000), one in a patient receiving amiodarone (Martínez-Marcos 2000), and a fatal stroke occurred on day 7 in a patient assigned to placebo and later treated with sotalol (Beatch 2016). There were no reported strokes in patients assigned to electrical cardioversion. Due to the extremely low number of events our review was not powered for analyses on this endpoint (Summary of Findings Table Figure 48)

This seems to be an extremely rare complication in patients having cardioversion when appropriately anticoagulated as per the guidelines, which is a reassuring finding.

IV. 30 day all cause mortality, 30 day cardiovascular mortaility

In total there were 14 instances of all cause mortality in the first 30 days post attempted cardioversion. Three cases occurred in patients randomized to placebo, one case occurred 8h after electrical cardioversion, and nine mortality events were observed for patients randomized to treatment with antiarrhythmic agents (7 deaths with Vernakalant, 1 with Dofetilide and 1 Ibutilide). Nine of these deaths were tought to be of cardiovascular cause.

The potential for fatal ventricular arrhythmias highlights the need for some caution and good patient selection when using some of these agents (i.e. not using Vernakalant in patients with underlying cardiac structural disease). Due to the extremely low number of events our review was not powered for analyses on this endpoint (Summary of Findings Table Figure 55 & Figure 60)

V. Quality of Life within the first year

Data on quality of life were scarce and of uncertain clinical significance.

Camm 2011 reported on quality of life measures assessed 2 hours post-cardioversion. Vernakalant was associated with a greater improvement in patient perception of state of health (EQ-5D quality of life visual analog scale).

We were uncertain about the data reported by Beatch 2016, and whether or not this represented an assessment of quality of life done with a validated instrument.

Yamashita 2009 assessed persistent quality of life of persistent AF patients treated with placebo vs bepridil at baseline, 4, 8 and 12-weeks, or at treatment discontinuation using the Japanase AF quality of life questionnaire

(AFQLQ) and the Japanese version 2 of SF-36. Potential benefit of Bepridil (200mg daily dose) was observed only whilst using the AFQLQ for variety and frequenty of symptoms, and for severity of symptoms.

Singh 2005 reported on the change in quality of life measured with the SF-36 questionnaire between baseline and the end of the first year of follow-up, but provided no results for comparisons across the different treatment groups (sotalol, amiodarone and placebo).

In sum, due to utilization of different scales (EQ-5D, SF-36 & AFQLQ), uncertainty of the measured parameter or scale in one study (Beatch 2016), and no mention to the measured QOL levels for each treatment group in other studies (e.g. Singh 2005; Yamashita 2009) no pooling of data was possible.

VI. Duration of hospitalisation

This was only reported in 3 studies and data could not be pooled as different intervals were measured (Summary of Findings Table Figure 61). Time in the Emergency department seems lower for AP BTE Incremental than for propafenone. Duration of cardioversion treatment was shorter with quinidine than sotalol (Bellone 2012). Time in the emergency room post-cardioversion in patients treated with AP BTE Incremental seemed to be shorter than hospital admission duration for sotalol and quinidine (Halinen 1995). In Scheuermeyer 2019 length of stay was shorter for patients assigned to electrical cardioversion first.

VII. Heart failure readmission within the first month post-cardioversion

There were no cases of heart failure readmission in the first month. However, as reported below, there were some cases of acute heart failure described in patients receiving anti-arrhythmic drugs or placebo.

VIII. Development of ventricular arrhythmias following cardioversion while in hospital

Life-threatening ventricular arrhythmias, torsade de pointes or ventricular fibrillation, were documented with Dofetilide (incidence of 3% to 8.3%), Quinidine (4 to 12%), Ibutilide (0.9% to 7.1%), Sotalol (1.9%), and Vernakalant (0.8 to 0.9%). This reinforces the need for carefull monitoring of these patients during administration of drugs and until the end of the drug's half life.

There was a very low incidence of life-threatening ventricular arrhythmias in electrical cardioversion trials. The only occurence was in Schmidt 2017 where there were 1 patient developped ventricular fibrillation in the AP PB Incremental arm due to a malfunctioning device which was asynchronously shocking patients.

IX. Development of bradyarrhythmias following cardioversion while in hospital

Sinus pauses were seen in 0 to 3.2% of patients treated with placebo, 0.9% of patients on amiodarone, 2.0% of patients on flecainide, 2.8% of ibutilide patients, and 3.8% to 8.2% of propafenone patients. Electrical cardioversion was also associated with pauses in 1.4% to 3.1%. Underlying sinus node disease may be an important contributor to this.

Slow junctional rhythm was observed in 2.5% of ibutilide patients, 1% to 6% propafenone patients, flecainide in 4%, and procainamide in up to 11.5%.

Transient complete atrioventricular block was observed in 0.4% of those treated with vernakalant, up to 2.5% treated with flecainide and 0.9% treated with sotalol. Second or 3rd degree atriventricuclar block was observed in 1.6% of patients receiving AP BTE maximum energy cardioversion and advanced 2:1 atrioventricular block was found in 0.4% receiving AP BTE incremental energy cardioversion.

X. Immediate (< 24 hours) procedure-related complications

XI. Complications deemed to be related to the procedure occurring within the first week.

Due to most trials reporting mainly inpatient complications, these endpoints are jointly discussed on this section, being that for complications observed after discharge information is scare.

Electrical cardioversion displayed a favorable complications profile. Skin burns (blistering and necrosis) were reported only in 0.1% of patients treated with electrical cardioversion, and were observed only for AP MDS incremental cardioversion (Page 2002). Sedation-related complications were not reported in any of the included trials. No acute heart failure events were reported for patients treated with electrical cardioversion.

A few acute heart failure events were observed (0.5 to 5.1%) in patients treated with amiodarone, propafenone, flecainide, sotalol, and vernakalant, suggesting that in patients where this is likely to happen, electrical cardioversion should be the preferred cardioversion modality.

Phlebitis was a common complication in amiodarone treated patients (2.5% to 35.3%) of patients suggesting the need for specific precautions when utilizing this agent intravenously (e.g. considering only short duration iv use and, ideally, through a central venous line). Dysgeusia (5.6% to 38.5%) and sneezing (3.4% to 17.6%) are frequent vernakalant side effects that the clinician should also be aware of.

Overall completeness and applicability of evidence

The included data in this review allows us to provide the bulk available evidence regarding patients with paroxysmal & persistent AF, and atrial flutter receiving pharmacological and electrical cardioversion. Trial setting is similar to the setting these patients are managed Worldwide. This data is, therefore, applicable to clinical practice anywhere in the World, but has a few limitations (i.e. it was not able to address all of the proposed aims).

Local availability of some anti-arrhythmic drug agents

Bepridil is available and licensed for cardioversion in AF patients in Japan, and Antazoline is available in Poland. Trials for those agents were conducted in Japan and Poland, respectively. Difficult access to these drugs is likely in other countries.

Efficacy Outcomes

Data on the efficacy of cardioversion at different timepoints was insufficient. Most studies provided information regarding rhythm at discharge only. Information about acute success or early relapses were not usually provided. Similarly, no data was usually available on rhythm within the first month (following discharge).

Inconsistent reporting of complications, adverse events and clinical outcomes

There was inconsistent reporting of complications: type of complications reported and timing of complications. Some of the endpoints (e.g. mortality, stroke, torsade de pointes, etc) are infrequent, and trials were not powered to allow for comparisons.

This contributes to a considerable level uncertainty in our analyses / observations.

Incomplete 30-day data

Most studies had short follow-up (e.g. until discharge or immediately after cardioversion) and did not provide enough information about possible procedure-related complications, efficacy, and stroke and systemic embolism or mortality in the first 30 days.

Even though the risks associated with cardioversion modalities seem low, the fact that most studies provided no information on events after discharge and within the first 30 days, results in some uncertainty.

Comparison of electrical to pharmacological modalities.

As mentioned there was only one trial, including paroxysmal AF patients, that compared electrical to pharmacological interventions. This was included into our network meta-analysis, but the very high observed heterogeneity leads to uncertainty about the reliability and applicability of the data.

It is therefore difficult to say which cardioversion modality has higher efficacy for paroxysmal AF. For persistent AF and atrial flutter, uncertainty seems to be lower regarding the higher efficacy of electrical cardioversion vs. pharmacological cardioversion.

Lack of Placebo (or sham-procedure) or Drug-controlled electrical cardioversion studies

There were no placebo-controlled studies assessing electrical cardioversion. A trial of "sham procedure: vs. electrical cardioversion (NCT05136131) is currently ongoing. Direct comparisons of fast acting drugs like vernakalant, ibutilide, flecainide vs. electrical cardioversion are absent or sparse. Addressing this knowledge gap will allow us to understand with more certainty whether or not electrical and pharmacological cardioversion are comparable across the universe of atrial fibrillation and flutter.

Insuficient data on pharmacological cardioversion in persistent AF

Some of the drugs included in this review (e.g. vernakalant, flecainide) had no trials in the persistent AF setting, and therefore, there is uncertainty about their effect in that setting.

Quality of Life

Our data fail to answer the question of whether cardioversion leads to an improvement in quality of life, and which strategy leads to the best reponse. The abovementioned NCT05136131 trial will look at quality of life as assessed through the Atrial Fibrillation Effect on QualiTy of Life (AFEQT) questionaire at 4 weeks, and will provide more information on this matter.

Magnesium

Treatment arms in all studies looking at magnesium utilized different doses, leading to some difficulty on how to extrapolate the results to clinical practice.

Despite this, we believe this evidence can be used to help guide the management of patients with paroxysmal and persistent AF and atrial flutter who are being considered for cardioversion, and to help define the best cardioversion strategy.

Quality of the evidence

112 trials and 15,968 patients were included in the analysis. For the efficacy endpoints, we used 35 trials of patients with paroxysmal AF, 26 trials of persistent AF and 14 trials with results for atrial flutter patients.

The overal quality of the evidence for nearly all outcomes ranged from "very low" to "high".

High level of certainty was observed in the persistent AF electrical cardioversion network, with AP BTE maximum energy with patches and active compression BTE incremental energy with patches vs. AP BTE incremental energy with patches for the outcome: maintenance of sinus rhythm until hospital discharge or end of study follow-up..

Moderate certainty of evidence was available for:

- Some of the comparisons in the electrical cardioversion strategies for persistent AF, with likely lower efficacy observed for AP & AA MDS Incremental energy with Patches, AA & AP RBW Incremental energy with Patches

and AA MDS Incremental energy with Paddles vs. AP BTE Incremental energy with Patches.

- Some of the comparisons in the paroxysmal AF network for the primary endpoint, with AP/AA BTE Incremental energy, Quinidine, Ibutilide, Propafenone, Amiodarone, Sotalol, and Procainamide being likely more effective than Placebo.

High heterogeneity for some of the comparisons (e.g. acute procedural success and sinus rhythm at discharge or end of study follow-up), and and multiple items of the risk of bias tool with unclear or high risk of bias were seen.

The network for "acute procedural success" in patients with paroxysmal AF had high global inconsistency.

Only one trial was low risk of bias for all domains when assessing all endpoints. When restricting the analysis to objective endpoints only (acute procedural success, all-cause mortality and stroke or systemic embolism; i.e. not as likely to be affected by lack of blinding), two further additional trials were considered low risk.

Random sequence generation and allocation concealment were not handled properly in most trials. Some studies showed numerical differences in baseline variables across the different intervention groups, which raised some concerns about quality of the randomization process.

Blinding (patient, personnel and assessor) was usually also an issue.

Attrition bias was also an issue for some studies with a high % of missing data. Selective reporting was also noted for some studies without previous publication of the protocol and no clarity on the pre-planned study outcomes.

Trials frequently had no proof of registration, or sometimes this occurred after the trial had already started enrolment.

Incoherence was observed for some of the comparisons (e.g. flecainide for the two efficacy endpoints in patients with paroxysmal AF).

Imprecision was also a significant issue, especially with efficacy in small trials and with rare adverse events.

Study design issues were observed for electrical cardioversion trials, as no placebo, anti-arrhythmic drug or sham-procedure arm was usually available.

Potential biases in the review process

While assessing the 2 efficacy endpoints of this review we split the population in groups while attempting to respect the transitivity assumption.

Patients were divided by AF type (paroxysmal AF, persistent AF, and atrial flutter) and by body mass index (> vs. $\leq 30 Kg/m^2$) to assure that more homogeneous populations were compared.

For objective endpoints (i.e. all-cause mortality, stroke or systemic embolism, and acute procedural success) we did not consider lack of blinding as a potential source of bias as this was unlikely to interfere. However, for endpoints like maintenance of sinus rhythm after discharge, quality of life, duration of hospitalization, lack of blinding can lead to bias in the way the patient is addressed and hence affect outcomes.

Our searches are up-to-date and we believe we have not missed any relevant trials.

High heterogeneity (68% and 71%) in paroxysmal AF drugs cardioversion efficacy outcomes recommends caution while interpreting the results of the networks for the efficacy outcomes. Sensitivity analyses did not help with handling of the heterogeneity.

The fact that Vernakalant was compared with amiodarone at 90min (and hence not yet at its peak of action) may have led to changes in the structure of the network an overestimation of Vernakalant's effect in the aforementioned efficacy comparisons. Similarly, the fact that Antazoline was compared with Placebo at 90min, which is before paroxysmal AF patients have time to spontaneously convert, may inflate the results of Antazoline in the network as for most of the antiarrhythmic agents compared to Placebo the follow-up was slightly longer.

Agreements and disagreements with other studies or reviews

Our study confirms that both electrical and pharmacological approaches are more useful than placebo for the treatment of paroxysmal AF, persistent AF and atrial flutter. Our review confirms previous evidence in this regard about the benefits of newer agents such as Vernakalant as well as previously known agents such as Flecainide (ESC Guidelines 2016, ESC Guidelines 2020). A recent meta-analysis by Desouza et al also showed the superiority of pharmacological therapy over placebo and the efficacy of Vernakalant and Flecainide in recent onset AF which is similar to our results. (Desouza 2020). The authors also found a spontaneous cardioversion rate of 50.5%. Their overall study quality was low and their network demonstrated inconsistency. The authors had also suggested that further high quality studies are required, which is something we are in agreement with.

Vernalakant is a newer antiarrhythmic agent which is atrial selective, rapid acting with multi ion channel activity. It is approved in Europe for use for cardioversion of AF (Ritchie 2020). It is still not approved in the US and the latest attempt in 2019 was denied and it was not mentioned in the latest guidance (2023 ACC/AHA/ACCP/HRS Guideline). It is mentioned in the Canadian guidelines as treatment for AF but no evidence grade is given (Andrade 2018). The ESC guidelines give a class I indication for usage in AF in patients without structural heart disease which would be in agreement with our data.(ESC Guidelines 2020)

Vernakalant is indicated overall in patients with recent onset AF (less than one week) and no heart disease or mild to moderate structural heart disease (Kossaify 2019). Mcintyre 2019 have shown that in their meta analysis of nine trials that Vernakalant is safe and useful for restoration of Sinus Rhythm in recent onset AF. It also had no significant difference in severe side effects compared with placebo, Ibutilide or amiodarone (McIntryre 2019). Ma 2020 carried out a meta analysis on Vernalakant with similar results. They found that although it was superior to placebo, it was not superior to Ibutilide. (Ma 2020). Our review gives further evidence that Vernakalant is useful along with Flecainide and Ibutilide for cardioversion in new onset AF in clinical practice. (Hall 2019)

Flecainide is a widely used medication for the treatment of new-onset Atrial fibrillation. Desouza 2020 have demonstrated its effectivess in a NMA of 21 studies (Desouza 2020). Markey et al looked at 11 studies looking at cardioversion for Flecainide and Acute AF and demonstrated that it was very effective (Markey 2018). Flecainide has widespread approval with the FDA approving it in 1984 (Arunachalam 2020). Flecainide is still first line for patients without structural heart disease in multiple guidelines (ACC/AHA/HRS Guidelines 2014; ESC Guidelines 2020;Andrade 2018;NICE 2014). Even though its usage has been reduced since the CAST trial due to fear of Ventricular Arrhythmia, this risk has not been found in patients without structural heart disease. (Echt 2020). Our data are in agreement with these guidelines in the recommendation of Flecainide for recent onset AF without structural heart disease.

Ibutilide is a class III antiarrhythmic drug which has been recommended in the latest ESC guidance. (ESC Guidelines 2020). It has a half life of six hours on average and requires monitoring for a period even after the infusion is stopped. (Szymanski 2020) Ibutilide has had approval from the FDA since 1998. (www.accessdata.fda.gov/drugsatfda_docs/nda/96/020491Orig1s000rev.pdf;ACC/AHA/HRS Guidelines 2014). This drug is not routinely available in the UK (but it is not mentioned in the British National Forumulary bnf.nice.org.uk/), and our data concur with all of these guidances in their recommendations.

Our study also confirms that the most widely used electrical cardioversion modality (i.e. biphasic electrical energy) was the most effective form of electrical energy, and suggests that maximum energy should be used from first cardioversion attempt. Electrical therapy has lower rate of side effects (e.g. life-threatening ventricular arrhythmias, acute heart failure) than pharmacological therapy which may lead to a stronger class of recommendation for electrical therapy than at present (2023 ACC/AHA/ACCP/HRS Guideline, ESC Guidelines 2020).

Biphasic shocks have been demonstrated to be superior to monophasic shocks in a network meta-analysis of 23 trials by Inacio et al. (Inacio 2016). Biphasic shocks require less energy and resulted in a higher chance of cardioversion after the first shock, after multiple events. DC Cardioversion is recommended as first line in multiple guidelines, and this indication can be supported by our data (Andrade 2018, 2023 ACC/AHA/ACCP/HRS Guideline, ESC Guidelines 2020, NICE 2014).

Previous meta-analyses have faced similar issues to the ones we encountered. Desouza (which included 21 studies) have called for further high quality trials (Desouza 2020). Similarly McIntyre 2019 and Ma 2020 looked at nine papers each on Vernalakant and also had issues with follow up beyond short periods (i.e. 2 hours). (McIntryre 2019; Ma 2020) These reviews also could not carry out subgroup analysis on patients with structural heart disease due to paucity of data in this area. All of these suggest that high quality trials with longer follow up periods, and post-hoc sub-group analyses for the main endpoints are needed.

It should be noted that a significant number of studies (7 in the ESC guidelines, 7 in the ACC/AHA/HRS and 11 in the CCS guidelines) about pharmacological therapy could not be included in this review as they did not meet the necessary inclusion criteria (ACC/AHA/HRS Guidelines 2014;Andrade 2018;ESC Guidelines 2016).

Authors' conclusions

Implications for practice

Our findings suggest that electrical cardioversion may be effective for cardioverting paroxysmal AF, persistent AF and atrial flutter. The most effective electrical cardioversion approach seems to be AP BTE maximum energy. Pharmacological cardioversion seems to be an effective option for paroxysmal AF but onset of action of the most effective options may vary from 30 to 90 minutes (e.g. vernakalant, flecainide, antazoline, and ibutilide) to longer, with other drugs (e.g. quinidine, propafenone, amiodarone, sotalol, procainamide, and propafenone) achieving maximum efficacy at up to 24h. Efficacy of antiarrhythmic agents for persistent AF seems to be lower, and for atrial flutter only ibutilide may have comparable efficacy to electrical cardioversion.

The reported frequencies of stroke, or embolism across all drugs and placebo were extremely low, and no events were observed for electrical cardioversion. Data was not powered to allow for meaningful comparisons. These data may reassure those wishing to carry on cardioversion procedures, but reinforce the need for adherence to guidelinesis and appropriate thromboprophylaxis or pre-procedural transoeophageal echocardiogram when required. Additionally, mortality in the setting of these procedures is extremely low (with uncertainty for most cases on whether it was related to the utilized treatment option).

Life-threatening ventricular arrhythmias (e.g. Torsade de pointes, sustained ventricular tachycardia or ventricular fibrillation) were observed for a small proportion of individuals treated with quinidine, dofetilide, ibutilide, sotalol and vernakalant (in descending order of frequency) and reinforce the need for electrocardiogram monitoring of these individuals when the drug is being administered and while effective concentration is still available in the bloodstream. These were only observed for electrical cardioversion when devices were not operated properly or failed (i.e. asynchronous shock being delivered).

Pauses, slow junctional rhythm and transient complete heart block were observed in a minority of patients, irrespectively of the utilized cardioversion strategy and were also observed in patients receiving placebo.

Skin burns were not observed for patients treated with biphasic electrical cardioversion and sedation-related complications were not reported for patients receiving electrical cardioversion in any of the included trials.

Acute heart failure seems to be infrequent and was described for patients treated with propafenone, flecainide, sotalol, amiodarone, vernakalant, and placebo. No events were observed in patients receiving electrical cardioversion.

Phlebitis seems to be frequent in patients treated with amiodarone, and dysgeusia and sneezing may occur frequently in patients treated with vernakalant.

There is no meaningful data to address differences in quality of life among the studied cardioversion strategies.

Data are scarse regarding hospitalization duration and have limitations with regards to comparing cardioversion approaches, but due to its immediate effect and no need for electrocardiogram monitoring post-procedure to exclude life-threatening ventricular arrhythmias (as is required for pharmacological cardioversion), it is possible that electrical cardioversion may lead to shorter duration hospitalization. This option appears a best fit for busy emergency departments or high turnover services with the capacity and means to safely deliver it. Physicians performing electrical cardioversion should acquire training in sedation (and dealing with its complications), and close cooperation with anesthetists is required for confidently and safely performing this approach. Pharmacological cardioversion may be an option for physicians without appropriate training in sedation and when anesthetic-cover is not available, or when the risk of sedation-related complications is deemed high and outweighs the risks associated with the available anti-arrhythmic agents.

Importantly, some of these drugs (i.e. ibutilide, dofetilide, antazoline & bepridil) are not available in all countries, and some agents (e.g. vernakalant, flecainide, propafenone, ibutilide) are or may be contraindicated in patients with structural heart disease and coronary artery disease.

Some aspects may be important for deciding which cardioversion strategy to utilize. Drugs like vernakalant, ibutilide and flecainide seem to be effective and with fast onset of action for paroxysmal AF, whilst drugs like amiodarone may be effective too, but require 24h or longer to cardiovert patients. Electrical cardioversion may immediately cardiovert most patients, but requires a physician with experience in sedating patients, or anesthetics support. Also, the drug side effect profile, and underlying patient comorbidities should also be considered. Finally, adherence to guidelines and appropriate thromboprophylaxis, when indicated, is essential to assure overall procedure safety.

We believe the findings of our review will contribute to improve the level of evidence of future guideline recommendations for cardioversion of AF patients, and support multiple new recommendations for the management of AF patients undergoing cardioversion with level of evidence A (i.e. arising from a meta-analysis).

Implications for research

Issues encountered in collating the data we had set out to in our protocol suggest that more and better quality evidence is required in the field.

Firstly, trials need to abide by the regulation and need to be registered before enrolment starts. Better planning is required when designing trials and making decisions on random sequence generation, and allocation concealment. Also, better planning and attempts at blinding are required. Future studies should consider including a "sham procedure" arms when assessing electrical cardioversion.

More studies comparing electrical vs. pharmacological cardioversion in paroxysmal AF, and looking at quality of life and duration of hospitalization outcomes are required.

More trials assessing some of the promising drugs identified in our search (i.e. Antazoline & Bepridil) but that have no data available outside countries like Poland and Japan would be of interest.

An expert consensus defining a core set of outcomes to be reported in cardioversion studies (e.g. acute procedural success, acute relapse, relapses after discharge, duration of hospitalization, mortality, stroke or systemic embolism within the first month, torsade de pointes, ventricular fibrillation, skin burns, sedation-related complicaitons, etc) is required. Availability of these data in future trials will vastly improve future evidence synthesis. As some of the outcomes (e.g. mortality & stroke) are rare and trials with enough power to assess for them unlikely to be conducted (as several thousand patients would be required), this would be a way to address this knowledge gap.

Longer-term follow-up (i.e. at least a month) should also be available to allow for better clinical and patient-informed decisions.

High heterogeneity in baseline population characteristics (AF duration, left atrial size, underlying comorbidity profile) and their reporting was observed across trials. Reporting of outcomes for different sub-groups of interest is absent in most trials. Reporting of outcomes for different paroxysmal AF, persistent AF, and atrial flutter, whenever these populations are included in the same trial, should be routinely available. Similarly, reporting of outcomes for patients with heart failure, hypertrophic cardiomyopathy, different age groups, women, etc should be performed. Datasets of trials should be made available to researchers to allow for sub-group analyses.

Finally, further and appropriately powered trials with cost-effectiveness analyses are required for comparing electrical cardioversion vs. the most effective anti-arrhythmic drugs, and clarifying the role of pharmacological cardioversion.

Acknowledgements

We would like to acknowledge Mrs. Charlene Bridges (Information Specialist - Cochrane Heart), Dr. Rachel Richardson (Associate Editor - Cochrane), Professor Michael Brown (Senior Editor of the Circulation & Breathing Network - Cochrane), Dr. Nuala Livingstone (Methods Reviewer - Cochrane Evidence Production and Methods Directorate), Dr. Tess Moore & Dr. Kerry Dwan (Methods Support Unit - Cochrane), Dr. Steve McDonald (Search Reviewer - Cochrane Australia), Professor Lisa Bero (Research Integrity Team - Cochrane), Professor Axel

Brandes (Clinical Peer Reviewer - Department of Cardiology, Odense University Hospital & Esbjerg Hospital - University Hospital of Southern Denmark, Denmark) & Dr. Michael Diamant (Clinical Peer Reviewer - Royal Columbian Hospital & University of British Columbia, Vancouver, Canada).

Data and analyses

Comparison 1

Flecainide vs Amiodarone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
1.1 Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)	2	180	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.87, 1.64]	
1.2 Acute procedural success (Paroxysmal AF)	2	180	Risk Ratio (M-H, Random, 95% CI)	2.02 [0.27, 14.91]	

Comparison 2

Flecainide vs Propafenone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
2.1 Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)	3	482	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.92, 1.22]	
2.2 Acute procedural success (Paroxysmal AF)	3	482	Risk Ratio (M-H, Random, 95% CI)	1.28 [1.02, 1.59]	

Comparison 3

Amiodarone vs Propafenone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
3.1 Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)	7	772	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.94, 1.07]	
3.2 Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)	2	126	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.68, 1.81]	
3.3 Acute procedural success (Paroxysmal AF)	7	772	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.36, 0.96]	

Comparison 4

Amiodarone vs Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)	7	718	Risk Ratio (M-H, Random, 95% CI)	1.68 [1.33, 2.11]
4.2 Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)	6	905	Risk Ratio (M-H, Fixed, 95% CI)	20.81 [7.89, 54.88]
4.3 30 day all-cause mortality	7	1048	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.02, 8.98]
4.4 30 day cardiovascular mortality	7	1048	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
4.5 Stroke or Systemic Embolism at 30 days	5	829	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
4.6 Acute procedural success (Paroxysmal AF)	7	718	Risk Ratio (M-H, Random, 95% CI)	1.64 [1.19, 2.25]

Comparison 5

Dofetilide vs Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Sinus rhythm until hospital discharge or end of study follow-up (Atrial Flutter)	3	43	Risk Ratio (M-H, Fixed, 95% CI)	6.88 [1.46, 32.36]
5.2 Acute procedural success (Atrial Flutter)	3	43	Risk Ratio (M-H, Fixed, 95% CI)	6.88 [1.46, 32.36]

Comparison 6

Propafenone vs Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)	9	1182	Risk Ratio (M-H, Random, 95% CI)	2.27 [1.68, 3.06]
6.2 Acute procedural	9	1182	Risk Ratio (M-H,	2.35 [1.68, 3.27]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
success (Paroxysmal AF)			Random, 95% CI)		

Comparison 7

Vernakalant vs Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
7.1 Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)	3	364	Risk Ratio (M-H, Random, 95% CI)	5.69 [0.14, 226.30]	
7.2 Acute procedural success (Paroxysmal AF)	3	364	Risk Ratio (M-H, Random, 95% CI)	8.20 [2.06, 32.71]	
7.3 Stroke or Systemic Embolism at 30 days	4	852	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 4.29]	
7.4 30 day all-cause mortality	5	963	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.34, 4.88]	
7.5 30 day cardiovascular mortality	5	963	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.25, 5.08]	

Comparison 8

Magnesium vs Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
8.1 Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)	3	112	Risk Ratio (M-H, Random, 95% CI)	1.71 [0.31, 9.32]	
8.2 Acute procedural success (Paroxysmal AF)	3	112	Risk Ratio (M-H, Random, 95% CI)	1.29 [0.45, 3.73]	

Comparison 9

Amiodarone vs Quinidine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
9.1 Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)	2	100	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.27, 1.19]	

Comparison 10

Ibutilide vs Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
10.1 Sinus rhythm until hospital discharge or end of study follow-up (Atrial Flutter)	2	178	Risk Ratio (M-H, Fixed, 95% CI)	21.89 [4.54, 105.61]	
10.2 Acute procedural success (Atrial Flutter)	2	178	Risk Ratio (M-H, Fixed, 95% CI)	21.89 [4.54, 105.61]	

Comparison 11

AP BTE Incremental vs AP MDS Incremental

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
11.1 Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)	2	319	Risk Ratio (M-H, Random, 95% CI)	1.23 [1.04, 1.46]	
11.2 Acute procedural success (Persistent AF)	2	319	Risk Ratio (M-H, Random, 95% CI)	1.23 [1.04, 1.46]	

Comparison 12

Sotalol vs Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
12.1 Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)	2	443	Risk Ratio (M-H, Fixed, 95% CI)	26.38 [5.14, 135.38]	
12.2 30 day cardiovascular mortality	2	443	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable	
12.3 30 day all cause mortality	2	443	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.01, 6.83]	

Comparison 13

Procainamide vs Amiodarone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
13.1 Sinus rhythm until	2	403	Risk Ratio (M-H,	0.89 [0.67, 1.17]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
hospital discharge or end of study follow-up (Paroxysmal AF)			Random, 95% CI)		
13.2 Acute procedural success (Paroxysmal AF)	2	403	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.67, 1.17]	

Comparison 14

Amiodarone vs Sotalol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
14.1 Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)	2	565	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.86, 1.52]	
14.2 30 day cardiovascular mortality	2	565	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable	
14.3 30 day all cause mortality	2	565	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable	

History

Protocol first published: Issue 3, 2019

Contributions of authors

KKR: data entry, study selection, risk of bias assessment, carrying out the analysis and writing up the review

MA: carried out data entry, study selection, and writing up the review

MC: study selection and data entry

AI: study selection and data entry

JT: study selection and data entry

YR: study selection and data entry

NP: data entry and clinical feedback

GEM: helped with methods and data

IIFN: helped with methods and data

FDA: helped with methods and data

SBW: provided clinical feedback

PL: provided clinical feedback

CAM: provided clinical feedback

JK: helped with methods and data

RP: writing the protocol, study selection, risk of bias assessment, editing the review, preparing the revised version & addressing reviewers' comments.

All authors have read and approved the review.

Declarations of interest

RP: none known

DC: none known

JT: none known

KKR: none known

MA: None known

NP: none known

AI: none known

GEM: none known

IIFN: none known

SBW: received unrestricted grant support from Medtronic Canada, Boston Scientific, and Abbott, for work unrelated to the review topic, and consulting fees from Arca Biopharma for work on an atrial fibrillation clinical trial

PL: receives speaker fees and educational grant funding from Boston Scientific, and educational grant funding from Medtronic for work unrelated to the content of this Cochrane Review

CAM: declared conflicts not related with the current work

RP, KKR and JSKW are Editors for Cochrane but were not involved in the editorial process.

Sources of support

Internal sources

- No sources of support provided

External sources

- NIHR, UK
  This project was supported by the NIHR via Cochrane Infrastructure funding to the Heart Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service (NHS) or the Department of Health and Social Care
- NIHR, UK
  This project was supported by the Complex Reviews Support Unit, funded by the NIHR (project number 14/178/29)
- The Cochrane Collaboration, Other
  Cochrane Review Support Program Grant (CRSP)

Differences between protocol and review

We did not use a machine learning filter or Cochrane crowd to aid in screening for studies.

We also included quasi-randomized controlled trials (randomized controlled trials where treatment allocation was obtained by alternation or other predictable methods).

For cluster-randomized trials, we planned extracting the estimates of the observed effect measure (for example, risk ratio and confidence interval) accounting for the cluster design. These effect estimates and their standard errors would then be meta-analysed with those from the studies with a parallel design using the generic inverse-variance method (Higgins 2019). If the study had not accounted for clustering and had analysed the individual as the unit of analysis, we would extract the number of clusters, total number of participants, average size of each cluster, the outcome data and an estimate of the intracluster correlation coefficient obtained from similar studies (Higgins 2019). These cluster-RCTs would be excluded from our sensitivity analysis. We identified no cluster-randomized trials for the purpose of our review.

Intervention drugs in this review had to be approved for routine clinical use in AF cardioversion in at least on country (e.g. Antazoline and Bepridil are examples of drugs in this situation, as to best of the authors' knowledge they are only used in Poland and Japan, respectively). We excluded non-approved drugs as this review aims to support clinical practice decisions.

For studies where only a subset of participants was eligible (e.g. study population including a small group of participants with AF due to reversible causes), individual patient-data or sub-group analysis excluding non-eligible patients was requested to the authors.

One secondary endpoint was changed to "Stroke or systemic embolism occurring within the first 30 days following cardioversion". Transient ischaemic attack was removed as it is not frequently used in this endpoint in the literature, it is a subjective diagnosis and its clinical impact is lower than stroke or systemic embolism.

Transient ischaemic attack as an outcome has been used less and less in reviews from the Cochrane Heart group due to this fact.

Acute procedural success was changed from "at least 30 seconds of sinus rhythm following cardioversion" to "at least one beat of sinus rhythm following cardioversion" Antman EM 2012 The former endpoint definition aimed to reinforce some stability of rhythm after reversal but it was based on an arbitrary cut-off of 30 seconds which was not based on any mechanistic process. This new definition is based on the pathophysiological assumption that immediate recurrence of AF is caused by atrial ectopy, or other mechanisms, (at least partialy) different from the ones which are targeted with cardioversion (Kirchhof 2005), and is broadly accepted (Mittal 2000). Also, the main aim of this review is to assess interventions leading to cardioversion/termination of the arrhythmia. Interventions leading to long-term maintenance of sinus rhythm following cardioversion fall outside its scope.

We removed the planned exception in risk of bias assessment for "electrical cardioversion studies" as there is now an ongoing "sham electrical cardioversion" trial (NCT05136131), which makes our previous comments on the matter obsolete (i.e. previous statement that it would be difficult to do a sham electrical cardioversion trial, and hence electrical cardioversion studies should not be downgrade based on lack of patient and/or personnel blinding).

Due to the NMA design and its complexity, and to reporting absolute risk differences already, we opted not to present NNTB or NNTH.

AF duration and type (paroxysmal or persistent) and body mass index (BMI) were considered as potential effect modifiers for the endpoints "Acute Procedural Success" and "Maintenance of sinus rhythm until hospital discharge or end of study follow-up". For that reason networks were split based on these to maintain the transitivity assumption within networks.

We changed the planned approach for the Summary of Findings table as the paper by Yepes-Nuñez 2019 was only published following development of our initial protocol, and we thought it provided a more appropriate framework for NMAs. Also, following this change we decided we would prefer to utilize this approach and not use CINeMA as we are more experienced with GRADE and felt it would be easier to interpret and follow by readers of the review.

We decided to remove plots and/or summary of findings tables regarding the following complication related endpoints: "Complications deemed to be related to the procedure occurring within the first week", "Immediate (< 24 hours) procedure-related complications", "Development of ventricular arrhythmias following cardioversion while in hospital" & "Development of bradyarrhythmias following cardioversion while in hospital". These were the reasons: first, these are composite endpoint that combines a diverse number of complications. This is problematic as we observed a strong discrepancy in report of complications across trials (e.g. while some trials reported every single complication, other trials were selective in the time of complications they were reporting, and some trials did not even report complications). Second, different trials were reporting complications at different timepoints. Third, meaningful interpretation of composite endpoints composed of heterogeneous components is confusing. We observed that these issues applied even to simpler endpoints like the ones regarding composite bradyarrhythmias and ventricular arrhythmias, as discrepancies in the definition of these endpoints across studies were also major. For the abovementioned reasons, we opted to describe only the findings across trials and to provide a supplementary table with detailed information on this matter (Supplementary Table 1).

We added a sub-group comparison ("d. Route of Anti-arrhythmic Administration: -Oral / -Intravenous") as this is of clinical importance for treatment decisions, and removed the sub-group comparison of "Patch/pad position for electrical cardioversion" as this division was already contemplated on the network, and a further sub-analysis would bring no further clinical insights.

Notes

This review supersedes two reviews that were in need of updating but have been merged and started as a new review (Cordina 2017; Mead 2017)

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Abi Mansour 1998

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 4h)
Participants	**Baseline Characteristics** Ibutilide Not given by treatment Placebo

	Not given by treatment AF type: 193 (77%) AF patients, type not given, 57 (33%) Atrial Flutter patients **Inclusion criteria:** Patients had to have sustained AFl or AF of >3 hours and <90 days. **Exclusion criteria:** Patients were excluded if they had a history of torsades de pointes; prior exposure to ibutilide; corrected QT interval (QTc) >440 msec on 12-lead electrocardiogram (ECG); hemodynamic instability; symptoms of unstable angina or congestive heart failure; heart rate <60 beats/min; myocardial infarction within the previous 30 days; clinical evidence of hyperthyroidism or serious pulmonary, hepatic, hematologic, metabolic, renal, gastrointestinal, central nervous system, psychiatric, or other disorder that could interfere with the conduct or validity of the study or compromise safety; participated in another drug study or received an investigational drug within 30 days; been treated with a class I or class III antiarrhythmic agent unless it was discontinued >5 half-lives before enrollment; clinical evidence of digitalis toxicity if receiving digoxin; serum levels of hepatic enzymes (alanine aminotransferase [ALT], aspartate aminotransferase [AST]) at or above twice the upper limit of normal; abnormal serum electrolytes; or if they were ≤18 years old; if they weighed ≤132 lbs (60 kg) or ≥300 lbs (136 kg); or if they were fertile (women only). Calcium channel blocking agents and β- adrenergic blocking agents were permitted for rate control. **Numbers:** 262 patients enrolled with 250 eligible for study, 209 patients to ibutilide arm (45 to flutter and 164 to AF), and 41 patients to placebo arm (12 to flutter and 29 to AF). No patients lost to follow up. **Anticoagulation:** Patients with AF duration of >3 days were given anticoagulation therapy unless transesophageal echocardiography confirmed the absence of a mural thrombus. **Monitoring:** Continuous ECG strip and 12 lead ECG at 30 min, termination of arrhythmia or any significant rhythm change. Max follow up 24h.
Interventions	Intravenous Ibutilide Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint No data available for any of the other endpoints of the systematic review.
Identification	**Sponsorship source:** Local and supported by Pharmic and Upjohn Inc **Country:** United States of America **Setting:** Not clear **Comments:** No conflicts of interest reported. Planned outcomes: termination of arrhythmia within 90 mins of infusion, arrhythmia at 24h, time to conversion, effect on ECG characteristics, adverse events including blood pressure and pulse rate changes. All planned outcomes were reported. No trial registration. **Authors name:** Pierre Abi-Mansour **Institution:** Christ Hospital Medical Center, Pharmacia & Upjohn, Charleston Area Medical Center, and The Christ Hospital **Email:** Not provided **Address:** Peter A. Carberry, MD, Pharmacia & Upjohn, 7031-227-600, 7000 Portage Rd., Kalamazoo, MI 49001-0199
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	No information provided on generation of randomization sequence.
Allocation concealment (selection bias)	Unclear risk	No information provided on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study is reported as double-blind. No information present on blinding to personnel. All patients received 2 infusions and based on description the infusion protocol was similar for the active drug and placebo.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	These are objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Study is reported as double-blind. No information present on whether there was a blinded adjudication committee.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	These are objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	All patients were followed up for the total study period
Selective reporting (reporting bias)	Unclear risk	No protocol was published online or made available prior to the study.
Other bias	Unclear risk	The study was approved by the institutional review board at each center. No published study protocol.

Aliot 1996

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Flecainide • Age (years) mean (SD): 62.4 (12.3) • Male (%): 25 (52) • Hypertension (%): 19 (40) • Valvular Heart Disease (%): 4 (8) • Heart Failure (%): 0 (0) • Cardiomyopathy (%): 0 (0) • Coronary Artery Disease (%): 2 (4) • Atrial Flutter (%): 4 (8) Propafenone • Age (years) mean (SD): 63.6 (12.2) • Male (%): 26 (53) • Hypertension (%): 12 (25) • Valvular Heart Disease (%): 2 (4) • Heart Failure (%): 1 (2) • Cardiomyopathy (%): 2 (4) • Coronary Artery Disease (%): 2 (4) • Atrial Flutter (%): 4 (8) Structural heart disease, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Pulmonary Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A

	Duration of episode: N/A AF type: definition not given for paroxysmal AF **Inclusion criteria:** Patients > 18 years of age with paroxysmal episodes of AF or atrial flutter associated with disabling symptoms. **Exclusion criteria:** Patients with a history of unstable angina or myocardial infarction, recent heart surgery within <2 months, episodes or history of sustained ventricular tachycardia (VT) or chronic AF or atrial flutter (lasting >72 hours) congestive heart failure (New York Heart Association [NYHA] class III or IV), left ventricular ejection fraction <35 %, PR interval > 0.28 sec or QRS duration > 0.15 sec in sinus rhythm; sinus dysfunction with absence of pacemaker, 2nd- or 3rd-degree AV block, or right bundle branch block associated with a left anterior hemiblock in the absence of a pacemaker. Other antiarrhythmic treatments had to be discontinued for at least the equivalent of 4 elimination half-lives, and for at least 3 months in the case of amiodarone (plasma level of amiodarone <0.5 ng/ml before entering the study). However, beta blockers and digitalis could be continued provided the treatment had been stable for at least 14 days prior to inclusion in the study. Finally, patients with either a concomitant disease likely to modify the absorption, metabolism, or excretion of the treatment, or having used treatments known for their organ toxicity during the 4 weeks prcccding inclusion, were excluded. **Numbers:** 97 patients enrolled. 48 randomised to flecainide and 49 to propafenone. 45 patients discontinued before end of follow up but determined as treatment failure. **Anticoagulation:** No anticoagulation protocol as arrhythmia classified as paroxysmal. **Monitoring:** Clinic visits at 1, 3, 6, 9, 12 months. 24 hr holter recorded at 1 month visit.
Interventions	Oral Flecainide Oral Propafenone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint No data available for any of the other endpoints of the systematic review.
Identification	**Sponsorship source:** Local **Country:** France **Setting:** Outpatient **Comments:** Planned outcomes: Sinus Rhythm at 1 year follow up, adverse events, discontinuation of treatement. Reported outcomes: Sinus Rhythm at various points during follow up, adverse events. No trial registration. **Authors name:** Etienne Aliot **Institution:** Cardiology Department, Central University Hospital, Nancy, France; Cordiology Department, Hôpital Lariboisière, Paris, France **Email:** Not provided **Address:** E. Aliot, MD, Department of Cordiology, Hôpital Central, 54035 Nancy, France.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention to method of sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention to method for allocation concealment.

Blinding of participants and personnel (performance bias) All other outcomes	High risk	Open-label trial.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	Open-label trial.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	All outcomes assessed for the first 30-days
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	All outcomes assessed for the first 30-days
Selective reporting (reporting bias)	Unclear risk	Could not see the study protocol prior to study enrolment to assess whether all planned outcomes were reported.
Other bias	Unclear risk	Approved by National Institutional review board. No proof of trial registration.

Alp 2000

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Crossover) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Fixed Paddles • Age (years) mean (SD):: 67 (8) • Men (%): 22 (76) • Ischaemic Heart Disease (%): 3 (10) • Hypertension (%): 11 (38) • Digoxin (%): 11 (38) • Amiodarone (%): 6 (21) • Calcium Channel Blocker (%): 0 (0) • Valvular Heart Disease (%): 1 (3) • Flecainide (%): 16 (55) • Sotalol (%): 1 (3) • AF duration (weeks) mean (range): 31 (8-104) AA MDS Fixed Paddles • Age (years) mean (SD): 68 (8) • Men (%): 22 (73) • Ischaemic Heart Disease (%): 6 (20) • Hypertension (%): 5 (17) • Digoxin (%): 15 (50) • Amiodarone (%): 8 (27) • Calcium Channel Blocker (%): 2 (7)

	• Valvular Heart Disease (%): 3 (10) • Flecainide (%): 14 (47) • Sotalol (%): 1 (3) • AF duration (weeks) mean (range): 23 (2-104) Structural heart disease, Stroke/TIA, Pulmonary disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus: N/A Beta-blocker, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LA dimensions and LVEF %: N/A All patients had persistent AF **Inclusion criteria:** Aged 18 or over and admitted for elective DCCV for persistent AF **Exclusion criteria:** Pregnancy, permanent pacemaker in situ, serum potassium less than 3.5 mmol / l, severe kyphoscoliosis, and inability to provide informed consent. **Numbers:** 72 patients Eligible for study, 59 patients randomised: 30 patients to AA arm and 29 patients to AP arm. No patients lost to follow up. **Anticoagulation:** All patients were anticoagulated with warfarin for at least 1 month prior to cardioversion (international normalised ratio greater than 2.0) **Monitoring:** with regular 12 lead ECG. Follow up duration not described.
Interventions	AP MDS Fixed Paddles AA MDS Fixed Paddles
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint No data available for any of the other endpoints of the systematic review.
Identification	**Sponsorship source:** Local **Country:** United Kingdom **Setting:** Elective Admission **Comments:** No conflicts identified. Planned outcomes: 12 lead evidence of sinus rhythm after cardioversion, which protocol more effective in restoring sinus rhythm, total energy required to achieve sinus rhythm. All planned outcomes reported. **Authors name:** N.J. Alp **Institution:** Cardiology Department, John Radcliffe Hospital, Headley Way, Oxford OX3 9DU, UK **Email:** 101323.2347@compuserve.com **Address:** 160 Old Road, Headington, Oxford, OX3 8SY, UK
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation done by a computerised randomised number generator in blocks of 20. With such a large block, this is a low risk method as it would be difficult for personell to perceive/predict the sequence.
Allocation concealment (selection bias)	Unclear risk	No documentation of allocation concealment
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	The fact that patients or personnel had knowledge of patch location had no impact on the only endpoint reported in the study - Acute Procedural Success - which is 100% objective.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	The fact that patients or personnel had knowledge of patch location had no impact on the only endpoint reported in the study - Acute Procedural Success - which is 100% objective.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	The fact that assessors had knowledge of patch location could have no impact on the only endpoint reported in the

		study - Acute Procedural Success. Sinus rhythm on an ECG strip is an objective outcome.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	The fact that assessors had knowledge of patch location could have no impact on the only endpoint reported in the study - Acute Procedural Success. Sinus rhythm on an ECG strip is an objective outcome.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints.
Other bias	Unclear risk	No proof of trial registration. Approved by the local ethics committee.

Azpitarte 1997

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD): 60 (12) • Male (%): 14 (48) • Duration of episode (h) mean (sd): 22.7 (41.7) • Valvular Heart Disease (%): 4 (14) • Dilated Cardiomyopathy (%): 1 (3) • LA diameter (mm) (sd): 35 (7) • Paroxysmal AF (%): 9 (31) Placebo • Age (years) mean (SD): 57 (14) • Male (%): 7 (27) • Duration of episode (h) mean (sd): 18 (39.8) • Valvular Heart Disease (%): 5 (19) • Dilated Cardiomyopathy (%): n/a (n/a) • LA diameter (mm) (sd): 37 (8) • Paroxysmal AF (%): 6 (23) Structural Heart Disease, Hypertension, Pulmonary Disease, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Diabetes Mellitus: N/A Beta-blocker, Calcium antagonist, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Digoxin, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LVEF %: N/A **Inclusion criteria:** Consecutive patients presenting to emergency department with recent onset atrial fibrillation. **Exclusion criteria:** Patients were excluded if they were taking antiarrhythmic medication, or if, after a complete medical history, physical examination, 12-lead ECG, chest X-ray, and routine biochemical laboratory testing, they had any of the following: a previous embolic event, a mean ventricular rate < 70 beats . min ', symptomatic ischaemic heart disease, dilated or hypertrophic cardiomyopathy, severe hypertension, atrial fibrillation with ventricular preexcitation, hepatic or renal dysfunction, severe pulmonary disease, intraventricular conduction defects, documented sick sinus syndrome, or haemodynamic instability (arterial systolic pressure less than IOOmmHg). Special care was taken to exclude left-sided heart failure because of the potentially adverse effects of propafenone in this clinical setting. If structural heart disease was present patients were only included if duration of AF was <72h **Numbers:** 55 patients Eligible for study, 55 patients randomised: 29 patients to Propafenone arm and 26 patients to placebo arm. No patients lost to follow up. **Anticoagulation:** Protocol not given. Recent onset defined as < 1 week. **Monitoring:** with regular ECG strip. Max follow up 24h.
Interventions	Oral Propafenone Oral Placebo

Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint No data available for any of the other endpoints of the systematic review.
Identification	**Sponsorship source:** Laboratories Knoll, Madrid, Spain **Country:** Spain **Setting:** Emergency Department **Comments:** Planned outcomes: Conversion to sinus rhythm, Reported outcome: As planned and adverse events. No trial registration. **Authors name:** Jose Azpitarte **Institution:** Division of Cardiology, Hospital Universitario Virgen de las Nieves, Granada, Spain **Email:** Not provided **Address:** Jose Azpitarte, Division of Cardiology, Hospital Universitario Virgen de las Nieves, Avda de la Constitution 100, 18012 Granada, Spain
Notes	Oral all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No info provided on this.
Allocation concealment (selection bias)	Unclear risk	No info provided on this.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Mention to "Placebo tablets had the same appearance as the propafenone tablets", which means that patients and personnel were likely blind to what treatment was being given. Reported outcomes - adverse effects.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Mention to "Placebo tablets had the same appearance as the propafenone tablets", suggesting that patients and personnel were likely blind to what treatment was being given. Reported outcome (conversion to sinus rhythm) is objective.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on this.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No information provided on this, but sinus rhythm is an objective outcome/not prone to any subjective interpretation of ECG tracing. Not expected to be exposed to bias.
Incomplete outcome data (attrition bias)	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.

Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications		
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	No proof of Protocol registration. Study protocol was approved by the human research committee of the authors' institution.

Balla 2011

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Flecainide • Age (years) mean (SD): 57.9 (9.5) • Male (%): 28 (70) • Duration of episode (h) mean (SD): 16.2 (9.1) • Hypertension (%): 18 (45) • Diabetes Mellitus (%): 10 (25) • LA diameter (mm) mean (SD): 36.1 (3.2) • Stroke/TIA (%): 0 (0) Amiodarone • Age (years) mean (SD): 58.9 (10.4) • Male (%): 29 (73) • Duration of episode (h) mean (SD): 19.1 (12.4) • Hypertension (%): 12 (30) • Diabetes Mellitus (%): 16 (40) • LA diameter (mm) mean (SD):42.3 (4.3) • Stroke/TIA (%): 0 (0) Propafenone • Age (years) mean (SD): 57.4 (9.8) • Male (%): 20 (50) • Duration of episode (h) mean (SD): 18.6 (4.2) • Hypertension (%): 20 (50) • Diabetes Mellitus (%): 12 (30) • LA diameter (mm) mean (SD): 34.4 (5.3) • Stroke/TIA (%): 0 (0) Placebo • Age (years) mean (SD): 58.6 (10.7) • Male (%): 24 (60) • Duration of episode (h) mean (SD): 17.8 (13.9) • Hypertension (%): 9 (23) • Diabetes Mellitus (%): 8 (20) • LA diameter (mm) mean (SD): 32.9 (6.3) • Stroke/TIA (%): 0 (0) Valvular heart disease, Structural heart disease, Pulmonary disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction: N/A Beta-blocker, Calcium Antagonist, Digoxin, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LA dimensions and LVEF %: N/A AF type: All patients had paroxysmal AF. **Inclusion criteria:** Recent onset AF <48h

	Exclusion criteria: Patients with uncontrolled congestive heart failure, acute myocardial infarction within 7 days, previous electrocardiographic documentation of atrioventricular block or sick sinus syndrome, patients on antiarrhythmic therapy at the time of admission, patients with prior thromboembolic episodes or stroke, patients with impaired hepatic or renal function, patients with advanced obstructive bronchopulmonary disease or pregnancy were excluded **Numbers:** 370 Eligible, 160 Randomised, Flecainide 40, Amiodarone 40, Propafenone 40, Placebo 40, No lost follow up. **Anticoagulation:** no protocol as recent onset AF. **Monitoring:** with continuous ECG and follow up was at 3, 6, 12 and 24 hours.	
Interventions	Oral Flecainide Oral Amiodarone Oral Propafenone Oral Placebo	
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Only side effect reported was mild diarrhea in two patients (amiodarone arm). "There were no significant adverse effects during the follow-up period". Therefore, we can assume there were no stroke/systemic embolism events during the 24h follow-up period. However, follow-up is not long enough (<30 days) for the data to be used for that endpoint. No other reported endpoints.	
Identification	**Sponsorship source:** Local **Country:** Albania **Setting:** Accident and Emergency **Comments:** Planned outcomes: SR at 24h, Blood pressure readings, side effects that patients reported, HR and arrhythmias Reported outcomes: SR at 24h, Adverse events. No trial registration. **Authors name:** Idriz Balla **Institution:** Departments of Cardiology and Public Health, University Hospital Center of Tirana, Tirana **Email:** idrizballa@yahoo.com **Address:** Idriz Balla, MD, Department of Cardiology, University Hospital Center of Tirana, Tirana-Albania	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	Antiarrhythmic drugs and placebo were coded with numbers (from 1 to 4) and placed in an envelope. Upon patient's arrival in the coronary care unit, patients were randomly assigned based on withdrawal of numbers from the envelope.
Allocation concealment (selection bias)	Unclear risk	The authors report that drugs were coded with numbers and placed in an envelope, but we do not know whether it was a sealed & opaque envelope, where it was kept, who had access to the envelopes and who was responsible for withdrawing the envelope for each patient (nurse? physician? secretary?).
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Study was single blinded on the patients side. Unclear if lack of blinding to personnel could have potentially led to bias as patients were blinded and the assessors were also blinded.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints which should not be affected by blinding.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	"monitoring and endpoint adjudication were performed by personnel who were unaware of the type of drug"
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	"monitoring and endpoint adjudication were performed by personnel who were unaware of the type of drug". However, these are objective endpoints which should not be affected by blinding.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Specified outcomes were reported in all patients. No patients lost to follow-up or with missing outcomes.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Approved by the local Ethics Committee.

Baroffio 1995

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Crossover) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD): 60 (14) • Male (%): 8 (32) • Duration of episode (h) mean (SD): 9 (14) • Hypertension (%): 11 (44) • Pulmonary disease (%): 2 (8) • LA diameter (mm) mean (SD): 33 (7) • LVEF % mean (SD): 59 (12) Placebo (Digoxin) • Age (years) mean (SD): 56 (12) • Male (%): 13 (52) • Duration of episode (h) mean (SD): 8 (10) • Hypertension (%): 7 (28) • Pulmonary disease (%): 1 (4) • LA diameter (mm) mean (SD): 33 (6) • LVEF % mean (SD): 56 (9) Valvular Heart Disease, Structural Heart Disease, Stroke/TIA, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease, Diabetes Mellitus: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF type: All patients had paroxysmal AF.

	Inclusion criteria: Patients aged over 18 years who presented to the emergency department with atrial fibrillation of recent onset <72 hours) with a heart rate of more than 80 beats per minute were considered for enrolment in the trial. **Exclusion criteria:** Patients were excluded if they had ongoing antiarrhythmic treatment or therapy with digitalis, had an acute myocardial infarction in the previous month or unstable angina. Had clinical findings of heart failure (NYHA class III or IV) or low cardiac output. There was presence of hypotension (systolic blood pressure <100mm Hg); Hyperthyroidism; Known sick sinus syndrome (not paced); Documented second- or third-degree atrioventricular block. Were in postoperative period following cardiac surgery. There was bifascicular block. They had chronic obstructive lung disease. There was Wolff-Parkinson-White syndrome (contraindication to digitalis). The patient was obese (patient weight >120kg). They were assessed or assumed for pregnancy. **Numbers:** 50 patients Eligible for study, 50 patients randomised: 25 patients to Propafenone arm and 25 patients to placebo arm. No patients lost to follow up. **Anticoagulation:** protocol not given but recent onset defined as < 72h. **Monitoring:** with regular ECG strip. Max follow up 3h.
Interventions	Intravenous Propafenone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint No data available for any of the other endpoints of the systematic review.
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Accident and Emergency **Comments:** Planned outcomes: SR at 1 and 3h, Blood pressure readings, side effects that patients reported, HR and arrhythmias Reported outcomes: All planned outcomes. No trial registration. **Authors name:** Rafaelle Barroffio **Institution:** Emergency and Cardiology Departments, Hospital of Saronno, Saronno, Italy **Email:** n/a **Address:** Dr Raffaele Baroffio, Via Galvani, 103 - 20025 Legnano (MI), Italy.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	A "randomization list" is mentioned, but there is no information on how it was generated, and whether or not this was a predictable sequence.
Allocation concealment (selection bias)	Unclear risk	No information provided on where and how the "randomization list" was kept..
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Study described as "open". Administered drugs had similar infusion protocols - administered during 10 minutes.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence unlikely to be affected by knowledge of the treatment arm.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	Study described as open.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence unlikely to be affected by knowledge of the treatment arm.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.

bradyarrhythmias, immediate procedure-related complications		
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	High risk	No proof of trial registration or mention to approval by the ethics committee. Propafenone arm is 4 years older and has 15% more patients with hypertension, but population is small.

Baroni 2011

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (mean +/- SD): 65 (10) • Men (%): 14 (47) • Coronary Artery Disease (%): 1 (3) • Hypertension (%): 15 (50) • LVEF (%) (mean +/- SD): 58 (1) • Left Atrial Diameter (mm) (mean +/- SD): 45 (3) • Valvular Heart Disease (%): 5 (17) Quinidine • Age (mean +/- SD): 64 (8) • Men (%): 17 (57) • Coronary Artery Disease (%): 3 (10) • Hypertension (%): 13 (43) • LVEF (%) (mean +/- SD): 58 (2) • Left Atrial Diameter (mm) (mean +/- SD): 46 (4) • Valvular Heart Disease (%): 2 (7) Amiodarone • Age (mean +/- SD): 63 (6) • Men (%): 17 (57) • Coronary Artery Disease (%): 7 (23) • Hypertension (%): 12 (40) • LVEF (%) (mean +/- SD): 59 (3) • Left Atrial Diameter (mm) (mean +/- SD): 47 (7) • Valvular Heart Disease (%): 4 (13) Structural heart disease, Stroke/TIA, Pulmonary disease, Cardiomyopathy, Ischaemic heart Disease, Myocardial Infarction, Diabetes Mellitus: N/A Calcium antagonists, digoxin, Beta-blocker, flecainide, sotalol, Diuretic, ACE inhibitor, Aspirin: N/A LVEF %: N/A BMI: N/A CHA2DS2VASc: N/A All patients had persistent AF. **Inclusion criteria:** AF lasting > 6 weeks, Age > 18 **Exclusion criteria:** Pts already on anti-arrhythmic drugs, hemodynamic instability (SBP lower than 90 mmHg, signs of shock), NYHA class III or IV heart failure, II or III degree atrioventricular block, ventricular pre-excitation (positive history and\or delta wave at ECG), long QT (corrected QT > 480ms or measured QT > 500ms), acute coronary syndrome on admission or in the previous three months, history of hyper-sensitivity to iodine compounds, COPD, liver cirrhosis (Child class B or C) or myasthenia gravis. **Numbers:** 90 Consecutive patients were Randomized: 30 to Propafenone, 30 to Quinidine, 30 to Amiodarone. No documentation of attrition after randomisation. **Anticoagulation:** INR between 2-3 for at least 4 weeks. **Monitoring:** was with continuous wireless ECG monitoring. Follow up was 24 hrs.
Interventions	Intravenous Propafenone Oral Quinidine Intravenous Amiodarone

Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint No mention of stroke or systemic embolism during the 24h follow-up period ("No differnece was found before and after the administration within the groups. No adverse effects requiring drug discontinuation occured, in particular there were no syncope or sustained ventricular tachycardia or torsade de pointes". However, follow-up is not long enough (<30 days) for the data to be used for that endpoint.
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Not Clear **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to SR within 24 hrs after administration of drugs. Pharmacological side effects. Reported outcomes: as above. No trial registration. **Authors name:** Matteo Baroni **Institution:** Cardiology Department of Policlinico San Pietro, Ponte S. Pietro, Bergamo, Italy **Email:** Not Provided **Address:** Dr. Matteo Baroni, Cardiology Department, Policlinico San Pietro. Via Forlanini 15, 24036 Ponte San Pietro (BG) Italy, MN 55112
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation was not described.
Allocation concealment (selection bias)	Unclear risk	Description of allocation distribution not described.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Trial is open-label However, "Low risk" for ventricular tachycardia as definition of ventricular tachycardia follows objective criteria and all treatment arms received similar monitoring during the 24h period. "High risk" for other outcomes (e.g. symptomatic bradycardia with no defined heart rate cut-off is included as part of the bradycardia endpoint and may be subjective to personnel and patients who may refer it or not depending on the assigned drug; adverse effects).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk for the outcome "*Sinus Rhythm Until Discharge/Inpatient Follow Up Period" as sinus rhythm is an objective outcome, and all treatment arms received similar monitoring during the 24h period.*

Blinding of outcome assessment (detection bias) All other outcomes	High risk	Trial is open label "Low risk" for ventricular tachycardia as definition of ventricular tachycardia follows objective criteria and all treatment arms received similar monitoring during the 24h period. "High risk" for other outcomes (e.g. symptomatic bradycardia with no defined heart rate cut-off is included as part of the bradycardia endpoint and may be subjective to the assessors physicians who may report it or not depending on the assigned drug; adverse effects).
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	"Low risk" for the outcome "*Sinus Rhythm Until Discharge/Inpatient Follow Up Period" as sinus rhythm is an objective outcome, and all treatment arms received similar monitoring during the 24h period.*
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There was no attrition during the study period so all outcomes specified were fully reported. No patients lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	Seemingly large differences in CAD across treatment groups. No p value given. No proof of trial registration. Local Ethics committee approval.

Beatch 2016

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 2hrs)
Participants	**Baseline Characteristics** Placebo • Age (sd): 60.8 (14.1) • Male (%): 45 (66.2) • Duration of episode h (sd): 41 (36.3) • Hypertension (%): 39 (57.4) • Valvular Heart Disease (%): 13 (9.1) • Diabetes Mellitus (%): 16 (23.5) • Ischaemic Heart Disease (%): 12 (17.6) • Myocardial Infarction (%): 7 (10.3) • Any Anti-Arrythmic drug (%): 0 (0) Vernakalant • Age (sd): 60.8 (14.1) • Male (%): 76 (58.9) • Duration of episode h (sd): 37.3 (37.6) • Hypertension (%): 89 (69.0) • Valvular Heart Disease (%): 27 (20.9) • Diabetes Mellitus (%): 18 (14.0) • Ischaemic Heart Disease (%): 18 (14.0) • Myocardial Infarction (%): 11 (8.5) • Any Anti-Arrythmic drug (%): 0 (0) Structural heart disease, Cardiomyopathy, Stroke/TIA, Pulmonary disease: N/A Beta-blocker, Calcium antagonist, Diuretic, ACE inhibitor, Aspirin, Digoxin: N/A LA dimensions and LVEF %: N/A BMI: N/A CHA2DS2VASc: N/A AF type: All patients had paroxysmal AF. **Inclusion criteria:** Included patients were adults aged 18 – 85 years with recent-onset (duration >3 h– ≤ 7 days) symptomatic AF for whom best management was determined by the investigator to be acute cardioversion to SR.

	Exclusion criteria: Patients were also required to be ad- equately hydrated (as determined by the investigator). If AF had continued for more than 48 h, patients were to be managed in accordance with the standard of care for anticoagulation, as recommended by the American College of Cardiology/American Heart Association/ European Society of Cardiology guidelines. Patients were excluded if they had evidence or a history of heart failure or evidence of left ventricular dysfunction, heart rate less than 50 beats per minute (bpm) or symptomatic bradycardia. an investigational drug within 30 days before enrollment; a reversible cause of AF; end-stage disease; previously failed electric conversion; uncorrected electrolyte imbalance; or digoxin toxicity. Patients were also excluded if they met any of the following criteria: had a QRS interval of more than 0.14 s without a pacemaker; an uncorrected QT interval of more than 0.44 s; typical atrial fluter; acute coronary syndrome or myocardial infarction; or cardiac surgery performed in the 30 days before planned enrolment. **Numbers:** 217 patients enrolled and randomised. 145 patients to Vernakalant arm and 72 patients to placebo arm. Enrollment suspended in 2010 due to adverse event in Vernakalant arm then terminated early. **Anticoagulation:** guidance was as per ACC/AHA/ESC guidelines. **Monitoring:** with continuous holter monitoring and intermitted 12 lead ECG. Max follow up 24 hr as inpatient and 1 week after. Patients were electrically cardioverted after 2 hrs if they did not respond.
Interventions	Intravenous Vernakalant Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported

	• **Direction**: Lower is better • **Data value**: Endpoint Quality of Life • **Outcome type**: Continuous • **Reporting**: only P value for the comparison was provided • **Direction**: Lower is better • **Data value**: Endpoint Clinicaltrials protocol mentions that this was assessed as number of patients that report no symptoms at 90min, but paper uses slightly different wording "impact of symptoms of AF on quality of life at 90 min after first drug exposure" and provides no explanation on how this was measured or if any scales were used. Previous studies of this drug development program (e.g. Beatch 2017; Camm 2011) assessed this same endpoint "the proportion of patients reporting AF symptoms at 90 minutes", but did not label it as "quality of life". Furthermore, Camm 2011 besides assessing the proportion of patients reporting AF symptoms at 90 minutes also assessed the change in EQ-5D quality of life assessment visual scale (VAS).
Identification	**Identification** **Sponsorship Source:** Astellas Pharma Global Development; Cardiome Pharma Corp.; and Merck Sharp & Dohme Corp. **Country:** Canada, United States of America, Chile, Israel, Mexico, Peru, South Africa **Setting:** Unclear **Comment:** Clinical trial reg NCT00989001. Planned Outcomes: Primary Efficacy end point was the proportion of patients with short duration AF in sinus rhythm for at least 1 minute within 90 minutes of drug initiation. Secondary endpoints; time to conversion and proportion of patients in Sinus Rhythm at 24 hours. Same outcomes for longer duration AF. Proportion of patients reporton no AF symptoms at 90 mins, and the the impact of symptoms of AF on quality of life after 90 mins. In addition adverse events were recorded, primary safety outcome was any of clinically significant hypotension, clinically significant ventricular arrhythmia or death within 2h of the start of exposure. Reported outcomes: as above. **Author's Name:** Gregory Beatch **Institution:** Cardiome Pharma Group **Email:** gbeatch@cardiome.com **Address:** Gregory Beatch, Cardiome Pharma Corp., 1441 Creekside Drive 6th Floor, Vancouver, BC V6J 4S7, Canada. 2PAREXEL International Corp., Lowell, MA, USA
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study was registered as double blind, but no information was provided on how this was achieved.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Study was registered as double blind, but no information was provided on how this was achieved. Sinus rhythm is an objective outcome, hence unlikely to be affected.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Study was registered as double blind, but no information was provided on how this was achieved.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Study was registered as double blind, but no information was provided on how this was achieved.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause	Unclear risk	Reported outcomes -stroke and mortality - during follow-up for 2 patients. Unclear if all other patients were alive and had no strokes at the end of month 1.

mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Unclear risk	All planned outcomes were reported. Quality of Life is not mentioned on clinicaltrials.gov (there is mention to symptoms) and also gets reported. Reported additional non-planned outcomes - stroke and mortality for a few patients, and it was unclear if remaining at no events.
Other bias	Low risk	Study protocol published and registered on clinicaltrials.gov (NCT00989001) nearly at the end of recruitment (2009-2010). However, study was assessed and reviewed by the FDA prior starting (i.e. protocol reviewed before study start and subsequently published on public repository), and hence there is irrefutable proof of trial registration. Approved by ethics committees at each study site.

Beatch 2017

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 2hrs)
Participants	**Baseline Characteristics** Placebo • Age (sd): 59.2 (12.0) • Male (%): 30 (54) • Duration of episode h (sd): 48 (35) • Structural Heart Disease (%): 13 (23) • Heart Failure (%): 3 (5) • Ischaemic Heart Disease (%): 7 (113) • Myocardial Infarction (%): 0 (0) • Valvular Heart Disease (%): 3 (5) • Any Anti-arrythmic drug: 0 Vernakalant • Age (sd): 60.7 (13.7) • Male (%): 37 (67) • Duration of episode h (sd): 48 (43) • Structural Heart Disease (%): 11 (20) • Heart Failure (%): 5 (9) • Ischaemic Heart Disease (%): 4 (7) • Myocardial Infarction (%): 1 (2) • Valvular Heart Disease (%): 2 (4) • Any Anti-arrythmic drug: 0 Stroke/TIA, cardiomyopathy, Diabetes Mellitus, Pulmonary disease, Hypertension: N/A Beta-blocker, Calcium antagonist, Diuretic, ACE inhibitor, Aspirin, Digoxin: N/A LA dimension and LVEF %: N/A BMI: N/A CHA2DS2VASc: N/A AF type: All patients had paroxysmal AF. **Inclusion criteria:** Included patients were adults aged 18 – 85 years with recent-onset (duration >3 h– ≤ 7 days) and dysrhythmic symptoms. Patients must have been hemo- dynamically stable for more than 12 hours before screening, adequately hydrated, and receiving sufficient anticoagulant therapy, as determined by the investigator. **Exclusion criteria:** Patient is pregnant, breast-feeding, or expecting to become pregnant during the study. Patient routinely consumes more than 2 alcoholic drinks per day. Patient has known or suspected prolonged QT, familial long QT syndrome, previous Torsades de Pointes, Brugada syndrome. Patient has known bradycardia, advanced AV block, or sick-sinus syndrome, unless controlled by a pacemaker. Patient has severe aortic stenosis. Patient has atrial flutter. Patient has Class IV congestive heart failure (CHF). Patient has had a myocardial infarction (MI) or acute coronary syndrome (ACS). Patient has had cardiac surgery within 30 days. Patient has known atrial thrombus. Patient has reversible causes of Atrial Fibrillation. Patient has failed electrical cardioversion during current episode of Atrial Fibrillation. Patient has uncorrected electrolyte imbalance. Patient has clinical evidence of digoxin toxicity. Patient has received certain antiarrhythmic drugs or intravenous amiodarone within 7 days. Patient is known to be HIV positive. Patient has a history of cancer within the past 5 years, except for certain skin or cervical cancer. **Numbers:** Original plan to enroll 615 patients from Taiwan, Korea, China, India and Hong Kong. However, due to early termination only 123 patients from Taiwan, Jorea and India were

	randomised, 61 to vernakalant and 62 to placebo. 4 patients in the vernakalant arm and 6 in the placebo arm were removed due to protocol violation. 1 patient in the vernakalant arm was removed due to physican decision and another due to patient choice. Only 111 patients recieved any study drug, 55 for vernakalant, 56 for placebo. **Anticoagulation:** protocol was to be determined by investigator. **Monitoring:** was with regular 12 lead electrocardiograms and continous telemetry. Patients were electrically cardioverted after 2 hrs if they did not respond. 24hrs inpatient follow up and 30 day follow up for adverse events.
Interventions	Intravenous Vernakalant Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Identification** **Sponsorship Source:** Cardiome Pharma Corp. and Merck AG **Country:** Taiwan, Korea, India **Setting:** Unclear **Comment:** Clinical trial reg NCT01174160. Planned Outcomes: Primary Efficacy end point was the proportion of patients with short duration AF

	in sinus rhythm for at least 1 minute within 90 minutes of drug initiation. Secondary endpoints; time to conversion and proportion of patients in Sinus Rhythm at 24 hours. Same outcomes for longer duration AF. Proportion of patients reporton no AF symptoms at 90 mins, and the the impact of symptoms of AF on quality of life after 90 mins. In addition adverse events were recorded, primary safety outcome was any of clinically significant hypotension, clinically significant ventricular arrhythmia or death within 2h of the start of exposure. Reported outcomes: as above. **Author's Name:** Gregory Beatch **Institution:** Cardiome Pharma Group **Email:** gbeatch@cardiome.com **Address:** Gregory Beatch, Cardiome Pharma Corp., 1441 Creekside Drive 6th Floor, Vancouver, BC V6J 4S7, Canada. 2PAREXEL International Corp., Lowell, MA, USA
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	An Interactive voice response system (central) would allocate treatment on contact by the pharmacist. No information on how the sequence was created.
Allocation concealment (selection bias)	Low risk	The pharmacist prepared the drug/placebo and this was brought to the assisting team and patient.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Pharmacist brings drug/placebo and administration/infusion is similar for both treatment groups.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Pharmacist brings drug/placebo and administration/infusion is similar for both treatment groups. These are objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Study described as double-blind and with an independent clinical events committee.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Study described as double-blind and with an independent clinical events committee. Also, these are objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients during hospitalization.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes reported for all patients up until day 10.
Selective reporting (reporting bias)	Low risk	Study protocol only mentioned the primary efficacy endpoint. Published study also published information on adverse events.
Other bias	Low risk	Protocol registered on clinicaltrials.gov (NCT01174160) (1 month after study start, but still 2 years before ending recruitment) and had Ethics approval at each site.

Bellandi 1995

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (sd): 65.15 (11.89) • Coronary Artery Disease (%): 24 (24.4) • Duration of episode h (sd): 56.97 (48.13)

	• Hypertension (%): 19 (19.3) • Dilated Cardiomyopathy (%): 6 (6) • Valvular Heart Disease (%): 20 (20.4) • LA diameter (mm) (sd): 41.12 (3.72) • Any Anti-arrythmic drug: 0 • Any rate control drugs: 0 Placebo • Age (sd): 66.12 (13.76) • Coronary Artery Disease (%): 19 (22.6) • Duration of episode h (sd): 49.78 (37.68) • Hypertension (%): 19 (22.6) • Dilated Cardiomyopathy (%): 5 (5.9) • Valvular Heart Disease (%): 17 (20.2) • LA diameter (mm) (sd): 42.22 (4.93) • Any Anti-arrythmic drug: 0 • Any rate control drugs: 0 Gender not given Stroke/TIA, Diabetes Mellitus, Pulmonary disease, Myocardial infarction, Heart failure: N/A Diuretic, ACE inhibitor, Aspirin: N/A % of LA diameter > 50mm, LVEF %: N/A BMI: N/A CHA2DS2VASc: N/A AF type: All patients had paroxysmal AF. **Included criteria:** Patients with recent onset AF determined as ≤7 days **Exclusion criteria:** Angina or clinical signs of heart failure (resting dyspnea, pulmonary congestion, systolic blood pressure <90 mmHg); spontaneous low mean ventricular rate (< 70 beat/min); and previous treatment with digoxin, beta blockers, calcium-channel blockers, or other antiarrhythmic drugs. **Numbers:** 182 patients randomised to propafenone (98) and placebo (84). There was no attrition. **Anticoagulation:** No recorded anticoagulation protocol given. **Monitoring:** Continuous telemetry and intermittent 12 lead ECG was used for monitoring. Maximum follow up was 24h.
Interventions	Intravenous Propafenone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h

	• **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Unclear **Comments:** Outcomes were coversion to sinus rhythm and time to conversion, conduction defects or changes to QRS or QTc duration, treatement side effects of hypotension, symptoms or signs of low cardiac output and pulmonary congestion, and mean ventricular rate of non-responsders at the end of infusion. All planed outcomes were reported as well as additional adverse events. No trial registration. **Authors name:** Francesco Bellandi **Institution:** Division of Medicine, Ospedale Misericordia e Dolce,Prato; *Clinics Medica I, University of Florence, Florence, Italy **Email:** Not provided **Address:** Prof. R.P. Dabizzi, Cardiologia, Clinica Medica I Universita di Firenze Viale Morgagni 85, 50100 Florence, Italy
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Two solutions were infused (one for 3 minutes, and then a subsequent one for 24h) for the propafenone group, and one solution only for the the placebo group (over 24h). Personnel would easily know who got the active drug.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints - unlikely to be affected.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on this.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints - unlikely to be affected.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	High risk	No mention to trial/protocol registration or Ethics approval. Questions about randomization method: with 98 patients assigned to propafenone and 84 to placebo.

Bellone 2012

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (Years) Mean (SD): 67 (14) • Sex (Male) n (%): 66 (52) • Weight (kg) Mean (SD): 71 (11) • Hypertension n (%): 67 (53) • Diabetes Mellitus n (%): 25 (20) • Duration of AF (h) Median (range): 4 (1-46) • Previous Symptomatic AF n (%): 2(1.6) • Dilated left atrium, n (%): 20 (16)

	• Digoxin n (%): 0 • Beta-blocker n (%): 40 (32) • ACE-I/ARB (%): 31 (25) • Aspirin (%): 43 (34) • Calcium antagonist n (%): 55 (44) Anteroposterior Biphasic Shock • Age (Years) Mean (SD): 68 (13) • Sex (Male) n (%): 65 (54) • Weight (kg) Mean (SD): 72 (15) • Hypertension n (%): 65 (54) • Diabetes Mellitus n (%): 22 (18) • Duration of AF (h) Median (range): 6 (1-28) • Previous Symptomatic AF n (%): 2(1.65) • Dilated left atrium, n (%): 20 (16) • Digoxin n (%): 0 • Beta-blocker n (%): 42 (35) • ACE-I/ARB (%): 25 (21) • Aspirin (%): 50 (41) • Calcium antagonist n (%): 45 (37) Valvular Heart Disease, Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction: N/A Sotalol, Diuretic, Amiodarone, Flecainide: N/A LVEF (%): N/A AF type: 100% patients had paroxysmal AF. **Inclusion criteria:** Patients of either sex were eligible for inclusion in the study if they were at least 18 years of age and presented with AF lasting less than 48 h. **Exclusion criteria:** Exclusion criteria consisted of AF lasting more than 48 h, haemodynamic instability defined as any patient with a systolic blood pressure less than 90 mm Hg and/or diastolic pressure less than 50 mm Hg, any valvular disease, acute onset AF due to acute coronary syndrome, electrolyte disturbances, sepsis, fever, hypothermia, untreated hyperthyroidism, daily home therapy with antiarrhythmic drugs(class I A, B, C and class III) and/or a high embolic risk with a CHADS2score of 2 or greater (congestive heart failure, hypertension, age>75 years, diabetes, previous stroke or transient ischaemic attacks). Patients presenting with an unclear duration of symptoms were presumed to have had them longer than 48 h and were excluded from the study. **Numbers:** 247 patients enrolled. Propafenone = 126 AP Biphasic = 121. No attrition reported. **Anticoagulation:** Protocol not given but duration less than 48 hours. No post cardioversion procotol given. **Monitoring:** Continous ECG monitoring and 12 lead ECG taken at intervals until 6 hours follow up. Patients followed up for 2 months.
Interventions	Intravenous Propafenone AP BTE Incremental
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism at 30d • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortaility • **Outcome type**: AdverseEvent

	• **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day all cause mortaility • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local funding **Country:** Italy **Setting:** Accident and Emergency **Comment:** No conflicts of interest reported. Planned outcomes: rate of successful cardioversion within 6h of treatment, adverse events, time spent in department, recurrence of AF within 2 months. Reported outcomes: as above, many patients lost to follow up so incomplete outcome for AF recurrence. Clinicaltrials.gov registration NCT00933634 **Author's Name:** Andrea Bellone **Institution:** Emergency Department, Valduce Hospital **Email:** andreabellone@libero.it **Address:** Dr Andrea Bellone, Emergency Department, Valduce Hospital, Via Dante 11, 22100 Como
Notes	Intravenous propafenone

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Computer based algorithm for randomisation "Patients were randomly assigned to receive either EC or PC and they were stratified according to our clinical centre with the use of an algorithm that ensured near balance in each group." However, no explanation of how the algorithm worked.
Allocation concealment (selection bias)	Unclear risk	The randomisation was placed in closed envelopes with identification numbers that were stored. However, we do not know who had access to the envelopes and who was responsible for withdrawing the envelope for each patient (nurse? physician? secretary?) and how long in advance that person would get/see the envelope. Were the envelopes opaque?
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Study design which would face some ethical issues/difficulty for blinding of participants/personel as it involves electrical cardioversion, which requires sedation, vs pharmacological cardioversion (doesn't require sedation). This would imply sedating patients in the pharmacological cardioversion group and performing a "sham procedure". There is currently an ongoing RCT using such a methodology, and therefore, this could have been possible.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as these are objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	Outcomes were assessed by the clinical staff during admission, no attempt of blinding
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as these are objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of	Low risk	All pre-specified end points were fully reported on

Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications		
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	High risk	Endpoints assessed after discharge. The authors state "the number of patients lost to follow-up was very high"
Selective reporting (reporting bias)	Low risk	Pre-specified end points in the methods section were fully reported. Protocol was published in 2009 in clinicaltrials.gov (i.e. prior to publication of the paper - 2012) which was after recruitment of all participants (patients were included between 2006 and 2008). Endpoints in the published 2012 manuscript are phrased in a different manner than in the 2009 protocol, and include one additional endpoint: time spent in ED after cardioversion. All endpoints mentioned in the published 2009 protocol are available in the 2012 publication.
Other bias	Unclear risk	Irrefutable proof of Trial registration: NCT00933634 As recruitment started before July 2008 (date specified in the methods) and the protocol was published in clinical trials after patient enrolment, we can still consider this trial as having irrefutable evidence of registration, despite registration after inclusion of patients. Mention to approval of the study by the institutional review board of the centre (Valduce Hospital in Como, Italy), which means there was a protocol before the start of inclusion.

Bertini 1990

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD): 62.58 (11.54) • Male (%): 9 (38) • Hypertension (%): 11 (46) • Diabetes Mellitus (%): 2 (8) • LA diameter (mm) mean (SD): 38 (3) Amiodarone • Age (years) mean (SD): 68.06 (7.35) • Male (%): 7 (47) • Hypertension (%): 6 (40) • Diabetes Mellitus (%): 2 (13) • LA diameter (mm) mean (SD): 38 (5) Structural heart disease, Valvular Heart Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Cardiomyopathy, Heart Failure, Coronary Artery Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LVEF %: N/A CHA2DS2VASc: N/A Duration of episode: N/A AF type: definition not given for paroxysmal AF **Inclusion criteria:** Patients with paroxysmal atrial fibrillation seen by mobile coronary care unit. **Exclusion criteria:** 1) history of coronary heart disease; 2) previous episodes of paroxysmal atrial tachydysrhythmias; 3) congenital or valvular heart disease; 4) history of WPW syndrome; 5) history of thyroid malfunction; 6) acute or chronic treatment with digoxin, betablockers, calcium antagonists, or other antidysrhythmic drugs; 7) age c 30 years; 8) complaint of chest pain; 9) clinical signs of heart failure; 10) an electrocardiogram suggestive of coronary artery disease, or 11) presence of bundle branch block.

	Numbers: 39 patients enrolled. 24 randomised to propafenone and 15 to amiodarone. No attrition recorded. **Anticoagulation:** No anticoagulation protocol as arrhythmia classified as paroxysmal. **Monitoring:** Continuous ECG monitoring throughout 120 minutes after drug infusion. If failure to convert, admitted to hospital for mangement over 48 hours.
Interventions	Intravenous Propafenone Intravenous Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local funding **Country:** Italy **Setting:** Mobile coronary care unit **Comment:** Planned outcomes: Conversion to sinus rhythm. Reported outcomes: as above, including adverse events. No trial registration. **Author's Name:** Giovanni Bertini **Institution:** Clinica Medica I, University of Florence, and Mobile Coronary Care Unit of the City of Florence **Email:** not provided **Address:** Giovanni Bertini, Associate Professor of Emergency Medicine, Clinica Medica I, University of Florence, Viale Morgagni 85, 50134 Florence, Italy
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quasirandomized design - by year of birth odd/even
Allocation concealment (selection bias)	High risk	Quasirandomized design - by year of birth odd/even
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Quasirandomized design - by year of birth odd/even - no information provided if personell and staff were aware of randomization method
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided if outcome assessors were aware of randomization method and were blinded to the year of birth/treatment arm.

Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes assessef for all patients.
Selective reporting (reporting bias)	Unclear risk	No protocol was published / available prior to the study publication, hence cannot say if all planned outcomes were reported.
Other bias	High risk	No proof of prior trial registration. No mention to Ethics approval. Quasirandomized design.

Bianconi 1998

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Crossover) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age mean (SD): 59 (13) • Male (%): 26 (63) • Duration of episode (h) mean (SD): 14 (17) • Hypertension (%): 11 (27) • Any Anti-arrythmic drug (%): 0 (0) Placebo (Digoxin and Placebo) • Age mean (SD): 60 (13) • Male (%): 38 (46) • Duration of episode (h) mean (SD):13.5 (18.9) • Hypertension (%): 25 (30) • Any Anti-arrythmic drug (%): 0 (0) Valvular Heart Disease, Structural Heart Disease, Stroke/TIA, Hypertension, Pulmonary Disease, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus, Cardiomyopathy: N/A Beta-blocker, Calcium antagonist, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A AF type all paroxysmal **Inclusion criteria:** All patients aged between 18 and 75 years presenting at the emergency room with atrial fibrillation lasting from 1 to 72 hours **Exclusion criteria:** Ongoing digitalis or class I or III antiarrhythmic drug therapy, myocardial infarction within the preceding month, postoperative period after heart surgery, unstable angina, clinical signs of heart failure or low cardiac output, clinical signs of hyperthyroidism, systolic blood pressure < 100 mm Hg, heart rate <80 beats/min, bifascicular block, known sick sinus syndrome or second- or third- degree atrioventricular block in absence of a cardiac pacemaker, Wolff-Parkinson-White syndrome, and ascertained or presumed pregnancy **Numbers:** 125 patients were enroled. 2 were excluded as sinus rhythm ocurred before randomisation. 123 were allocated to treatment with 41 to propafenone, and 82 to placebo (40 to digoxin and 42 to placebo pill). No patients lost to follow up. **Anticoagulation:** Protocol not given but recent onset defined as < 72h. **Monitoring:** With regular ECG strip. Observation time 1 hour, cross over to alternative active treatment if no response.
Interventions	Intravenous Propafenone Intravenous Placebo (Digoxin and Placebo)
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success

	• **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Knoll Farma- ceutici SpA, Medical Division, Muggio Milan, Italy. **Country:** Italy **Setting:** Emergency Department **Comments:** Planned outcomes were conversion to sinus rhythm within 1 hour from the start of the first treatment, (2) conversion to sinus rhythm within 1 hour from the start of the second treatment, (3) ventricular rate in nonconverters, and (4) frequency and severity of side effects. All planned outcomes were reported. No conflicts of interest reported. No trial registration. **Authors name:** Leopoldo Bianconi **Institution:** Department of Cardiology, San Filippo Neri Hospital, Rome, Italy **Email:** Not provided **Address:** Leopoldo Bianconi, MD, Via San Sotero 12, 00165 Rome, Italy.
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Computer generated ad-hoc list for each center guaranting that groups were balanced every 6 patients. However,not clear on the method.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Study described as "single-blind". Drugs infused with the same method of administration.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Drugs infused with the same method of administration. Objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	No information provided. Study reported as single-blind, and based on the above it is likely assessors were not blinded for the assessment of side effects.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No information provided, but these are objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	No proof of trial registration. Approved by the local ethics committee.

Bianconi 2000

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (allowed alternate cardioversion strategy after 3h)
Participants	**Baseline Characteristics** Dofetilide • Age (year) mean (SD): 64 (9) • Men (%): 28 (56) • Ischaemic Heart Disease (%): 6 (13) • Hypertension (%): 19 (40) • Beta-blocker (%): 7 (15) • Digoxin (%): 25 (52) • Cardiomyopathy (%): 2 (4) • Calcium Channel Blockers (%): 12 (25) • Left Atrial Diameter (mm) mean (SD): 44 (1)

	• Valvular Heart Disease (%): 12 (25) • Paroxysmal AF (%) : 23 (44) • Persistent AF (%): 27 (56) • Atrial Flutter (%): 12 (25) Amiodarone • Age (year) mean (SD): : 61 (12) • Men (%): 31 (57) • Ischaemic Heart Disease (%): 4 (18) • Hypertension (%): 24 (48) • Beta-blocker (%): 7 (14) • Digoxin (%): 34 (68) • Cardiomyopathy (%): 3 (6) • Calcium Channel Blockers (%): 13 (26) • Left Atrial Diameter (mm) mean (SD): 43 (1) • Valvular Heart Disease (%): 8 (16) • Paroxysmal AF (%): 27 (46) • Persistent AF (%): 27 (54) • Atrial Flutter (%): 9 (18) Placebo • Age (years) mean (SD): 61 (15) • Men (%): 29 (54) • Ischaemic Heart Disease (%): 6 (12) • Hypertension (%): 22 (42) • Beta-blocker (%): 8 (15) • Digoxin (%): 24 (46) • Cardiomyopathy (%): 0 (0) • Calcium Channel Blockers (%): 20 (38) • Left Atrial Diameter (mm) mean (SD): 45 (1) • Valvular Heart Disease (%): 4 (8) • Paroxysmal AF (%): 30 (52) • Persistent AF (%): 25 (48) • Atrial Flutter (%): 10 (19) Structural Heart Disease, Stroke/TIA, Pulmonary disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus: N/A Flecainide, Sotalol, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A LVEF%: N/A BMI: N/A CHA2DS2VASc: N/A Nearly equal split of paroxysmal and persistent AF. **Inclusion criteria:** Age between 18, 85, with AF or Atrial Flutter lasting from 2h to 6 months **Exclusion criteria:** Female patients of childbearing potential, Clinically unstable heart failure or distress (e.g. angina, dyspnoea) as a result of atrial fibrillation or flutter, Resting ventricular rate of <60 beats . min1or RR interval of >4 s, QRS interval of >180 ms or QT interval of >440 ms, History or clinical signs of thyrotoxicosis, History of cardiac surgery, myocardial infarction, unstable angina, or aborted sudden cardiac death within the last 3 weeks, Known sick sinus syndrome or atrioventricular block of greater than first degree, Cardiac pacemaker, History of polymorphic ventricular tachycardia secondary to drugs, Diastolic blood pressure of >110 mmHg or systolic blood pressure of <80 mmHg, Major haematological, hepatic, or renal disease, Plasma potassium level of <3·6 or >5·5 mmol /L, or known plasma magnesium level of <0·6 or >1·5mmol/L, Amiodarone treatment within previous 3 months or contraindications to amiodarone, History of substance abuse or dependence, Use of an experimental drug within the preceding month **Numbers:** 173 screen 158 eligible randomised to: Dofetilide 50, Amiodarone 54 and Placebo 54, 8 subjects excluded as timing of ECGs could not be verified (2 dofetilide, 4 amiodarone, 2 placebo). **Anticoagulation:** No anticoagulation protocol was described. **Monitoring:** Follow up duration was 12 hours as inpatient as well as clinic visit 3 to 7 days later. Monitoring of rhythm was with continuous ECG. If no cardioversion after 3 hours patients could be cardioverted using alternate means.
Interventions	Intravenous Dofetilide Intravenous Amiodarone

	Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Pfizer Central Research **Country:** Italy **Setting:** Not Clear **Comments:** No conflicts of interest reported but study was funded by industry. Planned outcomes were: incidence of conversion to sinus rhythm within 3 h of the start of infusion, incidence of side effects, mean time to conversion and (2) ventricular rate in non-converted patients after drug treatment with respect to baseline. Reported outcomes: as planned. No trial registration. **Authors name:** L. Bianconi **Institution:** Division of Cardiology, San Filippo Neri Hospital, Rome, Italy **Email:** kofler@opbg.net **Address:** Dr Leopoldo Bianconi, Via San Sotero 12, 00165 Rome, Italy
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Random sequence generation by permuted blocks. No information about the number of blocks.
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Process of allocation concealment not described.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Judgement Comment: Described as double blind, same length / duration of infusions given makes this possible.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Described as double blind, same length of duration infusions given makes this possible.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Judgement Comment: Reported as double blind but no description if data was independently assessed.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Reported as double blind but no description of how data was independently assessed. Unlikely to have had an impact on this as these are objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Judgement Comment: All patients were included in these analyses (i.e. no patients lost to follow-up)
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge:	Low risk	All patients were included in the 7-day safety analyses (i.e. no patients lost to follow-up)

Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	Judgement Comment: No proof of trial registration. The manuscript states that the protocol was reviewed and approved by the "European Ethical Committee and by local ethics committees, where present"

Blanc 1999

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (sd): 61 (12) • Men (%): 8 (2) • Hypertension (%): 8 (2) • Myocardial Infarction (%): 3 (7) • Stroke/TIA (%): 1 (2) Amiodarone • Age (sd): 64 (12) • Men (%): 8 (2) • Hypertension (%): 18 (42) • Myocardial Infarction (%): 0 (0) • Stroke/TIA (%): 4 (9) Valvular Heart Disease, Structural Heart Disease, Pulmonary Disease, Cardiomyopathy, Ischaemic Heart Disease, Heart Failure, Coronary Artery Disease: N/A Beta-blocker, Calcium antagonists, Digoxin, Flecainide, Sotalol, Diuretic, ACE inhibitor, Aspirin: N/A Duration of episode: N/A BMI: N/A CHA2DS2VASc: N/A AF type: could have been paroxysmal or persistent. **Inclusion criteria:** Patients between 25 and 80 years old with AF lasting for <2 weeks **Exclusion criteria:** NYHA class II or more before AF, hypotension (<90 mm Hg), brady-arrhythmia (<45 beats/min), dysthyroidism, second-or third-degree atrioventricular block without pacemaker, 3 mmol/L<kaliemia<5.5 mmol/L, stroke, or myocardial infarction in the 3 months preceding the study, severe obstructive bronchopathy, known hepatic or renal failure, and treatment with any antiarrhythmic drug at inclusion or one that had been discontinued for <5 half-lives. **Numbers:** No number given for eligible, Randomised 86, Propafenone 43, Amiodarone 43, None lost to follow up **Anticoagulation:** Heparin administered at admission for all pt, if >48 hours duration and no long term anticoagulation (not specified) TOE performed **Monitoring:** Holter monitoring and ECG. Max 48 hour follow up.
Interventions	Oral Propafenone Oral Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome

	• **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** France **Setting:** Elective Admission **Comments:** Primary Endpoint, delay between drug dose and recovery, Secondary Endpoint - proportion of cases in SR at 24 and 48hrs Reported as above and adverse events. No trial registration or conflict of interest reported. **Authors name:** Jean-Jacques Blanc **Institution:** Department of Cardiology, Brest University Hospital, Brest, Knoll France **Email:** not provided **Address:** Jean-Jacques Blanc, MD, De´ partement deCardiologie, CHU La Cavale Blanche 29609 Brest, Cedex, France
Notes	Oral all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No specifications provided
Blinding of participants and personnel (performance bias) All other outcomes	High risk	The authors mention: "Single-blind". We assume blinding is for patients and that only the caregivers know the treatment assignment. "Compliance to treatment was analyzed by tablet count" (amiodarone dose was 30mg/kg, meaning 10 to 12 pills over 2 to 3 minutes vs propafenone 600mg) - number of pills may have given a clue on the type of treatment. This could have had an effect mainly with regards to side effect reporting. As for documentation of sinus rhythm during the admission, there is always the potential question of management being affected when the physician knows the assigned drug and that having on results. It would still be possible, even though less likely.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Authors report Acute procedural success which is an objective outcome and not likely to be affected by lack of blinding.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Assessors of outcome (AF in Holter) were also blinded - Low risk. Other endpoints like VT, SVT and bradycardia were defined in an objective manner and were also assessed by blinded assessors - Low risk. With regards to other side effects like digestive disconfort it is uncertain, however the number of events was comparable.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Assessors of outcome (AF in Holter) were also blinded.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints of interest to this review were reported for all patients (none lost to follow-up), and confirmed by the %s reported in the paper.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. The manuscript states that the protocol was reviewed and approved by "our Ethics Committee" - Brest University Hospital, France.

Boriani 1997

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD):60 (12) • Male (%): 70 (59) • Duration of episode (h) mean (SD): 31 (36) • Hypertension (%): 37 (31) • Structural Heart Disease (%): 32 (27) • Coronary Artery Disease (%): 11 (9) • Cardiomyopathy (%): 7 (6) • Valvular Heart Disease (%): 8 (7) • Any Anti-arrythmic drug (%): 0 (0) • LA diameter (mm) mean (SD): 42 (6) Placebo • Age (years) mean (SD): 58 (13) • Male (%): 67 (55) • Duration of episode (h) mean (SD): 30 (34) • Hypertension (%): 37 (31) • Structural Heart Disease (%): 30 (25) • Coronary Artery Disease (%): 9 (7) • Cardiomyopathy (%): 8 (7) • Valvular Heart Disease (%): 9 (7) • Any Anti-arrythmic drug (%): 0 (0) • LA diameter (mm) mean (SD): 41 (7) Stroke/TIA, Pulmonary disease, Myocardial Infarction, Ischaemic Heart Disease, Heart Failure, Diabetes Mellitus: N/A Beta-blocker, Calcium antagonist, Diuretic, ACE inhibitor, Digoxin, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LVEF %: N/A All patients had paroxysmal AF **Inclusion criteria:** Consecutive patients presenting to emergency department with recent onset atrial fibrillation defined as less than or equal to 7 days. **Exclusion criteria:** Age > 80 years, heart failure > NYHA Class II, mean ventricular rate during atrial fibrillation < 70 beats/min, recent (< 6 months) myocardial infarction, unstable angina pectoris, electrocardiographic evidence (present or past) of ventricu- lar preexcitation or complete bundle branch block, previous electrocardiographic evidence of second- or third-degree atrioventricular or bifascicular block, sick sinus syndrome, hypokalemia (potassium < 3.5 mEq/L), renal or hepatic failure and severe hypoxia (partial pressure of oxygen < 55 mmHg), or severe metabolic disturbances or known thyroid dysfunction. Patients receiving digoxin or antiarrhythmic drugs chronically or within 8 hours prior to entry into the study were also excluded. Patients with atrial fibrillation lasting a 72 hours were enrolled only if chronically anticoagulated with warfarin. **Numbers:** 240 patients were enrolled. 119 randomised to propafenone group and 121 to placebo. No patients lost to follow up. **Anticoagulation:** Protocol not specified but chronic wafarinisation for AF duration >72h required. **Monitoring:** With regular ECG strip and 24 hour holter and intermitted 12 lead ECG strip. Max follow up 24h. Could switch to different treatment after 8 hours if needed.
Interventions	Oral Propafenone Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome

	• **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Unclear **Comments:** No conflicts of interest reported. Planned outcomes: SR at 24h, Blood pressure readings, side effects that patients reported, HR and arrhythmias Reported outcomes: SR at 24h, Adverse events. No trial registration. **Authors name:** Giuseppe Boriani **Institution:** Institute of Gardiology, University of Bologna, Bologna; Department of Gardiology, Ospedale S.Anna, Gomo; and Department of Gardiology, Ospedale Civile, Lugo, Italy **Email:** cardiol@almadns.unibo.it **Address:** Giuseppe Boriani, M.D., Institute of Cardiology, University of Bologna, Via Massarenti 9, 40138 Bologna, Italy.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Patients were given 300mg propafenone (2 tablets) or placebo (no specification on number of tablets). Mention of single-blind study - patients likely blind, but not the health professionals?
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided. Unclear if assisting physicians assessing inpatient adverse side effects were blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Holter tapes were assessed by blinded assessors. Objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were

		any other additional endpoints that were not reported.
Other bias	High risk	No mention to protocol/trial registration or Ethics approval.

Botto 1999

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Crossover) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA MDS Incremental Patches • Age (years) mean (SD): 62 (12) • Male (%): 94 (62) • Hypertension (%): 41 (27) • Valvular Heart Disease (%): 42 (28) • Cardiomyopathy (%): 15 (10) • Coronary Artery Disease (%): 14 (9) • Amiodarone (%): 62 (41) • Sotalol (%): 7 (5) • Flecainide (%): 3 (2) • Propafenone (%): 25 (17) • LA diameter (mm) mean (SD): 44 (6) • Duration of episode (days) mean (SD): 84 (92) AP MDS Incremental Patches • Age (years) mean (SD): 62 (11) • Male (%): 89 (59) • Hypertension (%): 40 (27) • Valvular Heart Disease (%): 43 (29) • Cardiomyopathy (%): 17 (11) • Coronary Artery Disease (%): 18 (12) • Amiodarone (%): 69 (46) • Sotalol (%): 6 (4) • Flecainide (%): 1 (1) • Propafenone (%): 18 (12) • LA diameter (mm) mean (SD): 45 (6) • Duration of episode (days) mean (SD): 92 (96) Structural Heart Disease, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure, Pulmonary Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LVEF %: N/A CHA2DS2VASc: N/A AF type: definition not given. **Inclusion criteria:** Patients scheduled for elective external cardioversion for stable atrial fibrillation. **Exclusion criteria:** Haemodynamically unstable atrial fibrillation in which cardioversion needed to be performed urgently; left atrial dimension > 60 mm measured by M mode echocardiography; arrhythmia duration either > 2 years or of unknown duration; and untreated hyperthyroidism. **Numbers:** 301 patients enrolled. 151 randomised to anteroapical group and 150 to anterolateral group. No attrition recorded. **Anticoagulation:** Patients with arrhythmia duration >72 hours had anticoagulation with warfarin for at least 3 weeks and then 4 weeks after cardioversion. **Monitoring:** ECG monitoring method not reported. Success defined as interruption of AF for 10 seconds. Cross-over to alternate posittion after 3rd shock.
Interventions	AA MDS Incremental Patches AP MDS Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported

	• **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Did not specify bradycardia episodes by group
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Elective Admission **Comments:** Planned outcomes: 12 lead evidence of sinus rhythm for 10 seconds after cardioversion. All planned outcomes reported. No trial registration. **Authors name:** G L Botto **Institution:** Department of Cardiology, Ospedale “Sant’ Anna”, Via Napoleona 60, 22100 Como, Italy **Email:** ccaec@tin.it **Address:** Correspondence address not provided
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided on sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information provided on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	No information provided on blinding, but blinding unlikely as pads were positioned and visible to patient personel.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Data reported for all patients.
Selective reporting (reporting bias)	Unclear risk	No published study protocol, hence cannot confirm if any of the plannet outcomes were left unreported.
Other bias	Unclear risk	Protocol approved by the local Ethics committee. No evidence of prior publication of study protocol.

Bouida 2019

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Magnesium • Male n (%): 183 (61) • Age (Years) Mean (SD): 67 (14) • Hypertension n (%): 145 (48) • Heart Failure n (%): 71 (24) • Beta-blocker n (%): 64 (21) • Calcium Antagonist n (%): 143 (48)

	• Digoxin n (%): 94 (31) • Stroke (%): 23 (8) Placebo • Male n (%): 86(60) • Age (Years) Mean (SD): 66.7 (12.3) • Hypertension n (%): 75 (50) • Heart Failure n (%): 32 (21) • Beta-blocker n (%): 33(22.1) • Calcium Antagonist n (%): 45 (30.2) • Digoxin n (%): 71 (47.7) • Stroke (%): 9 (6) Structural Heart Disease, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, yocardial Infarction, Ischaemic Heart Disease, Diabetes Mellitus: N/A Flecainide, Propafenone, Amiodarone, Sotalol, Diuretic, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF: N/A CHA2DS2VASc: N/A BMI: N/A AF type and duration: N/A **Inclusion criteria:** Over 18 years old admitted to the ED for rapid AF (>120 beats/min) were eligible for enrollment **Exclusion criteria:** Patients were ineligible in presence of arterial hypotension (systolic arterial pressure <90mmHg), if they have impaired consciousness, renal failure (serum creatinine >180 µmol/L), wide-complex ventricular response or contraindication to Magnesium Sulphate (MgS). We also excluded patients with acute myocardial infarction, acute congestive heart failure (New York Heart Association functional class 3 or 4), sick sinus syndrome, or rhythm other than AF. **Numbers:** 450 patients randomised to 149 in Placebo group and 301 in Magnesium group. **Anticoagulation:** No documentation of anticoagulation protocol. **Monitoring:** All patients had continuous ECG monitoring. Monitoring was for 24 hours until after randomisation.
Interventions	Intravenous Magnesium Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint

Identification	**Sponsorship Source:** Local **Country:** Tunisia **Setting:** Accident and Emergency **Comments:** No conflicts of interest reported. Planned outcomes: Sinus Rhythm conversion rate, adverse events, ventricular rate control and time elapsed from start of treatment to rate response. ClinicalTrials.gov Registry (NCT00965874) **Author's name:** Wahid Bouida **Institution:** Fattouma Bourguiba University Hospital **Email:** semir.nouira@rns.tn **Address:** Pr. Semir Nouira, Emergency Department and Laboratory Research (LR12SP18), Fattouma Bourguiba University Hospital, 5000, Monastir, Tunisia
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement Comment: Randomisation using random number tables was achieved by block of 3 packs.
Allocation concealment (selection bias)	Low risk	Randomization was done by a pharmacist not involvement in patient enrolement, data collection or analysis. Patient and Treating physicians were not aware of the assigned treatment (only a random number was shown by the pharmacist). The magnesium and placebo solutions were identical in appearance.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Physicians and patients were both blinded to the randomisation which was done by random number.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Physicians and patients were both blinded to the randomisation which was done by random number.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Physicians inserted outcome data into patients' notes and were blinded to the randomisation results. Therefore, blind outcome assignment.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Physicians inserted outcome data into patients' notes and were blinded to the randomisation results. Therefore, blind outcome assignment.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	All patients were followed up for the total duration of the study (24h after randomization)
Selective reporting (reporting bias)	Low risk	Pre-specified end points in the methods section were fully reported. Protocol posted on clinicaltrials.gov in August 2009 which was the start date for inclusion. Endpoints in the published clinicaltrials.gov protocol used for this systematic review did not change.
Other bias	Low risk	Irrefutable proof of Trial registration: NCT00965874 Protocol posted on clinicaltrials.gov in August 2009 which was the start date for inclusion. Mention to approval of the study by human research ethics committees of the participating centres.

Braždžionytė 2006

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Crossover) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA BTE Incremental Paddles • Age (years) mean (SD): 64 (12) • Male (%): 36 (66) • BMI (Kg/m^2) mean (SD): 30 (5) • Hypertension (%): 20 (36) • Valvular Heart Disease (%): 8 (15) • Coronary Artery Disease (%): 26 (47) • Beta-blocker (%): 17 (31)

	• Digoxin (%): 2 (4) • Amiodarone (%): 22 (40) • Propafenone (%): 8 (15) • LA diameter (mm) mean (SD): 46 (5) • LVEF (%) mean (SD): 49 (9) • Duration of episode <48h (%): 22 (40) • Duation of episode 48h - 1 month (%): 9 (16.4) • Duation of episode 1 - 6 months (%): 19 (34.5) • Duation of episode >6 months (%): 5 (9.1) AP BTE Incremental Paddles • Age (years) mean (SD): 62 (10) • Male (%): 29 (60) • BMI (Kg/m^2) mean (SD): 30 (5) • Hypertension (%): 19 (40) • Valvular Heart Disease (%): 11 (13) • Coronary Artery Disease (%): 16 (33) • Beta-blocker (%): 8 (17) • Digoxin (%): 2 (4) • Amiodarone (%): 24 (50) • Propafenone (%): 10 (21) • LA diameter (mm) mean (SD): 46 (5) • LVEF (%) mean (SD): 49 (6) • Duration of episode <48h (%): 12 (25) • Duation of episode 48h - 1 month (%): 6 (12.5) • Duation of episode 1 - 6 months (%): 23 (47.9) • Duation of episode >6 months (%): 7 (14.6) Structural Heart Disease, Cardiomyopathy, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure, Pulmonary Disease: N/A Calcium Antagonist, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A AF type: definition not given. **Inclusion criteria:** Patients scheduled for elective external cardioversion for atrial fibrillation who are above 18 years old and haemodynamically stable. **Exclusion criteria:** Not reported **Numbers:** 103 patients enrolled. 55 randomised to anteroapical group and 48 to anterolateral group. No attrition recorded. **Anticoagulation:** Patients with arrhythmia duration >48 hours had anticoagulation for at least 3 weeks for an INR $\geq$ 2. **Monitoring:** Continuous ECG monitoring during cardioversion. Success defined as presence of at least one clearly visible P wave within 30s of shock. Cross-over to alternate posittion after 4th shock.
Interventions	AA BTE Incremental Paddles AP BTE Incremental Paddles
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Lithuania **Setting:** Elective Admission

	Comments: No conflict of interest reported. Planned outcomes: 12 lead evidence of at least one p wave within 30s after cardioversion. All planned outcomes reported. No trial registration. **Authors name:** Julija Braždžionytė **Institution:** Department of Cardiology, Kaunas University of Medicine, Lithuania **Email:** giedre1972@yahoo.com **Address:** G. Stanaitienė, Department of Cardiology, Kaunas University of Medicine, Eivenių 2, 50009 Kaunas, Lithuania.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	No information on blinding method (if any), but due to study design patient and personnel knew the treatment arm.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information on blinding method (if any), for the outcome assessor.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Selective reporting (reporting bias)	Unclear risk	No published study protocol, hence could not confirm if any planned outcomes were not reported.
Other bias	High risk	No mention to Ethics approval. No evidence of prior trial protocol publication.

Brodsky 1994

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Magnesium • Age (years) mean (SD): 58.7 (14.9) • Male (%): 5 (50) • Hypertension (%): 5 (50) • Valvular Heart Disease (%): 1 (10) • Coronary Artery Disease (%): 0 (0) • Pulmonary Disease (%): 1 (10) • Digoxin (%): 1 (10) • LA diameter (mm) mean (SD): 42 (11.9) Placebo • Age (years) mean (SD): 55.6 (15.6) • Male (%): 5 (63) • Hypertension (%): 3 (38) • Valvular Heart Disease (%): 2 (25) • Coronary Artery Disease (%): 1 (13) • Pulmonary Disease (%): 1 (13) • Digoxin (%): 1 (13) • LA diameter (mm) mean (SD): 45.5 (8.7) Structural Heart Disease, Cardiomyopathy, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure: N/A Beta-Blocker, Calcium Antagonist, Amiodarone, Sotalol, Flecainide, Propafenon, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A

	BMI: N/A LVEF %: N/A AF type: All paroxysmal **Inclusion criteria:** Symptomatic AF of <7 days with ventricular response 100 to 200 beatslmin **Exclusion criteria:** Unstable cardiac, pulmonary, hepatic, endocrine, or renal disease, and therapy with class I to IV antiarrhythmic agents. Patients were accepted into the study if they gave a history of digoxin therapy, provided the level at admission was ≤0.8 nmol/liter. **Numbers:** 18 patients enrolled. 10 randomised to magnesium group and 8 to placebo. No attrition recorded. **Anticoagulation:** No anticoagulation protocol provided, patient population was paroxysmal AF. **Monitoring:** Continuous holter monitoring during therapy. Follow-up over 24hrs.
Interventions	Intravenous Magnesium Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** United States of America **Setting:** Unclear **Comments:** Planned outcomes: reduction in ventricular rate to less thatn 90 beats per minute either by cardioversion or slowdown of ventricular response. All planned outcomes reported, some adverse events reported. No trial registration. **Authors name:** Michael Brodsky **Institution:** University of California, Irvine, Division of Cardiology, Department of Medicine, University of California Irvine Medical Center, 101 City Drive South, Orange, California **Email:** not provided **Address:** not provided
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	

		No description of generation of randomization sequence
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study reported as double-blind, however not enough information provided on methods for blinding. Similar infusion protocols suggest blinding was attempted.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	objective outcomes, hence low risk
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on who the outcome assessors were or blinding method for allowing any judgement.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	objective outcomes, hence low risk
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	All outcomes reported for all patients - only inpatient outcomes.
Selective reporting (reporting bias)	Unclear risk	No protocol was published before online or as a manuscript.
Other bias	High risk	No proof of protocol registration or mention to Ethics approval.

Camm 2011

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV permitted 2h after infusion if no conversion)
Participants	**Baseline Characteristics** Vernakalant • Male n (%): 75 (64.7) • White n (%): 111 (95.7) • Age (Years) Mean (SD): 63.1 (10.8) • Previous Symptomatic AF n (%): 82 (70.7) • Duration of AF (h) Median (Q1 - Q3): 17.7 (9.1 - 28.7) • Hypertension n (%): 86 (74.1) • Structural Heart Disease n (%): 36 (31.0) • Ischaemic Heart Disease n (%): 22 (19.0) • Myocardial Infarction n (%): 11 (9.5) • Valvular Heart Disease n (%): 4 (3.4) • Heart Failure n (%): 20 (17.2) • LADD (mm) mean (SD): 40.6 (6.7) • LADD > 50mm n (%): 5 (4.3) • LVEF (%) mean (SD): 57.6 (7.3) • LVEF <50% n (%): 15 (12.9) • Any rate control n (%): 71 (61.2) • Beta-blocker n (%): 63 (54.3) • Calcium Antagonist n (%): 10 (8.6) • Digoxin n (%): 6 (5.2) Amiodarone • Male n (%): 71 (61.2) • White n (%): 111 (95.7) • Age (Years) Mean (SD): 62.2 (11.63) • Previous Symptomatic AF n (%): 83 (71.0) • Duration of AF (h) Median (Q1 - Q3): 17.9 (9.7 - 31.4) • Hypertension n (%): 80 (69.0) • Structural Heart Disease n (%): 45 (38.8) • Ischaemic Heart Disease n (%): 30 (25.9) • Myocardial Infarction n (%): 8 (6.9) • Valvular Heart Disease n (%): 12 (10.3) • Heart Failure n (%): 26 (22.4) • LADD (mm) mean (SD): 41.0 (6.04) • LADD > 50mm n (%): 7 (6.0)

	• LVEF (%) mean (SD): 59.5 (6.97) • LVEF <50% n (%): 4 (3.4) • Any rate control n (%): 78 (67.2) • Beta-blocker n (%): 76 (65.5) • Calcium Antagonist n (%): 4 (3.4) • Digoxin n (%): 10 (8.6) No class I or III antiarrhythmic drugs in the 24h pre and post study. Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Diabetes Mellitus: N/A Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LA dimensions and LVEF: N/A All patients had paroxysmal AF **Inclusion criteria:** Included if men and women between 18 and 85 years with symptomatic recent-onset AF (duration of 3 to 48 h) who were eligible for cardioversion, hemodynamically stable (systolic blood pressure 100 to 160 mm Hg and diastolic blood pressure 95 mm Hg), and taking adequate anticoagulation therapy (if recommended by American College of Cardiology/American Heart Association/European Society of Cardiology guidelines **Exclusion criteria:** Patients were excluded if they had an uncorrected QT interval >440 ms; familial long QT syndrome; previous torsades de pointes (TdP), ventricular fibrillation, or sustained ventricular tachycardia (VT); symptomatic bradycardia, known sick sinus syndrome, or ventricular rate <50 beats/min; o rQRS interval >140 ms. Patients with a pacemaker; atrial flutter (AFL); atrial thrombus; unstable congestive heart failure, New York Heart Association functional class IV heart failure, or heart failure requiring inotropes; myocardial infarction, acute coronary syndrome, or cardiac surgery within 30days prior to enrollment; cerebrovascular accident within 3months prior to enrollment; atrioventricular block; valvular stenosis, hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy, or constrictive pericarditis; or end-stage dis-ease states were also excluded from the study. Other exclusion criteria were previously failed electrical cardioversion, secondary causes of AF, uncorrected electrolyte imbalance, digoxin toxicity, contraindications to amiodarone, or previous exposure to vernakalant **Numbers:** 254 patient were enrolled and then 232 were randomised to 116 Vernakalant and 116 Amiodarone. **Anticoagulation:** Therapy was in line with ACC/AHA/ESC guidelines however all patients had recent onset AF so specific protocol was not specified. **Monitoring:** There was continuous ECG monitoring and patients were monitored until at least 6h after dose. There was a 7 day follow up visit and a 30 day telephone call.
Interventions	Intravenous Vernakalant Intravenous Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30 day all cause mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day CVD mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported

	• **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 1 week complications • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Stroke or systemic embolism at 30 day follow up. • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Quality of Life Change in EQ-5D quality of life assessment visual analog scale (VAS) from screening to hour 2 • **Outcome type**: ContinuousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Cardiome Pharma Corp, Local Funding **Country:** Australia, Canada, Europe **Setting:** Accident and Emergency **Comment:** No conflicts of interest. Planned outcomes: proportion of patients converting to SR within 90 minutes of treatment and for a minimum duration of 1 minute. Time to conversion, symptoms and quality of life visual analog scale parameters. Also Adverse events were monitored. Reported outcomes as above. Clinicaltrials.gov registration is NCT00668759 **Author's Name:** A. John Camm **Institution:** Clinical Cardiology, Cardiac and Vascular Sciences, St. George's University of London **E-mail:** jcamm@sgul.ac.uk **Address:** Dr. A. John Camm, Clinical Cardiology, Cardiac and Vascular Sciences, St. George's University of London, Cranmer Terrace, London SW17 0RE, United Kingdom
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information was supplied on this
Allocation concealment (selection bias)	Unclear risk	No information was supplied on this
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	To maintain blinding, patients in both treatment arms received similar duration and volume infusions and placebo (mimicking either vernakalant or amiodarone).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: To maintain blinding, patients in both treatment arms received similar duration and volume infusions and placebo (mimicking either vernakalant or amiodarone).
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	To maintain blinding, patients in both treatment arms received similar duration and volume infusions and placebo (mimicking either vernakalant or amiodarone). All ECG endpoints were assigned by a clinical events committee who was blinded to treatment allocation.

		Clinical endpoints were assined by treating physicians who were blinded to treatment allocation.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	To maintain blinding, patients in both treatment arms received similar duration and volume infusions and placebo (mimicking either vernakalant or amiodarone). All ECG endpoints were assigned by a clinical events committee who was blinded to treatment allocation. Clinical endpoints were assined by treating physicians who were blinded to treatment allocation.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Nearly all patients were followed up for the total duration of the study. Only one patient was lost to follow-up. Reason for patients who discontinued the study drug (adverse effects) or who were not dosed (spontaneous cardioversion - no longer meeting inclusion criteria) are explained in Figure 1. Occuring for only a very small minority of patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Nearly all patients were followed up for the total duration of the study (30 days). Only one patient was lost to follow-up. Reason for patients who discontinued the study drug (adverse effects) or who were not dosed (spontaneous cardioversion - no longer meeting inclusion criteria) are explained in Figure 1. Occuring for only a very small minority of patients.
Selective reporting (reporting bias)	Low risk	Pre-specified end points in the methods section were fully reported. Protocol posted on clinicaltrials.gov in April 2008 which was the start date for inclusion. Endpoints in the published clinicaltrials.gov protocol used for this systematic review did not change.
Other bias	High risk	Irrefutable proof of Trial registration: NCT00668759 Protocol posted on clinicaltrials.gov in April 2008 which was the start date for inclusion. Mention to approval of the study by institutional review board or ethics committee at each site. This study has, however a design flaw. It compares a very fast acting agent - vernakalant - vs. amiodarone which is a very slow action agent. With the definition of the efficacy endpoints we are able to observe the effect of vernakalant and proving its efficacy within a short time interval. Unfortunately, results for amiodarone at 24h to 48h are not presented in the paper. Therefore, despite proving that vernakalant is faster and more effective than amiodarone at cardioverting patients within 90min to a few hours, this trial fails to provide data on the true magnitude of effect of amiodarone (which would be at 24h or later), creating the artificial impression that amiodarone does not work .

Camm 2012

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Vernakalant • Age (mean +/- SD): 67 (11) • Men: 26 (67) • Atrial Flutter Duration (hours) median (range): 98 (5-784) • BMI (Kg/m^2) mean (SD): 29.3 (5.3) Placebo • Age (mean +/- SD): 69 (11) • Men: 12 (80) • Atrial Flutter Duration (hours) median (range): 178 (32-760) • BMI (Kg/m^2) mean (SD): 29.7 (7.0) Ischaemic Heart Disease, Hypertension, Valvular Heart Disease, Structural heart disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus, Heart Failure: N/A Beta-blocker, Propafenone, Diuretic, ACE inhibitor, Aspirin, Calcium Channel Blocker, Amiodarone, Flecainide, Sotalol, Digoxin: N/A

	CHA2DS2VASc: N/A LA dimensions and LVEF: N/A 100% of patients had atrial flutter. **Inclusion criteria:** Male or non-pregnant woman, Aged 18 or over with sustained flutter for. >3h and <45 days. Atrial flutter included typical AFL defined as an atrial rate between 220 and 320b.p.m. and a typical sawtooth pattern in electrocardiogram (ECG) leads II and III. Atypical AFL was included in the absence of a typical sawtooth pattern when there was clear evidence of regular, organized atrial activity in other leads (particularly lead V2) within this range of rates and fixed AV conduction (2 : 1, 3 : 1, etc.) **Exclusion criteria:** Pregnancy, those at risk of QT prolongation, bradycardia, or other proarrhythmia; haemo- dynamically unstable patients; and those with reversible causes of AFL or recent use of other antiarrhythmic drugs. **Numbers:** 60 patients Eligible for study, 6 patients did not recieve study drug (5 in placebo and one in vernakalant). 2 patients in placebo group spontaneously converted to sinus rhythm, one patient withdrew at baseline due to an observed thrombus on trans-oesophaeal echocardiogram, one withdrew consent and intravenous access was not possible to obtain for another. One of the vernakalant patients had a serum potassium level of 3.0 mmol/L at baseline. 15 Placebo patients completed the trial and 39 vernakalant. **Anticoagulation:** All patients were anticoagulated prior to inclusion but protocol not given. **Monitoring:** with regular 12 lead ECGs were done at several points during 24 hour period and at 7 days. Follow up duration was 30 days for adverse event monitoring.
Interventions	Intravenous Placebo Intravenous Vernakalant
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30 day all cause mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day CVD mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 1 week complications

	• **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Astellas Pharma Inc, Cardiome Pharma Corp. **Country:** United Kingdom, Denmark, Sweden, USA, Canada **Setting:** Elective Admission **Comments:** A.J.C. was a member of the Data and Safety Monitoring Board for this and other vernakalant studies; has been an advisor and member of a speakers' bureau for Cardiome, Astel- las, and Merck; and has been a consultant to Sanofi, Gilead, Menar- ini, Servier, Sention, Daiichi, and BMS. E.T., C.T.-P., S.J.-M., and D.G.W were steering committee members for this clinical trial, and P.V. and J.I. were principal investigators in this clinical trial. C.T.-P. has also received consultant fees, honoraria, and speaker's fees from Cardiome and Merck, and has been an advisory board and steering committee member for Cardiome and Merck. S.J.-M. is also a consultant to Merck. D.G.W. is also participating in studies sponsored by Boehringer Ingelheim, Bristol Myers Squibb/Pfizer, Sanofi Aventis, BIOTRONIK, Boston Scientfic/ Guident (Europe), Medtronic, and Merck, and has been a consult- ant to Merck. G.N.B. is a full time employee of Cardiome and G.D. is a consultant to Cardiome. Planned outcomes: 12 lead evidence of sinus rhythm after cardioversion, time to conversion, absolute reduction in ventricular rate and adverse events. All planned outcomes reported. Clinical Trial Registration—clinical- trials.gov. identifier: NCT00476112 **Authors name:** A. John Camm **Institution:** Cardiac and Vascular Sciences, St George's University of London **Email:** jcamm@sgul.ac.uk **Address:** Cardiac and Vascular Sciences, St George's University of London, Cranmer Terrace, London SW17 0RE.
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Sequence generation method was not specified.
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No documentation of how randomisation was concealed to participants
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Judgement Comment: Was reported as double-blinded. However no documentation of how treatments were blinded though this would have been possible based on the administration protocol (same volume of infusion & infusion time).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Although blinding process was not documented this would no have no effect on these outcomes as they are completely objective.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Judgement Comment: Conversion of AFL to sinus rhythm was confirmed by members of a Clinical Events Committee (who were blinded to treatment assignment), using the results of the Holter monitor and/or two consecutive 12-lead ECG recordings at least 1 min apart within 90 min of first exposure to study drug.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: As above there was a blinded clinical events comittee for the acute conversion outcome. The other outcomes are also completely objective so not likely to be affected by blinding.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Judgement Comment: No patients who were given the interventions were lost to follow up.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Judgement Comment: Only one patients lost to follow-up (vernakalant arm).
Selective reporting (reporting bias)	Low risk	

		Judgement Comment: Pre-specified end points in the methods section were fully reported. Protocol was published in 2007 in clinicaltrials.gov (i.e. prior to publication of the paper - 2012) which was after recruitment of all participants (finished in 2004). All endpoints mentioned in the published 2007 protocol are available in the 2012 publication. NCT00476112
Other bias	Unclear risk	Clinical trial registration given: NCT00476112 However, this was done in 2007 and according to the register enrolement for the trial was finished in 2004 (i.e. irrefutable evidence of registration, however only after trial enrolment). Approved by the institutional review board at each site.

Channer 2004

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (assisted electrical cardioversion, data taken before electrical cardioversion)
Participants	**Baseline Characteristics** Amiodarone • Age (years) mean (SD): 66 (10) • Male (%): 92 (75) • BMI (Kg/m^2) mean (SD): 30 (5) • Hypertension (%): 53 (43) • Coronary Artery Disease (%): 31 (25) • LA diameter (mm) mean (SD): 44 (7) • LVEF (%) mean (SD): 60 (11) • Digoxin (%): 65 (53) • Beta-Blocker (%): 29 (24) • Calcium Antagonist (%): 19 (15) • Recurrent AF (%): 3 (2) • Duration of AF (months) median (range): 5 (1-84) Placebo • Age (years) mean (SD): 68 (8) • Male (%): 30 (79) • BMI (Kg/m^2) mean (SD): 29 (4) • Hypertension (%): 14 (37) • Coronary Artery Disease (%): 14 (37) • LA diameter (mm) mean (SD): 44 (7) • LVEF (%) mean (SD): 57 (12) • Digoxin (%): 26 (68) • Beta-Blocker (%): 5 (13) • Calcium Antagonist (%): 7 (18) • Recurrent AF (%): 3 (8) • Duration of AF (months) median (range): 6 (1-180) Structural Heart Disease, Valvular Heart Disease, Cardiomyopathy, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure, Pulmonary Disease: N/A Amiodarone, Sotalol, Flecainide, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A AF type: All persistent **Inclusion criteria:** Patients aged over 18 years were recruited if they had sustained AF for more than 72 h. However a minimum of 2 weeks on anticoagulation with warfarin with an INR above 2 was required before randomisation. **Exclusion criteria:** AF due to an acute reversible condition. Echocardiographic exclusion criteria were: left ventricular ejection fraction less than 20%; mitral regurgitation worse than mild; mitral stenosis (valve area less than 2.0 cm^2); aortic stenosis (peak gradient more than 30 mmHg); severe tricuspid regurgitation; or elevated pulmonary artery systolic pressure (greater than 40 mmHg). Other exclusion criteria were: female of childbearing age (taken as under 50 years); previous long-term therapy with or intolerance to amiodarone; previous or active thyroid disease; abnormal liver function tests (a serum alanine aminotransferase concentration more than 2.5 times the upper limit of normal); chronic lung disease (FEV1 less

	than 1L); and any medical condition that would make survival for 1 year unlikely. Patients were not recruited if they had a contraindication to anticoagulation **Numbers:** 172 patients were enrolled. 4 were withdrawn due to protocol violations (2 with iron deficiency where anticoagulation is contraindicated and 2 with active thyroid disease precluding amiodarone therapy). A further 7 withdrew consent after randomisation before direct current cardioversion was performed. 38 patients randomised to placebo were available for analysis and 123 patients randomised to amiodarone (short term and long term post DCCV) were available for analysis. **Anticoagulation:** Patients were anticoagulated with warfarin for 2 weeks prior to randomisation aiming for an INR of greater than 2. **Monitoring:** ECG recording on attendance for electrical cardioversion 2 weeks after randomisation.
Interventions	Oral Amiodarone Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30 day all cause mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** United Kingdom **Setting:** Outpatient **Comments:** Planned outcomes: Planned outcomes were for after DCCV at which point data is not eligible for inclusion in systematic review. Reported outcomes include cardioversion prior to DCCV. Adverse events reported but time frame not given. No trial registration. **Authors name:** Kevin S. Channer **Institution:** Royal Hallamshire Hospital, Sheffield, UK, Sheffield Centre for Health and Related Research, Sheffield, UK, Rotherham District General Hospital, Rotherham, UK, Barnsley District General Hospital, Barnsley, UK, Mid Yorkshire NHS Trust, Wakefield, UK, Calderdale Royal Hospital, Halifax, UK **Email:** Kevin.channer@sth.nhs.uk **Address:** Dr Kevin S. Channer MD FRCP, Consultant Cardiologist, Royal Hallamshire Hospital, Glossop Rd., Sheffield S10 2JF, UK
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not clearly specified: "Patients were assigned their treatment group by a pharmacist using a random number sequence. No blocking or stratification was used."
Allocation concealment (selection bias)	Low risk	Pharmacist may have known the sequence, but based on description it is unlikely that physicians including patients knew. "Subjects recruited to the trial, investigators, and physicians involved in DCCV were blinded to treatment allocation."
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	No specification of how the "matching placebo" looked like and whether posology was the same (two tablets once a day?). "Subjects recruited to the trial, investigators, and physicians involved in DCCV were blinded to treatment allocation."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No specification of methods for blinding of outcome assessors. "Subjects recruited to the trial, investigators, and physicians involved in DCCV were blinded to treatment allocation."

Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes reported for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not assess pre-enrolment protocol to compare reported vs planned outcomes.
Other bias	Unclear risk	Approval by each Institution's Ethics Committee was gained. No evidence of trial registration on a publicly available platform.

Chiladakis 2001

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (Additional phamacological therapy after 6h if no conversion)
Participants	**Baseline Characteristics** Magnesium • Age (mean +/- SD): 61 (6) • Men (%): 12 (52) • Coronary Artery Disease (%): 2 (9) • Pulmonary Disease (%): 1 (4) • Hypertension: 8 (35) • Left Atrial Diameter (mm) (mean +/- SD): 37 (6) • LVEF (%) (mean +/- SD): 60 (9) Placebo (Diltiazem) • Age (mean +/- SD): 64 (4) • Men (%): 13 (57) • Coronary Artery Disease (%): 5 (22) • Pulmonary Disease (%): 1 (4) • Hypertension: 12 (52) • Left Atrial Diameter (mm) (mean +/- SD): 38 (5) • LVEF (%) (mean +/- SD): 59 (10) Valvular Heart Disease, Structural Heart Disease, Stroke/TIA, Heart Failure, Cardiomyopathy, Ischaemic Heart Disease, Myocardial Infarction, Diabetes Mellitus: N/A Beta-blocker, Digoxin, Calcium Antagonist, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A Duration of episode: N/A All patients had paroxysmal AF **Inclusion criteria:** Paroxysmal symptomatic episode of atrial fibrillation of <12h duration and mean ventricular response >100 beats/min **Exclusion criteria:** acute myocardial infarction, severe circulatory failure requiring inotropic agents, hypotension with a systolic blood pressure <90mmHg, electrocardiographic evidence of high-degree atrioventricular block or ventricular preexcitation, a history of sick sinus syndrome or known thyroid disease, pacemaker dependence, severe metabolic disturbances, women in pregnancy, patients on b-blockers, calcium channel blockers, digitalis and anti-arrythmic drugs were also excluded. **Numbers:** 46 patients randomised to 23 magnesium and 23 placebo. No attrition.

	Anticoagulation: Acute anticoagulation was with a bolus and infusion of heparin. No reported post cardioversion protocol. **Monitoring:** with 24 hour Holter during inpatient stay. Follow up duration was at least 6h.
Interventions	Intravenous Magnesium Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Greece **Setting:** Not Clear **Comments:** No conflicts of interest reported. Planned outcomes were Conversion to Sinus Rhythm in 6hr period, Reported outcomes as planned as well as heart rate, and adverse effects. No trial registration. **Authors name:** John A. Chiladakis **Institution:** Patras University Medical School,Cardiology Division, Rio, Patras, Greece **Email:** asm@otenet.gr **Address:** 41 Kourempana Street, Agios Dimitrios, Athens 173 43, Greece
Notes	Intravenous all arms

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No documentation of sequence generation
Allocation concealment (selection bias)	Unclear risk	No documentation of how randomisation allocation was concealed.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	No documentation of blinding
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Even without blinding, there would be no bias with the endpoint acute procedural success.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No documentation of blinding
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Even without blinding, there would be no bias with the endpoint acute procedural success.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No attrition in trial. Endpoints reported for all patients.
Selective reporting (reporting bias)	High risk	

		There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper fails to specify in the methods section all the endpoints that are reported in the results.
Other bias	High risk	No proof of trial registration. The manuscript does not mention protocol reviewal or ethics approval.

Chu 2009

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (clinicians allowed other anti-arrhythmic drugs or DCCV if needed during trial)
Participants	**Baseline Characteristics** Magnesium • Age (mean +/- SD): 47 (15) • Men (%): 19 (79) • Hypertension (%): 2 (8) • Congestive heart failure (%): 0 (0) • Mitral valve disease (%): 0 (0) Placebo • Age (mean +/- SD): 58 (18) • Men (%): 17 (71) • Hypertension (%): 6 (25) • Congestive heart failure (%): 0 (0) • Mitral valve disease (%): 0 (0) Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease, Diabetes Mellitus: N/A Beta-blocker, Calcium antagonists, Digoxin, Flecainide, Sotalol, Amiodarone, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF: N/A BMI: N/A CHA2DS2VASc: N/A All patients had paroxysmal AF **Inclusion criteria:** Patients aged 18 years and older presenting with paroxysmal AF of less than 48 hours' duration, plus a sustained ventricular rate of ‡ 100 beats/min. **Exclusion criteria:** Permanent, paroxysmal, and of more than 48 hours' duration or AF of unknown duration irrespective of whether the patient was anticoagulated. AF with a wide-complex ventricular response.Patients with systolic blood pressure of less than 90 mmHg, acute pulmonary edema, or electrocardiographic evidence of acute myocardial infarction. Patients unable to give consent, including those with an impaired level of consciousness. **Numbers:** Number of people eligible - not reported, the authors state that their aim was to assess every patient presenting with AF for eligibility, but it became evident during the course of the trial that this was not done because of medical and/or nursing staff turnover and/or work logistic reasons.N randomised, N completing treatment, N analysed - 24 for each group. N lost to follow-up - 0 in each group.Follow-up duration - 2 hours; patients lost to follow-up and withdrawals: 0. **Anticoagulation:** No anticoagulation protocol given. **Monitoring:** Method used for rhythm monitoring: cardiac monitor (telemetry) read every 15 minutes for 2 hours. Reports that clinicians could give other anti-arrhythmic drugs or dccv during treatment period.
Interventions	Intravenous Magnesium Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better

	• **Data value**: Endpoint
Identification	**Sponsorship source:** None reported **Country:** Australia **Setting:** Patients admitted to the Emergency department of the University Hospital **Comments:** No information on published protocol/clinical trial register entry trial authors' conflicts of interest. Planned outcomes: sinus rhythm after 2 hours, change in heart rate across 2 hours. Reported outcomes as planned. **Authors name:** Kevin Chu, MBBS, MS **Institution:** Department of Emergency Medicine, Royal Brisbane and Women's Hospital, Brisbane, Queensland **Email:** uqkchu@uq.edu.au **Address:** Royal Brisbane and Women's Hospital, Brisbane, Queensland
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Random allocation sequence was generated by pharmacist who was not involved in the enrolment. However, no description is available on how this was done.
Allocation concealment (selection bias)	Low risk	Random allocation concealment was implemented through the use of serially numbered, tamper-evident envelopes. The envelopes contained study data sheets together with experimental or placebo drug.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Double-blinded. MgSO4•7H2O 10 mmol (2.5 g) or normalsaline (NSal) were prepared in identical vials and inequivalent volumes (5 mL) by the central pharmacy. Their physical appearance was indistinguishable.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Double-blinded. MgSO4•7H2O 10 mmol (2.5 g) or normalsaline (NSal) were prepared in identical vials and inequivalent volumes (5 mL) by the central pharmacy. Their physical appearance was indistinguishable.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Double-blinded study with random allocation concelment implemented by the hospital pharmacist. The nurse caring for the patient read and recorded the heart rate, rhythm, and other vital signs directly from the cardiac monitor onto a study datasheet.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Double-blinded study with random allocation concelment implemented by the hospital pharmacist. The nurse caring for the patient read and recorded the heart rate, rhythm, and other vital signs directly from the cardiac monitor onto a study datasheet.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No attritions or exclusions for outcomes were reported. Endpoints reported for all patients in the Placebo group, and 23/24 in the Magnesium group.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. The manuscript mentions approval by the hospital's Human Research Ethics Committee - Royal Brisbane and Women's Hospital, Brisbane, Australia. Study received funding from the Emergency Medicine Research Foundation, Australia - i.e. Protocol had peer review.

Cotter 1999

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 24h, some cross-over to amiodarone)
Participants	**Baseline Characteristics** Placebo • Age (mean +/- SD): 68 (13) • Men (%): 19 (38) • Ischaemic Heart Disease (%): 19 (38) • Hypertension (%): 31 (62) • Heart Failure (%): 4 (8)

	Amiodarone • Age (mean +/- SD): 65 (14) • Men (%): 24 (48) • Ischaemic Heart Disease (%): 24 (48) • Hypertension (%): 36 (72) • Heart Failure (%): 2 (4) Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus: N/A Beta-blocker, Calcium antagonists, Diuretic, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF: N/A BMI: N/A CHA2DS2VASc: N/A All patients had paroxysmal AF **Inclusion criteria:** Paroxysmal atrial fibrillation lasting less than 48h and if they had at least 1 previous episode of paroxysmal AF. **Exclusion criteria:** severe bradyarrythmia, including significant sinoatrial and atrioventricular node disease, need for emergency cardioversion due to symptomatic hypotension, ischaemia or congestive symptoms, significant chronic lung disease, hepatic failure or active hepatitis, previous recent treatment with amiodarone or known hypersensitivity or significant side effects related to amiodarone, treatment with any class I or III antiarrhythmia drugs, recent treatment with digoxin or acute myocardial infarction in the previous 7 days **Numbers:** 100 patients eligible 50 randomised to placebo and 50 randomised for amiodarone. All patients received 2 doses of IV digoxin prior to randomization. **Anticoagulation:** No prior anticoagulation protocol as pts had AF<48h. No documented post cardioversion anticoagulation **Monitoring:** With continous ECG and 12 lead after cardioversion. Follow up for 24 as inpatients and 1 month as outpatient. As some cross over after 24h, no endpoints after this can be used for systematic review.
Interventions	Intravenous Placebo Intravenous Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local Funding **Country:** Israel **Setting:** Accident and Emergency

	Comments: No conflicts of interest reported. Planned outcomes were: Rate of conversion to normal sinus rhythm during first 24hr and time to conversion. Safety of high dose amiodarone (acute side effects). Heart rate control. Reported ouctomes were as planned. No trial registration. **Authors name:** G Cotter **Institution:** The Assaf Harofeh Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Israel **Email:** not provided **Address:** Dr Cotter at the Cardiology Institute, Assaf-Harofeh Medical Center, Zerifin 70300, Israel
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No documentation.
Allocation concealment (selection bias)	Unclear risk	No documentation how randomisation allocations were provided
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	No documentation of blinding throughout study - would be possible to do due to method of infusions.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Even though there was no documentation of blinding throughout study, these are objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	There is no documentation of blinding of outcome assessors
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Even though there was no documentation of blinding throughout study, these are objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Event rates are provided taking into account all 100 patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Event rates are provided taking into account all 100 patients. Follow-up period of 30 days.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	High risk	No proof of trial registration. The manuscript does not mention protocol review or ethics approval.

Cybulski 2003

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone • Age (years) mean (SD): 61.7 (13.8) • Male (%): 59 (56) • Duration of AF (h) mean (SD): 19.6 (8.1) • Hypertension (%): 55 (52) • Coronary Artery Disease (%): 29 (27) • Digoxin (%): 5 (5) • Beta-Blockers (%): 33 (31) • Diuretics (%): 17 (16) • ACE inhibitors (%): 39 (37) • Calcium antagonists (%): 18 (17) • LA diameter (mm) mean (SD): 42 (8)

	• LVEF (%) mean (SD): 60 (25) Placebo (Magnesium) • Age (years) mean (SD): 61.4 (10.8) • Male (%): 30 (54) • Duration of AF (h) mean (SD): 20.3 (10.2) • Hypertension (%): 29 (54) • Coronary Artery Disease (%): 14 (26) • Digoxin (%): 4 (7) • Beta-Blockers (%): 17 (32) • Diuretics (%): 8 (15) • ACE inhibitors (%): 22 (40) • Calcium antagonists (%): 10 (19) • LA diameter (mm) mean (SD): 41 (9) • LVEF (%) mean (SD): 58 (19) Structural Heart Disease, Cardiomyopathy, Diabetes Mellitus, Pulmonary Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Valvular Heart Disease, Heart Failure: N/A Amiodarone, Sotalol, Flecainide, Propafenone, Aspirin: N/A CHA2DS2VASc: N/A BMI: N/A AF type: All paroxysmal **Inclusion criteria:** Patients with recent onset AF <24h duration. **Exclusion criteria:** : (1) Age <18 years; (2) premenopausal women not using adequate birth control; (3) AF causing significant heart failure (New York Heart Association [NYHA] class > II) or anginal chest pain; (4) acute coronary event during the previous 3 weeks (myocardial infarction, unstable angina, percutaneous transluminal coronary angioplasty, or coronary artery bypass graft); (5) hemodynamically significant valvular heart disease; (6) contraindications to immediate rhythm reversion, such as history of an embolic event in a patient not receiving anticoagulation therapy; (7) Wolff-Parkinson-White syndrome; (8) sick sinus syndrome; (9) baseline systolic blood pressure < 100 mmHg or diastolic blood pressure > 110 mmHg; (10) contraindications to amiodarone: Mean heart rate during AF < 80/min, atrioventricular block, thyroid function disorders (currently treated thyroid disease or clinical symptoms), iodine hypersensitivity/allergy, porphyria, pregnancy, pulmonary fibrosis; (11) amiodarone therapy or prolonged antiarrhythmic therapy with another agent; (12) history of proarrhythmia following administration of drugs prolonging QT interval; (13) electrolyte imbalance (serum potassium < 3.5 mmol/l or/and serum magnesium <1.7 mg/dl; (14) renal or liver insufficiency, suprarenal gland insufficiency, myasthenia gravis; and (15) insulin-dependent diabetes **Numbers:** 160 patients enrolled. 106 randomised to amiodarone and 54 to placebo. No attrition recorded. **Anticoagulation:** No anticoagulation protocol provided, patient population was paroxysmal AF with duration < 24hrs **Monitoring:** Continuous ECG monitoring during therapy. Follow-up over 20 hrs, in order to provide time for electrical cardioversion before risk of atrial thrombosis too high.
Interventions	Intravenous Amiodarone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better

	• **Data value**: Endpoint
Identification	**Sponsorship source:** Study was supported by a grant of the State Committee for Scientific Research No. 4P05B 04914. **Country:** Poland **Setting:** Coronary Care Unit **Comments:** No conflicts of interest reported. Planned outcomes: Not specified but ECG recorded continuously as well as blood pressure. Reported ouctomes: Conversion to sinus rhythm and adverse reactions. No trial registration. **Authors name:** Jacek Cybulski **Institution:** Department of Cardiology, Postgraduate Medical School, Grochowski Hospital, Warsaw; Biegańskiego Hospital, Grudziądz; Dietla Hospital, Kraków; Provincial Hospital, Skierniewice, Poland **Email:** cybulski@kkcmkp.pl **Address:** Jacek Cybulski, M.D., Ph.D. Postgraduate Medical School Department of Cardiology Grochowski Hospital Grenadierów Str. 51/59 04-073 Warszawa, Poland
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization by central telephone assignment in the coordinating centre, but no mention to method.
Allocation concealment (selection bias)	Low risk	Randomization by central telephone assignment in the coordinating centre.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Two infusions used for the drug group, and only one for the controls.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low-risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low-risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not identify pre-enrolment version of the protocol to assess if all planned outcomes were reported.
Other bias	Unclear risk	Approved by the local Ethics Committee. No mention to study protocol publication.

Davey 2005

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Magnesium • Age (mean +/- SD): 71 (15) • Men (%): 46 (45) • Digoxin (%): 14 (14) • Beta-Blocker (%): 11 (11) • Calcium Channel Blockers (%): 2 (2) • Diuretic (%): 13 (13) Placebo • Age (mean +/- SD): 72 (15)

	• Men (%): 45 (46) • Digoxin (%): 12 (13) • Beta-Blocker (%): 9 (9) • Calcium Channel Blockers (%): 4 (4) • Diuretic (%): 25 (27) Valvular Heart Disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus, Heart Failure, Ischaemic Heart Disease: N/A Amiodarone, Sotalol, Flecainide, Propafenone, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF: N/A Study information not allowing accurate categorization into paroxysmal and persistent AF. Info on <24h, >24h and unknown AF duration only. **Inclusion criteria:** Older than 18 years and presenting to the ED with atrial fibrillation and a ventricular response rate greater than 120 beats/min **Exclusion criteria:** Hemodynamic instability defined as: Requirement for cardioversion, Systolic blood pressure<90 mm Hg, Symptomatic hypotensionHistory of renal failureHistory of atrioventricular node disease, including secondary and tertiary atrioventricular block, ‘‘tachy/bradycardia syndrome,’’ but excluding primary atrioventricular block and patients with permanent pacemakersAcute myocardial infarction with ECG criteria for thrombolysis **Numbers:** 199 Patients randomised Magnesium 102, Placebo. 97. 17 patients withdrew from trial (3 with creatinine clearance lower than 30 (1 magneisum, 2 placebo), 2 unkown reasons (1 in each arm), 1 with hypermagnesemia in magnesium arm, 4 with hypotension (3 magnesium, 1 placebo), 5 with minor adverse effects (2 magnesium, 3 placebo) and 2 other (1 each arm) This totals 9 in magnesium and 8 in placebo). **Anticoagulation:** There was no documentation of anticoagulation protocol. **Monitoring:** With continous vital sign monitoring and ECG before treatment and after conversion.Follow up was over 2h inpatient period
Interventions	Intravenous Magnesium Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Australia **Setting:** Accident and Emergency **Comments:** No conflicts of interest reported. Planned Outcomes were: HR <100, Pulse rate change at various intervals. Conversion to sinus Rhythm. Adverse events were collected but no pre-determined significance level was made. Reported outcomes as planned. No trial registration. **Authors name:** Michael Davey **Institution:** Emergency Department, Royal Adelaide Hospital,North Terrace, Adelaide, South Australia **Email:** mdavey@mail.rah.sa.gov.au **Address:** Michael John Davey, MBBS, FACEM, Emergency Department, Royal Adelaide Hospital, North Terrace, Adelaide, South Australia, Australia 5000
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	High risk	Block randomisation of 50 consecutive study numbers as either solution "A" or "B" (this seems to suggest alternation). As the blocks are quite large, after a while it is possible that the investigators started to become aware which patients would be getting drug or placebo.
Allocation concealment (selection bias)	Low risk	Pharmacists not involved in patient enrolment "prepared all solutions and decided which of "A" or "B" was to be the study and which the placebo solutions". Solutions had equivalent volume and perfusion rate.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Patients and personnel were not aware of allocations (double blinded, pharmacy labelled infusions A or B, infusions were identical in administration)
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Patients and personnel were not aware of allocations (double blinded, pharmacy labelled infusions A or B, infusions were identical in administration)
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Physicians and investigators were also blinded to study solutions and the statistical analysis was also performed blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Physicians and investigators were also blinded to study solutions and the statistical analysis was also performed blinded.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	High risk	7 to 8% of patients had missing data regarding outcomes. This was comparable between treatment arms, but being above 5% it can be considered a source of bias.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. The manuscript mentions "approval by the ethics committees of both participating hospitals".

Ellenbogen 1996

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Ibutilide • Age (years) Mean (SD): 64 (11) • Sex (Male) n (%): 69 (88) • Duration of AF (days) mean (SD): 27 (29) • Vavlular Heart Disease (%): 43 (55) • Dilated left atrium (%): 62 (80) • Heart Failure (%): 39 (50) • Digoxin (%): 62 (79) • Beta-blocker (%): 16 (20) • Calcium antagonist (%): 32 (41) • Any Anti-Arrythmic drug (%): 0 (0) • LA diameter (mm) mean (SD): 34 (13) Placebo • Age (years) Mean (SD): 61 (10) • Sex (Male) n (%): 17 (85) • Duration of AF (days) mean (SD): 27 (25) • Vavlular Heart Disease (%): 10 (50) • Dilated left atrium (%): 18 (90) • Heart Failure (%): 6 (70) • Digoxin (%): 12 (60) • Beta-blocker (%): 4 (20) • Calcium antagonist (%): 6 (30) • Any Anti-Arrythmic drug (%): 0 (0) • LA diameter (mm) mean (SD): 40 (12)

	Hypertension, Diabetes Mellitus, Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease: N/A Diuretic, ACE inhibitor, Aspirin: N/A LVEF %, BMI: N/A CHA2DS2VASc: N/A AF type: not clear (mixed population) Only data for Atrial Flutter used. **Inclusion criteria:** A sustained rhythm of atrial flutter of ~3 h duration or atrial librWion (duration 3 h to 90 days), hemodynamic stability during the atrial arrhythmia, with a systolic blood pressure >90 mm Hg, and no symptoms of unstable angina or uncontrolled heart failure.. **Exclusion criteria:** Patients were excluded from the study if they were of childbearing potential or had a myocardial infarction within the preceding 3 months. AU classl or III antiarrhythmic drugs were discontinued for at least 5 half-lives **Numbers:** 200 eligible patients were evaluated and 197 were randomised; 157 to ibutilide and 40 to placebo (78 flutter to ibutilide and 20 to placebo). 2 patients recieved incorrect doses of ibutilide and 1 did not have an arrhythmia before drug administration. **Anticoagulation:** Protocol was for ≥ 2 weeks if arrhythmia duration was ≥ 3 days. **Monitoring:** With continuous 3 lead ECG during infusion and then single lead after until 24h had elapsed. Cross over after second infusion means that data after this cannot be used for this systematic review.
Interventions	Intravenous Ibutilide Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local and support form a grant form the Upjohn Company Kalamazoo, Michigan **Country:** United States of America **Setting:** Unclear **Comment:** No conflicts of interest reported. Planned Outcomes: Not specified but to determine efficacy and to measure dose response for conversion of atrial arrhythmia to sinus rhythm. Reported outcomes: Conversion to sinus rhythm, time to conversion, ECG changes of QRS and QT inteval, Adverse outcomes. No trial registration. **Author's Name:** Kenneth Ellenbogen **Institution:** Department of Medicine, Medical College of Virgina and McGuire Veterans Affairs Medical Center, Richmond, Virgina; University of California at Los Angeles and Wadsworth Veterans Affairs Medical Center, Los Angeles, California; Long Beach Veterans Affairs Medical Center, Long Beach, California; Wayne State University Medical Center and the Allen Park Veterans Affairs Medical Center, Allen Park, Michigan; University of Florida, Tampa, Florida; Upjohn Company, Kalamazoo, Michigan. **Email:** not provided **Address:** GDr Kenneth A. Ellenbogen, Medical College of Virgina, P.O. Box 980053, Richmond, Virgina 23298-0053
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Study was labellet as double-blind and infusion was similar for placebo and ibutilide group (10min iv for each).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Study was labellet as double-blind and infusion was similar for placebo and ibutilide group (10min iv for each). Objective endpoint.

Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Study was labelled as double-blind but no information performed on whether outcome assessors where blinded (and how this was done)
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoint - sinus rhythm.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Study protocol was approved by the Institutional review board of each investigators hospital. No evidence of publication of study protocol prior to start of trial.

Fak 1997

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone Data not split by arm Placebo Data not split by arm Patients with AF 48 (80%), Patient with Atrial flutter 12 (20%). Definitions for acute and chronic arrhythmia given as greater or less than 72hrs duration **Inclusion criteria:** Patients (> 18 years) with new or late onset chronic or paroxysmal atrial fibrillation, and flutter were eligible for the study. **Exclusion criteria:** 1) history of myocardial infarction within I month, 2) systolic blood pressure < 90 mm Hg at presentation, 3) acute pulmonary edema, 4) symptoms or signs of digitalis toxicity, 5) any previously documented or suspected conduction disturbances of more than first-degree AV block (excluding bundle branch blocks) or spontaneous heart rate < 70 beats/min at presentation, 6) hyperthyroidism, 7) severe obstructive pulmonary disease, 8) Wolf-Parkinson-White syndrome, and 9) clinically important liver or renal disease or electrolyte imbalance. Atrial fibrillation patients with a known or suspected arrhythmia duration of more than 72 hours were included in the study after an oral anticoagulation period of 3-4 weeks. **Numbers:** 66 patients were enrolled. 3 converted to sinus rhythm after consent. 30 patients randomised to each arm. However proportions of patients by arrhythmia type not given by arm. **Anticoagulation:** Patients were anticoagulated orally for 3-4 weeks before inclusion if they had arrhythmia duration more than 72hrs. **Monitoring:** Continuous ECG monitoring for 1 hour after drug administration. After 60 minutes if there was no conversion the other drug was given.
Interventions	Intravenous Propafenone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Endpoints after cross-over cannot be included.
Identification	**Sponsorship source:** Local **Country:** Turkey **Setting:** Unclear

	Comments: Planned outcomes: Conversion to sinus rhythm within 60 minutes of infusion Reported outcomes: All planned outcomes. No trial registration. **Authors name:** Ali Serdar Fak **Institution:** Cardiology and Pharmacology Departments, Marmara University School of Medicine, Istanbul, Turkey **Email:** not provided **Address:** Prof. Ahmet Oktay, MD, Marmara, Üniversitesi Hastanesi, Kardiyoloji Anablilim Dali, Altunizade 81190 Istanbul Turkey
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details provided on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No details on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Drug and Placebo had same infusion protocol and patient is reported as blind (single-blind). No information on methods of blinding for personell.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No details on blinding attempts for outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Selective reporting (reporting bias)	Unclear risk	No protocol was available prior to the study publication and hence not able to assess if all planned outcomes were reported.
Other bias	Unclear risk	Study protocol was approved by the Institution's Ethics Committee. No proof of prior protocol registration/publication. No information provided on study baselines across treatment groups.

Falk 1997

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (Further dofetilide if no cardioversion after 1hr)
Participants	**Baseline Characteristics** Dofetilide • Age (mean): 64 • Men (%): 55 (90) • Myocardial Infarction (%): 9 (15) • Hypertension (%): 30 (49) • Heart Failure (%): 30 (49) • Cardiomyopathy (%): 14 (23) • Left Atrial Diameter (mm) (mean): 45 • Valvular Heart Disease (%): 3 (5) • Atrial Flutter (%): 11 (18) • Duration of episode (months) mean (range): 2 (0.5-6.8) Placebo • Age (mean): 67 • Men (%): 22 (73)

	• Myocardial Infarction (%): 6 (20) • Hypertension (%): 14 (47) • Heart Failure (%): 7 (23) • Cardiomyopathy (%): 6 (20) • Left Atrial Diameter (mm) (mean): 45 • Valvular Heart Disease (%): 3 (10) • Atrial Flutter (%): 5 (17) • Duration of episode (months) mean (range): 2.6 (0.5-7.9) Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Ischaemic Heart Disease, Coronary Artery Disease, Diabetes Mellitus: N/A Beta-blocker, Digoxin, Amiodarone, Sotalol, Propafenone, Flecainide, Calcium antagonists, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LVEF %: N/A Approximately 80% of patients had persistent AF and the rest with flutter. **Inclusion criteria:** Atrial fibrillation or atrial flutter lasting from 2 weeks to 6 months. Ventricular rate > 70 beats bpm Minimum of 2 weeks anticoagulation **Exclusion criteria:** All antiarrhythmic drugs, as well as diltiazem, verapamil and beta-adrenergic blocking agents were withdrawn for at least 5 half-lives before study drug administration, and subjects receiving drugs that may prolong the QT interval, such as antidepressants or phenothiazines, were excluded. Serum potassium concentrations were required to be within the range 4.0 to 5.5 mEq/liter and serum magnesium 1.5 to 2.5 mEq/liter. Subjects.75 years old, women of childbearing potential, patients with pre-excitation syndromes and those with uncontrolled hypertension were excluded, as were Patients with previous electrocardiographic(ECG) documentation of high degree atrioventricular block(unless protected by a permanent pacemaker), those with a QRS duration >= 180 ms or a QT interval>500 ms **Numbers:** 91 patents randomised 30 to placebo 32 to 4micrograms/kg Dofetilite and 29 to 8 micrograms/Kg dofetilide. The two different dofetilide doses and outcomes were combined for this analysis. There was no attrition. **Anticoagulation:** Minimum of 2 weeks prior to cardioversion, no post cardioversion protocol is given. **Monitoring:** With continuous ECG monitoring and patients were followed up for an additional 6hours after the infusion had finished. C
Interventions	Intravenous Dofetilide Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local Funding **Country:** United States of America **Setting:** Elective Admission

	Comments: No conflicts of interest reported. Planned outcomes were conversion to normal sinus rhythm, dofetilide levels and adverse events. Reported outcomes were also as planned. No trial registration. **Authors name:** Rodney H. Falk **Institution:** Division of Cardiology, Boston Medical Center, Boston, Massachusetts **Email:** rfalk@bu.edu **Address:** Dr. Rodney H. Falk, Division of Cardiology, Boston Medical Center, 1 Boston Medical Center Place, Boston, Massachusetts 02118
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	All infusions were identical in duration, this would make it easy to blind to both patients and investigators. It is mentioned that neither patients or investigators were aware of the identify of the therapy. However, there is no information describing the process.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	All infusions were identical in duration, this would make it easy to blind to both patients and investigators. It is mentioned that neither patients or investigators were aware of the identify of the therapy. These are objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	It is reported as double blind and the set up of the protocol does make it possible for the investigators to be blind to the allocations. However, no data is provided regarding outcome assessment.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	It is reported as double blind and the set up of the protocol does make it possible for the investigators to be blind to the allocations. These are objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Unclear risk	Unsure about reporting of adverse events, as no % is provided, only number of cases with no indication of total number of assessed patients. Some concern about quality of records and missing some events - e.g. 3 patients developped intermittent runs of broad complex tachycardia. Out of those 3 patients, only 1 had ECG tracings allowing proper analyses. For the acute procedural success endpoint data on all patients was available.
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper fails to specify in the methods section all the endpoints that are reported in the results.
Other bias	Unclear risk	No proof of trial registration. The manuscript mentions approval by the institution review board.

Fresco 1996

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age: 56.1 • Male (%): 22 (53.8) • LVEF %: 60.1 • LA diameter (mm) mean: 40.4 • LVEF (%) mean: 60.1 • Any Antiarrythmic drug (%): 0 (0) Placebo • Age (sd): 51.0 • Male (%): 28 (82.4) • LVEF %: 69.1 • LA diameter (mm) mean: 38.9

	• LVEF (%) mean: 69.1 • Any Antiarrythmic drug (%): 0 (0) Hypertension, Diabetes Mellitus, Valvular Heart Disease, Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease: N/A Beta-blocker, Calcium antagonist, Digoxin, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A BMI: N/A Duration of episode: N/A AF type: All patients had paroxysmal AF. **Inclusion criteria:** Recent onset AF defined as <72h **Exclusion criteria:** Age >70 years, clinical heart failure, recent (<6 months) acute myocardial infarction, Wolff-Parkinson-White syndrome, atrioventricular block, heart rate <70 beatdmin, current treatment with antiarrhythmic agents or digitalis, hyperthyroidism. **Numbers:** 75 patients recruited, 41 to propafenone and 34 to placebo. None lost follow up. **Anticoagulation:** No anticoagulation protocol as recent onset AF (although defined as <72h). **Monitoring:** Rhythm monitoring method not defined. Follow up duration 3h.
Interventions	Intravenous Propafenone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Unclear **Comments:** No conflict of interest reported. Planned outcomes: Conversion to sinus rhythm in 3h and reduction in heart rate in non responders. Reported outcomes: as above including some adverse events. No trial registration. **Authors name:** Claudio Fresco **Institution:** Istittito di Cardiologia Ospcdale S. Maria della Misericordia **Email:** not given **Address:** Claudio Fresco. M.D. Istituto di Cardiologia Ospcdale S. Maria della Misericordia Via Pieri *2* 33100 Udine, Italy
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	not specified
Allocation concealment (selection bias)	Unclear risk	Investigators were provided with numbered boxes - content unknown - and asked to provide boxes with starting with the lowest identification number. Unclear if boxes were opaque or if there was a way to predict what was inside (and hence what would be assigned to the next included patient).
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study reported as double-blind. Same volume of administered infusion was given, but for propafenone there was a change in infusion rate (not mentioned for placebo).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Endpoints are objective. Unlikely to be influenced.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Study reported as double-blind but no information was provided on outcome assessment process.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcome. No likely to be influenced.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	High risk	High likelihood of issues with randomization as 4 out of 13 reported baseline variables different significantly across treatment groups. No mention to Ethics approval or evidence of trial registration.

Galperín 2001

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (assisted electrical cardioversion, data taken before electrical cardioversion)
Participants	**Baseline Characteristics** Amiodarone • Age (years) mean (SD): 61.63 (7.52) • Male (%): 30 (64) • Hypertension (%): 22 (47) • Valvular Heart Disease (%): 14 (28) • Structural Heart Disease (%): 43 (91) • Cardiomyopathy (%): 7 (15) • Coronary Artery Disease (%): 4 (9) • LA diameter (mm) mean (SD): 37 (9) • Duration of episode (months) mean (SD): 35.73 (50.77) Placebo • Age (years) mean (SD): 65.10 (5.51) • Male (%): 39 (81) • Hypertension (%): 27 (56) • Valvular Heart Disease (%): 6 (13) • Structural Heart Disease (%): 47 (98) • Cardiomyopathy (%): 7 (15) • Coronary Artery Disease (%): 7 (15) • LA diameter (mm) mean (SD): 38 (8) • Duration of episode (months) mean (SD): 35.52 (33.05) Structural heart disease, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure, Pulmonary Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LVEF %: N/A CHA2DS2VASc: N/A

	AF type: all persistent **Inclusion criteria:** Patients with chronic atrial fibrillation lasting from 2 months to more than 10 years **Exclusion criteria:** age older than 75 years; paroxysmal atrial fibrillation (AF); acute myocardial infarction in the last 6 months; PR interval less than 0.24 seconds; second or third degree AV block in ECG recordings obtained before AF occurrence unless a permanent pacemaker was implanted; spontaneous heart rate of less than 50 beats per minute; history of sinus node disease without implanted pacemaker; QTc interval of less than 0.50 seconds; hypothyroidism or hyperthyroidism; pregnancy; impossibility to follow-up for any reason; comorbidities conditioning the short-term prognosis; **Numbers:** 95 patients enrolled. 47 randomised to amiodarone and 48 to placebo. No attrition reported. **Anticoagulation:** All patients anticoagulated for 3 weeks to an INR between 2 and 3 prior to randomisation. **Monitoring:** ECG at 30 days at which point patients would be due for electrical cardioversion if not cardioverted already.
Interventions	Oral Amiodarone Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism at 30 days • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day all cause mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local and part from GEMA and the Fundación de Investigaciones Cardiológicas Einthoven **Country:** Argentina **Setting:** Outpatient **Comments:** Planned outcomes: To assess efficacy of amiodarone alone or with electrical cardioversion for restoration of sinus rhythm and prevention of recurrence. However detailed outcome measurements not specified. Reported outcomes: Conversion to sinus rhythm at 30d, outcomes after this date cannot be included in systematic review. **Authors name:** Jorge Galperín **Institution:** Hospital Durand, Buenos Aires, Hospital Ramos Mejía, Buenos Aires, IInstituto del Corazón, Córdoba, G.E.M.A. Grupo de Estudios Multicéntricos Argentinos, Hospital de Clinicas, Buenos Aires, Argentina. **Email:** Not provided **Address:** Jorge Galperín, MD, Lafinur 2932-8 A, Buenos Aires-1425, Argentina.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No specification of method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No specification if any allocation concealment method was used.

Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	No description of methods for blinding of study personel and participants. No explanation on the nature and posology of placebo.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No specification of method for blinding outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all participants.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes reported for all participants for >30 days
Selective reporting (reporting bias)	Unclear risk	Could not assess pre-enrolment copy of protocol, and hence could not confirm if planned outcomes and reported outcomes overlapped.
Other bias	Unclear risk	Ethics approval gained by all participant hospitals. No proof of trial registration in publicly available platform.

Ganau 1998

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD): 59 (13) • Male (%): 25 (52) • Hypertension (%): 34 (42) • Diabetes Mellitus (%): 9 (11) • Duration of Episode (min) mean (SD): 486 (755) Placebo • Age (years) mean (SD): 57 (11) • Male (%): 26 (53) • Hypertension (%): 23 (32) • Diabetes Mellitus (%): 5 (7) • Duration of Episode (min) mean (SD): 489 (741) Structural Heart Disease, Valvular Heart Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure, Cardiomyopathy, Coronary Artery Disease, Pulmonary Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A AF type: All persistent AF **Inclusion criteria:** 1) patients arriving at the ED suffering from AF with a ventricular rate ≥ 110 beats/min; 2) AF symptoms (mainly palpitations) complained of by the patient for ≤ 72 h; 3) patients aged between 18 and 80 years; 4) patients with systolic blood pressure ≥ 110 mmHg; 5) availability, on admittance to the ED, of electrocardiographics (EKG) documentation of AF. **Exclusion criteria:** 1) refusal to give informed consent; 2) clinical evidence of acute or chronic congestive heart failure (lung rales and peripheral edema); 3) history of bronchial asthma or other severe respiratory disease; 4) history of severe hepatic or renal disease; 5) clinical hyperthyroidism; 6) myocardial infarction (in the previous 3 months); 7) bifascicular heart block or QRS width greater than 0.10 s; 8) known cardiac valve dysfunction; 9) presence of a prosthetic cardiac valve; 10) known sinoatrial node disease; 11)

	digitalis therapy; 12) antidysrhythmic therapy (including non-di-hydropiridinic calcium channel blockers, b-blockers, and digitalis) administered in the last 12 h; and 13) chronic amiodarone therapy. **Numbers:** 156 patients enrolled. 81 randomised to propafenone and 75 to placebo. No attrition reported. **Anticoagulation:** No anticoagulation protocol as arrhythmia classified as paroxysmal. **Monitoring:** Continous ECG monitoring and 12 lead ECG every 15 minutes for at least 2 hours. Follow up end when discharged from ED or admitted to hospital.
Interventions	Intravenous Propafenone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Emergency Department **Comments:** No conflicts of interest reported. Planned outcomes: Rate of conversion to sinus rhythm, time to conversion, changes from baseline ventricular rate and other ECG parameters, changes in blood pressure and signs of low cardiac output. Reported outcome: As planned and adverse events. No trial registration. **Authors name:** Gianfranco Ganau **Institution:** Emergency Department, Ospedale Civile, Sassari, Italy, and Emergency Department, Ospedale “M. Bufalini,” Cesena, Italy **Email:** Not provided **Address:** Tiziano Lenzi, Servizio di Pronto Soccorso-Medicina D’Urgenza, Ospedale “M. Bufalini,” Viale Ghirotti, 286–47023 Cesena, Italy
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention to method of randomization / how the sequence was obtained. "The randomization was performed by the centers on the basis of an ad hoc list (one for each center) generated by means of a specific software and guaranteeing that the groups were balanced every six patients."
Allocation concealment (selection bias)	Unclear risk	No specification of method (if any) for allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Mention to study being single-blind. Similar infusion protocol was used for both groups which means that patients were blinded. Unsure about methods for blinding of personell.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.

Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to blindind method (if any) for outcome assessors).
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes assessed for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not assess the pre-enrolment protocol to assess if all planned outcomes were assessed.
Other bias	Unclear risk	Study approved by the Scientific and Ethics Committees. No proof of prior protocol registration.

Halinen 1995

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (cardioversion at 12 hours with electrical or pharmacological method)
Participants	**Baseline Characteristics** Sotalol • Age (mean +/- SD): 54.9 (12.7) • Men: 21 (64) • Drinking Alcohol before Onset: 7 (21.2) • Myocardial Infarction: 2 (6.1) • Hypertension: 11 (33.3) • Angina Pectoris: 3 (9.1) • On Digoxin: 5 (15.2) • On Beta-Blocker: 6 (18.2) • On Verapamil/Diltiazem: 4 (12.1) • On Diuretic: 1 (3) • Valvular Heart Disease: 1 (3) • Other PMHx: 2 (6.1) • Duration of AF before Randomisation: 12.4 (10.8) Quinidine • Age (mean +/- SD): 53.2 (15.3) • Men: 19 (68) • Drinking Alcohol before Onset: 4 (14.2) • Myocardial Infarction: 3 (10.7) • Hypertension: 12 (42.9) • Angina Pectoris: 7 (25) • On Digoxin: 1 (3.6) • On Beta-Blocker: 13 (46.4) • On Verapamil/Diltiazem: 3 (10.7) • On Diuretic: 8 (28.6) • Valvular Heart Disease: 1 (3.6) • Other PMHx: 1 (3.6) • Duration of AF before Randomisation: 11.8 (11.5) Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Ischaemic Heart Disease, Coronary Artery Disease, Diabetes Mellitus: N/A Amiodarone, Flecainide, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF: N/A CHA2DS2VASc: N/A All patients had paroxysmal AF.

	Inclusion criteria: Recent onset of AF lasting <48 hours and subject to acute pharmacological cardioversion **Exclusion criteria:** Exclusion criteria were age <18 or >75 years; heart rate ~80 beats/min; systolic blood pressure ~120 mm Hg; clinical or radiologic signs of heart failure; chest pain with or without electrocardiographic changes suggesting acute myocardial infarction or unstable angina; history of bradyarrhythmia or sick sinus syndrome with significant bradyarrhythmia; and treatment with class I antiarrhythmic drugs. **Numbers:** N randomised = 61, 33 to Sotalol and 28 to Quinidine. In the Sotalol group 1 patient discontinued by request before administration and 1 due to symptoms of dyspnoea and hypotension before dose. Also 3 patients did not get ambulatory ECG in the sotalol group and 2 in the quinidine group. **Anticoagulation:** The patient population was recent onset AF <48h so there was no pre-specified anticoagulation protocol. There was no post cardioversion anticoagulation protocol. **Monitoring:** With continuous ambulatory ECG. Patients were discharged home after >3 hours of observation if successful cardioversion, otherwise kept for 12 hours before DCCV was scheduled.
Interventions	Oral Sotalol Oral Quinidine
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** The study was supported in part by the Bristol-Myers Squibb Company, Helsinki, Finland. **Country:** Finland **Setting:** Accident and emergency departments of Kuopio University Hospital, Central Hospital of Mikkeli, and Central Hospital of Savonlinna **Comments:** No reported conflict of interest, although there was an industry grant. Planned outcomes: The conversion of AF to sinus rhythm was the primary end point; The time of rhythm change; Possible adverse effects and proarrhythmia; occurrence of ventricular and supraventricular arrhythmia; and delay from admission to discharge from the hospital. Reported outcomes were the same. No trial registration. **Authors name:** Matti O. Halinen **Institution:** Departments of Medicine, Kuopio University Hospital, Kuo pio; Savonlinna Central Hospital, Savonlinna; and Mikkeli Central Hospital, Mikkeli, Finland. **Email:** Not Provided **Address:** Accident and Emergency Department, Kuo pio University Hosprtal, P.O.B. 1777, FIN-702 1 1 Kuopio, Finland.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No documentation of sequence generation
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias)	High risk	Medication administered in a way which makes blinding impossible, different amount of infusions and tablets given.

All other outcomes		One treatment group involved IV drug (depending on heart rate) + oral whereas the other group involved oral drug only.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as acute conversion to sinus rhythm is a very objective endpoint. The other endpoints were not reported.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information on an event adjudication committee, but as these were emergency department patients. It is possible that most of (or all) the events were adjudicated by the treating physicians, who likely knew what drug the patients were being given.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as acute conversion to sinus rhythm is a very objective endpoint. The other endpoints were not reported.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	High risk	Originally supposed to be 260 patients. An unplanned interim analysis after 60 patients because of suspected low efficacy, interrupted the trial. Also, "because of technical failure, the ambulatory electrocardiogram was not available in 3 patients in the Sotalol group (nearly 10%) and in 2 (7%) in the Digoxin group", which means that for some rhythm related outcomes (e.g. ventricular tachycardia or pronounced bradycardias) there was a significant portion of missing data (>5%)
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. The manuscript mentions approval by the ethics committee of the participating hospitals - Kupoio Universital Hospital, Central Hospital of Mikkeli and Central Hospital of Savonlinna (Finland).

Hohnloser 1995

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 7 days without response)
Participants	**Baseline Characteristics** Sotalol • Age (years) mean (SD): 60 (10) • Male (%): 8 (32) • Cardiomyopathy (%): 2 (8) • Hypertension (%): 4 (16) • Valvular Heart Disease (%): 6 (24) • Coronary Artery Disease (%): 9 (36) • Duration of Episode (days) mean (SD): 49 (63) Quinidine • Age (years) mean (SD): 65 (13) • Male (%): 10 (40) • Cardiomyopathy (%): 2 (8)) • Hypertension (%): 6 (24) • Valvular Heart Disease (%): 8 (32) • Coronary Artery Disease (%): 6 (24) • Duration of Episode (days) mean (SD): 39 (48) Structural Heart Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure, Diabetes Mellitus: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A AF type: AF type not split as chronic/persistent AF is defined as a duration greater than 48 hours. **Inclusion criteria:** Patients with chronic atrial fibrillation referred to arrythmia services with following critieria 1) age 18 to 80 years; 2) ECG documented persistent atrial fibrillation with a continuous duration between 48 h and 6 months; 3) symptoms such as palpitation, dyspnea, chest pain or light-headedness in association with atrial fibrillation; 4) provision of informed consent.

	Exclusion criteria: 1) acute myocardial infarction <4 weeks before entry in the study; 2) unstable angina pectoris; 3) congestive heart failure of New York Heart Association class IV; 4) uncorrected electrolyte disturbances (e.g., serum potassium <4.0 mEq/liter or magnesium <1.5 mEq/liter); 5) chronic obstructive pulmonary disease; 6) compromised renal function (i.e., serum creatinine >1.8 mg/dl); 7) hepatic insufficiency; 8) hyperthyroidism; 9) previous treatment with quinidine or sotalol; 10) concomitant therapy with other class I to IV antiarrhythmic agents **Numbers:** 50 patients enrolled, 25 randomised to quindine and 25 to sotalol. No attrition is documented. **Anticoagulation:** Patients were anticoagulated with warfarin to a target of partial thromboplastin time adjusted to 2 times upper limit of normal for more than 8 days before cardioversion. Anticoagulation was continued for 4 weeks after cardioversion and continuous if no response to therapy. **Monitoring:** 24 hour ambulatory ECG monitoring before enrollment. Rest ECGs 2hrs after first dose ant ehn daily therafter. Then a repeat 24 hour monitor on restoration of sinus rhythm or day 7 if no response after which patients had DCCV. Patients were followed up at outpatient clinic at 2 and 6 months
Interventions	Oral Sotalol Oral Quinidine
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 1 week complications • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported

	• **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Supported by research grant from Bristol-Myers Squibb, Munich, Germany **Country:** Germany **Setting:** Inpatient loading phase and outpatient follow up. **Comments:** Planned outcomes: Conversion to sinus rhythm, and maintenance of sinus rhythm. However specifics of outcome measurement not reported. Drug related pro-arrhtyhmic reactions and ECG changes. Reported outcome: As planned. No trial registration. **Authors name:** Stefan Hohnloser **Institution:** Department of Cardiology, University Hospital, Freiburg, Germany. **Email:** Not provided **Address:** Dr. Stefan H. Hohnloser, Department of Medicine, Division of Cardiology, J. W. Goethe University, Theodor-Stern-Kai 7, 60590 Frankfurt. 120 Germany
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information on method of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Patients treated with quinidine also received verapamil, and patients on sotalol only received sotalol. Hence, patients and personnel would know which treatment arm.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to methods (if any) for blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Follow-up obtained for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Follow-up obtained for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not identify a pre-published version of the protocol, hence unsure if all planned outcomes were reported.
Other bias	High risk	Could not identify proof of protocol registration. No mention to Ethics approval.

Jakobsson 1990

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA MDS Incremental Paddles • Age (years) mean (SD): 60 (8) • Male (%): 9 (60) • Digoxin (%) : 12 (80)

	• Duration of episode (months) median (range): 5 (1-18) AA MDS Incremental Patches • Age (years) mean (SD): 59 (7) • Male (%): 9 (81) • Digoxin (%) : 10 (91) • Duration of episode (months) median (range): 4 (1-8) Structural Heart Disease, Valvular Heart Disease, Cardiomyopathy, Hypertension, Pulmonary Disease, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Diabetes Mellitus: N/A Beta-blocker, Calcium antagonist, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LA dimensions and LVEF %: N/A **Inclusion criteria:** Consecutive patients planned fro elective cardioversion. **Exclusion criteria:** None reported **Numbers:** 26 patients Eligible for study, 15 patients to paddle arm and 11 patients to adhesive patch arm. No attrition reported. **Anticoagulation:** No anticoagulation protocol reported. **Monitoring:** ECG recorded before and after each shock up to 4 times (4 shocks maximum). Obsevation period after treatment 24h.
Interventions	AA MDS Incremental Paddles AA MDS Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Sweden **Setting:** Elective Admission **Comments:** Planned outcomes: Assessment of conversion rate, energy requirement, and enzyme release as indicator of muscle damage. Reported outcome: As planned and other adverse events. No trial registration. **Authors name:** J. Jakobsson

	Institution: Department of Anaesthesiology, Danderyds Hospital and Division of Cardiology. Department of Medicine, Karolinska Hospital, Karolinska Institute& Stockholm (Sweden) **Email:** Not provided **Address:** J. Jakobsson, Department of Anaesthesiology and Intensive Care, Danderyds Hospital, S-182 88 Danderyd, Sweden.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Paper mentions randomization according to date of birth, suggesting quasirandomized design.
Allocation concealment (selection bias)	High risk	No information on allocation concealment, however high risk as predictable - based on year of birth.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Patients under sedation - unsure if blinded. Personnel not blinded to treatment arm.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information on whether (and how) the outcome assessors were blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Selective reporting (reporting bias)	Unclear risk	As no pre-publication protocol could be identified, we could not confirm if all planned outcomes were reported.
Other bias	Unclear risk	Study was approved by the Local Ethics committee. No proof of prior Protocol Registration.

Joseph 2000

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone • Male n (%): 25 (64.10) • Age (Years) Mean (SD): 61.3 (2.6) • Hypertension n (%): 5 (12.82) • Structural Heart Disease n (%): 21 (53.85) • Ischaemic Heart Disease n (%): 8 (20.51) • Valvular Heart Disease n (%): 3 (7.69) • LADD (mm) mean (SD): 39.7 (1.1) • LVEF <50% n (%): 8 (20.51) • Cardiomyopathy n (%): 5 (12.82) Placebo (Digoxin) • Male n (%): 20 (55.56) • Age (Years) Mean (SD): 64.9 (2.0) • Hypertension n (%): 10 (27.78) • Structural Heart Disease n (%): 18 (50.00) • Ischaemic Heart Disease n (%): 3 (8.33) • Valvular Heart Disease n (%): 4 (11.11) • LADD (mm) mean (SD): 39.5 (1.0) • LVEF <50% n (%): 6 (16.67) • Cardiomyopathy n (%): 1 (2.78) Sotalol • Male n (%): 19 (47.50) • Age (Years) Mean (SD): 62.8 (2.4) • Hypertension n (%): 6 (15)

	• Structural Heart Disease n (%): 14 (35.00) • Ischaemic Heart Disease n (%): 7 (17.5) • Valvular Heart Disease n (%): 1 (2.5) • LADD (mm) mean (SD): 38.4 (1.0) • LVEF <50% n (%): 6 (15.00) • Cardiomyopathy n (%): 0 Stroke/TIA, Pulmonary disease, Coronary Artery Disease, Diabetes Mellitus, Myocardial Infarction, Heart Failure: N/A Beta blocker, Calcium Antagonist, Propafenone, Flecainide Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A All patients had paroxysmal AF. **Inclusion criteria:** AF onset within 24 h Consent obtained Serum K+>3.5 mmol/L and <5.5 mmol/L Serum creatinine <0.2 mmol/L **Exclusion criteria:** AF present within 7 d and >24 h No consent Serum K+<3.5 mmol/L and >5.5 mmol/L Serum creatinine >0.2 mmol/L Current β-blocker treatment Digoxin or sotalol treatment in last week Amiodarone treatment within 3 months Hypotension (MAP <70 mm Hg) Previous adverse reaction to any of trial medications Known thyroid disease Asthma/bronchospasm with β-blocker Wide-complex tachycardia Contraindication to anticoagulation Age <18 y Left ventricular dysfunction Pregnancy **Numbers:** 120 patients were enrolled and 5 had protocol violations (4 in placebo/digoxin arm and 1 in amiodarone arm). 36 were randomised to placebo, 39 to amiodarone and 40 to sotalol. No further attrition reported. **Anticoagulation:** Patients started on IV heparin after 24 hours if no cardioversion. Aim to achiever APTT of 2.0 to 2.5 times control and then subsequent DCCV at 48 hours if anticoagulation targets mainatined. No prior anticoagulation as duration of episode < 24h. **Monitoring:** Continuous ECG monitoring throughout 48 hour period.
Interventions	Intravenous Amiodarone Intravenous Placebo Intravenous Sotalol
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local Funding **Country:** Australia **Setting:** Accident and Emergency

	Comment: No conflicts of interest reported. Planned outcomes: Time of conversion to sinus rhythm, adverse events, ventricular rate at 4, 24, and 48hrs. Reported outcomes as above. No trial registration. **Author's Name:** Anthony P. Joseph **Institution:** Department of Emergency Medicine, Royal North Shore Hospital **Email:** toseph@med.usyd.edu.au **Address:** Anthony P. Joseph, MB BS, Department of Emergency Medicine, Royal North Shore Hospital, Pacific Highway, St. Leonards, New South Wales, 2065, Australia; 61-2-9926-7922
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The randomization process was computer-generated and administered centrally. However, no details are provided on the process.
Allocation concealment (selection bias)	High risk	For the first 85 patients, physicians knew which drug would be used before enrolling a patient: "The process was open, with the study drug known to the treating physicians. However, after the enrolment of 85 patients, the investigators believed it was preferable to blind the treating physicians to the selected drug until inclusion and exclusion criteria were met, and consent obtained"
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Posologies were different across different treatment arms allowing identification of allocated drug. Also, the manuscript specifies that there was no blinding of physicians for at least 85 patients (but based on the descrition there was no blinding for physicians after treatment allocation): "The process was open, with the study drug known to the treating physicians. However, after the enrolment of 85 patients, the investigators believed it was preferable to blind the treating physicians to the selected drug until inclusion and exclusion criteria were met, and consent obtained"
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Even though there was no blinding, Acute success if a very objective endpoint. There other 2 endpoints were not reported.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	Treating clinicians were aware of the treatment group at enrolment
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Even though there was no blinding, Acute success if a very objective endpoint. There other 2 endpoints were not reported.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	High risk	5 patients were excluded due to protocol violation. These were unequally distributed across the 3 treatment arms: 0 in the sotalol group, 1 (2.5%) in the amiodarone group and 4 (10%) in the digoxin group.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. The manuscript mentions approval of the protocol by the Medical Ethics Review Committee of the participating hospitals - Royal North Shore Hospital, Sidney; University of Sidney, New South Wales, Australia.

Kanoupakis 2003

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (assisted electrical cardioversion, data taken before electrical cardioversion)
Participants	**Baseline Characteristics** Amiodarone • Age (years) mean (SD): 64 (8) • Male (%): 28 (58) • Hypertension (%): 17 (35) • Valvular Heart Disease (%): 6 (13) • Coronary Artery Disease (%): 5 (10) • Digoxin (%): 17 (35) • LA diameter (mm) mean (SD): 43 (4)

	• LVEF (%) mean (SD): 58 (6) • Duration of episode (months) mean (SD): 10 (12) Placebo (Carvedilol and Placebo pill) • Age (years) mean (SD): 64 (10) • Male (%): 56 (60) • Hypertension (%): 30 (32) • Valvular Heart Disease (%): 8 (9) • Coronary Artery Disease (%): 10 (11) • Digoxin (%): 25 (27) • LA diameter (mm) mean (SD): 43 (5) • LVEF (%) mean (SD): 57 (8) • Duration of episode (months) mean (SD): 11 (13) Structural heart disease, Diabetes Mellitus, Cardiomyopathy, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure: N/A Beta-blocker, Calcium Antagonist, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF type: all persistent AF > 7 days **Inclusion criteria:** Patients with persistent AF lasting >7 days who were <80 years old, had ventricular rates at rest of >60 beats/min, systolic blood pressure >90mmHg, and left atrial diameter <50mm. **Exclusion criteria:** Patients with left ventricular ejection fraction of <40%, concomitant treatment with class I or III antiarrhythmic drugs, recorded amiodarone use during the preceding 6 months, and contraindications for beta-blocakde, such as conduction disturbances, asthma, or severe chronic obstructive pulmonary disease, were excluded. **Numbers:** 145 eligible patients enrolled. 48 randomised to amiodarone and 97 to placebo (carvedilol and placebo pill arms). 2 patients recieveing carvedilol had excessive bradycardia or hypotension and one patient recieving placebo had a myocardial infarction so was excluded from analysis. **Anticoagulation:** Patients were anticoagulated with acenocoumarol for an INR range of 2.5 to 3.5 for $\geq$ 4 weeks before cardioversion. **Monitoring:** Patients followed up at weekly intervals with rhythm check and treatment tollerance measured before DCCV at 4 weeks.
Interventions	Oral Amiodarone Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local

	Country: Greece **Setting:** Outpatient **Comments:** No conflicts of interest reported. Planned outcomes: Conversion and recurence rates, ECG characteristics, atrial refractory period. Reported outcomes: As planned including some adverse events. No trial registration. **Authors name:** Emmaneul Kanoupakis **Institution:** Department of Cardiology, Heraklion University Hospital, Heraklion, Greece. **Email:** cardio@med.uco.gr **Address:** Panos Vardas, Cardiology Department, Heraklion University Hospital, PO Box 1352 Stavrakia, Heraklion, Crete, Greece
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No specification of randomization method. "patients were randomly assigned to 3 treatment groups (A, B, or C) by a computer-generated model"
Allocation concealment (selection bias)	Unclear risk	No specification of method, if any, of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Carvedilol and amiodarone had different posologies, hence personnel and patients might know which drug was being used.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention/description of method for blinding outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes reported for all patients - followed for >28 days
Selective reporting (reporting bias)	Unclear risk	Not able access pre-enrolment protocol to compare with published reported outcomes.
Other bias	Unclear risk	Approval obtained from Ethics committee. No proof of registration/publication of protocol in open-access platform.

Khaykin 2003

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Maximum Patches • Male n (%): 23 (82) • Age (Years) Mean (SD): 59.7 (10.8) • Duration of AF (weeks) (sd): 26 (19) • BMI (Kg/m^2) mean (SD): 30 (12) • Hypertension n (%): 17 (61) • Myocardial Infarction n (%): 5 (18) • LADD (mm) mean (SD): 44 (5.8) • LVEF <50% n (%): 16 (56) • Any rate control n (%): 19 (68) • Beta-blocker n (%): 13 (46)

	• Calcium Antagonist n (%): 4 (15) • Digoxin n (%): 10 (36) • Diabetes (%): 2 (7) • Stroke/TIA (%): 1 (4) • Amiodarone (%): 12 (43) • Sotalol (%): 2 (7) • Class 1A/1C (%): 12 (43) • Any Antiarrhythmic (%): 20 (71) AP BTE Incremental Patches • Male n (%): 23 (82) • Age (Years) Mean (SD): 58.3 (14.6) • Duration of AF (weeks) (sd): 24 (18) • BMI (Kg/m^2) mean (SD): 30 (9) • Hypertension n (%): 16 (57) • Myocardial Infarction n (%): 6 (21) • LADD (mm) mean (SD): 46.9 (5.4) • LVEF <50% n (%): 17 (58) • Any rate control n (%): 16 (57) • Beta-blocker n (%): 12 (43) • Calcium Antagonist n (%): 4 (14) • Digoxin n (%): 4 (14) • Diabetes (%): 3 (11) • Stroke/TIA (%): 0 (0) • Amiodarone (%): 18 (64) • Sotalol (%): 1 (4) • Class 1A/1C (%): 8 (29) • Any Antiarrhythmic (%): 22 (79) Valvular Heart Disease, Structural heart disease, Hypertension, Pulmonary disease, Cardiomyopathy, Coronary Artery Disease, Diabetes Mellitus, Ischaemic Heart Disease: N/A Flecainide, Propafenone, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A All patients had persistent AF. **Inclusion criteria:** Requiring a cardioversion after failing at least one previous attempt at external cardioversion (for the current episode)using≥1 attempt with 360-J monophasic damped sinusoidal shocks, were enrolled into the trial. All patients were in continuous atrial fibrillation from the time of their failed cardioversion until study entry. **Exclusion criteria:** Not provided **Numbers:** 56 patients enrolled randomised to 28 to monophasic, 28 biphasic. **Anticoagulaion:** Anticoagulation was for at least 3 weeks prior to intervention. Not reported on how long anticoagulation continued afterwards. **Monitoring:** Method not documented. Total duration of study follow up not documented.
Interventions	AP MDS Maximum Patches AP BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported

	• **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local Funding, Medtronic Physio-Control **Country:** Canada **Setting:** Elective Admission **Comment:** Grant from Medtronic declared, no other Conflicts of Interest. Planned Outcomes: Primary endpoint was proportion of patients achieving sinus rhythm in each group after initial therapy. Reported Outcomes: As above and Adverse Events. No trial registration. **Author's Name:** Yaariv Khaykin **Institution:** Terrence Donnelly Heart Center, Department of Medicine, St Michael's Hospital **Email:** dorianp@smh.toronto.on.ca **Address:** Paul Dorian, M.D., Department of Medicine, St. Michael's Hospital, 30 Bond Street, 7-050Q; Toronto, Ontario, Canada
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of random sequence generation method (if any).
Allocation concealment (selection bias)	Unclear risk	No description on allocation concealment
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Not described. However, physicians and patients could see the cardioversion device, and hence likely not blinded. Likely high risk.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Event though blinding was likely not done, it is unlikely to have affected acute cardioversion success as an objective measure
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No description of who assessed outcomes or if there was a committee.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No description of who assessed outcomes or if there was a committee. However, unlikely to interfer with acute procedural success as objective measure.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Pre-specified end points were fully reported on
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. The manuscript mentions approval of the protocol by "St Michael's Hospital Research Ethics Board" (Ontario, Canada)

Kim 2003

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Crossover) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP BTE Incremental Patches • Age (years) mean (SD): 65 (15) • Men (%): 40 (54) • Coronary Artery Disease (%): 16 (22) • Cardiomyopathy (%): 6 (8) • Hypertension (%): 3 (4) • Beta-Blocker (%): 33 (45) • Digoxin (%): 23 (31)

	• Amiodarone (%): 15 (20) • Calcium Channel Blocker (%): 21 (28) • Valvular Heart Disease (%): 5 (7) • Sotalol (%): 8 (11) • Diuretic (%): 21 (28) • AF duration (days) mean (SD): 206 (512) • LA diameter (mm) mean (SD): 46 (11) • LVEF (%) mean (SD): 45 (7) AP RBW Incremental Patches • Age (years) mean (SD): 65 (15) • Men (%): 44 (62) • Coronary Artery Disease (%): 21 (30) • Cardiomyopathy (%): 6 (8) • Hypertension (%): 2 (3) • Beta-Blocker (%): 43 (61) • Digoxin (%): 19 (27) • Amiodarone (%): 9 (13) • Calcium Channel Blocker (%): 21 (30) • Valvular Heart Disease (%): 15 (21) • Sotalol (%): 2 (3) • Diuretic (%): 20 (28) • AF duration (days) mean (SD): 206 (512) • LA diameter (mm) mean (SD): 52 (14) • LVEF (%) mean (SD): 53 (15) Structural heart disease, Stroke/TIA, Pulmonary disease, Cardiomyopathy, Ischaemic Heart Disease, Myocardial Infarction, Diabetes Mellitus: N/A Propafenone, ACE inhibitor, Flecainide, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF type not given **Inclusion criteria:** Patients were eligible for this study if they were ≥ 18 years of age and were undergoing direct-current cardioversion for atrial fibrillation (AF). **Exclusion criteria:** Patients were excluded from the study if they were in atrial flutter or atrial tachycardia. **Numbers:** 145 patients enrolled, 74 patients randomised to BTE arm and 71 patients to RBW arm. No attrition reported. **Anticoagulation:** If arrhythmia duration was ≥ 48 hours patients had to undergo anticoagulation with warfarin for ≥ 3 weeks aiming for an INR ≥ 2.0 before enrollment. If they had not been anticoaglated then they were treated with heparin and screened for left atrial thrombus with transoesophageal echocardiograpy before cardioversion. Anticoagulation was continued for at least 3 to 4 weeks after cardioversion. **Monitoring:** There was continuous vital sign and rhythm monitoring throughout procedure but method not specified. 30 day outpatient follow up.
Interventions	AP BTE Incremental Patches AP RBW Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent

	• **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Stroke or systemic embolism at 30 days • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day all-cause mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day CVD mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** United States of America **Setting:** Unclear **Comments:** No conflicts identified. Planned outcomes: Sinus rhythm lasting > 5 seconds after defribrillation. All planned outcomes reported. No trial registration. **Authors name:** Maureen Kim **Institution:** Department of Pediatrics, Mount Sinai Medical Center, New York; Arrhythmia Service, Division of Cardiology, Montefiore Medical Center, Bronx; and Department of Medicine, Columbia Hospital Medical Center, New York, New York **Email:** skim@montefiore.org **Address:** Dr Maureen Kim, Division of Cardiology, Montefiore Medical Center, 111 East 210th Street, Bronx, New York 10467
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No information provided on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information provided on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Participants sedated and no information if they were blinded. As two different defibrillators were utilized, the personnel would not be blinded.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information on whether the outcome assessors were blinded (and how).
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of	Low risk	Endpoints reported for all patients at 30 days.

sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Unclear risk	Could not identify pre-published protocol, hence unsure if all planned outcomes were reported.
Other bias	Unclear risk	The study was approved by the institutional review board of Montefiore Medical Center. Authors mention in the limitations potential issues with quality of randomization.

Kirchhof 2005

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-over for waveform) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Incremental • Age (mean +/- SD): 63 (1) • Men (%): 68 (70) • Coronary Artery Disease (%): 22 (23) • Amiodarone (%): 20 (21) • Valvular Heart Disease (%): 13 (13) • Cardiomyopathy (%): 17 (18) • Flecainide (%): 15 (15) • Sotalol (%): 17 (18) • BMI (Kg/m^2) mean (SD): 27.2 (0.4) • Duration of episode (months) mean (SD): 7.1 (2) AP BTE Incremental • Age (mean +/- SD): 63 (1) • Men (%): 79 (76) • Coronary Artery Disease (%): 39 (38) • Amiodarone (%): 26 (25) • Valvular Heart Disease (%): 5 (5) • Cardiomyopathy (%): 17 (16) • Flecainide (%): 15 (14) • Sotalol (%): 11 (11) • BMI (Kg/m^2) mean (SD): 27.3 (0.4) • Duration of episode (months) mean (SD): 5.5 (1) Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Ischaemic Heart Disease, Myocardial Infarction, Diabetes Mellitus: N/A Beta blocker, Digoxin, Calcium Channel Blocker, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF: N/A CHA2DS2VASc: N/A All patients had persistent AF. **Inclusion criteria:** Clinical indication for external cardioversion of atrial fibrillation. Documented AF prior to procedure. **Exclusion criteria:** Atrial Flutter/Atrial Tachycardia **Numbers:** 313 screened, 202 patient enrolled, 97 monophasic, 104 biphasic. 1 patient had spontaneous termination of AF. **Anticoagulation:** INR 2-3 for weeks prior with phenprocoumon or TOE to exclude atrial appendage thrombus prior to procedure. **Monitoring:** Follow up period not specified, monitoring with 6 lead continuous ECG.
Interventions	AP MDS Incremental Paddles AP BTE Incremental Paddles AP MDS Incremental Patches AP BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported

	• **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Medtronic unrestricted grant **Country:** Germany **Setting:** Elective Admission **Comments:** www.controlled-trials.com, number ISRCTN42858989 Planned outcomes - Successful Cardioversion (includes patients with recurrence), Reported outcomes - As planned. No conflict of interest reported. **Authors name:** Paulus Kirchof **Institution:** Department of Cardiology and Angiology, Universitatsklinikum Munster **Email:** kirchhp@uni-muenster.de **Address:** Department of Cardiology and Angiology, Universitatsklinikum Munster, Albert-Schweitzer-Straße 33, D-48149 Munster, Germany
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	High risk. "Randomization was performed using a computer-read randomization list. This procedure guaranteed complete concealment of the study group from all personnel who participated in the trial." However, "Randomization was in blocks of 100 patients." and "The first 100 patients were cardioverted using commercially available gel-covered adhesive mesh-wire patch electrodes, the second half of the patients were cardioverted using sintered-steel hand-held paddle electrodes", suggesting that the personnel would know at some point which intervention would be assigned to patients included in the study at some point (i.e. at least it would be easy to predict if patients would be assigned patches of paddles).
Allocation concealment (selection bias)	High risk	High risk. "Randomization was performed using a computer-read randomization list. This procedure guaranteed complete concealment of the study group from all personnel who participated in the trial." However, "Randomization was in blocks of 100 patients." and "The first 100 patients were cardioverted using commercially available gel-covered adhesive mesh-wire patch electrodes, the second half of the patients were cardioverted using sintered-steel hand-held paddle electrodes", suggesting that the personnel would know at some point which intervention would be assigned to patients included in the study at some point.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Reported as blinded to personnel but different defibrillators required for different waveforms and patches vs. pads. Therefore, the physicians knew which treatment arm the patient had been allocated to.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Reported as blinded to personnel but different defibrillators required for different waveforms and patches vs. pads. Therefore, the physicians knew which treatment arm the patient had been allocated to. However, not likely to have influence in the endpoint "Acute procedural success".
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No description of an endpoint adjudicating committee. Likely, the treating physicians described adverse effects and procedural results.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No description of an endpoint adjudicating committee. Likely, the treating physicians described adverse effects and procedural results. However, not likely to have had impact on the outcome "Acute procedural success"
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Pre-specified end points were fully reported on
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	Trial registration - ISRCTN42858989 - on 15/06/2004, and enrolment started in 2001 (i.e. irrefutable evidence of registration, however only after trial enrolment). The manuscript mentions approval by the local ethics committee - Hospital of the University of Münster, Germany

Kochiadakis 1998

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (Cardioversion with drugs or defibrillator after 1 hour if not cardioversion)
Participants	**Baseline Characteristics** Procainamide • Age (mean +/- SD): 63.63 (10.48) • Men: 29 (51) • Duration of AF hours (mean +/- SD): 422.31 (1048.29) • Left Atrial Diameter (mm) (mean +/- SD): 43.03 (5.44) • LVEF (%) (mean +/- SD): 42 (18) Placebo • Age (mean +/- SD): 64.08 (9.87) • Men: 30 (53) • Duration of AF hours (mean +/- SD): 426.26 (1043.45) • Left Atrial Diameter (mm) (mean +/- SD): 44.29 (6.39) • LVEF (%) (mean +/- SD): 43 (12) Valvular Heart disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus: N/A Beta-blockers, Calcium antagonists, Digoxin, Propafenone, Flecainide, Sotalol, Amidoarone, Diuretics, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF type: mix of paroxysmal and persistent but amount not given. **Inclusion criteria:** AF lasting <6 months and ventricular rate >100 **Exclusion criteria:** Recent myocardial infarction, heart surgery within the last 6 months, unstable angina, acute myocarditis, acute pericarditis, severe uncontrolled heart failure (EF 30%), or cardiogenic shock were excluded, as were those with significant chronic obstructive pulmonary disease, pulmonary embolism, pneumonia, liver or kidney failure, thyroid disease, electrolyte disturbances, pregnancy or lactation, and age, 18 years. Also excluded were patients with sick sinus syndrome, a history of second or third degree AV block, as well as those who had had taken any other anti-arrhythmic drug apart from digoxin within a period less than five half-lives of the drug in question prior to the study **Numbers:** 114 Randomised: 57 to placebo, 57 to procainamide. None lost to follow up **Anticoagulation:** Anticoagulation >21 days with acenocoumarol INR 3 and also 21 days after successful cardioversion or indefinitely if unsuccessful. **Monitoring:** With 12 lead before and after intervention as well as continuous rhythm monitoring during infusion. Follow up inpatient up to 1hr and outpatient 30 days.
Interventions	Intravenous Procainamide Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent

	• **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Greece **Setting:** Elective Admission **Comments:** No conflicts of interest reported. Planned outcome cardioversion to sinus rhythm, plasma levels of drug. Reported fully, as well as adverse features and other ECG measurements. No trial registration. **Authors name:** George E. Kochiadakis **Institution:** Cardiology Department, University Hospital of Heraklion, Crete, Greece **Email:** cardccu@ikaros.edu.uch.gr **Address:** Prof. P.E. Vardas, MD, PhD (London), FESC, FACC, Cardiology Department, University Hospital of Crete, P.O. Box 1352, Heraklion, Crete, Greece
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No documentation of randomisation process.
Allocation concealment (selection bias)	Unclear risk	No documentation of allocation concealment
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	No mention to blinding of patients of staff. However, two interventions may have appeared different as may likely look and feel different to the patient and personnel during infusion. It was therefore possible for the staff to be aware. "Patients were randomized to receive either intravenous procainamide (1 g over 30 minutes, followed by an infusion of 2 mg/min over 1 hour) or a placebo." No information of where the infusions were prepared and labelled (if done in pharmacy, blinding would be more likely).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No mention to blinding of patients of staff. However it was possible for the staff and patients to be aware, this was an objective endpoint.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Not clear if all outcomes were blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	ECGs assessed by examiners who were blinded to the assigned intervention. Objective endpoint. "None of the observers knew whether the ECGs were from procainamide or placebo patients."
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No attrition in either arm, pre-specified end points were fully reported on
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	Unclear risk	No proof of trial registration. The manuscript mentions approval by the hospital's review board - Hospital of Heraklion, Greece. No information on enrolment dates.

Kochiadakis 1998a

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (mean +/- SD): 63 (9) • Men (%): 25 (54)

	• Left Atrial Diameter (mm) (mean +/- SD): 43 (6) • LVEF (%) (mean +/- SD): 51 (8) • Duration of episode (h) mean (SD): 16 (13) Amiodarone • Age (mean +/- SD): 63 (12) • Men (%): 27 (56) • Left Atrial Diameter (mm) (mean +/- SD): 43 (5) • LVEF (%) (mean +/- SD): 50 (8) • Duration of episode (h) mean (SD): 16 (14) Placebo • Age (mean +/- SD): 65 (9) • Men (%): 25 (51) • Left Atrial Diameter (mm) (mean +/- SD): 41 (6) • LVEF (%) (mean +/- SD): 50 (9) • Duration of episode (h) mean (SD): 18 (14) Valvular Heart Disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease, Diabetes Mellitus: N/A Beta-blockers, Calcium antagonists, Digoxin, Propafenone, Flecainide, Sotalol, Amidoarone, Diuretics, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A All patients had paroxysmal AF. **Inclusion criteria:** AF lasting< 48 hours. **Exclusion criteria:** recent myocardial infarction, heart surgery within the last 6 months, unstable angina, acute myocarditis, acute pericarditis, baseline systolic blood pressure < 100mmHg, hypertrophic obstructive cardiomyopathy, severe uncontrolled heart failure (EF < 30%), cardiogenic shock, severe COPD, pulmonary embolism, pneumonia, liver or kidney failure, thyroid disease, electrolyte disturbances, digoxin intoxication, pregnancy or lactation, or age < 18 years. Also excluded were patients with sick sinus syndrome, a history of second- or third-degree AV block, and those who had taken an anti-arrhythmic drug other than digoxin within less than five drug elimination half-lives prior to the study **Numbers:** 143 consecutive patients randomised, 46 to propafenone, 48 to amiodarone and 49 to placebo. There was no attrition. **Anticoagulation:** No anticoagulation protocol was described as patient had AF <48h **Monitoring:** Inpatient follow up period was 24h. Monitoring was with continuous ECG.
Interventions	Intravenous Propafenone Intravenous Amiodarone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint

	Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local Funding **Country:** Greece **Setting:** Not Clear **Comments:** No conflicts of interest reported. Planned outcomes, Sinus rhythm occurring in 24 hour study period. Reported outcomes, as planned but also adverse effects and predictors of conversion. No trial registration. **Authors name:** George E. Kochiadakis **Institution:** Cardiology Department, University Hospital of Heraklion, Crete, Greece **Email:** cardccu@ikaros.edu.uch.gr **Address:** Prof. P.E. Vardas, M.D. Cardiology De-partment, Heraklion University Hospital, P.O. Box 1352 Stavrakia, Heraklion, Crete, Greece
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No documentation of randomisation process
Allocation concealment (selection bias)	Unclear risk	No documentation of the process
Blinding of participants and personnel (performance bias) All other outcomes	High risk	It was not reported as blinded, but based on the way the infusions were designed, it would be possible to detect that they were different treatments (i.e. amiodarone included iv infusion and oral tablets; propafenone and digoxin only infusion)."Patients randomized to amiodarone beganwith 300 mg intravenously {IV) over 1 hour, followed hy 20 mg/kg over the next 24 hours. They also received simultaneously 1,800 mg/day orally in three divided doses. Patients randomized to propafenone began with IV 2 mg/kg over 15 minutes followed hy 10 mg/kg over 24 hours. Patientsin the placebo group received an identical amountof saline over 24 hours."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	It is unclear what information outcome assessors were given. No mention to event adjudication committee. If events were adjudicated by treating physicians, they would be likely aware of the intervention.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There was no attrition in this study. No missing data or patients lost to follow-up.
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	High risk	No proof of trial registration. No mention to ethics or institutional approval. No information on enrolment dates.

Kochiadakis 1999

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Placebo

	• Age (mean +/- SD): 63 (9) • Men: 16 (47) • Left Atrial Diameter (mm) (mean +/- SD): 46 (6) • LVEF (%) (mean +/- SD): 50 (8) • Duration of episode (h) mean (SD): 1400 (1433) Amiodarone • Age (mean +/- SD): 64 (9) • Men: 16 (49) • Left Atrial Diameter (mm) (mean +/- SD): 46 (8) • LVEF (%) (mean +/- SD): 50 (8) • Duration of episode (h) mean (SD): 1671 (1423) Valvular Heart Disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus: N/A Beta-blockers, Calcium antagonists, Digoxin, Propafenone, Flecainide, Sotalol, Amidoarone, Diuretics, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A All patients had persistent AF. **Inclusion criteria:** Patients with persistent AF (>48h) who came from the emergency department or were treated in clinic. **Exclusion criteria:** Recent myocardial infarction, heart surgery within the last 6 months, unstable angina, acute myocarditis, acute pericarditis, severe uncontrolled heart failure (ejection fraction, 30%), or cardiogenic shock were excluded from the study, as were those with significant chronic obstructive pulmonary dis-ease, pulmonary embolism, pneumonia, liver or kidney failure, thyroid disease, electrolyte disturbances, pregnancy or lactation, or those, 18 years of age. Also sick sinus syndrome, a history of second- or third-degree atrioventricular block, as well as those who had taken any other anti-arrhythmic drug apart from digoxin within a period, 5 half lives of the drug in question before the study. **Numbers:** 67 patients eligible for study randomised to: Placebo 34, Amiodarone 33. **Anticoagulation:** Acenocourmarol was used for anticoagulation for >21 days with an INR target of 3 before cardioversion and continued for 21 days after. (note: if some patients did not meet current day criteria for peristent AF, by the time they finished the 3 weeks of anticoagulation they were clearly persistent AF). **Monitoring:** Follow up period 30 days with clinic appointment where 12 lead ECG and echocardiogram were done. Continuous ECG monitoring was done as inpatient.
Interventions	Intravenous Placebo Intravenous Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism at 30 days • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day all-cause mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day CVD mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent

	• **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 1 Week Complication • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Greece **Setting:** Accident and Emergency or Elective **Comments:** No conflicts of interest reported. Planned outcomes: Sinus rhythm achieved within 1 month period. Reported outcomes: as planned but including adverse outcomes. Continuous ECG monitoring was obtained during first 24 hours of inpatient stay. No trial registration. **Authors name:** George E. Kochiadakis **Institution:** Cardiology Department, University Hospital of Heraklion, Crete, Greece **Email:** cardccu@ikaros.edu.uch.gr **Address:** Panos E. Vardas, MD, PhD, Cardiology Department, Heraklion University Hospital, P.O. Box 1352 Stavrakia, Heraklion, Crete, Greece
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No documentation of randomisation process
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No documentation of the process
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Judgement Comment: It was not reported as blinded, but based on the way the infusions were designed, it would be possible to detect that they were different treatments as saline and amiodarone infusions feel different to patients (amiodarone infusions are made in dextrose) . "Patients randomized to amiodarone received 300 mg intravenously for 1 hour andthen 20 mg/kg for 24 hours. At the same time, theywere given 600 mg/day orally, divided into 3 doses,for 1 week and thereafter 400 mg/day for 3 weeks.Patients in the placebo group received an identicalamount of saline the first day, 3 placebo tablets perday for 1 week and 2 per day for 3 weeks. Digoxin was administered to all patients who had not previ-ously received it."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Judgement Comment: It is unclear what information outcome assessors were given. No mention to event adjudication committee. If events were adjudicated by treating physicians, they would be likely aware of the intervention.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Judgement Comment: It does not appear that any patients were lost to follow up or did not report certain outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge:	Low risk	Judgement Comment: It does not appear that any patients were lost to follow up or did not report certain outcomes.

Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	High risk	Judgement Comment: There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report. Several measurements described in the protocol are not reported in the results.
Other bias	Unclear risk	Judgement Comment: No proof of trial registration. Mention to approval by the hospital's Ethics Committee - Hospital of Heraklion, Greece. No information on enrolment dates.

Kochiadakis 1999a

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone • Age (mean +/- SD): 64 (9) • Men: 16 (47) • Left Atrial Diameter (mm) (mean +/- SD): 47 (8) • LVEF (%) (mean +/- SD): 50 (8) • Duration of episode (days) mean (SD): 162 (95) Propafenone • Age (mean +/- SD): 64 (10) • Men: 16 (50) • Left Atrial Diameter (mm) (mean +/- SD): 48 (6) • LVEF (%) (mean +/- SD): 51 (6) • Duration of episode (days) mean (SD): 162 (100) Placebo • Age (mean +/- SD): 63 (9) • Men: 16 (46) • Left Atrial Diameter (mm) (mean +/- SD): 48 (6) • LVEF (%) (mean +/- SD): 50 (8) • Duration of episode (days) mean (SD): 163 (100) Valvular Heart disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease, Diabetes Mellitus: N/A Beta-blockers, Calcium antagonists, Digoxin, Propafenone, Flecainide, Sotalol, Amidoarone, Diuretics, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A All patients had persistent AF. **Inclusion criteria:** Patients with chronic atrial fibrillation presenting to emergency department or clinic. **Exclusion criteria:** Recent myocardial infarction, heart surgery within the last six months, acute pericarditis, severe uncontrolled heart failure (ejection fraction <30%) or cardiogenic shock, significant chronic obstructive pulmonary disease, thyroid disease, unstable angina, acute myocarditis, pulmonary embolism, pneumonia, liver or kidney failure, electrolyte disturbances, pregnancy or lactation, age <18 years, sick sinus syndrome, a history of second- or third-degree atrioventricular block or the taking of any other antiarrhythmic drug apart from digoxin within a period less than five half-lives of the drug in question before the study **Numbers:** 115 patients selected and 101 randomised to: 34 Amiodarone, 32 Propafenone, 35 Placebo. There were no lost to follow up. **Anticoagulation:** With acenocoumarol for more than 21 days until cardioversion with INR 2-3. Further 21 days anticoagulation after cardioversion or indefinite if unsuccessful.

	Monitoring: With continuous ECG over first 24h. Kept for observation for at least 2 days prior to discharge. Weekly physical examination and ECG until 30 days.
Interventions	Intravenous Amiodarone Intravenous Propafenone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism at 30 days • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day all-cause mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day CVD mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 1 Week Complication • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local funding **Country:** Greece **Setting:** Accident and Emergency and Elective and Outpatient follow up **Comments:** No conflicts of interest reported. Planned outcomes, successful cardioversion within study period, Sinus rhythm restored by end of 1 month study period. Reported outcomes as planned as well as adverse events and predictors of conversion. Continuous ECG monitoring was obtained during first 24 hours of inpatient stay. No trial registration. **Authors name:** George E. Kochiadakis **Institution:** Cardiology Department, University Hospital of Heraklion, Crete, Greece **Email:** cardio@danae.med.uoc.gr

	Address: Dr. P. E. Vardas, Cardiology Department, Heraklion University Hospital, P.O. Box 1352 Stavrakia, Heraklion, Crete, Greece
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No documentation of randomisation process
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No description of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Judgement Comment: It was not reported as blinded, but based on the way the infusions were designed, it would be possible to detect that they were different treatments . "Patients randomized to amiodarone received 300 mg intravenously for 1 h and then 20 mg/kg over 24 h. At the same time, they were given 600 mg per day in three doses, orally, for one week.Thereafter they received 400 mg per day for 3 weeks.Patients randomized to propafenone began with 2 mg/kg intravenously over 15 min, followed by 10 mg/kg over 24 hrs then 450 mg/day, orally, for one month. Patients in the placebo group received an identical amount of saline on the first day, and then oral placebo for one month. Digoxin (0.5 mg intravenously initially, followed by 0.25 mg at 2 hand 0.25 mg every 6 h thereafter) was administered for 24 h to all patients who had not previously received it."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Judgement Comment: It is unclear what information outcome assessors were given. No mention to event adjudication committee. If events were adjudicated by treating physicians, they would be likely aware of the intervention.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Judgement Comment: No patients were lost to follow up or did not report certain outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Judgement Comment: No patients were lost to follow up or did not report certain outcomes.
Selective reporting (reporting bias)	High risk	Judgement Comment: There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report. Several measurements described in the protocol are not reported in the results.
Other bias	Unclear risk	Judgement Comment: No proof of trial registration. Mention to approval by the hospital's Ethics Committee - Hospital of Heraklion, Greece. No information on enrolment dates.

Kochiadakis 2007

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Procainamide • Age (mean +/- SD): 64 (10) • Men (%): 42 (47) • Left Atrial Diameter (mm) (mean +/- SD): 41 (6) • LVEF (%) (mean +/- SD): 52 (10) Propafenone • Age (mean +/- SD): 64 (11)

	• Men (%): 42 (46) • Left Atrial Diameter (mm) (mean +/- SD): 42 (6) • LVEF (%) (mean +/- SD): 53 (10) Amiodarone • Age (mean +/- SD): 65 (11) • Men (%): 42 (46) • Left Atrial Diameter (mm) (mean +/- SD): 42 (5) • LVEF (%) (mean +/- SD): 52 (10) Placebo • Age (mean +/- SD): 66 (9) • Men (%): 40 (44) • Left Atrial Diameter (mm) (mean +/- SD): 41 (6) • LVEF (%) (mean +/- SD): 52 (10) Valvular Heart Disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus: N/A Beta-blockers, Calcium antagonists, Digoxin, Propafenone, Flecainide, Sotalol, Amidoarone, Diuretics, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A Duration of episode: N/A All patients had paroxysmal AF. **Inclusion criteria:** Patients presenting with AF of < 48 hours duration. **Exclusion criteria:** Patients with a recent myocardial infarction, heart surgery within the previous 6 months, unstable angina, acute myocarditis, acute pericarditis, baseline systolic blood pressure 100 mm Hg, hypertrophic obstructive cardiomyopathy, severe uncontrolled heart failure (left ventricular ejectionfraction [LVEF]30%), or cardiogenic shock, significant chronic obstructive pulmonary disease, pulmonary embolism, pneumonia, liver or kidney failure, thyroid disease, electrolyte disturbances, digoxin intoxication, pregnancy or lactation, or age< 18 years, sick sinus syndrome or a history of second- or third-degree atrioventricular block, as well as those who had taken any anti-arrhythmic drug other than digoxin within5 half-lives of the drug in question before the study **Numbers:** 362 patients randomised to: Procainamide 89, Propafenone 91, Amiodarone 92, Placebo 90. **Anticoagulation:** As less than 48 hour AF duration there was no need for an anticoagulation protocol prior to cardioversion. If cardioversion was not successful then patients were booked for DCCV after 3 weeks of anticoagulation with acenocoumarol at INR 2-3, or other anti-arrhythmics used. **Monitoring:** There was continuous ECG monitoring and patients were followed up for more than 2 days before discharge.
Interventions	Intravenous Procainamide Intravenous Propafenone Intravenous Amiodarone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported

	• **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local funding **Country:** Greece **Setting:** Accident and Emergency **Comments:** No conflicts of interest declared. Planned outcomes: Sinus Rhythm in 24 hour study period, Echocardiograpic features (LA diameter). Reported outcomes: as planned as well as adverse events including signs of phlebitis, arrhythmia and hypotension. No trial registration. **Authors name:** George E. Kochiadakis **Institution:** Cardiology Department, University Hospital of Heraklion, Crete, Greece **Email:** cardccu@ikaros.edu.uch.gr **Address:** Cardiology Department, University Hospital of Heraklion, Crete, Greece
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No documentation of randomisation process
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	It was not reported as blinded, but based on the way the infusions were designed (different rates), it would be possible to detect that they were different treatments. "Patients allotted to receive procainamide began with 1 g intravenously over 30 minutes, followedby 2 mg/min intravenously in the next 24 hours. Patients allotted to the propafenone group began with 2 mg/kg intravenously over 15 minutes, followed by 10 mg/kg intravenously in the next 24 hours. Patients allotted to the amiodarone group began with 300 mg intravenously over 1hour, followed by 20 mg/kg intravenously in the next 24 hours. Patients in the placebo group received an identical amount of saline solution intravenously over 24 hours."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	It is unclear what information outcome assessors were given. No mention to event adjudication committee. If events were adjudicated by treating physicians, they would be likely aware of the intervention.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoint - acute procedural success. Issues with blinding would not affect it.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Only 1 patient in the placebo group refused to continue treatment at 10 hours. Otherwise all other patients were available for follow-up.
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	Unclear risk	No proof of trial registration. Mention to approval by the hospital's Ethics Committee - Hospital of Heraklion, Greece. No information on enrolment dates.

Kosior 2009

Study characteristics	
Methods	**Study design:** Randomized controlled trial

	Study grouping: Parallel group
Participants	**Baseline Characteristics** Propafenone • Age (mean +/- SD): 62.1 (10.7) • Men (%): 21 (49) • Ischaemic Heart Disease (%): 26 (61) • Hypertension (%): 25 (58) • Myocardial Infarction (%): 8 (19) • Structural Heart Disease (%): 10 (22) • AF duration (h) (mean +/- SD): 14.5 (13.0) • Left Atrial Diameter (mm) (mean +/- SD): 43.9 (5.0) • LVEF (%) mean (SD): 56.4 (3.8) Quinidine • Age (mean +/- SD): 66.1 (12.4) • Men (%): 19 (54) • Ischaemic Heart Disease (%): 17 (49) • Hypertension (%): 19 (54) • Myocardial Infarction (%): 6 (17) • Structural Heart Disease (%): 8 (23) • AF duration (h) (mean +/- SD): 9.7 (7.7) • Left Atrial Diameter (mm) (mean +/- SD): 40.0 (3.0) • LVEF (%) mean (SD): 52.5 (6.2) Valvular Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Diabetes Mellitus, Coronary Artery Disease: N/A Beta-blockers, Calcium antagonists, Digoxin, Propafenone, Flecainide, Sotalol, Amidoarone, Diuretics, ACE-inhibitors, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A All patients had paroxysmal AF. **Inclusion criteria:** Age from 18 to 85 years, mean ventricular rate above70 beats per minute (calculated over at least 30 R-R cycles), as well as New York Heart Association (NYHA) functional class < II. **Exclusion criteria:** documented intolerance, ineffectiveness or contraindications for study drugs, thyroid dysfunction, myocardial infarction in the three months preceding the study, acute myocarditis, cardiac surgery in the 30 days prior to the study, hemodynamic instability defined as symptomatic heart failure or hypotension (systolic pressure < 90 mm Hg), systemic hypertension not responding to treatment (diastolic pressure > 115 mm Hg), valvular heart disease qualified for surgical treatment, R-R intervals exceeding more than 3 s, ventricular rhythm below 70/min (unrelated to drugs reducing ventricular rhythm), bundle branch block, electrocardiogram (ECG) evidence (past or present) of ventricular pre-excitation syndrome, QT segment prolongation (a corrected QT interval of more than 480 ms or an uncorrected QT interval of more than 500 ms), hypokalemia (serum potassium level < 3.5 mmol/L), pregnancy and lactation, liver, kidney or central nervous system damage, advanced chronic lung disease, or malignancy. Patients were also excluded from the study if they had been medicated with digitalis or subjected to any anti arrhythmic therapy in the previous 24 hours **Numbers:** 81 patients randomised: 46 to propafenone, 35 to quinidine. Unclear from data if 3 patients cross over to quinidine arm from propafenone. **Anticoagulation:** Anticocoagulation not specified as AF <48h **Monitoring:** Holter monitoring for 24hrs. Total study follow up 24hrs.
Interventions	Oral Propafenone Oral Quinidine
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent

	• **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Investigators stated that there were no strokes, pulmonary embolsim and deaths at 24h
Identification	**Sponsorship source:** Local **Country:** Poland **Setting:** Accident and Emergency **Comments:** No conflict of interest reported Planned outcomes: Conversion to Sinus Rhythm at specific time points, Adverse events observed by investigators and reported by patients (Proarrythmic events, and Haemodynamic changes), Reported ouctomes: as above. No trial registration. **Authors name:** Dariusz A. Kosior **Institution:** Department of Cardiology, Warsaw Medical University **Email:** dkosior@acn.waw.pl **Address:** Dariusz A. Kosior, Department of Cardiology, Warsaw Medical University, Banacha 1A, 02–097 Warszawa, Poland
Notes	Oral all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No documentation of how randomization was performed.
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Treatment protocol is different in terms of drug/tablet burden and infusion. Impossible to blind. "Group I received propafenone 600 mg orally as theinitial therapy and an additional dose of 300 mg af-ter eight hours, if the SR had not been restored bythen. Group II received digoxin 1 mg IV followedby an oral loading of quinidine (400 mg followed by200 mg every two hours, with the total dose notexceeding 1400 mg)"
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Treatment protocol is different in terms of drug/tablet burden and infusion. Impossible to blind. However, low risk, as acute procedural success is an objective endpoint and not likely to be influenced.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No description of independent adjudicating committee. Based on the manuscript it seems like treating physicians and patients reported side effects, and clinicians assessed presence of sinus rhythm.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No description of independent adjudicating committee. Based on the manuscript it seems like treating physicians and patients reported side effects, and clinicians assessed presence of sinus rhythm. Low risk for acute procedural success as it is an objective outcome.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There was no attrition in either arm for all outcomes.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Mention to approval by the Ethics Committee - Medical University of Warsaw, Poland.

Koster 2004

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA BTE Incremental • Age (mean +/- SD): 69.6 (10.9) • Men (%): 20 (57) • Duration of AF (days) (mean +/- SD): 82.2 (62.0) • Digoxin (%): 22 (63) • Beta-Blocker (%): 11 (31) • Verapamil/Diltiazem (%): 8 (23) • Amiodarone (%): 9 (26) • Sotalol (%): 7 (20) • Left Atrial Dimension (mm) (mean +/- SD): 45.0 (5.3) AA MDS Incremental • Age (mean +/- SD): 63.2 (15.8) • Men (%): 25 (68) • Duration of AF (days) (mean +/- SD): 94.3 (84.2) • Digoxin (%): 17 (46) • Beta-Blocker (%): 7 (19) • Verapamil/Diltiazem (%): 4 (11) • Amiodarone (%): 12 (32) • Sotalol (%): 9 (24) • Left Atrial Dimension (mm) (mean +/- SD): 46.2 (8.0) Valvular Heart Disease, Structural Heart Disease, Stroke/TIA, Pulmonary disease, Cardiomyopathy, Diabetes Mellitus, Heart Failure, Coronary Artery Disease, Ischaemic Heart Disease, Myocardial Infarction: N/A Propafenone, Flecainide, Diuretics, ACE-inhibitors, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LVEF% : N/A % of Paroxysmal or Persistent AF: N/A **Inclusion criteria:** Suitable for elective cardioversion for AF and >18 years **Exclusion criteria:** Subcutaneous of epicardial implantable defibrillator, on ibutilide, any IV antiarrythmic at time of cardioversion attempt. Cardiac surgery in the last 7 days, continuous AF >1yr, previous failed cardioversion from AF with monophasic energy. **Numbers:** 73 patients randomised: 37 to Monophasic and 35 to Biphasic one patient was treated with wrong energy so excluded **Anticoagulation:** With warfarin was required if AF >48h, not specified duration **Monitoring:** Follow up duration as IP not clear, at least 1 hour as pain rating at this point. ECG monitoring with 12 lead ECG pre and post.
Interventions	AA BTE Incremental Patches AA MDS Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Medtronic-Physio Control **Country:** Netherlands, Canada **Setting:** Elective Admission

	Comments: No conflicts of interest reported but industry grant who provided debfibrillators.Planned outcomes: Shock Success absence of AF post shock on ECG, Pain rating 1 hour after shock on visual analog scale. Reported outcomes were the same. No trial registration. **Authors name:** Rudolph W.Koster **Institution:** Department of Cardiology, Academic Medical Center, University of Amsterdam **Email:** R.W.Koster@amc.uva.nl **Address:** Rudolph W. Koster, MD, Department of Cardiology, F3-239, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No documentation of randomization method.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Patients were not aware of treatment allocation, however physicians performing cardioversion were as defibrillators were not identical. "Patients were randomly assigned in equal proportions to 2 groups, one initially treated with MDS and the other with BTE shocks. Because the defibrillators were not identical,shock waveform was not blinded to the physician, but patients were not informed of the type of waveform. "
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Patients were not identified of treatment allocation, however physicians performing cardioversion were as defibrillators were not identical. However, this would have no impact in the acute procedural success endpoint.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Two independent cardiologists blinded to allocation assessed the ECGs. Besides pain (assessed on a visual analogue scale by patients - who were blinded to the allocated treatment) there were no more reported endpoints. "each patient rated the pain across the chest felt at that moment by selecting a number on a visual analogue scale blind to both waveform and number of shocks delivered"
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Two independent cardiologists blinded to allocation assessed the ECGs. Besides pain (assessed on a visual analogue scale by patients - who were blinded to the allocated treatment) there were no more reported endpoints. "For classification of success of cardioversion, each pre- and postshock electrocardiogram was over-read by 2 independent cardiologists, blinded to the wave-form and the energy settings."
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Only one patient removed from study, all other outcomes, that were being assessed were fully reported
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Mention to approval by the Ethics Review Board for each center: Academic Medical Center, University of Amsterdam, The Netherlands; St Michael's Hospital, Toronto, Canada. Some baseline differences in the % of Beta-blockers, Digoxin and Calcium Antagonists.

Kumagai 2000

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Pilsicainide • Age (years) mean (SD): 57 (15) • Men (%): 30 (75) • Coronary Artery Disease (%): 0 (0) • Cardiomyopathy (%): 1 (3) • Hypertension (%): 8 (20) • Valvular Heart Disease (%): 2 (5) • AF duration (min) mean (SD): 321 (444)

	Disopyramide • Age (years) mean (SD): 59 (12) • Men (%): 21 (66) • Coronary Artery Disease (%): 1 (3) • Cardiomyopathy (%): 1 (3) • Hypertension (%): 6 (19) • Valvular Heart Disease (%): 2 (6) • AF duration (min) mean (SD): 247 (403) Structural Heart Disease, Stroke/TIA, Pulmonary disease, Ischaemic Heart Disease Myocardial Infarction, Diabetes Mellitus: N/A Beta-blocker, Digoxin, Calcium Channel Blocker, Amiodarone, Sotalol, Flecainide, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LA dimensions and LVEF %: N/A All patients had paroxysmal AF duration < 48 hours **Inclusion criteria:** Documented symptomatic paroxysmal AF lasting < 48 hours. The main criteria to define the time of AF onset were either electrocardiographic documentation during hospitalisation, or a sudden, well-defined onset of palpitations with subsequent electrocardiographic findings of AF on admission to the hospital. **Exclusion criteria:** (a) congestive heart failure with New York Heart Association functional Class II, (b) myocardial infarction or unstable angina pec- toris within 6 months of the study, (c) sick sinus syndrome in absence of a permanent pacemaker, (d) bifascicular block or bundle branch block, (e) con comitant use of other antiarrhythmic drugs, includ ing beta-adrenoreceptor blocking agents, calcium antagonists, or other antiarrhythmic drugs, (f) long QT syndrome, and (g) hyperthyroidism **Numbers:** 72 patients Eligible for study, 40 patients randomised to pilsicainide arm and 32 patients to disopyramide arm. No attrition reported. **Anticoagulation:** No protocol reported, AF duration < 48 hours **Monitoring:** Continous electrocardiographic monitoring from 30 minutes before treatment to 120 minutes after drug. Success if conversion in 120 minutes after administration. No other follow up duration reported.
Interventions	Intravenous Pilsicainide Oral Disopyramide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Japan **Setting:** Unclear Hospital Setting **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm within 120 minutes after drug administration. Reported outcome: As planned and adverse events. No trial registration.

	Authors name: Koichiro Kumagai **Institution:** Department of Cardiology, Fukuoka University School of Medicine, Fukuoka, Japan; Department of 2nd Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan; and the Department of Internal Medicine III, Kurume University School of Medicine, Kurume, Japan **Email:** kxk@fukuoka-u.ac.jp **Address:** Koichiro Kumagai, M.D., Department of Cardiology, Fukuoka University School of Medicine, 7-45-1, Nanakuma, Jonan-ku, Fukuoka, 814-0180 Japan
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No specification of the method of sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention to allocation concealment or how it was done.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Oral drug compared to iv drug, hence patients and personell highly likely to know assigned drug.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to method (if any) of allocation concealment.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients were lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	Could not access the pre-enrolment protocol and hence not able to confirm if all planned outcomes were reported.
Other bias	Unclear risk	Study approved by the Institutional Review Board in each centre. No evidence of protocol registration/publication.

Kühlkamp 1991

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Crossover) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Flecainide No baseline characteristics reported by treatment arm Cibenzoline No baseline characteristics reported by treatment arm All patients • Age (years) mean (SD): 56 (9) • Men (%): 17 (55) • Hypertension (%): 5 (16) • Cardiomyopathy (%): 3 (10) • Coronary Artery Disease (%): 3 (10) • LA diameter (mm) mean (SD): 45 (9) • Amiodarone (%): 0 (0) • Valvular Heart Disease (%): 8 (26) • AF duration (days) mean (SD): 168 (373) All patients had persistent AF Structural heart disease, Stroke/TIA, Pulmonary disease, Myocardial Infarction, Diabetes Mellitus, Ischaemic Heart Disease: N/A Beta-blocker, Propafenone, Diuretic, Sotalol, Flecainide, ACE inhibitor, Aspirin, Calcium Antagonist, Digoxin: N/A

	BMI: N/A CHA2DS2VASc: N/A **Inclusion criteria:** Patients admitted to hospital for conversion of atrial fibrillation that had lasted more than 7 days. **Exclusion criteria:** Patients with the paroxysmal form of atrial fibrillation, renal impairment (serum creatinine ≥ 1.5 mg/dl), uncontrolled arterial hypertension, recent (≤ 3 months) myocardial infarction or cardiac failure NYHA III or IV. Hyperthyroidism also had to be exclued. Class I anti-arrhythmic drugs and beta-adrenergic blocking drugs were withdrawn prior to the study for at least 5 drug half-lifes. No patients were on amiodarone but cardiac glycosides or verapamil were allowed. **Numbers:** 31 patient enrolled, 19 patients randomised to Cibenzoline arm and 12 patients to Flecainide arm. No attrition reported. **Anticoagulation:** Patients had to be anticoagulated for at least 14 days with intravenous heparin or oral phenprocoumoune. **Monitoring:** Daily 12 lead resting ECG. 5 day follow up after which washout for cross over began.
Interventions	Oral Flecainde Oral Cibenzoline
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Germany (Federal Republic of Germany) **Setting:** Unclear hospital settting **Comments:** No conflicts identified. Planned outcomes: Conversion to sinus rhythm and maintenance of sinusy rhythm for 1 year. However outcomes after 5 days cannot be included in systematic review due to cross-over. Effects of drug therapy on ECG characteristics. All planned outcomes reported including adverse effects however cannot determine if before or after cross-over. **Authors name:** Volker Kühlkamp **Institution:** Medizinische Klinik Abteilung III der Eberhard-Karls-Universität, Tübingen, F.R.G **Email:** not provided **Address:** V. Kühlkamp, M.D., Abteilung III der Medizinischen Universitätsklinik, Otfried Müller Str. 10, D- 7400 Tübingen, F.R.G.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quasirandomized design: by year of birth (odd/even).
Allocation concealment (selection bias)	High risk	Quasirandomized design: by year of birth (odd/even).
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Study personell likely to know treatment as randomization method is predictable.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to whether (any) blinding of outcome assessors was performed
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients were lost to follow-up.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure	Low risk	No patients were lost to follow-up. Followed for > 30 days.

admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Unclear risk	Could not find a pre-enrolment version of the protocol to confirm if all planned outcomes were reported.
Other bias	Unclear risk	Study approved by the Institutional Committee on Human Research. No Proof of prior protocol registration/publication.

Lindeboom 2000

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Dofetilide • Age (years) mean (range): 62 (30-75) • Men (%): 35 (67) • Hypertension (%): 13 (25) • Paroxysmal AF (%): 14 (27) • Persistent AF (%): 30 (59) • Atrial Flutter (%): 7 (14) • Valvular Heart Disease (%): 1 (2) • Coronary Artery Disease (%): 11 (22) • Hypertrophic Cardiomyopathy (%): 2 (4) • LA diameter (mm) mean: 43 • Any Anti-Arrythmic drug (%): 0 (0) Placebo • Age (years) mean (range): 59 (29-75) • Men (%): 11 (61) • Hypertension (%): 2 (11) • Paroxysmal AF (%): 4 (22) • Persistent AF (%): 11 (61) • Atrial Flutter (%): 3 (17) • Valvular Heart Disease (%): 1 (6) • Coronary Artery Disease (%): 5 (28) • Hypertrophic Cardiomyopathy (%): 0 (0) • LA diameter (mm) mean: 41 • Any Anti-Arrythmic drug (%): 0 (0) Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Myocardial Infarction, Ischaemic Heart Disease, Heart Failure, Diabetes Mellitus: N/A Beta-blocker, Calcium antagonists, Digoxin, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LVEF %: N/A CHA2DS2VASc: N/A Duration of episode: N/A AF type: mixed **Inclusion criteria:** Adult men and postmenopausal or surgically sterilized women aged between 18 and 75 years were eligible for inclusion if there was electrocardio- graphically documented evidence of AF or AFl (duration, <6 months, as estimated by onset of symptoms) **Exclusion criteria:** Patients were excluded from the study if they had severe heart failure (New York Heart Association class IV), recent unstable angina pectoris or myocardial infarction (within 2 weeks of entering the study), hypertension (>200 mm Hg systolic pressure or >110 mm Hg diastolic pressure) or hypotension (<90 mm Hg systolic pressure), or a slow ventricular rate (<70 beats/min). Further exclusion criteria were thyrotoxicosis, documented Wolff-Parkinson-White syndrome, resting QTc interval >500 ms, QRS width >180 ms, and clinically significant laboratory test abnormalities. All class I or III antiarrhythmic drugs were discontinued for at least 5 half-lives **Numbers:** 69 patients were randomized to 4 treatment groups, placebo (18), and three different dofetilide doses (51). None were lost to follow up. **Anticoagulation:** No anticoagulation protocol was provided. **Monitoring:** Holter for rhythm monitoring. Follow up period was for 12 hours after final treatment. However cross-over if failure at 1 hour.
Interventions	Intravenous Dofetilide Intravenous Placebo

Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint No adverse events outcomes taken due to cross over
Identification	**Sponsorship source:** Supported by research grant from Pfizer In. Sandwich, Uniked Kingdom **Country:** The Netherlands **Setting:** Unclear **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm within 60 minutes after infusion, Conversion after second infusion for non responders. Reported outcomes as planned as well as adverse events. No trial registration. **Authors name:** Jan-Eize Lindeboom **Institution:** Department of Cardiology, St Antonius Hospital, Nieuwegein; University Hospital Groningen, Groningen; and Ignatius Hospital Breda, Breda, The Netherlands. **Email:** Not provided **Address:** Dr. J. Herre Kingma, St. Antonius Hospital, R & D Cardiologie, Koekoek- slaan 1, 3435 CM Nieuwegein, The Netherlands
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	There is mention of double-blind study and infusion, but no detail is provided.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	There is mention of double-blind study and infusion, but no detail is provided. Objective endpoint - not affected.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	There is mention of double-blind study and infusion, but no detail is provided.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	There is mention of double-blind study and infusion, but no detail is provided. Objective endpoint - not affected.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome in the methods section, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Protocol approved by the institution review board of the 3 hospitals. No evidence of protocol publication prior to starting the study.

Maciag 2017

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group

Participants	**Baseline Characteristics** Antazoline • Age (years) mean (SD): 69 (13) • Hypertension (%): 52 (70) • Pulmonary Disease (%): 1 (3) • Coronary Artery Disease (%): 13 (36) • Beta-Blocker (%): 27 (78) • Calcium Antagonist (%): 4 (11) • Amiodarone (%): 4 (11) • Propafenone (%): 10 (28) • Diuretic (%): 15 (42) • ACE Inhibitor/ARB (%): 23 (64) • Duration of episode (h) mean (SD): 11.2 (10) Placebo • Age (years) mean (SD): 68 (12) • Hypertension (%): 27 (75) • Pulmonary Disease (%): 2 (5) • Coronary Artery Disease (%): 9 (24) • Beta-Blocker (%): 31 (82) • Calcium Antagonist (%): 3 (8) • Amiodarone (%): 1 (3) • Propafenone (%): 18 (47) • Diuretic (%): 16 (42) • ACE Inhibitor/ARB (%): 21 (55) • Duration of episode (h) mean (SD): 8.8 (8.2) Gender not split by intervention, 39 (53%) are male. Structural Heart Disease, Valvular Heart Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Cardiomyopathy, Heart Failure, Diabetes Mellitus: N/A Digoxin, Sotalol, Flecainide, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A AF type: All paroxysmal AF all patients had duration < 43h hours **Inclusion criteria:** Paroxysmal AF with standard indication for the cardioversion, age above 18 years, potassium blood concentration over 3.5 mmol/l, stable cardiopulmonary state defined as the absence of symptoms of acute coronary syndrome or heart failure exacerbation. **Exclusion criteria:** AF lasting more than 43h, lack of written informed consent, allergy to antazoline, AF related to significant valvular dis- ease, clinically significant heart failure or ejection fraction less than 55%, sys- tolic blood pressure (BP) less than 100mmHg, history of significant bradyarrhythmias without permanent pacemaker implantation, QT pro- longation over 440ms or QTc (Bazett's formula) over the population norm, heart rate more than 160', advanced liver or kidney failure, history of acute coronary syndrome, coronary artery by-pass grafting, stroke or tran- sient ischemic attack within 30 days before enrollment, pre-excitation in the ECG, signs and symptoms of ischemia related to current episode of AF, an investigational drug used within 30 days before enrollment, pregnancy or breast feeding. The b-blockers, calcium antagonist and digoxin, were permitted for up to 2 h before study drug infusion. Treatment with intra- venous anti-arrhythmic drug was not allowed for current incident of AF. Background therapy of any oral anti-arrhythmics was allowed in the study (however data given separately for those without AADs permits inclusion in systematic review). **Numbers:** 74 patients enrolled. 36 randomised to antazoline and 38 to placebo. No attrition recorded. **Anticoagulation:** No anticoagulation protocol as arrhythmia classified as paroxysmal and < 43 hours duration **Monitoring:** Continuous ECG monitoring throughout 90 minutes after drug infusion. No other follow up duration noted.
Interventions	Intravenous Antazoline Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome

	• **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Supported by Institute of Cardiology, Warsaw, Poland Scientific Grant [2.27/4/12] **Country:** Poland **Setting:** Emergency Department **Comment:** No conflict of interest reported. Planned outcomes: Conversion to sinus rhythm by end of 90 min observation period. Time to conversion, reutrn of SR directly at end of infusion, serious adverse event requiring hospitalisation or prolonged observation. BP less than 90mmHg, AV conduction disturbances, sustanted SVT, new ventricular arrhythmia, other adverse events and ECG changes. Reported outcomes: as above, including adverse events (adverse effects outcomes not reported separately for drug naive patients). Clinical trial registration number NCT01527279 **Author's Name:** Aleksandr Maciag **Institution:** The 2nd Department of Coronary Artery Disease, Institute of Cardiology, Spartanska 1, 02-637 Warsaw, Poland **Email:** mfarkowski@gmail.com **Address:** Not provided
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization will be provided by the independent statistician using SAS.9.2 software, SAS Institute Inc., Cary, NC, U.S.A.. Permuted block randomization will be used with a block size (AB, BA) not known by the investigators."
Allocation concealment (selection bias)	Unclear risk	"A Random allocation sequence will be implemented using numbered sealed envelopes opened after inclusion of the patient for the study. Contacted authors that clarified that opaque sealed envelopes were used.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	"The patient, enrolling physician, and nurse who administering the drug will all be blinded to the treatment. The study nurse who prepares the syringes I will be unblinded to the patient's assignment."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	The clinician reviewing the clinical outcomes will be blinded to the treatment. The statistician, and clinician involved in safety control will be unblinded to the patient's assignment.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Selective reporting (reporting bias)	Low risk	All planned outcomes in the published protocol and clinicaltrials.gov have been published.
Other bias	High risk	Protocol registered on clinicaltrials.gov NCT01527279 - registered before enrolment started. Study had Ethics approval. Active drug compared with placebo and results assessed at 90 min which might overinflate the results in favour of Antazoline (usually it takes longer for patients with paroxysmal AF to revert to sinus rhythm whilst on placebo). Other studies with assessment of efficacy of fast cardioverting agents usually had an active treatment comparator arm.

Madrid 1993

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics**

	Flecainide • Age (years) mean (SD): 54 (14) • Male (%): 27 (68) • LA diameter (mm) mean (SD): 38 (-) • Duration of episode (h) mean (SD): 5.9 (5.5) Procainamide • Age (years) mean (SD): 55 (14) • Male (%): 23 (58) • LA diameter (mm) mean (SD): 40 (15) • Duration of episode (h) mean (SD): 8.9 (8.1) Structural Heart disease, Valvular Heart Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Cardiomyopathy, Heart Failure, Coronary Artery Disease, Diabetes Mellitus, Hypertension, Pulmonary Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LVEF %: N/A CHA2DS2VASc: N/A AF type: All paroxysmal and duration less than 24hrs **Inclusion criteria:** Paroxysmal atrial fibrillation lasting < 24 h and if they were aged less than 75 years. **Exclusion criteria:** Any clinical or radiological sign of acute heart failure, conduction disturbances, known sick sinus syndrome, severe hypoxaemia (oxygen partial pressure <55mmHg) acute ischaemic events, acute myo- cardial infarction or electrolyte alterations. Patients with atrial flutter were excluded, as were those currently receiving antiarrhythmic drugs. Anyone with slow ventricular raate (<100 beats per min) **Numbers:** 80 patients enrolled. 40 randomised to flecainide and 40 to procainamide. No attrition recorded. **Anticoagulation:** No anticoagulation protocol as arrhythmia classified as paroxysmal and duration <24h. **Monitoring:** Intermittent 12 lead ECG every 15 mins during infusion and as soon as conversion to sinus rhythm. Continous rhythm monitoring but method not specified. Success recorded as conversion within 1 hour of starting infusion. Patients switched to other drug after 1 hour washout.
Interventions	Intravenous Flecainide Intravenous Procainamide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local funding **Country:** Spain **Setting:** Unclear Hospital Setting **Comment:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm within 1 hour of infusion. Reported outcomes: as above, including adverse events but as cross over study cannot use endpoints after cross over for systematic review. No trial registration. **Author's Name:** Antonio H. Madrid **Institution:** Arrhythmia Unit, Ramón y Cajal Hospital, Madrid, Spain **Email:** not provided **Address:** Antonio H. Madrid, Arrhythmia Unit, Ramón y Cajal Hospital, Ctra de Colmenar Viejo Km 9, 100, 29034, Madrid, Spain
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	

		no information provided on random sequence generation.
Allocation concealment (selection bias)	Unclear risk	no information available on allocation concealment
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Two different infusion rates were used. Hence personnel was not blinded. Unsure about patient.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on whether blinding of outcome assessors was performed.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Only reported inpatient outcomes. No missing data for any patients
Selective reporting (reporting bias)	Unclear risk	No evidence of Protocol published prior to the study - hence, unable to assess
Other bias	Unclear risk	No proof of trial protocol registration. Protocol approved by the local Ethics committee.

Manegold 2007

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Incremental Paddles Data not given by intervention arm AP RBW Incremental Paddles Data not given by intervention arm All Patients • Age (years) mean (SD): 70 (10) • Male (%): 31 (70) • BMI (Kg/m^2) mean (SD): 27 (4) • Hypertension (%): 29 (66) • Coronary Artery Disease (%): 14 (32) • Cardiomyopathy (%): 18 (41) • Valvular Heart Disease (%): 18 (41) • Beta-Blocker (%): 37 (84) • Amiodarone (%): 20 (45) • Digoxin (%): 20 (45) • ACE-I/ARB (%): 33 (75) • LA diameter (mm) mean (SD): 48 (7) • LVEF (%) mean (SD): 43 (18) • Duraition of episode (days) median (range): 21 (1-1359) Structural Heart Disease, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure, Pulmonary Disease: N/A Calcium Antagonist, Propafenone, Sotalol, Flecainide, Diuretic, Aspirin: N/A CHA2DS2VASc: N/A AF type: range of AF duration encompasses both paroxsymal and persistent cutoffs. No split of data by type. **Inclusion criteria:** All patients with implanted rhythm devices referred for electrical cardioversion of AF **Exclusion criteria:** Patients with implanted systems with evidence of pre-existing technical problems (e.g. undersensing or exit block) not correctable by device reprogramming were excluded from participation. Further exclusion criteria were the presence of contraindications for ECV, pregnancy, and age < 18 years. **Numbers:** 44 patients enrolled. 21 randomised to MDS waveform and 23 to RBW waveform. No attrition recorded. **Anticoagulation:** Guideline driven - oral anticoagulation aiming for INR between 2-3 for at least 3 weeks prior to cardioversion or TOE to rule out atrial thrombus if no prior

	anticoagulation. In those without prior anticoagulation treatment with fractionated or unfractionated heparin was applied. After cardioversion patients were anticoagulated with warfarin for at least 4 weeks. **Monitoring:** ECG recorded prior during and after cardoversion as well as 1 hour later. No continous monitoring reported other than that from defibrillator as well as information from implanted device. Repeat interrogation 1 hr after cardioversion and 1 week later.
Interventions	AP MDS Incremental Paddles AP RBW Incremental Paddles
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local funding **Country:** Germany **Setting:** Unclear Hospital Setting **Comment:** No conflict of interest reported. Planned outcomes: Energy required for successful cardioversion, Adverse events including lead or device failure. Influcence of anti-arrhythmic drugs on pacing performance. Reported outcomes: as planned. No trial registration. **Author's Name:** Johannes Manegold **Institution:** Division of Cardiology, Department of Medicine, J. W. Goethe University Hospital, Theodor-Stern-Kai 7, 60590 Frankfurt, Germany **Email:** hohnloser@em.uni-frankfurt.de **Address:** not provided
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was performed using an unblocked randomization scheme without stratification prepared by a computer program.
Allocation concealment (selection bias)	Low risk	Sequentially numbered opaque sealed envelopes were opened immediately before cardioversion.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	All pads were positioned in AP position. Two different devices were used for monophasic and biphasic cardioversion, hence the personnel would know most likely which treatment arm.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to method (if any) of blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization,	Low risk	Outcome data available for all patients.

Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications		
Selective reporting (reporting bias)	Unclear risk	Could not access a published version of the pre-enrolment protocol, hence could not confirm if all planned outcomes were assessed.
Other bias	Unclear risk	Study approved by the Institutional Review Board. Could not identify proof of protocol registration.

Martínez-Marcos 2000

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone • Age (mean +/- SD): 62 (14) • Men (%): 24 (48) • Pulmonary disease (%): 1 (2) • Hypertension (%): 27 (54) • Digoxin (%): 2 (4) • Beta-Blocker (%): 0 (0) • Calcium Channel Blocker (%): 4 (8) • Left Atrial Diameter (mm) (mean +/- SD): 40 (5) • LVEF (%) (mean +/- SD): 62 (7) • Duration of episode (h) median (range): 5 (1-48) Propafenone • Age (mean +/- SD): 62 (11) • Men (%): 20 (40) • Pulmonary disease (%): 3 (6) • Hypertension (%): 30 (60) • Digoxin (%): 2 (4) • Beta-Blocker (%): 2 (4) • Calcium Channel Blocker (%): 4 (8) • Left Atrial Diameter (mm) (mean +/- SD): 40 (3) • LVEF (%) (mean +/- SD): 64 (7) • Duration of episode (h) median (range): 6 (1-48) Flecainide • Age (mean +/- SD): 57 (14) • Men (%): 26 (52) • Pulmonary disease (%): 1 (2) • Hypertension (%): 27 (54) • Digoxin (%): 2 (4) • Beta-Blocker (%): 3 (6) • Calcium Channel Blocker (%): 1 (2) • Left Atrial Diameter (mm) (mean +/- SD): 39 (5) • LVEF (%) (mean +/- SD): 63 (7) • Duration of episode (h) median (range): 7 (1-33) Valvular Heart Disease, Structural Heart Disease, Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Coronary Artery Disease, Ischaemic Heart Disease, Myocardial Infarction: N/A Sotalol, Diuretics, ACE-inhibitors, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A 100% patients with paroxysmal AF <48h **Inclusion criteria:** Patients presenting to emergency department with AF <48h **Exclusion criteria:** uncertain or >48 hours duration of symptoms; known left ventricular ejection fraction <35%, usual New York Heart Association functional class>II, current chest x-ray film with cardiothoracic ratio >0.6, or clinical or radiologic signs of congestive heart failure; baseline systolic blood pressure<100 mm Hg; baseline mean ventricular rate <110 beats/min; unstable angina or myocardial infarction within the preceding month; known sick sinus syndrome or high-degree atrioventricular block; overt thyroid disease; anti-arrhythmic therapy with the trial drugs within the

	previous 3 months; pulmonary fibrosis; hepatic dysfunction; renal insufficiency (creatinine >2.5mg/dl); pregnancy or lactation; age <18, unable or unwilling to give informed consent **Numbers:** 150 patients enrolled and randomised to 50 Amiodarone, 50 Propafenone, 50 Flecainide. There was no attrition. **Anticoagulation:** AF less than 48h there was no prior anticoagulation protocol. There was no documented post cardioversion anticoagulation protocol. **Monitoring:** Follow up duration was for a 12 hour inpatient period. Monitoring was with continuous ECG.
Interventions	Intravenous Amiodarone Intravenous Propafenone Intravenous Flecainide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local Funding **Country:** Spain **Setting:** Accident and Emergency **Comments:** No conflicts of interest reported. Planned outcome for primary end point was stable sinus rhythm within 12 hours of starting medication. Reported outcome was as planned but also time to cardioversion and adverse effects. No trial registration. **Authors name:** Francisco J. Martínez-Marcos **Institution:** Servicio de Cuidados Crıticos-Urgencias and Servicio de Cardiologıa, Hospital Juan Ramo n Jimenez, Huelva, Spain **Email:** cavaleri@viautil.com **Address:** Francisco J. Martínez-Marcos, MD, Unidadde Cuidados Intensivos, Servicio de Cuidados Crıticos-Urgencias, Hospital Juan Ramon Jimenez, Ronda Norte, s/n. 21005 Huelva, Spain
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Reported as "computer-generated randomization schedule". However, no details on the randomization process.
Allocation concealment (selection bias)	Unclear risk	It is not clear how allocations of treatment were concealed.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Although it was reported as a single blind trial, and that drugs were administered in this way, the amiodarone infusion protocol was different to placebo and propafenone. Therefore it would be difficult to completely blind to personnel. "Flecainide and propafenone wereadministered as an intravenous bolus of 2 mg/kg in 20minutes. A second bolus of 1 mg/kg in 20 minutes wasadministered if conversion to sinus rhythm was notachieved within 8 hours after the first bolus. Thesecond bolus was half of the first one to minimize anyproarrhythmic risk. Amiodarone was administered asan intravenous bolus of 5 mg/kg in 20 minutes followed by a continuous infusion of 50 mg/hour. Patients were observed for a 12-hour period."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-	Low risk	Although it was reported as a single blind trial, and that drugs were administered in this way, the amiodarone infusion protocol was different to placebo and propafenone. Therefore it would be difficult to completely blind to personnel. "Flecainide and

Cause Mortality, and Stroke or Systemic Embolism		propafenone wereadministered as an intravenous bolus of 2 mg/kg in 20minutes. A second bolus of 1 mg/kg in 20 minutes wasadministered if conversion to sinus rhythm was notachieved within 8 hours after the first bolus. Thesecond bolus was half of the first one to minimize anyproarrhythmic risk. Amiodarone was administered asan intravenous bolus of 5 mg/kg in 20 minutes followed by a continuous infusion of 50 mg/hour. Patients were observed for a 12-hour period." However, "Low Risk" as these were objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	The trial was only single blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	One patient in each group (1/50) did not terminate the study protocol.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Approved by the local ethical committee.

Mattioli 1998

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 48 hours)
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD): 64.3 (12) • Men (%): 26 (68) • BMI (kg/m^2) mean: 25.6 • Hypertension (%): 6 (16) • Coronary Artery Disease (%): 4 (10.5) • Structural Heart Disease (%): 15 (39.5) • Any Anti-Arrythmic drug (%): 0 (0) • Any rate control drug (%): 0 (0) Procainamide • Age (years) mean (SD): 63 (13) • Men (%): 29 (76) • BMI (kg/m^2) mean: 26.5 • Hypertension (%): 5 (13) • Coronary Artery Disease (%): 5 (13) • Structural Heart Disease (%): 16 (42) • Any Anti-Arrythmic drug (%): 0 (0) • Any rate control drug (%): 0 (0) Valvular Heart Disease, Cardiomyopathy, Stroke/TIA, Pulmonary Disease, Myocardial Infarction, Ischaemic Heart Disease, Diabetes Mellitus: N/A Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A LA dimensions and LVEF %: N/A AF type mixed duration **Inclusion criteria:** Patients in AF with age >I8 years and recent onset AF (lasting $\leq$ 2 weeks) and chronic AF (lasting $\geq$ 2 weeks), either as a first or a recurrent episode. **Exclusion criteria:** Signs or symptoms of heart failure on physical examination, recent myocardial infarctionor cardiac surgery (< 3 months), cardiogenic shock or hypotension (systemic arterial pressure <90 mmHg), electrocardiographic (ECG) evidence of ventricular preexcitation, second- or third- degree atrioventricular block, previous diagnosis of sinus node disease, unstable hepatic or

	renal function, or evidence of digitalis intoxication and hypokalemia. Patients were also excluded if they had been treated with amiodarone, if, they were currently receiving treatment with antiarrhythmic drugs, digoxin, Ca antagonist, and beta blockers, or if they had a known allergy to one ofthe drugs. **Numbers:** 117 patients were enrolled into the study but 41 spontaenously converted to sinus rhythm before therapy. Of the remaining 76, 38 were randomised to propafenone and 38 to procainamide. None were lost to follow up. **Anticoagulation:** If patients had AF lasting more than 48 hours or unknown duration anticoagulation was administered for 3 weeks before and 4 weeks after cardioversion, all patients with duration greater than 48 hours had transoesophageal echocardiogram, if this was negative then they were treated with short term anticoagulation (IV heparin for 48 hours before cardioversion) and then 4 weeks of anticoagulation after cardioversion. **Monitoring:** Continuous heart rhythm monitoring and 12 lead ECG on conversion. Follow up period was for 48 hours after final treatment, if no conversion DCCV.
Interventions	Intravenous Propafenone Intravenous Procainamide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint No 24 endpoint for adverse events given.
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Inpatient **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm. Reported outcomes as planned as well as time to conversion and adverse events. No trial registration. **Authors name:** Anna Vittoria Mattioli **Institution:** Department of Cardiology, Internal Medicine, University of Modena, Modena, Italy **Email:** Not provided **Address:** Dr. Anna Vittoria Mattioli, Dept. of Cardiology, University of Modena Via del pozzo, 71, 41100, Modena, Italy
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No info provided
Allocation concealment (selection bias)	Unclear risk	No info provided
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Different infusion protocols. Personnel would know what drug a given patient was receiving.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-	Low risk	Objective outcome - unlikely to be affected.

Cause Mortality, and Stroke or Systemic Embolism		
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention of any effors to blind outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcome - unlikely to be affected.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome in the methods section, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Study protocol approved by University's Ethics committee. No mention of trial protocol registration/publication.

Mittal 2000

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP RBW Incremental • Age (mean +/- SD): 65 (12) • Men (%): 59 (67) • Coronary Artery Disease (%): 22 (25) • Hypertension (%): 7 (8) • Digoxin (%): 38 (43) • Beta-Blocker (%): 41 (47) • Calcium Channel Blockers (%): 27 (31) • Diuretic (%): 19 (22) • Valvular Heart Disease (%): 18 (21) • ACE Inhibitor (%): 23 (26) • Amiodarone (%): 24 (27) • Sotalol (%): 8 (9) • Cardiomyopathy (%): 3 (3) • LVEF (%) (mean +/- SD): 50 (14) • Left Atrial Diameter (mm) (mean +/- SD): 47 (10) AP MDS Incremental • Age (mean +/- SD): 66 (12) • Men (%): 56 (73) • Coronary Artery Disease (%): 24 (31) • Hypertension (%): 3 (4) • Digoxin (%): 35 (45) • Beta-Blocker (%): 35 (45) • Calcium Channel Blockers (%): 26 (33) • Diuretic (%): 21 (27) • Valvular Heart Disease (%): 13 (18) • ACE Inhibitor (%): 23 (30) • Amiodarone (%): 18 (23) • Sotalol (%): 6 (8) • Cardiomyopathy (%): 8 (18) • LVEF (%) (mean +/- SD): 48 (14) • Left Atrial Diameter (mm) (mean +/- SD): 46 (8)

	Structural Heart Disease, Heart Failure, Stroke/TIA, Diabetes Mellitus, Pulmonary Disease, Myocardial Infarction, Ischaemic Heart Disease: N/A Propafenone, Flecainide, Diuretics, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A 20% patients with paroxysmal AF <48h Remaining patients had AF >48h to 6 months (i.e. mixed AF duration population) **Inclusion criteria:** Patients were eligible for the study if they were undergoing electrical cardioversion of atrial fibrillation **Exclusion criteria:** Patients were ineligible if they were <18 years of age, were pregnant, or were undergoing cardioversion of an atrial arrhythmia other than atrial fibrillation. **Numbers:** 174 Patients enrolled, 9 excluded from analysis: 7 failed to follow pre-specified step up shock protocol, 1 had pre-treatment with ibutilide, 1 had computer issues which made shock data inaccessible. 88 randomised to biphasic, 77 randomised to monophasic. **Anticoagulation:** Patients who had AF >48 hrs were anticoagulated with warfarin for >3 weeks with INR >2.0, if not long enought anticoagulation then pt had TOE guided cardioversion. All patients had 3-4 weeks anticoag after procedure. **Monitoring:** With electrodes on device, unclear follow up duration.
Interventions	AP RBW Incremental Patches AP MDS Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Zoll Medical Co-orporation **Country:** United States of America **Setting:** Elective Admission **Comments:** Dr Lerman is a consultant to Zoll Medical Corporation and Mr Ayati is and employee of Zoll Medical Corporation Planned outcomes: Conversion to SR - AF> 30s after the shock. Reported outcomes as above and Energy, voltage current and impedance for first shock. No trial registration. **Authors name:** Suneet Mittal **Institution:** Division of Cardiology, The New York Hospital-Cornell Medical Center **Email:** blerman@mail.med.cornell.edu **Address:** Bruce B. Lerman, MD, Division of Cardiology, The New York Hospital-Cornell Medical Center, 525 East 68th Street, Starr 4, NewYork, NY 10021
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Simple block randomization scheme. No details provided on how it was done.
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Allocation concealment not specified.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Judgement Comment: "Patients randomized to the monophasic protocol received sequential shocks of 100, 200, 300, and 360 J, if necessary.If the 360-J shock failed to cardiovert the patient, a final 170-Jbiphasic shock was delivered. Patients randomized to the biphasicprotocol received sequential shocks of 70, 120, 150, and 170 J, ifnecessary. If the 170-J shock failed to cardiovert the patient, a final 360-J monophasic shock was delivered." Operator was aware of different voltages being used.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Low risk as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Judgement Comment: Unclear if the assessors were blinded.

Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: Low risk as endpoints are objective.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	High risk	Judgement Comment: Clear definition for outcome of SR, 10 patient difference in groups, this mainly due to failure of adherence to protocol. "Nine patientswere excluded from analysis. Reasons for exclusion included(1) failure of the investigator to follow the prespecifiedstep-up shock protocol (n 57), (2) pretreatment with ibutilide(n 51), and (3) inability to access cardioversion shock datadue to a computer malfunction (n 51)" 77 patients vs. 88 patients makes us believe that there was unequal exclusion of patients across the 2 groups.
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	Judgement Comment: No proof of trial registration. The Institutional Review Board at each participating institution approved the investigational protocol.

Mortensen 2007

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Incremental • Age (years) (sd): 62 (13) • Male (%): 36 (77) • Hypertension (%): 20 (43) • Coronary Artery Disease (%): 9 (19) • Valvular Heart Disease (%): 7 (15) • Cardiomyopathy (%): 2 (4) • Amiodarone (%): 4 (9) • Flecainide (%): 5 (11) • Beta-blocker (%): 16 (34) • Sotalol (%): 1 (2) • BMI (Kg/m^2) mean (SD): 26 (4) AP RBW Incremental • Age (years) (sd): 62 (12) • Male (%): 34 (71) • Hypertension (%): 20 (42) • Coronary Artery Disease (%): 13 (27) • Valvular Heart Disease (%): 7 (15) • Cardiomyopathy (%): 4 (8) • Amiodarone (%): 7 (15) • Flecainide (%): 6 (13) • Beta-blocker (%): 14 (29) • Sotalol (%): 4 (8) • BMI (Kg/m^2) mean (SD): 27 (5) Structural Heart Disease, Stroke/TIA, Diabetes Mellitus, Heart Failure, Ischaemic Heart Disease, Pulmonary Disease, Myocardial Infarction: N/A Calcium channel blocker, Digoxin, ACE-I/ARB Propafenone, Diuretics, Aspirin: N/A LA dimensions and LVEF%: N/A CHA2DS2VASc: N/A 100% of patients had atrial flutter **Inclusion criteria:** Patients were eligible for the study if electrical cardioversion was indicated for atrial flutter according to the current guidelines for acute electrical cardioversion, e.g. patients were symptomatic, had imminent cardial decompensation, hypotension or angina. **Exclusion criteria:** Patients were ineligible for this study if they were less than 18 years of age, pregnant or were undergoing cardioversion for other arrhythmias than atrial flutter.

	Numbers: 97 eligible patients randomised, 48 to RBW and 47 to MDS. No attrition reported **Anticoagulation:** All patients underwent diagnostic procedures and eventual treatment for the prevention of embolic stroke and systemic embolism according to actual guidelines for the management of patients with atrial fibrillation or flutter. After cardioversion, all patients were required to be anticoagulated for ≥4 weeks. **Monitoring:** Rhythm monitoring method not specified, likely via defibrillator. A crossover between electrode positions was planned in case of a futile shock of 200 J for a final second shock of 200 J with the alternative electrode position.
Interventions	AP MDS Incremental Patches AP RBW Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local Funding **Country:** Germany **Setting:** Outpatient clinic, Emergency room, Intensive care unit, or Wards **Comments:** No conflicts of interest reported. Planned outcomes: Successful cardioversion. All planned outcomes reported as well as adverse events. No clinical trial registration. **Authors name:** Kai Mortensen **Institution:** Department of Cardiology, University Heart Center Martinstrasse **Email:** k.mortensen@uke.uni-hamburg.de **Address:** University Hospital Hamburg-Eppendorf, Heart Center, Department of Cardiology, Hamburg, Germany; Martinistraße 52, 20246 Hamburg, Germany
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of randomization was not described.
Allocation concealment (selection bias)	Unclear risk	Randomization done right before the cardioversion, but not explained by whom and if operators were blinded.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Not explained. No mention of potential strategies for blinding. Patient and personnel would understand due to the nature of the study, unless a sophisticated approach or extra-staff were involved (and this is not decribed).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No clarification if there was an independent/blinded adjudication committee.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.

Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, a copy of the original protocol with date of publication is not available for confirming if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No irrefutable proof of trial registration. Local ethics committee approved the study.

Muñoz-Martínez 2010

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA BTE Incremental Patches • Age (years) mean (SD): 63 (9) • Male (%): 40 (87) • LA diameter (mm) mean (SD): 46 (5) • LVEF (%) mean (SD): 59 (7) • Duration of episode (days) median (range): 89 (5-1210) AP BTE Incremental Patches • Age (years) mean (SD): 55 (13) • Male (%): 35 (78) • LA diameter (mm) mean (SD): 47 (5) • LVEF (%) mean (SD): 55 (13) • Duration of episode (days) median (range): 98 (1-485) Structural heart disease, Diabetes Mellitus, Hypertension, Valvular Heart Disease, Heart Failure, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF type: Mixed population of persistent and paroxysmal AF based on range of AF duration. **Inclusion criteria:** 1) Patients aged 18 or older, 2) Persistent AF, 3)Haemodynamically stable, 4) No respiratory compromise SpO2> 90% 5) effective anticoagulation by ACC guidelines 2008 or demonstration of no intra-cardiac thrombus but TOE. 6) informed consent **Exclusion criteria:** 1) Patients younger than 18 2) Persistent AF, 3)Haemodynamically compromise or SpO2< 90% 4) Reduced conscious level 5) Clinical or electrical evidence of digitalis toxicity 6) Pregnancy 7) AF in context of myocardial infarction 8) Barrier to correct electrode placement (e.g. wall deformity, burns or device implant) 9) Electrolyte disturbance 10) increased thrombotic risk due to innappropriate anticoagulation or echocardiogaphy findings. **Numbers:** 92 patients enrolled. 46 randomised to anteroapical arm and 46 randomised to anteroposterior arm. Only one patient in the anteroapical arm cardioverted spontaenously. **Anticoagulation:** As per 2008 ACC guidelines for antithombotic therapy in atrial fibrillation or demonstration of intracardiac thrombus by TOE. **Monitoring:** 3 lead continous rhythm monitoring. Patient cross over to alternative position after 3rd shock if no success. Data after this not suitable for inclusion in systematic review.
Interventions	AA BTE Incremental Patches AP BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported

	• **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Spain **Setting:** ICU (patients referred specifically for cardioversion) **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm, number of shocks required, total energy used and need to change pad position. Other adverse effects. Reported outcomes: As planned however data after conversion not suitable for inclusion in systematic review. No trial registration. **Authors name:** Tomas Muñoz-Martínez **Institution:** Unidad de Cuidados Intensivos, Hospital Txagorritxu, Vitoria, España **Email:** tomas.munozmartinez@osakidetza.net, tomas@arconte.jazztel.es **Address:** not provided
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not specification of method for sequence generation. Paper mentions "random sequence" but provides no detail on how it was generated.
Allocation concealment (selection bias)	Low risk	Study reports that patients were assigned a pad position (AA or AL) following a random sequence that was kept in the Research unit and kept hidden to clinicians until the moment of patient inclusion in the study.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Patients and personnel not blinded to location of pads.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No specification to method of blinding, if any, of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcome data provided for all participants.
Selective reporting (reporting bias)	Unclear risk	Pre-enrolment protocol not accessible and hence could not confirm if planned outcomes were as reported on the paper.
Other bias	Unclear risk	Study approved by the Local Research council. No proof of publication of protocol in open-access platform.

Negrini 1994

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group

Participants	**Baseline Characteristics** Amiodarone • Age (sd): 61 (10) • Male (%): 12 (40) • Duration of episode h (sd): 31.1 (40.4) • Hypertension (%): 9 (30) • Coronary Artery Disease (%): 2 (6) • Valvular Heart Disease (%): 3 (10) • LA diameter (mm) (sd): 40 (7) Propafenone • Age (sd): 57 (12) • Male (%): 17 (55) • Duration of episode h (sd): 25.8 (39.3) • Hypertension (%): 7 (23) • Coronary Artery Disease (%): 2 (6) • Valvular Heart Disease (%): 4 (13) • LA diameter (mm) (sd): 38 (6) Structural Heart Disease, Ischaemic Heart Disease, Pulmonary Disease, Cardiomyopathy, Myocardial Infarction, Stroke/TIA, Diabetes Mellitus: N/A Sotalol, Flecainide, Beta-blocker, Calcium antagonist, Digoxin, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LVEF %: N/A AF type: All patients had paroxysmal AF. **Inclusion criteria:** All patients with recent-onset AF (defined as ≤1 week, who were admitted to the emergency department for primary evaluation or treatment. **Exclusion criteria:** New York Heart Association functional class >II or clinical evidence of heart failure, a ventricular heart rate <90 beats/min, systolic blood pressure < 100 mm Hg, recent myocardial infarc- tion within 3 months, unstable angina pectoris, evidence of left bundle branch block, previously documented high-degree atrioventricular block or bifascicular block, diagnosed sick sinus syndrome, thyroid or pulmonary diseases, or electrolyte imbalance. Long term anti-arrhythmi therapy within 5 half-lives of the drug. **Numbers:** 61 patients randomised, 31 to propafenone and 30 to amiodarone. None were lost to follow up. **Anticoagulation:** No anticoagulation protocol as recent onset AF (although defined as ≤1 week). **Monitoring:** Was with continuous ECG and recording of rhythm strips at any rhythm change. 12 lead ECG was recorded prior to treatment and at resumption of sinus rhythm. Follow up was for 24h.
Interventions	Intravenous Amiodarone Intravenous Propafenone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent

	• **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Total Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Accident and Emergency **Comments:** No conflicts of interest reported. Planned outcomes: SR at 1h, Blood pressure readings. Reported outcomes: As above including adverse effects. No trial registration. **Authors name:** Marco Negrini **Institution:** Division of Cardiology, Fatebenefratelli Hospital, and Division of Cardiology, Cernusco Hospital, Milan, Italy **Email:** not given **Address:** Dr. Marco Negrini, Via G. Govone 100, 20155 Milano, Italy.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	No information given on sequence generation.
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used and patients elected their own envelope.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study referred as single-blind - paper mentions that patients were anaware of the drug being given. Infusion protocols seem to be similar, but no further information was given on preparation.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objetive endpoints, not likely to be affected.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information given on whether the assessors were blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objetive endpoints, not likely to be affected.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported. Authors say that primary endpoint was defined before the start of the study.
Other bias	High risk	No mention of ethics and approval and no evidence of protocol registration. AF mean duration was 5h longer in the amiodarone, but the difference was not considered to be significant and numbers were small.

Neumann 2004

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Incremental • Age (mean +/- SD): 64 (11) • Men (%): 38 (67) • Ischaemic Heart Disease (%): 10 (18) • Hypertension (%): 25 (44)

	• Amiodarone (%): 11 (19) • Beta-Blocker (%): 19 (33) • Sotalol (%): 12 (21) • Valvular Heart Disease (%): 3 (5) • Cardiomyopathy (%): 4 (7) • LVEF (%) mean (SD): 51 (11) • LA diameter (mm) mean (SD): 40 (6) • Duration of episode (months) mean (SD): 9 (13) AP BTE Incremental • Age (mean +/- SD): 62 (11) • Men (%): 45 (74) • Ischaemic Heart Disease (%): 11 (18) • Hypertension (%): 24 (39) • Amiodarone (%): 13 (21) • Beta-Blocker (%): 24 (39) • Sotalol (%): 7 (12) • Valvular Heart Disease (%): 7 (11) • Cardiomyopathy (%): 3 (3.3) • LVEF (%) mean (SD): 49 (11) • LA diameter (mm) mean (SD): 41 (5) • Duration of episode (months) mean (SD): 7 (10) Structural Heart Disease, Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Pulmonary Disease, Coronary Artery Disease, Heart Failure, Myocardial Infarction: N/A Calcium Channel Blocker, Digoxin, Propafenone, Flecainide, ACE-inhibitor, Diuretics, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A 100% of patients had persistent AF. **Inclusion criteria:** Symptomatic persistent AF, worsening of pre-existing heart failure with atrial fibrillation, need to interrupt anticoagulation because of bleeding risk. **Exclusion criteria:** Inadequate anticoagulation, age<18, pregnancy, presence of other atrial arrhythmia other than atrial fibrillation **Numbers:** 118 patients were randomised to Monophasic (57), Biphasic (61). No attrition. **Anticoagulation:** Anticoagulation for at least 3 weeks, INR 2-3. Advised anticoagulation for at least 3 months after. **Monitoring:** Upto 48hrs inpatient monitoring if QT changes, otherwise 4-5 hrs monitoring post cardioversion. ECG monitoring with defibrillation and repeat ECG after.
Interventions	AP MDS Incremental Patches AP BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia

	• **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Germany **Setting:** Elective Admission **Comments:** No conflicts of interest reported. Planned outcomes not reported. Reported outcomes were cumulative success, success at energy levels, SR at discharge and acute thromboembolic or arrhythmic events. No trial registration. **Authors name:** Thomas Neumann **Institution:** Department of Cardiology, Kerchof Clinic, Benekstrasse 2-8, 61231 Bad Nauheim, Germany **Email:** Not Provided **Address:** Department of Cardiology, Kerchof Clinic, Benekstrasse 2-8, 61231 Bad Nauheim, Germany
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not described.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Different defibrillators used for different waveforms so personnel could not be blinded. "electrical cardioversion were randomized to receive either monophasic (n = 57) or biphasic shocks (n = 61)" Reported as single-blind.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Different defibrillators used for different waveforms so personnel could not be blinded. "electrical cardioversion were randomized to receive either monophasic (n = 57) or biphasic shocks (n = 61)" However, "low risk" as these are objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	It is not clear if outcome assessors were aware, study is reported as single blind, however not clear who is blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as these are objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients were lost to follow-up.
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	High risk	No proof of trial registration. No mention to Ethics Approval.

Noc 1990

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone Data not given by intervention arm Placebo (Verapamil) Data not given by intervention arm All patients • Age (years) mean (SD): 71 (9.6) • Male (%): 15 (63) • Duration of episode (range): 20 minutes to 48 hours

	Structural Heart Disease, Diabetes Mellitus, Hypertension, Valvular Heart Disease, Heart Failure, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A Duration of episode: N/A AF type: paroxysmal AF, duration <48 hours **Inclusion criteria:** Patients with paroxysmal atrial fibrillation. **Exclusion criteria:** Known or suspected conduction disturbances, including preexcitation; sick sinus syndrome; hyperthyroidism; concomitant therapy with antiarrhythmic drugs: arrhythmia-related systemic arterial hypotension; and any sign of heart failure. **Numbers:** 97 patients enrolled. 48 randomised to flecainide and 49 to propafenone. 45 patients discontinued before end of follow up but determined as treatment failure. **Anticoagulation:** No anticoagulation protocol as arrhythmia < 48 duration. **Monitoring:** Continuous holter monitoring througout. Cross over after 3 hours if no success. Data after this point cannot be used for systematic review.
Interventions	Intravenous Amiodarone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Slovenia (Yugoslavia) **Setting:** Unclear hospital setting **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm within 3 hours after drug administration. Reported outcomes: As planned plus adverse events but not specified if before cross-over so cannot be used in systematic review. No trial registration. **Authors name:** Marko Noc **Institution:** Center for Intensive Internal Medicine, University Clinical Center Ljubljana, Zaloska 7,610OO Ljubljana, Yugoslavia. **Email:** Not provided **Address:** Not provided
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Reported as single blind, but differrenet drug administration regimens were used, and hence patients and personell could know the assigned treatment.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Mention to study being single-blinded. However, no info on method of blinding for outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization,	Low risk	All endpoints were reported.

Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications		
Selective reporting (reporting bias)	Unclear risk	Could not find a copy of the pre-enrolment protocol, hence could not confirm if all planned outcomes were reported.
Other bias	Unclear risk	Protocol approved by the Stage Ethics Committee. No proof of trial registration prior to starting enorommnent.

Nogic 2022

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Magnesium • Age (years) mean (SD): 72 (14) • Male (%): 32 (45) • Hypertension (%): 38 (52) • Valvular Heart Disease (%): 4 (8) • Heart Failure (%): 7 (10) • Diabetes Mellitus (%): 13 (18) • Coronary Artery Disease (%): 8 (11) Placebo • Age (years) mean (SD): 71 (13) • Male (%): 31 (42) • Hypertension (%): 43 (59) • Valvular Heart Disease (%): 2 (4) • Heart Failure (%): 11 (15) • Diabetes Mellitus (%): 10 (14) • Coronary Artery Disease (%): 7 (10) Structural Heart Disease, Valvular Heart Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A Duration of episode: N/A AF type: definition and duration not given **Inclusion criteria:** 1. Greater than or equal to 18 years of age 2. ECG at presentation to Emergency Department greater than or equal to a ventricular rate of 120 3. Presenting complaint attributable to atrial fibrillation 4. Able to give informed consent **Exclusion criteria:** 1. Haemodynamically instability, in this study, defined as Systolic Blood Pressure less than 90mmHg 2. Suspected acute myocardial infarction 3. Overt sepsis suspected by treating clinician 4. Known renal impairment (egfr <30) **Numbers:** 144 patients enrolled. 71 randomised to magnesium and 73 to placebo. No attrition reported. **Anticoagulation:** No anticoagulation protocol provided. **Monitoring:** Telemetry during whole of ED stay. Medications as per ED clinician preference given after 2 hours.
Interventions	Intravenous Magnesium Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success

	• **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Australia **Setting:** Emergency Department **Comments:** No conflict of interest reported. Planned outcomes: Reduction of ventricular rate to less than 100 beats per minute, conversion to sinus rhythm within 1 hour, time to conversion or rate reduction, additional medications needed for rate reduction. Also duration of ED stay, need for hospial admission. Death at 30 day and representation at 30 reported but unclear if other anti-arrythmic drugs given in interim so endpoint cannot be used for systematic review. Reported outcomes: As planned. Australian Clinical Trial reg ACTRN12619000532101 **Authors name:** Jason Nogic **Institution:** Departments of Cardiology and Emergency Medicine Eastern Health 8 Arnold Street Box Hill Melbourne, Victoria 3128, Australia **Email:** andrew.teh@easternhealth.org.au **Address:** Not provided
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Sequentially numbered magnesium and normal saline bags which will be identical in appearance and numbered from 1-200, randomly ordered. These will be prepared in advance in batches of 10 by the hospital pharmacy department with random allocation of each unit to either contain the control drug or placebo. Only the pharmacy will be aware of which number corresponds to placebo or magnesium and both bags will be identical in appearance. " However, there is no specification on method of randomization. Mention to "batches of 10", but unsure if this implies block randomization. Also mention to "A bag (randomly chosen) by the treating team at time of recruitment shall be taken and administered and that bags number recorded for eventual analysis by a researcher."
Allocation concealment (selection bias)	Low risk	Sequentially numbered magnesium and normal saline bags which will be identical in appearance and numbered from 1-200, randomly ordered. These will be prepared in advance in batches of 10 by the hospital pharmacy department with random allocation of each unit to either contain the control drug or placebo. Only the pharmacy will be aware of which number corresponds to placebo or magnesium and both bags will be identical in appearance. Once a bag has been taken sequentially, this will become the study participants ID number to ensure accurate data analysis post hoc. This method will ensure blinding and allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	"Only the pharmacy will be aware of which number corresponds to placebo or magnesium and both bags will be identical in appearance." Similar administration protocol.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	"Only the pharmacy will be aware of which number corresponds to placebo or magnesium and both bags will be identical in appearance."
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke	Low risk	Outcomes reported for all patients. No patients seemed to have been lost to follow-up at 30 days

or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Low risk	All outcomes in the protocol seem to have reported.
Other bias	Low risk	Found trial registration on Australian government site and on the trial registration site below ACTRN12619000532101 https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=377117 Ethics approval by local institutions (proof of Ethics approval attached).

Norgaard 1999

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 3 hours or other anti-arrhythmic drug after 8 hours if no cardioversion)
Participants	**Baseline Characteristics** Dofetilide • Age (mean +/- SD): 64 (13) • Men (%): 45 (68) • Ischaemic Heart Disease (%): 13 (20) • Hypertension (%): 18 (27) • Heart Failure (%): 24 (36) • Digoxin (%): 48 (73) • Beta-Blocker (%): 7 (11) • Calcium Channel Blockers (%): 23 (35) • Valvular Heart Disease (%): 5 (8) • Left Atrial Size (mm) (mean +/- SD): 49 (13) • Duration of episode median (IQR): 64 (33 - 130) Placebo • Age (mean +/- SD): 62 (10) • Men (%): 23 (77) • Ischaemic Heart Disease (%): 11 (35) • Hypertension (%): 10 (33) • Heart Failure (%): 15 (50) • Digoxin (%): 22 (73) • Beta-Blocker (%): 5 (17) • Calcium Channel Blockers (%): 8 (27) • Valvular Heart Disease (%): 1 (3) • Left Atrial Size (mm) (mean +/- SD): 51 (12) • Duration of episode median (IQR): 51 (39 - 112) Structural Heart Disease, Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Coronary Artery Disease, Pulmonary Disease, Myocardial Infarction: N/A Sotalol, Amiodarone, Propafenone, Flecainide, ACE-inhibitor, Diuretics, Aspirin: N/A LVEF %: N/A BMI: N/A CHA2DS2VASc: N/A 19% atrial flutter no precise info on paroxysmal and persistent AF %; however, it is stated that 21% of all atrial arrhythmias lasted < 7 days. **Inclusion criteria:** Patients with a sustained rhythm of AF or AFL of a duration from 1 hour to 6 months, with haemodynamic stability and without symptoms of uncontrolled heart failure, were eligible for inclusion. **Exclusion criteria:** Previous myocardial infarction, unstable angina pectoris, or cardiac arrest or had undergone any form of heart surgery within the past 3 weeks (or any other kind of surgery <24hours). Further exclusion criteria were age <18 years, child-bearing potential, presence of thyrotoxicosis, major haematologic, hepatic, or renal disease, and history of Torsade de pointes ventricular tachycardia (TdP), a serum-potassium level <3.6 or >5.5 mmol/L, a resting ventricular rate <60beats/min, or a QT (or QTc) interval >440 ms

	Numbers: 98 patients were randomised to treatment: 67 to dofetilide, 31 to placebo. 2 were excluded because of protocol violations from each arm, for efficacy analysis. All randomised pts who received drug were included in safety analysis. **Anticoagulation:** protocol, not provided however no stroke recorded in study period. **Monitoring:** Holter monitoring was recorded throughout study period. Primary outcome follow up up to 8hrs, Adverse events during or within 30 days after study drug admission however some of this population had DCCV.
Interventions	Intravenous Dofetilide Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint No other adverse endpoints due to cross-over, however all recorded arrhythmic events before cross over
Identification	**Sponsorship source:** Local **Country:** Denmark, United Kingdom **Setting:** Not Clear **Comments:** No conflicts of interest identified.Planned outcomes: SR within 3 hours of infusion, ventricular rate before and after drug adminisatraion. Blood pressure, adverse events including Torsade de points. Reported outcomes: As planned above. No trial registration. **Authors name:** Bjarne Linde Norgaard **Institution:** Department of Medicine and Cardiology, Aarhus University Hospital **Email:** Not provided **Address:** Bjarne Linde Nørgaard, MD, Department of Medicine and Cardiology, Aarhus University Hospital, DK-8000 Aarhus C, Denmark
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention to randomization process.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not documented
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Reported as double blind study - single infusion of study drug or placebo allows for easy blinding. "Study patients received a single infusion of 8 µg/kg dofetilide or placebo through a peripheral venous catheter at a constant rate over a period of 30 minutes."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Reported as double blind study - single infusion of study drug or placebo allows for easy blinding. "Study patients received a single infusion of 8 µg/kg dofetilide or placebo through a peripheral venous catheter at a constant rate over a period of 30 minutes." However, unlikely to have an impact on objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Reported as double-blind but protocol unclear about this "The electrocardiographic recordings were interpreted by the individual investigators." No mention to endpoint assignment committee or investigator, and whether or not blinding was performed (and how).

Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Reported as double-blind but protocol unclear about this "The electrocardiographic recordings were interpreted by the individual investigators." No mention to endpoint assignment committee or investigator, and whether or not blinding was performed (and how). However, unlikely to impact on objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Only one patient in each arm lost to attrition.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No Proof of trial registration. Protocol approved by the Regional Scientific Ethical Committee of the participant centres. Some differences in baselines, but likely non-significant.

Okishige 2000

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV at 4 weeks)
Participants	**Baseline Characteristics** Pilsicainide • Age (years) mean (SD): 61 (10) • Male (%): 49 (92) • Hypertension (%): 9 (17) • Valvular Heart Disease (%): 14 (27) • Cardiomyopathy (%): 2 (4) • Coronary Artery Disease (%): 3 (6) • LA diameter (mm) mean (SD): 42 (5) • Duration of episode (months) mean (SD): 22.3 (3.8) Placebo • Age (years) mean (SD): 55 (9) • Male (%): 8 (80) • Hypertension (%): 4 (40) • Valvular Heart Disease (%): 2 (20) • Cardiomyopathy (%): 0 (0) • Coronary Artery Disease (%): 0 (0) • LA diameter (mm) mean (SD): 38 (6) • Duration of episode (months) mean (SD): 21.8 (4.2) Structural heart disease, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LVEF %: N/A CHA2DS2VASc: N/A AF type: Chronic AF deined as repeatedly documented arrythmia without intercurrent sinus rhythm on consecutive outpatient visits before cardioversion. All patients with persistent AF duration > 6 months. **Inclusion criteria:** Patients with chronic AF persisting longer than 6 months. Age > 20 years. **Exclusion criteria:** Paroxysmal AF, myocardial infarction within 12 months before entry into the study, unstable angina, sick sinus syndrome in the absence of an artificial pacemaker, severe systemic disease, hyperthyroidism, impaired left ventricular function, and long QT syndrome. **Numbers:** 62 patients enrolled. 50 randomised to pilsicainide and 10 to placebo. No reported attrition.

	Anticoagulation: Oral anticoagulation to maintain prothrombin times within a target range of 1.5 to 2.0 times value found in normal subjects not having anticoagulation. Otherwise transoesophageal echocardiogram was performed to rule out atrial thrombus. **Monitoring:** Baseline 12 lead ECG and then rhythm check at 4 weeks where patients had DCCV if no response. Effiacy outcomes after this cannot be included in systematic review.
Interventions	Oral Pilsicainide Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Japan **Setting:** Outpatient **Comments:** No conflicts of interest reported. Planned outcomes: Recurrence of AF or atrial flutter during follow-up. Side effects not amenable to dose reduction leading to discontinuation. End points after 4 weeks for efficacy cannot be used for systematic review. Reported outcomes: As planned as well as adverse events. No trial registration. **Authors name:** Kaoru Okishige **Institution:** Department of Cardiology, Yokohama Red Cross Hospital, Yokohama Minami-Kyosai Hospital, and Yokosuka Kyosai Hospital **Email:** Not provided **Address:** Kaoru Okishige, MD, Cardiovascular Division, Yokohama Red Cross Hospital 2-85 Negishi, Naka-Ku, Yokohama-City, Japan
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No specification of method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No specification if any allocation concealment was present.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study reported as double-blind but no specification of methods for blinding.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Study reported as double-blind but no specification of methods for blinding.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural	Low risk	Outcomes available for all patients.

Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications		
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes available for all patients for 28 days.
Selective reporting (reporting bias)	Unclear risk	Could not access pre-enrolment protocol to confirm if all planned outcomes were reported.
Other bias	Unclear risk	Protocol approved by the Ethics committees of participating hospitals.

Okishige 2006

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Pilsicainide • Age (years) mean (SD): 58 (9) • Male (%): 45 (78) • LA diameter (mm) mean (SD): 42 (6) • LVEF (%) mean (SD): 62 (9) • Duration of episode (days) mean (SD): 43 (34) Placebo • Age (years) mean (SD): 60 (10) • Male (%): 39 (78) • LA diameter (mm) mean (SD): 41 (7) • LVEF (%) mean (SD): 64 (10) • Duration of episode (days) mean (SD): 58 (46) Structural heart disease, Diabetes Mellitus, Hypertension, Valvular Heart Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF type: Persistent AF but defined as > 48 hours and < 6 months **Inclusion criteria:** Aged between 20 and 75 years and had persistent AF defined as AF lasting ≥48 h but not exceeding 6 months **Exclusion criteria:** (1) no necessity of digitalis administration for the appropriate rate control of AF; (2) sick sinus syndrome, intraventricular conduction disturbance, high degree atrioventricular block, or bifascicular block; (3) congestive heart failure or remarkable cardiomegaly; (4) myocardial infarction within the previous 28 days; (5) hypertrophic or dilated cardiomyopathy; (6) renal dysfunction (creatinine clearance <50ml/min) or on hemodialysis; (7) prior administration of pilsicainide; (8) contraindication of digitalization or anticoagulation with warfarin; and (9) were pregnant or lactating **Numbers:** 117 patients enrolled, 9 withdrew due to protocol violation. 108 randomised 58 to pilsicainide and 50 to placebo. No reported attrition after randomisation. **Anticoagulation:** Oral anticoagulation with warfarin to maintain prothrombin times within a target range of 1.5 to 2.0 times value found in normal subjects not having anticoagulation for more than 3 weeks prior to enrolment. Otherwise transoesophageal echocardiogram was performed to rule out atrial thrombus. **Monitoring:** Baseline 12 lead ECG and then 12 lead at 2 weeks. No patients followed up after 2 weeks.
Interventions	Oral Pilsicainide Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint

Identification	**Sponsorship source:** Local **Country:** Japan **Setting:** Outpatient **Comments:** Drugs provided by Daiichi Pharmaceutical Co, Ltd and Daiichi Asubio Pharma Co, Ltd. Planned outcomes: Efficacy outcome not specified. Reported outcomes: Conversion to sinus rhythm and adverse effects reported, however time point not given so cannot obtain data for 1 week complications. No trial registration. **Authors name:** Kaoru Okishige **Institution:** Yokohama City Bay Red Cross Hospital, Yokohama, Osaka General Medical Center, Osaka, Fukuoka University Hospital, Fukuoka, Nippon Medical School, Tama-Nagayama Hospital, Tokyo and University of Toyama, Toyama, Japan **Email:** okishige@yo.rim.or.jp **Address:** Kaoru Okishige, MD, Division of Cardiology, Heart Center, Yokohama City Bay Red Cross Hospital, 3-12-1 Shinyamashita, Naka-ku, Yokohama 231-8682, Japan
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention to method of sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention to method (if any) of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study reported as double-blind but no description of methods for blinding.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk, objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Study reported as double-blind but no description of methods for blinding.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk, objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes reported for all patients - followed for at least 2 weeks
Selective reporting (reporting bias)	Unclear risk	Could not confirm whether all planned outcomes were reported as pre-enrolment protocol not available.
Other bias	Unclear risk	Study design approved by the local Ethics committees of participant centres. No proof of protocol registration/publication.

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Incremental • Age (mean +/- SD): 65 (13) • Men (%): 73 (68) • Ischaemic Heart Disease (%): 20 (19) • Cardiomyopathy (%): 7 (7) • Hypertension (%): 31 (29) • Digoxin (%): 40 (37) • Beta-Blocker (%): 45 (42) • Calcium Channel Blocker (%): 27 (25)

	• Diuretic (%): 49 (46) • Valvular Heart Disease (%): 23 (21) • ACE Inhibitor (%): 36 (34) • Left Atrial Diameter (mm) (mean +/- SD): 48 (7) • LVEF <55%: 41% (29) AP BTE Incremental • Age (mean +/- SD): 65 (14) • Men (%): 69 (72) • Ischaemic Heart Disease (%): 23 (24) • Cardiomyopathy (%): 4 (4) • Hypertension (%): 33 (34) • Digoxin (%): 41 (43) • Beta-Blocker (%): 32 (33) • Calcium Channel Blocker (%): 33 (34) • Diuretic (%): 51 (53) • Valvular Heart Disease (%): 19 (20) • ACE Inhibitor (%): 34 (35) • Left Atrial Diameter (mm) (mean +/- SD): 48 (8) • LVEF <55%: 38% (25) Structural Heart Disease, Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Pulmonary Disease, Myocardial Infarction, Coronary Artery Disease, Heart Failure: N/A Sotalol, Amiodarone, Propafenone, Flecainide, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF <48h in 20% AF >48h to 6months 60% AF >6 months to 1 year 17% AF > 1 year 8% **Inclusion criteria:** 18 years or older, Haemodynamically Stable and scheduled for Elective cardioversion of AF **Exclusion criteria:** Epicardial defibrillator electrodes, pacemaker dependence, participation in a double-blind anti-arrhythmic trial, dependence of vasopressors or inability to place defibrillation electrodes in the positions defined by the study. **Numbers:** 210 patients eligible. 1 patient excluded due to incorrect electrode placement and 6 patients excluded due to later assessment that the original rhythm was not AF. Randomized to 107 Monophasic and 96 Biphasic (15 cross over to biphasic and 6 cross over to monophasic) **Anticoagulation:** if AF>48h duration with INR >2.0 for 3 weeks or heparin + TOE negative for LA thrombus. Anticoagulation required for 4 weeks after cardioversion. **Monitoring:** Follow up up to 48 h after procedure. Monitoring with 12 Lead ECG and a Holter monitor.
Interventions	AP MDS Incremental AP BTE Incremental
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint

	Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Grant from Heartstream, Philips Medical Systems. **Country:** United Kingdom, United States of America **Setting:** Elective Admission **Comments:** Other than industry funding, no conflicts of interest declared.Planned outcomes: Success as 2 consecutive p waves uninterrupted by AF in 30s after shock. Skin burns as identified by standardised scale. No trial registration. **Authors name:** Richard Page **Institution:** Department of Internal Medicine, University of Texas Southwestern Medical Center **Email:** rpage@parknet.pmh.org **Address:** Dr. Richard L. Page, Department of Internal Medicine (Cardiology, Clinical CardiacE lectrophysiology), University of Texas Southwestern Medical Center, Room CS7.102, 5323 Harry Hines Boulevard, Dallas, Texas 75390-9047
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Random sequence generation not described.
Allocation concealment (selection bias)	Unclear risk	Allocations were provided in sealed envelopes. Mention to the fact that devices were placed out of the view of the investigator, but no information provided on opacity of envelope.
Allocation concealment (selection bias)	Unclear risk	Allocations were provided in sealed envelopes. Mention to the fact that devices were placed out of the view of the investigator, but no information provided on opacity of envelope.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Reported as double blind. "Defibrillators were outwardly identical and differed only in serial number."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Reported as double blind. "Defibrillators were outwardly identical and differed only in serial number." Objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Investigators kept blind of allocation as device was kept out of their view. The same people were kept blind to waveform when assessing skin burn. "All ECG review was blinded as to treatment"
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Investigators kept blind of allocation as device was kept out of their view. The same people were kept blind to waveform when assessing skin burn. "All ECG review was blinded as to treatment"
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Only minimal attrition from study. Equivalent amounts of patients in each arm. Patients followed up with telephone call for skin burn to avoid missing outcomes.
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: According to the paper, prespecified outcomes were all reported. However, there is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	Judgement Comment: No proof of trial registration. Trial approved by institutional review board.

Pratt 2010

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group

Participants	**Baseline Characteristics** Placebo • Age (mean +/- SD): 62 (14) • Men (%): 86 (66) • Myocardial Infarction (%): 8 (6) • Hypertension (%): 53 (41) • Diabetes Mellitus (%): 18 (14) • Digoxin (%): 27 (21) • Beta-Blocker (%): 81 (62) • Calcium Channel Blockers (%): 32 (25) • Coronary Artery Disease (%): 16 (12) • Heart Failure (%): 25 (19) Vernakalant • Age (mean +/- SD): 61 (15) • Men (%): 92 (70) • Myocardial Infarction (%): 9 (7) • Hypertension (%): 62 (47) • Diabetes Mellitus (%): 10 (8) • Digoxin (%): 20 (15) • Beta-Blocker (%): 83 (63) • Calcium Channel Blockers (%): 24 (18) • Coronary Artery Disease (%): 17 (13) • Heart Failure (%): 27 (20) Structural Heart Disease, Stroke/TIA, Cardiomyopathy, Valvular Heart Disease, Ischaemic Heart Disease, Pulmonary Disease: N/A Sotalol, Amiodarone, Propafenone, Flecainide, ACE-inhibitor, Diuretics, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A Duration of episode: N/A LA dimensions and LVEF%: N/A Atrial flutter 23 (8.7%), paroxysmal AF 170 (64.2%), persistent AF 70 (26.4%) **Inclusion criteria:** sustained AF or AFL for3 hours but45 days **Exclusion criteria:** age18 years, body weight 45 to 136 kg (99 to 300lb), adequate anticoagulation, and systolic blood pressure90 and160 mm Hg and diastolic blood pressure95mmHg, QRS0.14 seconds without a pacemaker, a ventricular rate of50 beats/min without a pacemaker, an uncorrected QT interval of0.440 seconds, class IV heart failure, acute coronary syndrome, and myocardial infarction or cardiac surgery within 30 days before randomization. The protocol was amended on March24, 2005 to include severe valvular stenosis, hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy, or constrictive pericarditis as exclusion criteria. Patients were ineligible if they had received intravenous class I or III anti-arrhythmics, including amiodarone, within 24 hours before study drug infusion **Numbers:** 305 assessed for eligibility, 265 Randomised: 131 Placebo 134 Vernakalant. **Anticoagulation:** Protocol not specified. **Monitoring:** Continuous Holter monitoring up to 24 hours after dosing. Follow up inpatient follow up to 24hrs, then 7 day follow up and 30 day phone call.
Interventions	Intravenous Placebo Intravenous Vernakalant
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30-day all-cause mortality • **Outcome type**: AdverseEvent

	• **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day CVD mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 1 Week Complication • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Astellas Pharma US Inc, Illinois and Cardiome Pharma Corp **Country:** United States of America, Argentina, Sweden, Canada, Denmark **Setting:** Not Clear **Comments:** Drs Pratt, Roy and Wyse have previously received consulting fees for Cardiome or Astellas.Clinical Trial Reg: NCT00115791 Planned Outcomes: Conversion to SR for >1 min within 90 minutes of infusion. Time to conversion, Adverse events. Reported outcomes: as above. **Authors name:** Craig M. Pratt **Institution:** Department of Cardiology, Methodist DeBakey Heart and Vascular Center, Methodist Research Institute **Email:** cpratt@tmhs.org **Address:** Department of Cardiology, Methodist DeBakey Heart and Vascular Center, Methodist Research Institute, Houston, Texas
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No documentation of random sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No description of how allocation information was provided.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Judgement Comment: Study is double blinded although no description on how this is done. However as the administration infusion could be matched for placebo it would not be difficult to do. Therefore we will accept this as double-blind as it seems there was an effort to make it so. "Patients received either a 10-minute infusion of vernakalant (3 mg/kg)or placebo, followed by a 15-minute observation period. If the patient was still in AF or AFL, an additional 10-minuteinfusion of vernakalant (2 mg/kg) or placebo was administered."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: As above, but unlikely to impact on objective outcomes.

Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Judgement Comment: A core electrocardiogram laboratory enables blinding of outcome assessors. "The protocol included a clinical events committee and a core electrocardiogram laboratory." Information on clinicaltrials.gov stating that the committee was also blinded..
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Judgement Comment: As above, but unlikely to have had an impact on objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Judgement Comment: 1 patient died who received vernakalant, 1 patient from each arm violated protocol due to incomplete ECG data. 1 excluded from Vernakalant arm due to not having AF/AFL. 1 patient did not receive proper infusion and another did not return to follow up in placebo arm. Overall this is minimal attrition.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Judgement Comment: As above. Data in figure 2 shows that only a minor percentage of patients were lost to follow-up (n=3).
Selective reporting (reporting bias)	Low risk	Judgement Comment: Pre-specified end points were fully reported on according to protocol available on clinicaltrials.gov. However, this was posted only after the enrolment finished. NCT00115791
Other bias	Unclear risk	Judgement Comment: Trial with irrefutable proof of registration. clinicaltrials.gov NCT00115791 Cardiome Pharma, Vancouver, British Columbia, Canada, Protocol 1235-0504 Fujisawa Healthcare, North Deerfield, Illinois, protocol 04-70-10 Institutional or Regional review board at each site approved the protocol. Significant baseline differences for some of the variables.

Rajagopalan 2014

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Magnesium • Male n (%): 89 (67.4) • Age (Years) Mean (SD): 65.4 (10.4) • Duration of AF(d) mean (SD): 111.5 (231.7) • LADD (mm) mean (SD): 48 (7) • LVEF (%) mean (SD): 52.6 (11.5) • Beta-blocker n (%): 94 (71.2) • Calcium Antagonist n (%): 47 (35.6) • Digoxin n (%): 23 (16.7) • Amiodarone (%): 20 (15.2) • Sotalol (%): 15 (11.4) • Propafenone (%): 6 (4.5) • Flecainide (%): 19 (14.4) • ACE-I/ARB (%): 55 (41.7) • BMI (Kg/m^2) mean (SD): 31.3 (6.8) Placebo • Male n (%): 91 (70.5) • Age (Years) Mean (SD): 65.6 (11.9) • Duration of AF (d) mean (SD): 85.2 (114.9) • LADD (mm) mean (SD): 48 (7) • LVEF (%) mean (SD): 51.2 (11.4) • Beta-blocker n (%): 95 (73.6) • Calcium Antagonist n (%): 48 (37.2)

	• Digoxin n (%): 14 (10.9) • Amiodarone (%): 20 (15.5) • Sotalol (%): 9 (7.0) • Propafenone (%): 7 (5.4) • Flecainide (%): 15 (11.6) • ACE-I/ARB (%): 61 (47.3) • BMI (Kg/m^2) mean (SD): 32.6 (7.0) Structural Heart Disease, Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Coronary Artery Disease, Ischaemic Heart Disease, Heart Failure, Valvular Heart Disease, Pulmonary Disease, Myocardial Infarction: N/A Diuretics, Aspirin: N/A CHA2DS2VASc: N/A 85% persistent AF, 15% paroxysmal AF **Inclusion criteria:** New onset Atrial fibrillation less than 48 hours after onset undergoing electrical cardioversion. Patients with atrial fibrillation longer than 48 hours on warfarin with documented therapeutic INR levels >2 for at least 3 weeks prior to the cardioversion, or been on dabigatran for 3 weeks, or a transesophageal echocardiogram on the day of the procedure that excludes intracardiac thrombi, undergoing electrical cardioversion. **Exclusion criteria:** Creatinine >2.0 mg/dl, Potassium level less than 3.5 mmol/dl, TSH < 0.5, Magnesium levels >3.0 mg/dl, Urgent need for cardioversion (e.g., hemodynamic instability, unstable angina, pulmonary edema), Patients with recent (less than 6 weeks) acute myocardial infarction, Patients post-cardiac surgery, Pregnant women, Patients who are being treated with antiarrhythmic drugs who have received less than five doses of the drug. For amiodarone, patients who have received less than three weeks prior to cardioversion are excluded **Numbers:** 261 patients were enrolled, 132 were allocated to magnesium and 129 to placebo. 4 cardiuverted out of protocol for magnesium arm and 3 cardioverted out of protocol for placebo arm. **Anticoagulation:** All patients were anticoagulated effectively for at least 3 weeks with warfarin or a newer anticoagulant, or they underwernt transoeseophageal echocardiogram to rule out a left atrial appendage thrombus. All patients were anticoagulated for at least 4 weeks after cardioversion. **Monitoring:** Method was not specified although probably with defibrillator. Max follow up 1 hour.
Interventions	**Intervention Characteristics** Magnesium Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	Sponsorship Source: Local Country: USA Setting: Elective Admission

	Comment: No conflicts of interest reported. Planned outcomes were successful cardioversion of AF to sinus hrythm lasting at least 1 hour. However data regarding cardioversion prior to electrical cardioversion was provided. Clinicaltrials registration was NCT01597557 Author's Name: Bharath Rajagopalan Institution: Department of Medicine, University at Buffalo, Buffalo General Medical Centre, Buffalo, USA Email: abcurtis@buffalo.edu Address: Anne B. Curtis, MD, Department of Medicine, University at Buffalo, Buffalo General Medical Center, D2-76, 100 High St, Buffalo, NY 14203
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Computer generated randomised sequence at individual local centres. No information provided on how the sequence was generated.
Allocation concealment (selection bias)	Unclear risk	Randomization done at the pharmacy. No documentation of concealment method / No information if the infusions were prepared by the pharmacy (that could be an effective concealment method).
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Double blinding is mentioned and it is demonstrated how this may work with the protocol for patients, and for personel regarding the Magnesium Sulphate solution (same infusion volume, therefore possible if it comes prepared from the pharmacy or is prepared away from the treating physician).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Double blinding was mentioned but method not described
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above but low risk as the endpoints were objective.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Data assessed for all patients.
Selective reporting (reporting bias)	Low risk	Pre-specified end points available on clinicaltrials.gov and were fully reported. Protocol and endpoints published in May 2012. Enrolment started April 2012.
Other bias	Unclear risk	Irrefutable proof of trial registration. clinicaltrials.gov NCT01597557 Protocol and endpoints published in May 2012. Enrolment started April 2012. Approved by the Institutional Review Board at the University at Buffalo

Reisinger 1998

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Flecainide • Male n (%): 30 (56) • Age (Years) Mean (SD): 65 (12) • Previous Symptomatic AF n (%): • Duration of AF (h) Median (Q1 - Q3): 12.72 (0.1 - 1.50) • Hypertension n (%): 15 (28) • Structural Heart Disease n (%): 5 (9) • Coronary Artery Disease n (%): 9 (17) • Valvular Heart Disease n (%): 5 (9) • Heart Failure n (%): 15 (28) • LADD (mm) mean (SD): 58 (8) • LVEF <50% n (%): 15 (28) • Any rate control n (%): 12(22)

	• Beta-blocker n (%): 0 (0) • Calcium Antagonist n (%): 0 (0) • Digoxin n (%): 12 (22) • BMI (Kg/m^2) mean (SD): 27 (4) Sotalol • Male n (%): 31 (60) • Age (Years) Mean (SD): 59 (15) • Previous Symptomatic AF n (%): • Duration of AF (h) Median (Q1 - Q3): 9.84 (0.18 - 1.48) • Hypertension n (%): 16 (31) • Structural Heart Disease n (%): 5 (10) • Coronary Artery Disease n (%): 6 (12) • Valvular Heart Disease n (%): 5 (10) • Heart Failure n (%): 14 (27) • LADD (mm) mean (SD): 57 (8) • LVEF <50% n (%): 14 (27) • Any rate control n (%): 14 (24) • Beta-blocker n (%): 0 (0) • Calcium Antagonist n (%): 0 (0) • Digoxin n (%): 14 (27) • BMI (Kg/m^2) mean (SD): 26 (4) Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Pulmonary Disease, Ischaemic Heart Disease: N/A Amiodarone, Propafenone, ACE-inhibitor, Diuretics, Aspirin: N/A CHA2DS2VASc: N/A 81% paroxysmal AF and 19% persistent AF **Inclusion criteria:** Sustained AF lasting 15 minutes to 6 months with a ventricular rate of more than 80 beats/min at rest **Exclusion criteria:** Clinical signs of congestive heart failure (New YorkHeart Association functional class.II), Severely reduced left ventricular systolic function, Unstable angina pectoris, Acute myocardial infarction within the preceding 6 weeks, Hypotension (systolic blood pressure,100 mm Hg) Obstructive pulmonary disease, Recent antiarrhythmic therapy (treatment with antiarrhythmicagents of class I to IV within the previous 48 hours or amiodarone within the previous 6 months), Documented conduction disturbances of more than first-degree atrioventricular block or sick sinus syndrome (unless protected by a permanent pacemaker), Prolongation of the corrected QT (QTc) interval(450 ms), AF lasting > 48 hours without appropriate anticoagulation therapy, Compromised renal function(i.e., serum creatinine >2.5 mg/dl), Hepatic insufficiency, Uncorrected hypokalemia, Flecainide or sotalol hypersensitivity, Pregnancy and lactation, Age less than 16 or greater than 85 years,Inability or unwillingness to give written informed consent. **Numbers:** 106 patients randomised; 54 to flecainide, 52 to sotalol. There was no attrition. **Anticoagulation:** Anticoagulation protocol was not specified but patients with AF >48h with inadequate anticoagulation were excluded. **Monitoring:** There was continuous cardiac rhythm monitoring and patients were followed up for up to 2hrs as inpatients.
Interventions	Intravenous Flecainide Intravenous Sotalol
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint

	Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** This study was supported byresearch grants from F. Joh. Kwizda GmbH, and Bristol-Myers SquibbGmbH, Vienna, Austria. **Country:** Austria **Setting:** Not clear **Comments:** The study protocol was approved by the institutional committees on human research of the participating hospitals. There were no conflicts of interest. Planned outcomes: Sinus Rhythm within 2 hours of starting medication also adverse events, cardioversion predictors, and rate slowing. Reported outcomes: as planned. No trial registration. **Authors name:** Johann Reisinger **Institution:** Department of Internal Medicine, Krankenhaus Barmherzige Schwestern, Austria **Email:** Not documented **Address:** Department of Internal Medicine, Krankenhaus Barmherzige Schwestern, Seilerstaette 4, A-4020 Linz, Austria.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No clear method for sequence generation identified/how patients split into treatment groups
Allocation concealment (selection bias)	Unclear risk	Not documented
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Reported as single blinded and protocol amenable to participant blinding. "Trial medication was given by infusion over 15 minutes at a dose of 1.5mg/Kg body weight (maximum 150mg) and all patients were monitored for 2 hours". No details were given on who was blinded, but we assume the patients were most likely blinded.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above. However, this should have no impact on objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Blinding not clearly documented. "Cardiac rhythm was monitored continuously for 4 h after starting medication. A 12-lead electrocardiogramwas recorded at the time of conversion to sinus rhythm or on the appearance of a significant rhythm change and at 90 minafter starting medication." No information on the outcome assessor.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No information on the outcome assessor. However, not likely to have had an impact on objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes clearly stated. All patient and outcomes accounted for (54 in Flecainide group, 52 in Sotalol group).
Selective reporting (reporting bias)	Unclear risk	All pre-specified end points were fully reported on. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Approved by the local ethical committees of the participating hospitals.

Reisinger 2004

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 90 min if failure)
Participants	**Baseline Characteristics** Flecainide • Age mean (SD): 63 (15)

	• Male (%): 61 (60) • Coronary Artery Disease (%): 17 (17) • Hypertension (%): 44 (44) • Valvular heart disease (%): 7 (7) • Duration of AF (hours) mean (SD): 11.5 (5.3, 22.9) • Digoxin (%): 29 (29) • Beta-blocker (%): 31 (31) • Calcium Antagonists (%): 24 (24) • BMI (Kg/m^2) mean (SD): 28 (4) • LA diameter (mm) mean (SD): 52 (8) Ibutilide • Age mean (SD): 63 (13) • Male (%): 67 (63) • Coronary Artery Disease (%): 13 (12) • Hypertension (%): 47 (44) • Valvular heart disease (%): 5 (5) • Duration of AF (hours) mean (SD): 13.3 (7.3, 23.0) • Digoxin (%): 30 (28) • Beta-blocker (%): 32 (31) • Calcium Antagonists (%): 21 (20) • BMI (Kg/m^2) mean (SD): 27 (5) • LA diameter (mm) mean (SD): 50 (9) Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Ischaemic Heart Disease, Myocardial Infarction, Pulmonary Disease: N/A Amiodarone, Propafenone, Sotalol, ACE-inhibitor, Diuretics, Aspirin: N/A LVEF%: N/A CHA2DS2VASc: N/A All patients had AF < 48h **Inclusion criteria:** Sustained AF with a ventricular rateP60beats/min at rest, lasting > 1h and < 48 h. **Exclusion criteria:** Exclusion criteria were clinical signs of congestive heart failure (New York Heart Association functional class>II), severely reduced left ventricular systolic function (mean left ventricular fractional shortening<20%), unstable angina pectoris, acute myocardial infarction within the pre-ceding 6 weeks, hypotension (systolic blood pressure<100mmHg), recent anti-arrhythmic therapy (treatment with anti-arrhythmic agents of class I or III within the previous 48 h or amiodarone within the previous 6 months), any previously documented atrio-ventricular or intraventricular conduction disturbances of more than first degree atrio-ventricular block or of more than unifascicular block, sick sinus syndrome (unless protected by a permanent pacemaker), prolongation of the QTc(corrected QT interval; Fridericia's correction) >450 ms, compromised renal function (i.e., serum creatinine>2.5 mg/dl), hepatic insufficiency, uncorrected hypokalaemia or hypomagnesaemia, flecainide or ibutilide hypersensitivity, pregnancy and lactation, age<19 or>90 years, and inability or unwillingness to give written informed consent. **Numbers:** 207 Patients randomised to Flecanide N=101 Ibutilide N=106. No attrition documented. **Anticoagulation:** Anticoagulation protocol prior not defined as recent onset AF. No post cardioversion protocol given. **Monitoring:** Cardiac Rhythm monitoring continuously for 4h after starting medication. Total follow up duration was 4h.
Interventions	Intravenous Flecainide Intravenous Ibutilide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported

	• **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Pharmacia-Austria gmbH, F. Joh, Kwizda GmbH **Country:** Austria **Setting:** Accident and Emergency **Comment:** No conflicts of interest reported other than research grant. Planned outcomes: Conversion of AF to SR within 90 min after start of medication. Differences in the frequency of adverse events and difference between two drugs in slowing of the ventricular rate in non-converters. Reported outcomes: as above. No trial registration. **Author's Name:** Johann Reisinger **Institution:** Department of Internal Medicine/Cardiology, Krankenhaus Barmherzige Schwestern **Email:** johann.reisinger@bhs.at **Address:** Department of Internal Medicine/Cardiology, Krankenhaus Barmherzige Schwestern, Seilerstatte 4, A-4020 Linz, Austria
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomisation was done. No desciption on how it was done (size of blocks)
Allocation concealment (selection bias)	Unclear risk	Method not documented
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Reported as single-blind. No mention of blinding or method, but drugs given as different duration infusions. Therefore, only patients were blinded most likely.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but low risk as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention of event adjudicating committee.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients. No patients lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: All pre-specified end points were fully reported on. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	Judgement Comment: No proof of trial registration. Protocol approved by the institutional committees on human research of the 10 participating hospitals.

Ricard 2001

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA BTE Fixed

	• Age (mean +/- SD): 69 (10) • Men (%): 22 (73) • Coronary Artery Disease (%): 6 (20) • Hypertension (%): 11 (37) • Valvular Heart Disease (%): 7 (23) • Cardiomyopathy (%): 1 (3) • Left Atrial Diameter mm (mean +/- SD): 46 (6) • LVEF % (mean +/- SD): 58 (10) • Paroxysmal AF (%): 2 (7) • Chronic AF (%): 28 (93) AA MDS Incremental • Age (mean +/- SD): 66 (12) • Men (%): 17 (63) • Coronary Artery Disease (%): 2 (7) • Hypertension (%): 8 (30) • Valvular Heart Disease (%): 9 (33) • Cardiomyopathy (%): 2 (7) • Left Atrial Diameter mm (mean +/- SD): 46 (6) • LVEF % (mean +/- SD): 56 (11) • Paroxysmal AF (%): 2 (7) • Chronic AF (%): 25 (93) Stroke/TIA, Structural Heart Disease, Pulmonary Disease, Diabetes Mellitus, Heart Failure, Ischaemic Heart Disease: N/A Beta-blocker, Calcium antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, ACE-inhibitor, Diuretics, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A Persistent AF in 93%, paroxysmal in 7%. **Inclusion criteria:** (1) AF lasting more than 48 h either paroxysmal (current episode7 days) or chronic (current episode >7 days)(2) Absence of thrombus on the transoesophageal echocardiogram per-formed in all patients within 48 h prior to cardioversion(3) A minimum of 4 weeks anticoagulation with warfarin or a similar agent and an INR>2·5 or intravenous or subcutaneous heparin for72 h according to the recommendations of the Working Group on Arrhythmias of the European Society of Cardiology(4) Informed consent to participate in the study under the approval of the Institutional Review Board. **Exclusion criteria:** Patients with hyperthyroidism, patients under 18 years of age and pregnant women were excluded from the study **Numbers:** 57 Eligible Randomised: Biphasic 30, Monophasic 27, None lost to follow up. **Anticoagulation:** 4 weeks anticoagulation INR >2.5 with Warfarin, or IV/SC heparing for >= 72h **Monitoring:** Method not specified. No follow up duration specified.
Interventions	AA BTE Fixed Patches AA MDS Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** France **Setting:** Not Clear **Comments:** No conflicts of interest reported. Planned outcome: Successful Shock if Sinus Rhythm >=5min, Reported Outcomes: Successful Restoration of Sinus Rhythm (>=5min), Cardiac Enzymes. No trial registration.

	Authors name: S.Levy **Institution:** Division of Cardiology, Hospital Nord **Email:** slevy@ap-hm.fr **Address:** Professor Samuel Levy, MD, Division of Cardiology, Hopital Nord, 13015 Marseille, France.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No documentation of sequence generation
Allocation concealment (selection bias)	Unclear risk	Randomised concealment in series of 10 envolopes. No information provided on opacity of envelope, and where these are kept. Envelope was opened by nurse right before the procedure.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Not documented if patients were blinded, "Patients randomized to the monophasicgroup received an initial shock of 150 J and (if neces-sary) a second shock of 360 J. In case of failure, thepatient was crossed oved to the biphasic protocol. Patients randomized to biphasic waveform shocks received afirst 150 J shock and (if necessary) a second150 J shock. The energy of 150 J was selected as it is the highest energy that the defibrillator used could deliver." Different defibrillators were used for mono or biphasic shocks, therefore it is unlikely the performing clinician was not blinded.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No documentation of whether outcome assessors were aware of allocation.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above but low risk as objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No significant patient numbers lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	All pre-specified end points were fully reported on. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Protocol approved by the institutional review board.

Risius 2009

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA RBW Incremental • Age (mean +/- SD): 62 (13) • Men (%): 35 (73) • Coronary Artery Disease (%): 19 (39) • Hypertension (%): 20 (42) • Valvular Heart Disease (%): 11 (23) • Cardiomyopathy (%): 4 (8) • Amiodarone (%): 7 (15) • Flecainide (%): 5 (10) • Beta-blockers (%): 11 (23) • Sotalol (%): 5 (10) • BMI (kg/m^2) mean (sd): 24 (4) • Duration of episode < 48h (%): 24 (50) • Duration of episode > 48h (%): 24 (50)

	AP RBW Incremental • Age (mean +/- SD): 62 (12) • Men (%): 37 (77) • Coronary Artery Disease (%): 11 (23) • Hypertension (%): 21 (44) • Valvular Heart Disease (%): 5 (10) • Cardiomyopathy (%): 1 (2) • Amiodarone (%): 5 (10) • Flecainide (%): 5 (10) • Beta-blockers (%): 11 (23) • Sotalol (%): 5 (10) • BMI (kg/m^2) mean (sd): 26 (5) • Duration of episode < 48h (%): 24 (50) • Duration of episode > 48h (%): 24 (50) Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Pulmonary Disease, Heart Failure, Ischaemic Heart Disease, Myocardial Infarction: N/A Calcium channel blockers, Digoxin, Propafenone, ACE-inhibitor, Diuretics, Aspirin: N/A CHA2DS2VASc: N/A LA dimensions and LVEF %: N/A All atrial flutter patients. **Inclusion criteria:** Patients were eligible for the study if according to current guidelines, the electrical cardioversion of atrial flut- ter was indicated by, for example, imminent cardiac decompensation, hypotension, or angina pectoris. **Exclusion criteria:** Aged <18 years, pregnant, or planned for cardioversion of arrhythmias other than com- mon atrial flutter **Numbers:** 98 Eligible Randomised: 48 to anteroapical arm and 48 to anteroposterior arm. None lost to follow up. No follow up duration specified. **Anticoagulation:** 4 weeks anticoagulation after cardioversion. Patients were investigated and managed for embolic stroke or systemic embolism prior to cardioversion though protocol is not given. **Monitoring:** Method not specified. Max follow up duration not provided.
Interventions	AA RBW Incremental Patches AP RBW Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Germany **Setting:** Outpatient Clinic, Emergency Room, ICU or Wards

	Comments: No conflicts of interest reported. Planned outcome: Successful Shock if Sinus Rhythm >=30s, Reported Outcomes: Successful Restoration of Sinus Rhythm (>=30s), Skin irritations. Clinical trials registration number UKE-2383. **Authors name:** Tim Risius **Institution:** University Hospital Hamburg-Eppendorf, Heart Center, Department of Cardiology **Email:** risius@uke.uni-hamburg.de **Address:** University Hospital Hamburg-Eppendorf, Heart Center, Department of Cardiology, Hamburg, Germany
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomization was not described.
Allocation concealment (selection bias)	Unclear risk	Randomization done right before the cardioversion, but not explained by whom and if operators were blinded.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Not explained. No mention of potential strategies for blinding. Patient and personnel would understand due to the nature of the study, unless a sophisticated approach or extra-staff were involved (and this is not decribed).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No clarification if there was an independent/blinded adjudication committee.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Selective reporting (reporting bias)	Low risk	According to the paper, prespecified outcomes were all reported. The study was registered at ClinicalTrials.gov (NCT00860314) only after the end of enrolment. However study also had a local protocol record UKE-2383.
Other bias	Unclear risk	Proof of trial registration. The study was registered at ClinicalTrials.gov (NCT00860314) only after the end of enrolment. However study also had a local protocol record UKE-2383. Local ethics committee approved the study.

Romano 2001

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 24 hours)
Participants	**Baseline Characteristics** Flecainide • Age (sd): 59 (12) • Male (%): 65 () • Duration of episode h (sd): 11.3 (16) • Hypertension (%): 63 (45.6) • Diabetes Mellitus (%): 10 (7.2) • Ischaemic Heart Disease (%): 6 (4.3) • Valvular Heart Disease (%): 9 (6.5) • LA diameter (mm) (sd): 38 (5) • LVEF >55% (%): 129 (93.5) • BMI (kg/m^2) (sd): 27 (5) • Any Antiarrythmic drug: 0 (0) Propafenone • Age (sd): 59 (13) • Male (%): 79 (48)

	• Duration of episode h (sd): 11.8 (12) • Hypertension (%): 77 (46.9) • Diabetes Mellitus (%): 13 (7.9) • Ischaemic Heart Disease (%): 10 (6.1) • Valvular Heart Disease (%): 10 (6.1) • LA diameter (mm) (sd): 37 (5) • LVEF >55% (%): 153 (93.4) • BMI (kg/m^2) (sd): 27 (4) • Any Antiarrythmic drug: 0 (0) Placebo • Age (sd): 60 (8) • Male (%): 23 (46) • Duration of episode h (sd): 10.9 (10) • Hypertension (%): 19 (35.2) • Diabetes Mellitus (%): 4 (7.4) • Ischaemic Heart Disease (%): 2 (3.7) • Valvular Heart Disease (%): 4 (7.4) • LA diameter (mm) (sd): 35 (6) • LVEF >55% (%): 52 (96.3) • BMI (kg/m^2) (sd): 27 (5) • Any Antiarrythmic drug: 0 (0) Structural Heart Disease, Pulmonary Disease, Cardiomyopathy, Myocardial Infarction, Stroke/TIA, Heart Failure: N/A Beta-blocker, Calcium antagonist, Digoxin, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A AF type: All patients had paroxysmal AF. **Inclusion criteria:** All patients who came to the emergency room of our hospital with AF lasting < 72 hours, with ventricular rate > 100 beats/min and with hemodynamic stability (NYHA class I or II) **Exclusion criteria:** Widening of the QRS, anamnestic sinus node disease, permanent pacemaker implanted, ongoing treatment with antiarrhythmic drugs or digitalis, known intolerance towards flecainide or propafenone, ongoing myocardial ischemia , recent myocardial infarction or cardiac surgery (<4 weeks), severe liver or kidney disease, pregnancy or any disease with a poor short-term prognosis. **Numbers:** Of 352 eligible patients 302 were randomised to treatments, 138 to flecainide and 164 to propafenone. The other 50 patients were those who refused informed consent to pharmacological treatment were assigned to the control group. None were lost follow up. **Anticoagulation:** None given as recent onset AF, although the definition was <72h. **Monitoring:** With continuous ECG. Maximum inpatient follow up was 24h.
Interventions	Intravenous Flecainide Intravenous Propafenone Intravenous Placebo (Not randomised)
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia

	• **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Accident and Emergency **Comments:** No conflicts of interest reported. Planned outcomes: None specified although sinus rhythm at 3h is measured to deterimine dischargability. Reported outcomes: Sinus rhythm at 1, 3, 6 and 24hrs as well as adverse events. No Trial registration. **Authors name:** Salvatore Romano **Institution:** Dipartimento di Cardiologia, Azienda Ospedaliera Ospedale Civile, Caserta **Email:** not given **Address:** Dr Luciano Fattore, Dipartimento di Cardiologia, U.O Eletrofisologia ed Elettrostimolazione, Azienda Ospedaliera, Via Tescione, 81100 Caserta
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Mention of "causally alternating drugs" - antiarrhythmics - given to consecutive patients attending the ED. Seems like a predictable A/B sequence, not a random sequence. Placebo seems to have been assigned to patients that did not consent for active antiarrhythmic treatment, based on description.
Allocation concealment (selection bias)	High risk	Mention of "causally alternating drugs" given to patients attending the ED. allocation could be predicted from previous patient as it is simple "alternation"
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Infusion protocols are different - propafenone runs in 10 min and flecainide runs in 20 min, which means personnel will know which drug was assigned.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, not likely to be affected.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to blinding of assessors or who the assessors were.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, not likely to be affected.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	High risk	No mention to Ethics approval of protocol registration. Randomization methods not likely ideal and numbers in the two treatment arms are slightly different (138 vs 164).

Roy 2004

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Vernakalant • Male n (%): 20 (56) • Age (Years) Mean (SD): 60 (16)

	• Hypertension n (%): 23 (64) • Diabetes Mellitus n (%): 8 (23) • B-Blocker n (%): 23 (64) • ACE Inhibitor n (%): 9 (25) • Calcium Channel Blocker n (%): 10 (28) • Digoxin n (%): 6 (17) • Duration of episode median (range): 13.3 (5.1-59.4) Placebo • Male n (%): 14 (70) • Age (Years) Mean (SD): 63 (13) • Hypertension n (%): 9 (45) • Diabetes Mellitus n (%): 5 (25) • B-Blocker n (%): 15 (75) • ACE Inhibitor n (%): 6 (30) • Calcium Channel Blocker n (%): 6 (30) • Digoxin n (%): 6 (30) • Duration of episode median (range): between 11.5 to 19.5 (5.1-70.4) Stroke/TIA, Pulmonary Disease, Coronary Artery Disease, Structural Heart Disease, Ischaemic Heart Disease, Valvular Heart Disease, Cardiomyopathy: N/A Amiodarone, Sotalol, Flecainide, Propafenone, Diuretic, Aspirin: N/A LA dimensions and LVEF: N/A BMI: N/A CHA2DS2VASc: N/A Patients had a mix of recent onset and recurrent AF **Inclusion criteria:** To be eligible, patients with recent onset AF (recurrent or new onset) had to have AF with a continuous duration of 3 to 72 h at the time of randomization. Patients had to be over 21 years of age and had to be haemodynamically stable (Systolic blood pressure from 90mmHg to 160mmHg as well as a diastolic blood pressure <95mmHg), they should also be able to provide written consent. **Exclusion criteria:** Exclusion criteria included female patients of child-bearing potential; weight >136Kg; history of long QT syndrome, torsade de pointes, or an uncorrected QT interval of 450 ms; QRS >120ms; myocardial infarction; symptoms of angina; congestive heart failure; stroke within the previous three months; cardiac surgery in the previous six months; bradycardia (<50 beats/min) or sick sinus syndrome, unless controlled by a pacemaker; digoxin toxicity; reversible cause of AF (such as hyperthyroidism, pulmonary embolism, alcohol intoxication, acute pericarditis); Wolff-Parkinson-White syndrome; chronic obstructive pulmonary disease requiring daily bronchodilation therapy; cyanotic or other significant congenital heart disease; concurrent treatment with known QT-prolonging drugs or class I or III anti-arrhythmic agents (unless the medication was discontinued more than five half-lives before enrollment); oral amiodarone in the prior six months or intravenous amiodarone in the previous month; endstage disease; and the following laboratory abnormalities: serum potassium <3.5 mEq/L, magnesium <1.5 mEq/L, serum creatinine >= 1.8mg/dl, haemoglobin <9g/dl in women or <11g/dl in men, and liver enzymes 1.5 times the maximal normal values. No alcohol, caffeine, herbal remedies, or smoking was permitted during the study. Preenrollment treatment with beta-adrenergic blocking agents, calcium antagonists, and digoxin for control of ventricular rate was permitted. **Numbers:** 65 patients were elegible and were randomised, however 9 patients who were randomised did not recieve the study drug (7 were not in AF at the time of the intended study drug administration, one had a screening failure and one withdrew consent); patients were randomised 20 to placebo and 36 to Vernakalant. No patients were lost to follow up. **Anticoagulation:** Patients were managed according to the American College of Cardiology/American Heart Association/European Society of Cardiology anticoagulation practice guidelines. **Monitoring:** Patients were continously monitored with a holter rhythm strip as well as 12 lead ECGs before dosing as well as every minute during infusion to 5 mins after and at various intervals until discharge 24h and 1 week after.
Interventions	Intravenous Vernakalant Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported

	• **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Cardiome Pharma **Country:** Canada **Setting:** Unclear **Comment:** No conflicts of interest reported. Planned outcomes: Conversion to Sinus within 30min of first infusion, Remaining in sinus rhythm at 30 mins at 1hr and 24 hours. Reported outcomes as above. No trial registration. **Author's Name:** Denis Roy **Institution:** Montreal Heart Institute, University of Montreal, Montreal, Quebec, Canada **Email:** d_roy@icm-mhi.com **Address:** Dr. Denis Roy, Montreal Heart Institute, 5000 Belanger Street, Montreal, Quebec, Canada, H1T 1C8
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information available.
Allocation concealment (selection bias)	Unclear risk	No information available.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	The authors stated that: "This was a prospective double-blinded, placebo- controlled, randomized, dose-response trial. Multiple levels of blinding were employed, including the treating physician, patient, treating nurse, research nurse, family physician, follow-up assessment, and outcome adjudicators." Even though there is no specification of how blinding of patients and physicians/nurses is performed, the explanation below seems to allow for blinding: "Patients were randomized to one of three groups and in each group received up to two 10-min intravenous infusions, separated by 30 min. Infusions were placebo followed by placebo, 0.5 mg/kg followed by 1.0 mg/kg RSD1235 if required, or 2.0 mg/kg followed by 3.0 mg/kg RSD1235 if required."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above. Objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	The authors specifify that blinding was present for "outcome adjudicators." "Efficacy outcomes were adjudicated by Drs. Dickinson, Rowe, and Ezrin before unblinding of treatment allocation"
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of	High risk	Protocol contemplated electrical cardioversion if no success within a certain timeframe. Authors state that: "Patients who were electrically cardioverted were not evaluated for secondary end points." This means that for some endpoints, data are not available for 30 to 40% of patients.

ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications		
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	High risk	Protocol contemplated electrical cardioversion if no success within a certain timeframe. Authors state that: "Patients who were electrically cardioverted were not evaluated for secondary end points." This means that for some endpoints, data are not available for 30 to 40% of patients. Follow-up data available for 7 days.
Selective reporting (reporting bias)	High risk	All pre-specified efficacy end points were fully reported on. However, safety/adverse events are reported and not mentioned in the methods section. There is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	Judgement Comment: No proof of trial registration. "The study protocol was approved by the institutional or ethics review boards at each of the participating sites." "Nine patients were randomized but did not receive the study drug (seven not remaining in AF at the time of intended study drug administration; one with screening failure; and one who withdrew consent), and they were withdrawn from further participation in the study" - We do not know if this affected all groups equally and it is possible that it may have interfered with the randomization process. There seem to be numerical differences in the duration of AF, prevalence of hypertension, utilization of beta-blockers, etc.

Roy 2008

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Vernakalant • Male n (%): 159 (71.9) • White n (%): 212 (95.9) • Age (Years) Mean (SD): 62.3 (13.7) • Duration of AF (h) Median (Q1 - Q3): 59.1 (1.2, 1041) • Hypertension n (%): 91 (41) • Ischaemic Heart Disease n (%): 44 (20) • Myocardial Infarction n (%): 24 (11) • Heart Failure n (%): 32 (14) • Beta-blocker n (%): 128 (57.9) • Calcium Antagonist n (%): 40 (18.1) • Digoxin n (%): 55 (24.9) • Class I anti arrhythmic n (%): 14 (6.3) • Class III anti arrhythmic n (%): 12 (5.4) Placebo • Male n (%): 75 (65.2) • White n (%): 113 (98.3) • Age (Years) Mean (SD): 61.5 (11.3) • Duration of AF (h) Median (Q1 - Q3): 41.8 (1.2, 1082) • Hypertension n (%): 53 (46) • Ischaemic Heart Disease n (%): 24 (21) • Myocardial Infarction n (%): 9 (8) • Heart Failure n (%): 18 (16) • LADD (mm) mean (SD): • Beta-blocker n (%): 71 (61.7) • Calcium Antagonist n (%): 27 (23.5)

	• Digoxin n (%): 36 (31.3) • Class I anti arrhythmic n (%): 8 (7.0) • Class III anti arrhythmic n (%): 5 (4.3) Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Valvular Heart Disease, Pulmonary Disease: N/A Sotalol, ACE-inhibitor/ARB, Diuretics, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LA dimensions and LVEF%: N/A 65% of patients had paroxysmal AF and 35% persistent AF **Inclusion criteria:** To be eligible, patients had to have sustained AF for 3 hours to 45days, be18 years of age, have a body weight of 45 to 136 kg, be receiving adequate anticoagulation, and have a systolic blood pressure 90 mm Hg and 160 mm Hg and a diastolic blood pressure 95 mm Hg. Women could not be pregnant or nursing and, if premenopausal, had to use an effective form of birth control **Exclusion criteria:** Patients were excluded if they had sick-sinus syndrome or QRS more than 0.14 seconds without a pacemaker; ventricular rate of 50 bpm; uncorrected QT more than 0.440 seconds; typical atrial flutter; New York Heart Association class IV heart failure; acute coronary syndrome, myocardial infarction, or cardiac surgery within 30 days before enrollment; an investigational drug within 30 days before enrollment; a reversible cause of AF; end-stage disease; previously failed electric conversion; uncorrected electrolyte imbalance; or digoxin toxicity. **Numbers:** 356 Patients randomised. 20 patients did not receive study drug and were withdrawn: 14 spontaneously converted to sinus rhythm; 2 violated inclusion or exclusion criteria; 2 were diagnosed with myocardial infarction; 1 could not obtain the study drug; and 1 discontinued for an unspecified reason. This left 336 randomised: 221 to Vernakalant, 115 to Placebo. **Anticoagulation:** Anticoagulation protocol was not specified. **Monitoring:** Follow up was for at least 8 hours and continuous ECG monitoring was done for 24 hours.
Interventions	Intravenous Vernakalant Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30 day cardiovascular mortaility • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day all cause mortaility • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h

	• **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Astellas Pharama US, Cardiome Pharma Group Canada **Country:** Canada, United States of America, Denmark, Sweden **Setting:** Elective Admission **Comment:** Clinical trial reg NCT00468767. Funding from Astellas Pharma and Cardiome Pharma Corp. Dr Roy has received consultant fees from and is an advisory board member for Cardiome Pharma Corp, Astellas Pharma US, Inc, Sanofi-aventis, and CryoCath Technologies Inc. Dr Roy also held stock in Cardiome Pharma Corp and is fully divested. Dr Pratt has received consultant fees and honoraria from Astellas Pharma US, Incand Cardiome Pharma Corp. Dr Torp-Pedersen has received grant support and honoraria from Astellas Pharma US, Inc and Cardiome Pharma Corp. Dr Wyse has received consultant fees from Astellas Pharma US, Inc, Boehringer Ingelheim, Cardiome Pharma Corp, CVTherapeutics, Medtronic, Novartis, Sanofi-aventis, and Transoma Medical; grant support from Astellas Pharma US, Inc, Cardiome Pharma Corp, and Medtronic; and speaker's fees from Astellas Pharma US, Inc, Cardiome Pharma Corp, and Eisai Inc. Dr Stiell has received research support from the Canadian Institutes of HealthResearch and the National Institutes of Health. Dr Ip has received grant support from Aryx Therapeutics, Astellas Pharma US, Inc, Biotronik, Cardiome Pharma Corp, Guidant, Reliant Pharmaceuticals, Inc, SCTR/NIH, St Jude, and Vitatron. Dr Pritchett has received consultant fees from Astellas Pharma US, Inc, Cardiome Pharma Corp, NovaCardia Inc, Procter & Gamble, Reliant Pharmaceuticals,Inc, Sanofi-aventis, and Solvay Pharma BV. Dr Camm has received consultant fees, honoraria, and speaker's fees from Astellas Pharma US, Inc and Cardiome Pharma Corp. The remaining authors report no conflicts. Planned Outcomes: Primary Efficacy end point was the proportion of patients with short duration AF in sinus rhythm for at least 1 minute within 90 minutes of drug initiation. Also time to conversion and proportion of patients in Sinus Rhythm at 24 hours. Same outcomes for longer duration AF. In addition adverse events were recorded. Reported outcomes: as above. **Author's Name:** Denis Roy **Institution:** Montreal Heart Institute **Email:** d_roy@icm-mhi.com **Address:** Dr Denis Roy, Montreal Heart Institute, 5000 Belanger St, Montreal, Quebec H1T 1C8, Canada.
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomisation was used, but no details on how it was performed.
Allocation concealment (selection bias)	Unclear risk	No information provided on this.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Described as double-blind. Infusions were similar in length of time given. "Patients received a 10-minute infusion of vernakalant (3.0 mg/kg) orplacebo, followed by a 15-minute observation period. If the patient did not convert to sinus rhythm, an additional dose of vernakalant(2.0 mg/kg) or placebo was administered."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above and objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	"Conversion to sinus rhythm and termination of AF were adjudi-cated by a Clinical Events Committee blinded to treatment assign-ment. The Clinical Events Committee also reviewed all episodes ofsuspected torsade de pointes. All 12-lead ECGs and 24-hour Holter recordings were reviewed by a cardiologist at the central ECGlaboratory who was blinded to treatment assignment." Trial data outcomes adjucation clearly blinded.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above and objective endopints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Low risk. Acute outcomes available for all patients. More vernakalant patients (n=16; 6.8%) did not receive treatment after randomisation than placebo (n=4; 3.3%), however the provided reason was conversion to sinus rhythm prior to drug administration.
Incomplete outcome data (attrition bias) Outcomes assessed also after	Low risk	5 patients with vernakalant (2%) were lost to follow-up vs 1 (1%) in the placebo group. Follow-up for 30 days.

discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Low risk	Pre-specified end points were fully reported on. However, protocol available on clinicaltrials in 2007 and enrolment finished in 2004.
Other bias	Unclear risk	Irrefutable proof of trial registration, but only available on clinicaltrials.gov after the end of enrolment. Protocol approved by the institution or regional review board.

Satullo 1996a

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Propafenone Data not given by treatment arm Quinidine Data not given by treatment arm All patients • Age (years) mean (range): 58.2 (30-75) • Male (%): 51 (64) Structural heart disease, Diabetes Mellitus, Hypertension, Valvular Heart Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Heart Failure: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A Duration of episode: N/A AF type: Recent onset AF defined as <10 days ago **Inclusion criteria:** Patients with recent onset AF beggining less than 10 days ago. **Exclusion criteria:** NYHA class III and IV, acute myocardial infarction, any degree of persistent AV block, AF with haemodynamic compromise, WPW syndrome, hepatic or renal insufficiency, sinus node dysfunction based on history of syncope or previous ECG, QRS prolongation more than 120ms, acute illness capable of compromising haemodynamic status or patients general condition, ongoing therapy with digoxin or class I/III antiarrythmics. **Numbers:** 80 patients enrolled. Numbers randomised not given but outcome totals indicate 41 in propafenone arm and 37 in quinidine. Reasons for loss of 2 patients: 1 in propafenone arm due to documentation of dilated cardiomyopathy and 1 in quinidine arm due to development of urticarial rash. **Anticoagulation:** No protocol reported. **Monitoring:** Baseline 12 lead ECG and then every 8 hours for 3 days or when sinus rhythm achieved. If no conversion after 3 days then a 2 day washout period was permitted before alternative drug prescribed. Data after initiation of washout period cannot be used for systematic review.
Interventions	Oral Propafenone Oral Quinidine
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome

	• **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Total adverse events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Unclear hospital setting **Comments:** No conflicts of interest reported. Planned outcomes not specified. Reported outcomes were conversion to sinus rhythm and adverse events. No trial registration. **Authors name:** G Satullo **Institution:** Ospedale di Papardo, Messina, Servisio di Cardiologia con UTIC, Policlinico Universitario, Messina, Cattedra di Cardiologia, Ospedale Margherita, Messina Servizio di Cardiologia **Email:** Not Provided **Address:** G Satullo, Via Lepanto, 7 -98122 Messina
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	The two drugs compared had different posology with propafenone given three times daily and quinidine every 4 hours +- digoxin.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information on blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Selective reporting (reporting bias)	Unclear risk	No protocol available regarding the pre-publication period, and hence could not assess if all planned outcomes were assessed.
Other bias	High risk	No information on Ethics approval and no proof of prior trial registration.

Scheuermeyer 2019

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV at 2 hours in chemical cardioversion arm)
Participants	**Baseline Characteristics** Procainamide • Age (years) mean (SD): 57 (13) • Male (%): 26 (63) • Heart Failure (%): 0 (0) • Hypertension (%): 10 (24) • Stroke/TIA (%): 0 (0) • Diabetes Mellitus (%): 1 (2) • Beta-blocker (%): 3 (7) • Digoxin (%): 0 (0) • Calcium Antagonist (%): 2 (5) • Amiodarone (%): 0 (0) • Sotalol (%): 0 (0) • Propafenone (%): 3 (7) • Aspirin (%): 18 (44) • CHADS2 score 0 (%): 29 (70.7) • CHADS2 score 1 (%): 12 (29.3) • CHADS2 score 2 (%): 0 (0) BTE Incremental • Age (years) mean (SD): 59 (11) • Male (%): 26 (60) • Heart Failure (%): 0 (0) • Hypertension (%): 14 (33) • Stroke/TIA (%): 0 (0) • Diabetes Mellitus (%): 2 (5) • Beta-blocker (%): 3 (7) • Digoxin (%): 0 (0) • Calcium Antagonist (%): 0 (0) • Amiodarone (%): 1 (2) • Sotalol (%): 3 (7) • Propafenone (%): 1 (2) • Aspirin (%): 19 (44) • CHADS2 score 0 (%): 25 (58.1) • CHADS2 score 1 (%): 15 (34.9) • CHADS2 score 2 (%): 3 (7.0) Structural heart disease, Valvular Heart Disease, Heart Failure, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease: N/A Flecainide, Diuretic, ACE inhibitor: N/A BMI: N/A CHA2DS2VASc: N/A, only older CHADS2 score values given LA dimensions and LVEF %: N/A Duration of episode: N/A AF type: All paroxysmal, duration less than 48 hours. **Inclusion criteria:** Patients between 18 and 75 years of age with episode of AF less than 48 hours' duration as the primary diagnosis were screened by emergency physicians and referred for enrollment **Exclusion criteria:** Patients who attended the ED for other reasons (for example, trauma or gout and were found to have incidental AF) were not included as the AF had likely been present for an unknown length of time. Hemodynamically unstable patients (those with altered mental status, acute chest pain or heart failure, or systolic blood pressure less than 90 mm Hg) were excluded as such patients are often treated with rapid electrical countershock. Patients with atrial flutter were ineligible since this dysrhythmia does not readily convert with procainamide. AF patients with an acute underlying medical illness were also excluded, since they respond poorly to rhythm control. Patients could not have had a cardiac procedure such as coronary artery bypass grafting, percutaneous coronary intervention, electrophysio- logic ablation, or pacemaker or defibrillation insertion within the prior 2 weeks, as such patients are typically managed by cardiologists or surgeons. Finally, patients who were acutely intoxicated or withdrawing from alcohol or illicit drugs were ineligible. **Numbers:** 135 eligble patients considered. 49 declined enrollment. 86 patients enrolled. 42 randomised to procainamide first arm and 44 randomised to BTE incremental only arm. One

	patient in each arm withdrew after randomisation, one self withdrew in the chemical first arm and another in the BTE only arm was found to have an elevated troponin. None were lost to longer term follow up. **Anticoagulation:** Arrhythmia duration was less than 48 hours. **Monitoring:** Monitoring method not repoted. Patients followed up for 3 days post dishcharge and 30 days. However patients in procainamide arm had DCCV after 2 hours if no conversion, that efficacy data cannot be used for systematic review.
Interventions	Intravenous propafenone BTE Incremental
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Stroke or systemic embolism at 30 days • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day all cause mortality • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Canada **Setting:** Accident and Emergency **Comments:** No conflicts of interest reported. Planned outcomes: Proportion of patients discharged within 4 hours of ED arrival. ED length of stay, ED based adverse events, 30 day patient-centered outcomes, quality of life assessment. Reported outcomes: As planned however data after conversion not suitable for inclusion in systematic review. NCT01994070

	Authors name: Frank X. Scheuermeyer **Institution:** Department of Emergency Medicine, St Paul's Hospital and the University of British Columbia **Email:** frank.scheuermeyer@gmail.com **Address:** not provided
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomly assigned to receive one of two treatments: Using the RedCap (Vanderbilt University, Nashville, TN,) online algorithm, consenting eligible patients were block-randomized in groups of four at each site in a 1:1 fashion using concealed allocation.
Allocation concealment (selection bias)	Low risk	Using RedCap features, the assigned intervention is concealed in an effective manner.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Electrical cardioversion arm required sedation, involvement of a specialized team and the use of a defibrillator.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	"Two emergency physicians blinded to allocation reviewed each event to ascertain whether it was truly an adverse event"
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes reported for all patients - at 30 days.
Selective reporting (reporting bias)	Low risk	All initially planned endpoints were reported.
Other bias	Low risk	Ethics approval gained. Proof of prospective trial registration at clinicaltrials.gov NCT01994070 (prior to study start).

Schmidt 2017

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP BTE Incremental • Age mean (SD): 67 (8) • Male (%): 51 (78) • AF duration in months median (IQR): 5 (2, 24) • BMI (Kg/m^2) mean (SD): 30 (6) • Hypertension (%): 51 (78) • Congestive heart failure (%): 12 (19) • Ischaemic heart disease (%): 12 (18)

	• Pulmonary Disease (%): 5 (8) • Valvular heart disease (%): 7 (11) • Prior stroke / TIA (%): 4 (6) • Prior myocardial infarction (%): 5 (8) • Amiodarone (%): 18 (28) • Beta-blocker (%): 53 (82) • Digoxin (%): 18 (28) • Flecainide (%): 1 (2) • ACE-I/ARB (%): 40 (62) • Calcium Antagonist (%): 20 (31) AP PB Incremental • Age mean (SD): 66 (9) • Male (%): 51 (74) • AF duration in months median (IQR): 3 (2, 9) • BMI (Kg/m^2) mean (SD): 29 (6) • Hypertension (%): 51 (74) • Congestive heart failure (%): 20 (29) • Ischaemic heart disease (%): 13 (19) • Pulmonary Disease (%): 2 (3) • Valvular heart disease (%): 3 (4) • Prior stroke / TIA (%): 6 (9) • Prior myocardial infarction (%): 1 (1) • Amiodarone (%): 6 (9) • Beta-blocker (%): 57 (83) • Digoxin (%): 14 (19) • Flecainide (%): 1 (1) • ACE-I/ARB (%): 44 (64) • Calcium Antagonist (%): 16 (23) Coronary Artery Disease, Cardiomyopathy, Diabetes Mellitus: N/A Sotalol, Propafenone, Diuretics, Aspirin: N/A LA dimensions and LVEF%: N/A CHA_2DS_2-VASc: N/A % of patients with persistent AF and paroxysmal AF not clear. Nearly 14% had atrial flutter. **Inclusion criteria:** All patients admitted for elective cardioversion of AF or atrialflutter were eligible for inclusion. **Exclusion criteria:** The exclusion criteria were age<18 years, pregnancy, untreated hyperthyroidism, or an oxygen saturation<92% and supra-ventricular arrhythmias other than AF or atrial flutter. **Numbers:** 144 patients assessed for eligibility, 137 randomised: 70 to PB Incremental and 67 to BTE Incremental . 1 in PB group was unable to follow protocol due to adverse event and 2 in BTE group developed SR before treatment. **Anticoagulation:** All patients were required to be adequately anti-coagulated or alternatively have undergone a recent transesophageal echocardiography documenting the absence of intra cardiac thrombi (ESC guidance is quoted) **Monitoring:** With continuous ECG and the duration of. inpatient follow up was for 4 hours.
Interventions	AP BTE Incremental Patches AP PB Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia

	• **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local Funding, Marie de Lancy Pedersen's Foundation **Country:** Denmark **Setting:** Elective Admission **Comment:** Disclosures: Deakin served as the immediate past chair of ILCOR Advanced Life Support task force. The remaining authors have no disclosures to report. Planned outcomes: Primary end point was successful cardioversion defined as sinus rhythm 4 hours after cardioversion, secondary points were sinus rhythm 1 to 30 minutes after cardioversion, troponin levels before and after, complications such as arrhythmia detected on ECG and other adverse events such as skin burns. Reported outcomes: as above. Clinical trial registration: NCT02317029 **Author's Name:** Anders S. Schmidt **Institution:** Department of Internal Medicine, Regional Hospital of Randers **Email:** bl@clin.au.dk **Address:** Bo Løfgren, MD, PhD, Department of Internal Medicine,Regional Hospital of Randers, Skovlyvej 15, 8930 Randers NE, Denmark
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomized using simple randomization with random numbers from 1 to 4 in sealed envelopes. These were only opened at the time of cardioversion.
Allocation concealment (selection bias)	Unclear risk	Allocations were done in sealed envelopes which were only opened at the time of randomization. However, there is no information on whether the envelope is opaque and appropriate for the purpose.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	No mention of blinding or methods
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No mention of blinding on methods, but unlikely to impact on objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention of blinding or methods
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	No mention of blinding on methods, but unlikely to impact on objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Only a very small number of patients were not included in the final analysis (3 out of 137; 2%). Reasons provided are acceptable (2 patients already in SR right before cardioversion and 1 patient with a side effect not allowing following the protocol), and patients equally distributed through the 2 intervention arms.
Selective reporting (reporting bias)	Unclear risk	Study protocol published in clinicaltrials.gov NCT02317029 However, enrolment started in September 2013 and the protocol was only submitted to clinicaltrials.gov in March 2014, and outcomes available in December 2014 (enrolment ended in August 2014). Secondary Endpoints: sinus rhythm 1 and 30 minutes after cardioversion not mentioned on the clincial trials entry.
Other bias	Unclear risk	Irrefutable proof of Trial registration: NCT02317029 Even though recruitment started before the date of protocol registration on clinicaltrials.gov, the protocol was published in clinical trials before study publication. Study approved by the National Committee on Health Research Ethics (no. 1-10-720150-13) and the Danish Data Protection Agency (no. 1-16-02-425-13),

		both dated 2013, which means there was a peer-reviewed protocol before the start of inclusion.

Schmidt 2019

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP BTE Maximum Fixed • Age (years) (sd): 68 (9) • Male (%): 90 (70) • BMI (Kg/m^2) mean (SD): 30 (6) • Hypertension (%): 84 (65) • Heart Failure (%): 39 (30) • Valvular Heart Disease (%): 9 (7) • Ischaemic Heart Disease (%): 9 (7) • Diabetes Mellitus (%): 11 (9) • Stroke/TIA (%): 15 (12) • Amiodarone (%): 10 (8) • LA volume (ml/m^2): 37 (13) • CHA_2DS_2-VASc = 0 (%): 7 (5) • CHA_2DS_2-VASc = 1 (%): 21 (16) • CHA_2DS_2-VASc $\geq$ 2 (%): 101 (78) • Duration of episode < 1 month (%): 14 (11) • Duration of episode 1-12 month (%): 77 (60) • Duration of episode > 12 month (%): 37 (29) AP BTE Incremental • Age (years) (sd): 68 (8) • Male (%): 109 (74) • BMI (Kg/m^2) mean (SD): 29 (6) • Hypertension (%): 81(55) • Heart Failure (%): 36 (25) • Valvular Heart Disease (%): 17 (12) • Ischaemic Heart Disease (%): 16 (11) • Diabetes Mellitus (%): 13 (9) • Stroke/TIA (%): 11 (7) • Amiodarone (%): 12 (8) • LA volume (ml/m^2): 39 (13) • CHA_2DS_2-VASc = 0 (%): 11 (7) • CHA_2DS_2-VASc = 1 (%): 32 (22) • CHA_2DS_2-VASc $\geq$ 2 (%): 104 (71) • Duration of episode < 1 month (%): 17 (11) • Duration of episode 1-12 month (%): 85 (58) • Duration of episode > 12 month (%): 45 (31) Stroke/TIA, Cardiomyopathy, Diabetes Mellitus, Pulmonary Disease: N/A Beta-blocker, Digoxin, Calcium channel blocker, Propafenone, Diuretics, Aspirin ACE-I/ARB: N/A LVEF%: N/A All patients had persistent AF. **Inclusion criteria:** Persistent atrial fibrillation scheduled for elective direct-current cardioversion were eligible for participation in the study. We defined persistent atrial fibrillation in accordance with the 2016 ESC guidelines on the management of atrial fibrillation. The inclusion criteria were an electrocardiogram (ECG) documenting atrial fibrillation, age>_18 years, and ability to sign the informed consent **Exclusion criteria:** Exclusion criteria were patients with haemodynamic unstable atrial fibrillation, untreated hyperthyroidism, pregnancy, and previous enrolment in the study.Patients were required to receive sufficient anticoagulation or alternatively a

	transoesophageal echocardiogram documenting the absence of intra-cardiac thrombi according to guidelines **Numbers:** 296 Patients assessed for eligibility, 276 patients randomised: 129 for BTE Maximum Fixed, 145 to BTE incremental, 2 in BTE incremental also received 1 maximum energy shock. **Anticoagulation:** Patients were required to receive sufficient anticoagulation or alternatively a transoesophageal echocardiogram documenting the absence of intra-cardiac thrombi according to guidelines (2016 ESC). **Monitoring:** With 12 lead ECG 1 min after cardioversion and continuous ECG surveillance over 4 hours.
Interventions	AP BTE Maximum Fixed Patches AP BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local Funding **Country:** Denmark **Setting:** Elective Admission **Comments:** No conflicts of interest reported. Planned outcomes: presence of sinus rhythm on 12 lead ECG recorded 1 min after cardioversion. First shock efficacy. Safety endpoints including any arrhythmia, myocardial injury measured by troponin and skin irritation or redness. Reported outcomes: as above. Clinicaltrials.gov registration: NCT02923414 **Authors name:** Anders S. Schmidt **Institution:** Clinical Research Unit, Randers Regional Hospital **Email:** bl@clin.au.dk **Address:** Clinical Research Unit, Randers Regional Hospital, Skovlyvej 15, 8930 Randers NE, Denmark
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomisation (1:1) using computer generated random numbers.
Allocation concealment (selection bias)	Low risk	"The numbers were placed in consecutive numbered, sealed, opaque envelopes. The envelopes were opened by the treating physician immediately prior to cardioversion."
Blinding of participants and personnel (performance bias) All other outcomes	High risk	"The patients and care providers were blinded to the intervention but due to the nature of the study, the physician delivering the shocks was not blinded."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but these endpoints are objective.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Although the physician delivering the shocks was not blinded, the nurse measuring the nurse and investigator analysing ECGs were.

Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above. Objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There were no missing data on the primary endpoint, and no patients were excluded from the intention-to-treat analysis.
Selective reporting (reporting bias)	Low risk	Numbers were reported on all outcomes. The outcome definitions make selective reporting unlikely. NCT02923414 Protocol available on clinicaltrials.gov at the time enrolment started.
Other bias	Low risk	Irrefutable proof of trial registration (a few days study started; study lasted for 3 years). NCT02923414 The protocol was approved by the Danish Research Ethical Committee for the Central Denmark Region and the Danish Data Protection Agency.

Schmidt 2021

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA BTE Incremental • Age (mean +/- SD): 69 (10) • Men (%): 156 (67) • Ischaemic Heart Disease (%): 28 (12) • Hypertension (%): 149 (64) • Valvular Heart Disease (%): 26 (11) • Diabetes (%): 23 (10) • Previous Stroke/TIA (%): 21 (9) • Heart Failure (%): 67 (29) • CHA_2DS_2-VASc mean (SD): 2.6 (1.7) • On Digoxin (%): 42 (18) • Beta-blocker (%): 194 (83) • Amiodarone (%): 39 (17) • Flecainide (%): 4 (2) • ACE inhibitor or ARB (%): 123 (53) • AF duration (days) median (IQR): 27 (10-51) • BMI (Kg/m^2) mean (SD): 28.8 (5.8) AP BTE Incremental • Age (mean +/- SD): 69 (9) • Men (%): 158 (68) • Ischaemic Heart Disease (%): 27 (12) • Hypertension (%): 151 (65) • Valvular Heart Disease (%): 33 (14) • Diabetes (%): 22 (9) • Previous Stroke/TIA (%): 17 (7) • Heart Failure (%): 54 (23) • CHA_2DS_2-VASc mean (SD): 2.5 (1.5) • On Digoxin (%): 32 (14) • Beta-blocker (%): 179 (76) • Amiodarone (%): 30 (13) • Flecainide (%): 2 (1) • ACE inhibitor or ARB (%): 114 (49) • AF duration (days) median (IQR): 30 (10-518) • BMI (Kg/m^2) mean (SD): 28.9 (5.4) Approximately 80% persistent AF and 20% paroxysmal AF

	Structural Heart Disease, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction: N/A Sotalol, Calcium Channel Blocker, Propafenone, Diuretic, Aspirin: N/A LA dimensions and LVEF: N/A **Inclusion criteria:** Adult patients (≥18 years of age) with AF who were scheduled for elective cardioversion. **Exclusion criteria:** Arrhythmias other than AF; implantable devices (eg, pacemaker or implantable cardioverter defibrillator); hemodynamically unstable AF; untreated hyperthyroidism; known or suspected pregnancy. **Pretreatment:** 468 patients Eligible for study, 1 patient was accidentally randomised twice. 467 patients randomised: 233 patients to AA arm and 234 patients to AP arm. No patients lost to follow up. **Anticoagulation:** All patients were anticoagulated or had TOE to exclude LA thrombus prior to procedure. **Monitoring:** Rhythm monitoring method not documented. 2 hours of continuous monitoring post cardioversion. Long term follow up duration not described.
Interventions	AP BTE Incremental Patches AA BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Health Research Foundation of Cen- tral Denmark Region, Aarhus University, A.P. Møller Fonden, Rosa og Asta Jen- sens Fond (Rosa and Asta Jensens Foundation), and Direktør Kurt Bønnelycke og Hustru Grethe Bønnelyckes Fond (Managing Director Kurt Bønnelycke and Mrs Grethe Bønnelyckes Foundation) **Country:** Denmark **Setting:** Elective Admission **Comment:** Dr Schmidt received a consulting fee from Ooono A/S. Dr Møller has been an advisory board member for Bayer and has received speaker's honoraria from Bayer, Bristol Meyers Squibb, Boehringer Ingelheim, Merck Sharp and Dohme, and Pfizer. All other authors have nothing to disclose relevant to this study. Clinical trials registration: NCT03817372 **Author's Name:** Anders Schmidt **Institution:** Department of Internal Medicine, Randers Regional Hospital **Email:** bl@clin.au.dk **Address:** Professor Bo Løfgren, MD, PhD, Department of Internal Medicine, Randers Regional Hospital, Skovlyvej 15, 8930 Randers NE, Denmark
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was stratified according to study site and with variable block sizes of 4, 6, or 8.
Allocation concealment (selection bias)	Low risk	Randomisation was performed by an external service to ensure concealment of assignments

Blinding of participants and personnel (performance bias) All other outcomes	High risk	It was not possible to blind physicians delivering the shock to the pad positions due to the nature of the study.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Assessment of these outcomes is objective and therefore not subject to influence from allocation blinding.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Blinded assessment of the outcomes was performed centrally by an investigator through an electronic review of the cardiover- sion attempts using CODE-STAT 10 data review software (Stryker/Physio-Control Inc). Due to the nature of the study the authors considered it was impossible to blind nurses assessing adverse events to the allocations.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Blinded assessment of the outcomes was performed centrally by an investigator through an electronic review of the cardioversion attempts using CODE-STAT 10 data review software (Stryker/Physio-Control Inc). Objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Low risk	All endpoints present in the protocol were reported in the manuscript.
Other bias	Low risk	Trial registered on NCT03817372 and outcomes defined and unchanged prior to the start of enrolment. Approved by The Research Ethics Committee for the Central Denmark Region (registration no. 1-10-72-332-18).

Siaplaouras 2004

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Incremental • Age (mean +/- SD): 65 (10) • Men (%): 78 (72) • Coronary Artery Disease (%): 18 (17) • Hypertension (%): 33 (31) • Cardiomyopathy (%): 12 (11) • Digoxin (%): 8 (7) • Beta-Blocker (%): 25 (23) • Sotalol (%): 28 (26) • Valvular Heart Disease (%): 29 (27) • Amiodarone (%): 30 (28) • LVEF (%) (mean +/- SD): 62 (15) • LA diameter (mm) (mean +/- SD): 48 (6) • Duration of episode (months) mean (SD): 3.2 (4) • BMI (Kg/m^2) mean (SD): 27.4 (4) AP RBW Incremental • Age (mean +/- SD): 66 (10) • Men (%): 77 (71) • Coronary Artery Disease (%): 22 (20) • Hypertension (%): 37 (34) • Cardiomyopathy (%): 11 (10) • Digoxin (%): 4 (4) • Beta-Blocker (%): 42 (39) • Sotalol (%): 18 (17) • Valvular Heart Disease (%): 25 (23) • Amiodarone (%): 31 (29) • LVEF (%) (mean +/- SD): 59 (13) • LA diameter (mm) (mean +/- SD): 48 (7) • Duration of episode (months) mean (SD): 4.1 (10)

	• BMI (Kg/m^2) mean (SD): 27.9 (4) Structural Heart Disease, Pulmonary Disease, Heart Failure, Stroke/TIA, Ischaemic Heart Disease, Myocardial Infarction: N/A Calcium Antagonist, Propafenone, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A All patients had persistent AF **Included criteria:** Patients with symptomatic persistent AF referred for elective cardioversion. **Excluded criteria:** acute cardiopulmonary decompensation, significant electrolyte imbalance (potassium<3.5 or>5.0 mM), a reversible cause of AF (e.g. hyperthyroidism), ineffective anticoagulation during the last 4 weeks prior to cardioversion (international normalized ratio [INR] target range: 2–3), and an AF duration>1 year **Numbers:** 216 patients fulfilled criteria. Randomised to 108 Monophasic, 108 Biphasic. There was no attrition. **Anticoagulation:** Protocol was 4 weeks prior to cardioversion with INR 2-3. **Monitoring:** Follow up duration was for at least 3 hours after cardioversion and monitoring was with continuous ECG.
Interventions	AP MDS Incremental Patches AP RBW Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local funding **Country:** Germany **Setting:** Elective Admission **Comments:** No conflicts of interest reported. Planned Outcomes: Successful cardioversion defined as termination of AF with at least 2 consecutive sinus beats. ERAF was defined as a relapse of AF within 1 minute after a successful cardioversion. Reported Outcomes: As planned. No trial registration. **Authors name:** Stephanos Siaplaouras **Institution:** Klinik fur Innere Medizin, Kardiologie, Angiologie und Internistische Intensivmedizin, Universitatsklinikum des Saarlandes, Homburg/Saar, Germany **Email:** siaplaouras@aol.com **Address:** Stephanos Siaplaouras, M.D, Klinik fur In-nere Medizin, Kardiologie, Angiologie und Internistische Intensivmedizin, Universitatsklinikum des Saarlandes, D-66421 Homburg, Germany
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No documentation of sequence generation method
Allocation concealment (selection bias)	Unclear risk	It is not shown how the randomizations were concealed
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Authors considered it would be impossible to blind patients or personel in this study design
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	It is not clear if those assessing conversion to sinus rhythm and adverse events were aware of the treatment allocations
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above but objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization,	Low risk	There was no attrition in this study

Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications		
Selective reporting (reporting bias)	Unclear risk	All pre-specified end points were fully reported on. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	High risk	No proof of trial registration. No mention to Ethics Approval.

Siaplaouras 2005

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP RBW Incremental • Age (mean +/- SD): 67 (10) • Men (%): 40 (67) • LVEF (%) (mean +/- SD): 60 (13) • Ischaemic Heart Disease (%): 10 (16) • Hypertension (%): 26 (44) • Cardiomyopathy (%): 3 (5) • Sotalol (%): 9 (15) • Beta-Blocker (%): 29 (48) • Amiodarone (%): 16 (27) • Digoxin (%): 2 (3) • Valvular Heart Disease (%): 14 (23) • Left Atrial Diameter (mm) (mean +/- SD): 49 (7) • Duration of episode (months) mean (SD): 3.0 (5) • BMI (Kg/m^2) mean (SD): 27.7 (4) AA RBW Incremental • Age (mean +/- SD): 66 (10) • Men (%): 47 (75) • LVEF (%) (mean +/- SD): 59 (13) • Ischaemic Heart Disease (%): 16 (25) • Hypertension (%): 18 (28) • Cardiomyopathy (%): 11 (17) • Sotalol (%): 13 (21) • Beta-Blocker (%): 19 (30) • Amiodarone (%): 19 (30) • Digoxin (%): 4 (6) • Valvular Heart Disease (%): 11 (18) • Left Atrial Diameter (mm) (mean +/- SD): 48 (7) • Duration of episode (months) mean (SD): 3.8 (9) • BMI (Kg/m^2) mean (SD): 28.2 (5) Structural Heart Disease, Pulmonary Disease, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Heart Failure: N/A Propafenone, Flecainide, Sotalol, Calcium Channel Blocker, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A All patients had persistent AF **Inclusion criteria:** Symptomatic persistent AF. **Exclusion criteria:** Arrhythmias other than AF, implanted pacemakers, cardiopulmonary decompensation at the time of presentation, significant electrolyte imbalance (potassium <3.5 or >5.0 mmol/L), and an ineffective anticoagulation during the last 4 weeks before CV (international normalized ratio target range 2-3). **Numbers:** 123 patients randomised. 60 to Anteroposterior and 63 to Anteroapical. **Anticoagulation:** Effective anticoagulation was INR 2-3 for at least 4 weeks before procedure.

	Monitoring: With was with continuous ECG and the follow up duration was up to 3 hours after cardioversion.
Interventions	AP RBW Incremental Patches AA RBW Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Germany **Setting:** Elective Admission **Comments:** No conflict of interest reported. Planned outcomes were: successful cardioversion as defined by termination of AF with at least 2 consecutive sinus beats. Early recurrence atrial fibrillation was defined as a relapse of AF within 1 minute after a primarily successful cardioversion. Reported outcomes were as above. No trial registration. **Authors name:** Stephanos Siaplaouras **Institution:** Internal Medicine Clinic, Saarlandes University **Email:** siaplaouras@aol.com **Address:** Dr Stephanos Siaplaouras, Klinik fur Innere Medizin III (Kardiologie, Angiologie und Internistische Intensivmedizin), Universitatsklinikum des Saarlandes, Kirrberger Strasse, D-66421 Homburg, German
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not specified.
Allocation concealment (selection bias)	Unclear risk	Concealment method or if attempt to conceal was not mentioned.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	It would be unlikely patients or personel could be blinded to either group because of the pad positions.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but unlikely to have an impact as these are objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	A blinding method or attempt to blind outcome assessors was not described.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but unlikely to have an impact as these are objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There was no attrition in the groups
Selective reporting (reporting bias)	Unclear risk	All pre-specified end points were fully reported on. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	High risk	No proof of trial registration. No mention to Ethics Approval.

Simon 2017

Study characteristics	
Methods	**Design:** Randomized controlled trial **Group:** Parallel group (DCCV after 2 hours)
Participants	**Baseline Characteristics** Vernakalant

	• Age (Years) Mean (SD): 56 (14) • Sex (Male) n (%): 34 (69) • Hypertension n (%): 30 (61) • Ischaemic Heart Disease n (%): 3 (6) • Digoxin n (%): 2 (4) • Beta-blocker n (%): 24 (47) • Duration of episode (h) mean (SD): 10.9 (9.9) • CHA2DS2VASc mean (IQR): 1.7 (1-2) Ibutilide • Age (Years) Mean (SD): 57 (16) • Sex (Male) n (%): 34 (67) • Hypertension n (%): 36 (71) • Ischaemic Heart Disease n (%): 4 (8) • Digoxin n (%): 1 (2) • Beta-blocker n (%): 29 (57) • Duration of episode (h) mean (SD): 8.7 (6.2) • CHA2DS2VASc mean (IQR): 1.8 (1-3) Stroke/TIA, Pulmonary disease, Coronary Artery Disease, Diabetes Mellitus, Heart Failure, Cardiomyopathy, Valvular Heart Disease: N/A Calcium antagonist, Propafenone, Flecainide, Diuretic, Amiodarone, Sotalol, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF%: N/A BMI: N/A AF type: duration of symptoms< 48 hours however baseline characteristics report some persistent **Inclusion criteria:** Recent-onset AF (symptoms of AF since no longer than 48 h) Male and female patients between 18 and 90 years were included in the study. **Exclusion criteria:** Exclusion criteria were necessity for immediate electrical cardioversion due to haemodynamic instability; heart failure NYHA III/IV;a previously documented left ventricular ejection fraction of ≤35%; history or signs of acute coronary syndrome within the last 30 days; a rest-ing ventricular rate of, 80 bpm without pacemaker backup; a QT interval of.440 ms; presence of Wolff–Parkinson–White syndrome; history of Torsade de pointes (TdP) arrhythmia or other polymorphic ventricular tachycardias (VTs); signs of thyrotoxicosis, sick sinus syndrome or atrioventricular block II and III, severe valvular heart disease, clinically meaningful hypertrophic obstructive cardiomyopathy, restrictive cardiomyopathy, or constrictive pericarditis; serious disorders of the hepatic, renal, pulmonary, gastrointestinal, haematological, or central nervous system; serious psychiatric disorders; abnormal serum electrolytes despite adequate therapy; intravenous use of any Class I or III anti-arrhythmic drugs within 4 h prior to study drug application; pregnancy; and known hypersensitivity to study medications.We did not include patients with atrial flutter as vernakalant treatment is not indicated in this patient group due to lack of efficacy **Numbers:** 209 patients assessed for eligibility, 101 underwent randomisation: 49 to Vernakalant and 51 to Ibutilide. **Anticoagulation:** No prior anticoagulation protocol defined but this population was AF duration < 48h. However it was reported that patients without sufficient anticoagulation received 1mg/kg of enoxaparin. There was no post-cardioversion anti-coagulation protocol reported. **Monitoring:** Patients were monitored with continuous ECG monitoring and follow up duration was 6h as inpatient. DCCV after 2 hours so no efficacy end points can be used after this.
Interventions	Intravenous Vernakalant Intravenous Ibutilide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint

	Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Jubilaeumsfonds of the Austrian National Bank **Country:** Austria **Setting:** Accident and Emergency **Comment:** No conflicts of interest declared. Planned outcomes: Time to SR and conversion to SR within 90 mins. Reported outcomes: As above including adverse outcomes including arrhythmias. Clinicaltrials.gov registration: NCT01447862 **Author's Name:** Alexander Simon **Institution:** Department of Emergency Medicine, Medical University of Vienna **Email:** hans.domanovits@meduniwien.ac.at **Address:** Department of Emergency Medicine, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomization into two treatment groups with variable block sizes of four to six was performed by an independent epidemiologist using www.randomization.com
Allocation concealment (selection bias)	Low risk	To conceal allocation we used sequentially numbered, sealed, opaque envelopes, which were produced before initiation of the study.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	This was an open label non-blinded trial. Different infusion regimens.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but low risk as objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	This was an open label non-blinded trial
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but low risk as objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Only 1 patients excluded from trial due to side effects.
Selective reporting (reporting bias)	Low risk	Outcomes were well defined on the protocol and reported fully and appropriately. Protocol published in clinicaltrials.gov in October 2011 and enrolmente finished in 2015.
Other bias	Unclear risk	Irrefutable proof of trial registration. Registered at Clinicaltrials.gov as NCT01447862 (EudraCT number 2011-000695-34). Approved by the independent Ethics Committee of the Medical University of Vienna (EK NR: 220/2011) Nearly 60% with persistent AF in one treatment arm vs 40% only in the other - questions about quality of randomization.

Singh 2000

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV if no cardioversion after 5 doses)
Participants	**Baseline Characteristics** Dofetilide

	• Age (years) mean (SD): 67 (-) • Male (%): 200 (83) • Hypertension (%): 114 (47) • Structural Heart Disease (%): 161 (67) • Digoxin (%): 194 (80) • Calcium Antagonist (%): 56 (23) • Diuretic (%): 110 (46) • Persistent AF (%): 210 (87) • Atrial Flutter (%): 31 (12) Placebo • Age (years) mean (SD): 67 (-) • Male (%): 73 (90) • Hypertension (%): 39 (46) • Structural Heart Disease (%): 58 (69) • Digoxin (%): 67 (80) • Calcium Antagonist (%): 20 (24) • Diuretic (%): 40 (48) • Persistent AF (%): 67 (80) • Atrial Flutter (%): 17 (20) Diabetes Mellitus, Valvular Heart Disease, Heart Failure, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease: N/A Beta-blocker, Amiodarone, Propafenone, Sotalol, Flecainide, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LVEF % and LA diameter: N/A Duration of episode: N/A AF type: Duration of AF > 2 weeks so all AF is persistent. **Inclusion criteria:** Patients 18 to 85 years of age with AF/AFl for 2 to 26 weeks, confirmed by ECG, were screened. **Exclusion criteria:** Women of childbearing potential; inability to tolerate withdrawal from current antiarrhythmic therapy; syncope of unknown origin in the preceding 6 months; active thyrotoxicosis, AF, or AFl from reversible noncardiac diseases; uncompensated or rapidly progressive congestive heart failure; myocardial infarction or unstable angina pectoris within the preceding month or percutaneous transluminal coronary angioplasty within the preceding 3 months; heart surgery in the preceding 2 months; significant sinus node abnormalities, including sick sinus syndrome, or greater than first-degree atrioventricular block, unless treated with a properly functioning pacemaker; ECG intervals exceeding the following limits in the drug-free state and in the absence of preexcitation syndrome and bundle-branch block: QRS of >180 ms, QT interval of >440 ms, or both; in the case of bundle-branch block, the QT or QTc was not to exceed 500 ms; R-R interval of >3.5 seconds; ventricular rate of <50 bpm on 12-lead ECG; systolic blood pressure of <90 mm Hg or diastolic blood pressure of >110 mm Hg (>105 mm Hg at Canadian centers after the January 1994 protocol amendment); major hematological, pulmonary, hepatic, or renal disease (serum creatinine of >221 mmol/L or, after the April 1994 protocol amendment, calculated ClCr of <0.3334 mL/s); serum potassium of <4.0 or >5.5 mmol/L and serum magnesium of <0.75 or >1.25 mmol/L at screening, 1 week before entry, and immediately before entry into study; concomitant therapy with other antiarrhythmic agents, verapamil, diltiazem, diuretics (if serum potassium was out of the specified limits), antihistamines, tricyclic antidepressants, anticonvulsants or phenothiazines, digoxin (allowed if the dosage was constant during the study), cimetidine (after the April 5, 1994, protocol amendment), and amiodarone (if blood levels of amiodarone >0.3 mg/mL); history of polymorphic ventricular tachycardia associated with antiarrhythmic drugs or other drugs known to prolong the QT interval; history of substance dependency or abuse; any experimental medication con- comitantly or within the 4 weeks of the study; and participation in a previous dofetilide study **Numbers:** 327 patients enrolled. 241 randomised to dofetilide arm (3 doses) and 84 randomised to placebo arm. Only 250 followed up in maintenance phase (181 dofetilide, 68 placebo), reasons for attrition not given. **Anticoagulation:** Anticoagulation therapy initiated before cardioversion and continued for a minimum of 3-4 weeks after cardioversion. No specifics provided for drug therapy and pre-cardioversion duration. **Monitoring:** Minimum of 3 days inpatient loading on telemetry. DCCV after 5 doses so efficacy data cannot be taken after this end point. Follow up clinic visit from 2 weeks to 1 year at regular intervals.
Interventions	Oral Dofetilide Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint

	Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint No data available for any of the other endpoints of the systematic review. Mortality data not given for 30d endpoint.
Identification	**Sponsorship source:** Study supported by grant from Pfizer **Country:** United States of America **Setting:** Unclear hospital setting for loading and then Outpatient **Comments:** Planned outcomes: Sinus Rhythm at 1 year follow up, adverse events, discontinuation of treatement, arrhythmia relapse, adverse events. Reported outcomes: As planned, however efficacy outcomes cannot be assessed after inpatient DCCV, data not given split via arrhythmia type. No trial registration. **Authors name:** Steven Singh **Institution:** Veterans Affairs Medical Center, Washington, DC; James A. Haley Medical Center, Tampa, Fla; Cardiology Associates Medical Group of East San Diego, Inc, San Diego, Calif; the Division of Cardiology, University of California–Irvine Medical Center; the Division of Cardiology, University of California–San Diego Medical Center; the Division of Cardiology, Presbyterian Hospital of Dallas, Dallas, Tex; and Pfizer Inc, Groton, Conn **Email:** snsingh@erols.com **Address:** Dr Steven Singh, Veterans Affairs Medical Center, 50 Irving St NW, Room 1E301, Washington, DC 20422
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No specification of method of sequence generation.
Allocation concealment (selection bias)	Unclear risk	No description of method, if any, of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study reported as double-blind but no description of blinding methods.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Study reported as double-blind but no description of blinding methods.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Follow-up and outcome information available for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or	Low risk	Follow-up and outcome information available for all patients.

systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Unclear risk	Could not assess pre-enrolment protocol and hence not able to confirm if initially planned outcomes were as reported in the published study. Timing of mortality reported only for one patient treated with dofetilide in the first month. Cannot say if other deaths occurring in the first year also occurred in the first month.
Other bias	Unclear risk	The Institutional Review Board at each center approved the study. Study protocol not published on open access protocol platform.

Singh 2005

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV at 28 days if no conversion)
Participants	**Baseline Characteristics** Placebo • Age (years) mean (SD): 68 (10) • Male (%): 136 (99) • BMI (Kg/m^2) mean (SD): 31 (5) • Heart Failure (%): 33 (24) • Hypertension (%): 76 (56) • Valvular Heart Disease (%): 8 (6) • Stroke/TIA (%): 20 (15) • Pulmonary Disease (%): 15 (11) • Cardiomyopathy (%): 7 (5) • Ischaemic Heart Disease (%): 31 (23) • Diabetes Mellitus (%): 33 (24) • LA diameter (mm) mean (SD): 49 (7) • LVEF (%) mean (SD): 49 (13) • Duration of episode ≤ 1yr (%): 110 (80) • Duration of episode > 1yr (%): 23 (17) Amiodarone • Age (years) mean (SD): 67 (9) • Male (%): 265 (99) • BMI (Kg/m^2) mean (SD): 32 (6) • Heart Failure (%): 67 (25) • Hypertension (%): 194 (73) • Valvular Heart Disease (%): 19 (7) • Stroke/TIA (%): 33 (12) • Pulmonary Disease (%): 36 (14) • Cardiomyopathy (%): 25 (10) • Ischaemic Heart Disease (%): 71 (27) • Diabetes Mellitus (%): 67 (25) • LA diameter (mm) mean (SD): 48 (7) • LVEF (%) mean (SD): 51 (12) • Duration of episode ≤ 1yr (%): 197 (74) • Duration of episode > 1yr (%): 61 (23) Sotalol • Age (years) mean (SD): 67 (9) • Male (%): 257 (99) • BMI (Kg/m^2) mean (SD): 32 (6) • Heart Failure (%): 72 (28) • Hypertension (%): 172 (66) • Valvular Heart Disease (%): 17 (7)

	• Stroke/TIA (%): 30 (12) • Pulmonary Disease (%): 31 (12) • Cardiomyopathy (%): 19 (7) • Ischaemic Heart Disease (%): 66 (25) • Diabetes Mellitus (%): 72 (28) • LA diameter (mm) mean (SD): 48 (7) • LVEF (%) mean (SD): 52 (12) • Duration of episode ≤ 1yr (%): 206 (79) • Duration of episode > 1yr (%): 53 (20) Structural heart disease, Coronary Artery Disease, Myocardial Infarction: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A AF type: All perisisten AF patients **Inclusion criteria:** Electrocardiographically documented atrial fibrillation for at least 72 hours, still had atrial fibrillation at randomization, and were taking anticoagulants. Eligibility screening spanned 3 or 4 visits at 7 day intervals. **Exclusion criteria:** Patients with atrial flutter or paroxysmal atrial fibrillation were excluded. Other exclusion criteria included New York Heart Association class III or IV heart failure, a calculated creatinine clearance below 60 ml per minute, intolerance of beta-blockers, and a history of the long-QT syndrome. Originally, patients who had had atrial fibrillation for more than 12 months were excluded. **Numbers:** 665 patients enrolled. 267 randomised to amiodarone arm and 261 randomised to sotalol arm and 137 to placebo. In the amiodarone arm, 31 withdrew consent and 11 were lost to follow up, in the sotalol arm, 27 withdrew consent and 12 were lost to follow up and in the placebo arm, 23 withdrew consent and 5 were lost to follow up. **Anticoagulation:** INR had to be stable between 2.0 to 3.0 before cardioversion. However duration prior to cardioversion and after not specified. **Monitoring:** Follow up visits every 4 weeks with ECG. Electrical cardioversion at 28 days so efficacy outcome after this cannot be used in systematic review.
Interventions	Oral Amiodarone Oral Sotalol Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day all cause mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Quality of Life outcomes • **Outcome type**: Scale • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint

	No data available for any of the other endpoints of the systematic review.
Identification	**Sponsorship source:** Support from Cooperative Studies Program of the Depart- ment of Veterans Affairs Office of Research and Development (Washington, D.C.) and by unrestricted grants-in-aid from Berlex Labora- tories and Wyeth–Ayerst Laboratories. **Country:** United States of America **Setting:** Outpatient **Comments:** B. Singh had acted in advisory capacity and speaker for Wyeth-Ayerst Laboratoties, Sanofi-Synthelabo Laboratories, and Berlex Laboratories. Dr Reda reports having recieved grant support from Novartis Pharmaceuticals. Planned outcomes: Time to first recurrence of atrial fibrillation after sinus rhythm restored. Failed cardioversion determined as persistence of atrial fibrillation on day 28. Reported outcomes: As planned including adverse events, however efficacy analysis after 28 days cannot be included in systematic review. No trial registration. **Authors name:** Bramah N. Singh **Institution:** Department of Veterans Affairs Medical Center, West Los Angeles, Calif.; the Department of Veterans Affairs Medical Center, Washington, D.C.; the Department of Veter- ans Affairs Hospital, Hines, Ill.; the Department of Veterans Affairs Medical Center, Albuquerque, N.M.; the Department of Veterans Affairs Medical Center, Providence, R.I.; Walter Reed Army Medical Center, Washington, D.C.; the Department of Veterans Affairs Medical Center, Loma Linda, Calif.; the Department of Veterans Affairs Medical Center, Kansas City, Mo.; and Hahnemann University and the Department of Veterans Affairs Medical Center Philadelphia — both in Philadelphia **Email:** bsingh@ucla.edu **Address:** Dr. Singh at the Veterans Affairs Medical Center of West Los Angeles, 11301 Wilshire Blvd., Los Angeles, CA 90073
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization of eligible patients was performed by permuted block design, with stratification according to the participating hospital, whether the patient was symptomatic or had ischemic heart disease."
Allocation concealment (selection bias)	Unclear risk	Not specified.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Study reported as double-blind, however, sotalol was given twice-daily and amiodarone once daily.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints, hence low-risk.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Endpoints comittee was blinded to treatment allocation.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints, hence low risk. Endpoints comittee was blinded to treatment allocation.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Low risk. Only 4% of patients lost to follow-up. Follow-up > 30 days.
Selective reporting (reporting bias)	Low risk	All planned outcomes were reported.
Other bias	Unclear risk	Study approved by the Hines VA Cooperative Studies Coordinating Center Human Rights Committee as well as by the local institutional review board. Could not find evidence of trial registration and protocol publication on a platform. Protocol was published in the Am J Cardiol after the end of enrolment and follow-up.

Squara 2021

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional cross-over)

	Study grouping: Parallel group
Participants	**Baseline Characteristics** Active Compression AP BTE Incremental Patches • Male (%): 70.8 (10.3) • Age (years) mean (SD): 25 (50) • Duration of AF (months) mean (SD): 5.8 (10.3) • Hypertension (%): 28 (56) • Diabetes Mellitus (%): 8 (16) • Ischaemic Cardiomyopathy (%): 10 (20) • COPD (%): 4 (8) • BMI (kg/m^2) mean (SD): 28.0 (4.9) • Class I Anti-Arrhythmic (flecainide) (%): 3 (6) • Class III Anti-Arrhythmic (amiodarone or sotalol) (%): 17 (34) • LVEF (%) mean (SD): 45.9 (14) • Left Atrial size (cm^2) mean (SD): 28.1 (5.1) AP BTE Incremental Patches • Male (%): 69.6 (10.2) • Age (years) mean (SD): 19 (38) • Duration of AF (months) mean (SD): 6.1 (16.9) • Hypertension (%): 28 (56) • Diabetes Mellitus (%): 9 (18) • Ischaemic Cardiomyopathy (%): 10 (20) • COPD (%): 4 (8) • BMI (kg/m^2) mean (SD): 28.9 (7.7) • Class I Anti-Arrhythmic (flecainide) (%): 3 (6) • Class III Anti-Arrhythmic (amiodarone or sotalol) (%): 21 (42) • LVEF (%) mean (SD): 49.1 (14.2) • Left Atrial size (cm^2) mean (SD): 28.9 (4.8) Structural Heart disease, Valvular heart disease, Myocardial Infarction, Heart Failure, Coronary Artery Disease, Stroke/TIA: N/A Propafenone, Diuretic, ACE inhibitor, Aspirin, Beta-Blocker, Calcium Channel Blocker, Digoxin: N/A CHA2DS2VASc: N/A All patients had persistent AF. **Inclusion criteria:** 18 years or older who were undergoing elective ECV for persistent AF (duration ≥7 days) **Exclusion criteria:** Any other atrial arrhythmia than AF was excluded—that is, atrial flutter or atrial tachycardia—by a careful analysis of the 12-lead electrocardiogram (ECG) by a senior electrophysiologist on the day of the cardioversion procedure. Also excluded patients with a history of median sternotomy, of osteoporotic fracture, of multiple myeloma, and of sternal radiotherapy. **Numbers:** 100 patients randomised, 50 to active compression, 50 to standard anterior-posterior group. **Anticoagulation:** If patients were anticoagulated for <3 weeks transoesophageal echocardiogram was perfomed to rule out intracardiac thrombus. **Monitoring:** Patients were monitored wtih 6 lead continuous ECG. Follow up duration was for at least 6 hours.
Interventions	Active Compression AP BTE Incremental Patches AP BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint

	Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local **Country:** France **Setting:** Elective Admission **Comment:** No conflicts of interest reported. Planned Outcomes: Primary Efficacy end point was the defibrillation threshold defined as the lowest defibrillation energy required for successful termination of AF and presence of sinus rhythm. Secondary endpoints; cardioversion success, total energy delivery, number of shocks, and success rate after crossover. Reported outcomes: as above including adverse events. No trial registration given. **Author's Name:** Fabien Squara **Institution:** CHU de Nice, Hôpital Pasteur, Service de Cardiologie, Nice, France, and CH de Cannes, Service de Cardiologie, Cannes, France **Email:** squara.f@chu-nice.fr **Address:** Dr Fabien Squara, CHU de Nice, H^opital Pasteur, Service de Cardiologie, 30 avenue de la Voie Romaine, CS 51069, 06001 Nice Cedex 1, France
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Mention to computer-generated list - completely random without any sequence (no blocks/clusters).
Allocation concealment (selection bias)	Low risk	Opaque envelopes were used (information after contacting authors).
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Mention to patients being blinded to treatment group which is possible as they would be under general anaesthetic for the cardioversion and pad location was AP for both groups. Personnel would see the active pressure intervention, hence not blinded. However, as all the study endpoints are objective and related to procedural result (sinus rhythm or AF) which is objectively taken from an ECG, this is considered low risk.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints. No influence.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	All endpoints were objective endpoints. No influence.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	All endpoints were objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome in the methods section, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Local ethics approval. No trial/protocol registration.

Stambler 1996

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics**

	Ibutilide • Age (sd): 68 (10) • Male (%): 127 (77) • Duration of episode d (sd): 15 (13) • Atrial Flutter (%): 80 (48) • Paroxysmal AF (%): 37 (23) • Persistent AF(%): 44 (27) • Valvular Heart Disease (%): 48 (30) • LA diameter (mm) (sd): 46 (8) • LVEF % (sd): 43 (18) • Digoxin (%): 92 (57) • Beta-Blocker (%): 26 (16) • Calcium Channel Blocker (%): 75 (47) • Any Antiarrythmic drug (%): 0 (0) Placebo • Age (sd): 66 (13) • Male (%): 68 (84) • Duration of episode d (sd): 12 (14) • Atrial Flutter (%): 41 (51) • Paroxysmal AF (%): n/a (n/a) • Persistent AF(%): n/a (n/a) • Valvular Heart Disease (%): n/a (n/a) • LA diameter (mm) (sd): 45 (7) • LVEF % (sd): 45 (17) • Digoxin (%): 40 (49) • Beta-Blocker (%): 27 (33) • Calcium Channel Blocker (%): 32 (40) • Any Antiarrythmic drug (%): 0 (0) Valvular Heart Disease, Structural Heart disease, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Stroke/TIA, Hypertension, Diabetes Mellitus, Heart Failure, Ischaemic Heart Disease: N/A Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A AF type: cannot determine based on provided data, likely mix of peristent and paroxysmal. **Inclusion criteria:** The patient had to have a rhythm of sustained atrial flutter or atrial fibrillation with a duration of >3 hours and <45 days. If the duration of atrial fibrillation was >3 days, ≥2 weeks of anticoagulation before enrollment was needed. **Exclusion criteria:** The patient could not be <18 years of age, of child-bearing potential, weigh >300 lb, have a history of torsade de pointes or a corrected QT interval (QTc) of >440 ms, have received ibutilide previously, have had a myocardial infarction or cardiac surgery within the previous 30 days, or have clinical evidence of digoxin toxicity or hyperthyroidism. The patient had to be hemodynamically stable (systolic blood pressure >90 mm Hg and diastolic blood pressure <105 mm Hg) without symptoms of angina or congestive heart failure, have normal serum electrolytes (potassium ≥4.0 mEq/L), and have liver enzymes less than twice maximal normal values. The patient could not be receiving class I or III antiarrhythmic agents unless the medication was discontinued more than five half-lives before enrollment. β-Adrenergic–blocking agents, calcium antagonists, and digoxin were permitted, but heart rate could not be <60 bpm. **Numbers:** 266 patients were randomised, 86 patients to placebo and 180 to ibutilide. 24 were excluded from efficaciy analysis due to protocol violation, 13 due to recieving an incorrect dose of study drug, 8 due to having an arrhythmia duration of > 45 days, 3 recieving other drugs within 3 hal-lives of the study, 1 due to having a rhythm that was not atrial fibrillation or flutter at start of treatment and one which was electrically cardioverted before hour 1.5. **Anticoagulation:** Required for ≥2 weeks if not recent onset arrhythmia but that was defined as ≥72h. No post cardioversion protocol given. **Monitoring:** With continuous ECG and 12 lead ECGs were perfomed at mulitple intervals. Follow up was for 90 minutes after which electrical cardioversion or pacing was performed or other anti-arrythmic agents used if 4h after infusion unless earlier cardioversion determined necessary by investigator.
Interventions	Intravenous Ibutilide Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better

	• **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local and grant from The Upjohn Company, Kalamazoo, Mich. **Country:** United States of America **Setting:** Unclear **Comments:** Planned outcomes: Treatment-induced termiantion of atrial fibrillation or flutter, adverse events such as blood pressure drop or sudden rhythm change were also monitored. ECG parameter changes of QRS duration and QT interval were monitored. Reported outcomes: as above including other adverse events. No trial registration. **Authors name:** Bruce Stambler **Institution:** West Roxbury Veterans Administration Medical Center and Harvard Medical School **Email:** not given **Address:** Bruce S. Stambler, MD, Cardiology Section (111A), West Roxbury VA Medical Center, 1400 VFW Pkwy, West Roxbury, MA 02132
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	There is mention to blinding of patients and the study being double blind. No sure about personnel, but unlikely to have an impact due to protocol and them not being the outcome assessors.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints - not at risk of bias.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Outcome assessors were blinded to treatment group
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Outcome assessors were blinded to treatment group
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome in the methods section, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Study protocol was approved by the institutional review boards at each of the participating sites. No mention of protocol/trial registration.

Stanaitienė 2008

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** BTE Incremental • Age (years) mean (SD): 63 (11) • Male (%): 68 (61) • BMI (Kg/m^2) mean (SD): 30 (5) • Hypertension (%): 47 (42) • Beta-blocker (%): 47 (42) • Digoxin (%): 4 (4) • Amiodarone (%): 47 (42) • Propafenone (%): 18 (16) • Duration of episode (days) mean (SD): 98 (147) MDS Incremental • Age (years) mean (SD): 65 (9) • Male (%): 70 (63) • BMI (Kg/m^2) mean (SD): 30 (5) • Hypertension (%): 48 (43) • Beta-blocker (%): 50 (45) • Digoxin (%): 3 (3) • Amiodarone (%): 67 (60) • Propafenone (%): 10 (9) • Duration of episode (days) mean (SD): 80 (93) Structural Heart Disease, Valvular Heart Disease, Heart Failure, Cardiomyopathy, Coronary Artery Disease, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease: N/A Calcium Antagonist, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF %: N/A CHA2DS2VASc: N/A AF type: mixed duration of AF **Inclusion criteria:** Patients > 18 years of age who were haemodynamically stable. **Exclusion criteria:** Not specified **Numbers:** 224 patients enrolled. 112 randomised to BTE arm and 112 to MDS arm. No attrition reported. **Anticoagulation:** Any AF lasting more than 48 hours was anticoagulated with warfarin aiming for an INR from 2 to 3.5 for at least 3 weeks. Duration not given for post cardioversion anticoagulation. **Monitoring:** ECG before procedure, continuous monitoring not specified other than from device. Max follow up at 24h but cross-over after 5th shock if failure to cardiovert. Therefore data after this end point cannot be used for efficacy in systematic review.
Interventions	BTE Incremental MDS Incremental
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local

	Country: Lithuania **Setting:** Unclear hospital setting **Comments:** No conflicts of interest reported. Planned outcomes: Successful cardioversion determined as sinus rhythm within 30s of shock, early relapse within 2 mins and acute within 24h Reported outcomes: As planned, adverse events not reported. No trial registration. **Authors name:** Giedrė Stanaitienė **Institution:** Kauno medicinos universiteto Kardiologijos klinika **Email:** giedre1972@yahoo.com **Address:** G. Stanaitienė, KMU Kardiologijos klinika, Eivenių 2, 50009 Kaunas
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No specification of method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention of method, if any, of allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	No mention to method of blinding, but two different defibrillators were used (one for each treatment arm).
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to if blinding of outcome assessors was present.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not assess pre-enrolment protocol, hence could not confirm if all planned outcomes were reported.
Other bias	High risk	No mention to Ethics approval. No irrefutable proof of trial registration or publication of protocol in open-access repository.

Stroobandt 1997

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV if no conversion within 24-48h)
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD): 61 (11) • Male (%): 77 (76) • Heart Failure (%): 8 (8) • Hypertension (%): 18 (18) • Valvular Heart Disease (%): 12 (12) • Structural Heart Disease (%): 72 (71) • Cardiomyopathy (%): 8 (8) • Coronary Artery Disease (%): 14 (14) • Digoxin (%): 73 (72) • LA Diameter (mm) mean (SD): 38 (7) • Duration of episode ≤ 2 weeks (%): 49 (49) • Duration of episode > 2 weeks (%): 52 (51) Placebo • Age (years) mean (SD): 64 (9) • Male (%): 12 (35) • Heart Failure (%): 2 (6) • Hypertension (%): 6 (17) • Valvular Heart Disease (%): 4 (11) • Structural Heart Disease (%): 25 (71) • Cardiomyopathy (%): 2 (6)

	• Coronary Artery Disease (%): 9 (26) • Digoxin (%): 19 (54) • LA Diameter (mm) mean (SD): 41 (7) • Duration of episode ≤ 2 weeks (%): 14 (40) • Duration of episode > 2 weeks (%): 21 (60) Diabetes Mellitus, Myocardial Infarction, Pulmonary Disease, Stroke/TIA, Ischaemic Heart Disease: N/A Beta-blocker, Amiodarone, Propafenone, Calcium Antagonist, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A LVEF %: N/A CHA2DS2VASc: N/A BMI: N/A AF type: mixed duration of AF **Inclusion criteria:** Aged >18 years, were included into the study if they presented with 1 of the following forms of atrial fibrillation: recent-onset atrial fibrillation (defined as lasting not >2 weeks) and chronic atrial fibrillation (lasting >2 weeks), occurring either as a first episode or as a recurrent episode. **Exclusion criteria:** New York Heart Association functional class >II or symptoms of heart failure on physical examination, recent myocardial infarction or cardiac surgery (<2 months before trial entry), cardiogenic shock or hypotension (systemic arterial pressure <90 mm Hg), New York Heart Asociation class III or IV angina pectoris, electrocardiographic evidence of ventricular pre-excitation, previous electrocardiographic ev- idence of second- to third-degree atrioventricular block, sinus bradycardia (<50 beat/min) or known sick sinus syndrome, a history of life-threatening ventricular arrhythmias, severe obstructive lung disease, pulmonary embolism, metabolic disturbances or known thyroid dysfunctions, unstable hepatic or renal function, and evidence of digitalis intoxication and hypokalemia (potassium <4.0 mEq/L). Patients were also excluded if they were treated with amiodarone within the preceding 6 months, or were currently receiving treatment with antiarrhythmic or cardiovascular drugs (except for digitalis and/or diuretics) such as b-blockers, verapamil, or diltiazem not discontinued 5 half-lives before the start of the study. **Numbers:** 136 patients enrolled. 101 randomised to propafenone arm and 35 to placebo arm. 1 patient in each arm converted before therapy. 3 patients who did not respond to therapy before DCCV withdrew, one from propafenone arm because of excessive bradycardia and another two in placebo arms due to protocol violation and discovery of a left ventricular thrombus. **Anticoagulation:** Anticoagulation protocol was instituted according to common practice of investigator. **Monitoring:** Continuous rhythm monitoring before and after drug administration. Follow up was for 24-48 hours after which if no cardioversion DCCV was performed. efficacy outcomes after this cannot be used for systematic review. Patients were then followed up at clinic visits at 1, 3 and 6 months.
Interventions	Intravenous Propafenone Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Adverse events not reported with time points consistently allowing to determine which ones were inpatient time frame. Time points for serious (death) not given.
Identification	**Sponsorship source:** Supported by Knoll, Belgium N.V. Brussels, Belgium **Country:** Belgium **Setting:** Unclear hospital setting then outpatient **Comments:** No conflicts of interest reported. Planned outcomes: Number of patients who maintained sinus rhythm at 6 months, efficacy of initial drug therapy before DCCV, Long term safety of drug. Reported outcomes: As planned, adverse events not reported with time frames relevant to planned endpoints of systematic review. No trial registration. **Authors name:** Roland Stroobandt **Institution:** Department of Cardiology, St-Jozef Hospital, Oostende, Bel- gium; and Knoll, Belgium N.V., Brussels, Belgium **Email:** not provided

	Address: Roland Stroobandt, MD, PhD, Department of Cardiology, St.-Jozef Hospital, B-8400 Oostende, Belgium
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Study described as double-blind but no information providing on methods. Administation of drug and placebo followed same protocol, suggesting likely blinding of patients and/or personell.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objetcive outcome, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on method for outcome assessor, despite mention to double blind study.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcome, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Follow-up data available for all patients. Patients followed for 6 months.
Selective reporting (reporting bias)	Unclear risk	Could not access the pre-publication protocol, hence could not confirm if all planned outcomes were reported.
Other bias	Unclear risk	Protocol approved by each center's Ethics committee. No proof of prior protocol registration/publication.

Sun 2005

Study characteristics

Methods	**Design:** Randomized controlled trial **Group:** Parallel group
Participants	**Baseline Characteristics** Ibutilide • Age (Years) Mean (SD): 62 (7) • Sex (Male) n (%): 12 (60) • Hypertension n (%): 12 (60) • Hypertrophic Cardiomyopathy n (%): 2 (10) • Valvular Heart Disease n (%): 2 (10) • Digoxin n (%): 6 (30) • LA size mm (SD): 43 (7) • LVEF % (SD): 62 (15) Propafenone • Age (Years) Mean (SD): 60 (11) • Sex (Male) n (%): 10 (50)

	• Hypertension n (%): 10 (50) • Hypertrophic Cardiomyopathy n (%): 2 (10) • Valvular Heart Disease n (%): 2 (10) • Digoxin n (%): 7 (35) • LA size mm (SD): 39 (3) • LVEF % (SD): 61 (11) Stroke/TIA, Pulmonary Disease, Coronary Artery Disease, Diabetes Mellitus, Heart Failure: N/A Beta-blocker, Propafenone, Amiodarone, Sotalol, Calcium channel blocker, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A All patients with atrial flutter **Inclusion criteria:** Patients older than 18 years but less than 75 years with sustained atrial flutter (3 hours–90 days) were eligible when they were haemodynamically stable with a systolic blood pressure >110 mmHg, had a body weighty >60 kg, a normal serum potassium concentration (≥4 mEq/L), a ventricular rate of >50 beats/min and a rate corrected QT interval of no more than 440 ms in their 12 lead electrocardiogram (ECG) **Exclusion criteria:** Patients with hyperthyroidism, or with a history or evidence of unstable angina pectoris, bronchospastic disease, myocardial infarction or cardiac surgerywithin the previous 30 days, known sinus node dysfunction, second or third degree atrioventricular (AV) block, bundle branch block, Wolff-Parkinson-White syndrome and/or torsade de pointes were not included. Also, concurrent treatment with verapamil, or drugs that prolong the QT interval was not allowed. Treatment with class I or III antiarrhythmic agents, if present, was discontinued for more than five half lives before enrolment **Numbers:** 40 patients were eligible and 20 were randomised to ibutilide with 20 to propafenone. No patients were lost to follow up. **Anticoagulation:** No prior anticoagulation protocol defined, the text notes that this was left up to the investigators. There was no post-cardioversion anti-coagulation protocol reported. **Monitoring:** Patients were monitored with continuous ECG monitoring and follow up duration was 4h as inpatient.
Interventions	Intravenous Ibutilide Intravenous Propafenone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local **Country:** China **Setting:** Not clear **Comment:** No conflicts of interest declared. Planned outcomes: Conversion to SR within 90 mins, time to conversion, QT interval changes, other adverse events including arrhythmias. Reported outcomes: As above.. No trial registration. **Author's Name:** Jian-Ling Sun **Institution:** Electrophysiology Group, Department of Cardiology, People's Hospital, Peking University

	Email: sunjianling2000@yahoo.com **Address:** Electrophysiology Group, Department of Cardiology, People's Hospital, Peking University, Xi Zhi Men Nan Da Jie 11, Beijing 100044, PRC
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Methods not described.
Allocation concealment (selection bias)	Low risk	"Drugs were prepared in ampoules of 20 ml and were administered as a single 10 min intra- venous infusion using a similar infusion rate. Blinding was maintained by the drug being prepared by an independent individual not involved in the study."
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	"Drugs were prepared in ampoules of 20 ml and were administered as a single 10 min intra- venous infusion using a similar infusion rate. Blinding was maintained by the drug being prepared by an independent individual not involved in the study." Therefore, personnel and patients not able to discriminate the 2 drugs and not involved in preparation.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	"Drugs were prepared in ampoules of 20 ml and were administered as a single 10 min intra- venous infusion using a similar infusion rate. Blinding was maintained by the drug being prepared by an independent individual not involved in the study." Therefore, personnel and patients not able to discriminate the 2 drugs and not involved in preparation.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints reported for all patients.
Selective reporting (reporting bias)	Unclear risk	All pre-specified end points were fully reported on. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Ethics committee approval.

Suttorp 1989

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over for placebo arm) **Study grouping:** Parallel group (Electrical or pharmacological cardioversion if no conversion)
Participants	**Baseline Characteristics** Flecainide • Age (years) mean (SD): 60 (13) • Male (%): 19 (95) • Hypertension (%): 5 (25) • Valvular Heart Disease (%): 0 (0) • Coronary Artery Disease (%): 6 (30) • Beta-Blocker (%): 4 (20) • Digoxin (%): 4 (20) • LA Diameter (mm) mean (SD): 33 (5) • Duration of episode < 24hrs AF (%): 11 (65) • Duration of episode < 24hrs Flutter (%): 1 (5) • Atrial Flutter (%): 3 (15) Placebo (Verapamil)

	• Age (years) mean (SD): 58 (11) • Male (%): 13 (65) • Hypertension (%): 4 (20) • Valvular Heart Disease (%): 2 (10) • Coronary Artery Disease (%): 4 (20) • Beta-Blocker (%): 3 (15) • Digoxin (%): 4 (20) • LA Diameter (mm) mean (SD): 33 (8) • Duration of episode < 24hrs AF (%): 13 (76) • Duration of episode < 24hrs Flutter (%): 0 (0) • Atrial Flutter (%): 3 (15) Heart Failure, Structural Heart Disease, Pulmonary Disease, Cardiomyopathy, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease: N/A Amiodarone, Propafenone, Calcium Antagonist, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A LVEF %: N/A CHA2DS2VASc: N/A BMI: N/A AF type: mixed duration of AF max duration 6 months **Inclusion criteria:** AF or AFl lasting <6 months and a ventricular rate >100 beats/mm at rest and no signs of heart failure. **Exclusion criteria:** Previous documented or suspected conduction disturbances more than first-degree atrioventricular block, concomitant therapy with antiarrhythmic drugs, Wolff-Parkinson-White syndrome, sick sinus syndrome, acute myocardial infarction, hyperthyroidism, left atrial enlargement with AF or AFl lasting >2 days without appropriate anticoagulation therapy and a body weight of over 100 kg **Numbers:** 40 patients enrolled. 20 randomised to flecainide arm and 20 to placebo arm. No attrition reported. **Anticoagulation:** Anticoaultion protocol not provided **Monitoring:** Continuous rhythm monitoring method not reported. Switch to flecainide after 60 minus if no cardioversion in placebo arm. Efficacy outcomes after this cannot be used for systematic review.
Interventions	Intravenous Flecainide Intravenous Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** France **Setting:** Outpatient **Comments:** Planned outcomes: Sinus Rhythm at 1 year follow up, adverse events, discontinuation of treatement. Reported outcomes: Sinus Rhythm at various points during follow up, adverse events. No trial registration. **Authors name:** Etienne Aliot **Institution:** Cardiology Department, Central University Hospital, Nancy, France; Cordiology Department, Hôpital Lariboisière, Paris, France **Email:** Not provided **Address:** E. Aliot, MD, Department of Cordiology, Hôpital Central, 54035 Nancy, France.
Notes	**Sponsorship source:** Local **Country:** The Netherlands **Setting: Unclear hospital setting** **Comments:** No conflicts of interest reported. Planned outcomes: None specified. Reported outcomes: Conversion to sinus rhythm, time to conversion and adverse events

	(cannot be used for systematic review due to cross-over). No trial registration. **Authors name:** Maarten Suttorp **Institution:** Department of of Cardiology, St. Antonius Hospital Nieuwegein, Koekoekslaan CM Nieuwegein, the Netherlands. **Email:** Not provided **Address:** J. Herre Kingma, MD, PhD, Department of of Cardiology, St. Antonius Hospital Nieuwegein, Koekoekslaan CM Nieuwegein, the Netherlands.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information provided on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Study described as single-blind, but infusion protocols were different.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	All outcomes were reported for all patients.
Selective reporting (reporting bias)	Unclear risk	No protocol published prior to study publication, hence could not confirm if all planned outcomes were reported.
Other bias	High risk	No mention to Ethics approval. No clear proof of prior Protocol registration. Concerns about randomization method. Table shows differernces across treatment groups: 1 variable out of 9.

Suttorp 1990

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (Electrical or pharmacological cardioversion if no conversion)
Participants	**Baseline Characteristics** Flecainide • Age (years) mean (SD): 61 (13) • Male (%): 15 (60) • Hypertension (%): 2 (8) • Valvular Heart Disease (%): 4 (16) • Pulmonary Disease (%): 1 (4) • Coronary Artery Disease (%): 7 (28) • Beta-Blocker (%): 6 (24) • Digoxin (%): 3 (12) • Calcium Antagonist (%): 4 (16) • LA Diameter (mm) mean (SD): 38 (7) • Duration of episode < 24hrs AF (%): 14 (70) • Duration of episode < 24hrs Flutter (%): 1 (20) • Atrial Flutter (%): 5 (20) Propafenone • Age (years) mean (SD): 58 (15) • Male (%): 19 (76) • Hypertension (%): 2 (8) • Valvular Heart Disease (%): 3 (12) • Pulmonary Disease (%): 1 (4) • Coronary Artery Disease (%): 7 (28)

	• Beta-Blocker (%): 3 (12) • Digoxin (%): 4 (16) • Calcium Antagonist (%): 1 (4) • LA Diameter (mm) mean (SD): 37 (7) • Duration of episode < 24hrs AF (%): 14 (70) • Duration of episode < 24hrs Flutter (%): 2 (40) • Atrial Flutter (%): 5 (20) Heart Failure, Structural Heart Disease, Cardiomyopathy, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease: N/A Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A LVEF %: N/A CHA2DS2VASc: N/A BMI: N/A AF type: mixed duration of AF max duration 6 months **Inclusion criteria:** AF or AFl lasting <6 months and a ventricular rate >100 beats/mm at rest and no signs of heart failure. **Exclusion criteria:** Previous documented or suspected conduction disturbances more than first-degree atrioventricular block, concomitant therapy with calss I antiarrhtymic drugs, Wolff-Parkinson-White syndrore, sick sinus syndrome, acute myocardial infarction, cardiac surgery within two weeks before start of study, hyperthyroidism, left atrial enlargement with AF or AFl lasting >2 days without appropriate anticoagulation therapy and a body weight of over 100 kg **Numbers:** 50 patients enrolled. 25 randomised to flecainide arm and 25 to propafenone arm. No attrition reported. **Anticoagulation:** Anticoaultion protocol not provided **Monitoring:** Continuous rhythm monitoring method not reported. Switch to either electrical or pharmacological cardioversion after 60 mins if not conversion. Outcomes after this cannot be used for systematic review.
Interventions	Intravenous Flecainide Intravenous Propafenone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** The Netherlands **Setting: Unclear hospital setting** **Comments:** No conflicts of interest reported. Planned outcomes: None specified. Reported outcomes: Conversion to sinus rhythm, time to conversion and adverse events (cannot be used for systematic review due to cross-over). No trial registration. **Authors name:** Maarten Suttorp **Institution:** Department of of Cardiology, St. Antonius Hospital Nieuwegein, Koekoekslaan CM Nieuwegein, the Netherlands and Department of Cardiology, University Hospital Gronigen, Oostersingel 59, 9713 EZ Gronigen, The Netherlands **Email:** Not provided **Address:** Maarten J Suttorp, MD, Department of of Cardiology, St. Antonius Hospital Nieuwegein, Koekoekslaan 1, 3435, CM Nieuwegein, the Netherlands.
Notes	Intravenous all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention to method of sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention to allocation concealment.

Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Similar infusion protocol, but no specification to blinding or methods.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk of bias.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No specification to methods of blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk of bias.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Results provided for all patients. No patients lost to follow-up.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Results provided for all patients. No patients lost to follow-up - mean 11 months.
Selective reporting (reporting bias)	Unclear risk	No publication of study protocol, hence could not confirm if any planned outcomes were not reported.
Other bias	Unclear risk	Could not find evidence of prior study protocol registration. Study approved by the Institutional Review board.

Taha 2022

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone • Age (years) mean (SD): 54.7 (5.3) • Male (%): 61 (61) • Hypertension (%): 34 (34) • Diabetes Mellitus (%): 49 (49) • LA diameter (mm) (SD): 41.2 (2.4) • LVEF % mean (SD): 56.41 (11.4) • CHA_2DS_2-VASc Score mean (SD): 2.31 (1.38) • Any Anti-Arrythmic drug (%): 0 (0) • Any rate control drug (%): 0 (0) • Stroke/TIA (%): 0 (0) • Valvular Heart Disease (%): 0 (0) • Structural Heart Disease (%): 0 (0) • Pulmonary Disease (%): 0 (0) • Heart Failure (%): 0 (0) Propafenone • Age (years) mean (SD): 53.9 (7.4) • Male (%): 63 (63) • Hypertension (%): 36 (36) • Diabetes Mellitus (%): 47 (47) • LA diameter (mm) (SD): 39.7 (8.4) • LVEF % mean (SD): 57.26 (9.3) • CHA_2DS_2-VASc Score mean (SD): 2.26 (1.28) • Any Anti-Arrythmic drug (%): 0 (0) • Any rate control drug (%): 0 (0) • Stroke/TIA (%): 0 (0) • Valvular Heart Disease (%): 0 (0) • Structural Heart Disease (%): 0 (0) • Pulmonary Disease (%): 0 (0) • Heart Failure (%): 0 (0)

	Coronary Artery Disease, Myocardial Infarction, Ischaemic Heart Disease: N/A Diuretic, ACE inhibitor, Aspirin: N/A % of LA diameter > 50mm, duration of AF episode, BMI: N/A AF type: All patients had paroxysmal AF. **Inclusion criteria:** Recent onset paroxysmal AF (defined as a palpitation that proved to be attributable to AF within 48 hours of presentation) who were eligible for pharmacological cardioversion. **Exclusion criteria:** Uncontrolled congestive heart failure, acute myocardial infarction within 7 Days, previous atrial flutter (for fear of 1:1 AV conduction with propafenone), previous thromboembolic episodes or stroke, presence of left atrial thrombi, a known hepatic or renal impairment, advanced bronchopulmonary disease, rheumatic valvular heart disease or significant valve stenosis or regurgitation, significant structural heart disease, ejection fraction (EF) < 50%, long QT or pre-excitation syndrome, pregnancy, haemodynamic instability (baseline systolic Bp 90 mmHg), previous electrocardiographic documentation of atrioventricular block or sick sinus syndrome, use of antiarrhythmic drugs at the time of admission (e.g., Beta Blockers (BBs) or Calcium Channel Blockers (CCBs)) and history of hypersensitivity to any of the study medications. **Numbers:** 200 patients randomised equally to amiodarone or propafenone. None were lost to follow up. **Anticoagulation:** All patients were provided heparin or low molecular weight heparin. **Monitoring:** With continuous 24 hour ECG. Follow up duration was for 24 hrs.
Interventions	Intravenous Amiodarone Oral Propafenone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Egypt **Setting:** Accident and Emergency **Comments:** Local ethics committee approved study with registration I-140314. Planned outcomes: Success rate, and time to conversion to sinus rhythm. Impact of biomarkers on conversion to sinus rhythm. Reported outcomes: As above including adverse events in monitoring period. No conflicts of interest reported **Authors name:** Hesham S. Taha **Institution:** Cardiology Department, Faculty of Medicine, Cairo University, Cairo, Egypt, National Heart Institute, Cairo, Egypt and Clinical Pathology Department, Faculty of Medicine, Cairo University, Cairo, Egypt **Email:** ghadayoussef@kasralainy.edu.eg **Address:** Ghada Youssef, Cardiology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	no info provided
Allocation concealment (selection bias)	Unclear risk	no info provided
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Infusion vs. oral drug. Patients and personnel would know administered drug.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints - not at risk of bias
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on blinding of outcome assessors
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints - not at risk of bias
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome in the methods section, selective reporting on this is not likely. Could not access the registered protocol to confirm if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Local ethics committee approval, and study registration number was provided: I-140314. However, no proof of registration or publication on a trial plaftform.

Thomas 2004

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 12 hours if no cardioversion)
Participants	**Baseline Characteristics** Amiodarone • Age (years) mean (SD): 54 (16) • Male (%): 35 (67) • Hypertension (%): 8 (15) • Valvular Heart Disease (%): 1 (2) • Ischaemic Heart Disease (%): 4 (7) • Duration of episode < 48hrs (%): 41 (79) Sotalol • Age (years) mean (SD): 58 (16) • Male (%): 27 (60) • Hypertension (%): 6 (14) • Valvular Heart Disease (%): 1 (2) • Ischaemic Heart Disease (%): 2 (4) • Duration of episode < 48hrs (%): 39 (87) Placebo (Digoxin) • Age (years) mean (SD): 56 (17) • Male (%): 33 (77) • Hypertension (%): 3 (8) • Valvular Heart Disease (%): 3 (7) • Ischaemic Heart Disease (%): 2 (4) • Duration of episode < 48hrs (%): 33 (77)

	Heart Failure, Structural Heart Disease, Pulmonary Disease, Cardiomyopathy, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Coronary Artery Disease: N/A Beta-blocker, Digoxin, Amiodarone, Propafenone, Calcium Antagonist, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A LA dimension and LVEF %: N/A CHA2DS2VASc: N/A BMI: N/A AF type: possible mixed duration of AF, max duration not given **Inclusion criteria:** Patients with symptomatic atrial fibrillation who came to the emergency department were considered for the trial. **Exclusion criteria:** Patients who had taken amiodarone or sotalol in the preceding month or who had previously had an adverse reaction to a trial drug were excluded. Patients who had previously experienced atrial fibrillation while taking amiodarone or sotalol were also excluded. Other exclusion criteria were: Asthma or chronic airway limitation, signs or symptoms of heart failure, known or suspected pulmonary fibrosis, pregnancy, uncorrectable hypotension (<90 mmHg), sick sinus syndrome, bradycardia (<50 beats/min), QTc > 450 ms, active hepatitis, postoperative patients (1 month), patients previously randomised to the trial. **Numbers:** 140 patients enrolled. 52 randomised to amiodarone arm, 45 to sotalol arm and 43 to digoxin arm. No attrition reported. **Anticoagulation:** Unfractional heparin was administered to patietns with a target activated partial thromboplastin time range to 2- to 3- time the baseline level. Heparin was given continuously until cardioversion or end of the trial period. Afterwards anticoagulation was given at the discretion of the treating cardiologist. Patients with atrial fibrillation for >48 hours underwent transoeseophageal echocardiography before electrical cardioversion to exclude atrial thrombus. **Monitoring:** Heart rhythm was documented at intervals between 15 minutes to 1 hour to determine time of cardioversion. If there was no cardioversion after 12 hours patients were referred for electrical cardioversion. No further follow duration reported.
Interventions	Intravenous Amiodarone Intravenous Sotalol
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Two investigators are research scholars funded by National Heart Foundation of Australia (PM98S 0015, PM94S 204). **Country:** Australia **Setting:** Emergency Departement **Comment:** No conflicts of interest reported. Planned Outcomes: No primary outcome specified, patients examined for adverse reactions and early return of atrial fibrillation before discharge. Reported outcomes: as above, effiacy outcome for cardioversion cannot be used after DCCV in this systematic review. No trial registration given. **Author's Name:** Stuart P. Thomas **Institution:** Departments of Cardiology and Emergency Medicine, Westmead Hospital, Westmead, Department of Emergency Medicine, Blacktown Hospital, Blacktown, New South Wales, and Mt Druitt Hospital, Mt Druitt and the University of Sydney, New South Wales, Australia.

	Email: stuartpt@yahoo.com **Address:** Stuart P. Thomas, PhD, Department of Cardiology, Westmead Hospital, Westmead, NSW, Australia 2145
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information provided on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Infusion protocols of the 3 drugs were different, hence participants and personell could know which drug they were receiving.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcome, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on whether blinding of outcome assessors was performed and how.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcome, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoint reported for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not assess pre-publication protocol, and hence not able to confirm if all planned outcomes were reported.
Other bias	Unclear risk	Study approved by the Western Sydney Area Health Service Human Ethics Committee. No evidence of prior publication/registration of the study protocol.

Treglia 1994a

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (Electrical or pharmacological cardioversion if no conversion over 48h)
Participants	**Baseline Characteristics** Propafenone • Age (years) mean (SD): 58 (10) • Male (%): 13 (48) • Hypertension (%): 3 (11) • Valvular Heart Disease (%): 2 (7) • Ischaemic Heart Disease (%): 4 (15) • LA diameter (mm) mean (SD): 49 (7) • Duration of episode (h) mean (SD): 39.5 (52.3) Amiodarone • Age (years) mean (SD): 57 (10) • Male (%): 10 (37) • Hypertension (%): 2 (7) • Valvular Heart Disease (%): 2 (7) • Ischaemic Heart Disease (%): 2 (7) • LA diameter (mm) mean (SD): 48 (7) • Duration of episode (h) mean (SD): 35.9 (61.5) Structural Heart Disease, Coronary Artery Disease, Myocardial Infarction, Pulmonary Disease, Cardiomyopathy, Stroke/TIA, Diabetes Mellitus, Heart Failure: N/A

	Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A LVEF (%): N/A BMI: N/A AF type: All patients with AF <7 days **Inclusion criteria:** Patients referred to ICU for cardioversion of recent onset atrial fibrillation. **Exclusion criteria:** Patients with acute myocardial infarction, treatement with concurrent antiarrythmics, decompensated heart failure with NYHA score IV, arrhyhmia duation >7 days **Numbers:** 54 patients enrolled. 27 randomised to amiodarone arm and 27 randomised to propafenone arm. No attrition reported. **Anticoagulation:** Patients wwere given subcutaenous heparin 12,500 units every 12 hours. **Monitoring:** Continuous ECG monitoing over 48 hours after which patients were given other drugs or electrical cardioversion if no conversion. Data after this cannot be used for systematic review.
Interventions	Intravenous Propafenone Intravenous Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Italy **Setting:** Unclear hospital setting **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm within 48 hours of drug administration. Reported outcomes: As planned and adverse events. No trial registration. **Authors name:** A. Treglia **Institution:** Regione Lazio - USL LT/6 - Formia (Latina), Presidio Ospedaliero di Formia, Sezione Autonoma di Cardiologia **Email:** Not provided **Address:** A. Treglia, Via Rotabile, 67 - 04023 Formia (LT)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention to method of sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention to method (if any) for allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Different administration protocol for the two infusions, allowing personell and possibly patients to know which treatmetn they were on.

Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to method (if any) of blinding for outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not access pre-enrolment protocol, hence not possible to confirm if all planned outcomes were assessed/published.
Other bias	High risk	No mention to Ethics approval. No proof of protocol registration.

Trendafilova 2021

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AA BTE Fixed Patches • Age (years) mean (SD): 61 (9) • Male (%): 25 (66) • BMI (Kg/m^2) mean (SD): 31 (6) • Heart Failure (%): 16 (42) • Hypertension (%): 21 (55) • Valvular Heart Disease (%): 7 (18) • Structural Heart Disease (%): 33 (87) • Pulmonary Disease (%): 9 (24) • Cardiomyopathy (%): 3 (8) • Coronary Artery Disease (%): 2 (5) • Beta-Blocker (%): 28 (74) • Digoxin (%): 4 (11) • Calcium Antagonist (%): 0 (0) • Amiodarone (%): 29 (76) • Propafenone (%): 8 (21) • ACE Inhibitor/ARB (%): 20 (53) • LA diameter > 50mm (%): 21 (55) • LA Diameter (mm) mean (SD): 50 (10) • LVEF < 50% (%): 12 (32) • LVEF (%) mean (SD): 57 (-) • Duration of episode (days) median (IQR): 42 (30-180) • Persistent AF (%): 17 (45) AA PB Fixed Patches • Age (years) mean (SD): 64 (10) • Male (%): 21 (60) • BMI (Kg/m^2) mean (SD): 31 (6) • Heart Failure (%): 13 (37) • Hypertension (%): 20 (56) • Valvular Heart Disease (%): 6 (17) • Structural Heart Disease (%): 31 (89) • Pulmonary Disease (%): 10 (29) • Cardiomyopathy (%): 3 (8) • Coronary Artery Disease (%): 2 (6) • Beta-Blocker (%): 26 (74) • Digoxin (%): 7 (17) • Calcium Antagonist (%): 1 (3)

	• Amiodarone (%): 28 (80) • Propafenone (%): 7 (20) • ACE Inhibitor/ARB (%): 19 (54) • LA diameter > 50mm (%): 14 (40) • LA Diameter (mm) mean (SD): 49 (8) • LVEF < 50% (%): 10 (29) • LVEF (%) mean (SD): 52 (-) • Duration of episode (days) median (IQR): 60 (30-120) • Persistent AF (%): 43 (15) Diabetes Mellitus, Myocardial Infarction, Ischaemic Heart Disease: N/A Sotalol, Flecainide, Diuretic, Aspirin: N/A CHA2DS2VASc: N/A AF type: unclear definition for duration of first detected AF, potentially mixed group. **Inclusion criteria:** ≥ 18 years and had symptomatic (EHRA score 2–4) persistent AF or symptomatic first detected AF or persistent AF after successful causal therapy **Exclusion criteria:** Atrial Flutter; Spontaneous HR <60/min; Digitalis intoxication; Impossibility to maintain sinus rhythm irrespective to antiarrhythmic therapy and frequent cardioversions; Conduction disturbances (without fascicular block and AV block 1 degree) in patients without pacemaker; Asymptomatic patients with AFIB for > 1 year; Thyroid dysfunction: euthyroid status of at least one month is required (TSH is measured); Thrombosis in cardiac cavities, assessment performed using Transesophageal echocardiography (TEE); Spontaneous echo contrast > 2 degree (TEE); Patients with planned cardiac operation in the next three months; Patients with embolic event in the last three months; Patients <18 years of age; Pregnancy **Numbers:** 78 patients enrolled. 39 randomised to BTE arm and 39 to PB arm. 1 patient in the BTE arm recieved wrong intervention (different shock energy), 1 patient in the PB arm recieved the wrong intervention (different shock energy) and another 3 were treated with a different defibrillator. **Anticoagulation:** Anticoagultion protocol not specified, just appropriate standard anticoagulation with unfractionated heparin or acenocoumarol or direct oral anticoagulants were applied before and after cardioversion. **Monitoring:** Continuous ECG monitoring method. 2 hour follow up in ICU including assessment of adverse events. Further clinic follow up at 24 hours.
Interventions	AA BTE Fixed Patches AA PB Fixed Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Total Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local. Schiller Médical, Wissembourg, France provided defibrillators and pads to the principal investigator before the start of this study.

	Country: Bulgaria **Setting:** Referral to intensive care for cardioversion **Comments:** One author is an employee of Schillér Medical, Wissembourg, France. Planned outcomes: None specified. Reported outcomes: Conversion to sinus rhythm, time to conversion and adverse events (cannot be used for systematic review due to cross-over). Clinical Trial registration number NCT04032678. **Authors name:** Elina Trendafilova **Institution:** Intensive Cardiology Care Unit, Cardiology Clinic, National Cardiology Hospital, 65 Konyovitza Str., 1309 Sofia, Bulgaria; Schiller Médical SAS, 4 rue L. Pasteur, F-67160 Wissembourg, France; Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Acad. G. Bonchev Str. Bl 105, 1113 Sofia, Bulgaria **Email:** vessika@biomed.bas.bg **Address:** Vessela Krasteva, Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Acad. G. Bonchev Str. Bl 105, 1113 Sofia, Bulgaria
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Alternating intervention assignment.
Allocation concealment (selection bias)	High risk	"While cardiologists were not blinded to the used defibrillator, however, they could not control the order of patient admittance in ICCU-NCH", which implies that assigned treatment could be predicted by clinicians.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Clinicians were not blinded: Two different defibrillators were used/compared. According to publication, patients were blinded.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention to method, if any, of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients.
Selective reporting (reporting bias)	Low risk	All planned outcomes in the protocol were reported.
Other bias	Unclear risk	Approval by the Local Ethics Committee - project identification code, date: № 2902-2536, 23 July 2018. Irrefutable proof of trial registration on clinicaltrials.gov NCT04032678 - registration in July 2019 (halfway through study: started in February 2019 and finished in March 2020).

Vardas 2000

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Placebo • Age (mean +/- SD): 65 (9) • Men (%): 49 (49) • Left Atrial Diameter (mm) (mean +/- SD): 43 (7) • LVEF (%) (mean +/- SD): 50 (8) Amiodarone • Age (mean +/- SD): 64 (10) • Men (%): 53 (49)

	• Left Atrial Diameter (mm) (mean +/- SD): 44 (6) • LVEF (%) (mean +/- SD): 51 (9) Valvular Heart Disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus: N/A Amiodarone, Sotalol, Flecainide, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A At least 50% of patients have paroxysmal AF, and are defined as <24h duration. Cases last >1 month are considered chronic AF and currently fulfil criteria for persistent AF. Nearly 25% of patients are in that situation. However, persistent AF cases as reported in the stud last between 24h and 1 month, which currently includes paroxysmal AF (up to 7 days) and persistent AF (lasting > 7 days). **Inclusion criteria:** symptomatic atrial fibrillation **Exclusion criteria:** recent myocardial infarction, heart surgery within the last 6 months, unstable angina, acute myocarditis, acute pericarditis, severe uncontrolled heart failure (ejection fraction <30%), or cardiogenic shock were excluded, as were those with significant COPD, pulmonary embolism, pneumonia, liver or kidney failure, thyroid disease, electrolyte disturbances, pregnancy or lactation, and age<18 years, sick sinus syndrome, a history of second-or third-degree atrioventricular block, as well as those who had taken any other anti-arrhythmic drug apart from digoxin within a period prior to the study of less than five half-lives of the drug in question **Numbers:** 208 patients randomised to Amiodarone (108) and Placebo (100). **Anticoagulation:** Anticoagulation for AF >48h was for 21 days at INR 2-3 with acenocoumarol. This was also continued for 21 days after cardioversion. **Monitoring:** Monitoring was with continous ECG during first 24 hrs. Follow up duration was for 3 days as an inpatient and then at 30 days of treatment
Interventions	Intravenous Placebo Intravenous Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Stroke or systemic embolism at 30 days • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30-day CVD mortality • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better

	• **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local Funding **Country:** Greece **Setting:** Accident and Emergency or Clinic **Comments:** No conflicts of interest identified. Planned outcome were successful cardioversion within study period. Reported outcome were as planned but also conversion in outpatient follow up period, adverse effects. No trial registration. **Authors name:** Panos E. Vardas **Institution:** Cardiology Department and the Unit of Toxicology, Heraklion University Hospital, Crete, Greece **Email:** cardio@med.uoc.gr **Address:** Panos E. Vardas, MD, PhD, Cardiology Department, Heraklion University Hospital, PO Box 1352 Stavrakia, Heraklion, Crete, Greece
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Random sequence generation with computerised random number algorithm." - no further details given.
Allocation concealment (selection bias)	Unclear risk	No documentation of how random allocation was concealed to participants.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	No documentation of blinding, Process of medication admission would make blinding difficult as the regimens were different.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but low risk as these are objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No documentation of blinding process for outcome assessors
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but low risk as these are objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Endpoints seem to havebeen reported for every patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Endpoints seem to havebeen reported for every patients. Follow-up 30 days.
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	Unclear risk	No proof of trial registration. Approved by the Ethics committee of the hospital.

Vijayalakshmi 2006

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV if no conversion at 6 weeks)
Participants	**Baseline Characteristics** Placebo • Age (years) mean (SD): 65 (9) • Male (%): 17 (54) • Heart Failure (%): 1 (3) • Hypertension (%): 11 (36) • Coronary Artery Disease (%): 2 (7) • Myocardial Infarction (%): 2 (7) • Diabetes Mellitus (%): 4 (13) • LA Diameter (mm) mean (SD): 43 (7) • LVEF (%) mean (SD): 40 (-) • Duration of episode (months) mean (SD): 7 (4) Amiodarone • Age (years) mean (SD): 66 (11) • Male (%): 20 (74) • Heart Failure (%): 1 (3) • Hypertension (%): 11 (41) • Coronary Artery Disease (%): 2 (7) • Myocardial Infarction (%): 2 (7) • Diabetes Mellitus (%): 2 (8) • LA Diameter (mm) mean (SD): 42 (7) • LVEF (%) mean (SD): 51 (-) • Duration of episode (months) mean (SD): 6.6 (3.9) Sotalol • Age (years) mean (SD): 63 (9) • Male (%): 30 (83) • Heart Failure (%): 1 (3) • Hypertension (%): 11 (31) • Coronary Artery Disease (%): 1 (3) • Myocardial Infarction (%): 2 (6) • Diabetes Mellitus (%): 2 (6) • LA Diameter (mm) mean (SD): 45 (7) • LVEF (%) mean (SD): 40 (-) • Duration of episode (months) mean (SD): 7.3 (4.4) Valvular Heart Disease, Structural Heart Disease, Cardiomyopathy, Pulmonary Disease, Stroke/TIA, Ischaemic Heart Disease: N/A Beta-blocker, Digoxin, Amiodarone, Propafenone, Calcium Antagonist, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A BMI: N/A AF type: All persistent AF, max duration 1 year. **Inclusion criteria:** Patients in whom DCCV of AF was planned were eligible for the study. Only patients with the time of onset of AF within the last 1 year were included. **Exclusion criteria:** Patients < 18 years old; AF more than 1 year duration; AF associated with evidence of rheumatic mitral valve disease; AF associated with prosthetic mitral valves; AF after cardiac surgery within the previous 30 days; Patients with a contraindication to beta-blockers (heart block, significant chronic obstructive airways disease, and asthma); Patients with marked left ventricular dysfunction (NYHA class $\geq$ 3 or ejection fraction $\leq$ 30%); Patients with Wolff-Parkinson-White syndrome; Patients with AF in the context of thyrotoxicosis or pregnancy; Prior participation in the trial; and Patients who were unable to provide informed consent. **Numbers:** 94 patients enrolled. 31 randomised to placebo arm and 27 to amiodarone arm and 36 patients to sotalol. No attrition reported. **Anticoagulation:** Anticoagulation protocol was with warfarin 6 weeks before electrical cardioversion with INR of 1.8 to 2.5. **Monitoring:** Rhythm check done at pre-admission visit before electrical cardioversion. This was at 6 weeks after randomisation. Efficacy data after this cannot be used for systematic review.

Interventions	Oral Placebo Oral Amiodarone Oral Sotalol
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** United Kingdom **Setting:** Outpatient **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm, maintenance of sinus rhythm over 6 months. Reported outcomes: As planned including adverse events, effiacy data after 6 weeks cannot be used for the systematic review. No trial registration. **Authors name:** Kunadian Vijayalakshmi **Institution:** Department of Cardiology, The James Cook University Hospital, Middlesbrough, United Kingdom, and School of Health and Social Care, University of Teesside, Middlesbrough, United Kingdom **Email:** mark.debelder@stees.nhs.uk **Address:** Mark A. de Belder, MA, MD, FRCP, The James Cook University Hospital, Middlesbrough, TS4 3BW, United Kingdom.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No specification of randomization method used in the randomization sheet "Randomly assigned using a computer-generated randomization sheet to receive either no additional treatment, amiodarone or sotalol"
Allocation concealment (selection bias)	Unclear risk	No specification of method, if any, for allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	No blinding was performed.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Blinding of outcome assessment (detection bias) All other outcomes	High risk	No blinding was performed.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcomes, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Follow-up obtained for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality	Low risk	Follow-up obtained for all patients. > 4 weeks

of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.		
Selective reporting (reporting bias)	Unclear risk	Could not assess pre-enrolment protocol to confirm if all planned outcomes were reported.
Other bias	Unclear risk	Local Ethics approval gained. No irrefutable proof of trial registration on an open platform.

Vogiatzis 2009

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP MDS Incremental Patches • Age (mean +/- SD): 61.6 (7.2) • Men (%): 20 (65) • Coronary Artery Disease (%): 6 (20) • Hypertension (%): 4 (13) • Digoxin (%): 14 (46) • Beta-Blocker (%): 15 (50) • Calcium Channel Blockers (%): 5 (16) • Valvular Heart Disease (%): 5 (17) • Duration of AF days (mean +/- SD): 51.25 (13.75) • Left Atrial Diameter mm (mean +/- SD): 44.3 (8.7) • LVEF % (mean +/- SD): 51.9 (4.1) • BMI (Kg/m^2) mean (SD): 26 (4) AA MDS Incremental Patches • Age (mean +/- SD): 60.1 (8.6) • Men: 21 (66) • Coronary Artery Disease (%): 4 (13) • Hypertension (%): 4 (13) • Digoxin (%): 18 (56) • Beta-Blocker (%): 16 (50) • Calcium Channel Blockers (%): 8 (25) • Valvular Heart Disease (%): 6 (19) • Duration of AF days (mean +/- SD): 49.13 (21.84) • Left Atrial Diameter mm (mean +/- SD): 41.2 (9.9) • LVEF % (mean +/- SD): 52.4 (3.7) • BMI (Kg/m^2) mean (SD): 27 (4) Structural Heart Disease, Pulmonary Disease, Cardiomyopathy, Myocardial Infarction, Ischaemic Heart Disease, Heart Failure, Stroke/TIA, Diabetes Mellitus: N/A Amiodarone, Sotalol, Flecainide, Propafenone, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A All patients had persistent AF. **Inclusion criteria:** Chronic atrial fibrillation **Exclusion criteria:** No previous cardioversion **Numbers:** 62 patients were eligible, Randomisation: AP monophasic 32, AA monophasic 30, No attrition. No documentation of monitoring methods. **Anticoagulation:** Patients anticoagulated to INR 2-3 for 4 weeks with acenocoumarol. **Monitoring:** Follow up duration not specified. Continous ECG monitoring method not specified other than defibrillator
Interventions	AP MDS Incremental Patches AA MDS Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better

	• **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Greece **Setting:** Elective Admission **Comments:** No conflicts of interest reported. No specific planned outcomes reported, successful shock determined as sinus rhythm immediately after shock (even if early AF recurrence). Reported outcomes were Shock success, Cumulative shock success and Cardiac enzymes. No trial registration. **Authors name:** I. Vogiatzis **Institution:** Department of Cardiology, General Hospital of Veria, Greece **Email:** ivogia@otenet.gr **Address:** 3a Stougiannaki st., Panorama, Thessaloniki, P.C.55236, Greece.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No documentation of random sequence generation.
Allocation concealment (selection bias)	Unclear risk	No documentation of allocation concealment
Blinding of participants and personnel (performance bias) All other outcomes	High risk	It is not documented as to whether shock administrators or participants were aware of allocation. However, in face of no specific measures for blinding (i.e. no described measures) it seems like the study was open.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but endpoints are objective.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No documentation of if those assessing conversion were aware of allocation
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but endpoints are objective.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There was no attrition and all outcome data was reported
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	Unclear risk	No proof of trial registration. Ethics approval by the Scientific Committee of the hospital.

Vogziatis 2017

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV after 2 hours)
Participants	**Baseline Characteristics** Vernkalant • Male n (%): 25 (67) • Age (Years) Mean (SD): 62 (7) • Hypertension n (%): 27 (75) • Coronary Artery Disease n (%): 18 (50) • Valvular Heart Disease n (%): 5 (14) • LADD (mm) mean (SD): 43 (7) • LVEF <50% n (%): 3 (8) • LVEF % mean (SD): 57 (9)

	Ibutilide • Male n (%): 32 (76) • Age (Years) Mean (SD): 65 (6) • Hypertension n (%): 23 (55) • Coronary Artery Disease n (%): 13 (31) • Valvular Heart Disease n (%): 6 (14) • LADD (mm) mean (SD): 42 (6) • LVEF <50% n (%): 3 (7) • LVEF % mean (SD): 59 (8) Stroke/TIA, Pulmonary Disease, Ischaemic Heart Disease, Cardiomyopathy,Structural Heart Disease, Diabetes Mellitus, Heart Failure: N/A Diuretic, ACE inhibitor, Aspirin, Beta-Blocker, Calcium Channel Blocker, Digoxin, other anti-arrhythmics: N/A BMI: N/A CHA2DS2VASc: N/A All patients had paroxysmal AF. **Inclusion criteria:** AF onset was < 48h, All eligible patients were hemodynamically stable with systolic blood pressure (SBP) >100 mmHg and <160 mmHg, and were receiving anticoagulant treat- ment if it was considered necessary **Exclusion criteria:** a QTc interval on the ECG >440 msec, history of recent TdP, symptomatic bradycardia, sinus node dysfunction, and QRS >140 msec. Also, patients who had recently failed cardioversion were excluded, while exclusion was also considered if there were electrolyte disturbances or digi- talis toxicity, contraindications to ibutilide or recent ad- ministration of vernakalant. Finally, cases of congestive heart failure (CHF; stage >III, NYHA), acute coronary syndromes (ACS), pacemakers, cardiac surgery in the preceding 30 days, atrioventricular block and end-stage disease, were excluded **Numbers:** 78 patients were eligible for enrollemnt and 36 patients were randomised to vernakalant whilst 42 were randomised to Ibutilide. **Anticoagulation:** All patients who needed anticoagulation recieved it but AF onset was less that 48 hours in all cases. **Monitoring:** With ECG but not clear whether this was continuous or at intervals. DCCV was performed after 2 hours if no cardioversion and then a further 6-8 hour follow up as inpatient.
Interventions	Intravenous Vernakalant Intravenous Ibutilide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship Source:** Local Funding **Country:** Greece **Setting:** Unclear

	Comment: No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm, Time to conversion within 2hrs. Adverse events.. Reported outcomes as above. No trial registration **Author's Name:** Ioannis Vogiatzis **Institution:** Department of Cardiology, General Hospital of Veroia, Veroia, Greece **Email:** ivogia@hotmail.gr **Address:** Dr Ioannis Vogiatzis, 3a Stougiannaki str, Panorama, 55236 Thessaloniki, Greece, tel: +302310345709
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	The authors state that randomization was performed by patients' "registry number: odd numbers allocated to group A, and even to group B". There is no information to explain how the registry number is created, and whether it is done in a random manner, but this seems highly suggested of a quasi-randomized design.
Allocation concealment (selection bias)	High risk	The authors state that randomization was performed by patients' "registry number: odd numbers allocated to group A, and even to group B". This could have led to patients knowing in advance which treatment would be allocated and deciding whether or not to include them in the study.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Knowing the patient's registry number, the treating physician and team would know the assigned medication. Also, the administration regimen (infusions) was different for both drugs.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints. Not likely to be impacted.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	There is no mention to an adjudicating committee. It is uncertain how outcomes were assessed.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective endpoints. Not likely to be impacted.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes appear to be reported for every patient.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	No outcomes reported beyond initial hospitalization.
Selective reporting (reporting bias)	High risk	The study protocol was approved by the Ethical Committee of the General Hospital of Veroia (decision No: 13, 10/2/2014). Despite being available prior to start of enrolment, this is not available in a repository or published as a manuscript, and we cannot see which were the planned outcomes for assessment in the protocol. We do not know if any of the originally planned outcomes were left out, or if any additional ones were added. The paper does not clearly define all the endpoints it will report (i.e. dysgeusia is reported in the results section but not even mentioned in the methods).
Other bias	Unclear risk	Not registered on clincialtrials.gov or other trial repository. The study protocol was approved by the Ethical Committee of the General Hospital of Veroia (decision No: 13, 10/2/2014).

Volgman 1998

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV or pacing after 90 min)
Participants	**Baseline Characteristics** Ibutilide • Age (years) mean: 64.3 • Men (%): 45 (75)

	• Duration of episode (days) mean (SD): 22.3 (24.7) • Coronary Artery Disease (%): 23 (38.3) • Valvular Heart Disease (%): 14 (23.3) • Any Anti-Arrythmic drug (%): 0 (0) • Heart Failure (%): 0 (0) • Atrial Flutter (%): 20 (33) Procainamide • Age (years) mean: 67.7 • Men (%): 42 (70) • Duration of episode (days) mean (SD): 17.0 (23.0) • Coronary Artery Disease (%): 32 (53.3) • Valvular Heart Disease (%): 15 (25.0) • Any Anti-Arrythmic drug (%): 0 (0) • Heart Failure (%): 0 (0) • Atrial Flutter (%): 20 (33) Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Myocardial Infarction, Diabetes Mellitus: N/A Calcium Channel Blocker, Digoxin, Beta-blocker, Diuretic, ACE inhibitor, Aspirin: N/A LA dimensions and LVEF: N/A BMI: N/A CHA2DS2VASc: N/A There was a mix of atrial fibrillation and flutter but there is no data on atrial fibrillation type. **Inclusion criteria:**Patients were ≥ 18 years of age, had body weights ≥ 132 lb and ≤ 300 lb and had no previous exposure to ibutilide. Enrollment into the study was limited to six men for every four women enrolled at each site, with the exception of participating Veterans Affairs Medical Centers. Female patients were surgically sterile or postmenopausal. All patients had sustained atrial flutter or fibrillation persisting for at least 3 h and <90 days **Exclusion criteria:** Patients were excluded if they had histories of myocardial infarc- tion within the previous 30 days, torsade de pointes, second- or third-degree heart block, congestive heart failure (New York Heart Association class III or higher) or any serious medical condition that could interfere with the conduct or interpreta- tion of the study results. They were also excluded if they did not have (QTc) ≤ 440 ms on a 12-lead electrocardiogram (ECG), were not hemodynamically stable (ventricular heart rate ≥60 beats/min, systolic blood pressure >90 mm Hg, diastolic blood pressure >60 mm Hg) and were had symptoms of unstable angina or congestive heart failure. **Numbers:** 127 patients were enrolled and only 120 were evaluated for efficacy. 60 patients to each arm and 20 each had atrial flutter. The patients who were not included for evaluation were done so due to protocol violation. **Anticoagulation:** Patients were anticoagulated before being given study medication if the arrhythmia had been present for more than 3 days unless atrial clot had been ruled out with transoeseophageal echocardiography. However the anticoagulation protocol was not specifed. **Monitoring:** with continuous 1 lead ECG monitoring an intermitted 12-lead ECGs. Follow up was 24 hrs. Conversion with DCCV or pacing after 90mins if no conversion.
Interventions	Intravenous Ibutilide Intravenous Procainamide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent

	• **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Sponsored by Pharmacia and Upjohn **Country:** United States of America **Setting:** Not Clear **Comments:** No conflicts of interest reported. Planned outcomes not specified however patients were monitored for rhythm change and adverse events. Reported outcomes were conversion rates, time to conversion and adverse events. No trial registration. **Authors name:** Anabelle S. Volgman **Institution:** Rush–Presbyterian–St. Luke's Medical Center, Chicago, Illinois; Pharmacia & Upjohn, Kalamazoo, Michigan; West Roxbury Veterans Affairs Medical Center, West Roxbury, Massachusetts; University of California at Davis, Sacramento, California; and Mainline Arrhythmia and Cardiology Associates, Wynnewood, Pennsylvania **Email:** pacarber@am.pnu.com. **Address:** Dr. Peter A. Carberry, Pharmacia & Upjohn, 7031-298-142, 7000 Portage Road, Kalamazoo, Michigan 49001-0199
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	Not specified.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Different infusion protocols: two infusions of ibutilide and up to three infusions of procainamide. Personnel could understand which drug was being given.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No information provided on blinding of outcome assessors.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow up. Only reported intra-hospital procedural outcomes.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome in the methods section, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Mention to Ethics/Human subjects committee approval at each site. No information on protocol/trial registration.

Vos 1998

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Ibutilide • Age (years) mean (range): 60.7 (21-89) • Men (%): 142 (67.2) • Duration of Episode (days) median (range): between 5.4 and 16.0 (0.3-90.7) • Any Anti-Arrythmic drug (%): 0 (0) • Digoxin (%): 81 (38.3)

	• Calcium Channel Blocker (%): 0 (0) • Beta-Blocker (%): 0 (0) • Atrial Flutter (%): 36 (17.5) Sotalol • Age (years) mean (range): 59.2 (24-85) • Men (%): 81 (75) • Duration of Episode (days) median (range): 7.2 (0.5-83.4) • Any Anti-Arrythmic drug (%): 0 (0) • Digoxin (%): 33 (30.6) • Calcium Channel Blocker (%): 0 (0) • Beta-Blocker (%): 0 (0) • Atrial Flutter (%): 21 (20.3) Valvular Heart Disease, Coronary Artery Disease, Cardiomyopathy, Hypertension, Structural Heart Disease, Stroke/TIA, Pulmonary Disease, Myocardial Infarction, Diabetes Mellitus: N/A Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A LA size, LA diameter, % of LA diameter > 50mm, and LVEF %: N/A **Inclusion criteria:** Patients older than 18 years with recent onset sustained atrial flutter or fibrillation (defined as between 3h and 45 days) were eligible when they: were haemodynamically stable (systolic blood pressure > 90 mm Hg and diastolic blood pressure < 105 mm Hg); had a normal serum potassium concentration (> 4 mEq/l); had a ventricular rate of > 60 beats/min; and had a rate corrected QT interval of no more than 440 ms in their 12 lead electrocardiogram (ECG). **Exclusion criteria:** Patients with hyperthyroidism, or with a history or evidence of unstable angina pectoris, bronchospastic disease, myocardial infarction or cardiac surgery within the previous 30 days, known sinus node dysfunction, second or third degree atrioventricular (AV) block, bundle branch block, Wolff-Parkinson-White syndrome and/or torsade de pointes were not included. Concurrent treatment with verapamil, diltiazem, or drugs that prolong the QT interval was not allowed. Treatment with class I or III antiarrhythmic agents or with beta adrenoceptor blocking agents was discontinued for more than five half lives before enrolment. **Numbers:** 69 patients were randomized to 4 treatment groups, placebo (18), and three different dofetilide doses (51). None were lost to follow up. **Anticoagulation:** No anticoagulation protocol was provided. **Monitoring:** Continous ECG monitoring. Follow up period was for 12 hours after final treatment.
Interventions	Intravenous Ibutilide Intravenous Sotalol
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Higher is better
Identification	**Sponsorship source:** Supported in part by a grant from the Upjohn Company (Pharmacia & Upjohn), Europe **Country:** The Netherlands, Russia, Germany, United States of America, France, United Kingdom

	Setting: Unclear **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm within 60 minutes after infusion, Conversion after second infusion for non responders. Reported outcomes as planned as well as adverse events. No trial registration. **Authors name:** M A Vos **Institution:** University Hospital, Maastricht, Netherlands; Cardiology Research Centre, Moscow, Russia; Humholdt University, Berlin, Germany; St Chr Ziekenhuis Refaja, Stadskanaal, Netherlands; Pharmacia & Upjohn, Crawley, West Sussex, UK; Pharmacia & Upjohn, Kalamazoo, Michigan, USA; Hospitaux de Lyon, Lyon, France; Klinikum Grosehadern of the University of Munich, Germany **Email:** Not provided **Address:** Dr M A Vos, Department of Cardiology, Cardiovascular Research Institute Maastricht, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, Netherlands.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Mention to study being double blind and that drugs were prepared by an individual not responsible for making assessments. However, no information on who that person was (pharmacist? treating physician? assisting nurse?) and where the preparation of the drug was done.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk of bias as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Mention to study being double blind and that drugs were prepared by an individual not responsible for making assessments.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Mention to study being double blind and that drugs were prepared by an individual not responsible for making assessments.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Unclear risk	Not mentioned how many patients, if all, were reached on the 72h phone call. Also, manuscript is a bit unclear about whether or not all patients had a holter as despite being in the protocol at some point there is mention to 76 patients having a Holter monitor - likely to be the patients in whom arrhythmia was terminated without any complications in <7h.
Selective reporting (reporting bias)	Unclear risk	Clearly defined prespecified primary outcome in the methods section, selective reporting on this is not likely. No information available or pre-publication of protocol saying if there were any other additional endpoints that were not reported.
Other bias	Unclear risk	Ethics approval by all participating centers. No proof of trial or protocol registration. Study partially funded by a grant from the Upjohn Company (pharmaceutical company).

Voskoboinik 2018

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP/AA Biphasic Paddles • Male n (%): 44(71) • Age (Years) Mean (SD): 60(10) • Duration of AF h (range): 5 (5) • Hypertension n (%): 31 (50) • LVEF (%) mean (SD): 53 (10) • LA diamater mm mean (SD) 41 (10) • Any rate control n (%): 7(11) • Beta-blocker n (%): 7 (11) • Calcium Antagonist n (%): 0 (0)

	• Digoxin n (%): 0 (0) • BMI (Kg/m^2) mean (SD): 35 (6) AP/AA Biphasic Patches • Male n (%): 47(75) • Age (Years) Mean (SD): 61(11) • Duration of AF h (range): 4 (9) • Hypertension n (%): 26 (41) • LVEF (%) mean (SD): 50 (12) • LA diamater mm mean (SD) 44 (9) • Any rate control n (%): 11(18) • Beta-blocker n (%): 11 (18) • Calcium Antagonist n (%): 0 (0) • Digoxin n (%): 0 (0) • BMI (Kg/m^2) mean (SD): 35 (5) Structural Heart disease, Pulmonary disease, Cardiomyopathy, Valvular Heart Disease, Myocardial Infarction, Stroke/TIA, Diabetes Mellitus: N/A Propafenone, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A All patients had persistent AF. CHA2DS2VASc: N/A **Inclusion criteria:** Atrial Fibrilation BMI 30 or more, Planned ECV **Exclusion criteria:** Patient refusal, LA thrombus/appendage, Spontaneous cardioversion to sinus rhythm, Atrial Flutter **Numbers:** 125 patients randomised, 63 to patch, 62 to paddle. **Anticoagulation:** Clear anticoagulation protocol not determined. **Monitoring:** Follow up duration not specified. Monitoring was not specified but likely with defibrillator to assess outcome.
Interventions	AP/AA Biphasic Paddles AP/AA Biphasic Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	Sponsorship Source: Australian Govt Funding Country: Australia Setting: Elective Admission Comment: Australian New Zealand Clinical Trials Registry (ANZCTR: 12616000302459). No conflicts of interest reported. Planned outcomes were first or second shock success. Reported outcome: as planned. Author's Name: Aleksander Voskoboinik Institution: Heart Centre, The Alfred Hospital, Melbourne, Australia Email: peter.kistler@baker.edu.au

	Address: Professor Peter Kistler Director of Cardiac Electrophysiology, Alfred Hospital, Melbourne, Australia
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computerized central randomization scheme was generated using block randomization and sets of randomly selected blocks were provided to the investigating sites. "A computerized central randomization scheme was generated using block randomization and sets of randomly selected blocks were provided to the investigating sites. Randomization occurred prior to ECV to enable appropriate patient positioning prior to administration of sedation. Thus, operators were not blinded to group allocation."
Allocation concealment (selection bias)	Unclear risk	Allocation sequence itself was done prior to distribution to individual centres, operators and patients. Operators were not blind to the allocation.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Operators and patients not blinded. Both aware of shock vector and use of pad/patches prior to patient sedation. "Thus, operators were not blinded to group allocation."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Operators and patients not blinded. Both aware of shock vector and use of pad/patches prior to patient sedation. However, these are objective endpoints.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Operators and patients not blinded. Both aware of shock vector and use of pad/patches prior to patient sedation.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Operators and patients not blinded. Both aware of shock vector and use of pad/patches prior to patient sedation. However, these are objective endpoints.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No significant attrition reported
Selective reporting (reporting bias)	Low risk	Trial submitted and registered ANZCTR: 12616000302459 in March 2016 (months before starting enrolment). Pre-specified primary outcome fully reported. One of the endpoints, maintenance of sinus rhythm at 3 months was not reported. However, this was not one of the endpoints we had planned to use.
Other bias	Low risk	No other sources of bias detected. Trial with irrefutable proof with registration ANZCTR: 12616000302459 prior to starting enrolment. The trial was approved by the Alfred, Melbourne, Cabriniand Western Health Human Research Ethics Committees.

Walsh 2005

Study characteristics

Methods	**Study design:** Randomized controlled trial (Conditional Cross-over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** AP BTE Incremental Patches • Age (mean +/- SD): 66 (14) • Men (%): 100 (64) • Hypertension (%): 81 (52) • Ischaemic Heart Disease (%): 61 (39) • Digoxin (%): 61 (39) • Beta-Blocker (%): 93 (59) • Amiodarone (%): 15 (10) • Sotalol (%): 6 (4) • Valvular Heart Disease (%): 26 (17) • Flecainide (%): 3 (2) • Propafenone (%): 10 (6) • Calcium Channel Blocker (%): 5 (3) • LA diameter (mm) mean (SD): 47 (8) • LVEF < 55%: 21.6 (19) • Duration of episode (weeks) mean (SD): 26 (48)

	• BMI (Kg/m^2) mean (SD): 28 (5) AA BTE Incremental Patches • Age (mean +/- SD): 67 (10) • Men (%): 95 (63) • Hypertension (%): 57 (38) • Ischaemic Heart Disease (%): 47 (31) • Digoxin (%): 63 (42) • Beta-Blocker (%): 89 (59) • Amiodarone (%): 14 (9) • Sotalol (%): 5 (3) • Valvular Heart Disease (%): 36 (24) • Flecainide (%): 3 (2) • Propafenone (%): 10 (7) • Calcium Channel Blocker (%): 7 (5) • LA diameter (mm) mean (SD): 46 (6) • LVEF < 55%: 26.3 (25) • Duration of episode (weeks) mean (SD): 19 (33) • BMI (Kg/m^2) mean (SD): 29 (5) Structural Heart disease, Heart Failure, Stroke/TIA, Diabetes Mellitus, Pulmonary Disease, Cardiomyopathy, Myocardial infarction, Coronary Artery Disease: N/A Diuretic, ACE inhibitor, Aspirin: N/A CHA2DS2VASc: N/A AF type: definition not given for paroxysmal AF Patients classified as persistent AF 2/3 and paroxysmal or recurrent 1/3. However, difficult to ascertain what is meant by recurrent. **Inclusion criteria:** Patients eligible for elective cardioversion for AF **Exclusion criteria:** 18 years old, unable to provide informed consent or had any contraindication to the procedure (inadequate anticoagulation, electrolyte disturbance, digoxin toxicity, known intra-cardiac thrombus). Patients with atrial flutter were also excluded. **Numbers:** 322 patients were screened. Of these 2 refused consent, 13 with atrial flutter were excluded. 13 were automatically defaulted to AP if pacemaker in situ. 294 were randomised with 150 assigned to AA and 144 assigned to AP. **Anticoagulation:** Inadequate anticoagulation in exclusion but protocol not identified. **Monitoring:** ECG monitoring method not identified. Follow up period not defined.
Interventions	AP BTE Incremental Patches AA BTE Incremental Patches
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local (Northern Ireland Health and Personal Social Services Office) **Country:** United Kingdom **Setting:** Elective Admission **Comments:** Phillips medical provided defibrillators and pads for the study. Planned Outcomes: Stage in protocol at which patient was successfully cardioverted. Success defined as restoration of sinus rhythm for at least 30s. Reported Outcomes: as planned. No trial registration. **Authors name:** Jennifer Adgey **Institution:** Regional Medical Cardiology Centre, Royal Victoria Hospital **Email:** jennifer.adgey@royalhospital.n-i.nhs.uk **Address:** Regional Medical Cardiology Centre, Royal Victoria Hospital, Grosvenor Road, Belfast, BT12 6BA

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided on method.
Allocation concealment (selection bias)	High risk	Method of concealing randomisation not reported clearly but based on the description seems like high-risk of bias. "pad position was assigned according to a prepared schedule and was based on the order of the patient's arrival on the ward on the day of the procedure"
Blinding of participants and personnel (performance bias) All other outcomes	High risk	There is no report of whether patients or personnel were aware of allocations but the nature of the therapy makes this difficult as positions are different. "All cardioversions were performed using a HeartstreamXL defibrillator (formerly Agilent Technologies, now Philips MedicalSystems, Andover, MA, USA) and self-adhesive electrode pads(Agilent Adult Plus Electrode pads ref: M3713A)." No description of any measures intended for blinding.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above but low risk as objective endpoint.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	There is no mention to an independent committee assessing endpoints.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above but low risk as objective endpoint.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There does not seem to be any attrition on either side after randomisation.
Selective reporting (reporting bias)	Unclear risk	All pre-specified end points were fully reported on. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	Unclear risk	No proof of trial registration. Ethics approval was obtained from the Queen's University Belfast Research Ethics Committee

Xanthos 2007

Study characteristics

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone • Age (mean +/- SD): 64.13 (11.34) • Men: 78 (69) • LAD (mm) (SD): 43.02 (5.44) • LVEF (%) (SD): 44 (18) Procainamide • Age (mean +/- SD): 63.67 (10.56) • Men: 75 (68) • LAD (mm) (SD): 43.56 (5.87) • LVEF (%) (SD): 43 (16) Valvular Heart Disease, Structural Heart Disease, Hypertension, Stroke/TIA, Pulmonary Disease, Cardiomyopathy, Coronary Artery Disease, Myocardial Infarction, Diabetes Mellitus Heart Failure: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Sotalol, Flecainide, Propafenone, Diuretic, ACE inhibitor, Aspirin: N/A LA > 50mm and LVEF <50%: N/A All patients had paroxysmal AF. CHA2DS2VASc: N/A Duration of episode: N/A BMI: N/A **Inclusion criteria:** AF lasting <24h

	Exclusion criteria: Age <18 years, Heart surgery within last 6 months, Unstable Angina, Acute Myocarditis, Hypertrophic Obstructive Cardiomyopathy, Severe Uncontrolled heart failure, Severe chronic obstructive pulmonary disease, pulmonary embolism, liver or renal failure, thyroid disease, pregnancy, lactation, patients with sick sinus syndrome, a history of second or third degree heart block, baseline systolic blood pressure <100mmHg, electrolyte disturbances, pre-treatment with any antiarrhythmic drug other than digoxin, documented permanent AF, atrial flutter and a QTc interval >440ms **Numbers:** 354 patients eligible, 124 Excluded due to spontaneous cardioversion, 225 randomised: 113 to Amiodarone, 112 to Procainamide, 2 lost to follow up from procainamide arm as wanted private treatment. **Anticoagulation:** AF less than 24hrs so no peri-procedural anticoagulation required **Monitoring:** Follow up was 24hrs, ECG monitoring was with Holter.
Interventions	Intravenous Amiodarone Intravenous Procainamide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute procedural success • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Tot Adverse Events 24h • **Outcome type**: AdverseEvent • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Greece **Setting:** Acute Cardiology Deparment **Comments:** No conflicts of interest Planned outcomes : Conversion to sinus rhythm, HR below 95, Reported outcomes: Heart Rate response, Conversion to Sinus rhythm, time to cardioversion, Blood pressure response to therapy, ECG changes, Side effects. No trial registration. **Authors name:** T. Xanthos **Institution:** Department of Experimental Surgery and Surgical Research **Email:** theodorosxanthos@yahoo.com **Address:** Dr T. Xanthos, University of Athens, Medical School, Department of Experimental Surgery and Surgical Research, 15B Agiou Thoma Street, 11527, Athens, Greece.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not documented
Allocation concealment (selection bias)	Unclear risk	"Sealed envelopes" were used. No information if these were opaque, where they were kept and when they were opened.
Blinding of participants and personnel (performance bias)	Unclear risk	Not clear if patients and personnel were aware of allocation. Drugs however given over same period of time, so there seems to have been an attempt at

All other outcomes		blinding.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but low risk as objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Unclear if doctors aware of allocation
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	As above, but low risk as objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Low attrition, only 2 lost to follow up on one arm
Selective reporting (reporting bias)	High risk	There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	Unclear risk	Registered trial ISRCTN28131679 - date of registration after study enrolment. Approved by the Local Ethics Committee.

Yamase 2012

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group (DCCV if no cardioversion at 3 months)
Participants	**Baseline Characteristics** Bepridil • Age (years) mean (SD): 62 (8) • Male (%): 17 (85) • Hypertension (%): 16 (80) • Ischaemic Heart Disease (%): 2 (10) • Diabetes Mellitus (%): 2 (10) • Beta-blocker (%): 5 (25) • Digoxin (%): 6 (30) • Calcium Antagonist (%): 5 (25) • ACE-I/ARB (%): 11 (55) • LA diameter (mm) mean (SD): 46 (5) • LVEF (%) mean (SD): 61 (11) • Duration of episode (months) mean (SD): 12.5 (6.0) Amiodarone • Age (years) mean (SD): 61 (10) • Male (%): 18 (90) • Hypertension (%): 12 (60) • Ischaemic Heart Disease (%): 0 (0) • Diabetes Mellitus (%): 7 (35) • Beta-blocker (%): 8 (40) • Digoxin (%): 8 (40) • Calcium Antagonist (%): 6 (30) • ACE-I/ARB (%): 9 (45) • LA diameter (mm) mean (SD): 45 (4) • LVEF (%) mean (SD): 62 (10) • Duration of episode (months) mean (SD): 15.9 (9.5) Heart Failure, Coronary Artery Disease, Cardiomyopathy, Structural Heart Disease, Valvular Heart Disease, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Pulmonary Disease: N/A

	Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, Aspirin: N/A BMI: N/A CHA2DS2VASc: N/A AF type: all persistent patients **Inclusion criteria:** Not specified other than persitent AF **Exclusion criteria:** Patients were excluded from the study when the AF persisted for more than 2 years, when direct current (DC) cardioversion was attempted more than twice on the separate occasion at least 2 months interval or when the QT interval on the baseline ECG was already longer than 0.5 s **Numbers:** 40 patients enrolled. 20 randomised to bepridil and 20 to amiodarone. No attrition reported. **Anticoagulation:** All patients received anticoagulation therapy with warfarin, with appropriate control by international normalised ratio testing. However durations not specified. **Monitoring:** Clinic visits at 1, 2 and 3 months with ECG. Holter monitor was provided in case of conversion to sinus rhythm to assess for recurrence.
Interventions	Oral Bepridil Oral Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Japan **Setting:** Outpatient **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm and maintenance of sinus rhythm. Adverse events. Reported outcomes: As planned. No trial registration. **Authors name:** Miki Yamase **Institution:** Department of Cardiology, Juntendo University Urayasu Hospital, Urayasu-city, Chiba, Japan; Department of Cardiology, Juntendo University, Tokyo, Japan **Email:** ynkzt@juntendo-urayasu.jp **Address:** Professor Yuji Nakazato, Department of Cardiology, Juntendo University Urayasu Hospital, Tomioka 2-1-1, Urayasu-city, Chiba 279-0021, Japan
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided on method for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information provided on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	open-label study
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	objective endpoints, low risk

Blinding of outcome assessment (detection bias) All other outcomes	High risk	open-label study
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	objective endpoints, low risk
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Short-term outcomes reported for all patients.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Long-term outcomes reported for all patients.
Selective reporting (reporting bias)	Unclear risk	Could not a published protocol and hence could not confirm if all planned outcomes were reported.
Other bias	Unclear risk	Could not find proof of protocol registration. Study had Ethics approval.

Yamashita 2009

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Bepridil • Age (years) mean (SD): 64 (11) • Male (%): 49 (80) • Hypertension (%): 36 (59) • Valvular Heart Disease (%): 7 (11) • Ischaemic Heart Disease (%): 7 (11) • LA diameter (mm) mean (SD): 44 (5) • LVEF (%) mean (SD): 63 (10) • Duration of episode (days) mean (SD): 100.9 (83.3) Placebo • Age (years) mean (SD): 63 (9) • Male (%): 25 (86) • Hypertension (%): 14 (48) • Valvular Heart Disease (%): 12 (41) • Ischaemic Heart Disease (%): 1 (3) • LA diameter (mm) mean (SD): 43 (7) • LVEF (%) mean (SD): 61 (6) • Duration of episode (days) mean (SD): 85.8 (65.0) Heart Failure, Coronary Artery Disease, Cardiomyopathy, Diabetes Mellitus, Structural Heart Disease, Myocardial Infarction, Stroke/TIA, Pulmonary Disease: N/A Beta-blocker, Digoxin, Calcium antagonist, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, Aspirin, ACE-I/ARB: N/A BMI: N/A CHA2DS2VASc: N/A AF type: all persistent patients **Inclusion criteria:** Not specified other than persistent AF **Exclusion criteria:** (1) patients under 20 years of age; (2) patients with AF having been persisting for 1 year or longer; (3) patients within 1 month after cardiac surgery or acute myocardial infarction; (4) patients with AF presumably attributable to the following underlying disorders: sick sinus syndrome, giant left atrium (left atrial diameter > 50mm), severe conduction system disturbances, hyperthyroidism, or mitral stenosis; (5) patients with a left ventricular ejection fraction of <40% or with a Class III or IV heart failure; (6) patients with bradycardia (<50 beats/ min); (7) patients with QT interval prolongation (QTc ≥ 460ms); (8) patients with a history of syncope due to polymorphic ventricular tachycardia or antiarrhythmic drugs; (9) patients with severe hepatic or renal dysfunction; and (10) patients who were pregnancy or were lactating, and women of child-bearing potential. **Numbers:** 112 patients enrolled. 92 randomised: 62 randomised to bepridil (two arms different doses) and 30 to placebo. 20 patients withdrawn during observation period for the following reasons: deviation

	from inclusion criteria (n=11), withdrawal of informed consent (n=4), deviation from exclusion criteria (n=3), and other reasons (n=1). **Anticoagulation:** Anticoagulation protocol not reported. **Monitoring:** Transtelephonic ECG at 2,4 8, and 12 weeks. No follow up reported after this.
Interventions	Oral Bepridil Oral Placebo
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Quality of Life Outcome • **Outcome type**: Scale • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** Japan **Setting:** Outpatient **Comments:** No conflicts of interest reported. Planned outcomes: Conversion to sinus rhythm and maintenance of sinus rhythm, quality of life improvement, and adverse events. Reported outcomes: As planned. No trial registration. **Authors name:** Takeshi Yamashita **Institution:** The Cardiovascular Institute, Cardio-pulmonary Division, Department of Medicine, Keio University School of Medicine, Tokyo, First Department of Internal Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Department of Internal Medicine, Nippon Medical School, Tama-Nagayama Hospital, Tama, Second Department of Internal Medicine, University of Toyama, Toyama, Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Otsu, The First Department of Internal Medicine, Nippon Medical School, Third Department of Internal Medicine, Showa University School of Medicine, Tokyo, Cardiovascular Division, Osaka National Hospital, Osaka, International University of Health and Welfare, Fukuoka, Department of Cardio-Angiology, Kitasato University School of Medicine, Sagamihara, Division of Cardiology, International Medical Center of Japan, Tokyo, Division of Cardiology, Hirosaki University School of Medicine, Hirosaki, Department of Cardiology, Fukuoka University School of Medicine, Fukuoka, Division of Cardiology, Tokai University School of Medicine, Isehara and Department of Biostatistics, University of Toyama, Toyama, Japan **Email:** yamt-tky@umin.ac.jp **Address:** Takeshi Yamashita, MD, The Cardiovascular Insitute, 7-3-10 Roppongi, Minato-ku, Tokyo 106-0032, Japan.
Notes	Oral all arms

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided on sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information provided on allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	Low risk	Study reported as double blind. The test drugs and matching placebo, which were indistinguishable in size, weight, color and taste and were provided + packaged by the drug manufacturer (Schering-Plough KK). It is likely therefore that both patients and personnel were blinded.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-	Low risk	Objective outcome, hence low risk.

Cause Mortality, and Stroke or Systemic Embolism		
Blinding of outcome assessment (detection bias) All other outcomes	Low risk	Outcomes assessed by an external ECG centre. Reported as double-blind and outcome assessors likely blind.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Objective outcome, hence low risk.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	Outcomes reported for all patients throughout study duration.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	Outcomes reported for all patients throughout study duration.
Selective reporting (reporting bias)	Low risk	Protocol available and all endpoints reported. A few more endpoints were reported with different wording from the online protocol were reported (i.e., "quality of life" reported instead of "improvement rate of subjective symptom"; QOL was assessed with AFQLQ and looked at 2 subscales: frequenty and variety, and severity of symptoms), and paper also reports adverse events. https://rctportal.niph.go.jp/en/detail?trial_id=jRCT1091220005
Other bias	Low risk	Evidence of Study protocol registration JRCT ID: jRCT1091220005 on 15/02/2006 - prior to first enrolment.

Yu 2013

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** No baseline characteristics provided although study did report that there was no statisticlly significant difference betweent the two arms for: duration of arrhythmia, coronary artery disease, hypertension, diabetes, rheumatic heart disease, left atrial diameter, left ventricular ejection fraction, resting heart rate and QTc % of paroxysmal and persistent AF not known. **Inclusion criteria:** Paroxysmal and Persistent AF/AFL of < 3 month duration, Age 18-75, HR greater than 60, Weight 60-100Kg, Serum K >4mmoL, QTc interval less than or equal to 440ms, Class I and III antiarrhythmic drugs stopped for at least 5 half lives, No previous history of Torsades des points or Ventricular Tachycardia **Exclusion criteria:** Acute Myocardial Infarction or unstable Angina, Severe congestive heart failure (LVEF<35%), Sick Sinus Syndrome without pacing, uncontrolled hypothyroidism, second or third degree conduction block, Liver and kidney function damage (exceeding twice the upper limit of normal), pregnancy or lactation, uncontrolled severe hypertension (Systolic pressure greater than 180mmHg or diastolic pressure greater than 105 mmHg), hypotension with systolic less than 90mmHg, refusal to sign informed consent, history of embolism or intracardiac thrombus **Numbers:** 99 patients randomised to Ibutilide 49 or Propafenone 50. **Anticoagulation:** With warfarin for more than 3 weeks, post cardioversion. protocol was not documented. **Monitoring:** Study follow up period was 24 hours. Patients were monitored with continuous ECG.
Interventions	**Intervention Characteristics** Ibutilide Propafenone

Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Acute Procedural Success • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: Adverse Event • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: Adverse Event • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local funding **Country:** China **Setting:** Not Clear **Comments:** No conflicts of interest reported. Planned outcomes: Sinus Rhythm within 90 minutes of infusion. Adverse events. Reported outcomes as above. No trial registration **Authors name:** Zhong Yu **Institution:** Department of Cardiology, Hangzhou First Municipal Hospital, Hangzhou 310006, China **Email:** cyq6395@sina.com **Address:** Department of Cardiology, Hangzhou First Municipal Hospital, Hangzhou 310006, China
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reported as a randomised trial but no documentation of sequence generation."Patients were assigned randomly into two groups"
Allocation concealment (selection bias)	Unclear risk	It is not reported how the random allocation was concealed "Patients were assigned randomly into two groups"
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Not reported as blinded personnel. "49 patients in ibutilide group received ibutilide 1 mg, then repeated if AF/AFL was not converted after 10 min; 50 patients in propafenone group received propafenone 70 mg, then repeated if AF/AFL persisted after 10 min. Two drugs were diluted by 50 ml of 5% glucose and injected intravenously within 10 min."
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Not reported as blinded personnel. Low risk as these are objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	There is no documentation of investigators being blinded
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Low risk as these are objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	There was no attrition as of 99 patients at start of trial "AF/AFL were converted in 34 of 49 patients (69.4 %) in ibutilide group and in 22 of 50 patients (44.0 %) in propafenone group (P <0.05)".
Selective reporting (reporting bias)	High risk	

		There is no reference to the original protocol (and it does not apper to have been published prior to the study publication) and if any of the originally planned outcomes were left out. The paper does not clearly define all the endpoints it will report.
Other bias	High risk	No proof of trial registration. Approval by local ethics committee. No table with baseline characteristics.

Zehender 1994

Study characteristics	
Methods	**Study design:** Randomized controlled trial (Conditional Cross-Over) **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Amiodarone • Age (years) mean (SD): 59 (5) • Male (%): 12 (60) • Hypertension (%): 2 (10) • Valvular Heart Disease (%): 5 (25) • Cardiomyopathy (%): 4 (20) • Coronary Artery Disease (%): 4 (20) • LA diameter (mm) mean (SD): 50 (5) • Duration of episode (months) mean (SD): 6.1 (3.7) Quinidine • Age (years) mean (SD): 57 (6) • Male (%): 11 (55) • Hypertension (%): 3 (15) • Valvular Heart Disease (%): 5 (25) • Cardiomyopathy (%): 4 (20) • Coronary Artery Disease (%): 4 (20) • LA diameter (mm) mean (SD): 49 (4) • Duration of episode (months) mean (SD): 4.8 (3.9) Structural heart disease, Diabetes Mellitus, Myocardial Infarction, Stroke/TIA, Ischaemic Heart Disease, Pulmonary Disease, Heart Failure: N/A Beta-blocker, Calcium Antagonist, Digoxin, Amiodarone, Propafenone, Sotalol, Flecainide, Diuretic, ACE inhibitor, Aspirin: N/A BMI: N/A LVEF %: N/A CHA2DS2VASc: N/A AF type: all persistent AF **Inclusion criteria:** Chronic AF duration 4 weeks to 2 years **Exclusion criteria:** Severe heart disease limiting chance of 2 year follow up, pulmonary capilliary pressure > 30mmHg, NYHA class V heart failure, MI < 6 months ago, left atrial thrombus, thyroid disorder, treatement previously with amiodarone, quinidine or verapamil. **Numbers:** 40 patients enrolled. 20 randomised to amiodarone and 20 to quinidine. No attrition reported. **Anticoagulation:** Patients treated with 15,000 units of subcutaneous heparin on a 5 day lead in phase, no documentation of post cardioversion follow up. **Monitoring:** Holter on day 1 and 6 of inpatient stay as well as daily ECG. Follow up monthly for a year then at 18 and 24 months.
Interventions	Oral Quinidine Intravenous Amiodarone
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Higher is better

	• **Data value**: Endpoint 30 day mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint 30 day cardiovascular mortality • **Outcome type**: DichotomousOutcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local funding **Country:** Germany **Setting:** Unclear inpatient setting and outpatient follow up **Comments:** No conflicts of interest reported. Planned outcomes: Sinus Rhythm during inpatient stay, ECG changes, long term maintenance. Reported outcomes as above Including adverse events.. No trial registration **Authors name:** M. Zehender **Institution:** Abteilungen für Kardiologie, Innere Medizin III, Universitätsklinik Freiburg. i Br. und Allgemeines Krankenhaus St. Georg, Hamburg **Email:** not provided **Address:** not provided
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention to methods for sequence generation.
Allocation concealment (selection bias)	Unclear risk	No mention to allocation concealment.
Blinding of participants and personnel (performance bias) All other outcomes	High risk	Amiodarone was given iv during the first three days and quinidine was given orally, hence participants and personnel were not blinded.
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	objective endpoints, hence low risk
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	No mention/description of blinding of outcome assessor.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	objective endpoints, hence low risk
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	All patients were followed through the study period.
Incomplete outcome data (attrition bias) Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-cause mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.	Low risk	All patients were followed through the study period. Good survival curves with number of patients at risk.
Selective reporting (reporting bias)	Unclear risk	No publication of study protocol prior to study was available, hence could no confirm if any of the planned endpoints were not reported.
Other bias	High risk	No evidence of prior protocol registration and no mention to Ethics approval.

Zhang 2005

Study characteristics	
Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** No baseline charactersistics given

	Inclusion criteria: Age: 18 to 70 years old with weight ≥60 kg Patients with atrial fibrillation (75 patients) and atrial flutter (32 patients) with a clear ECG diagnosis, Duration of fibrillation/atrial flutter < 90 d Patients on class I or III antiarrhythmics must discontinue the drug for at least 5 half-lives Signed informed consent. **Exclusion criteria:** (1) Acute myocardial infarction, unstable Angina (2) Heart function ≥ Grade III (3) Sick sinus syndrome or ventricle 4) Rate <50~/min (5) Atrioventricular block of second degree or above (5)Have a history of torsade de pointes ventricular tachycardia (6) systolic blood pressure <90 mm Hg (1 millimeter Hg = 0.133 kPa) or> 180 mm Hg, 7) Diastolic blood pressure <50 mmHg or >110mmHg; (7)Serum potassium <4.0 mMol/L (8) QTc>440 ms. **Numbers:** 212 patients randomised, 107 to Ibutilide and 105 to propafenone. There was no attrition at inpatient follow up. **Anticoagulation:** No anticoagulation protocol is specified **Monitoring:** Patients were mointored with continuous ECG as inpatient. Follow up was 90 mins to 4hrs as inpatient.
Interventions	**Intervention Characteristics** Propafenone Ibutilide
Outcomes	Sinus rhythm until hospital discharge or end of study follow-up • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint Bradycardia • **Outcome type**: Adverse Event • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Ventricular Tachycardia • **Outcome type**: Adverse Event • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint Total Adverse Events 24h • **Outcome type**: Adverse Event • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Local **Country:** China **Setting:** Elective Admission **Comments:** No conflicts of interest reported. Planned outcome: Sinus rhythm wihin 90 after the start of administration. Bleeding or embolism within 4 hrs of start, Ventricular tachycardia or other adverse events. Reported outcomes: as planned **Authors name:** Zhang Haicheng **Institution:** Peoples Hostal, Peking University **Email:** not provided

	Address: Department of Cardiology, Peoples Hostal, Peking University, Bing 100044, China
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Utilized SAS program to generate random numbers, stratified by centre, and creation of a table for 220 participants. The patients were assigned treatments depending on the order.
Allocation concealment (selection bias)	Unclear risk	Concealment method not specified.
Blinding of participants and personnel (performance bias) All other outcomes	Unclear risk	Not clear if participants and personnel blinded Same length of duration infusions given makes blinding possible."Receiving intravenous injection of ibutilide 1 mg over 10 minutes)and propafenone group as control group(n=105 ，including 76 AF cases and 29 AFL casesreceiving intravenous injecfion of propafenone 70 mg over 10 minutes)".
Blinding of participants and personnel (performance bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Not clear if participants blinded. However, low risk as these are objective outcomes.
Blinding of outcome assessment (detection bias) All other outcomes	Unclear risk	Not clear if outcome assessors were blinded to the intervention drug.
Blinding of outcome assessment (detection bias) Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism	Low risk	Not clear if outcome assessors were blinded to the intervention drug. However, low risk as these are objective outcomes.
Incomplete outcome data (attrition bias) Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate procedure-related complications	Low risk	No patients lost to follow-up or with missing outcomes.
Selective reporting (reporting bias)	Unclear risk	According to the paper, prespecified outcomes were all reported. However, there is no reference original protocol (and it does not appear to have been published prior to the study publication) and if any of the originally planned outcomes were left out.
Other bias	High risk	Details on baseline characteristics not given. No irrefutable proof of trial registration - protocol not available on clinicaltrials.gov or other repository. Approved by the Ethics Committee of the Peking University People's Hospital

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Aizawa 2010	Wrong study design - Patients not randomised by intervention
Akel 2018	Wrong study design - Meta-Analysis
Alboni 2004	Wrong study design - Participants were not allocated randomly
Alpert 2000	Wrong study design - Report on a included trial
Benhalla 2015	Wrong patient population - All have acute heart failure
Borgeat 1986	Wrong study design - No mention of randomisation
Boriani 1998	Wrong study design - Case analysis of multiple trials
Botto 1996	Wrong study design - No mention of randomisation
Camm 2022	Wrong study design - Single-arm trial
Conde 2013	Wrong study design - No mention of randomisation
Crijns 1994	Wrong study design - No mention of randomisation
CTRI/2018/01/011248 2018	Wrong study design - Single arm study
Dankner 2009	Wrong study design - No mention of randomisation
Deedwania 1998	Wrong patient popultion - All patients have heart failure
Dittrich 2015	Wrong comparator - Drug not routinely used for cardioversion
Dluzniewski 1994	Wrong patient population - Patients with supraventricular tachycardias
Donovan 1991	Wrong patient population - Patients had recent cardiac surgery
Donovan 1995	Wrong patient population - Patients had recent cardiac surgery
Forney 2000	Wrong study design - Report on a included trial
Galve 1996	Wrong population: included post-cardiac surgery patients
Gullestad 1993	Wrong patient population - Patients with supraventricular tachycardias
Guo 1996	Duplicate - Sub-analyses of patients from two included studies
Hermida 1995	Wrong comparator - Drug compared in 2 dosages
Hohnloser 2004	Wrong comparator - Drug not routinely used for cardioversion
Hou 1995	Wrong patient population - Patients with acute MI

Study	Reason for exclusion
Huang 2003	Wrong comparator - Drug not routinely used for cardioversion / rate control agents
Jacobs 1998	Wrong study design - Assisted electrical cardioversion study
Kafkas 2007	Wrong study design - Patients already on anti-arrhythmics
Kanoupakis 2003a	Wrong patient population - Patients with concurrent anti-arrhythmic therapy for pharmacological cardioversion
Katcher 1997	Wrong study design - Report on a included trial
Kerin 1996	Wrong study design: Cross-over study with no results provided prior to cross-over phase
Kingma 1992	Wrong study design - Participants were not allocated randomly
Kirchhof 2002	Wrong patient population - All patients had EP study prior to cardioversion
Kirilmaz 2001	Wrong study design - Not a controlled trial
Kowey 2009	Wrong patient population - Patients had recent cardiac surgery
Levi 1973	Wrong comparator - Drug not routinely used for cardioversion
Marrouche 2000	Wrong comparator - Drug not routinely used for cardioversion
Martinelli 2003	Wrong comparator - Drug not routinely used for cardioversion
Masini 1990	Wrong comparator - Drug not routinely used for cardioversion
Mathew 1999	Wrong patient population - Patients had recent cardiac surgery
Mieure 2011	Wrong comparator - Drug not routinely used for cardioversion / rate control drugs; Retrospective design
Mironov 2019	Wrong comparator - Drug not routinely used for cardioversion
Nieuwlaat 2011	Wrong study design - Outcome assessed is AF recurrence
Niwano 2009	Wrong study design - Not a controlled trial
Oral 1999	Wrong study design - No mention of randomisation
Pedersen 2001	Wrong patient population - All patients have heart failure
Peuhkurinen 2000	Wrong study design - Patients already on anti-arrhythmics
Pluymaekers 2019	Wrong study design - Compares cardioversion timeframe
Pohjantahti-Maaroos 2017	Wrong study design - No mention of randomisation
Rashba 2002	Wrong comparator - Compares shock polarity
Rho 2003	Wrong study design - Report on a included trial
Sosnowski 2004	Wrong study design - Cardioversion was not the intervention; outcome assessed is AF recurrence
Stambler 1997	Wrong study design - Case analysis of multiple trials
Stiell 2020	Wrong study design - Assisted electrical cardioversion study
Stiell 2021	Wrong study design - Case analysis of multiple trials
Sung 1995	Wrong study design - Cross-over study, inadequate duration before crossover
Torp-Pedersen 2013	Wrong study design - Case analysis of multiple trials
Tuseth 2005	Wrong comparator - Compares different doses of same drug
Villani 2000	Wrong comparator - Drug not routinely used for cardioversion
Vita 1989	Wrong study design - Cross-over study, inadequate duration before crossover
Weiner 1994	Wrong patient population - Patients with acute MI
Zadura 2001	Wrong comparator - comparison of different routes of same drug
Zhan 2003	Wrong comparator - Drug not routinely used for cardioversion

Characteristics of studies awaiting classification [ordered by study ID]

Antonelli 2004

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Baldi 1990

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Baldi 1992

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Botto 1993

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Botto 1995

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Botto 1996a

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Capucci 1991

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Capucci 1992

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Capucci 1993

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Capucci 1994

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Capucci 1999

Methods	
Participants	
Interventions	
Outcomes	
Notes	Awaiting response as data required not presented in paper

Cesar 1994

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Chen 2003

Methods	
Participants	
Interventions	
Outcomes	
Notes	Awaiting response as data required not presented in paper

Fera 1993

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Fernßndez 1998

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Forgione 2000

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Giliarov 2007

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Joshi 1995

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Kalusche 1994

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Kazuzo 1991

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Kazuzo 1995

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Kmec 2006

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Kondili 1990

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Lakananurak 2022

Methods	
Participants	
Interventions	
Outcomes	
Notes	Awaiting correspondence for full text

Lalor 2014

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Negrini 1990

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Negrini 1990a

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Niu 2006

Methods	

Participants	
Interventions	
Outcomes	
Notes	Full text not available

Satullo 1996

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Taha 2013

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Tarasov 2019

Methods	
Participants	
Interventions	
Outcomes	
Notes	Awaiting response as data required not presented in paper

Treglia 1994

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Tsaknakis 1999

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Vaisman 2005

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Vardas 2003

Methods	
Participants	
Interventions	
Outcomes	
Notes	Awaiting response as potential duplicate

Villani 1990

Methods	
Participants	

Interventions	
Outcomes	
Notes	Full text not available

Wu 2010

Methods	
Participants	
Interventions	
Outcomes	
Notes	Full text not available

Zhang 2005a

Methods	
Participants	
Interventions	
Outcomes	
Notes	Awaiting response as potential duplicate

Characteristics of ongoing studies [ordered by study ID]

ChiCTR1900024500

Study name	Effect of Different Discharge Energy on the Efficacy of Transthoracic Cardioversion in Patients With Persistent Atrial Fibrillation
Methods	**Study type:** Interventional study **Study design:** Parallel: yes Randomised: yes
Participants	Inclusion criteria: 1 Aged 18 to 75 years; 2 Subjects with persistent AF documented by ECG recording and history; 3 Patient willing to sign the informed consent. Exclusion criteria: 1 Moderate to severe valvular disease; 2 With congenital heart disease; 3 K+ <3.5 mmol/ L. 4 Left atrial diameter = 55 mm; 5 Left ventricular ejection fraction <40%; 6 Significant pulmonary dysfunction; 7 Thrombus in the left atrium despite anticoagulation in therapeutic range; 8 Contraindication to anticoagulation therapy; 9 History of cardiac surgery; 10 Subjects that are pregnant; 11 Life expectancy <12 months; 12 Digitalis intoxication. Age minimum: 18 Age maximum: 75 Gender: Both
Interventions	Procedure: DCCV 100J protocol; Procedure: DCCV 150J protocol; Procedure: DCCV 200J protocol;
Outcomes	**Primary Outcome(s)** Restore sinus rhythm after first-shock.; **Secondary Outcome(s)** Myocardial injury; Complications;
Starting date	2019-07-01
Contact information	Name: Bing Han Address: 199 Jiefang Road South, Quanshan District, Xuzhou, Jiangsu, China 221000 Telephone: +86 15305218127 Email:

	hbing@hotmail.com Affiliation: Xuzhou Central Hospital
Notes	Ongoing Recruitment

EUCTR2021-001627-40-CZ

Study name	A Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial of Flecainide Acetate Inhalation Solution for Cardioversion of Recent-Onset, Symptomatic Atrial Fibrillation to Sinus Rhythm
Methods	**Study type:** Interventional clinical trial of medicinal product **Study design:** Controlled: yes Randomised: yes Double blind: yes Parallel group: no Cross over: no
Participants	**Inclusion criteria:** 1. >=18 and <=85 years of age 2. Recent onset of symptomatic newly diagnosed or paroxysmal AF a) Recent onset is defined as a symptom duration =1 and =48 hours at time of dosing. b) Newly diagnosed AF is AF that has not been diagnosed previously, independent of its duration. c) Paroxysmal AF is defined as recurrent AF in a patient whose previous AF episode(s) self-terminated (ie, without treatment) or terminated with intervention <=7 days of onset. d) A symptomatic recent-onset AF episode post cardiac ablation for paroxysmal AF would be considered eligible. Are the trial subjects under 18? no Number of subjects for this age range: F.1.2 Adults (18-64 years) yes F.1.2.1 Number of subjects for this age range 200 F.1.3 Elderly (>=65 years) yes F.1.3.1 Number of subjects for this age range 200 **Exclusion criteria:** 1. History of non self-terminating AF/atrial flutter: a) One or more failed attempts to restore SR with pharmacological therapy b) ECV procedure for an AF episode =1 year prior to screening. Exception: One (1) prior ECV is allowed if no option for pharmacological conversion was previously available c) More than 3 ECV procedures in =5 years prior to screening 2. Current diagnosis of persistent AF 3. One or more episodes of AFL =6 months prior to randomization 4. Hemodynamic or cardiac instability during AF, defined as at least 3 consecutive measurements of any of the following during screening: a) Systolic blood pressure (SBP) <100 or =160 mmHg b) Diastolic blood pressure (DBP) =95 mmHg c) Ventricular HR <80 or >160 bpm 5. Respiratory rate >22 breaths per minute 6. History of decompensated heart failure 7. Evidence of significant HF defined as any of the following: a) Hospitalization in the last 12 months for HF or suspected HF event b) Most recent assessment of left ventricular ejection fraction <45% c) New York Heart Association Class II-IV symptoms d) Medication history suggestive of HF per the Investigator's discretion 8. Signs or symptoms of ongoing myocardial ischemia, including any of the following: a) Significant ST segment elevation or depression (ie, =2 mm) on a standard 12-lead ECG b) Echocardiogram findings (eg, wall motion abnormalities) suggestive of acute myocardial infarction c) Angina pectoris, atypical angina pectoris, or receiving antianginal medication for ischemia 9. History of MI =3 months of screening 10. History of uncorrected moderate or severe aortic or mitral valvular stenosis, in the opinion of the Investigator a) If an echocardiogram is performed at screening, moderate or severe valvular stenosis observed during the examination is considered exclusionary. 11. History of LV hypertrophy with LV thickness >12 mm as observed in the most recent assessment, ie, an echocardiogram 12. Stroke (including transient ischemic attack) =3 months prior to randomization 13. History of any of the following cardiac abnormalities: a) Long QT syndrome b) Conduction system disease c) Brugada syndrome d) Torsade de pointes e) Diagnosed with sinus node dysfunction or any of the following: i. History of unexplained or cardiovascular syncope ii. Bradycardia suggestive of sinus node dysfunction iii. Prior electrical or pharmacological cardioversion associated with sinus or ventricular pause >3 seconds or ventricular heart rate <45 bpm at time of conversion 14. Any of the following ECG-related features at screening: a) QT interval corrected for heart rate using the Fridericia formula (QTcF) >480 msec

	b) Wide QRS complex (ie, duration =120 msec) or history of documented wide QRS complex tachycardia (ie, wide QRS complex with ventricular heart rate >100 bpm) c) Presence of VT. Site telemetry should be equipped with an alarm system for VT and premature ventricular complexes (PVCs) or be continuously visually observed prior to dosing. 15. Presence of a pacemaker 16. Cardiac surgery for any of the exclusionary conditions (eg, valvular disease, hypertrophy, coronary artery disease) =6 months prior to randomization 17. Known severe renal impairment or patient receiving dialysis 18. Known abnormal liver function, including hepatic disease or biochemical evidence of significant liver derangement 19. Uncorrected hypokalemia 20. Uncorrected hypomagnesemia 21. Chronic obstructive pulmonary disease or other established pulmonary disease
Interventions	**Drug:** Flecainide **Drug:** Placebo
Outcomes	**Primary Outcome(s)** Primary end point(s): The proportion of patients whose AF converts to SR =90 minutes after initiation of dosing Timepoint(s) of evaluation of this end point: =90 minutes after initiation of dosing Secondary Objective: To compare the effects of flecainide acetate inhalation solution and placebo on the time to conversion of AF to SR, AF-related symptoms, hospitalizations, AF-related interventions, and the time to discharge in patients with recent-onset, symptomatic newly diagnosed or paroxysmal AF Main Objective: To compare the efficacy of flecainide acetate inhalation solution and placebo for the conversion of atrial fibrillation (AF) to sinus rhythm (SR) in patients with recent-onset, symptomatic newly diagnosed or paroxysmal AF **Secondary Outcome(s)** Timepoint(s) of evaluation of this end point: 1) =90 minutes after initiation of dosing 2) 90 minutes after initiation of dosing 3) prior to discharge 4) discharge-eligible status Secondary end point(s): 1) The time to conversion of AF to SR =90 minutes after initiation of dosing 2) The proportion of patients with AF-related symptoms at the 90 minute time point 3) The proportion of patients requiring hospitalization prior to discharge 4) The prevalence (ie, events per patient) of additional AF-related interventions required prior to discharge 5) The time to discharge-eligible status
Starting date	18/05/2022
Contact information	Name: RESTORE-1 Study Lead Address: 39899 Balentine Drive, Suite 185 CA 94560 Newark United States Telephone: +1510422 5522 Email: RESTORE-1@incardatherapeutics.com Affiliation: InCarda Therapeutics, Inc.
Notes	Ongoing Recruitment

NCT04485195

Study name	RAFF4 Trial: Vernakalant vs. Procainamide for Acute Atrial Fibrillation in the Emergency Department
Methods	**Allocation:** Randomized **Intervention Model:** Parallel Assignment **Masking:** None (Open Label)
Participants	**Ages Eligible for Study:** 18 Years and older (Adult, Older Adult) **Sexes Eligible for Study:** All **Accepts Healthy Volunteers:** No **Criteria** **Inclusion Criteria:** The investigators will include stable (see below) patients presenting with an episode of acute non-valvular AF of at least 3 hours duration and no greater than 7 days, where symptoms require urgent management and where immediate cardioversion is a reasonable option because: 1. The patient has been adequately anticoagulated for a minimum of 3 weeks (warfarin and INR > 2.0 or novel oral anticoagulants [dabigatran, rivaroxaban, edoxaban, and apixaban]), or 2. The patient is not adequately anticoagulated for > 3 weeks, has no history of stroke or TIA, and does not have valvular heart disease, AND: i) onset < 12 hours ago, or ii) if onset 12 - 48 hours ago and there are <2 of these CHADS-65 criteria (age ≥ 65, diabetes, hypertension, heart failure), or iii) negative for thrombus on transesophageal echocardiography. Of note, we will not exclude patients with prior episodes of acute AF. Patients will only be enrolled if the attending physician is confident about time of

	onset, based upon the patient's symptoms. Physicians are well aware of the importance of this determination and will not attempt to cardiovert patients otherwise. **Exclusion Criteria:** The investigators will exclude patients who have any of the reasons listed below. **Appropriateness:** 1. unable to understand the study and integrated consent due to language barrier and/or cognitive impairment; 2. have permanent (chronic) AF; 3. have valvular heart disease (mitral stenosis, rheumatic or mechanical); 4. increased risk of stroke because onset not clearly <48 hours and not anticoagulated (or abnormal TEE); or do not meet the inclusion criteria a or b; 5. deemed unstable and require immediate cardioversion: i) systolic blood pressure <100 mmHg; ii) rapid ventricular preexcitation (Wolff-Parkinson-White syndrome); iii) acute coronary syndrome - chest pain and acute ischemic changes on ECG; or iv) pulmonary edema - severe dyspnea requiring immediate IV diuretic, nitrates, or BIPAP; 6. primary presentation was for another condition; examples include pneumonia, pulmonary embolism, and sepsis; 7. convert spontaneously to sinus rhythm prior to randomization; 8. were previously enrolled in the study; or 9. have atrial flutter. **Safety** 1. has heart failure Class NYHA III or NYHA IV; left ventricular ejection fraction <30%; or has clinical or radiological evidence of acute HF; 2. has presented with an acute coronary syndrome or acute decompensated heart failure, in the last 30 days; or has had a recent myocardial infarction (< 3 months); 3. has severe aortic stenosis; 4. has a systolic blood pressure < 100 mmHg; 5. has a significantly prolonged QT interval at baseline e.g. uncorrected > 440 msec, congenital or acquired long QT syndrome; or a family history of Long QT syndrome; or ECG shows QTc >460ms (when heart rate >100 measured by the Fridericia formula); 6. has severe bradycardia (heart rate < 55 bpm), sinus node dysfunction, or second or third degree atrioventricular heart block, in the absence of an in situ properly functioning pacemaker; or, has Brugada syndrome (genetic disease with increased risk of sudden cardiac death); 7. has received an intravenous antiarrhythmic drug Class I, e.g. procainamide, or Class III, e.g. amiodarone or ibutilide, within the prior 4 hours; or currently takes oral class I or III antiarrhythmic drugs other than amiodarone (last dose < 5 half-lives before enrollment); 8. has received an IV beta-blocker within the 2 hours prior 9. has hypersensitivity to the active substance or to any of the ingredients of either drug; 10. has advanced or end-stage liver disease; or 11. is breast feeding or pregnant (safety not established).
Interventions	**Drug:** Vernakalant **Drug:** Procainamide
Outcomes	**Primary Outcome Measures :** 1. Conversion to sinus rhythm for a minimum duration of 30 minutes [Time Frame: During any time following randomization until 30 minutes past the completion of the drug infusion] Conversion to and maintenance of sinus rhythm for at least 30 minutes at any time following randomization until 30 minutes past the completion of the drug infusion. Heart rhythm will be determined by an electrocardiogram (ECG). **Secondary Outcome Measures :** 1. Normal sinus rhythm [Time Frame: At the time of patient disposition (approximately 3 hours after arrival)] Being in normal sinus rhythm at the time of ED disposition (discharge or admission). Heart rhythm will be determined by an electrocardiogram (ECG). 1. Patient disposition (admission or discharge) [Time Frame: At the time of patient admission or discharge (approximately 3 hours after arrival)] Whether the patient was discharged home or admitted to the hospital. 1. Length of stay in ED [Time Frame: From time of arrival until time of discharge or admission (approximately 3 hours)] Length of stay in ED in minutes, from time of arrival to time of discharge or admission 1. Time to discharge [Time Frame: From time of randomization until time of discharge or admission (approximately 3 hours)] Time to discharge in minutes, from time of randomization to time of discharge or admission

	1. Time to conversion [Time Frame: From time of infusion start until time of conversion to sinus rhythm (approximately 0 - 90 minutes)] Time to conversion to sinus rhythm in minutes, from time of start of study drug infusion 1. Whether the patient required electrical cardioversion [Time Frame: From 30 minutes after the study drug infusion is completed.] Whether the patient required electrical cardioversion to restore normal sinus rhythm in the ED 1. Adverse events [Time Frame: 0-12 hours] will be classified as serious or other, whether occurring 0-2 hours or 2-12 hours after infusion, whether infusion had to be halted or discontinued, or treatment required **Other Outcome Measures:** 1. Maintenance of normal sinus rhythm [Time Frame: 30 days post discharge] Maintenance of normal sinus rhythm at 30 days after ED disposition, to be verified by hospital records, patient report, or by a smartphone application. 1. Recurrence of acute AF [Time Frame: 30 days] Recurrence of acute atrial fibrillation requiring an emergency department visit 1. Death [Time Frame: 30 days] within 30 days of ED disposition 1. Stroke [Time Frame: 30 days] transient ischemic attack, myocardial infarction, or other thromboembolic event within 30 days of ED disposition 1. Return to normal activities [Time Frame: 30 days] Return to normal daily activities measured in days
Starting date	June 17, 2021
Contact information	Contact: Ian G Stiell, MD, MSc 613-798-5555 ext 18683 istiell@ohri.ca Contact: Erica Brown 613-798-5555 ericbrown@ohri.ca
Notes	Ongoing Recruitment

NCT04594746

Study name	Oral Amiodarone for Acute Cardioversion of Atrial Fibrillation Study (AAA)
Methods	**Allocation:** Randomized **Intervention Model:** Parallel Assignment **Masking:** Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) **Masking Description:** Drug and placebo will be encapsulated and blinded by the investigational pharmacy.
Participants	**Ages Eligible for Study:** 18 Years and older (Adult, Older Adult) **Sexes Eligible for Study:** All **Accepts Healthy Volunteers:** No **Criteria** **Inclusion Criteria:** • Acute persistent or paroxysmal atrial fibrillation or atrial flutter with duration < 14 days (continuous with no spontaneous conversions), confirmed by ECG or cardiac telemetry • History of symptoms associated with atrial fibrillation • Appropriate anticoagulation (warfarin with an international normalized ratio (INR) > 2.0 or direct oral anticoagulant) **Exclusion Criteria:**

	• Received > 10 g of amiodarone in the prior 6 months, or other Class III anti-arrhythmic agents in the prior 3 months • previous severe adverse event following a cardioversion for atrial fibrillation • Hypothyroid and not on thyroid replacement therapy • Recent myocardial infarction (within 2 weeks) • Acute pulmonary oedema requiring hospital admission or New York Heart Association (NYHA) class IV heart failure • Severe left ventricular dysfunction or left ventricular ejection fraction < 36%, as determined by cardiac imaging • Sick sinus syndrome, high grade atrioventricular block, ventricular rate < 50 beats per minute in the absence of a mechanical pacemaker • Severe renal or hepatic disease • Known congenital long QT syndrome • Hypotension with systolic blood pressure < 90 mmHg • Pregnant or breast-feeding women
Interventions	**Drug:** Amiodarone Hydrochloride **Drug:** Placebo
Outcomes	**Primary Outcome Measures :** 1. Time to Successful Reversion to Sinus Rhythm [Time Frame: 48 hours of intervention administration] Time to successful reversion to sinus rhythm (continuous variable), as documented by continuous cardiac monitoring **Secondary Outcome Measures :** 1. Conversion Rate to Sinus Rhythm [Time Frame: 48 hours of intervention administration] Conversion rate to sinus rhythm (dichotomous variable), as documented by continuous cardiac monitoring 1. Early Recurrence of Atrial Fibrillation After Initial Reversion to Sinus Rhythm [Time Frame: 48 hours of intervention administration] Early recurrence of atrial fibrillation (lasting > 6 minutes) after initial reversion to sinus rhythm (dichotomous variable), as documented by continuous cardiac monitoring
Starting date	February 3, 2022
Contact information	Contact: Satish R Raj, MD MSCI 4032106152 autonomic.research@ucalgary.ca Contact: Rasha Hamzeh, RN rasha.hamzeh1@ucalgary.ca
Notes	Ongoing Recruitment

NCT04680026

Study name	A Study of IV HBI-3000 for the Conversion Recent Onset Atrial Fibrillation (AF)
Methods	**Allocation:** Randomized **Intervention Model**: Parallel Assignment **Intervention Model Description:** **Allocation:** Stage A: non-randomized; Stage B: randomized, double-blind and placebo-controlled Intervention **Model:** Two-stage study Masking: None; Stage A (open label); Stage B: randomized, double-blind and placebo-controlled **Masking:** Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Participants	**Ages Eligible for Study:** 18 Years to 80 Years (Adult, Older Adult) **Sexes Eligible for Study:** All **Accepts Healthy Volunteers:** No **Criteria** **Inclusion Criteria:** • 18 to 80 years of age • Sustained AF of > 2 hours and < 72 hours duration • Eligible for cardioversion (electrical and pharmacologic)

	• On adequate anticoagulant therapy or eligible for anticoagulation during treatment and for at least 30 days duration after treatment if indicated by ACC/AHA/HRS or country specific national or international guidelines for thromboembolic risk reduction related to AF **Exclusion Criteria:** • Atrial fibrillation < 2 hours or > 72 hours duration or with duration not reliably established at the time of dosing • Hemodynamic instability that may require emergency electrical cardioversion • Atrial flutter • Moderate to severe HF • Clinical or ECG signs of acute cardiac ischemia or digitalis toxicity • Known or suspected hyperthyroidism • Cardiac surgery, stroke, TIA, acute MI/ PCI, unstable angina, or persistent angina at rest within the previous 3 months • Presence of LA thrombus by TEE or TTE • Presence of concurrent myocarditis or endocarditis • ECG abnormalities: Current QTcF > 480 msec; QRS interval > 120 msec and/or a complete bundle branch block (BBB)l Delta wave or other pre-excitation pattern consistent with WPW syndrome; Acute coronary ischemia patterns • Use of medication that prolongs the QTc interval or history of: Long QT syndrome, congenital or acquired; Torsades de Pointes (TdP); Brugada Syndrome; Ventricular arrhythmia (not including infrequent isolated PVC) • Concurrent treatment with Class I or III antiarrhythmic drugs, metformin or strong CYP2D6 inhibitors (unless the medication is discontinued > 5 half-lives before enrollment) • Treatment with oral amiodarone in the previous 3 months or IV amiodarone administered within 24 hours prior to planned Study Drug administration • Use of vernakalant, or any experimental drug within 30 days or five half-lives (whichever is longer) of Study Drug administration, or use of an invasive investigational medical device within 2 months prior to Study Drug administration, or current enrollment in another study with investigational agent or procedure • Clinically significant laboratory abnormalities
Interventions	**Drug:** HBI-3000 **Drug:** Placebo
Outcomes	**Primary Outcome Measures :** 1. Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by the incidence of adverse events (AEs) [Time Frame: 30 days] Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by the incidence of adverse events (AEs) 1. Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by changes in heart rate (HR) [Time Frame: 90 minutes] Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by change in heart rate (HR) from baseline (prior to Study Drug infusion) to study timepoints during and after Study Drug infusion, specifically: HR < 40 bpm for 2 minutes or longer within 90 minutes of initiation of the infusion HR increase > 25 percent before conversion to SR (based on one minute averages compared between the event and the first minute of stable telemetry) HR > 120 bpm for one minute or longer after conversion to SR and within 90 minutes of initiation of the infusion 1. Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by change in blood pressure (BP) [Time Frame: 90 minutes] Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by changes in blood pressure (BP) from baseline (prior to Study Drug infusion) to study timepoints during and after Study Drug infusion, specifically: Systolic BP < 90 mmHg for > 1 minute during SR and within 90 minutes of initiation of the infusion 1. Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by ECG interval changes above a specific level [Time Frame: 24 hours] Evaluate the safety of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset, as measured by ECG interval changes from baseline (prior to Study Drug infusion) to 24 hour post-infusion, specifically: QTcF: > 500 msec and > 60 msec above the 24-hour post-conversion level during SR PR: > 50 percent above the 24-hour post-conversion level during SR QRS: ≥ 33 percent above the 24-hour post-conversion level during SR 1. The efficacy of intravenously (IV) administered HBI-3000 as measured by the proportion of patients with AF of recent onset who convert to SR [Time Frame: 120 minutes]

	Evaluate the efficacy of intravenously (IV) administered HBI-3000 in patients with Atrial Fibrillation (AF) of recent onset as measured by the proportion of patients with AF of recent onset who convert to SR (for a duration of at least one minute) within 120 minutes of the start of infusion **Secondary Outcome Measures :** 1. Evaluate the time to conversion to SR from start of infusion [Time Frame: 24 hours] Efficacy as measured by the time from the start of infusion to the time of conversion to SR for a duration of at least one minute 1. Evaluate the proportion of patients with sustained AF or late conversion to SR [Time Frame: 12 hours, 24 hours and 7 days] Efficacy as measured by the proportion of patients with sustained or late conversion of AF of recent onset to SR at 12 hours, 24 hours and 7 days after start of infusion
Starting date	June 1, 2021
Contact information	Contact: Jerry Riebman, MD, FACS, FACC 858-798-8800 jriebman@huyabio.com Contact: Suzanne Romano, PhD 858-798-8800 sromano@huyabio.com
Notes	Ongoing Recruitment

NCT05148923

Study name	Comparison of Two DCCV Algorithms - Rational Versus Maximum Fixed Energy (PROTOCOLENERGY)
Methods	**Allocation:** Randomized **Intervention Model:** Parallel Assignment **Masking:** Single (Participant)
Participants	**Ages Eligible for Study:** 18 Years and older (Adult, Older Adult) **Sexes Eligible for Study:** All **Accepts Healthy Volunteers:** No **Criteria** **Inclusion Criteria:** 1. Patients must have atrial fibrillation or atrial tachycardia. 2. Patients must be on therapeutic anticoagulation at least three weeks prior to DCCV or undergo esophageal echocardiography to rule out intracardiac thrombus. 3. Patients come on an empty stomach. 4. Patients must be over 18 years of age. 5. Patients must provide verbal and written informed consent to participate in the study. **Exclusion Criteria:** 1. Omitting oral anticoagulant treatment in the last three weeks. 2. Unclear time of onset of palpitations in acute patients without anticoagulation therapy. 3. A different type of arrhythmia than atrial fibrillation or atrial tachycardia.
Interventions	**Procedure:** Direct current cardioversion (DCCV) Rational Energy Algorithm **Procedure:** Direct current cardioversion (DCCV) Maximum Fixed Energy Algorithm
Outcomes	**Primary Outcome Measures :** 1. Heart rhythm after DCCV [Time Frame: one minute after DCCV] sinus rhythm 1. Incidence of Neurological Adverse Events [Time Frame: two hours after DCCV] neurological complications **Secondary Outcome Measures :** 1. Incidence of skin changes [Time Frame: two hours after DCCV] none, skin redness, skin burns

	1. Chest pain [Time Frame: one day after DCCV] 0-10 scale of pain severity
Starting date	January 1, 2022
Contact information	Lucjan Rucki, Principal Investigator: lucjan.rucki@npo.agel.cz
Notes	Completed, awaiting correspondance from author.

NCT05511389

Study name	Anteroposterior Versus Anterolateral Electrode Position for Electrical Cardioversion of Atrial Fibrillation (SHOCK-VECTOR)
Methods	**Allocation:** Randomized **Intervention Model:** Parallel Assignment **Intervention Model Description:** With a partial factorial randomization to manual pressure versus not (second intervention) if the first randomized attempt is unsuccessful at restoring normal heart rhythm **Masking:** None (Open Label)
Participants	**Ages Eligible for Study:** 18 Years and older (Adult, Older Adult) **Sexes Eligible for Study:** All **Accepts Healthy Volunteers:** No **Criteria** **Inclusion Criteria:** Consenting adult patients scheduled for non-emergent electrical cardioversion of Atrial Fibrillation or Flutter **Exclusion Criteria:** 1. Insufficiently anticoagulation for cardioversion as per Canadian Cardiovascular Society guidelines or have not undergone trans-esophageal echocardiography to rule out left atrial thrombus 2. Anatomic contraindication to anterolateral or anteroposterior placement (e.g. skin conditions or wounds)
Interventions	**Other:** Anterolateral electrode position **Other:** Anteroposterior electrode position **Other:** Manual pressure
Outcomes	**Primary Outcome Measures :** 1. First-shock cardioversion success [Time Frame: At time of intervention] Reversion to sinus rhythm (5 consecutive P waves within 5 seconds of shock) **Secondary Outcome Measures :** 1. Cumulative cardioversion success for anterolateral versus anteroposterior placement afte [Time Frame: At time of intervention] Reversion to sinus rhythm (5 consecutive P waves within 5 seconds of shock) 1. Second shock success for manual pressure versus none [Time Frame: At time of intervention] Reversion to sinus rhythm (5 consecutive P waves within 5 seconds of shock) **Other Outcome Measures:** 1. Descriptive analysis of techniques and results for third, unrandomized, clinician directed shock [Time Frame: At time of intervention] Reversion to sinus rhythm (5 consecutive P waves within 5 seconds of shock) 1. First shock cardioversion success (subgroup analysis) by electrode position [Time Frame: At time of intervention] As above; exploratory subgroup analysis of: Males vs females, BMI > 30 vs BMI < 30, First episode atrial fibrillation versus recurrent, Duration of current episode >30 days vs <30 days, Left ventricular ejection fraction > 40% vs <40%, Left atrial volume index >34ml/m2 vs not, Premedication with amiodarone , sotalol or class 1 antiarrhythmic drugs versus not, History of cardiac surgery versus not 1. Second shock cardioversion success by manual pressure versus none [Time Frame: At time of intervention] As above; exploratory subgroup analysis of: Males vs females, BMI > 30 vs BMI < 30, First episode atrial fibrillation versus recurrent, Duration of current episode >30 days vs <30 days, Left ventricular ejection fraction > 40% vs <40%, Left atrial volume index >34ml/m2 vs not, Premedication with amiodarone , sotalol or class 1 antiarrhythmic drugs versus not, History of cardiac surgery versus not

	1. Total number of shocks by electrode positioning [Time Frame: At time of intervention] Reversion to sinus rhythm (5 consecutive P waves within 5 seconds of shock)
Starting date	February 22, 2023
Contact information	Contact: William McIntyre, MD william.mcintyre@phri.ca
Notes	Ongoing Recruitment

NCT05549752

Study name	Flecainide Versus Amiodarone in the Cardioversion of Paroxysmal Atrial Fibrillation at the Emergency Department, in Patients With Coronary Artery Disease Without Residual Ischemia (FLECA-ED)
Methods	**Allocation:** Randomized **Intervention Model:** Parallel Assignment **Masking:** Single (Outcomes Assessor)
Participants	**Ages Eligible for Study:** 18 Years to 85 Years (Adult, Older Adult) **Sexes Eligible for Study:** All **Accepts Healthy Volunteers:** No **Criteria** **Inclusion Criteria:** 1. Age: 18-85 years old Paroxysmal Atrial Fibrillation, documented by 12-lead ECG, with one of the following: 1. Atrial Fibrillation onset less than 48 hours from the time of presentation to the Emergency Department 2. Atrial Fibrillation onset between 48 hours and 7 days from the time of presentation to the Emergency Department, and patient has been on anticoagulation for at least 30 days History of Coronary Artery Disease without residual ischemia, defined by one of the following criteria: • PCI <= 1 year, or • CABG <= 3 years, or Negative imaging-based stress testing within 1 year, and: • History of known coronary artery stenosis > 60% without revascularization, or • PCI >= 1 year, or • CABG >= 3 years 1. Ejection Fraction > 35% (documented by cardiac ultrasound at the Emergency Department, or within 1 year) 2. Signed informed consent from the patient or legal representative. **Exclusion Criteria:** Based on ECG at the Emergency Department: 1. Atrial Flutter 2. Newly documented Left Bundle Branch Block (LBBB) 3. Newly documented Right Bundle Branch Block (RBBB) with QRS duration > 150ms 4. Previously documented 24-hour ECG holter monitoring with > 720 poly PVCs/24hours, or non sustained ventricular tachycardia 5. No history of coronary artery disease 6. ST-Segment Elevation Myocardial Infarction (STEMI) Non-ST-Segment Elevation Myocardial Infarction (NSTEMI), according to ESC 2020 guidelines on NSTEMI: 1. If troponin at t0h is over the "low" criterion on table of the cutoff values 2. If the change of troponin (Δtroponin) at t1h is over the respective cutoff value at the table for the cutoff values 3. Unstable angina, defined as myocardial ischemia at rest or at minimum effort, in the absence of acute injury/necrosis of myocardial cells Known residual ischemia: 1. Positive imaging-based stress testing Negative imaging-based stress testing >= 1 year, and: • History of known coronary artery stenosis > 60% without revascularization, or • PCI >= 1 year, or • CABG >= 3 years 1. History of acute coronary syndrome within 1 year 2. Severe Aortic Valve Stenosis (mean pressure gradient > 40mmHg, AVA < 1cm/m^2) 3. Severe Chronic Kidney Disease (stage >= 4)

	4. Severe systematic disease, including neoplasmatic disease under any antineoplasmatic treatment, liver failure, infection with fever 5. Use of strategy "pill in the pocket", by taking flecainide (max 200mg) or propafenone (max 600mg) within 6 hours prior to Emergency Department visit 6. Known dysanexia or allergy to flecainide or amiodarone 7. Pregnancy or/and breastfeeding 8. Participation in any other clinical trial 9. Life expectancy less than 1 year 10. Inappropriate, unfit, or unwilling to follow the desingated protocol procedures.
Interventions	**Drug:** Flecainide Injectable Solution **Drug:** Amiodarone Injectable Solution
Outcomes	**Primary Outcome Measures :** 1. The frequency of successful cardioversion to sinus rhythm [Time Frame: From the drug initiation and for 6 hours] 1. The combined frequency of premature ventricular contractions (PVCs), non-sustained ventricular tachycardia (NSVT), sustained ventricular tachycardia (SVT), bradycardia < 50bpm and systolic blood pressure < 90mmHg. [Time Frame: From the drug initiation and for 6 hours] **Secondary Outcome Measures :** 1. The frequency of patient discharges from the Emergency Department in sinus rhythm [Time Frame: From the drug initiation and for 6 hours] 1. The frequency of successful cardioversion to sinus rhythm [Time Frame: From the drug initiation and for 24 hours, 24 hour ECG Holter monitoring] 1. The time until the cardioversion to sinus rhythm [Time Frame: From the drug initiation and for 6 hours] 1. The frequency of electrical cardioversion [Time Frame: From the drug initiation and for 24 hours] 1. The frequency of arrhythmias: burden of PVCs, NSVT episodes, SVT episodes [Time Frame: From the drug initiation and for 24 hours] 1. The frequency, severity and type of Adverse Events [Time Frame: From the drug initiation and for 30 days]
Starting date	March 24, 2023
Contact information	Contact: Konstantinos P Tsioufis, Professor 2132088000 ktsioufis@hippocratio.gr
Notes	Ongoing Recruitment

Appendices

Appendix 1. MEDLINE search strategy

1 Electric Countershock/

2 Cardioversion*.tw.

3 countershock*.tw.

4 electroversion*.tw.

5 defibrillation*.tw.

6 exp Anti-Arrhythmia Agents/

7 (anti arrhythmi* or antiarrhythmic* or antifibrillatory).tw.

8 ((cardiac or myocardial) adj2 (depressant* or dysrhythmia)).tw.

9 exp Adrenergic beta-Antagonists/

10 (beta adj2 (adrenergic* or antagonist* or block* or receptor*)).tw.

11 acebutolol.tw.

12 Adenosine.tw.

13 Ajmaline.tw.

14 amiodarone.tw.

15 atenolol.tw.

16 azimilide.tw.

17 bisoprolol.tw.

18 Carvedilol.tw.

19 digoxin.tw.

20 diltiazem.tw.

21 disopyramide.tw.

22 dofetilide.tw.

23 Dronedarone.tw.

24 Encainide.tw.

25 esmolol.tw.

26 flecainide.tw.

27 ibutilide.tw.

28 Lidocaine.tw.

29 metoprolol.tw.

30 Mexiletine.tw.

31 moricizine.tw.

32 nadolol.tw.

33 Nebivolol.tw.

34 oxprenolol.tw.

35 Phenytoin.tw.

36 procainamide.tw.

37 propafenone.tw.

38 propranolol.tw.

39 quinidine.tw.

40 sotalol.tw.

41 Timolol.tw.

42 Tocainide.tw.

43 verapamil.tw.

44 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43

45 Atrial Fibrillation/

46 Atrial Flutter/

47 ((atrial or atrium or auricular) adj3 (fibrillat* or flutter*)).tw.

48 45 or 46 or 47

49 44 and 48

50 randomized controlled trial.pt.

51 controlled clinical trial.pt.

52 randomized.ab.

53 placebo.ab.

54 clinical trials as topic.sh.

55 randomly.ab.

56 trial.ti.

57 50 or 51 or 52 or 53 or 54 or 55 or 56

58 exp animals/ not humans.sh.

59 57 not 58

60 49 and 59

Appendix 2. CENTRAL search strategy

#1 MeSH descriptor: [Electric Countershock] this term only

#2 Cardioversion*

#3 countershock*

#4 electroversion*

#5 "counter shock" OR "counter shocks"

#6 cardioconversion*

#7 electroconversion*

#8 electrocardioversion*

#9 "electric conversion" OR "electric conversions"

#10 defibrillation*

#11 MeSH descriptor: [Anti-Arrhythmia Agents] explode all trees

#12 (anti NEXT arrhythmi*) OR antiarrhythmic* or antifibrillatory

#13 ((cardiac or myocardial) NEAR/2 (depressant* or dysrhythmia))

#14 MeSH descriptor: [Adrenergic beta-Antagonists] explode all trees

#15 (beta NEAR/2 (adrenergic* or antagonist* or block* or receptor*))

#16 acebutolol OR Adenosine OR Ajmaline OR amiodarone OR atenolol OR azimilide OR bisoprolol OR Carvedilol OR digoxin OR diltiazem OR disopyramide OR dofetilide OR Dronedarone OR Encainide OR esmolol OR flecainide OR ibutilide OR Lidocaine OR metoprolol OR Mexiletine OR moricizine OR nadolol OR Nebivolol OR oxprenolol OR Phenytoin OR procainamide OR propafenone OR propranolol OR quinidine OR sotalol OR Timolol OR Tocainide OR verapamil

#17 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16

#18 MeSH descriptor: [Atrial Fibrillation] this term only

#19 MeSH descriptor: [Atrial Flutter] this term only

#20 ((atrial or atrium or auricular) NEAR/3 (fibrillat* or flutter*))

#21 #18 OR #19 or #20

Appendix 3. Embase Ovid search strategy

1. cardioversion/

2. Cardioversion*.tw.

3. countershock*.tw.

4. "counter shock*".tw.

5. electroversion*.tw.

6. defibrillation*.tw.

7. "electric conversion*".tw.

8. cardioconversion*.tw.

9. electrocardioversion*.tw.

10. electroconversion*.tw.

11. exp antiarrhythmic agent/

12. (anti arrhythmi* or antiarrhythmic* or antifibrillatory).tw.

13. ((cardiac or myocardial) adj2 (depressant* or dysrhythmia)).tw.

14. exp beta adrenergic receptor blocking agent/

15. (beta adj2 (adrenergic* or antagonist* or block* or receptor*)).tw.

16. acebutolol.tw.

17. Adenosine.tw.

18. Ajmaline.tw.

19. amiodarone.tw.
20. atenolol.tw.
21. azimilide.tw.
22. bisoprolol.tw.
23. Carvedilol.tw.
24. digoxin.tw.
25. diltiazem.tw.
26. disopyramide.tw.
27. dofetilide.tw.
28. Dronedarone.tw.
29. Encainide.tw.
30. esmolol.tw.
31. flecainide.tw.
32. ibutilide.tw.
33. Lidocaine.tw.
34. metoprolol.tw.
35. Mexiletine.tw.
36. moricizine.tw.
37. nadolol.tw.
38. Nebivolol.tw.
39. oxprenolol.tw.
40. Phenytoin.tw.
41. procainamide.tw.
42. propafenone.tw.
43. propranolol.tw.
44. quinidine.tw.
45. sotalol.tw.
46. Timolol.tw.
47. Tocainide.tw.
48. verapamil.tw.
49. or/1-48
50. exp atrial fibrillation/
51. heart atrium flutter/
52. ((atrial or atrium or auricular) adj3 (fibrillat* or flutter*)).tw.
53. or/50-52
54. 49 and 53
55. random$.tw.
56. factorial$.tw.
57. crossover$.tw.
58. cross over$.tw.
59. cross-over$.tw.
60. placebo$.tw.
61. (doubl$ adj blind$).tw.
62. (singl$ adj blind$).tw.
63. assign$.tw.
64. allocat$.tw.
65. volunteer$.tw.
66. crossover procedure/

67. double blind procedure/

68. randomized controlled trial/

69. single blind procedure/

70. 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69

71. (animal/ or nonhuman/) not human/

72. 70 not 71

73. 54 and 72

Appendix 4. CPCI-S search strategy

#18 #17 AND #16

#17 TS=(random* or blind* or allocat* or assign* or trial* or placebo* or crossover* or cross-over*)

#16 #15 AND #14

#15 TS=((atrial fibrillat*) OR (atrial flutter*) OR (atrium fibrillat*) OR (atrium flutter*) OR (auricular fibrillat*) OR (auricular flutter*))

#14 #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1

#13 TS=(acebutolol OR Adenosine OR Ajmaline OR amiodarone OR atenolol OR azimilide OR bisoprolol OR Carvedilol OR digoxin OR diltiazem OR disopyramide OR dofetilide OR Dronedarone OR Encainide OR esmolol OR flecainide OR ibutilide OR Lidocaine OR metoprolol OR Mexiletine OR moricizine OR nadolol OR Nebivolol OR oxprenolol OR Phenytoin OR procainamide OR propafenone OR propranolol OR quinidine OR sotalol OR Timolol OR Tocainide OR verapamil)

#12 TS=((beta adrenergic*) OR (beta antagonist*) OR (beta block*) OR (beta receptor*))

#11 TS=((cardiac depressant*) OR (cardiac dysrhythmia) OR (myocardial depressant*) or (myocardial dysrhythmia))

#10 TS=((anti arrhythmi*) OR antiarrhythmic* OR antifibrillatory)

#9 TS=defibrillation*

#8 TS="electric conversion*"

#7 TS=electrocardioversion*

#6 TS=electroconversion*

#5 TS=cardioconversion*

#4 TS="counter shock*"

#3 TS=electroversion*

#2 TS=Cardioversion*

#1 TS=countershock*

Appendix 5. Clinicaltrials.gov search strategy

Intervention: cardioversion

Condition: atrial fibrillation OR atrial flutter

Study type: Interventional studies (clinical trials)

Appendix 6. WHO ICTRP search strategy

Condition: atrial fibrillation OR flutter

Intervention: cardioversion

Recruitment status: ALL

Appendix 7. ISRCTN

Condition: atrial fibrillation

Intervention: cardioversion

Appendix 8. Characteristics of Excluded Studies

Study	Reason for Exclusion
Aizawa 2010	Wrong study design - Patients not randomized by intervention

Akel 2018	Wrong study design - Meta-analysis
Alboni 2004	Wrong study design - Participants were not allocated randomly
Alpert 2000	Wrong study design - Report on a included trial
Benhalla 2015	Wrong patient population - All have acute heart failure
Borgeat 1986	Wrong study design - No mention of randomization
Boriani 1998	Wrong study design - Case analysis of multiple trials
Botto 1996	Wrong study design - No mention of randomization
Camm 2022	Wrong study design - Single-arm trial
Conde 2013	Wrong study design - No mention of randomization
Crijns 1994	Wrong study design - No mention of randomization
CTRI/2018/01/011248 2018	Wrong study design - Single arm study
Dankner 2009	Wrong study design - No mention of randomization
Deedwania 1998	Wrong patient population - All patients have heart failure
Dittrich 2015	Wrong comparator - Drugs not routinely used for cardioversion
Dluzniewski 1994	Wrong patient population - Patients with supraventricular tachycardias
Donovan 1991	Wrong patient population - Patients had recent cardiac surgery
Donovan 1995	Wrong patient population - Patients had recent cardiac surgery
Forney 2000	Wrong study design - Report on a included study
Galve 1996	Wrong patient population - Included post-cardiac surgery patients
Gullestad 1993	Wrong patient population - Patients with supraventricular tachycardias
Hermida 1995	Wrong comparator - Drug compared in 2 dosages
Hohnloser 2004	Wrong comparator - Drug not routinely used for cardioversion
Hou 1995	Wrong patient population - Patients with acute MI
Huang 2003	Wrong comparator - Drug not routinely used for cardioversion / rate control agents
Jacobs 1998	Wrong study design - Assisted electrical cardioversion study
Kafkas 2007	Wrong study design - Patients already on anti-arrhythmics
Kanoupakis 2003a	Wrong patient population - Patients with concurrent anti-arrhythmic therapy for pharmacological cardioversion
Katcher 1997	Wrong study design - Report on a included trial
Kerin 1996	Wrong study design - Cross-over study with no results provided prior to cross-over phase
Kingma 1992	Wrong study design - Participants were not allocated randomly
Kirchhof 2002	Wrong patient population - All patients had EP study prior to cardioversion
Kirilmaz 2001	Wrong study design - Not a controlled trial
Kowey 2009	Wrong patient population - Patient had recent cardiac surgery
Levi 1973	Wrong comparator - Drug not routinely used for cardioversion
Marrouche 2000	Wrong comparator - Drug not routinely used for cardioversion
Martinelli 2003	Wrong comparator - Drug not routinely used for cardioversion
Masini 1990	Wrong comparator - Drug not routinely used for cardioversion
Mieure 2011	Wrong comparator - Drug not routinely used for cardioversion / rate control drugs; Retrospective design
Mironov 2019	Wrong comparator - Drug not routinely used for cardioversion
Nieuwlaat 2011	Wrong study design - Outcome assessed is AF recurrence
Niwano 2009	Wrong study design - Not a controlled trial
Oral 1999	Wrong study design - No mention of randomization
Pedersen 2001	Wrong patient population - All patients have heart failure
Peuhkurinen 2000	Wrong study design - Patients already on anti-arrhythmics
Pluymaekers 2019	Wrong study design - Compares cadioversion timeframe
Pohjantahti-Maaroos 2017	Wrong study design - No mention of randomisation
Rashba 2002	Wrong comparator - Compares shock polarity
Rho 2003	Wrong study design - Report on a included trial
Sosnowski 2004	Wrong study design - Outcome assessed is AF recurrence / Intervention is not cardioversion
Stambler 1997	Wrong study design - Case analysis of multiple trials
Stiell 2020	Wrong study design - Assisted electrical cardioversion study
Stiell 2021	Wrong study design - Case analysis of multiple trials
Sung 1995	Wrong study design - Cross-over study; inadequate duration before crossover
Torp-Pedersen 2013	Wrong study design - Case analysis of multiple trials
Tuseth 2005	Wrong comparator - Compares different doses of same drug
Villani 2000	Wrong comparator - Drug not routinely used for cardioversion
Vita 1989	Wrong study design - inadequate duration before crossover
Weiner 1994	Wrong patient population - Patients with acute MI
Zadura 2001	Wrong comparator - comparison of different routes of same drug
Zhan 2003	Wrong comparator - Drug not routinely used for cardioversion

References

References to studies included in this review

Abi Mansour 1998 {published data only}

studyIdentifiers

Abi-Mansour, P, Carberry, P A, McCowan, R J, Henthorn, R W, Dunn, G H, Perry, K T. Conversion efficacy and safety of repeated doses of ibutilide in patients with atrial flutter and atrial fibrillation. Study Investigators. Am Heart J 1998;136(4 Pt 1):632-42.

Aliot 1996 {published data only}

studyIdentifiers

Aliot, E, Denjoy, I. Comparison of the safety and efficacy of flecainide versus propafenone in hospital out-patients with symptomatic paroxysmal atrial fibrillation/flutter. The Flecainide AF French Study Group. Am J Cardiol 1996;77(3):66A-71A.

Alp 2000 {published data only}

studyIdentifiers

* Alp, NJ, Rahman, S, Bell, JA, Shahi, M . Randomised comparison of antero-lateral versus antero-posterior paddle positions for DC cardioversion of persistent atrial fibrillation. Int J Cardiol 2000;75:211 - 216.

Azpitarte 1997 {published data only}

studyIdentifiers

Azpitarte, J, Alvarez, M, Baun, O, Garcia, R, Moreno, E, Martin, et al. Value of single oral loading dose of propafenone in converting recent-onset atrial fibrillation. Results of a randomized, double-blind, controlled study. Eur Heart J 1997;18(10):1649-54.

Balla 2011 {published data only}

studyIdentifiers

* Balla, I, Petrela, E, Kondili, A. Pharmacological conversion of recent atrial fibrillation: a randomized, placebo-controlled study of three antiarrhythmic drugs. Anadolu Kardiyol Derg 2011;11(7):600-6. [DOI: https://dx.doi.org/10.5152/akd.2011.162]

Balla, I, Bardhaj, G, Shota, E, Petrela, E, Gace, A, Kondili, et al. Pharmacological conversion of recent atrial fibrillation: A randomized study of three antiarrhythmic. Eur. Heart J. 2006;27:888.

Baroffio 1995 {published data only}

studyIdentifiers

Baroffio, R, Tisi, G, Guzzini, F, Milvio, E, Annoni, P. A randomised study comparing digoxin and propafenone in the treatment of recent onset atrial fibrillation. Clinical Drug Investigation 1995;9(5):277-283.

Baroni 2011 {published data only}

studyIdentifiers

* Baroni, M, Kheir, A, Manfredi, M, Pattarino, F, Doni, F. Quinidine for Pharmacological Cardioversion of Long-lasting Atrial Fibrillation. J Atr Fibrillation 2011;4(2):350. [DOI: https://dx.doi.org/10.4022/jafib.350]

Beatch 2016 {published data only}

studyIdentifiers

Beatch, G N, Mangal, B. Safety and efficacy of vernakalant for the conversion of atrial fibrillation to sinus rhythm; a phase 3b randomized controlled trial. BMC Cardiovasc Disord 2016;16:113.

Beatch 2017 {published data only}

studyIdentifiers

Beatch, G N, Bhirangi, K, Juul-Moller, S, Rustige, J. Efficacy and Safety of Vernakalant for Cardioversion of Recent-onset Atrial Fibrillation in the Asia-Pacific Region: A Phase 3 Randomized Controlled Trial. J Cardiovasc Pharmacol 2017;69(2):86-92. [DOI: https://dx.doi.org/10.1097/FJC.0000000000000445]

Bellandi 1995 {published data only}

studyIdentifiers

Bellandi, F, Cantini, F, Pedone, T, Palchetti, R, Bamoshmoosh, M, Dabizzi, et al. Effectiveness of intravenous propafenone for conversion of recent-onset atrial fibrillation: a placebo-controlled study. Clin Cardiol

1995;18(11):631-4.
Bellandi, F, Dabizzi, R P, Cantini, F, Natale, M D, Niccoli, L . Intravenous propafenone: efficacy and safety in the conversion to sinus rhythm of recent onset atrial fibrillation--a single-blind placebo-controlled study. . Cardiovasc Drugs Ther 1996;10 (2):153-7.

Bellone 2012 {published data only}

studyIdentifiers

* Bellone, A, Etteri, M, Vettorello, M, Bonetti, C, Clerici, D, Gini, G, Maino, C, Mariani, M, Natalizi, A, Nessi, I, Rampoldi, A, Colombo, L. Cardioversion of acute atrial fibrillation in the emergency department: a prospective randomised trial. Emerg Med J 2012;29(3):188-91. [DOI: https://dx.doi.org/10.1136/emj.2010.109702]

Bertini 1990 {published data only}

studyIdentifiers

Bertini, G, Conti, A, Fradella, G, Francardelli, L, Giglioli, C, Mangialavori, et al. Propafenone versus amiodarone in field treatment of primary atrial tachydysrhythmias. J Emerg Med 1990;8(1):15-20.

Bianconi 1998 {published data only}

studyIdentifiers

Bianconi, L, Mennuni, M. Comparison between propafenone and digoxin administered intravenously to patients with acute atrial fibrillation. PAFIT-3 Investigators. The Propafenone in Atrial Fibrillation Italian Trial. Am J Cardiol 1998;82(5):584-8.

Bianconi 2000 {published data only}

studyIdentifiers

* Bianconi, L, Castro, A, Dinelli, M, Alboni, P, Pappalardo, A, Richiardi, E, Santini, M. Comparison of intravenously administered dofetilide versus amiodarone in the acute termination of atrial fibrillation and flutter. A multicentre, randomized, double-blind, placebo-controlled study. Eur Heart J 2000;21(15):1265-73.

Blanc 1999 {published data only}

studyIdentifiers

* Blanc, J J, Voinov, C, Maarek, M. Comparison of oral loading dose of propafenone and amiodarone for converting recent-onset atrial fibrillation. PARSIFAL Study Group. Am J Cardiol 1999;84(9):1029-32.

Boriani 1997 {published data only}

studyIdentifiers

Boriani, G, Biffi, M, Capucci, A, Botto, G L, Broffoni, T, Rubino, et al. Oral propafenone to convert recent-onset atrial fibrillation in patients with and without underlying heart disease. A randomized, controlled trial. Ann Intern Med 1997;126(8):621-5.
Boriani, G, Biffi, M, Capucci, A, Botto, G L, Broffoni, T, Rubino, et al. Oral loading with propafenone: a placebo-controlled study in elderly and nonelderly patients with recent onset atrial fibrillation.. Pacing Clin Electrophysiol 1998;21(11 Pt 2):2465-9.

Botto 1999 {published data only}

studyIdentifiers

Botto, G L, Politi, A, Bonini, W, Broffoni, T, Bonatti, R. External cardioversion of atrial fibrillation: role of paddle position on technical efficacy and energy requirements. Heart 1999;82(6):726-30.

Bouida 2019 {published data only}

studyIdentifiers

* Bouida, W, Beltaief, K, Msolli, M A, Azaiez, N, Ben Soltane, H, Sekma, A, Trabelsi, I, Boubaker, H, Grissa, M H, Methemem, M, Boukef, R, Dridi, Z, Belguith, A, Nouira, S. Low-dose Magnesium Sulfate Versus High Dose in the Early Management of Rapid Atrial Fibrillation: Randomized Controlled Double-blind Study (LOMAGHI Study). Academic Emergency Medicine 2019;26(2):183-191. [DOI: http://dx.doi.org/10.1111/acem.13522]

Braždžionytė 2006 {published data only}

studyIdentifiers

Brazdzionyte, J, Babarskiene, R M, Stanaitiene, G. Anterior-posterior versus anterior-lateral electrode position for biphasic cardioversion of atrial fibrillation. Medicina (Kaunas) 2006;42(12):994-8.

Brodsky 1994 {published data only}

studyIdentifiers

Brodsky, M A, Orlov, M V, Capparelli, E V, Allen, B J, Iseri, L T, Ginkel, M, Orlov, Y S. Magnesium therapy in new-onset atrial fibrillation. Am J Cardiol 1994;73(16):1227-9.

Camm 2011 {published data only}

studyIdentifiers

* Camm, A J, Capucci, A, Hohnloser, S H, Torp-Pedersen, C, Van Gelder, I C, Mangal, B, Beatch, G, Investigators, Avro. A randomized active-controlled study comparing the efficacy and safety of vernakalant to amiodarone in recent-onset atrial fibrillation. J Am Coll Cardiol 2011;57(3):313-21. [DOI: https://dx.doi.org/10.1016/j.jacc.2010.07.046]

Camm 2012 {published data only}

studyIdentifiers

* Camm, A J, Toft, E, Torp-Pedersen, C, Vijayaraman, P, Juul-Moller, S, Ip, et al. Efficacy and safety of vernakalant in patients with atrial flutter: a randomized, double-blind, placebo-controlled trial. Europace 2012;14(6):804-9.

Channer 2004 {published data only}

studyIdentifiers

Channer, K S, Birchall, A, Steeds, R P, Walters, S J, Yeo, W W, West, J N, Muthusamy, R, Rhoden, W E, Saeed, B T, Batin, P, Brooksby, W P, Wilson, I, Grant, S. A randomized placebo-controlled trial of pre-treatment and short- or long-term maintenance therapy with amiodarone supporting DC cardioversion for persistent atrial fibrillation. Eur Heart J 2004;25(2):144-50.

Chiladakis 2001 {published data only}

studyIdentifiers

* Chiladakis, J A, Stathopoulos, C, Davlouros, P, Manolis, A S. Intravenous magnesium sulfate versus diltiazem in paroxysmal atrial fibrillation. Int J Cardiol 2001;79(2-3):287-91.

Chu 2009 {published data only}

studyIdentifiers

* Chu, K, Evans, R, Emerson, G, Greenslade, J, Brown, A. Magnesium sulfate versus placebo for paroxysmal atrial fibrillation: a randomized clinical trial. Acad Emerg Med 2009;16(4):295-300. [DOI: https://dx.doi.org/10.1111/j.1553-2712.2009.00360.x]

Cotter 1999 {published data only}

studyIdentifiers

* Cotter, G, Blatt, A, Kaluski, E, Metzkor-Cotter, E, Koren, M, Litinski, I, Simantov, R, Moshkovitz, Y, Zaidenstein, R, Peleg, E, Vered, Z, Golik, A. Conversion of recent onset paroxysmal atrial fibrillation to normal sinus rhythm: the effect of no treatment and high-dose amiodarone. A randomized, placebo-controlled study. Eur Heart J 1999;20(24):1833-42.

Cybulski 2003 {published data only}

studyIdentifiers

Cybulski J, Kułakowski P, Budaj A, Danielewicz H, Maciejewicz J, Kawka-Urbanek T, Ceremuzyński L. Intravenous amiodarone for cardioversion of recent-onset atrial fbrillation.. Clin Cardiol. 2003;26(7):329–35.. [DOI: 10.1002/clc.4950260707]

Davey 2005 {published data only}

studyIdentifiers

* Davey, M J, Teubner, D. A randomized controlled trial of magnesium sulfate, in addition to usual care, for rate control in atrial fibrillation. Ann Emerg Med 2005;45(4):347-53.

Ellenbogen 1996 {published data only}

studyIdentifiers

* Ellenbogen, K A, Stambler, B S, Wood, M A, Sager, P T, Wesley, R C Jr, Meissner, M C, Zoble, R G, Wakefield, L K, Perry, K T, Vanderlugt, J T. Efficacy of intravenous ibutilide for rapid termination of atrial fibrillation and atrial flutter: a dose-response study. J Am Coll Cardiol 1996;28(1):130-6.

Fak 1997 {published data only}

studyIdentifiers

Fak, A S, Tezcan, H, Caymaz, O, Tokay, S, Oktay, S, Oktay, et al. Efficacy of intravenous propafenone in converting atrial fibrillation and flutter in sinus rhythm.. [Turkish]. Turk Kardiyoloji Dernegi Arsivi 1997;25(7):406-411+390-391.

Fak, A S, Tezcan, H, Caymaz, O, Tokay, S, Oktay, S, Oktay, A. Intravenous Propafenone for Conversion of Atrial Fibrillation or Flutter to Sinus Rhythm: A Randomized, Placebo-controlled, Crossover Study. J Cardiovasc Pharmacol Ther 1997;2(4):251-258.

Falk 1997 {published data only}

studyIdentifiers

* Falk, R H, Pollak, A, Singh, S N, Friedrich, T. Intravenous dofetilide, a class III antiarrhythmic agent, for the termination of sustained atrial fibrillation or flutter. Intravenous Dofetilide Investigators. J Am Coll Cardiol 1997;29(2):385-90.

Fresco 1996 {published data only}

studyIdentifiers

Fresco, C, Proclemer, A, Pavan, A, Buia, G, Vicentini, A, Pavan, et al. Intravenous propafenone in paroxysmal atrial fibrillation: a randomized, placebo-controlled, double-blind, multicenter clinical trial. Paroxysmal Atrial Fibrillation Italian Trial (PAFIT)-2 Investigators. Clin Cardiol 1996;19(5):409-12.

Galperín 2001 {published data only}

studyIdentifiers

Galperin, J, Elizari, M V, Chiale, P A, Molina, R T, Ledesma, R, Scapin, A O, Vazquez Blanco, M, Gefca Investigators-Gema Group, Buenos Aires Argentina. Efficacy of amiodarone for the termination of chronic atrial fibrillation and maintenance of normal sinus rhythm: a prospective, multicenter, randomized, controlled, double blind trial. J Cardiovasc Pharmacol Ther 2001;6(4):341-50.

Ganau 1998 {published data only}

studyIdentifiers

Ganau, G, Lenzi, T. Intravenous propafenone for converting recent onset atrial fibrillation in emergency departments: a randomized placebo-controlled multicenter trial. FAPS Investigators Study Group. J Emerg Med 1998;16(3):383-7.

Halinen 1995 {published data only}

studyIdentifiers

* Halinen, M O, Huttunen, M, Paakkinen, S, Tarssanen, L. Comparison of sotalol with digoxin-quinidine for conversion of acute atrial fibrillation to sinus rhythm (the Sotalol-Digoxin-Quinidine Trial). Am J Cardiol 1995;76(7):495-8.

Hohnloser 1995 {published data only}

studyIdentifiers

Hohnloser, S H, Loo, Avd, Baedecker, F, Hablawetz, E, Jh. Effectivity and safety of Sotalol verses Chinidin in the conversion therapy of persistent atrial fibrillation: a prospective randomised comparison. Zeitschrift fur kardiologie 1994;83 Suppl 1:13.

Hohnloser, S H, van de Loo, A, Baedeker, F. Efficacy and proarrhythmic hazards of pharmacologic cardioversion of atrial fibrillation: prospective comparison of sotalol versus quinidine. J Am Coll Cardiol 1995;26(4):852-8.

Jakobsson 1990 {published data only}

studyIdentifiers

Jakobsson, J, Odmansson, I, Nordlander, R. Comparison of two different electrodes for the delivery of dc-shocks. Resuscitation 1990;20(1):25-9.

Joseph 2000 {published data only}

studyIdentifiers

* Joseph, A P, Ward, M R. A prospective, randomized controlled trial comparing the efficacy and safety of sotalol, amiodarone, and digoxin for the reversion of new-onset atrial fibrillation. Ann Emerg Med 2000;36(1):1-9.

Kanoupakis 2003 {published data only}

studyIdentifiers

Kanoupakis, E M, Manios, E G, Mavrakis, H E, Tzerakis, P G, Mouloudi, H K, Kallergis, E M, Kambouraki, D C, Vardas, P E. Effects of carvedilol and amiodarone on persistent atrial fibrillation conversion and recurrence rates. A randomized controlled study. Eur. Heart J. 2003;24:367-367. [DOI: 10.1016/s0195-668x(03)95012-3]

Khaykin 2003 {published data only}

studyIdentifiers

* Khaykin, Y, Newman, D, Kowalewski, M, Korley, V, Dorian, P. Biphasic versus monophasic cardioversion in shock-resistant atrial fibrillation. J Cardiovasc Electrophysiol 2003;14(8):868-72.

Kim 2003 {published data only}

studyIdentifiers

Kim ML, Kim SG, Park DS, Gross JN, Ferrick KJ, Palma EC, Fisher JD. Comparison of rectilinear biphasic waveform energy versus truncated exponential biphasic waveform energy for transthoracic cardioversion of atrial fibrillation. Am J Cardiol 1st December 2004;94(11):1438-1440. [DOI: 10.1016/j.amjcard.2004.07.149] [PMID: 15566922]

Kim, S G, Kim, M, Park, D, Gross, J N, Ferrick, K J, Palma, et al. Prospective Randomized comparison of rectilinear biphasic waveform shock versus truncated exponential biphasic waveform shock for transthoracic cardioversion of atrial fibrillation. J. Am. Coll. Cardiol. 2003;41(6):138A.

Kirchhof 2005 {published data only}

studyIdentifiers

* Kirchhof, P, Monnig, G, Wasmer, K, Heinecke, A, Breithardt, G, Eckardt, L, Bocker, D. A trial of self-adhesive patch electrodes and hand-held paddle electrodes for external cardioversion of atrial fibrillation (MOBIPAPA). Eur Heart J 2005;26(13):1292-7.

Kochiadakis 1998 {published data only}

studyIdentifiers

* Kochiadakis, G E, Igoumenidis, N E, Solomou, M C, Parthenakis, F I, Christakis-Hampsas, M G, Chlouverakis, G I, Tsatsakis, A M, Vardas, P E. Conversion of atrial fibrillation to sinus rhythm using acute intravenous procainamide infusion. Cardiovasc Drugs Ther 1998;12(1):75-81.

Kochiadakis 1998a {published data only}

studyIdentifiers

* Kochiadakis, G E, Igoumenidis, N E, Simantirakis, E N, Marketou, M E, Parthenakis, F I, Mezilis, N E, Vardas, P E. Intravenous propafenone versus intravenous amiodarone in the management of atrial fibrillation of recent onset: a placebo-controlled study. Pacing Clin Electrophysiol 1998;21(11 Pt 2):2475-9.

Kochiadakis 1999 {published data only}

studyIdentifiers

* Kochiadakis, G E, Igoumenidis, N E, Solomou, M C, Kaleboubas, M D, Chlouverakis, G I, Vardas, P E. Efficacy of amiodarone for the termination of persistent atrial fibrillation. Am J Cardiol 1999;83(1):58-61.

Kochiadakis 1999a {published data only}

studyIdentifiers

* Kochiadakis, G E, Igoumenidis, N E, Parthenakis, F I, Chlouverakis, G I, Vardas, P E. Amiodarone versus propafenone for conversion of chronic atrial fibrillation: results of a randomized, controlled study. J Am Coll Cardiol 1999;33(4):966-71.

Kochiadakis 2007 {published data only}

studyIdentifiers

* Kochiadakis, G E, Igoumenidis, N E, Hamilos, M E, Marketou, M E, Chlouverakis, G I, Vardas, P E. A comparative study of the efficacy and safety of procainamide versus propafenone versus amiodarone for the conversion of recent-onset atrial fibrillation. Am J Cardiol 2007;99(12):1721-5.

Kosior 2009 {published data only}

studyIdentifiers

* Kosior, D A, Kochanowski, J, Scislo, P, Piatkowski, R, Postula, M, Rabczenko, D, Opolski, G. Efficacy and tolerability of oral propafenone versus quinidine in the treatment of recent onset atrial fibrillation: A randomized, prospective study. Cardiol J 2009;16(6):521-7.

  Kosior, D, Kochanowski, J, Niemczyk, M, Scislo, P, Rabczenko, D, Og. Efficacy and tolerability of oral propafenone vs quinidine in treatemnt of new-onset of atrial fibrillation: a randomized, double-blind controlled study. Kardiologia polska 2002;57(Suppl. II):II-240.

Koster 2004 {published data only}

studyIdentifiers

* Koster, R W, Dorian, P, Chapman, F W, Schmitt, P W, O'Grady, S G, Walker, R G. A randomized trial comparing monophasic and biphasic waveform shocks for external cardioversion of atrial fibrillation. Am Heart J 2004;147(5):e20.

Kühlkamp 1991 {published data only}

studyIdentifiers

Kuhlkamp, V, Schmid, F, Risler, T, Seipel, L. Randomized comparison of flecainide and cibenzoline in the conversion of atrial fibrillation. Int J Cardiol 1991;31(1):65-9.

Kumagai 2000 {published data only}

studyIdentifiers

Kumagai, K, Abe, H, Hiraki, T, Nakashima, H, Oginosawa, Y, Ikeda, et al. Single oral administration of pilsicainide versus infusion of disopyramide for termination of paroxysmal atrial fibrillation: a multicenter trial. Pacing Clin Electrophysiol 2000;23(11 Pt 2):1880-2. [DOI: 10.1111/j.1540-8159.2000.tb07043.x]

Lindeboom 2000 {published data only}

studyIdentifiers

Lindeboom, J E, Kingma, J H, Crijns, H J, Dunselman, P H. Efficacy and safety of intravenous dofetilide for rapid termination of atrial fibrillation and atrial flutter. Am J Cardiol 2000;85(8):1031-3.

Maciag 2017 {published data only}

studyIdentifiers

Farkowski, M, Maciag, A, Chwyczko, T, Beckowski, M, Syska, P, Kowalik, et al. Clinical efficacy of antazoline in rapid cardioversion of paroxysmal atrial fibrillation: A single centre, randomized, double blind, placebo controlled study. . In: European Heart Journal. Vol. Suppl 1. 2015:906. 19330748]

Maciag, A, Farkowski, M M, Chwyczko, T, Beckowski, M, Syska, P, Kowalik, et al. Efficacy and safety of antazoline in the rapid cardioversion of paroxysmal atrial fibrillation (the AnPAF Study). Europace 2017;19(10):1637-42.

Madrid 1993 {published data only}

studyIdentifiers

Madrid, A H, Moro, C, Marin-Huerta, E, Mestre, J L, Novo, L, Costa, A. Comparison of flecainide and procainamide in cardioversion of atrial fibrillation. Eur Heart J 1993;14(8):1127-31.

Madrid, Moro, Costa, Lloret, Marfn, H, Novo, Mestre, L. Flecainide versus procainamide in the treatment of paroxystic atrial fibrillation.. Revista espanola de cardiologia 1992 ;45(Suppl 1):43.

Manegold 2007 {published data only}

studyIdentifiers

Manegold, J C, Israel, C W, Ehrlich, J R, Duray, G, Pajitnev, D, Wegener, F T, Hohnloser, S H. External cardioversion of atrial fibrillation in patients with implanted pacemaker or cardioverter-defibrillator systems: a randomized comparison of monophasic and biphasic shock energy application. Eur Heart J 2007;28(14):1731-8.

Martínez-Marcos 2000 {published data only}

studyIdentifiers

* Martinez-Marcos, F J, Garcia-Garmendia, J L, Ortega-Carpio, A, Fernandez-Gomez, J M, Santos, J M, Camacho, C. Comparison of intravenous flecainide, propafenone, and amiodarone for conversion of acute atrial fibrillation to sinus rhythm. Am J Cardiol 2000;86(9):950-3.

Mattioli 1998 {published data only}

studyIdentifiers

Mattioli, A V, Lucchi, G R, Vivoli, D, Mattioli, G. Propafenone versus procainamide for conversion of atrial fibrillation to sinus rhythm. Clin Cardiol 1998;21(10):763-6.

Mittal 2000 {published data only}

studyIdentifiers

* Mittal, S, Ayati, S, Stein, K M, Schwartzman, D, Cavlovich, D, Tchou, P J, Markowitz, S M, Slotwiner, D J, Scheiner, M A, Lerman, B B. Transthoracic cardioversion of atrial fibrillation: comparison of rectilinear biphasic versus damped sine wave monophasic shocks. Circulation 2000;101(11):1282-7.

Mortensen 2007 {published data only}

studyIdentifiers

* Mortensen K, Risius T, Schwemer TF, Aydin MA, Köster R, Klemm HU, Lutomsky B, Meinertz T, Ventura R, Willems S. Biphasic versus monophasic shock for external cardioversion of atrial flutter: a prospective, randomized trial. Cardiology 2008;111:57-62.

Risius, T, Mortensen, K, Schwerner, T, Aydin, M A, Henne, S, Koster, et al. Atrial flutter: Is biphasic superior to monophasic external cardioversion? A randomized comparison. J. Am. Coll. Cardiol. 2005;45(3):222A.

Muñoz-Martínez 2010 {published data only}

studyIdentifiers

Munoz-Martinez, T, Castaneda-Saiz, A, Vinuesa-Lozano, C, Aretxabala-Kortajarena, N, Dudagoitia-Otaolea, J L, Iribarren-Diarasarri, S, Ruiz-Zorrilla, J M, Hernandez-Lopez, M, Castillo-Arenal, C. [Electrode position in elective electrical cardioversion of atrial fibrillation. A randomized study]. Med 2010;34(4):225-30. [DOI: https://dx.doi.org/10.1016/j.medin.2009.10.004]

Negrini 1994 {published data only}

studyIdentifiers

Negrini, M, Gibelli, G, De Ponti, C. A comparison of propafenone and amiodarone in reversion of recent-onset atrial fibrillation to sinus rhythm. Current Therapeutic Research - Clinical and Experimental 1994;55(11):1345-54.

Neumann 2004 {published data only}

studyIdentifiers

* Neumann, T, Erdogan, A, Reiner, C, Siemon, G, Kurzidim, K, Berkowitsch, A, Kuniss, M, Sperzel, J, Hamm, C W, Pitschner, H F. [Ambulatory electrocardioversion of atrial fibrillation by means of biphasic versus monophasic shock delivery. A prospective randomized study]. Z Kardiol 2004;93(5):381-7.

Noc 1990 {published data only}

studyIdentifiers

Noc, M, Stajer, D, Horvat, M. Intravenous amiodarone versus verapamil for acute conversion of paroxysmal atrial fibrillation to sinus rhythm. Am J Cardiol 1990;65(9):679-80.

Nogic 2022 {published data only}

studyIdentifiers

* Nogic, J, MacPherson, M, Aldrige, E, Sajeev, JK, Roberts, L, Lowman, D, Sze, S, Kwong, A, Buntine, P, Teh, AW. Magnesium in the Management of Atrial Fibrillation With Rapid Ventricular Response. JACC: Clinical Electrophysiology 2022.

Norgaard 1999 {published data only}

studyIdentifiers

* Norgaard, B L, Wachtell, K, Christensen, P D, Madsen, B, Johansen, J B, Christiansen, E H, Graff, O, Simonsen, E H. Efficacy and safety of intravenously administered dofetilide in acute termination of atrial fibrillation and flutter: a multicenter, randomized, double-blind, placebo-controlled trial. Danish Dofetilide in Atrial Fibrillation and Flutter Study Group. Am Heart J 1999;137(6):1062-9.

Okishige 2000 {published data only}

studyIdentifiers

Okishige, K, Nishizaki, M, Azegami, K, Igawa, M, Yamawaki, N, Aonuma, et al. Pilsicainide for conversion and maintenance of sinus rhythm in chronic atrial fibrillation: a placebo-controlled, multicenter study. Am Heart J 2000;140(3):e13.

Okishige 2006 {published data only}

studyIdentifiers

Okishige, K, Fukunami, M, Kumagai, K, Atarashi, H, Inoue, H, Pilsicainide Suppression Trial for Persistent Atrial Fibrillation, et al. Pharmacological conversion of persistent atrial fibrillation into sinus rhythm with oral pilsicainide: pilsicainide suppression trial for persistent atrial fibrillation II. Circ J 2006;70(6):657-61.

Page 2002 {published data only}

studyIdentifiers

* Page, R L, Kerber, R E, Russell, J K, Trouton, T, Waktare, J, Gallik, D, Olgin, J E, Ricard, P, Dalzell, G W, Reddy, R, Lazzara, R, Lee, K, Carlson, M, Halperin, B, Bardy, G H, BiCard, Investigators. Biphasic versus monophasic shock waveform for conversion of atrial fibrillation: the results of an international randomized, double-blind multicenter trial. J Am Coll Cardiol 2002;39(12):1956-63.

Pratt 2010 {published data only}

studyIdentifiers

* Pratt, C M, Roy, D, Torp-Pedersen, C, Wyse, D G, Toft, E, Juul-Moller, S, Retyk, E, Drenning, D H, Atrial Arrhythmia Conversion Trial, Investigators. Usefulness of vernakalant hydrochloride injection for rapid conversion of atrial fibrillation. Am J Cardiol 2010;106(9):1277-83. [DOI: https://dx.doi.org/10.1016/j.amjcard.2010.06.054]

Rajagopalan 2014 {published data only}

studyIdentifiers

* Bharath Rajagopalan, Zubair Shah, Deepika Narasimha, Ashish Bhatia, Chee H Kim, Donald F Switzer, Gregory H Gudleski, Anne B Curtis. Efficacy of Intravenous Magnesium in Facilitating Cardioversion of Atrial Fibrillation. Circ Arrhythm Electrophysiol. 2016;9:e003968.

Rajagopalan, B, Narasimha, D, Bhatia, A, Kim, C H, Switzer, D F, Curtis, A B. Efficacy of intravenous magnesium for cardioversion of atrial fibrillation. Circulation. Conference: American Heart Association's 2014;130:SUPPL. 2.

Reisinger 1998 {published data only}

studyIdentifiers

* Reisinger, J, Gatterer, E, Heinze, G, Wiesinger, K, Zeindlhofer, E, Gattermeier, M, Poelzl, G, Kratzer, H, Ebner, A, Hohenwallner, W, Lenz, K, Slany, J, Kuhn, P. Prospective comparison of flecainide versus sotalol for immediate cardioversion of atrial fibrillation. Am J Cardiol 1998;81(12):1450-4.

Reisinger, J, Gatterer, E, Slany, K, P. Comparison between Flecainid and Sotalol in the conversion treatment of atrial fibrillation. Zeitschrift fur kardiologie 1998;87(5):390.

Reisinger 2004 {published data only}

studyIdentifiers

* Reisinger, J, Gatterer, E, Lang, W, Vanicek, T, Eisserer, G, Bachleitner, T, Niemeth, C, Aicher, F, Grander, W, Heinze, G, Kuhn, P, Siostrzonek, P. Flecainide versus ibutilide for immediate cardioversion of atrial fibrillation of recent onset. Eur Heart J 2004;25(15):1318-24.

Ricard 2001 {published data only}

studyIdentifiers

* Ricard, P, Levy, S, Boccara, G, Lakhal, E, Bardy, G. External cardioversion of atrial fibrillation: comparison of biphasic vs monophasic waveform shocks. Europace 2001;3(2):96-9.

Risius 2009 {published data only}

studyIdentifiers

* Tim Risius, Kai Mortensen, Tjark F Schwemer, Muhammet A Aydin, Hanno U Klemm, Rodolfo Ventura, Achim Barmeyer, Boris Hoffmann, Thomas Rostock, Thomas Meinertz, Stephan Willems. Comparison of antero-lateral versus antero-posterior electrode position for biphasic external cardioversion of atrial flutter. Am J Cardiol 2009;104:1547-50.

Romano 2001 {published data only}

studyIdentifiers

Romano, S, Fattore, L, Toscano, G, Corsini, F, Coppo, A, Catanzaro, et al. Intravenous treatment with propafenone and flecainide in recent-onset atrial fibrillation. Italian Heart Journal Supplement 2001;2(1):41-5.

Romano, S, Fattore, L, Toscano, G, Corsini, F, Coppo, A, Catanzaro, et al. [Effectiveness and side effects of the treatment with propafenone and flecainide for recent-onset atrial fibrillation]. Ital 2001;2(1):41-5.

Romano, Toscano, S. Propafenone and e.v. flecainide in paroxysmal atrial fibrillation. Giornale italiano di cardiologia 1997;27(Suppl 1):58.

Romano, Toscano, S. Propafenone or flecainide e.v. in atrial paroxistic fibrillation. Giornale italiano di cardiologia 1995;25(Suppl 1):445.

Roy 2004 {published data only}

studyIdentifiers

Harris, S, Tepper, D, Ip, R. Vernakalant hydrochloride for rapid conversion of atrial fibrillation: A phase 3, randomized, placebo-controlled trial. Congestive Heart Failure 2013;14:4.

* Roy, D, Rowe, BH, Stiell, IG, Coutu, B, Ip, JH, Phaneuf, D, Lee, J, Vidaillet, H, Dickinson, G, Grant, S, Ezrin, AM, Beatch, GN, . A Randomized, Controlled Trial of RSD1235, a Novel Anti-Arrhythmic Agent, in the Treatment of Recent Onset Atrial Fibrillation. JACC 2004;44:2355-2361.

Roy 2008 {published data only}

studyIdentifiers

* Roy, D, Pratt, C M, Torp-Pedersen, C, Wyse, D G, Toft, E, Juul-Moller, S, Nielsen, T, Rasmussen, S L, Stiell, I G, Coutu, B, Ip, J H, Pritchett, E L, Camm, A J, Atrial Arrhythmia Conversion Trial, Investigators. Vernakalant hydrochloride for rapid conversion of atrial fibrillation: a phase 3, randomized, placebo-controlled trial. Circulation 2008;117(12):1518-25. [DOI: https://dx.doi.org/10.1161/CIRCULATIONAHA.107.723866]

Satullo 1996a {published data only}

studyIdentifiers

Satullo, G, Arrigo, F, Cavallaro, L, Coglitore, A, Fazio, F, Saporito, et al. [A comparison between propafenone and hydroquinidine perorally in the treatment of recent-onset atrial fibrillation]. Minerva Cardioangiol 1996;44(3):141-4.

Scheuermeyer 2019 {published data only}

studyIdentifiers

Scheuermeyer, FX, Andolfatto, G, Christenson, J, Couperthwaite, S, Villa-Roel, C, Lobay, K, Rowe, BH. LO100: Electrical vs chemical cardioversion in patients with acute atrial fibrillation: A multicenter parallel group randomized controlled clinical trial.. In: CEJM. 2016:S64 - S65.

Scheuermeyer, FX, Andolfatto, G, Christenson, J, Couperthwaite, S, Villa-Roel, C, Lobay, K, Rowe, BH. LO100: Electrical vs chemical cardioversion in patients with acute atrial fibrillation: A multicenter parallel group randomized controlled clinical trial.. In: CJEM. 2016:S64 - S65.

* Scheuermeyer, Frank X, Andolfatto, Gary, Christenson, Jim, Villa-Roel, Cristina, Rowe, Brian. A Multicenter Randomized Trial to Evaluate a Chemical-first or Electrical-first Cardioversion Strategy for Patients With Uncomplicated Acute Atrial Fibrillation. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine 2019;26(9):969-981. [DOI: https://dx.doi.org/10.1111/acem.13669]

Schmidt 2017 {published data only}

studyIdentifiers

* Schmidt, A S, Lauridsen, K G, Adelborg, K, Torp, P, Bach, L F, Jepsen, S M, Hornung, N, Deakin, C D, Rickers, H, Lofgren, B. Cardioversion Efficacy Using Pulsed Biphasic or Biphasic Truncated Exponential Waveforms: A Randomized Clinical Trial. J Am Heart Assoc 2017;6(3):08. [DOI: https://dx.doi.org/10.1161/JAHA.116.004853]

Schmidt 2019 {published data only}

studyIdentifiers

* Schmidt, A, Lauridsen, K, Torp, P, , Bach, L, Rickers, H, Løfgren, B. Comparison of High Versus Escalating Shocks in Cardioverting Atrial Fibrillation. Eur H J 2019;41(5):626-631. [DOI: 10.1093/eurheartj/ehz627]

Schmidt 2021 {published data only}

studyIdentifiers

* Schmidt, AS, Lauridsen, KG, Møller, DS, Christensen, PD, Dodt, KK, Rickers, H, Løfgren, B, Albertsen, AE. Anterior–Lateral Versus Anterior–Posterior Electrode Position for Cardioverting Atrial Fibrillation. Circulation 2021;144:1995-2003.

Siaplaouras 2004 {published data only}

studyIdentifiers

* Siaplaouras, S, Buob, A, Rötter, C, Böhm, M, Jung, J. Impact of Biphasic Electrical Cardioversion of Atrial Fibrillation on Early Recurrent Atrial Fibrillation and Shock Efficacy. J Cardiovasc Electrophysiol 2004;15:895-897. [DOI: 10.1046/j.1540-8167.2004.04027.x]

Siaplaouras 2005 {published data only}

studyIdentifiers

* Siaplaouras, S, Buob, A, Rötter, C, Böhm, M, Jung, J. Randomized comparison of anterolateral versus anteroposterior electrode position for biphasic external cardioversion of atrial fibrillation. Am Heart J 2005;150:150 - 152.

Simon 2017 {published data only}

studyIdentifiers

* Simon, A, Niederdoeckl, J, Skyllouriotis, E, Schuetz, N, Herkner, H, Weiser, C, Laggner, A N, Domanovits, H, Spiel, A O. Vernakalant is superior to ibutilide for achieving sinus rhythm in patients with recent-onset atrial fibrillation: a randomized controlled trial at the emergency department. Europace 2017;19(2):233-240. [DOI: https://dx.doi.org/10.1093/europace/euw052]

Simon, A, Niederdockl, J, Skyllouriotis, E, Schutz, N, Weiser, C, Herkner, et al. Vernakalant shows superiority to ibutilide in recent-onset atrial fibrillation: A randomized controlled trial at the emergency department. Circulation. Conference: American Heart Association's 2015;SUPPL. 3:132.

Singh 2000 {published data only}

studyIdentifiers

Singh, S, Zoble, R G, Yellen, L, Brodsky, M A, Feld, G K, Berk, M, Billing, C B Jr. Efficacy and safety of oral dofetilide in converting to and maintaining sinus rhythm in patients with chronic atrial fibrillation or atrial flutter: the symptomatic atrial fibrillation investigative research on dofetilide (SAFIRE-D) study. Circulation 2000;102(19):2385-90.

Singh 2005 {published data only}

studyIdentifiers

* Singh BN, Singh SN, Reda DJ, Tang XC, Lopez B, Harris CL, Fletcher RD, Sharma SC, Atwood JE, Jacobson AK, Lewis HD Jr, Raisch DW, Ezekowitz MD, Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T) Investigators. Amiodarone versus Sotalol for Atrial Fibrillation. N Engl J Med May 5, 2005;352:1861-1872. [DOI: 10.1056/NEJMoa041705.] [PMID: 15872201]

Singh, B N, Singh, S N, Reda, D J, Tang, C X, Lopez, B, Fye, C L, Fletcher, R D, Sharma, S C, Atwood, E J, Jacobson, A, Lewis, D, Ezekowitz, M. Efficacy of sotalol, amiodarone and placebo for cardioversion and maintenance of sinus rhythm in patients with atrial fibrillation: A veterans administration cooperative study. Circulation 2003;108(17):508-508.

Singh, S N, Tang, X C, Reda, D, Singh, B N . Systematic electrocardioversion for atrial fibrillation and role of antiarrhythmic drugs: a substudy of the SAFE-T trial.. Heart Rhythm 2009;6(2):152-5.

Steven N Singh, Bramah N Singh, Domenic J Reda, Carol L Fye, Michael D Ezekowitz, Ross D Fletcher, Satish C Sharma, J Edwin Atwood, Alan K Jacobson, H Daniel Lewis Jr, Eliott M Antman, Rodney H Falk, Becky Lopez, X Charlene Tang. Comparison of sotalol versus amiodarone in maintaining stability of sinus rhythm in patients with atrial fibrillation (Sotalol-Amiodarone Fibrillation Efficacy Trial [Safe-T]). Am J Cardiol August 15, 2003;92(4):468-72. [DOI: 10.1016/s0002-9149(03)00671-4] [PMID: 12914883]

Squara 2021 {published data only}

studyIdentifiers

* Squara, F, Elbaum, C, Garret, G, Liprandi, L, Scarlatti, D, Bun, S, Mossaz, B, Rocher, M, Bateau, J, Moceri, P, Ferrari, E. Active compression versus standard anterior-posterior defibrillation for external cardioversion of atrial fibrillation: A prospective randomized study. Heart Rhythm 2021;18:360 -365.

Stambler 1996 {published data only}

studyIdentifiers

Stambler, B S, Wood, M A, Ellenbogen, K A, Perry, K T, Wakefield, L K, VanderLugt, et al. Efficacy and safety of repeated intravenous doses of ibutilide for rapid conversion of atrial flutter or fibrillation. Ibutilide Repeat Dose Study Investigators. Circulation 1996;94(7):1613-21.

Stanaitienė 2008 {published data only}

studyIdentifiers

Stanaitiene, G . Low energy electrical cardioversion of atrial fibrillation.. Cardiology 2009;1:67. [DOI: dx.doi.org/10.1159/000223370]

Stanaitiene, G, Babarskiene, R M. [Impact of electrical shock waveform and paddle positions on efficacy of direct current cardioversion for atrial fibrillation]. Medicina (Kaunas) 2008;44(9):665-72.

Stroobandt 1997 {published data only}

studyIdentifiers

Stroobandt, R, Stiels, B, Hoebrechts, R. Propafenone for conversion and prophylaxis of atrial fibrillation. Propafenone Atrial Fibrillation Trial Investigators. Am J Cardiol 1997;79(4):418-23.

Sun 2005 {published data only}

studyIdentifiers

* Sun, J L, Guo, J H, Zhang, N, Zhang, H C, Zhang, P. Clinical comparison of ibutilide and propafenone for converting atrial flutter. Cardiovasc Drugs Ther 2005;19(1):57-64.

Suttorp 1989 {published data only}

studyIdentifiers

Suttorp, M J, Kingma, J H, Lie, A Huen L, Mast, E G. Intravenous flecainide versus verapamil for acute conversion of paroxysmal atrial fibrillation or flutter to sinus rhythm. Am J Cardiol 1989;63(11):693-6.

Suttorp 1990 {published data only}

studyIdentifiers

Suttorp, M J, Kingma, J H, Jessurun, E R, Lie, A Huen L, van Hemel, N M, Lie, et al. The value of class IC antiarrhythmic drugs for acute conversion of paroxysmal atrial fibrillation or flutter to sinus rhythm. J Am Coll Cardiol 1990;16(7):1722-7.

Taha 2022 {published data only}

studyIdentifiers

Taha HS, Youssef G, Omar RM, Kamal El Din AM, Shams El Din AA, Meshaal MS . Efcacy and speed of conversion of recent onset atrial fbrillation using oral propafenone versus parenteral amiodarone: a randomized controlled comparative study. Indian Heart J. 2022;74(3):212–217 . [DOI: 10.1016/j.ihj.2022.04.006]

* Taha, H S, Youssef, G, Omar, R M, Kamal El Din, A M, Shams El Din, A A, Meshaal, M S. Efficacy and speed of conversion of recent onset atrial fibrillation using oral propafenone versus parenteral amiodarone: A randomized controlled comparative study. Indian Heart Journal 2022;17(4):121-217.

Thomas 2004 {published data only}

studyIdentifiers

Thomas, S P, Guy, D, Wallace, E, Crampton, R, Kijvanit, P, Eipper, V, Ross, D L, Cooper, M J. Rapid loading of sotalol or amiodarone for management of recent onset symptomatic atrial fibrillation: a randomized, digoxin-controlled trial. Am Heart J 2004;147(1):E3.

Treglia 1994a {published data only}

studyIdentifiers

Treglia, A, Alfano, C, Rossini, E. [A comparison between propafenone and amiodarone in the conversion to sinus rhythm of atrial fibrillation of recent onset]. Minerva Cardioangiol 1994;42(6):293-7.

Trendafilova 2021 {published data only}

studyIdentifiers

* Trendafilova, E, Dimitrova, E, Didon, J P, Krasteva, V. A randomized comparison of delivered energy in cardioversion of atrial fibrillation: biphasic truncated exponential versus pulsed biphasic waveforms. Diagnostics 2021;11:1107.

Vardas 2000 {published data only}

studyIdentifiers

* Vardas, P E, Kochiadakis, G E, Igoumenidis, N E, Tsatsakis, A M, Simantirakis, E N, Chlouverakis, G I. Amiodarone as a first-choice drug for restoring sinus rhythm in patients with atrial fibrillation: a

randomized, controlled study. Chest 2000;117(6):1538-45.

Vijayalakshmi 2006 {published data only}

studyIdentifiers

Vijayalakshmi, K, Whittaker, V J, Sutton, A, Campbell, P, Wright, R A, Hall, J A, Harcombe, A A, Linker, N J, Stewart, M J, Davies, A, de Belder, M A. A randomized trial of prophylactic antiarrhythmic agents (amiodarone and sotalol) in patients with atrial fibrillation for whom direct current cardioversion is planned. Am Heart J 2006;151(4):863.e1-6.

Vijayalakshmi, K, Sutton, A G C, Campbell, P, Davies, A, Stewart, M J, Linker, et al. Randomised trial of two anti-arrhythmic agents (amiodarone and sotalol) in patients with atrial fibrillation for whom DC cardioversion is planned. Heart 2003;89:A40.

Vogiatzis 2009 {published data only}

studyIdentifiers

* Vogiatzis, I A, Sachpekidis, V, Vogiatzis, I M, Kambitsi, E, Karamitsos, T, Samanidis, D, Tsagaris, V, Simeonidou, O. External cardioversion of atrial fibrillation: the role of electrode position on cardioversion success. Int J Cardiol 2009;137(1):e8-10. [DOI: https://dx.doi.org/10.1016/j.ijcard.2008.05.038]

Vogziatis 2017 {published data only}

studyIdentifiers

* Vogiatzis, I, Papavasiliou, E, Dapcevitch, I, Pittas, S, Koulouris, E, . Vernakalant versus ibutilide for immediate conversion of recent-onset atrial fibrillation. Hippokratia 2017;21:67-73.

Volgman 1998 {published data only}

studyIdentifiers

Volgman, A S, Carberry, P A, Stambler, B, Lewis, W R, Dunn, G H, Perry, K T, Vanderlugt, J T, Kowey, P R. Conversion efficacy and safety of intravenous ibutilide compared with intravenous procainamide in patients with atrial flutter or fibrillation. J Am Coll Cardiol 1998;31(6):1414-9.

Vos 1998 {published data only}

studyIdentifiers

Vos, M A, Golitsyn, S R, Stangl, K, Ruda, M Y, Van Wijk, L V, Harry, et al. Superiority of ibutilide (a new class III agent) over DL-sotalol in converting atrial flutter and atrial fibrillation. The Ibutilide/Sotalol Comparator Study Group. Heart 1998;79(6):568-75.

Voskoboinik 2018 {published data only}

studyIdentifiers

* Voskoboinik A, Moskovitch J, Plunkett G, Bloom J, Wong G, Nalliah C, Prabhu S, Sugumar H, Paramasweran R, McLellan A, Ling LH, Goh CY, Noaman S, Fernando H, Wong M, Taylor AJ, Kalman JM, Kistler PM. Cardioversion of atrial fibrillation in obese patients: Results from the Cardioversion-BMI randomized controlled trial. J Cardiovasc Electrophysiol 2019;30:155-161.

Voskoboinik, A, Moskovitch, J, Bloom, J, Nalliah, C J, Prabhu, S, Wong, G, Sugumar, H, Wong, M, McLellan, A J A, Ling, L H, Plunkett, G, Kalman, J M, Kistler, P M. Hand-held paddles more effective than adhesive patches for cardioversion of atrial fibrillation in obese patients: Results from the dcr-bmi multicenter randomized controlled trial. Heart Rhythm 2018;15 (5 Supplement 1):S261-S262.

Walsh 2005 {published data only}

studyIdentifiers

* Walsh, S J, McCarty, D, McClelland, A J, Owens, C G, Trouton, T G, Harbinson, M T, O'Mullan, S, McAllister, A, McClements, B M, Stevenson, M, Dalzell, G W, Adgey, A A. Impedance compensated biphasic waveforms for transthoracic cardioversion of atrial fibrillation: a multi-centre comparison of antero-apical and antero-posterior pad positions. Eur Heart J 2005;26(13):1298-302.

Xanthos 2007 {published data only}

studyIdentifiers

* Xanthos, T, Prapa, V, Papadimitriou, D, Papadimitriou, L. Comparative study of intravenous amiodarone and procainamide in the treatment of atrial fibrillation of recent onset. Minerva Cardioangiol 2007;55(4):433-41.

Yamase 2012 {published data only}

studyIdentifiers

Yamase, M, Nakazato, Y, Enjyoji, Y. Convertion to sinus rhythm: Efficacy of amiodarone vs bepridil for persistent atrial fibrillation.. Journal of Interventional Cardiac Electrophysiology 2012;33(3):331.. [DOI: dx.doi.org/10.1007/s10840-012-9674-5]

Yamase, M, Nakazato, Y, Daida, H. Effectiveness of amiodarone versus bepridil in achieving conversion to sinus rhythm in patients with persistent atrial fibrillation: a randomised trial. Heart 2012;98(14):1067-71.

Yamashita 2009 {published data only}

studyIdentifiers

Yamashita, T, Ogawa, S, Sato, T, Aizawa, Y, Atarashi, H, Fujiki, A, Inoue, H, Ito, M, Katoh, T, Kobayashi, Y, Koretsune, Y, Kumagai, K, Niwano, S, Okazaki, O, Okumura, K, Saku, K, Tanabe, T, Origasa, H, Investigators, J Baf. Dose-response effects of bepridil in patients with persistent atrial fibrillation monitored with transtelephonic electrocardiograms: a multicenter, randomized, placebo-controlled,double-blind study (J-BAF Study). Circ J 2009;73(6):1020-7.

Yu 2013 {published data only}

studyIdentifiers

* Yu, Z, Xiang, M, Ma, C, Zhang, S, Yang, Y. [Efficacy and safety of ibutilide for conversion of atrial fibrillation/flutter]. Zhejiang Da Xue Xue Bao Yi Xue Ban 2013;42(2):212-6.

Zehender 1994 {published data only}

studyIdentifiers

Zehender, M, Meinertz, T, Just, H. Amiodaron and verapamil/chinidin in the treatment of patients with chronic atrial fibrillation. [German]. Zeitschrift fur Kardiologie 1994;83(SUPPL. 5):101-8.

Zhang 2005 {published data only}

studyIdentifiers

* Zhang, H C, Guo, J H, Fang, Q, Zheng, Y A, Sun, Y M, Zhu, W Q, Wan, Z, Guo, J X, Ge, J B, Han, S M. [Immediate cardioversion of atrial fibrillation and atrial flutter lasting less than 90 days by ibutilide versus propafenone: a multicenter study]. Chung Hua I Hsueh Tsa Chih 2005;85(12):798-801.

References to studies excluded from this review

Aizawa 2010 {published data only}

studyIdentifiers

Aizawa, Y, Kohsaka, S, Suzuki, S, Atarashi, H, Kamakura, S, Sakurai, et al. Comparison of antiarrhythmics used in patients with paroxysmal atrial fibrillation: Subanalysis of J-RHYTHM study. Circulation Journal 2010;74(1):71-6.

Akel 2018 {published data only}

studyIdentifiers

Akel, T, Lafferty, J. Efficacy and safety of intravenous vernakalant for the rapid conversion of recent-onset atrial fibrillation: A meta-analysis. Ann Noninvasive Electrocardiol 2018;23(3):e12508.

Alboni 2004 {published data only}

studyIdentifiers

Alboni, P, Botto, G L, Baldi, N, Luzi, M, Russo, V, Gianfranchi, et al. Outpatient treatment of recent-onset atrial fibrillation with the "pill-in-the-pocket" approach. N Engl J Med 2004;351(23):2384-91.

Alpert 2000 {published data only}

studyIdentifiers

Alpert, M A. Medical cardioversion of atrial fibrillation. Chest 2000;117(6):1529-31.

Benhalla 2015 {published data only}

studyIdentifiers

Benhalla, H, Fennich, N. What about magnesium sulfate in atrial fibrillation with acute heart failure? European Journal of Heart Failure 2015;1):400.

Borgeat 1986 {published data only}

studyIdentifiers

Borgeat, A, Goy, J J, Maendly, R, Kaufmann, U, Grbic, M, Sigwart, et al. Flecainide versus quinidine for conversion of atrial fibrillation to sinus rhythm. Am J Cardiol 1986;58(6):496-8.

Boriani 1998 {published data only}

studyIdentifiers

Boriani, G, Biffi, M, Capucci, A, Botto, G, Broffoni, T, Ongari, et al. Conversion of recent-onset atrial fibrillation to sinus rhythm: effects of different drug protocols. Pacing Clin Electrophysiol 1998;21(11 Pt 2):2470-4.

Botto 1996 {published data only}

studyIdentifiers

Botto, G L, Bonini, W, Broffoni, T, Molteni, S, Lombardi, R, Alfieri, et al. Conversion of recent onset atrial fibrillation with single loading oral dose of propafenone: is in-hospital admission absolutely necessary? Pacing Clin Electrophysiol 1996;19(11 Pt 2):1939-43.

Camm 2022 {published data only}

studyIdentifiers

* Camm, A J, Crijns, H, Elvan, A, Tuininga, Y, Badings, E, Kuijper, A, de Jong, J, Lee, M, Schellings, D, Van Gelder, I C, Ruskin, J N, Kowey, P R, Dufton, C, Maupas, J, Belardinelli, L. Orally Inhaled Flecainide for the Conversion of Recent-Onset, Symptomatic Atrial Fibrillation to Sinus Rhythm: Final Results From the Phase 2 Instant Trial. In: Circulation. Vol. 146. 2022:A12420. [DOI: https://doi.org/10.1161/circ.146.suppl_1.12420]

Conde 2013 {published data only}

studyIdentifiers

Aragon, M, Conde, D, Costabel, J P, Lambardi, M F, Trivi, M, Giniger, et al. Comparing the efficacy, hospitalization time and safety of vernakalant to propafenone in recent-onset atrial fibrillation in the emergency department. . Europace 2013;2(Suppl):ii16.

Conde, D, Costabel, J P, Aragon, M, Lambardi, F, Klein, A, Corrales Barbosa, et al. Propafenone versus vernakalant for conversion of recent-onset atrial fibrillation. Cardiovasc Ther 2013;31(6):377-80.

Crijns 1994 {published data only}

studyIdentifiers

Crijns, H J, Van Gelder, I C, Kingma, J H, Dunselman, P H, Gosselink, A T, Lie, et al. Atrial flutter can be terminated by a class III antiarrhythmic drug but not by a class IC drug. Eur Heart J 1994;15(10):1403-8.

CTRI/2018/01/011248 2018 {published data only}

studyIdentifiers

* CTRI/2018/01/011248. An Open-Label, Multicentre, Prospective, Phase- IV Study to Evaluate the Efficacy and Safety of Ibutilide Fumarate Injection (0.1mg/ml) in the Treatment of Atrial Fibrillation and Flutter - IBUTILIDE PHASE IV. https://www.ctri.nic.in/Clinicaltrials/showallp.php?mid1=20124&EncHid=&userName=CTRI/2018/01/011248 2018.

Dankner 2009 {published data only}

studyIdentifiers

Dankner, R, Shahar, A, Novikov, I, Agmon, U, Ziv, A, Hod, et al. Treatment of stable atrial fibrillation in the emergency department: a population-based comparison of electrical direct-current versus pharmacological cardioversion or conservative management. Cardiology 2009;112(4):270-8.

Deedwania 1998 {published data only}

studyIdentifiers

Deedwania, P C, Singh, B N, Ellenbogen, K, Fisher, S, Fletcher, R, Singh, S N. Spontaneous conversion and maintenance of sinus rhythm by amiodarone in patients with heart failure and atrial fibrillation: observations from the veterans affairs congestive heart failure survival trial of antiarrhythmic therapy (CHF-STAT). The Department of Veterans Affairs CHF-STAT Investigators. Circulation 1998;98(23):2574-9.

Dittrich 2015 {published data only}

studyIdentifiers

Dittrich, H C, Feld, G K, Bahnson, T D, Camm, A J, Golitsyn, S, Katz, et al. COR-ART: A multicenter, randomized, double-blind, placebo-controlled dose-ranging study to evaluate single oral doses of vanoxerine for conversion of recent-onset atrial fibrillation or flutter to normal sinus rhythm. Heart Rhythm 2015;12(6):1105-12.

Dluzniewski 1994 {published data only}

studyIdentifiers

Dluzniewski, M, Krol, J, Kuch, M, Syska-Suminska, J, Cedro, K. Increased efficacy of ajmaline after magnesium administration in the treatment of paroxysmal supraventricular tachyarrhythmias. [Polish]. Kardiologia Polska 1994;41(9):201-6.

Donovan 1991 {published data only}

studyIdentifiers

Donovan, K D, Dobb, G J, Coombs, L J, Lee, K Y, Weekes, J N, Murdock, et al. Reversion of recent-onset atrial fibrillation to sinus rhythm by intravenous flecainide. Am J Cardiol 1991;67(2):137-41.
Donovan, K D, Dobb, G J, Coombs, L J, Lee, K Y, Weekes, J N, Murdock, et al. Efficacy of flecainide for the reversion of acute onset atrial fibrillation. . Am J Cardiol 1992;70(5):50A-54A; discussion 54A-55A.. [DOI: 10.1016/0002-9149(92)91078-i]

Donovan 1995 {published data only}

studyIdentifiers

Donovan, K D, Power, B M, Hockings, B E, Dobb, G J, Lee, K Y. Intravenous flecainide versus amiodarone for recent-onset atrial fibrillation. Am J Cardiol 1995;75(10):693-7.

Forney 2000 {published data only}

studyIdentifiers

Forney, A J, Schooff, M. Is either sotalol or amiodarone more effective than digoxin for converting patients with new-onset atrial fibrillation (AF) to sinus rhythm within 48 hours? J Fam Pract 2000;49(11):982.

Galve 1996 {published data only}

studyIdentifiers

Galve, E, Rius, T, Ballester, R, Artaza, M A, Arnau, J M, Garcia-Dorado, et al. Intravenous amiodarone in treatment of recent-onset atrial fibrillation: results of a randomized, controlled study. J Am Coll Cardiol 1996;27(5):1079-82.

Gullestad 1993 {published data only}

studyIdentifiers

Gullestad, L, Birkeland, K, Molstad, P, Hoyer, M M, Vanberg, P, Kjekshus, et al. The effect of magnesium versus verapamil on supraventricular arrhythmias. Clin Cardiol 1993;16(5):429-34.

Guo 1996 {published data only}

studyIdentifiers

Guo, G B, Ellenbogen, K A, Wood, M A, Stambler, B S. Conversion of atrial flutter by ibutilide is associated with increased atrial cycle length variability. J Am Coll Cardiol 1996;27(5):1083-9.

Hermida 1995 {published data only}

studyIdentifiers

Hermida, J S, Mabo, P, Rouesnel, P, Scheck, F, Canler, A, Barthelemy, et al. [Comparative study of the efficacy and tolerability of 2 modalities of intravenous cibenzoline administration in the reduction of recent spontaneous atrial arrhythmia]. Ann Cardiol Angeiol (Paris) 1995;44(1):49-55.

Hohnloser 2004 {published data only}

studyIdentifiers

Hohnloser, S H, Dorian, P, Straub, M, Beckmann, K, Kowey, P. Safety and efficacy of intravenously administered tedisamil for rapid conversion of recent-onset atrial fibrillation or atrial flutter. J Am Coll Cardiol 2004;44(1):99-104.

Hou 1995 {published data only}

studyIdentifiers

Hou, Z Y, Chang, M S, Chen, C Y, Tu, M S, Lin, S L, Chiang, et al. Acute treatment of recent-onset atrial fibrillation and flutter with a tailored dosing regimen of intravenous amiodarone. A randomized, digoxin-controlled study. Eur Heart J 1995;16(4):521-8.

Huang 2003 {published data only}

studyIdentifiers

Huang, S W, Wang, L, Xia, J Z. Comparison of the efficacy and safety of intravenous esmolol and deslanoside in decreasing heart rate of patients with rapid atrial fibrillation. Journal of binzhou medical college 2003;26(2):95-97.

Jacobs 1998 {published data only}

studyIdentifiers

Jacobs, L O, Andrews, T C, Pederson, D N, Donovan, D J. Effect of intravenous procainamide on direct-current cardioversion of atrial fibrillation. Am J Cardiol 1998;82(2):241-2.

Kafkas 2007 {published data only}

studyIdentifiers

* Kafkas, N V, Patsilinakos, S P, Mertzanos, G A, Papageorgiou, K I, Chaveles, J I, Dagadaki, O K, Kelesidis, K M. Conversion efficacy of intravenous ibutilide compared with intravenous amiodarone in patients with recent-onset atrial fibrillation and atrial flutter. Int J Cardiol 2007;118(3):321-5.

Kanoupakis 2003a {published data only}

studyIdentifiers

Kanoupakis, E M, Kochiadakis, G E, Manios, E G, Igoumenidis, N E, Mavrakis, H E, Vardas, P E. Pharmacological cardioversion of recent onset atrial fibrillation with intravenous amiodarone in patients receiving long-term amiodarone therapy: is it reasonable? J Interv Card Electrophysiol 2003;8(1):19-26.

Katcher 1997 {published data only}

studyIdentifiers

Katcher, M S, Estes, N A, 3rd. Pharmacologic conversion of atrial fibrillation and atrial flutter to normal sinus rhythm: the role of ibutilide. Pharmacotherapy 1997;17(1):177-80.

Kerin 1996 {published data only}

studyIdentifiers

Kerin, N Z, Faitel, K, Naini, M. The efficacy of intravenous amiodarone for the conversion of chronic atrial fibrillation. Amiodarone vs quinidine for conversion of atrial fibrillation. Arch Intern Med 1996;156(1):49-53.

Kingma 1992 {published data only}

studyIdentifiers

Kingma, J H, Suttorp, M J. Acute pharmacologic conversion of atrial fibrillation and flutter: the role of flecainide, propafenone, and verapamil. Am J Cardiol 1992;70(5):56A-60A; discussion 60A-61A.

Kingma, J H, Suttorp, M J . ACUTE PHARMACOLOGICAL CONVERSION OF ATRIAL-FIBRILLATION AND FLUTTER - THE ROLE OF FLECAINIDE, PROPAFENONE, AND VERAPAMIL. . Am. J. Cardiol. 1992;70(5):A56-A61 . [DOI: 10.1016/0002-9149(92)91079-j; CRS ID: 19330800]. [DOI: 10.1016/0002-9149(92)91079-j]

Kirchhof 2002 {published data only}

studyIdentifiers

Kirchhof, P, Eckardt, L, Loh, P, Weber, K, Fischer, R J, Seidl, K H, Bocker, D, Breithardt, G, Haverkamp, W, Borggrefe, M. Anterior-posterior versus anterior-lateral electrode positions for external cardioversion of atrial fibrillation: a randomised trial. Lancet 2002;360(9342):1275-9.

Kirilmaz 2001 {published data only}

studyIdentifiers

Kirilmaz, A, Erinc, K, Kilicarslan, F, Demirtas, E. Fourier transformation analysis of atrial fibrillation intervals following ibutilide and procainamide to predict successful cardioversion. Turk Kardiyoloji Dernegi Arsivi 2001;29(8):481-487+462.

Kowey 2009 {published data only}

studyIdentifiers

Kowey, P R, Dorian, P, Mitchell, L B, Pratt, C M, Roy, D, Schwartz, et al. Vernakalant hydrochloride for the rapid conversion of atrial fibrillation after cardiac surgery a randomized, double-blind, placebo-controlled trial. Circulation: Arrhythmia and Electrophysiology 2009;2(6):652-9.

Levi 1973 {published data only}

studyIdentifiers

Levi, G, Proto, C, Rovetta, A. Double-blind evaluation of practolol and quinidine in the treatment of chronic atrial fibrillation. Cardiology 1973;58(6):364-8.

Marrouche 2000 {published data only}

studyIdentifiers

Marrouche, N F, Reddy, R K, Wittkowsky, A K, Bardy, G H. High-dose bolus lidocaine for chemical cardioversion of atrial fibrillation: a prospective, randomized, double-blind crossover trial. Am Heart J 2000;139(6):E8-11.

Martinelli 2003 {published data only}

studyIdentifiers

Martinelli, M M, Dragagna, G, Vitali, A, Fedele, F. [Verapamil in the cardioversion of atrial fibrillation. Clinical study]. Minerva Cardioangiol 2003;51(1):49-53.

Masini 1990 {published data only}

studyIdentifiers

Masini, M, Ieri, A, Lorenzoni, R, Bartoli, P, Lencioni, G, Zipoli, et al. [Comparison of lidoflazine and quinidine in the conversion to sinusal rhythm in atrial fibrillation of recent onset]. G Ital Cardiol 1990;20(3):202-6.

Mathew 1999 {published data only}

studyIdentifiers

Mathew, T P, Moore, A, McIntyre, M, Harbinson, M T, Campbell, N P, Adgey, et al. Randomised comparison of electrode positions for cardioversion of atrial fibrillation. Heart 1999;81(6):576-9.

Mieure 2011 {published data only}

studyIdentifiers

Mieure, K D, Moranville, M P, Park, J J, Lat, I, Jennings, H R, Lazar, et al. A comparison of intravenous rate control agents for new onset atrial fibrillation with rapid ventricular rate. Heart Rhythm 2011;1):S216-7.

Mironov 2019 {published data only}

studyIdentifiers

Mironov, N Yu, Vlodzyanovskiy, V V, Yuricheva, Y A, Sokolov, S F, Golitsyn, S P, Rosenstraukh, et al. Safety and effectiveness of electrical and pharmacological cardioversion in persistent atrial fibrillation. Part I: Study rationale, design and assessment of effectiveness. [Russian]. . Rational Pharmacotherapy in Cardiology 2018;14(5):664-9. [CRS ID: 19330840].

Mironov, N, Vlodzyanovsky, V, Yuricheva, Y, Sokolov, S, Golitsyn, S, Rosenstraukh, et al. SAFETY AND EFFECTIVENESS OF PHARMACOLOGICAL CONVERSION AND DIRECT CURRENT CARDIOVERSION IN PERSISTENT ATRIAL FIBRILLATION: RESULTS OF RANDOMIZED TRIAL. Journal of the american college of cardiology 2019;73(9):298-.

Nieuwlaat 2011 {published data only}

studyIdentifiers

Nieuwlaat, R, Hohnloser, S H, Connolly, S J. Effect of dronedarone in patients with permanent atrial fibrillation during the ATHENA study. European Heart Journal 2011;1):618.

Niwano 2009 {published data only}

studyIdentifiers

Niwano, S, Sasaki, T, Kurokawa, S, Kiryu, M, Fukaya, H, Hatakeyama, et al. Predicting the efficacy of antiarrhythmic agents for interrupting persistent atrial fibrillation according to spectral analysis of the fibrillation waves on the surface ECG. Circ J 2009;73(7):1210-8.

Oral 1999 {published data only}

studyIdentifiers

Oral, H, Brinkman, K, Pelosi, F, Flemming, M, Tse, H F, Kim, et al. Effect of electrode polarity on the energy required for transthoracic atrial defibrillation. Am J Cardiol 1999;84(2):228-30, A8.

Pedersen 2001 {published data only}

studyIdentifiers

Pedersen, O D, Bagger, H, Keller, N, Marchant, B, Kober, L, Torp-Pedersen, C. Efficacy of dofetilide in the treatment of atrial fibrillation-flutter in patients with reduced left ventricular function: a Danish investigations of arrhythmia and mortality on dofetilide (diamond) substudy. Circulation 2001;104(3):292-6.

Peuhkurinen 2000 {published data only}

studyIdentifiers

* Peuhkurinen, K, Niemela, M, Ylitalo, A, Linnaluoto, M, Lilja, M, Juvonen, J. Effectiveness of amiodarone as a single oral dose for recent-onset atrial fibrillation. Am J Cardiol 2000;85(4):462-5.

Pluymaekers 2019 {published data only}

studyIdentifiers

* NAHA Pluymaekers, EAMP Dudink, JGLM Luermans, JG Meeder, T Lenderink, J Widdershoven, JJJ Bucx, M Rienstra, O Kamp, JM Van Opstal, M Alings, A Oomen, CJ Kirchhof, VF Van Dijk, H Ramanna, A Liem, LR Dekker, BAB Essers, JGP Tijssen, IC Van Gelder, and HJGM Crijns. Early or Delayed Cardioversion in Recent-Onset Atrial Fibrillation. N Engl J Med 2019;380:1499-1508. [DOI: 10.1056/NEJMoa1900353]

Pohjantahti-Maaroos 2017 {published data only}

studyIdentifiers

Pohjantahti-Maaroos, H, Hyppola, H, Lekkala, M, Sinisalo, E, Heikkola, A, Hartikainen, et al. Intravenous vernakalant in comparison with intravenous flecainide in the cardioversion of recent-onset atrial fibrillation. Europ Heart J Acute Cardiovasc Care 2019;8(2):114-120..

Rashba 2002 {published data only}

studyIdentifiers

Rashba, E J, Bouhouch, R, MacMurdy, K A, Shorofsky, S R, Peters, R W, Gold, M R. Effect of shock polarity on the efficacy of transthoracic atrial defibrillation. Am Heart J 2002;143(3):541-5.

Rho 2003 {published data only}

studyIdentifiers

Rho, R W, Page, R L. Biphasic versus monophasic shock waveform for conversion of atrial fibrillation. Card Electrophysiol Rev 2003;7(3):290-1.

Sosnowski 2004 {published data only}

studyIdentifiers

Anonymous. Trial finds sustained release propafenone increases time to recurrent atrial fibrillation compared with placebo. Evid 2004;8(1):44-5; discussion 46-7.

Stambler 1997 {published data only}

studyIdentifiers

Stambler, B S, Wood, M A, Ellenbogen, K A. Antiarrhythmic actions of intravenous ibutilide compared with procainamide during human atrial flutter and fibrillation: electrophysiological determinants of enhanced conversion efficacy. Circulation 1997;96(12):4298-306.

Stiell 2020 {published data only}

studyIdentifiers

Stiell, I, Perry, J, Birnie, D, Macle, L, Vadeboncoeur, A, Thiruganasambandamoorthy, V, Borgundvaag, B, Brison, R, Hohl, C, McRae, A, Rowe, B, Sivilotti, M, Morris, J, Mercier, E, Clement, C, Brinkhurst, J, Taljaard, M, Wells, G. A randomized, controlled comparison of electrical versus pharmacological cardioversion for emergency department patients with recent-onset atrial fibrillation. In: CEJM. 2019:S5.

Stiell, I, Sivilotti, M, Taljaard, M, Birnie, D, Vadeboncoeur, A, Hohl, C, McRae, A, Rowe, B, Brison, R, Thiruganasambandamoorthy, V, MacLe, L, Borgundvaag, B, Morris, J, Mercier, E, Clement, C, Brinkhurst, J, Brown, E, Nemnom, M, Wells, G, Perry, J. A randomized, controlled comparison of

electrical versus pharmacological cardioversion for emergency department patients with atrial flutter.. Canadian Journal of Emergency Medicine 2020;22:S9.

* Stiell, Ian G, Sivilotti, Marco L A, Taljaard, Monica, Birnie, David, Vadeboncoeur, Alain, Hohl, Corinne M, McRae, Andrew D, Rowe, Brian H, Brison, Robert J, Thiruganasambandamoorthy, Venkatesh, Macle, Laurent, Borgundvaag, Bjug, Morris, Judy, Mercier, Eric, Clement, Catherine M, Brinkhurst, Jennifer, Sheehan, Connor, Brown, Erica, Nemnom, Marie-Joe, Wells, George A, Perry, Jeffrey J. Electrical versus pharmacological cardioversion for emergency department patients with acute atrial fibrillation (RAFF2): a partial factorial randomised trial. Lancet (London, England) 2020;395(10221):339-349. [DOI: https://dx.doi.org/10.1016/S0140-6736(19)32994-0]

Stiell 2021 {published data only}

studyIdentifiers

* Stiell, IG, Eagles, D, Nemnom, MJ, Brown, E, Taljaard, M, Archambault, P M, Birnie, D, Borgundvaag, B, Clark, G, Davis, P, Godin, D, Hohl, C M, Mathieu, B, McRae, A D, Mercier, E, Morris, J, Parkash, R, Perry, J J, Rowe, B H, Thiruganasambandamoorthy, V, Scheuermeyer, F, Sivilotti, M L A, Vadeboncoeur, A. Adverse Events Associated With Electrical Cardioversion in Patients With Acute Atrial Fibrillation and Atrial Flutter. The Canadian Journal of Cardiology 2021;37:1775 -1782.

Sung 1995 {published data only}

studyIdentifiers

Sung, R J, Tan, H L, Karagounis, L, Hanyok, J J, Falk, R, Platia, et al. Intravenous sotalol for the termination of supraventricular tachycardia and atrial fibrillation and flutter: a multicenter, randomized, double-blind, placebo-controlled study. Sotalol Multicenter Study Group. Am Heart J 1995;129(4):739-48.

Torp-Pedersen 2013 {published data only}

studyIdentifiers

Torp-Pedersen, C, Camm, A J, Butterfield, N N, Dickinson, G, Beatch, G N. Vernakalant: conversion of atrial fibrillation in patients with ischemic heart disease. Int J Cardiol 2013;166(1):147-51.

Tuseth 2005 {published data only}

studyIdentifiers

Tuseth, V, Jaatun, H J, Dickstein, K. Amiodarone infusion in the treatment of acute atrial fibrillation or flutter: high versus low dose treatment. Heart 2005;91(7):964-5.

Villani 2000 {published data only}

studyIdentifiers

Villani, G Q, Piepoli, M F, Terracciano, C, Capucci, A. Effects of diltiazem pretreatment on direct-current cardioversion in patients with persistent atrial fibrillation: a single-blind, randomized, controlled study. Am Heart J 2000;140(3):e12.

Vita 1989 {published data only}

studyIdentifiers

Vita, J A, Friedman, P L, Cantillon, C, Antman, E M. Efficacy of intravenous propafenone for the acute management of atrial fibrillation. American journal of cardiology 1989;63(17):1275-1278.

Weiner 1994 {published data only}

studyIdentifiers

Weiner, P, Ganam, R, Ganem, R, Zidan, F, Rabner, M. Clinical course of recent-onset atrial fibrillation treated with oral propafenone. Chest 1994;105(4):1013-6.

Zadura 2001 {published data only}

studyIdentifiers

Zadura, M, Grossmann, G, Modrzewska, A, Klecha, T, Klepacka, H, Ruminski, et al. [Comparison of efficacy, safety and cost-effectiveness of intravenous versus oral propafenone in paroxysmal atrial fibrillation]. Pol Merkuriusz Lek 2001;11(62):137-9.

Zhan 2003 {published data only}

studyIdentifiers

Zhan, C Y, Zhou, D X, Yang, G T, Deng, P Z. A comparative study on the efficacy and safety of intravenous amiodarone and lanatoside C for the treatment of rapid ventricular rate in patients with atrial fibrillation and

congestive heart falure. Journal of emergency medicine 2003;12(3):188-190.

References to studies awaiting assessment

Antonelli 2004 {published data only}

studyIdentifiers

Antonelli, D, Freedberg, N A, Feldman, A, Darawsha, A, Rosenfeld, T. Intravenous propafenone for conversion of atrial fibrillation in the emergency room. [Hebrew]. Harefuah 2004;143(7):471-474+551-552.

Baldi 1990 {published data only}

studyIdentifiers

Baldi, N, Marasco, G, Russo, V A, Lenti, V, Polimeni, G, Montervino, et al. Flecainide acetate vs digoxin in acute treatment of atrial fibrillation of recent onset: A randomized study. New Trends in Arrhythmias 1990;6(1-2):867-72.

Baldi 1992 {published data only}

studyIdentifiers

Baldi, N, Lenti, V, Marasco, G, Russo, V A, Montervino, C. Propafenone vs flecainide in the acute treatment of atrial fibrillation of recent onset: A randomized study. New Trends in Arrhythmias 1992;8(1-2):499-505.

Botto 1993 {published data only}

studyIdentifiers

Botto, Falcone, G L. A randomized controlled study between placebo vs propafenone per os in a recent cardioversion of atrial fibrillation. Giornale italiano di cardiologia 1993;23(Suppl 1):141.

Botto 1995 {published data only}

studyIdentifiers

Botto, Politi, G L. The efficacy of transthoracic electric cardioversion of the atrial fibrillation is not influeced by the position of the defriblillation platelets. A randomized controlled cross-over study. Giornale italiano di cardiologia 1995;25(Suppl 1):271.

Botto 1996a {published data only}

studyIdentifiers

Botto, Bonini, G L. Oral propafenone or digoxin in the treament of early atrial fibrillation cardioversion: a randomized study controlled with placebo. Giornale italiano di cardiologia 1996;26(Suppl 1):32.

Capucci 1991 {published data only}

studyIdentifiers

Capucci, Lenzi, A. Effect of fleicainide per os and amiodarione i.v. in the cardioversion of atrial fibrillation: a randomized study controlled with palcebo. Giornale italiano di cardiologia 1991;21(Suppl 1):36.

Capucci 1992 {published data only}

studyIdentifiers

Capucci, A, Lenzi, T, Boriani, G, Trisolino, G, Binetti, N, Cavazza, et al. Effectiveness of loading oral flecainide for converting recent-onset atrial fibrillation to sinus rhythm in patients without organic heart disease or with only systemic hypertension. Am J Cardiol 1992;70(1):69-72.

Capucci 1993 {published data only}

studyIdentifiers

Capucci, Boriani, A. Controlled clinical trial on the efficacy of propafenone or flecainide per os in the conversion of sinus rhythm of early atrial fibrillation. Giornale italiano di cardiologia 1993;23(Suppl 1):142.

Capucci 1994 {published data only}

studyIdentifiers

Capucci, A, Boriani, G, Rubino, I, Della Casa, S, Sanguinetti, M, Magnani, et al. A controlled study on oral propafenone versus digoxin plus quinidine in converting recent onset atrial fibrillation to sinus rhythm. Int J Cardiol 1994;43(3):305-13.

Capucci 1999 {published data only}

studyIdentifiers

Capucci, A, Villani, G Q, Aschieri, D, Piepoli, M. Safety of oral propafenone in the conversion of recent onset atrial fibrillation to sinus rhythm: a prospective parallel placebo-controlled multicentre study. Int J Cardiol 1999;68(2):187-96.

Capucci, Villani, A. Oral propafenone in the conversion of atrial fibrillation. The multicentric study SATE. Giornale italiano di cardiologia 1996;26(Suppl 1):32.

Cesar 1994 {published data only}

studyIdentifiers

Cesar, L A, Serrano, C V, Pamplona, D, D'Avila, A L, Ferreira, J F, Amato, et al. [Acute atrial fibrillation in the emergency room. Which is the best drug for a rapid sinus rhythm conversion?]. Arq Bras Cardiol 1994;63(6):481-4.

Chen 2003 {published data only}

studyIdentifiers

Chen, C J, Guo, G B. External cardioversion in patients with persistent atrial fibrillation: a reappraisal of the effects of electrode pad position and transthoracic impedance on cardioversion success. Jpn Heart J 2003;44(6):921-32.

Fera 1993 {published data only}

studyIdentifiers

Fera, Carunchio, M S. Propafenone and flecainide in pharmacological acute conversion of the paroxistic atrial fibrillation. Giornale italiano di cardiologia 1993;23(Suppl 1):141.

Fernßndez 1998 {published data only}

studyIdentifiers

Fernßndez, Martfnez, M, Ortega, Garcfa, Camacho, Santos, Martfn, Rodrfguez, G. Comparative study of propafenone, amiodarone and flecainide in the treatment of paroxystic atrial fibrillation. Revista espanola de cardiologia 1998;51(Suppl 5):84.

Forgione 2000 {published data only}

studyIdentifiers

Forgione, F N, Limido, A, Caico, I, Saveri, C, Provasoli, S, Binaghi, et al. Comparison with different sites of adhesive pad electrodes versus hand-held paddle electrodes for elective cardioversion of atrial fibrillation. New Trends in Electrocardiology 2000;na:93-98.

Giliarov 2007 {published data only}

studyIdentifiers

Giliarov, Mlu, Novikova, N A, Sulimov, V A, Suchkova, S A, Syrkin, A L. [Comparison of the efficacy and safety of electrical cardioversion and pharmacological cardioversion with nibentan in patients with persisting atrial fibrillation and flutter]. Vestn Ross Akad Med Nauk 2007;5:22-6.

Joshi 1995 {published data only}

studyIdentifiers

Joshi, P P, Deshmukh, P K, Salkar, R G. Efficacy of intravenous magnesium sulphate in supraventricular tachyarrhythmias. J Assoc Physicians India 1995;43(8):529-31.

Kalusche 1994 {published data only}

studyIdentifiers

Kalusche, D, Stockinger, J, Betz, P, Roskamm, H. [Sotalol and quinidine/verapamil (Cordichin) in chronic atrial fibrillation--conversion and 12-month follow-up--a randomized comparison]. Z Kardiol 1994;83 Suppl 5:109-16.

Kazuzo 1991 {published data only}

studyIdentifiers

Kazuzo, Kato, Iinuma, H, Sugimoto, T, Hosoda, S, Takao, Kato, Hiejima, K, Hirosawa, K, Gotoh, Y, Hashiba, K. Clinical Evaluation of Intravenous Cibenzoline in Treatment of Paroxysmal Atrial Fibrillation or

Paroxysmal Atrial Flutter. A Multicenter Double-blind Study in Comparison with Placebo. Rinsho hyoka (clinical evaluation) 1991;19(4):477-490.

Kazuzo 1995 {published data only}

studyIdentifiers

Kato Kazuzo, ea. Clinical Effect of E0735 (Flecainide) Injection on Paraxysmal Atrial Fibrillation/Flutter: a Multicenter Double-Blind Placebo-Controlled Comparative Study. Rinsho to kenkyu (the japanese journal of clinical and experimental medicine) 1995;72(2):491-503.

Kmec 2006 {published data only}

studyIdentifiers

Kmec, J. Comparison the effectiveness of damped sine wave monophasic and rectilinear biphasic shocks in patients with persistent atrial fibrillation. [Czech]. Kardiologia 2006;15(5):265-78.

Kondili 1990 {published data only}

studyIdentifiers

Kondili, A, Kastrati, A, Popa, Y. Comparative evaluation of verapamil, flecainide and propafenone for the acute conversion of atrial fibrillation to sinus rhythm. Wien Klin Wochenschr 1990;102(17):510-3.

Lakananurak 2022 {published data only}

studyIdentifiers

* Lakananurak, C, Cutting, D, Lockwood, E. PAD TYPE AND MANUAL PRESSURE AUGMENTATION WITH MAXIMUM OUTPUT SHOCKS IN ATRIAL FIBRILLATION CARDIOVERSION: A RANDOMIZED CONTROLLED TRIAL (PRESS-AF STUDY). In: J Am Coll Cardiol. Vol. 79. 2022:(9_Supplement) 79. [DOI: https://doi.org/10.1016/S0735-1097(22)01070-1]

Lalor 2014 {published data only}

studyIdentifiers

Lalor, N, Conde, D, Caro, M, Rodriguez, L, Elissamburu, P. Vernakalant versus Flecainide and Propafenone in acute atrial fibrillation. Global Heart 2014;1):e62.

Negrini 1990 {published data only}

studyIdentifiers

Negrini, Gibelli, M. Comparison between Iv propafenone and amiodarone in the cardioversion of atrial fibrillation. Giornale italiano di cardiologia 1990;20:14-207.

Negrini 1990a {published data only}

studyIdentifiers

Negrini, M, Gibelli, G, De Ponti, C. [Comparison of amiodarone and quinidine in the conversion to sinusal rhythm of atrial fibrillation of recent onset]. G Ital Cardiol 1990;20(3):207-14.

Niu 2006 {published data only}

studyIdentifiers

Niu, F, Huang, C X, Jiang, H, Yang, B, Guo, W L, Chen, et al. [Effects of amiodarone versus sotalol in treatment of atrial fibrillation: a random controlled clinical study]. Chung Hua I Hsueh Tsa Chih 2006;86(2):121-3.

Satullo 1996 {published data only}

studyIdentifiers

Satullo, G, Arrigo, F, Cavallaro, L, Coglitore, A, Fazio, F, Saporito, F, Sorrenti, S, Oreto, G. Propafenone versus quinidine in recent onset atrial fibrillation. [Italian]. Minerva Cardioangiologica 1996;44(3):141-144.

Taha 2013 {published data only}

studyIdentifiers

Taha, H S, Mashaal, M S, Omar, R M. Pharmacological conversion of recent onset atrial fibrillation: A randomized study of propafenone and amiodarone. Cardiology (Switzerland) 2013;2):175.

Tarasov 2019 {published data only}

studyIdentifiers

Tarasov, A, Davtyan, K, Protasova, D, Blokhina, A, Drapkina, O. Comparison of the efficacy and safety of injectable propafenone and amiodarone for elimination of paroxysmal atrial fibrillation in patients without organic heart disease. Europace 2019;21:ii273-.

Treglia 1994 {published data only}

studyIdentifiers

Treglia, A, Alfano, C, Rossini, E. Propafenone compared with amiodarone for conversion to sinus rhythm of recent onset atrial fibrillation. [Italian]. Minerva Cardioangiologica 1994;42(6):293-7.

Tsaknakis 1999 {published data only}

studyIdentifiers

Tsaknakis, T K, Douras, A L, Malamos, A A, Oikonomou, D S, Georgakli, K A. Comparison of a single oral dose of propafenone with a single intravenous dose of amiodarone in converting paroxysmal atrial fibrillation. [Greek]. Hellenic Journal of Cardiology 1999;40(5):408-12.

Vaisman 2005 {published data only}

studyIdentifiers

Vaisman, M, Bittencourt, M, I, Rey, H C, V, Rangel, F O D, Rocha, R M, Costa Filho, et al. Comparison of monophasic versus biphasic cardioversion for atrial fibrillation. Critical care (london, england) 2005;9(Suppl 2):28.

Vardas 2003 {published data only}

studyIdentifiers

Vardas, P E, Kochiadakis, G E. Amiodarone for the restoration of sinus rhythm in patients with atrial fibrillation. Card Electrophysiol Rev 2003;7(3):297-9.

Villani 1990 {published data only}

studyIdentifiers

Villani, G Q, Rosi, A, Piepoli, M, Gandolfini, A, Groppi, F, Groppi, et al. [The efficacy of oral treatment with flecainide for paroxysmal atrial fibrillation: correlation with plasma concentration]. G Ital Cardiol 1990;20(6):564-8.

Wu 2010 {published data only}

studyIdentifiers

Wu, Y, Jiang, W, Yan, X W, Hu, D Y, Liu, X H, Jia, et al. Comparison of converting therapy between ibutilide and propafenone in Chinese patients with atrial fibrillation and atrial flutter. Cardiology 2010;1):126.

Zhang 2005a {published data only}

studyIdentifiers

Zhang, N, Guo, J H, Zhang, HCh, Li, X B, Zhang, P, Xn, et al. Comparison of intravenous ibutilide vs. propafenone for rapid termination of recent onset atrial fibrillation. Int J Clin Pract 2005;59(12):1395-400.

References to ongoing studies

ChiCTR1900024500 {unpublished data only}

studyIdentifiers

* Bing Han. Effect of Different Discharge Energy on the Efficacy of Transthoracic Cardioversion in Patients With Persistent Atrial Fibrillation. https://trialsearch.who.int/Trial2.aspx?TrialID=ChiCTR1900024500.

EUCTR2021-001627-40-CZ {unpublished data only}

studyIdentifiers

* RESTORE-1 Study Lead. A Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial of Flecainide Acetate Inhalation Solution for Cardioversion of Recent-Onset, Symptomatic Atrial Fibrillation to Sinus Rhythm - RESTORE-1. https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2021-001627-40-CZ.

NCT04485195 {unpublished data only}

studyIdentifiers

* Ian G Stiell. RAFF4 Trial: Vernakalant vs. Procainamide for Acute Atrial Fibrillation in the Emergency Department. https://classic.clinicaltrials.gov/ct2/show/NCT04485195.

NCT04594746 {unpublished data only}

studyIdentifiers

* Satish R Raj. Oral Amiodarone for Acute Cardioversion of Atrial Fibrillation Study (AAA). https://classic.clinicaltrials.gov/ct2/show/NCT04594746?term=NCT04594746&draw=2&rank=1.

NCT04680026 {published data only}

studyIdentifiers

* HUYABIO International, LLC. A Study of IV HBI-3000 for the Conversion Recent Onset Atrial Fibrillation (AF). https://classic.clinicaltrials.gov/ct2/show/NCT04680026?term=NCT04680026&draw=2&rank=1 2020.

NCT05148923 {unpublished data only}

studyIdentifiers

* Lucjan Rucki. Comparison of Two DCCV Algorithms - Rational Versus Maximum Fixed Energy (PROTOCOLENERGY). https://classic.clinicaltrials.gov/ct2/show/NCT05148923?term=NCT05148923&draw=2&rank=1.

NCT05511389 {published data only}

studyIdentifiers

* Omar Ibrahim. Anteroposterior Versus Anterolateral Electrode Position for Electrical Cardioversion of Atrial Fibrillation (SHOCK-VECTOR). https://classic.clinicaltrials.gov/ct2/show/NCT05511389?term=NCT05511389&draw=2&rank=1.

NCT05549752 {unpublished data only}

studyIdentifiers

* Konstantinos P Tsioufis. Flecainide Versus Amiodarone in the Cardioversion of Paroxysmal Atrial Fibrillation at the Emergency Department, in Patients With Coronary Artery Disease Without Residual Ischemia (FLECA-ED). https://classic.clinicaltrials.gov/ct2/show/NCT05549752.

Additional references

2023 ACC/AHA/ACCP/HRS Guideline

José A Joglar, Mina K Chung, Anastasia L Armbruster, Emelia J Benjamin, Janice Y Chyou, Edmond M Cronin, Anita Deswal, Lee L Eckhardt, Zachary D Goldberger, Rakesh Gopinathannair, Bulent Gorenek, Paul L Hess, Mark Hlatky, Gail Hogan, Chinwe Ibeh, Julia H Indik, Kazuhiko Kido, Fred Kusumoto, Mark S Link, Kathleen T Linta, Gregory M Marcus, Patrick M McCarthy, Nimesh Patel, Kristen K Patton, Marco V Perez, Jonathan P Piccini, Andrea M Russo, Prashanthan Sanders, Megan M Streur, Kevin L Thomas, Sabrina Times, James E Tisdale, Anne Marie Valente and David R Van Wagoner. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 30 November 2023;148:e•••–e•••. [DOI: 10.1161/CIR.0000000000001193] [PMID: 38033089]

ACC/AHA/HRS Guidelines 2014

January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland J, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology 2014;64:e1-76.

Andrade 2018

Andrade JG, Verma A, Mitchell LB, Parkash R, Leblanc K, CCS Atrial Fibrillation Guidelines Committee et al . Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Canadian Journal of Cardiology 2018;34(11):1371-1392..

Antman EM 2012

Antman EM (Editor). Cardiovascular Therapeutics: A Companion to Braunwald's Heart Disease.. 4th Edition. Saunders, 2012.

Arunachalam 2020

Arunachalam K, Alzahrani T Flecainide. Flecainide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2020 Apr 20.;NA:NA.

Benjamin 1998

Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 1998;98(10):946-52.

Bialy 1992

Bialy D, Lehmann MH, Schumacher DN, Steinman RT, Meissner MD. Hospitalisation of arrhythmias in the United States: importance of atrial fibrillation. Journal of the American College of Cardiology 1992;19:41A.

Björck 2013

Björck S, Palaszewski B, Friberg L, Bergfeldt L. Atrial fibrillation, stroke risk, and warfarin therapy revisited: a population-based study. Stroke 2013;44(11):3103-8.

Blackshear 2003

Blackshear JL, Safford RE. AFFIRM and RACE trials: implications for the management of atrial fibrillation. Cardiac Electrophysiology Review 2003;7(4):366-9.

Boriani 2004

Boriani G, Diemberger I, Biffi M, Martignani C, Branzi A. Pharmacological cardioversion of atrial fibrillation: current management and treatment options. Drugs 2004;64(24):2741-62.

Brignardello-Petersen 2018

Brignardello-Petersen R, Bonner A, Alexander PE, Siemieniuk RA, Furukawa TA, Rochwerg B, Hazlewood GS, Alhazzani W, Mustafa RA, Murad MH, Puhan MA, Schünemann HJ, Guyatt GH, GRADE Working Group. Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis . J Clin Epidemiol 2018 ;93:36-44.

Cakulev 2010

Cakulev I, Efimov IR, Waldo AL. Cardioversion: past, present, and future. Circulation 2010;120(16):1623-32.

Caldwell 2005

Caldwell D, Ades A, Higgins J . Simultaneous comparison of multiple treatments: combining direct and indirect evidence as well.. JAMA 2005;331:897-900.

Camm 2011

Camm AJ, Capucci A, Hohnloser SH, Torp-Pedersen C, Van Gelder IC, Mangal B, et al. A randomized active-controlled study comparing the efficacy and safety of vernakalant to amiodarone in recent-onset atrial fibrillation. Journal of the American College of Cardiology 2011;57:313-21.

Catala-Lopez 2014

Catala-Lopez F, Tobias A, Cameron C, Moher D, Hutton B. Network meta-analysis for comparing treatment effects of multiple interventions: an introduction.. Rheumatology International 2014;34(11):1489-1496..

Chen 1991

Chen PS, Wolf PD, Ideker RE. Mechanism of cardiac defibrillation. A different point of view. Circulation 1991;84:913-9.

Chugh 2014

Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014;129:837-47.

Cipriani 2013

Cipriani A, Higgins JP, Geddes JR, Salanti G. Conceptual and technical challenges in network meta-analysis.. Annals of Internal Medicine 2013; 159(2):130-137.

Cochrane 2022

The Cochrane Collaboration. CRS (Cochrane Register of Studies). community.cochrane.org/tools/data-management-tools/crs (accessed 21 February 2022).

Cochrane EPOC 2018

Cochrane Effective Practice and Organisation of Care (EPOC). Reporting the effects of an intervention in EPOC reviews. EPOC Resources for review authors, available at. epoc.cochrane.org/resources/epoc-resources- review-authors (accessed 23 March 2022) 2018.

Connolly 2009

Connolly SJ, Crijns HJ, Torp-Pedersen C, van Eickels M, Gaudin C, Page RL, et al. Analysis of stroke in ATHENA: a placebo-controlled, double-blind, parallel-arm trial to assess the efficacy of dronedarone 400 mg BID for the prevention of cardiovascular hospitalization or death from any cause in patients with atrial fibrillation/atrial flutter. Circulation 2009;120:1174-80.

Connolly 2011

Connolly SJ, Camm AJ, Halperin JL, Joyner C, Alings M, Amerena J, et al. Dronedarone in high-risk permanent atrial fibrillation. New England Journal of Medicine 2011;365(24):2268-76.

Cordina 2005

Cordina J, Mead GE. Pharmacological cardioversion for atrial fibrillation and flutter. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No: CD003713. [DOI: 10.1002/14651858.CD003713.pub2]

Cordina 2017

Cordina J, Mead GE. Pharmacological cardioversion for atrial fibrillation and flutter. Cochrane Database of Systematic Reviews 2017, Issue 11. Art. No: CD003713. [DOI: 10.1002/14651858.CD003713.pub3]

Corley 2004

Corley SD, Epstein AE, DiMarco JP, Domanski MJ, Geller N, Greene HL, et al. Relationships between sinus rhythm, treatment, and survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) study. Circulation 2004;109(12):1509-13.

Covidence [Computer program]

Covidence. Melbourne, Australia: Vertitas Health Innovation Ltd, accessed prior to 12 January 2019. Available at www.covidence.org.

Dalzell 1990

Dalzell GW, Anderson J, Adgey AA. Factors determining success and energy requirements for cardioversion of atrial fibrillation. Quarterly Journal of Medicine 1990;76:903-13.

Desouza 2020

deSouza IS, Tadrous M, Sexton T, Benabbas R, Carmelli G, Sinert R. Pharmacologic cardioversion of recent-onset atrial fibrillation: a systematic review and network meta-analysis.. Europace. 2020 Jun 1;;22(6)::854-869.. [DOI: doi: 10.1093/europace/euaa024. PMID: 32176779.]

EAST-AFNET 4

Kirchhof P, Camm AJ, Goette A, Brandes A, Eckardt L, Elvan A, Fetsch T, van Gelder IC, Haase D, Haegeli LM, Hamann F, Heidbüchel H, Hindricks G, Kautzner J, Kuck KH, Mont L, Ng GA, Rekosz J, Schoen N, Schotten U, Suling A, Taggeselle J, Themistoclakis S, Vettorazzi E, Vardas P, Wegscheider K, Willems S, Crijns HJGM, Breithardt G, EAST-AFNET 4 Trial Investigators. Early Rhythm-Control Therapy in Patients with Atrial Fibrillation.. New England Journal of Medicine 29th August 2020;383(14):1305-1316. [PMID: 32865375]

Echt 2020

Echt DS, Ruskin JN. Use of Flecainide for the Treatment of Atrial Fibrillation.. American Journal of Cardiology. 2020 Apr 1;;125(7):1123-1133.. [DOI: doi: 10.1016/j.amjcard.2019.12.041. Epub 2020 Jan 9. PMID: 32044037.]

EMEA 2001

European Medicines Agency. NOTE FOR GUIDANCE ON CHOICE OF CONTROL GROUP IN CLINICAL TRIALS(CPMP/ICH/364/96). https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-10-choice-control-group-clinical-trials-step-5_en.pdf 2001.

ESC Guidelines 2016

Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace 2016;18(11):1609-78.

ESC Guidelines 2020

Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, Boriani G, Castella M, Dan GA, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL, ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS).. European Heart Journal 29th August 2020;ehaa612:ehaa612. [PMID: 32860505]

FDA 2011

Food and Drug Administration. FDA Drug Safety Communication: Review update of Multaq (dronedarone) and increased risk of death and serious cardiovascular adverse events. www.fda.gov/Drugs/DrugSafety/ucm283933.htm (accessed prior to 12 January 2019).

Feld 1992

Feld GK, Fleck RP, Chen PS, Boyce K, Bahnson TD, Stein JB, et al. Radiofrequency catheter ablation for the treatment of human type 1 atrial flutter. Identification of a critical zone in the reentrant circuit by endocardial mapping techniques. Circulation 1992;86:1233-40.

Friberg 2016

Friberg L, Tabrizi F, Englund A. Catheter ablation for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries. European Heart Journal 2016;37:2478-87.

Go 2011

Go AS, Hylek EM, Phillips KA, Chang Y, Hanault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001;285(18):2370-5.

Gunton 1964

Gunton RW. Drugs for arrhythmias. Canadian Medical Association Journal 1964;90:1361-2.

Haim 2015

Haim M, Hoshen M, Reges O, Rabi Y, Balicer R, Leibowitz M. Prospective national study of the prevalence, incidence, management and outcome of a large contemporary cohort of patients with incident non-valvular atrial fibrillation. Journal of the American Heart Association 2015;4(1):e001486.

Hall 2019

Hall AJ, Mitchell AR. Introducing Vernakalant into Clinical Practice.. Arrhythmia Electrophysiology Review. 2019 Mar;;8(1)::70-74.. [DOI: doi: 10.15420/aer.2018.71.2. PMID: 30918671; PMCID: PMC6434499.]

Haïssaguerre 1998

Haïssaguerre M, Jaïs P, Shah DC, Takahashi A, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. New England Journal of Medicine 1998;339(10):659-66.

HHS 2015

List of Clinical Registries available on the US Department of Health and Human Services. www.hhs.gov/ohrp/international/clinical-trial-registries/index.html 28 May 2015.

Higgins 1996

Higgins J, Whitehead A. Borrowing strength from external trials in a meta-analysis.. Statistics in Medicine 1996;15:2733-2749.

Higgins 2002

Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in Medicine 2002;21(11):1539-58.

Higgins 2003

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-60.

Higgins 2011

Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Higgins 2012

Higgins JP, Jackson D, JK Barrett JK, Lu G, Ades AE, Whitea IR. Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. Res Synth Methods 2012 Jun;3(2):98–110. [DOI: 10.1002/jrsm.1044] [PMID: 26062084]

Higgins 2016

Higgins JP, Lasserson T, Chandler J, Tovey D, Churchill R. Methodological Expectations of Cochrane Intervention Reviews. London: Cochrane, 2016.

Higgins 2019

Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions. . 2nd Edition. Chichester (UK): John Wiley & Sons, 2019.

Hohnloser 2009

Hohnloser SH, Crijns HJ, van Eickels M, Gaudin C, Page RL, Torp-Pedersen C, et al. Effect of dronedarone on cardiovascular events in atrial fibrillation. New England Journal of Medicine 2009;360(7):668-78.

Hróbjartsson 2014

Hróbjartsson A, Emanuelsson F, Skou Thomsen AS, Hilden J, Brorson S. Bias due to lack of patient blinding in clinical trials. A systematic review of trials randomizing patients to blind and nonblind sub-studies. International Journal of Epidemiology 2014;43(4):1272-83.

Inacio 2016

Inácio JF, da Rosa Mdos S, Shah J, Rosário J, Vissoci JR, Manica AL, Rodrigues CG. Monophasic and biphasic shock for transthoracic conversion of atrial fibrillation: Systematic review and network meta-analysis.. Resuscitation. 2016 Mar;;100:66-75.. [DOI: doi: 10.1016/j.resuscitation.2015.12.009. Epub 2016 Jan 8. PMID: 26777209.]

ISRCTN

ISRCTN. www.isrctn.com.

Iwasaki 2011

Iwasaki Y, Nishida K, Kato T, Nattel S. Atrial fibrillation pathophysiology implications for management. Circulation 2011;124:2264-74.

Jackson 2015

Jackson D, Boddington P, White IR. The design-by-treatment interaction model: a unifying framework for modelling loop inconsistency in network meta-analysis. Research Synthesis Methods 20 November 2015;7(3):329-332. [DOI: doi.org/10.1002/jrsm.1188]

Kirchhof 2002

Kirchhof P, Eckardt L, Loh P, Weber K, Fischer RJ, Seidl KH, et al. Anterior-posterior versus anterior-lateral electrode positions for external cardioversion of atrial fibrillation: a randomised trial. Lancet 2002;360:1275-9.

Knight 2015

Knight BP. Cardioversion (Beyond the Basics). www.uptodate.com/contents/cardioversion-beyond-the-basics 2015.

Knight 2017

Knight BP. Patient education: cardioversion (Beyond the Basics). www.uptodate.com/contents/cardioversion-beyond-the-basics (accessed 29 January 2019).

Kossaify 2019

Kossaify A. Vernakalant in Atrial Fibrillation: A Relatively New Weapon in the Armamentarium Against an Old Enemy.. Drug Target Insights. 2019 Jul;3:13. [DOI: 1177392819861114. doi: 10.1177/1177392819861114. PMID: 31320795; PMCID: PMC6610431.]

Krijthe 2013

Krijthe BP, Kunst A, Benjamin EJ, Lip GY, Franco OH, Hofman A, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. European Heart Journal 2013;34:2746-51.

König 2013

König, J, Krahn, U, Binder, H. Visualizing the flow of evidence in network meta-analysis and characterizing mixed treatment comparisons. Statistics in Medicine 2013;32:5414–29. [DOI: https://doi.org/10.1002/sim.6001]

Laine 2007

Laine C, Horton R, DeAngelis CD, Drazen JM, Frizelle FA, Godlee F, et al. Clinical trial registration-looking back and moving ahead. New England Journal of Medicine 2007;356:2734-6.

Laupacis 1995

Laupacis A, Albers G, Dalen J, Dunn M, Feinberg W, Jacobson A. Antithrombotic therapy in atrial fibrillation.. Chest 1995;108(Suppl4):352S-359S. [DOI: 10.1161/01.CIR.94.7.1613]

Le Heuzey 2012

Le Heuzey JY, De Ferrari GM, Radzik D, Santini M, Zhu J, Davy JM. A short-term, randomized, double-blind, parallel-group study to evaluate the efficacy and safety of dronedarone versus amiodarone in patients with persistent atrial fibrillation: the DIONYSOS study. Journal of Cardiovascular Electrophysiology 2012;21(6):597-605.

Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Lip 2010

Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation.. Chest 2010;137:263-72.

Lloyd-Jones 2004

Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation 2004;110:1042-6.

Lown 1962

Lown B, Amarasingham R, Neuman J. New method for terminating cardiac arrhythmias: use of synchronized capacitor discharge. JAMA 1962;182:548-55.

Lown 1963

Lown B, Perlroth MG, Kaidbey S, Abe T, Harken DE. “Cardioversion” of atrial fibrillation: a report on the treatment of 65 episodes in 50 patients. New England Journal of Medicine 1963;269:325-31.

Lu 2006

Lu G, Ades A. Assessing evidence inconsistency in mixed treatment comparisons. Journal of American Statistical Association 2006;101:447-59.

Lévy 1992

Lévy S, Lauribe P, Dolla E, Kou W, Kadish A, Calkins H, et al. A randomized comparison of external and internal cardioversion of chronic atrial fibrillation. Circulation 1992;86:1415-20.

Ma 2020

Ma W, Guo X, Wang Q, Sun G, Wang J. Systematic Review and Meta-analysis Appraising Efficacy and Safety of Vernakalant for Cardioversion of Recent-Onset Atrial Fibrillation.. Journal of Cardiovascular

Pharmacology. 2 020 Jul;76(1)::32-41.. [DOI: doi: 10.1097/FJC.0000000000000832. PMID: 32251022.]

Maddox 2008

Maddox TM, Nash IS, Fuster V. Economic costs associated with atrial fibrillation. In: Natale A, Jalie J, editors(s). Atrial Fibrillation from Bench to Bedside. Springer, 2008:13-26.

Magnani 2011

Magnani JW, Rienstra M, Lin H, Sinner MF, Lubitz SA, McManus DD, et al. Atrial fibrillation: current knowledge and future directions in epidemiology and genomics. Circulation 2011;124(18):1982-93.

Markey 2018

Markey GC, Salter N, Ryan J. Intravenous Flecainide for Emergency Department Management of Acute Atrial Fibrillation.. J Emerg Med. 2018 Mar;;54(3)::320-327.. [DOI: doi: 10.1016/j.jemermed.2017.11.016. PMID: 29269083.]

Marrouche 2018

Marrouche NF, Brachmann J, Andresen D, Siebels J, Boersma L, Jordaens L, et al. Catheter ablation for atrial fibrillation with heart failure. New England Journal of Medicine 2018;378(5):217-27.

McIntryre 2019

McIntyre WF, Healey JS, Bhatnagar AK, Wang P, Gordon JA, Baranchuk A, Deif B, Whitlock RP, Belley-Côté ÉP. Vernakalant for cardioversion of recent-onset atrial fibrillation: a systematic review and meta-analysis.. Europace 2019 Aug 1;;21(8):1159-1166.. [DOI: doi: 10.1093/europace/euz175. PMID: 31292622; PMCID: PMC6680366.]

Mead 2005

Mead GE, Elder A, Flapan AD, Cordina J. Electrical cardioversion for atrial fibrillation and flutter. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No: CD002903. [DOI: 10.1002/14651858.CD002903.pub2]

Mead 2017

Mead GE, Elder A, Flapan AD, Cordina J. Electrical cardioversion for atrial fibrillation and flutter. Cochrane Database of Systematic Reviews 2017, Issue 11. Art. No: CD002903. [DOI: 10.1002/14651858.CD002903.pub3]

Mills 2012

Mills EJ, Ioannidis JP, Thorlund K, Schunemann HJ, Puhan MA, Guyatt GH. How to use an article reporting a multiple treatment comparison meta-analysis.. JAMA 2012;308:1246-1253.

Miyasaka 2006

Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation 2006;114:119-25.

Mont 2014

Mont L, Bisbal F, Hernández-Madrid A, Pérez-Castellano N, Viñolas X, Arenal A, et al. Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study). European Heart Journal 2014;35:501-7.

NCT05136131

Ottawa Heart Institute. QOL Improvement After Cardioversion of Persistent AF (QOL-CAFRCT) (QOL-CAFRCT). https://clinicaltrials.gov/ct2/show/NCT05136131 12th November 2021.

netmeta

Rücker G, Schwarzer G, Krahn U, König J. Network Meta-Analysis Using Frequentist Methods. cran.r-project.org/web/packages/netmeta/netmeta.pdf 9 August 2017.

Neupane 2014

Neupane B, Richer D, Bonner AJ, Kibret T, Beyene J. Network meta-analysis using R: a review of currently available automated packages. Plos One 2014;9:e115065.

NICE 2013

National Institute for Health and Clinical Excellence. Review of TA197; Dronedarone for the treatment of non-permanent atrial fibrillation. www.nice.org.uk/guidance/ta197/documents/appendix-b-proposal-paper-presented-to-the-institutes-guidance-executive2 2013.

NICE 2014

National Institute for Health and Clinical Excellence (NICE). Atrial fibrillation: management. NICE guidelines [CG180]. nice.org.uk/guidance/cg180 2014.

Olshansky 2005

Olshansky B, Heller EN, Mitchell B, Chandler M, Slater W, Green M, et al. Are transthoracic echocardiographic parameters associated with atrial fibrillation recurrence or stroke? Results from the atrial fibrillation follow-up investigation of rhythm management (AFFIRM) study. Journal of the American College of Cardiology 2005;45(12):2026-33.

Oral 2002

Oral H, Knight BP, Tada H, Özaydın M, Chugh A, Hassan S, et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation 2002;105:1077-81.

Packer 2019

Packer DL, Mark DB, Robb RA, Monahan KH, Bahnson TD, Poole JE, Noseworthy PA, Rosenberg YD, Jeffries N, Mitchell LB, Flaker GC, Pokushalov E, Romanov A, Bunch TJ, Noelker G, Ardashev A, Revishvili A, Wilber DJ, Cappato R, Kuck KH, Hindricks G, Davies DW, Kowey PR, Naccarelli GV, Reiffel JA, Piccini JP, Silverstein AP, Al-Khalidi HR, Lee KL, CABANA Investigators. Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial.. JAMA 2nd April 2019;321(13):1261-1274. [DOI: 10.1001/jama.2019.0693.] [PMID: 30874766]

Pappone 2012

Pappone C, Santinelli V. Post ablation left atrial tachycardia: understanding mechanism, prevention and treatment. Journal of Atrial Fibrillation 2012;5:525.

Pocock 2015

Pocock SJ, Clayton TC, Stone GW. Design of major randomized trials: part 3 of a 4-part series on statistics for clinical trials. Journal of the American College of Cardiology 2015;66(24):2757-66.

Puhan 2014

Puhan MA, Schünemann HJ, Murad MH, Li T, Brignardello-Petersen R, Singh JA, Kessels AG, Guyatt GH, GRADE Working Group. A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis.. BMJ 2014;349:g5630.

R 2017 [Computer program]

R: A language and environment for statistical computing. Version 3.4.2. Vienna, Austria: R Foundation for Statistical Computing, 2017. Available at www.R-project.org.

Resnekov 1968

Resnekov L, McDonald L. Appraisal of electroconversion in treatment of cardiac dysrhythmias. British Heart Journal 1968;30:786-811.

RevMan Web 2023 [Computer program]

Review Manager Web (RevMan Web). Version 6.4.2. The Cochrane Collaboration, 2023. Available at revman.cochrane.org.

Ritchie 2020

Ritchie LA, Qin S, Penson PE, Henney NC, Lip GY. Vernakalant hydrochloride for the treatment of atrial fibrillation: evaluation of its place in clinical practice.. Future Cardiol. 2020 Nov;;16(6)::585-595. [DOI: doi: 10.2217/fca-2020-0039. Epub 2020 May 28. PMID: 32460637.]

Rücker 2012

Rücker G. Network meta-analysis, electrical networks and graph theory. Res Synth Methods 2012 December;3(4):312-324. [DOI: 10.1002/jrsm.1058] [PMID: 26053424]

Rücker 2015

Rücker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. BMC Medical Research Methodology 2015;15:58.

Salanti 2009

Salanti G, Marinho V, Higgins J. A case study of multiple-treatments meta-analysis demonstrates that covariates should be considered. Journal of Clinical Epidemiology 2009;62:857-64.

Scheuermeyer 2011

Scheuermeyer FX, Grafstein E, Heilbron B, Innes G. Emergency department management and 1-year outcomes of patients with atrial flutter. Annals of Emergency Medicine 2011;57:564-71.

Schwarzer 2015

Schwarzer G, Carpenter JR, Rücker G. Chapter 8: network meta-analysis. In: Meta-Analysis with R. Springer International Publishing Switzerland, 2015.

Sim 2006

Sim I, Chan AW, Gulmezoglu A, Evans T, Pang T. Clinical trial registration: transparency is the watchword. Lancet 2006;367:1631-3.

Supplementary Table 1

Same authors of this Network Meta-Analysis. Supplementary Table 1 - Adverse Effects or Complications. available online at FigShare: https://dx.doi.org/10.6084/m9.figshare.20179154 28th June 2022. [FIGSHARE: dx.doi.org/10.6084/m9.figshare.20179154]

Szymanski 2020

Szymanski MW, Cassagnol M Ibutilide. Ibutilide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan 2020 Nov 4.;NA:NA.

Tunick 1992

Tunick PA, McElhinney L, Mitchell T, Kronzon I. The alternation between atrial flutter and atrial fibrillation. Chest 1992;101:34-6.

Van Gelder 2002

Van Gelder IC, Hagens VE, Bosker HA, Kingma JH, Kamp O, Kingma T, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. New England Journal of Medicine 2002;347(23):1834-40.

Vaughan Williams 1984

Vaughan Williams EM. A classification of antiarrhythmic actions reassessed after a decade of new drugs. Journal of Clinical Pharmacology 1984;24(4):129-47.

Verma 2015

Verma A, Jiang C, Betts TR, Chen J, Deisenhofer I, Mantovan R, et al. Approaches to catheter ablation for persistent atrial fibrillation. New England Journal of Medicine 2015;372:1812-22.

Vos 1998

Vos MA, Golitsyn SR, Stangl K, Ruda MY, Van Wijk LV, Harry JD, et al. Superiority of ibutilide (a new class III agent) over DL-sotalol in converting atrial flutter and atrial fibrillation. Heart 1998;79(6):568-75.

Wenckbach 1923

Wenckbach KF. Cinchona derivates in the treatment of heart disorders. JAMA 1923;81:472-4.

WHO 2006

World Health Organization. The International Clinical Trials Registry Platform. www.who.int/ictrp/en 2006.

WHO 2012

World Health Organization. International standards for Clinical Trial Registries. apps.who.int/iris/bitstream/10665/76705/1/9789241504294_eng.pdf?ua=1&ua=1 (accessed 6 November 2017).

Wolf 1978

Wolf PA, Dawber TR, Thomas HE Jr, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham study. Neurology 1978;28(10):973-7.

Wyse 2002

Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. New England Journal of Medicine 2002;347(23):1825-33.

Yepes-Nuñez 2019

Yepes-Nuñez JJ, Li SA, Guyatt G, Jack SM, Brozek JL, Beyene J, Murad MH, Rochwerg B, Mbuagbaw L, Zhang Y, Flórez ID, Siemieniuk RA, Sadeghirad B, Mustafa R, Santesso N, Schünemann HJ. Development of the summary of findings table for network meta-analysis. J Clin Epidemiol 2019;115:1-13.

Additional tables

Table 1

Baseline Characteristics - Demographics and Co-Morbidities

Study Identifier	Intervention	Numbers	Age (Years) mean (SD)	Men (%)	BMI (Kg/m2)	Heart Failure (%)	Hypertension (%)	Valvular Heart Disease (%)	Structural Heart Disease n (%)	Stroke/TIA (%)	Pulmonary disease (%)	Ca
Abi Mansour 1998	Ibutilide	209	–	–	–	–	–	–	–	–	–	–
Abi Mansour 1998	Placebo	41	–	–	–	–	–	–	–	–	–	–
Aliot 1996	Flecainide	48	62 (12)	25 (52)	–	0 (0)	19 (40)	4 (8)	–	–	–	0
Aliot 1996	Propafenone	49	64 (12)	26 (53)	–	1 (2)	12 (25)	2 (4)	–	–	–	2
Alp 2000	AA MDS Fixed Paddles	30	68 (8)	22 (73)	–	–	5 (17)	3 (10)	–	–	–	–
Alp 2000	AP MDS Fixed Paddles	29	67 (8)	22 (76)	–	–	11 (38)	1 (3)	–	–	–	–
Azpitarte 1997	Placebo	26	57 (14)	7 (37)	–	–	–	5 (19)	–	–	–	–
Azpitarte 1997	Propafenone	29	60 (12)	14 (48)	–	–	–	4 (14)	–	–	–	1
Balla 2011	Amiodarone	40	59 (10)	29 (73)	–	–	12 (30)	–	–	–	–	–
Balla 2011	Flecainide	40	58 (10)	28 (70)	–	–	18 (45)	–	–	–	–	–
Balla 2011	Placebo	40	59 (11)	24 (60)	–	–	9 (23)	–	–	–	–	–
Balla 2011	Propafenone	40	57 (10)	20 (50)	–	–	20 (50)	–	–	–	–	–
Baroffio 1995	Digoxin	25	56 (12)	13 (52)	–	–	7 (28)	–	–	–	1 (4)	–
Baroffio 1995	Propafenone	25	60 (14)	8 (32)	–	–	11 (44)	–	–	–	2 (8)	–
Baroni 2011	Amiodarone	30	63 (6)	17 (57)	–	–	12 (40)	4 (13)	–	–	–	–
Baroni 2011	Propafenone	30	65 (10)	14 (47)	–	–	15 (50)	5 (17)	–	–	–	–
Baroni 2011	Quinidine	30	64 (8)	17 (57)	–	–	13 (43)	2 (7)	–	–	–	–
Beatch 2016	Placebo	68	61 (14)	45 (66)	–	–	39 (57)	13 (9)	–	–	–	–
Beatch 2016	Vernakalant	129	64 (13)	76 (59)	–	–	89 (69)	27 (21)	–	–	–	–
Beatch 2017	Placebo	56	59 (12)	30 (54)	–	3 (5)	–	3 (5)	13 (23)	–	–	–
Beatch 2017	Vernakalant	55	61 (14)	37 (67)	–	5 (9)	–	2 (4)	11 (20)	–	–	–
Bellandi 1995	Placebo	84	66 (14)	–	–	–	19 (23)	17 (20)	–	–	3 (4)	5
Bellandi 1995	Propafenone	98	65 (12	–	–	–	19 (19)	20 (20)	–	–	5 (5)	6
Bellone 2012	BTE Incremental	121	68 (13)	65 (54)	–	–	65 (54)	–	–	–	–	–
Bellone 2012	Propafenone	126	67 (14)		–	–	67 (53)	–	–	–	–	–

				66 (52)								
Bertini 1990	Amiodarone	15	68 (7)	7 (47)	–	–	6 (40)	–	–	–	–	–
Bertini 1990	Propafenone	24	63 (12)	9 (38)	–	–	11 (46)	–	–	–	–	–
Bianconi 1998	Placebo	82	60 (13)	38 (46)	–	–	25 (30)	–	–	–	–	–
Bianconi 1998	Propafenone	41	59 (13)	26 (63)	–	–	11 (27)	–	–	–	–	–
Bianconi 2000	Amiodarone	50	61 (12)	31 (57)	–	–	24 (48)	8 (16)	–	–	–	2
Bianconi 2000	Dofetilide	48	64 (9)	28 (56)	–	–	19 (40)	12 (25)	–	–	–	3
Bianconi 2000	Placebo	52	61 (15)	29 (54)	–	–	22 (42)	4 (8)	–	–	–	0
Blanc 1999	Amiodarone	43	64 (12)	8 (2)	–	–	18 (42)	–		4 (9)	–	–
Blanc 1999	Propafenone	43	61 (12)	8 (2)	–	–	17 (40)	–	–	1 (2)	–	–
Boriani 1997	Placebo	121	58 (13)	67 (55)	–	–	37 (31)	9 (7)	30 (25)	–	–	8
Boriani 1997	Propafenone	119	59 (12)	70 (59)	–	–	37 (31)	8 (7)	32 (27)	–	–	7
Botto 1999	AA MDS Incremental Patches	151	62 (12)	94 (62)	–	–	41 (27)	42 (28)	–	–	–	15
Botto 1999	AP MDS Incremental Patches	150	62 (11)	89 (59)	–	–	40 (27)	43 (29)	–	–	–	17
Bouida 2019	Magnesium	301	67 (14)	183 (61)	–	71 (24)	145 (48)	–	–	23 (8)	–	–
Bouida 2019	Placebo	149	67 (12)	86 (60)	–	32 (21)	75 (50)	–	–	9 (6)	–	–
Braždžionytė 2006	AA BTE Incremental Paddles	55	64 (12)	36 (66)	30 (5)	–	20 (36)	8 (15)	–	–	–	–
Braždžionytė 2006	AP BTE Incremental Paddles	48	62 (10)	29 (60)	30 (5)	–	19 (40)	11 (13)	–	–	–	–
Brodsky 1994	Magnesium	10	59 (15)	5 (50)	–	–	5 (50)	1 (10)	–	–	1 (10)	–
Brodsky 1994	Placebo	8	56 (16)	5 (63)	–	–	3 (38)	2 (25)	–	–	1 (13)	–
Camm 2011	Amiodarone	116	62 (12)	71 (61)	–	26 (22)	80 (69)	12 (10)	45 (39)	–	–	–
Camm 2011	Vernakalant	116	63 (11)	75 (65)	–	20 (17)	86 (74)	4 (3)	36 (31)	–	–	–
Camm 2012	Placebo	15	69 (11)	12 (80)	29 (5)	–	–	–	–	–	–	–
Camm 2012	Vernakalant	39	67 (11)	26 (67)	30 (7)	–	–	–	–	–	–	–
Channer 2004	Placebo	38	68 (8)	30 (79)	29 (4)	–	14 (37)	–	–	–	–	–
Channer 2004	Amiodarone	123	66 (10)	92 (75)	30 (5)	–	53 (43)	–	–	–	–	–
Chiladakis 2001	Magnesium	23	61 (6)	12 (52)	–	–	8 (35)	–	–	–	1 (4)	–
Chiladakis 2001	Placebo	23	64 (4)	13 (57)	–	–	12 (52)	–	–	–	1 (4)	–
Chu 2009	Magnesium	24	47 (15)	19 (79)	–	0 (0)	2 (8)	–	–	–	–	–
Chu 2009	Placebo	24	58 (18)	17 (71)	–	0 (0)	6 (25)	–	–	–	–	–
Cotter 1999	Amiodarone	50	65 (14)	24 (48)	–	2 (4)	36 (72)	–	–	–	–	–
Cotter 1999	Placebo	50	68 (13)	19 (38)	–	4 (8)	31 (62)	–	–	–	–	–
Cybulski 2003	Amiodarone	106	62 (14)	59 (56)	–	–	55 (52)	–	–	–	–	–
Cybulski 2003	Placebo	54	61 (11)	30 (54)	–	–	29 (54)	–	–	–	–	–
Davey 2005	Magnesium	95	71 (15)	46 (45)	–	–	–	–	–	–	–	–
Davey 2005	Placebo	91	72 (15)	45 (46)	–	–	–	–	–	–	–	–
	Ibutilide	157	64 (10		–	–	–	91 (58)	–	–	–	–

Ellenbogen 1996				140 (89)								
Ellenbogen 1996	Placebo	40	63 (9)	37 (92)	–	–	–	23 (57)	–	–	–	–
Fak 1997	Placebo	30	–	–	–	–	–	–	–	–	–	–
Fak 1997	Propafenone	30	–	–	–	–	–	–	–	–	–	–
Falk 1997	Dofetilide	61	64 (-)	55 (90)	–	30 (49)	30 (49)	3 (5)	–	–	–	14
Falk 1997	Placebo	30	67 (-)	22 (73)	–	7 (23)	14 (47)	3 (10)	–	–	–	6
Fresco 1996	Placebo	34	51 (-)	28 (82)	–	–	–	–	–	–	–	–
Fresco 1996	Propafenone	41	56 (-)	22 (54)	–	–	–	–	–	–	–	–
Galperín 2001	Amiodarone	47	62 (8)	30 (64)	–	–	22 (47)	14 (28)	43 (91)	–	–	7
Galperín 2001	Placebo	48	65 (6)	39 (81)	–	–	27 (56)	6 (13)	47 (98)	–	–	7
Ganau 1998	Placebo	75	57 (11)	44 (59)	–	–		–	–	–	–	–
Ganau 1998	Propafenone	81	59 (13)	44 (54)	–	–	34 (42)	–	–	–	–	–
Halinen 1995	Quinidine	28	53 (15)	19 (68)	–	–	12 (43)	1 (4)	–	–	–	–
Halinen 1995	Sotalol	33	55 (13)	21 (64)	–	–	11 (33)	1 (3)	–	–	–	–
Hohnloser 1995	Quinidine	25	65 (13)	10 (40)	–	–	6 (24)	8 (32)	–	–	–	2
Hohnloser 1995	Sotalol	25	60 (10)	8 (32)	–	–	4 (16)	6 (24)	–	–	–	2
Jakobsson 1990	AA MDS Incremental Paddles	11	59 (7)	9 (81)	–	–	–	–	–	–	–	–
Jakobsson 1990	AA MDS Incremental Patches	15	60 (8)	9 (60)	–	–	–	–	–	–	–	–
Joseph 2000	Amiodarone	39	61 (3)	25 (64)	–	–	5 (13)	3 (8)	21 (54)	–	–	5
Joseph 2000	Placebo	36	65 (2)	20 (56)	–	–	10 (28)	4 (11)	18 (50)	–	–	1
Joseph 2000	Sotalol	40	63 (2)	19 (48)	–	–	6 (15)	1 (3)	14 (35)	–	–	0
Kanoupakis 2003	Amiodarone	48	64 (8)	28 (58)	–	–	17 (35)	6 (13)	–	–	–	–
Kanoupakis 2003	Placebo	94	64 (10)	56 (60)	–	–	30 (32)	8 (9)	–	–	–	–
Khaykin 2003	AP MDS Maximum Patches	28	59 (11)	23 (82)	30 (12)	–	17 (61)	–	–	1 (4)	–	–
Khaykin 2003	AP BTE Incremental Patches	28	58 (15)	23 (82)	30 (9)	–	16 (57)	–	–	0 (0)	–	–
Kim 2003	AP BTE Incremental Patches	74	65 (15)	40 (54)	–	–	3 (4)	5 (7)	–	–	–	6
Kim 2003	AP RBW Incremental Patches	71	64 (15)	44 (62)	–	–	2 (3)	15 (21)	–	–	–	6
Kirchhof 2005	AP BTE Incremental Paddles/Patches	104	63 (1)	79 (76)	27 (0.4)	–	–	5 (5)	–	–	–	17
Kirchhof 2005	AP MDS Incremental Paddles/Patches	97	63 (1)	68 (70)	27 (0.4)	–	–	13 (13)	–	–	–	17
Kochiadakis 1998	Placebo	57	64 (10)	30 (53)	–	–	–	–	–	–	–	–
Kochiadakis 1998	Procainamide	57	64 (11)	29 (51)	–	–	–	–	–	–	–	–
Kochiadakis 1998a	Amiodarone	46	63 (12)	27 (56)	–	–	–	–	–	–	–	–
Kochiadakis 1998a	Placebo	49	65 (9)	25 (51)	–	–	–	–	–	–	–	–
Kochiadakis 1998a	Propafenone	48	63 (9)	25 (54)	–	–	–	–	–	–	–	–
	Amiodarone	34	64 (9)		–	–	–	–	–	–	–	–

Kochiadakis 1999				16 (49)								
Kochiadakis 1999	Placebo	33	63 (9)	16 (47)	–	–	–	–	–	–	–	–
Kochiadakis 1999a	Amiodarone	34	64 (9)	16 (47)	–	–	–	–	–	–	–	–
Kochiadakis 1999a	Placebo	35	63 (9)	16 (46)	–	–	–	–	–	–	–	–
Kochiadakis 1999a	Propafenone	32	64 (10)	16 (50)	–	–	–	–	–	–	–	–
Kochiadakis 2007	Amiodarone	92	65 (11)	42 (46)	–	–	–	–	–	–	–	–
Kochiadakis 2007	Placebo	90	66 (9)	40 (44)	–	–	–	–	–	–	–	–
Kochiadakis 2007	Procainamide	89	64 (10)	42 (47)	–	–	–	–	–	–	–	–
Kochiadakis 2007	Propafenone	91	64 (11)	42 (46)	–	–	–	–	–	–	–	–
Kosior 2009	Propafenone	46	62 (11)	21 (49)	–	–	25 (58)	–	10 (22)	–	–	–
Kosior 2009	Quinidine	35	66 (12)	19 (54)	–	–	19 (54)	–	8 (23)	–	–	–
Koster 2004	AA BTE Incremental Patches	35	70 (11)	20 (57)	–	–	–	8 (23)	–	–	–	–
Koster 2004	AA MDS Incremental Patches	37	63 (16)	25 (68)	–	–	–	4 (11)	–	–	–	–
Kühlkamp 1991	Cibenzoline	28	–	–	–	–	–	–	–	–	–	–
Kühlkamp 1991	Flecainide	23	–	–	–	–	–	–	–	–	–	–
Kumagai 2000	Disopyramide	32	59 (12)	21 (66)	–	–	6 (19)	2 (6)	–	–	–	1
Kumagai 2000	Pilsicainide	40	57 (15)	30 (75)	–	–	8 (20)	2 (5)	–	–	–	1
Lindeboom 2000	Dofetilide	51	62 (-)	35 (67)	–	–	13 (25)	1 (2)	–	–	–	2
Lindeboom 2000	Placebo	18	59 (-)	11 (61)	–	–	2 (11)	1 (6)	–	–	–	0
Maciag 2017	Antazoline	36	69 (13)	–	–	–	52 (70)	–	–	–	1 (3)	–
Maciag 2017	Control	38	68 (12)	–	–	–	27 (75)	–	–	–	2 (5)	–
Madrid 1993	Flecainide	40	54 (14)	27 (68)	–	–	–	–	–	–	–	–
Madrid 1993	Procainamide	40	55 (14)	23 (58)	–	–	–	–	–	–	–	–
Mannegold 2007	AP MDS Incremental Paddles	21	–	–	–	–	–	–	–	–	–	–
Mannegold 2007	AP RBW Incremental Paddles	23	–	–	–	–	–	–	–	–	–	–
Martínez-Marcos 2000	Amiodarone	50	62 (14)	24 (48)	–	–	27 (54)	–	–	–	1 (2)	–
Martínez-Marcos 2000	Flecainide	50	57 (14)	26 (52)	–	–	27 (54)	–	–	–	1 (2)	–
Martínez-Marcos 2000	Propafenone	50	62 (11)	20 (40)	–	–	30 (60)	–	–	–	3 (6)	–
Mattioli 1998	Propafenone	38	64 (12)	26 (68)	26 (-)	–	6 (16)	–	15 (39)	–	–	–
Mattioli 1998	Procainamide	38	63 (12)	29 (76)	27 (-)	–	5 (13)	–	16 (42)	–	–	–
Mittal 2000	AP MDS Incremental Patches	82	66 (12)	56 (73)	–	–	3 (4)	13 (18)	–	–	–	8
Mittal 2000	AP RBW Incremental Patches	104	65 (12)	59 (67)	–	–	7 (8)	18 (21)	–	–	–	3
Mortensen 2007	AP MDS Incremental Patches	47	63 (13)	36 (77)	26 (4)	10 (21)	20 (43)	7 (15)	–	–	–	2
Mortensen 2007	AP RBW Incremental Patches	48	62 (12)	34 (71)	27 (5)	15 (31)	20 (42)	7 (15)	–	–	–	4
		46	63 (9)		–	–	–	–	–	–	–	–

Muñoz-Martínez 2010	AA BTE Incremental Patches			40 (87)								
Muñoz-Martínez 2010	AP BTE Incremental Patches	45	55 (13)	35 (78)	–	–	–	–	–	–	–	–
Negrini 1994	Amiodarone	30	61 (10)	12 (40)	-	–	9 (30)	3 (10)	-	–	–	–
Negrini 1994	Propafenone	31	57 (12)	17 (55)	-	–	7 (23)	4 (13)	-	–	–	–
Neumann 2004	AP BTE Incremental Patches	57	62 (11)	45 (74)	–	–	24 (39)	7 (11)	–	–	–	3
Neumann 2004	AP MDS Incremental Patches	61	64 (11)	38 (67)	–	–	25 (44)	3 (5)	–	–	–	4
Noc 1990	Amiodarone	13	–	–	–	–	–	–	–	–	–	–
Noc 1990	Placebo	11	–	–	–	–	–	–	–	–	–	–
Nogic 2022	Magnesium	71	72 (14)	32 (45)	–	7 (10)	38 (52)	–	–	–	–	–
Nogic 2022	Placebo	73	71 (13)	31 (42)	–	11 (15)	43 (59)	–	–	–	–	–
Norgaard 1999	Dofetilide	66	64 (13)	45 (68)	–	24 (36)	18 (27)	5 (8)	–	–	–	–
Norgaard 1999	Placebo	30	62 (10)	23 (77)	–	15 (50)	10 (33)	1 (3)	–	–	–	–
Okishige 2000	Pilsicainide	52	61 (10)	49 (92)	–	–	9 (17)	14 (27)	–	–	–	2
Okishige 2000	Placebo	10	55 (9)	8 (80)	–	–	4 (40)	2 (20)	–	–	–	0
Okishige 2006	Pilsicainide	58	58 (9)	45 (78)	–	–	–	–	–	–	–	–
Okishige 2006	Placebo	50	60 (10)	39 (78)	–	–	–	–	–	–	–	–
Page 2002	AP BTE Incremental	107	65 (14)	69 (72)	–	–	33 (34)	19 (20)	–	–	–	7
Page 2002	AP MDS Incremental	96	65 (13)	73 (68)	–	–	31 (29)	23 (21)	–	–	–	4
Pratt 2010	Placebo	134	62 (14)	86 (66)	–	25 (19)	53 (41)	–	–	–	–	–
Pratt 2010	Vernakalant	131	61 (15)	92 (70)	–	27 (20)	62 (47)	–	–	–	–	–
Rajagopalan 2014	Magnesium	132	65 (10)	89 (67)	31 (7)	–	–	–	–	–	–	–
Rajagopalan 2014	Placebo	129	66 (12)	91 (66)	33 (7)	–	–	–	–	–	–	–
Reisinger 1998	Sotalol	52	59 (15)	31 (60)	26 (4)	14 (27)	16 (31)	5 (10)	5 (10)	–	–	–
Reisinger 1998	Flecainide	54	65 (12)	30 (56)	27 (4)	15 (28)	15 (28)	5 (9)	5 (9)	–	–	–
Reisinger 2004	Ibutilide	106	63 (13)	67 (63)	27 (5)	–	47 (44)	5 (5)	–	–	–	–
Reisinger 2004	Flecainide	101	63 (15)	61 (60)	28 (4)	–	44 (44)	7 (7)	–	–	–	–
Ricard 2001	AA BTE Fixed Patches	30	69 (10)	22 (73)	-	–	11 (37)	7 (23)	1 (3)	–	–	–
Ricard 2001	AA MDS Incremental Patches	27	66 (12)	17 (63)	-	–	8 (30)	9 (33)	–	–	–	–
Risius 2009	AA RBW Incremental Patches	48	62 (13)	35 (73)	24 (4)	16 (33)	20 (42)	11 (23)	–	–	–	4
Risius 2009	AP RBW Incremental Patches	48	62 (12)	37 (77)	26 (5)	12 (25)	21 (44)	5 (10)	–	–	–	1
Romano 2001	Propafenone	164	59 (13)	79 (48)	27 (4)	–	77 (47)	10 (6)	–	–	–	–
Romano 2001	Flecainide	138	59 (12)	65 (47)	27 (5)	–	63 (45)	9 (7)	–	–	–	–
Roy 2004	Placebo	20	63 (13)	14 (70)	–	–	9 (45)	–	–	–	–	–
Roy 2004	Vernakalant	36	60 (16)	20 (56)	–	–	23 (64)	–	–	–	–	–
Roy 2008	Placebo	115	62 (11)	75 (65)	–	18 (16)	53 (46)	–	–	–	–	–

Roy 2008	Vernakalant	221	62 (14)	159 (72)	–	32 (14)	91 (41)	–	–	–	–	–
Satullo 1996a	Propafenone	42	–	–	–	–	–	–	–	–	–	–
Satullo 1996a	Quinidine	38	–	–	–	–	–	–	–	–	–	–
Scheuermeyer 2019	BTE Incremental	43	59 (11)	26 (60)	–	0 (0)	14 (33)	–	–	0 (0)	–	–
Scheuermeyer 2019	Procainamide	41	57 (13)	26 (63)	–	0 (0)	10 (24)	–	–	0 (0)	–	–
Schmidt 2017	AP BTE Incremental Patches	65	67 (8)	51 (78)	30 (6)	12 (19)	51 (78)	7 (11)	–	4 (6)	5 (8)	–
Schmidt 2017	AP PB Incremental Patches	69	66 (9)	51 (74)	29 (6)	20 (29)	51 (74)	3 (4)	–	6 (9)	2 (3)	–
Schmidt 2019	AP BTE Incremental Patches	147	68 (8)	109 (74)	29 (6)	36 (25)	81(55)	17 (12)	–	11 (7)	–	–
Schmidt 2019	AP BTE Maximum Patches	129	68 (9)	90 (70)	30 (6)	39 (30)	84 (65)	9 (7)	–	15 (12)	–	–
Schmidt 2021	AP BTE Incremental Patches	234	69 (9)	158 (68)	29 (5)	54 (23)	151 (65)	33 (14)	–	17 (7)	–	–
Schmidt 2021	AA BTE Incremental Patches	233	69 (10)	156 (67)	29 (6)	67 (29)	149 (64)	26 (11)	–	21 (9)	–	–
Siaplaouras 2004	AP MDS Incremental Patches	108	65 (10)	78 (72)	27 (4)	–	33 (31)	29 (27)	–	–	–	–
Siaplaouras 2004	AP RBW Incremental Patches	108	66 (10)	77 (71)	28 (4)	–	37 (34)	25 (23)	–	–	–	–
Siaplaouras 2005	AP RBW Incremental Patches	60	67 (10)	40 (67)	28 (4)	–	26 (44)	14 (23)	–	–	–	–
Siaplaouras 2005	AA RBW Incremental Patches	63	66 (10)	47 (75)	28 (5)	–	18 (28)	11 (18)	–	–	–	–
Simon 2017	Ibutilide	51	57 (16)	34 (67)	–	–	36 (71)	–	–	–	–	–
Simon 2017	Vernakalant	49	56 (14)	34 (69)	–	–	30 (61)	–	–	–	–	–
Singh 2000	Dofetilide	241	67 (-)	200 (83)	–	–	114 (47)	–	161 (67)	–	–	–
Singh 2000	Placebo	84	67 (-)	73 (90)	–	–	39 (46)	–	58 (69)	–	–	–
Singh 2005	Placebo	137	68 (10)	136 (99)	31 (5)	33 (24)	76 (56)	8 (6)	–	20 (15)	15 (11)	7
Singh 2005	Amiodarone	267	67 (9)	265 (99)	32 (6)	67 (25)	194 (73)	19 (7)	–	33 (12)	36 (14)	25
Singh 2005	Sotalol	261	67 (9)	257 (99)	32 (6)	72 (28)	172 (66)	17 (7)	–	30 (12)	31 (12)	19
Squara 2021	Active compression AP BTE Incremental Patches	50	71 (10)	25 (50)	28 (5)	–	28 (56)	–	–	–	4 (8)	30
Squara 2021	AP BTE Incremental Patches	50	70 (10)	31 (62)	29 (8)	–	28 (56)	–	–	–	4 (8)	32
Stambler 1996	Ibutilide	161	68 (10)	126 (78)	–	–	–	–	–	–	–	–
Stambler 1996	Placebo	81	66 (13)	68 (84)	–	–	–	–	–	–	–	–
Stanaitienė 2008	AP/AA BTE Incremental	112	63 (11)	68 (61)	30 (5)	–	47 (42)	–	–	–	–	–
Stanaitienė 2008	AP/AA MDS Incremental	112	65 (9)	70 (63)	30 (5)	–	48 (43)	–	–	–	–	–
Stroobandt 1997	Placebo	35	64 (9)	12 (35)	–	2 (6)	6 (17)	4 (11)	25 (71)	–	–	2
Stroobandt 1997	Propafenone	101	61 (11)	77 (76)	–	8 (8)	18 (18)	12 (12)	72 (71)	–	–	8
Sun 2005	Ibutilide	20	62 (7)	12 (60)	–	–	12 (60)	2 (10)	–	–	–	2
Sun 2005	Propafenone	20	60 (11)	10 (50)	–	–	10 (50)	6 (30)	–	–	–	2

Suttorp 1989	Flecainide	20	60 (13)	19 (95)	–	–	5 (25)	0 (0)	–	–	–	–
Suttorp 1989	Placebo	20	58 (11)	13 (65)	–	–	4 (20)	2 (10)	–	–	–	–
Suttorp 1990	Flecainide	25	61 (13)	15 (60)	–	–	2 (8)	4 (16)	–	–	1 (4)	–
Suttorp 1990	Propafenone	25	58 (15)	19 (76)	–	–	2 (8)	3 (12)	–	–	1 (4)	–
Taha 2022	Amiodarone	100	55 (5)	61 (61)	–	–	34 (34)	–	–	–	–	–
Taha 2022	Propafenone	100	54 (7)	63 (63)	–	–	36 (36)	–	–	–	–	–
Thomas 2004	Amiodarone	52	54 (16)	35 (67)	–	–	8 (15)	1 (2)	–	–	–	–
Thomas 2004	Placebo	43	56 (17)	33 (77)	–	–	3 (8)	3 (7)	–	–	–	–
Thomas 2004	Sotalol	45	58 (16)	27 (60)	–	–	6 (14)	1 (2)	–	–	–	–
Treglia 1994a	Amiodarone	27	57 (10)	10 (37)	–	–	2 (7)	2 (7)	–	–	–	–
Treglia 1994a	Propafenone	27	58 (10)	13 (48)	–	–	3 (11)	2 (7)	–	–	–	–
Trendafilova 2021	AA BTE Fixed Patches	38	61 (9)	25 (66)	31 (6)	16 (42)	21 (55)	7 (18)	33 (87)	–	9 (24)	3
Trendafilova 2021	AA PB Fixed Patches	35	64 (10)	21 (60)	31 (6)	13 (37)	20 (56)	6 (17)	31 (89)	–	10 (29)	3
Vardas 2000	Amiodarone	100	64 (10)	53 (49)	–	–	–	–	–	–	–	–
Vardas 2000	Placebo	108	65 (9)	49 (49)	–	–	–	–	–	–	–	–
Vijayalakshmi 2006	Amiodarone	27	66 (11)	20 (74)	–	1 (3)	11 (41)	–	–	–	–	–
Vijayalakshmi 2006	Placebo	31	65 (9)	17 (54)	–	1 (3)	11 (36)	–	–	–	–	–
Vijayalakshmi 2006	Sotalol	36	63 (9)	30 (83)	–	1 (3)	11 (31)	–	–	–	–	–
Vogiatzis 2009	AP MDS Incremental Patches	30	62 (7)	20 (65)	26 (4)	–	4 (13)	5 (17)	–	–	–	–
Vogiatzis 2009	AA MDS Incremental Patches	32	60 (9)	21 (66)	27 (4)	–	4 (13)	6 (19)	–	–	–	–
Vogiatzis 2017	Ibutilide	43	62 (7)	32 (76)	–	–	23 (55)	6 (14)	–	–	–	–
Vogiatzis 2017	Vernakalant	36	62 (7)	25 (67)	–	–	27 (75)	5 (14)	–	–	–	–
Volgman 1998	Ibutilide	60	64 (-)	45 (75)	–	–	–	14 (23)	–	–	–	–
Volgman 1998	Procainamide	60	68 (-)	42 (70)	–	–	–	15 (25)	–	–	–	–
Vos 1998	Ibutilide	211	61 (-)	142 (67)	–	–	–	–	–	–	–	–
Vos 1998	Sotalol	108	59 (-)	81 (75)	–	–	–	–	–	–	–	–
Voskoboinik 2018	AP/AA Biphasic Patches	63	61 (11)	47 (75)	35 (5)	–	26 (41)	–	–	–	–	–
Voskoboinik 2018	AP/AA Biphasic Paddles	62	60 (10)	44 (71)	35 (6)	–	31 (50)	–	–	–	–	–
Walsh 2005	AP BTE Incremental Patches	144	66 (14)	100 (64)	28 (5)	–	81 (52)	26 (17)	–	–	–	–
Walsh 2005	AA BTE Incremental Patches	150	67 (10)	95 (63)	29 (5)	–	57 (38)	36 (24)	–	–	–	–
Xanthos 2007	Amiodarone	113	64 (11)	78 (69)	–	–	–	–	–	–	–	–
Xanthos 2007	Procainamide	110	64 (11)	75 (68)	–	–	–	–	–	–	–	–
Yamase 2012	Amiodarone	20	61 (10)	18 (90)	–	–	12 (60)	–	–	–	–	–
Yamase 2012	Bepridil	20	62 (8)	17 (85)	–	–	16 (80)	–	–	–	–	–
Yamashita 2009	Bepridil	61	64 (11)	49 (80)	–	–	36 (59)	7 (11)	–	–	–	–
	Placebo	29	63 (9)		–	–	14 (48)	12 (41)	–	–	–	–

Yamashita 2009				25 (86)								
Yu 2013	Ibutilide	50	–	–	–	–	–	–	–	–	–	–
Yu 2013	Propafenone	49	–	–	–	–	–	–	–	–	–	–
Zehender 1994	Amiodarone	20	59 (5)	12 (60)	–	–	2 (10)	5 (25)	–	–	–	4
Zehender 1994	Quinidine	20	57 (6)	11 (55)	–	–	3 (15)	5 (25)	–	–	–	4
Zhang 2005	Ibutilide	107	–	–	–	–	–	–	–	–	–	–
Zhang 2005	Propafenone	105	–	–	–	–	–	–	–	–	–	–

Data given as mean (sd) or n (%). AP = Anteroposterior, AA = Anteroapical, BTE = Biphasic Truncated Exponential, RBW = Rectilinear Biphasic Waveform, MDS = Monophasic Damped Sinewave, PB = Pulsed Biphasic

Table 2

Baseline Characteristics - Drug therapy and Structural information

Study Identifier	Intervention	Numbers	Beta-Blocker (%)	Digoxin (%)	Calcium Antagonist (%)	Amiodarone (%)	Sotalol (%)	Flecainide (%)	Propafenone (%)	Diuretic (%)	Inhi
Abi Mansour 1998	Ibutilide	209	–	–	–	–	–	–	–	–	–
Abi Mansour 1998	Placebo	41	–	–	–	–	–	–	–	–	–
Aliot 1996	Flecainide	48	–	–	–	–	–	–	–	–	–
Aliot 1996	Propafenone	49	–	–	–	–	–	–	–	–	–
Alp 2000	AA MDS Fixed Paddles	30	–	15 (50)	2 (7)	8 (27)	1 (3)	14 (47)	–	–	–
Alp 2000	AP MDS Fixed Paddles	29	–	11 (38)	0 (0)	6 (21)	1 (3)	16 (55)	–	–	–
Azpitarte 1997	Placebo	26	–	–	–	–	–	–	–	–	–
Azpitarte 1997	Propafenone	29	–	–	–	–	–	–	–	–	–
Balla 2011	Amiodarone	40	–	–	–	–	–	–	–	–	–
Balla 2011	Flecainide	40	–	–	–	–	–	–	–	–	–
Balla 2011	Placebo	40	–	–	–	–	–	–	–	–	–
Balla 2011	Propafenone	40	–	–	–	–	–	–	–	–	–
Baroffio 1995	Digoxin	25	–	–	–	–	–	–	–	–	–
Baroffio 1995	Propafenone	25	–	–	–	–	–	–	–	–	–
Baroni 2011	Amiodarone	30	–	–	–	–	–	–	–	–	–
Baroni 2011	Propafenone	30	–	–	–	–	–	–	–	–	–
Baroni 2011	Quinidine	30	–	–	–	–	–	–	–	–	–
Beatch 2016	Placebo	68	–	–	–	–	–	–	–	–	–
Beatch 2016	Vernakalant	129	–	–	–	–	–	–	–	–	–
Beatch 2017	Placebo	56	–	–	–	–	–	–	–	–	–
Beatch 2017	Vernakalant	55	–	–	–	–	–	–	–	–	–
Bellandi 1995	Placebo	84	–	–	–	–	–	–	–	–	–
Bellandi 1995	Propafenone	98	–	–	–	–	–	–	–	–	–
Bellone 2012	BTE Incremental	121	42 (35)	0 (0)	45 (37)	–	–	–	–	–	25 (2
Bellone 2012	Propafenone	126	40 (32)	0 (0)	55 (44)	–	–	–	–	–	31 (2
Bertini 1990	Amiodarone	15	–	–	–	–	–	–	–	–	–
Bertini 1990	Propafenone	24	–	–	–	–	–	–	–	–	–
Bianconi 1998	Placebo	82	–	–	–	–	–	–	–	–	–
Bianconi 1998	Propafenone	41	–	–	–	–	–	–	–	–	–
Bianconi 2000	Amiodarone	50	7 (14)	34 (68)	13 (26)	–	–	–	–	–	–
Bianconi 2000	Dofetilide	48	7 (15)	25 (52)	12 (25)	–	–	–	–	–	–
Bianconi 2000	Placebo	52	8 (15)	24 (46)	20 (38)	–	–	–	–	–	–
Blanc 1999	Amiodarone	43	–	–	–	–	–	–	–	–	–
Blanc 1999	Propafenone	43	–	–	–	–	–	–	–	–	–
Boriani 1997	Placebo	121	–	–	–	–	–	–	–	–	–
Boriani 1997	Propafenone	119	–	–	–	–	–	–	–	–	–
Botto 1999	AA MDS Incremental Patches	151	–	–	–	62 (41)	7 (5)	3 (2)	25 (17)	–	–
Botto 1999	AP MDS Incremental Patches	150	–	–	–	69 (46)	6 (4)	1 (1)	18 (12)	–	–
Bouida 2019	Magnesium	301	64 (21)	143 (48)	94 (31)	–	–	–	–	–	–
Bouida 2019	Placebo	149	33 (22)	71 (48)	45 (30)	–	–	–	–	–	–

Braždžionytė 2006	AA BTE Incremental Paddles	55	17 (31)	2 (4)	–	22 (40)	–	–	8 (15)	–	–
Braždžionytė 2006	AP BTE Incremental Paddles	48	8 (17)	2 (4)	–	24 (50)	–	–	10 (21)	–	–
Brodsky 1994	Magnesium	10	–	1 (10)	–	–	–	–	–	–	–
Brodsky 1994	Placebo	8	–	1 (13)	–	–	–	–	–	–	–
Camm 2011	Amiodarone	116	76 (66)	10 (9)	4 (3)	–	–	–	–	–	–
Camm 2011	Vernakalant	116	63 (54)	6 (5)	10 (9)	–	–	–	–	–	–
Camm 2012	Placebo	15	–	–	–	–	–	–	–	–	–
Camm 2012	Vernakalant	39	–	–	–	–	–	–	–	–	–
Channer 2004	Placebo	38	5 (13)	26 (68)	7 (18)	–	–	–	–	–	–
Channer 2004	Amiodarone	123	29 (24)	65 (53)	19 (15)	–	–	–	–	–	–
Chiladakis 2001	Magnesium	23	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	–	–
Chiladakis 2001	Placebo	23	0 (0)	0 (0)	23 (100)	0 (0)	0 (0)	0 (0)	0 (0)	–	–
Chu 2009	Magnesium	24	–	–	–	–	–	–	–	–	–
Chu 2009	Placebo	24	–	–	–	–	–	–	–	–	–
Cotter 1999	Amiodarone	50	–	50 (100)	–	0 (0)	0 (0)	0 (0)	0 (0)	–	–
Cotter 1999	Placebo	50	–	50 (100)	–	0 (0)	0 (0)	0 (0)	0 (0)	–	–
Cybulski 2003	Amiodarone	106	33 (31)	5 (5)	18 (17)	–	–	–	–	17 (16)	39 (3
Cybulski 2003	Placebo	54	17 (32)	4 (7)	10 (19)	–	–	–	–	8 (15)	22 (4
Davey 2005	Magnesium	95	11 (11)	14 (14)	2 (2)	–	–	–	–	13 (13)	–
Davey 2005	Placebo	91	9 (9)	12 (13)	4 (4)	–	–	–	–	25 (27)	–
Ellenbogen 1996	Ibutilide	157	30 (19)	115 (73)	64 (41)	–	–	–	–	–	–
Ellenbogen 1996	Placebo	40	6 (15)	25 (62)	15 (37)	–	–	–	–	–	–
Fak 1997	Placebo	30	–	–	–	–	–	–	–	–	–
Fak 1997	Propafenone	30	–	–	–	–	–	–	–	–	–
Falk 1997	Dofetilide	61	–	–	–	–	–	–	–	–	–
Falk 1997	Placebo	30	–	–	–	–	–	–	–	–	–
Fresco 1996	Placebo	34	–	–	–	–	–	–	–	–	–
Fresco 1996	Propafenone	41	–	–	–	–	–	–	–	–	–
Galperín 2001	Amiodarone	47	–	–	–	–	–	–	–	–	–
Galperín 2001	Placebo	48	–	–	–	–	–	–	–	–	–
Ganau 1998	Placebo	75	–	–	–	–	–	–	–	–	–
Ganau 1998	Propafenone	81	–	–	–	–	–	–	–	–	–
Halinen 1995	Quinidine	28	13 (46)	1 (4)	3 (11)	–	0 (0)	0 (0)	0 (0)	8 (29)	–
Halinen 1995	Sotalol	33	6 (18)	5 (15)	4 (12)	–	0 (0)	0 (0)	0 (0)	1 (3)	–
Hohnloser 1995	Quinidine	25	–	–	–	–	–	–	–	–	–
Hohnloser 1995	Sotalol	25	–	–	–	–	–	–	–	–	–
Jakobsson 1990	AA MDS Incremental Paddles	11	–	10 (91)	–	–	–	–	–	–	–
Jakobsson 1990	AA MDS Incremental Patches	15	–	12 (80)	–	–	–	–	–	–	–
Joseph 2000	Amiodarone	39	0 (0)	–	–	–	–	–	–	–	–
Joseph 2000	Placebo	36	0 (0)	–	–	–	–	–	–	–	–
Joseph 2000	Sotalol	40	0 (0)	–	–	–	–	–	–	–	–
Kanoupakis 2003	Amiodarone	48	–	17 (35)	–	–	–	–	–	–	–
Kanoupakis 2003	Placebo	94	–	25 (27)	–	–	–	–	–	–	–
Khaykin 2003	AP MDS Maximum Patches	28	13 (46)	10 (36)	4 (15)	12 (43)	2 (7)	–	–	–	–
Khaykin 2003	AP BTE Incremental Patches	28	12 (43)	4 (14)	4 (14)	18 (64)	1 (4)	–	–	–	–
Kim 2003	AP BTE Incremental Patches	74	33 (45)	23 (31)	21 (28)	15 (20)	8 (11)	–	–	21 (28)	–

Kim 2003	AP RBW Incremental Patches	71	43 (61)	19 (27)	21 (30)	9 (13)	2 (3)	–	–	20 (28)	–
Kirchhof 2005	AP BTE Incremental Paddles/Patches	104	–	–	–	26 (25)	11 (11)	15 (14)	–	–	–
Kirchhof 2005	AP MDS Incremental Paddles/Patches	97	–	–	–	20 (21)	17 (18)	15 (15)	–	–	–
Kochiadakis 1998	Placebo	57	–	–	–	–	–	–	–	–	–
Kochiadakis 1998	Procainamide	57	–	–	–	–	–	–	–	–	–
Kochiadakis 1998a	Amiodarone	46	–	–	–	–	–	–	–	–	–
Kochiadakis 1998a	Placebo	49	–	–	–	–	–	–	–	–	–
Kochiadakis 1998a	Propafenone	48	–	–	–	–	–	–	–	–	–
Kochiadakis 1999	Amiodarone	34	–	–	–	–	–	–	–	–	–
Kochiadakis 1999	Placebo	33	–	–	–	–	–	–	–	–	–
Kochiadakis 1999a	Amiodarone	34	–	–	–	–	–	–	–	–	–
Kochiadakis 1999a	Placebo	35	–	–	–	–	–	–	–	–	–
Kochiadakis 1999a	Propafenone	32	–	–	–	–	–	–	–	–	–
Kochiadakis 2007	Amiodarone	92	–	–	–	–	–	–	–	–	–
Kochiadakis 2007	Placebo	90	–	–	–	–	–	–	–	–	–
Kochiadakis 2007	Procainamide	89	–	–	–	–	–	–	–	–	–
Kochiadakis 2007	Propafenone	91	–	–	–	–	–	–	–	–	–
Kosior 2009	Propafenone	46	–	–	–	–	–	–	–	–	–
Kosior 2009	Quinidine	35	–	–	–	–	–	–	–	–	–
Koster 2004	AA BTE Incremental Patches	35	11 (31)	22 (63)	11 (31)	9 (26)	7 (20)	–	–	–	–
Koster 2004	AA MDS Incremental Patches	37	7 (19)	17 (46)	23 (62)	12 (32)	9 (24)	–	–	–	–
Kühlkamp 1991	Cibenzoline	28	–	–	–	–	–	–	–	–	–
Kühlkamp 1991	Flecainide	23	–	–	–	–	–	–	–	–	–
Kumagai 2000	Disopyramide	32	–	–	–	–	–	–	–	–	–
Kumagai 2000	Pilsicainide	40	–	–	–	–	–	–	–	–	–
Lindeboom 2000	Dofetilide	51	–	–	–	–	–	–	–	–	–
Lindeboom 2000	Placebo	18	–	–	–	–	–	–	–	–	–
Maciag 2017	Antazoline	36	28 (78)	–	4 (11)	4 (11)	–	–	10 (28)	15 (42)	23 (6
Maciag 2017	Control	38	31 (82)	–	3 (8)	1 (3)	–	–	18 (47)	16 (42)	21 (5
Madrid 1993	Flecainide	40	–	–	–	–	–	–	–	–	–
Madrid 1993	Procainamide	40	–	–	–	–	–	–	–	–	–
Mannegold 2007	AP MDS Incremental Paddles	21	–	–	–	–	–	–	–	–	–
Mannegold 2007	AP RBW Incremental Paddles	23	–	–	–	–	–	–	–	–	–
Martínez-Marcos 2000	Amiodarone	50	0 (0)	2 (4)	4 (8)	–	–	–	–	–	–
Martínez-Marcos 2000	Flecainide	50	3 (6)	2 (4)	1 (2)	–	–	–	–	–	–
Martínez-Marcos 2000	Propafenone	50	2 (4)	2 (4)	4 (8)	–	–	–	–	–	–
Mattioli 1998	Propafenone	38	–	–	–	–	–	–	–	–	–
Mattioli 1998	Procainamide	38	–	–	–	–	–	–	–	–	–
Mittal 2000		82	35 (45)	35 (45)	26 (33)	18 (23)	6 (8)	–	–	21 (27)	23 (3

	AP MDS Incremental Patches										
Mittal 2000	AP RBW Incremental Patches	104	41 (47)	38 (43)	27 (31)	24 (27)	8 (9)	–	–	19 (22)	23 (2
Mortensen 2007	AP MDS Incremental Patches	47	16 (34)	–	–	4 (9)	1 (2)	5 (11)	–	–	–
Mortensen 2007	AP RBW Incremental Patches	48	14 (29)	–	–	7 (15)	4 (8)	6 (13)	–	–	–
Muñoz-Martínez 2010	AA BTE Incremental Patches	46	–	–	–	–	–	–	–	–	–
Muñoz-Martínez 2010	AP BTE Incremental Patches	45	–	–	–	–	–	–	–	–	–
Negrini 1994	Amiodarone	30	–	–	–	–	–	–	–	–	–
Negrini 1994	Propafenone	31	–	–	–	–	–	–	–	–	–
Neumann 2004	AP BTE Incremental Patches	57	24 (39)	–	–	13 (21)	7 (12)	–	–	–	–
Neumann 2004	AP MDS Incremental Patches	61	19 (33)	–	–	11 (19)	12 (21)	–	–	–	–
Noc 1990	Amiodarone	13	–	–	–	–	–	–	–	–	–
Noc 1990	Placebo	11	–	–	–	–	–	–	–	–	–
Nogic 2022	Magnesium	71	–	–	–	–	–	–	–	–	–
Nogic 2022	Placebo	73	–	–	–	–	–	–	–	–	–
Norgaard 1999	Dofetilide	66	7 (11)	48 (73)	23 (35)	–	–	–	–	–	–
Norgaard 1999	Placebo	30	5 (17)	22 (73)	8 (27)	–	–	–	–	–	–
Okishige 2000	Pilsicainide	52	–	–	–	–	–	–	–	–	–
Okishige 2000	Placebo	10	–	–	–	–	–	–	–	–	–
Okishige 2006	Pilsicainide	58	–	–	–	–	–	–	–	–	–
Okishige 2006	Placebo	50	–	–	–	–	–	–	–	–	–
Page 2002	AP BTE Incremental	107	32 (33)	41 (43)	33 (34)	–	–	–	–	51 (53)	34 (3
Page 2002	AP MDS Incremental	96	45 (42)	40 (37)	27 (25)	–	–	–	–	49 (46)	36 (3
Pratt 2010	Placebo	134	81 (62)	27 (21)	32 (25)	–	–	–	–	–	–
Pratt 2010	Vernakalant	131	83 (63)	20 (15)	24 (18)	–	–	–	–	–	–
Rajagopalan 2014	Magnesium	132	94 (71)	23 (17)	47 (35)	20 (15)	15 (11)	19 (14)	6 (5)	–	55 (4
Rajagopalan 2014	Placebo	129	95 (74)	14 (11)	48 (37)	20 (16)	9 (7)	15 (12)	7 (5)	–	61 (4
Reisinger 1998	Sotalol	52	0 (0)	14 (27)	0 (0)	–	–	–	–	–	–
Reisinger 1998	Flecainide	54	0 (0)	12 (22)	0 (0)	–	–	–	–	–	–
Reisinger 2004	Ibutilide	106	32 (31)	30 (28)	21 (20)	–	–	–	–	–	–
Reisinger 2004	Flecainide	101	31 (31)	29 (29)	24 (24)	–	–	–	–	–	–
Ricard 2001	AA BTE Fixed Patches	30	–	–	–	–	–	–	–	–	–
Ricard 2001	AA MDS Incremental Patches	27	–	–	–	–	–	–	–	–	–
Risius 2009	AA RBW Incremental Patches	48	11 (23)	–	–	7 (15)	5 (10)	5 (10)	–	–	–
Risius 2009	AP RBW Incremental Patches	48	12 (25)	–	–	5 (10)	1 (2)	5 (10)	–	–	–
Romano 2001	Propafenone	164	–	–	–	–	–	–	–	–	–
Romano 2001	Flecainide	138	–	–	–	–	–	–	–	–	–
Roy 2004	Placebo	20	15 (75)	6 (30)	6 (30)	–	–	–	–	–	6 (30
Roy 2004	Vernakalant	36	23 (64)	6 (17)	10 (28)	–	–	–	–	–	9 (25
Roy 2008	Placebo	115	71 (62)	36 (31)	27 (24)	–	–	–	–	–	–
Roy 2008	Vernakalant	221	128 (58)	55 (25)	40 (18)	–	–	–	–	–	–
Satullo 1996a	Propafenone	42	–	–	–	–	–	–	–	–	–
Satullo 1996a	Quinidine	38	–	–	–	–	–	–	–	–	–

Scheuermeyer 2019	BTE Incremental	43	3 (7)	0 (0)	0 (0)	1 (2)	3 (7)	–	1 (2)	–	–
Scheuermeyer 2019	Procainamide	41	3 (7)	0 (0)	2 (5)	0 (0)	0 (0)	–	3 (7)	–	–
Schmidt 2017	AP BTE Incremental Patches	65	53 (82)	18 (28)	20 (31)	18 (28)	–	1 (2)	–	–	40 (6
Schmidt 2017	AP PB Incremental Patches	69	57 (83)	14 (19)	16 (23)	6 (9)	–	1 (1)	–	–	44 (6
Schmidt 2019	AP BTE Incremental Patches	147	–	–	–	12 (8)	–	–	–	–	–
Schmidt 2019	AP BTE Maximum Patches	129	–	–	–	10 (8)	–	–	–	–	–
Schmidt 2021	AP BTE Incremental Patches	234	179 (76)	32 (14)	–	30 (13)	–	2 (1)	–	–	114
Schmidt 2021	AA BTE Incremental Patches	233	194 (83)	42 (18)	–	39 (17)	–	4 (2)	–	–	123
Siaplaouras 2004	AP MDS Incremental Patches	108	25 (23)	8 (7)	–	30 (28)	28 (26)	–	–	–	–
Siaplaouras 2004	AP RBW Incremental Patches	108	42 (39)	4 (4)	–	31 (29)	18 (17)	–	–	–	–
Siaplaouras 2005	AP RBW Incremental Patches	60	29 (48)	2 (3)	–	16 (27)	9 (15)	–	–	–	–
Siaplaouras 2005	AA RBW Incremental Patches	63	19 (30)	4 (6)	–	19 (30)	13 (21)	–	–	–	–
Simon 2017	Ibutilide	51	29 (57)	1 (2)	–	–	–	–	–	–	–
Simon 2017	Vernakalant	49	24 (47)	2 (4)	–	–	–	–	–	–	–
Singh 2000	Dofetilide	241	–	194 (80)	56 (23)	–	–	–	–	110 (46)	–
Singh 2000	Placebo	84	–	67 (80)	20 (24)	–	–	–	–	40 (48)	–
Singh 2005	Placebo	137	–	–	–	–	–	–	–	–	–
Singh 2005	Amiodarone	267	–	–	–	–	–	–	–	–	–
Singh 2005	Sotalol	261	–	–	–	–	–	–	–	–	–
Squara 2021	Active compression AP BTE Incremental Patches	50	–	–	–	–	–	3 (6)	–	–	–
Squara 2021	AP BTE Incremental Patches	50	–	–	–	–	–	3 (6)	–	–	–
Stambler 1996	Ibutilide	161	26 (16)	92 (57)	75 (47)	–	–	–	–	–	–
Stambler 1996	Placebo	81	27 (33)	40 (49)	32 (40)	–	–	–	–	–	–
Stanaitienė 2008	AP/AA BTE Incremental	112	47 (42)	4 (4)	–	47 (42)	–	–	18 (16)	–	–
Stanaitienė 2008	AP/AA MDS Incremental	112	50 (45)	3 (3)	–	67 (60)	–	–	10 (9)	–	–
Stroobandt 1997	Placebo	35	–	19 (54)	–	–	–	–	–	–	–
Stroobandt 1997	Propafenone	101	–	73 (72)	–	–	–	–	–	–	–
Sun 2005	Ibutilide	20	–	6 (30)	–	–	–	–	–	–	–
Sun 2005	Propafenone	20	–	7 (35)	–	–	–	–	–	–	–
Suttorp 1989	Flecainide	20	4 (20)	4 (20)	–	–	–	–	–	–	–
Suttorp 1989	Placebo	20	3 (15)	4 (20)	–	–	–	–	–	–	–
Suttorp 1990	Flecainide	25	6 (24)	3 (12)	4 (16)	–	–	–	–	–	–
Suttorp 1990	Propafenone	25	3 (12)	4 (16)	1 (4)	–	–	–	–	–	–
Taha 2022	Amiodarone	100	–	–	–	–	–	–	–	–	–
Taha 2022	Propafenone	100	–	–	–	–	–	–	–	–	–

Thomas 2004	Amiodarone	52	–	–	–	–	–	–	–	–	–
Thomas 2004	Placebo	43	–	–	–	–	–	–	–	–	–
Thomas 2004	Sotalol	45	–	–	–	–	–	–	–	–	–
Treglia 1994a	Amiodarone	27	–	–	–	–	–	–	–	–	–
Treglia 1994a	Propafenone	27	–	–	–	–	–	–	–	–	–
Trendafilova 2021	AA BTE Fixed Patches	38	28 (74)	4 (11)	0 (0)	29 (76)	–	–	8 (21)	–	20 (5
Trendafilova 2021	AA PB Fixed Patches	35	26 (74)	7 (17)	1 (3)	28 (80)	–	–	7 (20)	–	19 (5
Vardas 2000	Amiodarone	100	–	–	–	–	–	–	–	–	–
Vardas 2000	Placebo	108	–	–	–	–	–	–	–	–	–
Vijayalakshmi 2006	Amiodarone	27	–	–	–	–	–	–	–	–	–
Vijayalakshmi 2006	Placebo	31	–	–	–	–	–	–	–	–	–
Vijayalakshmi 2006	Sotalol	36	–	–	–	–	–	–	–	–	–
Vogiatzis 2009	AP MDS Incremental Patches	30	15 (50)	14 (46)	5 (16)	–	–	–	–	–	–
Vogiatzis 2009	AA MDS Incremental Patches	32	16 (50)	18 (56)	8 (25)	–	–	–	–	–	–
Vogiatzis 2017	Ibutilide	43	–	–	–	–	–	–	–	–	–
Vogiatzis 2017	Vernakalant	36	–	–	–	–	–	–	–	–	–
Volgman 1998	Ibutilide	60	–	–	–	–	–	–	–	–	–
Volgman 1998	Procainamide	60	–	–	–	–	–	–	–	–	–
Vos 1998	Ibutilide	211	–	82 (39)	17 (8)	–	–	–	–	–	–
Vos 1998	Sotalol	108	–	33 (31)	13 (12)	–	–	–	–	–	–
Voskoboinik 2018	AP/AA Biphasic Patches	63	11 (18)	0 (0)	0 (0)	–	–	–	–	–	–
Voskoboinik 2018	AP/AA Biphasic Paddles	62	7 (11)	0 (0)	0 (0)	–	–	–	–	–	–
Walsh 2005	AP BTE Incremental Patches	144	93 (59)	61 (39)	5 (3)	15 (10)	6 (4)	3 (2)	10 (6)	–	–
Walsh 2005	AA BTE Incremental Patches	150	89 (59)	63 (42)	7 (5)	14 (9)	5 (3)	3 (2)	10 (7)	–	–
Xanthos 2007	Amiodarone	113	–	–	–	–	–	–	–	–	–
Xanthos 2007	Procainamide	110	–	–	–	–	–	–	–	–	–
Yamase 2012	Amiodarone	20	8 (40)	8 (40)	6 (30)	–	–	–	–	–	9 (45
Yamase 2012	Bepridil	20	5 (25)	6 (30)	5 (25)	–	–	–	–	–	11 (5
Yamashita 2009	Bepridil	61	–	–	–	–	–	–	–	–	–
Yamashita 2009	Placebo	29	–	–	–	–	–	–	–	–	–
Yu 2013	Ibutilide	50	–	–	–	–	–	–	–	–	–
Yu 2013	Propafenone	49	–	–	–	–	–	–	–	–	–
Zehender 1994	Amiodarone	20	–	–	–	–	–	–	–	–	–
Zehender 1994	Quinidine	20	–	–	–	–	–	–	–	–	–
Zhang 2005	Ibutilide	107	–	–	–	–	–	–	–	–	–
Zhang 2005	Propafenone	105	–	–	–	–	–	–	–	–	–

Data given as mean (sd) or n (%). AP = Anteroposterior, AA = Anteroapical, BTE = Biphasic Truncated Exponential, RBW = Rectilinear Biphasic Waveform, MDS = Monophasic Damped Sinewave, PB = Pulsed Biphasic

Table 3

Baseline Characteristics - AF type and follow up duration

Study Identifier	Intervention	Numbers	Setting	Follow up periods IP	Longterm f/u	Arrhythmia <48h %	Paroxysmal AF %	Persistent AF %	Recurrent AF %	Atrial Flutte (%)
Abi Mansour 1998	Ibutilide	209	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	45 (22)
Abi Mansour 1998	Placebo	41	Hospital Setting: Not	24 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	12 (29)

			Clear							
Aliot 1996	Flecainide	48	Outpatient	Outpatient	12 months	Not provided	Not provided	Not provided	Not provided	4 (8)
Aliot 1996	Propafenone	49	Outpatient	Outpatient	12 months	Not provided	Not provided	Not provided	Not provided	4 (8)
Alp 2000	AA MDS Fixed Paddles	30	Elective Admission	Unclear end	Not provided	0 (0)	0 (0)	30 (100)	0 (0)	0 (0)
Alp 2000	AP MDS Fixed Paddles	29	Elective Admission	Unclear end	Not provided	0 (0)	0 (0)	29 (100)	0 (0)	0 (0)
Azpitarte 1997	Placebo	26	Accident and Emergency	24 hrs	Not provided	Not provided	6 (23)	Not provided	Not provided	0 (0)
Azpitarte 1997	Propafenone	29	Accident and Emergency	24 hrs	Not provided	Not provided	9 (31)	Not provided	Not provided	0 (0)
Balla 2011	Amiodarone	40	Accident and Emergency	24 hrs	Not provided	40 (100)	40 (100)	0 (0)	Not provided	0 (0)
Balla 2011	Flecainide	40	Accident and Emergency	24 hrs	Not provided	40 (100)	40 (100)	0 (0)	Not provided	0 (0)
Balla 2011	Placebo	40	Accident and Emergency	24 hrs	Not provided	40 (100)	40 (100)	0 (0)	Not provided	0 (0)
Balla 2011	Propafenone	40	Accident and Emergency	24 hrs	Not provided	40 (100)	40 (100)	0 (0)	Not provided	0 (0)
Baroffio 1995	Digoxin	25	Accident and Emergency	3 hrs	Not provided	Not provided	25 (100)	0 (0)	Not provided	0 (0)
Baroffio 1995	Propafenone	25	Accident and Emergency	3 hrs	Not provided	Not provided	25 (100)	0 (0)	Not provided	0 (0)
Baroni 2011	Amiodarone	30	Hospital Setting: Not Clear	24 hrs	Not provided	0 (0)	0 (0)	30 (100)	Not provided	0 (0)
Baroni 2011	Propafenone	30	Hospital Setting: Not Clear	24 hrs	Not provided	0 (0)	0 (0)	30 (100)	Not provided	0 (0)
Baroni 2011	Quinidine	30	Hospital Setting: Not Clear	24 hrs	Not provided	0 (0)	0 (0)	30 (100)	Not provided	0 (0)
Beatch 2016	Placebo	68	Hospital Setting: Not Clear	2 hrs	Not provided	44 (65)	68 (100)	0 (0)	Not provided	0 (0)
Beatch 2016	Vernakalant	129	Hospital Setting: Not Clear	2 hrs	Not provided	77 (67)	129 (100)	0 (0)	Not provided	0 (0)
Beatch 2017	Placebo	56	Hospital Setting: Not Clear	2 hrs	30 days	31 (55)	56 (100)	0 (0)	Not provided	0 (0)
Beatch 2017	Vernakalant	55	Hospital Setting: Not Clear	2 hrs	30 days	33 (60)	55 (100)	0 (0)	Not provided	0 (0)
Bellandi 1995	Placebo	84	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	84 (100)	0 (0)	Not provided	0 (0)
Bellandi 1995	Propafenone	98	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	98 (100)	0 (0)	Not provided	0 (0)
Bellone 2012	BTE Incremental	121	Accident and Emergency	6 hrs	60 days	121 (100)	121 (100)	0 (0)	Not provided	0 (0)
Bellone 2012	Propafenone	126	Accident and Emergency	6 hrs	60 days	126 (100)	126 (100)	0 (0)	Not provided	0 (0)
Bertini 1990	Amiodarone	15	Mobile CCU	120 mins	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Bertini 1990	Propafenone	24	Mobile CCU	120 mins	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Bianconi 1998	Placebo	82	Accident and Emergency	60 mins	Not provided	Not provided	82 (100)	0 (0)	Not provided	0 (0)
Bianconi 1998	Propafenone	41	Accident and Emergency	60 mins	Not provided	Not provided	41 (100)	0 (0)	Not provided	0 (0)
Bianconi 2000	Amiodarone	50	Hospital Setting: Not Clear	3 hrs	Not provided	9 (18)	Not provided	Not provided	Not provided	9 (18)
Bianconi 2000	Dofetilide	48	Hospital Setting: Not Clear	3 hrs	Not provided	7 (15)	Not provided	Not provided	Not provided	12 (25)
Bianconi 2000	Placebo	52	Hospital Setting: Not Clear	3 hrs	Not provided	7 (13)	Not provided	Not provided	Not provided	10 (19)
Blanc 1999	Amiodarone	43		48 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)

			Hospital Setting: Not Clear							
Blanc 1999	Propafenone	43	Hospital Setting: Not Clear	48 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Boriani 1997	Placebo	121	Hospital Setting: Not Clear	8 hrs	Not provided	Not provided	121 (100)	0 (0)	Not provided	0 (0)
Boriani 1997	Propafenone	119	Hospital Setting: Not Clear	8 hrs	Not provided	Not provided	119 (100)	0 (0)	Not provided	0 (0)
Botto 1999	AA MDS Incremental Patches	151	Elective Admission	10 seconds	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Botto 1999	AP MDS Incremental Patches	150	Elective Admission	10 seconds	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Bouida 2019	Magnesium	301	Accident and Emergency	4 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Bouida 2019	Placebo	149	Accident and Emergency	4 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Braždžionytė 2006	AA BTE Incremental Paddles	55	Elective Admission	30s	Not provided	22 (40)	Not provided	Not provided	Not provided	0 (0)
Braždžionytė 2006	AP BTE Incremental Paddles	48	Elective Admission	30s	Not provided	12 (25)	Not provided	Not provided	Not provided	0 (0)
Brodsky 1994	Magnesium	10	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	10 (100)	0 (0)	Not provided	0 (0)
Brodsky 1994	Placebo	8	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	8 (100)	0 (0)	Not provided	0 (0)
Camm 2011	Amiodarone	116	Accident and Emergency	4 hrs	Not provided	116 (100)	116 (100)	0 (0)	Not provided	0 (0)
Camm 2011	Vernakalant	116	Accident and Emergency	4 hrs	Not provided	116 (100)	116 (100)	0 (0)	Not provided	0 (0)
Camm 2012	Placebo	15	Hospital Setting: Not Clear	24 hrs	30 days	Not provided	0 (0)	0 (0)	0 (0)	15 (100
Camm 2012	Vernakalant	39	Hospital Setting: Not Clear	24 hrs	30 days	Not provided	0 (0)	0 (0)	0 (0)	39 (100
Channer 2004	Placebo	38	Outpatient	Outpatient	2 weeks	0 (0)	0 (0)	38 (100)	3 (8)	0 (0)
Channer 2004	Amiodarone	123	Outpatient	Outpatient	2 weeks	0 (0)	0 (0)	123 (100)	3 (2)	0 (0)
Chiladakis 2001	Magnesium	23	Accident and Emergency	6 hrs	Not provided	23 (100)	23 (100)	0 (0)	Not provided	0 (0)
Chiladakis 2001	Placebo	23	Accident and Emergency	6 hrs	Not provided	23 (100)	23 (100)	0 (0)	Not provided	0 (0)
Chu 2009	Magnesium	24	Hospital Setting: Not Clear	2 hrs	Not provided	24 (100)	24 (100)	0 (0)	Not provided	0 (0)
Chu 2009	Placebo	24	Hospital Setting: Not Clear	2 hrs	Not provided	24 (100)	24 (100)	0 (0)	Not provided	0 (0)
Cotter 1999	Amiodarone	50	Accident and Emergency	24 hrs	30 days	50 (100)	50 (100)	0 (0)	Not provided	0 (0)
Cotter 1999	Placebo	50	Accident and Emergency	24 hrs	30 days	50 (100)	50 (100)	0 (0)	Not provided	0 (0)
Cybulski 2003	Amiodarone	106	Coronary Care Unit	20 hrs	Not provided	106 (100)	106 (100)	0 (0)	Not provided	0 (0)
Cybulski 2003	Placebo	54	Coronary Care Unit	20 hrs	Not provided	5 (100)	5 (100)	0 (0)	Not provided	0 (0)
Davey 2005	Magnesium	95	Accident and Emergency	150 mins	Not provided	70 (69)	Not provided	Not provided	Not provided	0 (0)
Davey 2005	Placebo	91	Accident and Emergency	150 mins	Not provided	54 (56)	Not provided	Not provided	Not provided	0 (0)
Ellenbogen 1996	Ibutilide	157	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	20 (50)
Ellenbogen 1996	Placebo	40	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	78 (50)
Fak 1997	Placebo	30	Hospital Setting: Not	60 mins	Not provided	Not provided	Not provided	Not provided	Not provided	Not provide

			Clear							
Fak 1997	Propafenone	30	Hospital Setting: Not Clear	60 mins	Not provided	Not provided	Not provided	Not provided	Not provided	Not provide
Falk 1997	Dofetilide	61	Accident and Emergency	6 hrs	Not provided	0 (0)	0 (0)	50 (82)	Not provided	11 (18)
Falk 1997	Placebo	30	Accident and Emergency	6 hrs	Not provided	0 (0)	0 (0)	25 (83)	Not provided	5 (17)
Fresco 1996	Placebo	34	Hospital Setting: Not Clear	3 hrs	Not provided	Not provided	34 (100)	0 (0)	Not provided	0 (0)
Fresco 1996	Propafenone	41	Hospital Setting: Not Clear	3 hrs	Not provided	Not provided	41 (100)	0 (0)	Not provided	0 (0)
Galperín 2001	Amiodarone	47	Outpatient	Outpatient	4 weeks	0 (0)	0 (0)	47 (100)	Not provided	0 (0)
Galperín 2001	Placebo	48	Outpatient	Outpatient	4 weeks	0 (0)	0 (0)	48 (100)	Not provided	0 (0)
Ganau 1998	Placebo	75	Accident and Emergency	Unclear end	Not provided	Not provided	75 (100)	0 (0)	Not provided	0 (0)
Ganau 1998	Propafenone	81	Accident and Emergency	Unclear end	Not provided	Not provided	81 (100)	0 (0)	Not provided	0 (0)
Halinen 1995	Quinidine	28	Elective Admission	12 hrs	Not provided	28 (100)	28 (100)	0 (0)	Not provided	0 (0)
Halinen 1995	Sotalol	33	Elective Admission	12 hrs	Not provided	33 (100)	33 (100)	0 (0)	Not provided	0 (0)
Hohnloser 1995	Quinidine	25	Hospital Setting: Not Clear and Outpatient	2 hrs then daily until day 7 or conversion	6 months	0 (0)	Not provided	Not provided	Not provided	0 (0)
Hohnloser 1995	Sotalol	25	Hospital Setting: Not Clear and Outpatient	2 hrs then daily until day 7 or conversion	6 months	0 (0)	Not provided	Not provided	Not provided	0 (0)
Jakobsson 1990	AA MDS Incremental Paddles	11	Elective Admission	24 hrs	Not provided	0 (0)	0 (0)	11 (100)	Not provided	0 (0)
Jakobsson 1990	AA MDS Incremental Patches	15	Elective Admission	24 hrs	Not provided	0 (0)	0 (0)	15 (100)	Not provided	0 (0)
Joseph 2000	Amiodarone	39	Accident and Emergency	48 hrs	Not provided	39 (100)	39 (100)	0 (0)	0 (0)	0 (0)
Joseph 2000	Placebo	36	Accident and Emergency	48 hrs	Not provided	36 (100)	36 (100)	0 (0)	0 (0)	0 (0)
Joseph 2000	Sotalol	40	Accident and Emergency	48 hrs	Not provided	40 (100)	40 (100)	0 (0)	0 (0)	0 (0)
Kanoupakis 2003	Amiodarone	48	Outpatient	Outpatient	2 weeks	0 (0)	0 (0)	48 (100)	Not provided	0 (0)
Kanoupakis 2003	Placebo	94	Outpatient	Outpatient	2 weeks	0 (0)	0 (0)	94 (100)	Not provided	0 (0)
Khaykin 2003	AP MDS Maximum Patches	28	Elective Admission	Not provided	Not provided	0 (0)	0 (0)	28 (100)	Not provided	0 (0)
Khaykin 2003	AP BTE Incremental Patches	28	Elective Admission	Not provided	Not provided	0 (0)	0 (0)	28 (100)	Not provided	0 (0)
Kim 2003	AP BTE Incremental Patches	74	Hospital Setting: Not Clear	5s	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Kim 2003	AP RBW Incremental Patches	71	Hospital Setting: Not Clear	5s	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Kirchhof 2005	AP BTE Incremental Paddles/Patches	104	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	104 (100)	Not provided	0 (0)
Kirchhof 2005	AP MDS Incremental Paddles/Patches	97	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	97 (100)	Not provided	0 (0)
Kochiadakis 1998	Placebo	57	Elective Admission	1hr	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Kochiadakis 1998	Procainamide	57	Elective Admission	1hr	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Kochiadakis 1998a	Amiodarone	46	Hospital Setting: Not Clear	24 hrs	Not provided	46 (100)	46 (100)	0 (0)	Not provided	0 (0)
	Placebo	49		24 hrs		49 (100)	49 (100)	0 (0)		0 (0)

Kochiadakis 1998a			Hospital Setting: Not Clear		Not provided				Not provided	
Kochiadakis 1998a	Propafenone	48	Hospital Setting: Not Clear	24 hrs	Not provided	48 (100)	48 (100)	0 (0)	Not provided	0 (0)
Kochiadakis 1999	Amiodarone	34	Accident and Emergency or Elective	24 hrs	30 days	0 (0)	0 (0)	34 (100)	Not provided	0 (0)
Kochiadakis 1999	Placebo	33	Accident and Emergency or Elective	24 hrs	30 days	0 (0)	0 (0)	33 (100)	Not provided	0 (0)
Kochiadakis 1999a	Amiodarone	34	Accident and Emergency or Elective	24 hrs	30 days	0 (0)	0 (0)	34 (100)	Not provided	0 (0)
Kochiadakis 1999a	Placebo	35	Accident and Emergency or Elective	24 hrs	30 days	0 (0)	0 (0)	35 (100)	Not provided	0 (0)
Kochiadakis 1999a	Propafenone	32	Accident and Emergency or Elective	24 hrs	30 days	0 (0)	0 (0)	32 (100)	Not provided	0 (0)
Kochiadakis 2007	Amiodarone	92	Accident and Emergency	24 hrs	Not provided	92 (100)	92 (100)	0 (0)	Not provided	0 (0)
Kochiadakis 2007	Placebo	90	Accident and Emergency	24 hrs	Not provided	90 (100)	90 (100)	0 (0)	Not provided	0 (0)
Kochiadakis 2007	Procainamide	89	Accident and Emergency	24 hrs	Not provided	89 (100)	89 (100)	0 (0)	Not provided	0 (0)
Kochiadakis 2007	Propafenone	91	Accident and Emergency	24 hrs	Not provided	91 (100)	91 (100)	0 (0)	Not provided	0 (0)
Kosior 2009	Propafenone	46	Accident and Emergency	24 hrs	Not provided	46 (100)	46 (100)	0 (0)	Not provided	0 (0)
Kosior 2009	Quinidine	35	Accident and Emergency	24 hrs	Not provided	35 (100)	35 (100)	0 (0)	Not provided	0 (0)
Koster 2004	AA BTE Incremental Patches	35	Elective Admission	1 min	Not provided	8 (23)	Not provided	Not provided	Not provided	0 (0)
Koster 2004	AA MDS Incremental Patches	37	Elective Admission	1 min	Not provided	9 (24)	Not provided	Not provided	Not provided	0 (0)
Kühlkamp 1991	Cibenzoline	28	Hospital Setting: Not Clear	5 days	5 days	0 (0)	0 (0)	28 (100)	Not provided	0 (0)
Kühlkamp 1991	Flecainide	23	Hospital Setting: Not Clear	5 days	5 days	0 (0)	0 (0)	23 (100)	Not provided	0 (0)
Kumagai 2000	Disopyramide	32	Hospital Setting: Not Clear	120 mins	Not provided	32 (100)	32 (100)	0 (0)	Not provided	0 (0)
Kumagai 2000	Pilsicainide	40	Hospital Setting: Not Clear	120 mins	Not provided	40 (100)	40 (100)	0 (0)	Not provided	0 (0)
Lindeboom 2000	Dofetilide	51	Hospital Setting: Not Clear	60 mins	Not provided	Not provided	14 (27)	30 (59)	Not provided	7 (14)
Lindeboom 2000	Placebo	18	Hospital Setting: Not Clear	60 mins	Not provided	Not provided	4 (22)	11 (61)	Not provided	3 (17)
Maciag 2017	Antazoline	36	Accident and Emergency	90 mins	Not provided	36 (100)	36 (100)	0 (0)	Not provided	0 (0)
Maciag 2017	Control	38	Accident and Emergency	90 mins	Not provided	38 (100)	38 (100)	0 (0)	Not provided	0 (0)
Madrid 1993	Flecainide	40	Hospital Setting: Not Clear	60 mins	Not provided	40 (100)	40 (100)	0 (0)	Not provided	0 (0)
Madrid 1993	Procainamide	40	Hospital Setting: Not Clear	60 mins	Not provided	40 (100)	40 (100)	0 (0)	Not provided	0 (0)
Mannegold 2007	AP MDS Incremental Paddles	21	Hospital Setting: Not Clear	1hr	1 week	Not provided	Not provided	Not provided	Not provided	0 (0)
Mannegold 2007	AP RBW Incremental Paddles	23	Hospital Setting: Not Clear	1hr	1 week	Not provided	Not provided	Not provided	Not provided	0 (0)
Martínez-Marcos 2000	Amiodarone	50	Accident and Emergency	12 hrs	Not provided	50 (100)	50 (100)	0 (0)	Not provided	0 (0)
	Flecainide	50		12 hrs		50 (100)	50 (100)	0 (0)		0 (0)

Martínez-Marcos 2000			Accident and Emergency		Not provided				Not provided	
Martínez-Marcos 2000	Propafenone	50	Accident and Emergency	12 hrs	Not provided	50 (100)	50 (100)	0 (0)	Not provided	0 (0)
Mattioli 1998	Propafenone	38	Hospital Setting: Not Clear	48 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	Not provide
Mattioli 1998	Procainamide	38	Hospital Setting: Not Clear	48 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	Not provide
Mittal 2000	AP MDS Incremental Patches	82	Elective Admission	30s	Not provided	15 (17)	Not provided	Not provided	Not provided	0 (0)
Mittal 2000	AP RBW Incremental Patches	104	Elective Admission	30s	Not provided	15 (19)	Not provided	Not provided	Not provided	0 (0)
Mortensen 2007	AP MDS Incremental Patches	47	Hospital Setting: Not Clear	30s	Not provided	19 (41)	0 (0)	0 (0)	0 (0)	47 (100
Mortensen 2007	AP RBW Incremental Patches	48	Hospital Setting: Not Clear	30s	Not provided	21 (44)	0 (0)	0 (0)	0 (0)	48 (100
Muñoz-Martínez 2010	AA BTE Incremental Patches	46	Referral to ICU for Cardioversion	Acute outcome	Not provided	Not provided	Not provided	Not provided	Not provided	Not provide
Muñoz-Martínez 2010	AP BTE Incremental Patches	45	Referral to ICU for Cardioversion	Acute outcome	Not provided	Not provided	Not provided	Not provided	Not provided	Not provide
Negrini 1994	Amiodarone	30	Accident and Emergency	24 hrs	Not provided	Not provided	30 (100)	0 (0)	Not provided	0 (0)
Negrini 1994	Propafenone	31	Accident and Emergency	24 hrs	Not provided	Not provided	31 (100)	0 (0)	Not provided	0 (0)
Neumann 2004	AP BTE Incremental Patches	57	Elective Admission	Not provided	Not provided	0 (0)	0 (0)	57 (100)	Not provided	0 (0)
Neumann 2004	AP MDS Incremental Patches	61	Elective Admission	Not provided	Not provided	0 (0)	0 (0)	61 (100)	Not provided	0 (0)
Noc 1990	Amiodarone	13	Hospital Setting: Not Clear	3 hrs	Not provided	13 (100)	13 (100)	0 (0)	Not provided	0 (0)
Noc 1990	Placebo	11	Hospital Setting: Not Clear	3 hrs	Not provided	11 (100)	11 (100)	0 (0)	Not provided	0 (0)
Nogic 2022	Magnesium	71	Accident and Emergency	2 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Nogic 2022	Placebo	73	Accident and Emergency	2 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Norgaard 1999	Dofetilide	66	Hospital Setting: Not Clear	3 hrs	Not provided	Not provided	14 (21)	Not provided	Not provided	11 (17)
Norgaard 1999	Placebo	30	Hospital Setting: Not Clear	3 hrs	Not provided	Not provided	6 (20)	Not provided	Not provided	6 (20)
Okishige 2000	Pilsicainide	52	Outpatient	Outpatient	4 weeks	0 (0)	0 (0)	51 (100)	Not provided	0 (0)
Okishige 2000	Placebo	10	Outpatient	Outpatient	4 weeks	0 (0)	0 (0)	10 (100)	Not provided	0 (0)
Okishige 2006	Pilsicainide	58	Outpatient	Outpatient	2 weeks	0 (0)	Not provided	Not provided	Not provided	0 (0)
Okishige 2006	Placebo	50	Outpatient	Outpatient	2 weeks	0 (0)	Not provided	Not provided	Not provided	0 (0)
Page 2002	AP BTE Incremental	107	Elective Admission	30s	Not provided	11 (10)	Not provided	Not provided	Not provided	0 (0)
Page 2002	AP MDS Incremental	96	Elective Admission	30s	Not provided	10 (10)	Not provided	Not provided	Not provided	0 (0)
Pratt 2010	Placebo	134	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	86 (64)	37 (28)	Not provided	0 (0)
Pratt 2010	Vernakalant	131	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	84 (64)	32 (24)	Not provided	0 (0)
Rajagopalan 2014	Magnesium	132	Elective Admission	1hr	Not provided	Not provided	18 (14)	114 (86)	28 (21)	0 (0)
Rajagopalan 2014	Placebo	129	Elective Admission	1hr	Not provided	Not provided	21 (16)	108 (84)	27 (21)	0 (0)

Reisinger 1998	Sotalol	52	Hospital Setting: Not Clear	2 hrs	Not provided	36 (69)	42 (81)	10 (19)	Not provided	0 (0)
Reisinger 1998	Flecainide	54	Hospital Setting: Not Clear	2 hrs	Not provided	34 (65)	44 (82)	10 (18)	Not provided	0 (0)
Reisinger 2004	Ibutilide	106	Accident and Emergency	90 mins	Not provided	106 (100)	106 (100)	0 (0)	72 (68)	0 (0)
Reisinger 2004	Flecainide	101	Accident and Emergency	90 mins	Not provided	101 (100)	101 (100)	0 (0)	54 (54)	0 (0)
Ricard 2001	AA BTE Fixed Patches	30	Hospital Setting: Not Clear	5 min	Not provided	0 (0)	2 (7)	28 (93)	Not provided	0 (0)
Ricard 2001	AA MDS Incremental Patches	27	Hospital Setting: Not Clear	5 min	Not provided	0 (0)	2 (7)	25 (93)	Not provided	0 (0)
Risius 2009	AA RBW Incremental Patches	48	Outpatient, Accident and Emergency, Inpatient and Intensive Care	30s	Not provided	24 (50)	0 (0)	0 (0)	0 (0)	48 (100
Risius 2009	AP RBW Incremental Patches	48	Outpatient, Accident and Emergency, Inpatient and Intensive Care	30s	Not provided	24 (50)	0 (0)	0 (0)	0 (0)	48 (100
Romano 2001	Propafenone	164	Accident and Emergency	24 hrs	Not provided	Not provided	164 (100)	0 (0)	Not provided	0 (0)
Romano 2001	Flecainide	138	Accident and Emergency	24 hrs	Not provided	Not provided	138 (100)	0 (0)	Not provided	0 (0)
Roy 2004	Placebo	20	Hospital Setting: Not Clear	1hr	7 days	Not provided	Not provided	Not provided	Not provided	0 (0)
Roy 2004	Vernakalant	36	Hospital Setting: Not Clear	1hr	7 days	Not provided	Not provided	Not provided	Not provided	0 (0)
Roy 2008	Placebo	115	Elective Admission	24 hrs	Not provided	61 (53)	75 (65)	40 (35)	Not provided	0 (0)
Roy 2008	Vernakalant	221	Elective Admission	24 hrs	Not provided	103 (47)	145 (66)	76 (34)	Not provided	0 (0)
Satullo 1996a	Propafenone	42	Hospital Setting: Not Clear	Unclear end (max 3 days)	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Satullo 1996a	Quinidine	38	Hospital Setting: Not Clear	Unclear end (max 3 days)	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Scheuermeyer 2019	BTE Incremental	43	Accident and Emergency	2 hrs	Not provided	43 (100)	43 (100)	0 (0)	22 (51)	0 (0)
Scheuermeyer 2019	Procainamide	41	Accident and Emergency	2 hrs	Not provided	41 (100)	41 (100)	0 (0)	21 (54)	0 (0)
Schmidt 2017	AP BTE Incremental Patches	65	Elective Admission	4 hrs	Not provided	0 (0)	Not provided	Not provided	Not provided	0 (0)
Schmidt 2017	AP PB Incremental Patches	69	Elective Admission	4 hrs	Not provided	0 (0)	Not provided	Not provided	Not provided	0 (0)
Schmidt 2019	AP BTE Incremental Patches	147	Elective Admission	4 hrs	Not provided	0 (0)	0 (0)	147 (100)	Not provided	0 (0)
Schmidt 2019	AP BTE Maximum Patches	129	Elective Admission	4 hrs	Not provided	0 (0)	0 (0)	129 (100)	Not provided	0 (0)
Schmidt 2021	AP BTE Incremental Patches	234	Outpatient, Accident and Emergency, Inpatient and Intensive Care	2 hrs	Not provided	Not provided	51 (22)	183 (78)	Not provided	0 (0)
Schmidt 2021	AA BTE Incremental Patches	233	Outpatient, Accident and Emergency, Inpatient and Intensive Care	2 hrs	Not provided	Not provided	42 (18)	191 (82)	Not provided	0 (0)
		108		1 min		0 (0)	0 (0)	108 (100)	0 (0)	0 (0)

Siaplaouras 2004	AP MDS Incremental Patches		Elective Admission		Not provided					
Siaplaouras 2004	AP RBW Incremental Patches	108	Elective Admission	1 min	Not provided	0 (0)	0 (0)	108 (100)	0 (0)	0 (0)
Siaplaouras 2005	AP RBW Incremental Patches	60	Elective Admission	1 min	Not provided	0 (0)	0 (0)	60 (100)	0 (0)	0 (0)
Siaplaouras 2005	AA RBW Incremental Patches	63	Elective Admission	1 min	Not provided	0 (0)	0 (0)	63 (100)	0 (0)	0 (0)
Simon 2017	Ibutilide	51	Accident and Emergency	2 hrs	Not provided	51 (100)	21 (41)	30 (59)	7 (14)	0 (0)
Simon 2017	Vernakalant	49	Accident and Emergency	2 hrs	Not provided	49 (100)	33 (59)	16 (41)	2 (4)	0 (0)
Singh 2000	Dofetilide	241	Hospital Setting: Not Clear and Outpatient	24 hrs	12 months	0 (0)	0 (0)	210 (87)	Not provided	31 (12)
Singh 2000	Placebo	84	Hospital Setting: Not Clear and Outpatient	24 hrs	12 months	0 (0)	0 (0)	67 (80)	Not provided	17 (20)
Singh 2005	Placebo	137	Outpatient	Outpatient	12 months	0 (0)	0 (0)	137 (100)	Not provided	0 (0)
Singh 2005	Amiodarone	267	Outpatient	Outpatient	12 months	0 (0)	0 (0)	267 (100)	Not provided	0 (0)
Singh 2005	Sotalol	261	Outpatient	Outpatient	12 months	0 (0)	0 (0)	261 (100)	Not provided	0 (0)
Squara 2021	Active compression AP BTE Incremental Patches	50	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	50 (100)	Not provided	0 (0)
Squara 2021	AP BTE Incremental Patches	50	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	50 (100)	Not provided	0 (0)
Stambler 1996	Ibutilide	161	Hospital Setting: Not Clear	90 mins	Not provided	Not provided	37 (23)	44 (27)	Not provided	80 (50)
Stambler 1996	Placebo	81	Hospital Setting: Not Clear	90 mins	Not provided	Not provided	Not provided	Not provided	Not provided	41 (51)
Stanaitienė 2008	AP/AA BTE Incremental	112	Hospital Setting: Not Clear	30s	Not provided	36 (32)	Not provided	Not provided	44 (40)	0 (0)
Stanaitienė 2008	AP/AA MDS Incremental	112	Hospital Setting: Not Clear	30s	Not provided	30 (27)	Not provided	Not provided	44 (50)	0 (0)
Stroobandt 1997	Placebo	35	Hospital Setting: Not Clear and Outpatient	48 hrs	6 months	Not provided	14 (40)	21 (60)	Not provided	0 (0)
Stroobandt 1997	Propafenone	101	Hospital Setting: Not Clear and Outpatient	48 hrs	6 months	Not provided	49 (49)	52 (51)	Not provided	0 (0)
Sun 2005	Ibutilide	20	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	0 (0)	0 (0)	0 (0)	20 (100
Sun 2005	Propafenone	20	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	0 (0)	0 (0)	0 (0)	20 (100
Suttorp 1989	Flecainide	20	Hospital Setting: Not Clear	60 mins	Not provided	Not provided	Not provided	Not provided	Not provided	3 (15)
Suttorp 1989	Placebo	20	Hospital Setting: Not Clear	60 mins	Not provided	Not provided	Not provided	Not provided	Not provided	3 (15)
Suttorp 1990	Flecainide	25	Hospital Setting: Not Clear	60 mins	Not provided	Not provided	Not provided	Not provided	Not provided	5 (20)
Suttorp 1990	Propafenone	25	Hospital Setting: Not Clear	60 mins	Not provided	Not provided	Not provided	Not provided	Not provided	5 (20)
Taha 2022	Amiodarone	100	Hospital Setting: Not	24 hrs	Not provided	100 (100)	100 (100)	0 (0)	Not provided	0 (0)

			Clear							
Taha 2022	Propafenone	100	Hospital Setting: Not Clear	24 hrs	Not provided	100 (100)	100 (100)	0 (0)	Not provided	0 (0)
Thomas 2004	Amiodarone	52	Accident and Emergency	12 hrs	Not provided	41 (79)	Not provided	Not provided	Not provided	0 (0)
Thomas 2004	Placebo	43	Accident and Emergency	12 hrs	Not provided	33 (77)	Not provided	Not provided	Not provided	0 (0)
Thomas 2004	Sotalol	45	Accident and Emergency	12 hrs	Not provided	39 (87)	Not provided	Not provided	Not provided	0 (0)
Treglia 1994a	Amiodarone	27	Referral to ICU for Cardioversion	48 hrs	Not provided	Not provided	27 (100)	0 (0)	Not provided	0 (0)
Treglia 1994a	Propafenone	27	Referral to ICU for Cardioversion	48 hrs	Not provided	Not provided	27 (100)	0 (0)	Not provided	0 (0)
Trendafilova 2021	AA BTE Fixed Patches	38	Referral to ICU for Cardioversion	2 hrs	Not provided	Not provided	Not provided	17 (45)	Not provided	0 (0)
Trendafilova 2021	AA PB Fixed Patches	35	Referral to ICU for Cardioversion	2 hrs	Not provided	Not provided	Not provided	43 (15)	Not provided	0 (0)
Vardas 2000	Amiodarone	100	Accident and Emergency or Clinic	24 hrs	30 days	49 (49)	unclear	unclear	Not provided	0 (0)
Vardas 2000	Placebo	108	Accident and Emergency or Clinic	24 hrs	30 days	57 (53)	unclear	unclear	Not provided	0 (0)
Vijayalakshmi 2006	Amiodarone	27	Outpatient	Outpatient	6 weeks	0 (0)	0 (0)	27 (100)	Not provided	0 (0)
Vijayalakshmi 2006	Placebo	31	Outpatient	Outpatient	6 weeks	0 (0)	0 (0)	31 (100)	Not provided	0 (0)
Vijayalakshmi 2006	Sotalol	36	Outpatient	Outpatient	6 weeks	0 (0)	0 (0)	36 (100)	Not provided	0 (0)
Vogiatzis 2009	AP MDS Incremental Patches	30	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	30 (100)	Not provided	0 (0)
Vogiatzis 2009	AA MDS Incremental Patches	32	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	32 (100)	Not provided	0 (0)
Vogiatzis 2017	Ibutilide	43	Hospital Setting: Not Clear	2 hrs	7 days	42 (100)	42 (100)	0 (0)	Not provided	0 (0)
Vogiatzis 2017	Vernakalant	36	Hospital Setting: Not Clear	2 hrs	7 days	36 (100)	36 (100)	0 (0)	Not provided	0 (0)
Volgman 1998	Ibutilide	60	Hospital Setting: Not Clear	90 mins	Not provided	Not provided	Not provided	Not provided	Not provided	20 (33)
Volgman 1998	Procainamide	60	Hospital Setting: Not Clear	90 mins	Not provided	Not provided	Not provided	Not provided	Not provided	20 (33)
Vos 1998	Ibutilide	211	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	36 (17)
Vos 1998	Sotalol	108	Hospital Setting: Not Clear	24 hrs	Not provided	Not provided	Not provided	Not provided	Not provided	21 (19)
Voskoboinik 2018	AP/AA Biphasic Patches	63	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	63 (100)	Not provided	0 (0)
Voskoboinik 2018	AP/AA Biphasic Paddles	62	Elective Admission	Acute outcome	Not provided	0 (0)	0 (0)	62 (100)	Not provided	0 (0)
Walsh 2005	AP BTE Incremental Patches	144	Elective Admission	30s	Not provided	Not provided	5 (3)	58 (40)	37 (26)	0 (0)
Walsh 2005	AA BTE Incremental Patches	150	Elective Admission	30s	Not provided	Not provided	3 (2)	63 (42)	35 (23)	0 (0)
Xanthos 2007	Amiodarone	113	Acute Cardiology Deparment	24 hrs	Not provided	113 (100)	113 (100)	0 (0)	Not provided	0 (0)
Xanthos 2007	Procainamide	110	Acute Cardiology Deparment	24 hrs	Not provided	110 (100)	110 (100)	0 (0)	Not provided	0 (0)
Yamase 2012	Amiodarone	20	Outpatient	Outpatient	3 months	0 (0)	0 (0)	20 (100)	Not provided	0 (0)

Yamase 2012	Bepridil	20	Outpatient	Outpatient	3 months	0 (0)	0 (0)	20 (100)	Not provided	0 (0)
Yamashita 2009	Bepridil	61	Outpatient	Outpatient	12 weeks	0 (0)	0 (0)	61 (100)	Not provided	0 (0)
Yamashita 2009	Placebo	29	Outpatient	Outpatient	12 weeks	0 (0)	0 (0)	29 (100)	Not provided	0 (0)
Yu 2013	Ibutilide	50	Hospital Setting: Not Clear	90 mins	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Yu 2013	Propafenone	49	Hospital Setting: Not Clear	90 mins	Not provided	Not provided	Not provided	Not provided	Not provided	0 (0)
Zehender 1994	Amiodarone	20	Hospital Setting: Not Clear and Outpatient	15 days	Not provided	0 (0)	0 (0)	20 (100)	Not provided	0 (0)
Zehender 1994	Quinidine	20	Hospital Setting: Not Clear and Outpatient	6 days	Not provided	0 (0)	0 (0)	20 (100)	Not provided	0 (0)
Zhang 2005	Ibutilide	107	Elective Admission	48 hrs	30 days	Not provided	Not provided	Not provided	Not provided	0 (0)
Zhang 2005	Propafenone	105	Elective Admission	48 hrs	30 days	Not provided	Not provided	Not provided	Not provided	0 (0)

Data given as mean (sd) or n (%). AP = Anteroposterior, AA = Anteroapical, BTE = Biphasic Truncated Exponential, RBW = Rectilinear Biphasic Waveform, MDS = Monophasic Damped Sinewave, PB = Pulsed Biphasic

Table 4

Efficacy of cardioversion strategies in sustained atrial arrhythmias: Maintenance of sinus rhythm until hospital discharge or end of study follow-up

	Paroxysmal AF		Persistent AF		Atrial Flutter	
Amiodarone	5.2% at 90min Camm 2011 14% at 1h Martinez-Marcos 2000 22.6% at 3h Cybulski 2003 76.9% at 3h Noc 1990 76.9% at 48h Joseph 2000	81.4% at 24h Xanthos 2007 83.3% at 24h Kochiadakis 1998a 85% at 24h Balla 2011 89.1% at 24h Kochiadakis 2007 92% at 24h Cotter 1999	6.25% at 4 weeks Kanoupakis 2003 10% at 3 days Zehender 1994 20% at 24h Baroni 2011 21.1% at 2 weeks Channer 2004 25.9% at 6 weeks Vijayalakshmi 2006	27.1% at 28 days Singh 2005 34.0% at 4 weeks Galperin 2001 35.0% at 3 months Yamase 2012 47% at 30 days Kochiadakis 1999a 60% at 14 days Zehender 1994	-	-
Antazoline	72.7% at 90min Maciag 2017	-	-	-	-	-
Bepridil	-	-	52.5% at 3 months Yamashita 2009	85% at 3 months Yamase 2012	-	-
Cibenzoline	-	-	36.8% at 9 days Kuhlkamp 1991	-	-	-
Disopyramide	56.3% at 2h Kumagai 2000	-	-	-	-	-
Dofetilide	-	-	21.3% at 6h Falk 1997	-	54.5% at 6h Falk 1997	63.6% at 3h Noorgard 1999 71.4% at 2h Lindeboom 2000
Ibutilide	52.4% at 90min Vogziatis 2017	53% at 90min Reisinger 2004	-	-	60% at 90min Abi-Mansour 1998 62.5% at 90min Stambler 1996	63.9% at 1h Vos 1998 75% at 90min Volgman 1998 90% at 90min Sun 2005
Flecainide	56.4% at 90min Reisinger 2004 72.5% at 60min Romano 2001 87.5% at 24h Balla 2011	90% at 12h Martinez-Marcos 2000 92.5% at 60min Madrid 1993	25% at 9 days Kuhlkamp 1991	-	0% at 1h Suttorp 1989	20% at 1h Suttorp 1990

Magnesium	8.7% at 2h Chu 2009	57% at 6h Chiladakis 2001	-	-	-	-
Quinidine	35.7% at 3h 86% at 12h Halinen 1995	52.6% at 8h 91.4% at 24h Kosior 2009	25% after 3 days Zehender 1994 53% at 24h Baroni 2011	80% after 7 days Zehender 1994	-	-
Pilsicainide	72.5% at 2h Kumagai 2000	-	21.2% at 4 weeks Okishige 2000	-	-	-
Placebo	0% at 90min Maciag 2017 0% at 3h Noc 1990 22% at 6h Chiladakis 2001 17.5% at 24h Balla 2011 25% at 2h Chu 2009 45.5% at 24h Roy 2004	55.1% at 24h Kochiadakis 1998a 58.3% at 48h Joseph 2000 61.1% at 24h Kochiadakis 2007 64% at 24h Cotter 1999	0% at 6h Falk 1997 0% at 2 weeks Channer 2004 0% at 4 weeks Okishige 2000 0% at 6 weeks Vijayalakshmi 2006	0% at 4 weeks Galperin 2001 0% at 30 days Kochiadakis 1999a 0.8% at 28 days Singh 2005 2.1% at 4 weeks Kanoupakis 2003 3.4% at 7 days Yamashita 2009	0% at 90 min Camm 2012 0% at 2h Lindeboom 2000 0% at 90min Abi-Mansour 1998	Noorgard 3.3% at 3h Noorgard 1999 0 at 6h Falk 1997 2.4% at 90min Stambler 1996
Procainamide	53.7 at 2h Scheuermeyer 2019 62.5% at 1h Madrid 1993	68.5% at 24h Kochiadakis 2007 82.7% at 24h Xanthos 2007	-	-	15% at 90min Volgman 1998	-
Propafenone	41.9% at 1h Negrini 1994 45.4% at 3h Boriani 1997 48.8% at 1h Bianconi 1998 58.5% at 3h Fresco 1996 72% at 12h Martinez-Marcos 2000	73.8% at 6h Bellone 2012 78.2% at 24h Kochiadakis 1998a 80.2% at 24h Kochiadakis 2007 85% at 24h Balla 2011 88% at 3h Baroffio 1995 90.7% at 24h Kosior 2009	20% at 24h Baroni 2011	40.6% at 30 days Kochiadakis 1999a	30% at 90 min Sun 2005	40% at 1h Suttorp 1990
Sotalol	52% at 18h Halinen 1995	87.5% at 48h Joseph 2000	19.4% at 6 weeks Vijayalakshmi 2006	24.2% at 28 days Singh 2005	19.0% at 1h Vos 1998	-
Vernakalant	36.1% at 60min Roy 2004 45.7% at 90 min Beatch 2016 51.7% at 90min Camm 2011 52.7% at 90 min Beatch 2017	52.8% at 90min Vogziatis 2017 69.6% at 24h Roy 2004 74.5% at 24h Beatch 2017	-	-	3% at 90 min Camm 2012	-
BTE active-compression AP patches	-	-	96.0% with 200J Squara 2021	-	-	-
BTE/PB fixed AA patches	-	-	94.3% with 200J PB 97.4% with 200J BTE Trendafilova 2021	-	-	-
BTE Incremental AA/AP patches	88.4% with 200J Scheuermeyer 2019	-	-	-	-	-
BTE/RBW incremental AA patches	-	-	62.5% with 200J BTE Voskoboinik 2018 95.2% with 200J RBW Siaplaouras	96.9% with 360J BTE Vogiatzis 2009	97.9% with 200J RBW Risius 2009	-

			2005				
BTE/RBW incremental AP patches	89.3% with 200J BTE Bellone 2012	-	61% with 360J BTE Khaykin 2003 66% with 360J BTE Schmidt 2019 74.2% with 200J BTE Voskoboinik 2018 84.0% with 200J BTE Squara 2021	94.3% with 360J RBW Siaplaouras 2004 94.9% with 200J RBW Siaplaouras 2005 95.8% with 360J BTE Kirchhof 2005 100% with 360J BTE Vogiatzis 2009 100% with 360J BTE Neumann 2004	97.9% with 200J RBW Risius 2009	100% with 200J RBW Mortensen 2007
BTE Incremental handheld paddles	-	-	90% with 200J AP Voskoboinik 2018 90.6% with 200J AA Voskoboinik 2018	100% with 360J AP Kirchhof 2005	-	-
BTE maximum fixed AP patches	-	-	88% with 360J Schmidt 2019	-	-	-
Monophasic incremental AP patches	-	-	73.7% with 360J Neumann 2004	79.6% with 360J Kirchhof 2005 96.8% with 360J Siaplaouras 2004	100% with 360J Mortensen 2007	-
Monophasic incremental AP paddles	-	-	91.7% with 360J Kirchhof 2005	-	-	-
Monophasic single-shock handheld AA paddles	-	-	60% with 360J Alp 2000	-	-	-
Monophasic single-shock handheld AP paddles	-	-	18% with 360J Khaykin 2003	34.5% with 360J Alp 2000	-	-

AA - anteroapical, AP - anteroposterior, BTE - biphasic trunkated exponential, PB - pulsed biphasic, RBW - rectilinear biphasic waveform.

Table 5

Cardioversion for Paroxysmal Atrial Fibrillation - Efficacy Outcomes Data

Study	Intervention	Route	Sample Size	SR until discharge of end of FUP, n	Acute Procedural Success, n	RR SR until discharge of end of FUP, 95%CI	RR Acute Procedural Success, 95%CI	Follow up periods IP	Longterm FUP
Balla 2011	Flecainide	Oral	40	35	29	5 (2.53-9.90)	7.25 (2.81-18.73)	3, 6, 12, 24h	NA
	Amiodarone	Oral	40	34	23	3.86 (2.45-9.64)	5.75 (2.19-15.12)		
	Propafenone	Oral	40	34	29	3.86 (2.45-9.64)	7.25 (2.81-18.73)		
	Placebo	Oral	40	7	4	Ref	Ref		
Baroffio 1995	Propafenone	Intravenous	25	22	22	2.75 (1.53-4.96)	2.75 (1.53-4.96)	3h	NA
	Placebo	Intravenous	25	8	8				
Beatch 2016	Vernakalant	Intravenous	129	56	59	29.52 (4.18, 208.62)	31.10 (4.40-219.60)	90 min, 24h	NA
	Placebo	Intravenous	68	1	1				
Beatch 2017	Vernakalant	Intravenous	55	41	29	1.10 (0.87-1.39)	4.22 (2.02-8.81)	90 min, 24h	10 days
	Placebo	Intravenous	56	38	7				
Bellandi 1995	Propafenone	Intravenous	98	89	89	2.83 (2.06-3.88)	2.83 (2.06-3.88)	every 10 mins and 24h	NA
	Placebo	Intravenous	84	27	27				
Bellone 2012	AP BTE Incremental		121	108	108	1.21 (1.07-1.36)	1.21 (1.07-1.36)	6h	60d
	Propafenone	Intravenous	126	93	93				
Bianconi 1998	Propafenone	Intravenous	41	20	20	2.11 (1.27-3.48)	2.11 (1.27-3.48)	1h	NA
	Placebo	Intravenous	82	19	19				
Boriani 1997	Propafenone	Oral	119	91	54	2.06 (1.60-2.65)	2.50 (1.63-3.82)	3,8,24h	NA
	Placebo	Oral	121	45	22				
Brodsky 1994	Magnesium	Intravenous	10	6	6	10.64 (0.69-164.43)	1.60 (0.57-4.47)	48h	NA
	Placebo	Intravenous	8	0	3				
Camm 2011	Vernakalant	Intravenous	116	63	60		10 (4.50-22.23)	90 min, 4h	NA

	Amiodarone	Intravenous	116	26	6	2.42 (1.66-3.53)			
Chiladakis 2001	Magnesium	Intravenous	23	13	13	2.60 (1.11-6.11)	2.60 (1.11-6.11)	6h	NA
	Placebo	Intravenous	23	5	5				
Chu 2009	Magnesium	Intravenous	24	2	2	0.33 (0.07-1.49)	0.33 (0.07-1.49)	2h	NA
	Placebo	Intravenous	24	6	6				
Cotter 1999	Amiodarone	Intravenous	50	46	31	1.44 (1.15-1.80)	1.07 (0.78-1.47)	8, 24h	NA
	Placebo	Intravenous	50	32	29				
Cybulski 2003	Amiodarone	Intravenous	106	88	24	1.87 (1.37-2.55)	1.75 (0.80-3.79)	3, 20h	NA
	Placebo	Intravenous	54	24	7				
Fresco 1996	Propafenone	Intravenous	41	24	24	1.99 (1.11-3.56)	2.21 (1.19-4.10)	3h	NA
	Placebo	Intravenous	34	10	9				
Ganau 1998	Propafenone	Intravenous	81	57	57	4.06 (2.43-6.79)	4.06 (2.43-6.79)	2,6,12,24h	15 days
	Placebo	Intravenous	75	13	13				
Halinen 1995	Quinidine	Oral	28	24	10	1.66 (1.16-2.39)	2.95 (1.04-8.37)	3, 8, 12h	NA
	Sotalol	Oral	33	17	4				
Joseph 2000	Amiodarone	Intravenous	39	30	30	1.32 (0.95-1.83)	1.32 (0.95-1.83)	4, 24, 48h	NA
	Sotalol	Intravenous	40	35	35	1.50 (1.11-2.02)	1.50 (1.11-2.02)		
	Placebo	Intravenous	36	21	21	Ref	Ref		
Kochiadakis 1998a	Amiodarone	Intravenous	48	40	40	1.51 (1.14-2.01)	1.51 (1.14-2.01)	24h	NA
	Propafenone	Intravenous	46	36	36	1.42 (1.06-1.91)	1.42 (1.06-1.91)		
	Placebo	Intravenous	49	27	27	Ref	Ref		
Kochiadakis 2007	Procainamide	Intravenous	89	61	61	1.12 (0.90-1.39)	1.12 (0.90-1.39)	24h	NA
	Amiodarone	Intravenous	92	82	82	1.46 (1.22-1.75)	1.46 (1.22-1.75)		
	Propafenone	Intravenous	91	73	73	1.31 (1.08-1.59)	1.31 (1.08-1.59)		
	Placebo	Intravenous	90	55	55	Ref	Ref		
Kosior 2009	Propafenone	Intravenous	43	39	36	0.98 (0.86-1.13)	1.59 (1.41-2.21)	8, 24h	NA
	Quinidine	Oral	38	35	20				
Kumagai 2000	Pilsicainide	Oral	40	29	29	1.29 (0.90-1.85)	1.29 (0.90-1.85)	120min	NA
	Disopyramide	Intravenous	32	18	18				
Maciag 2017	Antazoline	Intravenous	22	16	16	28.70 (1.84-448.40)	28.70 (1.84-448.40)	90min	
	Placebo	Intravenous	19	0	0				
Madrid 1993	Flecainide	Intravenous	40	37	37	1.48 (1.15-1.91)	1.48 (1.15-1.91)	1h	NA
	Procainamide	Intravenous	40	25	25				
Martinez-Marcos 2000	Flecainide	Intravenous	50	45	29	1.41 (1.12-1.77)	4.14 (2.00-8.57)	1, 8, 12h	NA
	Propafenone	Intravenous	50	36	30	1.13 (0.86-1.47)	4.29 (2.08-8.83)		
	Amiodarone	Intravenous	50	32	7	Ref	Ref		
Negrini 1994	Propafenone	Intravenous	31	27	13	1.09 (0.87-1.36)	4.19 (1.33-13.25)	1, 24h	NA
	Amiodarone	Intravenous	30	24	3				
Noc 1990	Amiodarone	Intravenous	13	10	10	18.00 (1.17-276.06)	18.00 (1.17-276.06)	3h	NA
	Placebo	Intravenous	11	0	0				
Reisinger 2004	Flecainide	Intravenous	101	57	57	1.13 (0.87-1.46)	1.13 (0.87-1.46)	90min	NA
	Ibutilide	Intravenous	106	53	53				
Romano 2001	Flecainide	Intravenous	138	124	100	0.98 (0.91-1.05)	1.34 (1.12-1.59)	1,3,24h	NA
	Propafenone	Intravenous	164	151	89				
Roy 2004	Vernakalant	Intravenous	36	12	13	6.67 (0.93-47.59)	7.22 (1.02-51.23)	30min, 1h	7d
	Placebo	Intravenous	20	1	1				
Scheuermeyer 2019	BTE Incremental		43	38	38	1.65 (1.21-2.23)	1.65 (1.21-2.23)	2h	NA
	Procainamide	Intravenous	41	22	22				
Taha 2022	Propafenone	Oral	100	85	47	1.02 (0.91-1.16)	2.94 (1.79-4.82)	3, 24h	NA
	Amiodarone	Intravenous	100	83	16				
Treglia 1994a	Propafenone	Intravenous	27	20	13	1.05 (0.76-1.47)	4.33 (1.39-13.50)	5h,48h	NA
	Amiodarone	Intravenous	27	19	3				
Vogiatzis 2017	Vernakalant	Intravenous	36	19	19	1.01 (0.66-1.54)	1.01 (0.66-1.54)	2h	7d
	Ibutilide	Intravenous	42	22	22				
Xanthos 2007	Procainamide	Intravenous	110	91	91	1.03 (0.91-1.16)	1.03 (0.91-1.16)	24h	NA
	Amiodarone	Intravenous	113	91	91				

SR - sinus rhythm, IP - inpatient, FUP - follow-up, RR - risk ratio, CI - confidence interval, BTE - biphasic trunkated exponential.

Table 6

League Table: Paroxysmal AF (Drugs): Sinus rhythm at hospital discharge or end of study follow-up

Direct evidence estimates										
Placebo	0.89 [0.55 - 1.44]	0.67 [0.40 - 1.13]	0.60 [0.48 - 0.75]	0.58 [0.26 - 1.26]	0.47 [0.38 - 0.57]	-	0.70 [0.44 - 1.11]	0.20 [0.09 - 0.45]	-	-
0.67 [0.51 - 0.88]	**Procainamide**	-	0.89 [0.65 - 1.23]	-	0.85 [0.54 - 1.36]	-	-	0.68 [0.41 - 1.11]	-	0.61 [0.36 - 1.03]
0.63 [0.43 - 0.92]	0.94 [0.61 - 1.46]	**Sotalol**	1.14 [0.71 - 1.83]	-	-	-	-	-	0.60 [0.34 - 1.05]	-
0.59 [0.50 - 0.70]	0.88 [0.69 - 1.13]	0.93 [0.64 - 1.36]	**Amiodarone**	-	0.99 [0.83 - 1.19]	-	0.41 [0.23 - 0.73]	0.84 [0.60 - 1.17]	-	-
0.58 [0.26 - 1.26]	0.86 [0.38 - 1.97]	0.91 [0.38 - 2.17]	0.98 [0.44 - 2.18]	**Magnesium**	-	-	-	-	-	-
0.51 [0.43 - 0.60]	0.75 [0.58 - 0.98]	0.80 [0.55 - 1.17]	0.86 [0.73 - 1.00]	0.88 [0.39 - 1.95]	**Propafenone**	-	-	0.93 [0.72 - 1.21]	0.98 [0.63 - 1.54]	0.83 [0.53 - 1.29]
0.50 [0.32 - 0.78]	0.75 [0.46 - 1.21]	0.79 [0.45 - 1.39]	0.85 [0.55 - 1.32]	0.87 [0.35 - 2.13]	0.99 [0.64 - 1.54]	**Ibutilide**	0.99 [0.54 - 1.81]	0.89 [0.54 - 1.46]	-	-
0.47 [0.33 - 0.66]	0.70 [0.47 - 1.05]	0.74 [0.45 - 1.21]	0.79 [0.56 - 1.12]	0.81 [0.35 - 1.90]	0.93 [0.65 - 1.32]	0.94 [0.60 - 1.46]	**Vernakalant**	-	-	-
0.46 [0.36 - 0.60]	0.69 [0.52 - 0.92]	0.73 [0.48 - 1.11]	0.78 [0.62 - 0.99]	0.80 [0.35 - 1.82]	0.91 [0.73 - 1.14]	0.92 [0.61 - 1.40]	0.98 [0.67 - 1.44]	**Flecainide**	-	-
0.45 [0.30 - 0.67]	0.67 [0.43 - 1.05]	0.71 [0.47 - 1.08]	0.76 [0.51 - 1.13]	0.78 [0.32 - 1.87]	0.89 [0.61 - 1.30]	0.89 [0.50 - 1.59]	0.96 [0.57 - 1.59]	0.97 [0.63 - 1.50]	**Quinidine**	-
0.41 [0.28 - 0.61]	0.62 [0.43 - 0.89]	0.65 [0.39 - 1.09]	0.70 [0.48 - 1.02]	0.72 [0.30 - 1.71]	0.82 [0.57 - 1.17]	0.83 [0.47 - 1.44]	0.88 [0.54 - 1.44]	0.89 [0.60 - 1.34]	0.92 [0.55 - 1.55]	**BTE Incremental**
0.03 [0.00 - 0.56]	0.05 [0.00 - 0.85]	0.06 [0.00 - 0.92]	0.06 [0.00 - 0.96]	0.06 [0.00 - 1.09]	0.07 [0.00 - 1.12]	0.07 [0.00 - 1.17]	0.07 [0.00 - 1.23]	0.08 [0.00 - 1.24]	0.08 [0.00 - 1.30]	0.08 [0.01 - 1.40]
Network estimates										

Table 7

Cardioversion for Persistent Atrial Fibrillation - Efficacy Outcomes Data

Study	Intervention	Route	Sample Size	SR until discharge or end of FUP, n	Acute Procedural Success, n	RR SR until discharge of end of FUP, 95%CI	RR Acute Procedural Success, 95%CI	Follow up periods IP	Longterm FUP
Alp 2000	AA MDS Fixed		30	18	18	1.74 (0.97-3.11)	1.74 (0.97-3.11)	30min	NA
	AP MDS Fixed		29	10	10				
Baroni 2011	Quinidine	Oral	30	16	16	2.67 (1.21-5.88)	2.67 (1.21-5.88)	24h	NA
	Propafenone	Intravenous	30	6	6	1.00 (0.36-2.75)	1.00 (0.36-2.75)		
	Amiodarone	Intravenous	30	6	6	Ref	Ref		
Channer 2004	Amiodarone	Oral	123	26	26	16.67 (1.04-267.25)	16.67 (1.04-267.25)	outpatient	1,4,8,12,26,52 weeks
	Placebo	Oral	38	0	0				
Falk 1997	Dofetilide	Intravenous	50	7	7	7.65 (0.45-128.74)	7.65 (0.45-128.74)	1, 6h	NA
	Placebo	Intravenous	25	0	0				
Galperin 2001	Amiodarone	Oral	47	16	16	33.69 (2.08-545.84)	33.69 (2.08-545.84)	NA	4 weeks
	Placebo	Oral	48	0	0				
Kanoupakis 2003	Amiodarone	Oral	48	3	3	2.94 (0.51-16.99)	2.94 (0.51-16.99)	outpatient	4 weeks
	Placebo	Oral	94	2	2				
Kochiadakis 1999a	Propafenone	Intravenous	32	3	3	7.64 (0.41-142.34)	7.64 (0.41-142.34)	24h	30d
	Amiodarone	Intravenous	34	16	0	33.94 (2.12-544.26)	NA		
	Placebo	Intravenous	35	0	0	Ref	Ref		
Khaykin 2003	AP BTE Incremental Patches		28	17	17	3.40 (1.46-7.94)	3.40 (1.46-7.94)	NA	NA
	AP MDS Single Max Patches		28	5	5				
Kirchhof 2005	AP BTE Incremental Paddles		56	56	56	1.25 (1.09-1.45)	1.25 (1.09-1.45)	NA	NA
	AP BTE Incremental Patches		48	46	46	1.20 (1.03-1.40)	1.20 (1.03-1.40)		

	AP MDS Incremental Paddles		48	44	44	1.15 (0.98-1.36)	1.15 (0.98-1.36)		
	AP MDS Incremental Patches		49	39	39	Ref	Ref		
Kuhlkamp 1991	Cibenzoline	Oral	19	7	7	1.47 (0.47-4.62)	1.47 (0.47-4.62)	9 days	9 days
	Flecainide	Oral	12	3	3				
Neumann 2004	AP BTE Incremental Patches		61	61	61	1.35 (1.16-1.58)	1.35 (1.16-1.58)	NA	NA
	AP MDS Incremental Patches		57	42	42				
Okishige 2000	Pilsicainide	Oral	52	11	11	4.77 (0.30-75.12)	4.77 (0.30-75.12)	4 weeks	4 weeks
	Placebo	Oral	10	0	0				
Schmidt 2019	AP BTE Maximum Patches		129	110	114	1.35 (1.17-1.55)	1.34 (1.17-1.53)	1 min, 4h	NA
	AP BTE Incremental Patches		147	93	97				
Siaplaouras 2004	AP MDS Incremental Patches		108	105	105	1.03 (0.97-1.09)	1.03 (0.97-1.09)	1 min	NA
	AP RBW Incremental Patches		108	102	102				
Siaplaouras 2005	AA RBW Incremental Patches		63	60	60	1.00 (0.93-1.09)	1.00 (0.93-1.09)	1 min	NA
	AP RBW Incremental Patches		60	57	57				
Singh 2005	Amiodarone	Oral	258	70	70	35.81 (5.03-254.95)	35.81 (5.03-254.95)	outpatient	12 months
	Sotalol	Oral	244	59	59	31.92 (4.47-227.76)	31.92 (4.47-227.76)		
	Placebo	Oral	132	1	1	Ref	Ref		
Squara 2021	Active compression AP BTE Incremental Patches		50	48	48	1.14 (1.00-1.31)	1.14 (1.00-1.31)	6h	NA
	AP BTE Incremental Patches		50	42	42				
Trendafilova 2021	AA BTE Fixed Patches		38	35	37	1.03 (0.94-1.14)	0.98 (0.86-1.11)	1min 2h, 24h	NA
	AA PB Fixed Patches		35	33	33				
Vijayalakshmi 2006	Amiodarone	Oral	27	7	7	17.14 (1.02-286.86)	17.14 (1.02-286.86)	outpatient	6 weeks, 6 months
	Sotalol	Oral	36	7	7	12.97 (0.77-218.37)	12.97 (0.77-218.37)		
	Placebo	Oral	31	0	0	Ref	Ref		
Vogiatzis 2008	AP MDS Incremental Patches		30	30	30	1.03 (0.94-1.12)	1.03 (0.94-1.12)	NA	NA
	AA MDS Incremental Patches		32	31	31				
Voskoboinik 2018	AP BTE Incremental Paddles		30	27	27	1.44 (1.07-1.93)	1.44 (1.07-1.93)	1min	NA
	AA BTE Incremental Paddles		32	29	29	1.45 (1.08-1.94)	1.45 (1.08-1.94)		
	AP BTE Incremental Patches		31	23	23	1.19 (0.85-1.67)	1.19 (0.85-1.67)		
	AA BTE Incremental Patches		32	20	20	Ref	Ref		
Yamase 2012	Bepridil	Oral	20	17	17	2.43 (1.30-4.54)	2.43 (1.30-4.54)	outpatient	3 months
	Amiodarone	Oral	20	7	7				
Yamashita 2009	Bepridil	Oral	61	32	32	15.21 (2.18-105.93)	15.21 (2.18-105.93)	outpatient	3 months
	Placebo	Oral	29	1	1				
Zehender 1994	Quinidine	Oral	20	11	5	0.92 (0.54-1.56)	2.50 (0.55-11.41)	3, 7 & 14 days	3 months
	Amiodarone	Oral	20	12	2				

SR - sinus rhythm, IP - inpatient, FUP - follow-up, RR - risk ratio, CI - confidence interval, BTE - biphasic trunkated exponential, MDS - monophasic dampened sinusoidal, RBW - rectilinear biphasic wafeform, PB - pulsed biphasic.

Table 8

League Table: Persistent AF (DCCV): Sinus rhythm at hospital discharge or end of study follow-up

Direct evidence estimates									
AA MDS Incremental Paddles	0.87 [0.72 - 1.05]	-	-	-	-	-	-	-	-
0.87 [0.72 - 1.05]	**AA MDS Incremental Patches**	-	-	0.97 [0.91 - 1.03]	-	-	-	-	-
					-	-	-	-	-

0.87 [0.71 - 1.07]	1.00 [0.92 - 1.08]	**AP RBW Incremental Patches**	1.00 [0.92 - 1.08]	0.97 [0.92 - 1.03]					
0.87 [0.69 - 1.08]	1.00 [0.89 - 1.12]	1.00 [0.92 - 1.08]	**AA RBW Incremental Patches**	-	-	-	-	-	-
0.84 [0.69 - 1.03]	0.97 [0.91 - 1.03]	0.97 [0.92 - 1.03]	0.97 [0.88 - 1.07]	**AP MDS Incremental Patches**	0.87 [0.74 - 1.02]	0.78 [0.70 - 0.87]	0.80 [0.69 - 0.92]	-	-
0.70 [0.55 - 0.89]	0.80 [0.69 - 0.93]	0.80 [0.69 - 0.93]	0.81 [0.68 - 0.95]	0.83 [0.72 - 0.95]	**AP MDS Incremental Paddles**	0.96 [0.86 - 1.06]	0.92 [0.84 - 1.00]	-	-
0.66 [0.53 - 0.83]	0.76 [0.67 - 0.86]	0.76 [0.68 - 0.86]	0.76 [0.66 - 0.88]	0.78 [0.70 - 0.87]	0.95 [0.86 - 1.05]	**AP BTE Incremental Patches**	0.96 [0.90 - 1.02]	0.88 [0.77 - 1.00]	0.74 [0.6 - 0.86]
0.64 [0.51 - 0.80]	0.74 [0.65 - 0.83]	0.74 [0.65 - 0.83]	0.74 [0.64 - 0.85]	0.76 [0.68 - 0.84]	0.92 [0.84 - 1.00]	0.97 [0.91 - 1.02]	**AP BTE Incremental Paddles**	-	-
0.58 [0.44 - 0.76]	0.67 [0.55 - 0.80]	0.67 [0.56 - 0.80]	0.67 [0.55 - 0.81]	0.69 [0.58 - 0.82]	0.83 [0.70 - 0.98]	0.87 [0.77 - 1.00]	0.90 [0.78 - 1.05]	**Active compression AP BTE Incremental Patches**	-
0.49 [0.38 - 0.64]	0.56 [0.47 - 0.68]	0.57 [0.47 - 0.68]	0.57 [0.46 - 0.70]	0.58 [0.49 - 0.70]	0.70 [0.59 - 0.84]	0.74 [0.64 - 0.86]	0.77 [0.66 - 0.89]	0.85 [0.70 - 1.03]	**AP BTE Maximu Patche**
Network estimates									

Table 9

League Table: Persistent AF (Drugs): Sinus rhythm at hospital discharge or end of study follow-up

Direct evidence estimates							
Placebo	0.22 [0.01 - 3.41]	0.03 [0.00 - 0.55]	0.04 [0.01 - 0.21]	0.11 [0.01 - 1.83]	0.07 [0.03 - 0.19]	-	0.07 [0.01 - 0.46]
0.22 [0.01 - 3.41]	**Pilsicainide**	-	-	-	-	-	-
0.11 [0.04 - 0.28]	0.49 [0.03 - 9.12]	**Propafenone**	-	-	0.90 [0.56 - 1.44]	0.38 [0.17 - 0.83]	-
0.10 [0.04 - 0.24]	0.44 [0.02 - 7.99]	0.90 [0.53 - 1.53]	**Sotalol**	-	0.88 [0.66 - 1.16]	-	-
0.11 [0.01 - 1.83]	0.50 [0.01 - 25.74]	1.01 [0.05 - 20.02]	1.13 [0.06 - 21.86]	**Dofetilide**	-	-	-
0.09 [0.04 - 0.20]	0.39 [0.02 - 7.01]	0.79 [0.50 - 1.25]	0.89 [0.67 - 1.18]	0.79 [0.04 - 15.12]	**Amiodarone**	0.69 [0.44 - 1.08]	0.41 [0.22 - 0.77]
0.06 [0.02 - 0.14]	0.26 [0.01 - 4.71]	0.52 [0.30 - 0.89]	0.58 [0.35 - 0.95]	0.51 [0.03 - 10.15]	0.65 [0.43 - 0.99]	**Quinidine**	-
0.04 [0.01 - 0.10]	0.17 [0.01 - 3.18]	0.35 [0.16 - 0.74]	0.39 [0.20 - 0.75]	0.34 [0.02 - 6.86]	0.44 [0.24 - 0.80]	0.67 [0.32 - 1.39]	**Bepridil**
Network estimates							

Table 10

Cardioversion for Atrial Flutter - Efficacy Outcomes Data

Study	Intervention	Route	Sample Size	SR until discharge or end of FUP, n	Acute Procedural Success, n	RR SR until discharge of end of FUP, 95%CI	RR Acute Procedural Success, 95%CI	Follow up periods IP	Longterm FUP
Abi-Mansour 1998	Ibutilide	Intravenous	45	27	27	15.45 (1.02-237.92)	15.45 (1.02-237.92)	90min	NA
	Placebo	Intravenous	12	0	0				
Camm 2012	Vernakalant	Intravenous	39	1	1	1.20 (0.05-27.94)	1.20 (0.05-27.94)	90min, 24h	7, 30d
	Placebo	Intravenous	15	0	0				
Falk 1997	Dofetilide	Intravenous	11	6	6	6.50 (0.43-97.14)	6.50 (0.43-97.14)	1, 6h	NA
	Placebo	Intravenous	5	0	0				
Lindeboom 2000	Dofetilide	Intravenous	7	5	5	5.50 (0.39-76.65)	5.50 (0.39-76.65)	2h	NA
	Placebo	Intravenous	3	0	0				
Mortensen 2007	AP RBW Incremental		48	48	48	1.00 (0.96-1.04)	1.00 (0.96-1.04)	30s	NA
	AP MDS Incremental		47	47	47				
Norgaard 1999	Dofetilide	Intravenous	11	7	7	8.75 (0.58-131.07)	8.75 (0.58-131.07)	3hrs	NA
	Placebo	Intravenous	6	0	0				
Risius 2009	AA RBW Incremental		48	48	48	1.00 (0.96-1.04)	1.00 (0.96-1.04)	30s	NA
	AP RBW Incremental		48	48	48				

Schmidt 2017	AP BTE Incremental		9	9	9	1.27 (0.86-1.86)	NA	1 min, 30min, 4h	NA
	AP PB Incremental		9	7	7				
Stambler 1996	Ibutilide	Intravenous	80	50	50	25.63 (3.67-178.91)	25.63 (3.67-178.91)	90min	NA
	Placebo	Intravenous	41	1	1				
Sun 2005	Ibutilide	Intravenous	20	18	16	3.00 (1.51-5.95)	16.00 (2.34-109.45)	90min, 24h	NA
	Propafenone	Intravenous	20	6	1				
Suttorp 1990	Flecainide	Intravenous	5	1	1	0.50 (0.06-3.91)	0.50 (0.06-3.91)	1h	NA
	Propafenone	Intravenous	5	2	2				
Suttorp 1989	Flecainide	Intravenous	3	0	0	NA	NA	60min	NA
	Placebo	Intravenous	3	0	0				
Volgman 1998	Ibutilide	Intravenous	20	15	15	5.00 (1.71-14.63)	5.00 (1.71-14.63)	1hr, 90min, 24,72h	NA
	Procainamide	Intravenous	20	3	3				
Vos 1998	Ibutilide	Intravenous	36	23	23	3.35 (1.34-8.38)	3.35 (1.34-8.38)	1, 7 38hrs	NA
	Sotalol	Intravenous	21	4	4				

SR - sinus rhythm, IP - inpatient, FUP - follow-up, RR - risk ratio, CI - confidence interval, MDS -monophasic dampened sinusoidal, RBW - rectilinear biphasic wafeform, PB - pulsed biphasic.

Table 11

League Table: Atrial Flutter (Drugs): Sinus rhythm at hospital discharge or end of study follow-up

Direct evidence estimates							
Placebo	0.85 [0.04 - 19.75]	-	-	-	0.16 [0.03 - 0.72]	-	0.05 [0.01 - 0.23]
0.85 [0.04 - 19.75]	**Vernakalant**	-	-	-	-	-	-
0.28 [0.02 - 4.09]	0.33 [0.01 - 20.58]	**Flecainide**	-	-	-	0.50 [0.06 - 3.91]	-
0.23 [0.03 - 1.58]	0.27 [0.01 - 10.90]	0.83 [0.07 - 9.35]	**Procainamide**	-	-	-	0.20 [0.07 - 0.59]
0.16 [0.03 - 0.97]	0.18 [0.00 - 7.00]	0.56 [0.05 - 5.87]	0.67 [0.16 - 2.75]	**Sotalol**	-	-	0.30 [0.12 - 0.74]
0.16 [0.03 - 0.72]	0.18 [0.01 - 6.07]	0.56 [0.03 - 12.24]	0.67 [0.06 - 7.75]	0.99 [0.09 - 10.83]	**Dofetilide**	-	-
0.14 [0.02 - 0.78]	0.16 [0.00 - 5.95]	0.50 [0.06 - 3.91]	0.60 [0.17 - 2.14]	0.89 [0.29 - 2.81]	0.90 [0.09 - 9.06]	**Propafenone**	0.33 [0.17 - 0.66]
0.05 [0.01 - 0.23]	0.05 [0.00 - 1.86]	0.17 [0.02 - 1.46]	0.20 [0.07 - 0.59]	0.30 [0.12 - 0.74]	0.30 [0.03 - 2.72]	0.33 [0.17 - 0.66]	**Ibutilide**
Network estimates							

Table 12

League Table: Paroxysmal AF (Drugs): Acute procedural success

Direct evidence estimates										
Placebo	0.67 [0.32 - 1.40]	0.61 [0.44 - 0.84]	0.69 [0.33 - 1.42]	0.89 [0.44 - 1.82]	-	0.44 [0.33 - 0.57]	-	0.11 [0.04 - 0.36]	-	0.16 [0.07 - 0.36]
0.74 [0.41 - 1.33]	**Sotalol**	1.14 [0.56 - 2.31]	-	-	0.34 [0.10 - 1.18]	-	-	-	-	-
0.67 [0.51 - 0.88]	0.90 [0.50 - 1.62]	**Amiodarone**	-	1.12 [0.69 - 1.83]	-	0.69 [0.50 - 0.95]	-	0.61 [0.35 - 1.08]	-	0.10 [0.04 - 0.28]
0.69 [0.33 - 1.42]	0.93 [0.36 - 2.37]	1.03 [0.47 - 2.24]	**Magnesium**	-	-	-	-	-	-	-
0.61 [0.41 - 0.93]	0.83 [0.42 - 1.64]	0.92 [0.63 - 1.35]	0.90 [0.39 - 2.07]	**Procainamide**	-	0.85 [0.42 - 1.72]	0.61 [0.29 - 1.28]	0.68 [0.33 - 1.39]	-	-
0.50 [0.25 - 1.01]	0.68 [0.31 - 1.49]	0.75 [0.38 - 1.52]	0.73 [0.27 - 2.01]	0.82 [0.38 - 1.75]	**Quinidine**	0.63 [0.30 - 1.33]	-	-	-	-
0.41 [0.32 - 0.52]	0.55 [0.30 - 1.01]	0.61 [0.47 - 0.80]	0.60 [0.28 - 1.29]	0.66 [0.45 - 0.98]	0.81 [0.42 - 1.58]	**Propafenone**	0.83 [0.42 - 1.65]	0.79 [0.52 - 1.21]	-	-
0.35 [0.20 - 0.63]	0.48 [0.22 - 1.05]	0.53 [0.30 - 0.94]	0.52 [0.20 - 1.31]	0.58 [0.33 - 0.99]	0.70 [0.30 - 1.64]	0.87 [0.51 - 1.48]	**BTE Incremental**	-	-	-
0.32 [0.22 - 0.48]	0.44 [0.23 - 0.86]	0.49 [0.33 - 0.71]	0.47 [0.21 - 1.08]	0.53 [0.34 - 0.82]	0.64 [0.31 - 1.36]	0.79 [0.56 - 1.13]	0.92 [0.50 - 1.69]	**Flecainide**	1.13 [0.55 - 2.33]	-
0.25 [0.13 -	0.34 [0.14 -	0.37 [0.19 - 0.72]	0.36 [0.14 - 0.97]	0.40 [0.20 - 0.82]	0.49 [0.20 - 1.24]	0.61 [0.32 - 1.17]	0.70 [0.31 - 1.60]	0.77 [0.42 - 1.40]	**Ibutilide**	0.99 [0.45 - 2.20]

0.48]	0.79]									
0.15 [0.09 - 0.28]	0.21 [0.09 - 0.47]	0.23 [0.13 - 0.42]	0.23 [0.09 - 0.57]	0.25 [0.13 - 0.49]	0.31 [0.13 - 0.74]	0.38 [0.21 - 0.69]	0.44 [0.20 - 0.95]	0.48 [0.26 - 0.88]	0.62 [0.33 - 1.17]	**Vernakalant**
0.03 [0.00 - 0.59]	0.05 [0.00 - 0.85]	0.05 [0.00 - 0.90]	0.05 [0.00 - 0.95]	0.06 [0.00 - 0.99]	0.07 [0.00 - 1.28]	0.09 [0.01 - 1.47]	0.10 [0.01 - 1.77]	0.11 [0.01 - 1.88]	0.14 [0.01 - 2.56]	0.23 [0.01 - 4.06]
Network estimates										

Table 13

League Table: Persistent AF (DCCV): Acute procedural success

Direct evidence estimates									
AA MDS Incremental Paddles	0.87 [0.72 - 1.05]	-	-	-	-	-	-	-	-
0.87 [0.72 - 1.05]	**AA MDS Incremental Patches**	-	-	0.97 [0.91 - 1.03]	-	-	-	-	-
0.87 [0.71 - 1.07]	1.00 [0.92 - 1.08]	**AP RBW Incremental Patches**	1.00 [0.92 - 1.08]	0.97 [0.92 - 1.03]	-	-	-	-	-
0.87 [0.69 - 1.08]	1.00 [0.89 - 1.12]	1.00 [0.92 - 1.08]	**AA RBW Incremental Patches**	-	-	-	-	-	-
0.84 [0.69 - 1.03]	0.97 [0.91 - 1.03]	0.97 [0.92 - 1.03]	0.97 [0.88 - 1.07]	**AP MDS Incremental Patches**	0.87 [0.74 - 1.02]	0.78 [0.70 - 0.87]	0.80 [0.69 - 0.92]	-	-
0.70 [0.55 - 0.89]	0.80 [0.69 - 0.93]	0.80 [0.69 - 0.93]	0.81 [0.68 - 0.95]	0.83 [0.72 - 0.95]	**AP MDS Incremental Paddles**	0.96 [0.86 - 1.06]	0.92 [0.84 - 1.00]	-	-
0.66 [0.53 - 0.83]	0.76 [0.67 - 0.86]	0.76 [0.68 - 0.86]	0.76 [0.66 - 0.88]	0.78 [0.70 - 0.87]	0.95 [0.86 - 1.05]	**AP BTE Incremental Patches**	0.96 [0.90 - 1.02]	0.88 [0.77 - 1.00]	0.74 [0.6 - 0.86]
0.64 [0.51 - 0.80]	0.74 [0.65 - 0.83]	0.74 [0.65 - 0.83]	0.74 [0.64 - 0.85]	0.76 [0.68 - 0.84]	0.92 [0.84 - 1.00]	0.97 [0.91 - 1.02]	**AP BTE Incremental Paddles**	-	-
0.58 [0.44 - 0.76]	0.67 [0.55 - 0.80]	0.67 [0.56 - 0.80]	0.67 [0.55 - 0.81]	0.69 [0.58 - 0.82]	0.83 [0.70 - 0.98]	0.87 [0.77 - 1.00]	0.90 [0.78 - 1.05]	**Active compression AP BTE Incremental Patches**	-
0.49 [0.38 - 0.64]	0.56 [0.47 - 0.68]	0.57 [0.47 - 0.68]	0.57 [0.46 - 0.70]	0.58 [0.49 - 0.70]	0.70 [0.59 - 0.84]	0.74 [0.64 - 0.86]	0.77 [0.66 - 0.89]	0.85 [0.70 - 1.03]	**AP BTE Maximu Patche**
Network estimates									

Table 14

League Table: Atrial Flutter (Drugs): Acute procedural success

Direct evidence estimates							
Flecainide	-	0.50 [0.06 - 3.91]	-	-	-	-	-
0.67 [0.03 - 16.93]	**Placebo**	-	0.85 [0.04 - 19.75]	-	0.16 [0.03 - 0.72]	-	0.05 [0.01 - 0.23]
0.50 [0.06 - 3.91]	0.75 [0.06 - 9.00]	**Propafenone**	-	-	-	-	0.06 [0.01 - 0.43]
0.57 [0.01 - 51.68]	0.85 [0.04 - 19.75]	1.14 [0.02 - 62.95]	**Vernakalant**	-	-	-	-
0.16 [0.01 - 3.18]	0.23 [0.03 - 1.58]	0.31 [0.03 - 2.83]	0.27 [0.01 - 10.90]	**Procainamide**	-	-	0.20 [0.07 - 0.59]
0.10 [0.00 - 3.72]	0.16 [0.03 - 0.72]	0.21 [0.01 - 3.89]	0.18 [0.01 - 6.07]	0.67 [0.06 - 7.75]	**Dofetilide**	-	-
0.10 [0.01 - 2.02]	0.16 [0.03 - 0.97]	0.21 [0.02 - 1.76]	0.18 [0.00 - 7.00]	0.67 [0.16 - 2.75]	1.01 [0.09 - 10.96]	**Sotalol**	0.30 [0.12 - 0.74]
0.03 [0.00 - 0.52]	0.05 [0.01 - 0.23]	0.06 [0.01 - 0.43]	0.05 [0.00 - 1.86]	0.20 [0.07 - 0.59]	0.30 [0.03 - 2.72]	0.30 [0.12 - 0.74]	**Ibutilide**
Network estimates							

Table 15

League Table: 30 day all cause mortality

Direct evidence estimates			

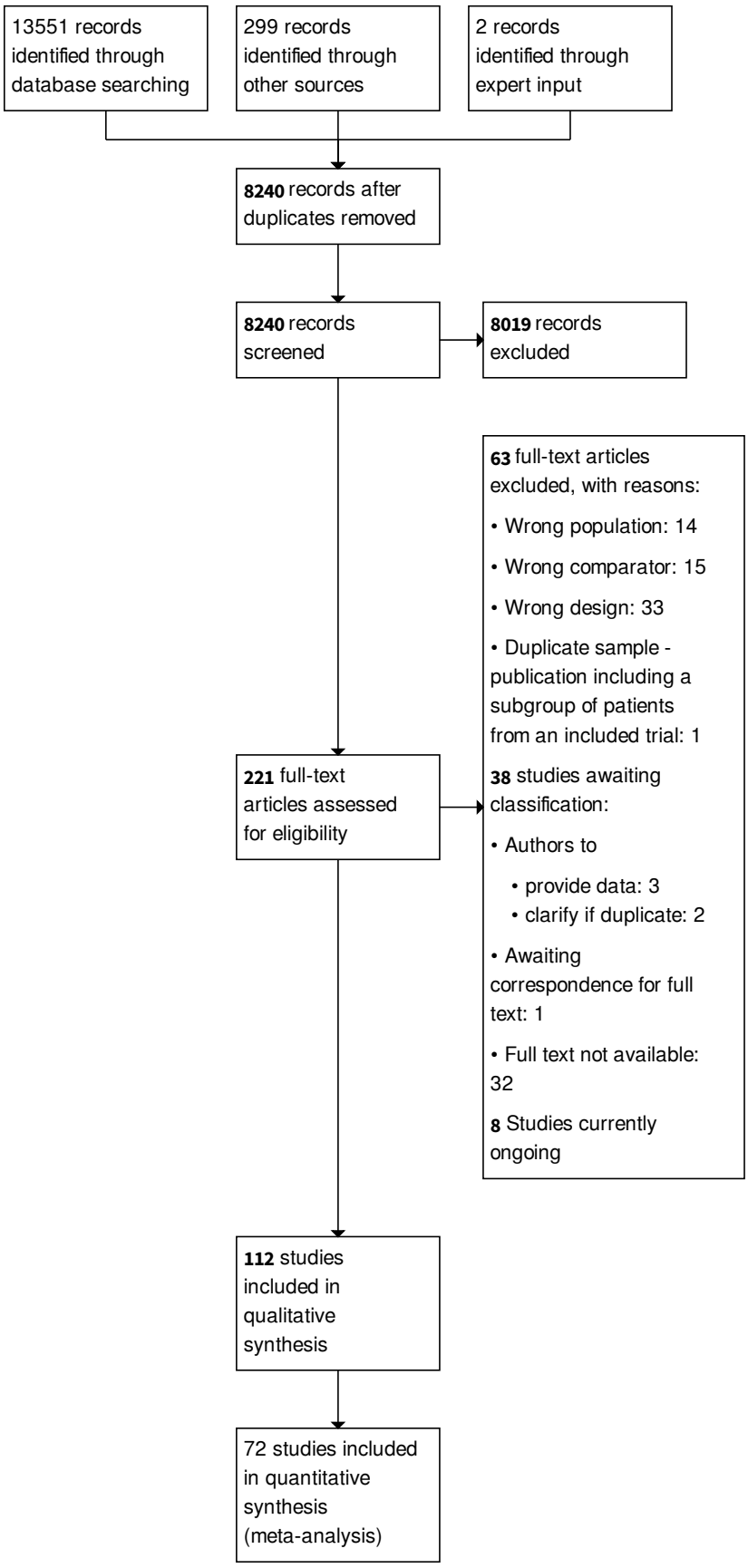
Sotalol	-	0.29 [0.01 - 6.81]	-
0.75 [0.01 - 85.57]	**Amiodarone**	-	0.33 [0.01 - 8.10]
0.29 [0.01 - 6.81]	0.38 [0.01 - 13.05]	**Placebo**	0.87 [0.19 - 3.90]
0.25 [0.01 - 8.30]	0.33 [0.01 - 8.10]	0.87 [0.19 - 3.90]	**Vernakalant**
Network estimates			

Table 16

League Table: 30 day cardiovascular mortality

Direct evidence estimates		
Amiodarone	-	0.33 [0.01 - 8.10]
0.38 [0.01 - 14.84]	**Placebo**	0.88 [0.14 - 5.37]
0.33 [0.01 - 8.10]	0.88 [0.14 - 5.37]	**Vernakalant**
Network estimates		

Figure 1



PRISMA Flow diagram

Figure 2

›cedure-related complications

use mortality, 30-day cardiovascular mortality, quality of life within the first year post-cardioversion, heart failure admission within the first month, complications occuring in the first week.

e generation (selection bias)

ment (selection bias)

pants and personnel (performance bias): All other outcomes

pants and personnel (performance bias): Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism

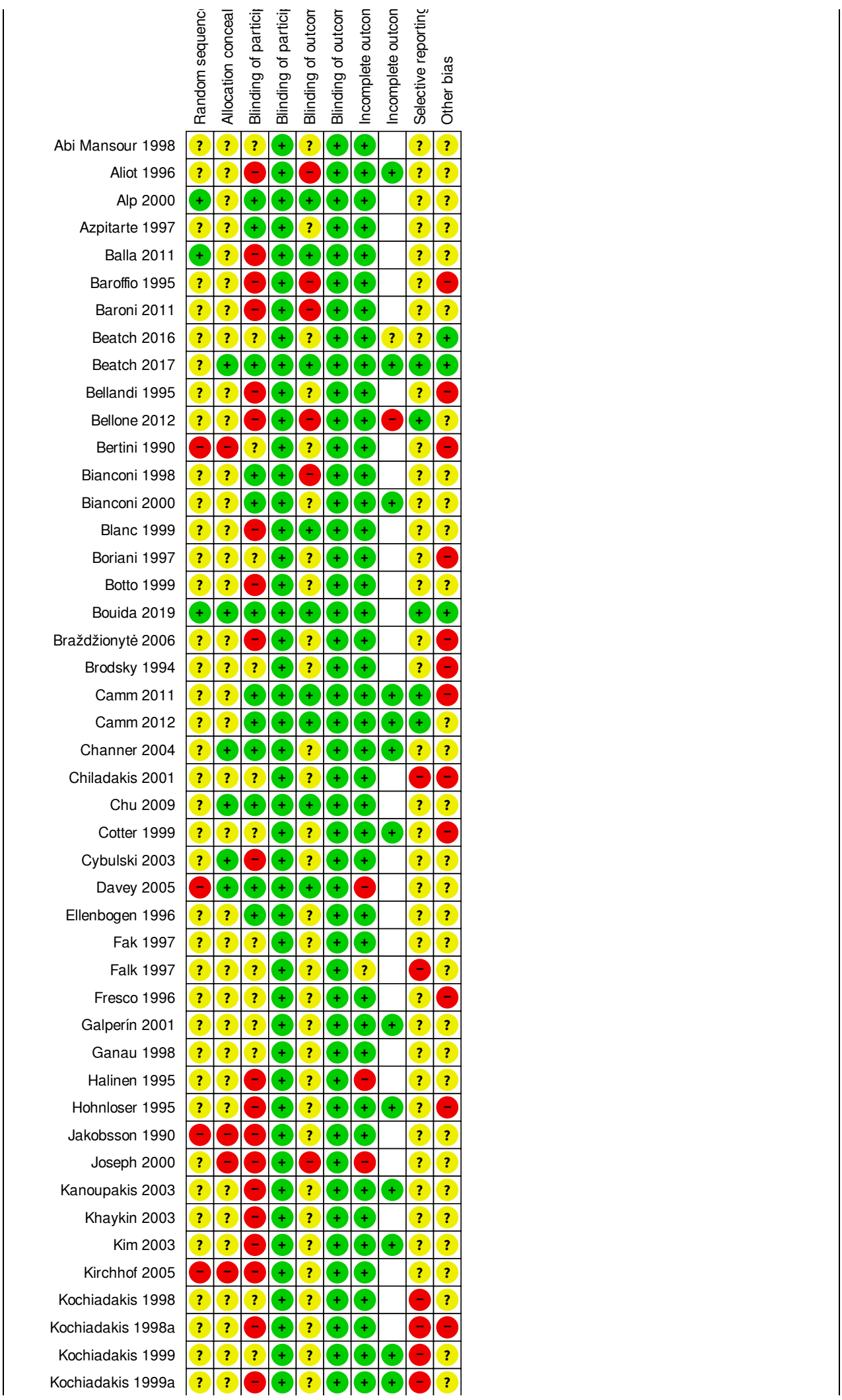
ne assessment (detection bias): All other outcomes

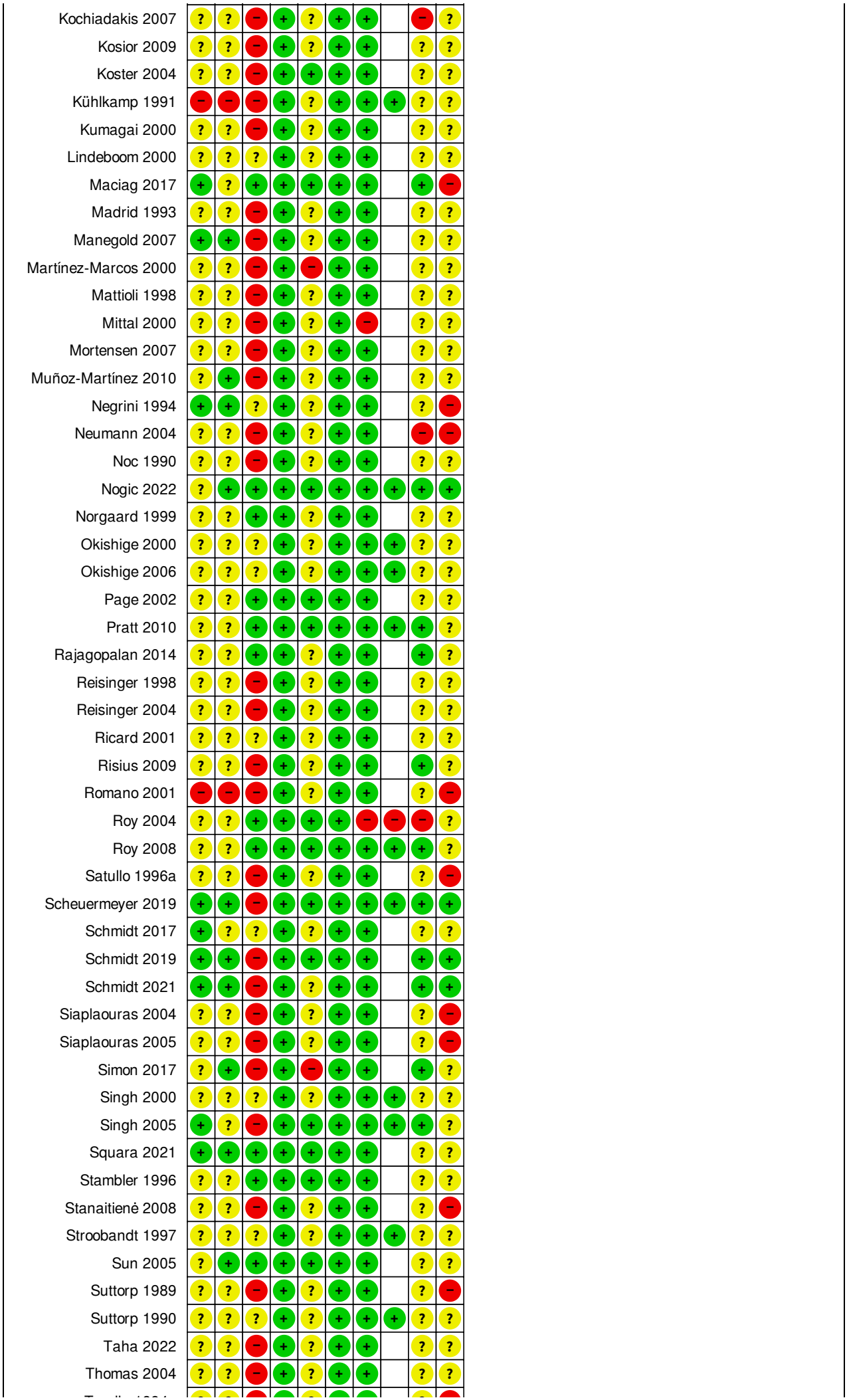
ne assessment (detection bias): Acute Procedural Success, All-Cause Mortality, and Stroke or Systemic Embolism

ne data (attrition bias): Outcomes assessed during index admission: Acute Procedural Success, Duration of Hospitalization, Development of ventricular arrhythmias, Development of bradyarrhythmias, immediate prc

ne data (attrition bias): Outcomes assessed also after discharge: Maintenance of sinus rhythm following discharge or at the end of study follow-up, Stroke or systemic embolism within the first 30 days, 30-day all-ca

g (reporting bias)


Random sequenc
Allocation conceal
Blinding of partici
Blinding of partici
Blinding of outcom
Blinding of outcom
Incomplete outcon
Incomplete outcon
Selective reportin
Other bias
Abi Mansour 1998
Aliot 1996
Alp 2000
Azpitarte 1997
Balla 2011
Baroffio 1995
Baroni 2011
Beatch 2016
Beatch 2017
Bellandi 1995
Bellone 2012
Bertini 1990
Bianconi 1998
Bianconi 2000
Blanc 1999
Boriani 1997
Botto 1999
Bouida 2019
Braždžionytė 2006
Brodsky 1994
Camm 2011
Camm 2012
Channer 2004
Chiladakis 2001
Chu 2009
Cotter 1999
Cybulski 2003
Davey 2005
Ellenbogen 1996
Fak 1997
Falk 1997
Fresco 1996
Galperín 2001
Ganau 1998
Halinen 1995
Hohnloser 1995
Jakobsson 1990
Joseph 2000
Kanoupakis 2003
Khaykin 2003
Kim 2003
Kirchhof 2005
Kochiadakis 1998
Kochiadakis 1998a
Kochiadakis 1999
Kochiadakis 1999a


Kochiadakis 2007
Kosior 2009
Koster 2004
Kühlkamp 1991
Kumagai 2000
Lindeboom 2000
Maciag 2017
Madrid 1993
Manegold 2007
Martínez-Marcos 2000
Mattioli 1998
Mittal 2000
Mortensen 2007
Muñoz-Martínez 2010
Negrini 1994
Neumann 2004
Noc 1990
Nogic 2022
Norgaard 1999
Okishige 2000
Okishige 2006
Page 2002
Pratt 2010
Rajagopalan 2014
Reisinger 1998
Reisinger 2004
Ricard 2001
Risius 2009
Romano 2001
Roy 2004
Roy 2008
Satullo 1996a
Scheuermeyer 2019
Schmidt 2017
Schmidt 2019
Schmidt 2021
Siaplaouras 2004
Siaplaouras 2005
Simon 2017
Singh 2000
Singh 2005
Squara 2021
Stambler 1996
Stanaitienė 2008
Stroobandt 1997
Sun 2005
Suttorp 1989
Suttorp 1990
Taha 2022
Thomas 2004

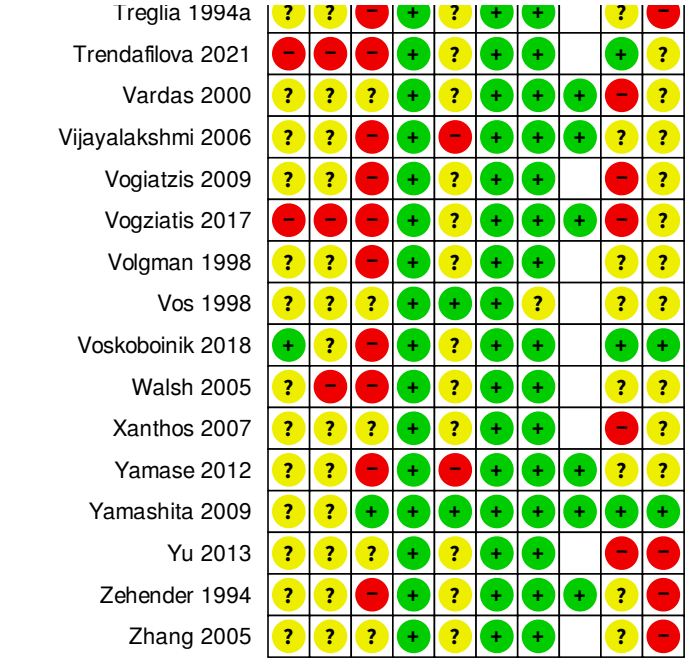
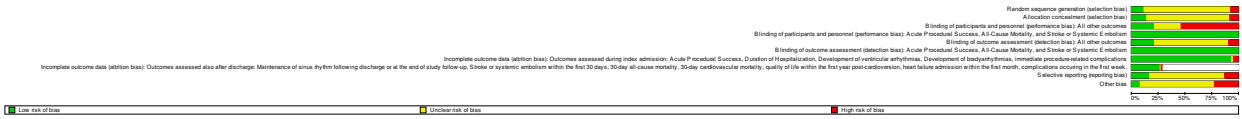


Figure 3



Risk of Bias proportions

Figure 4

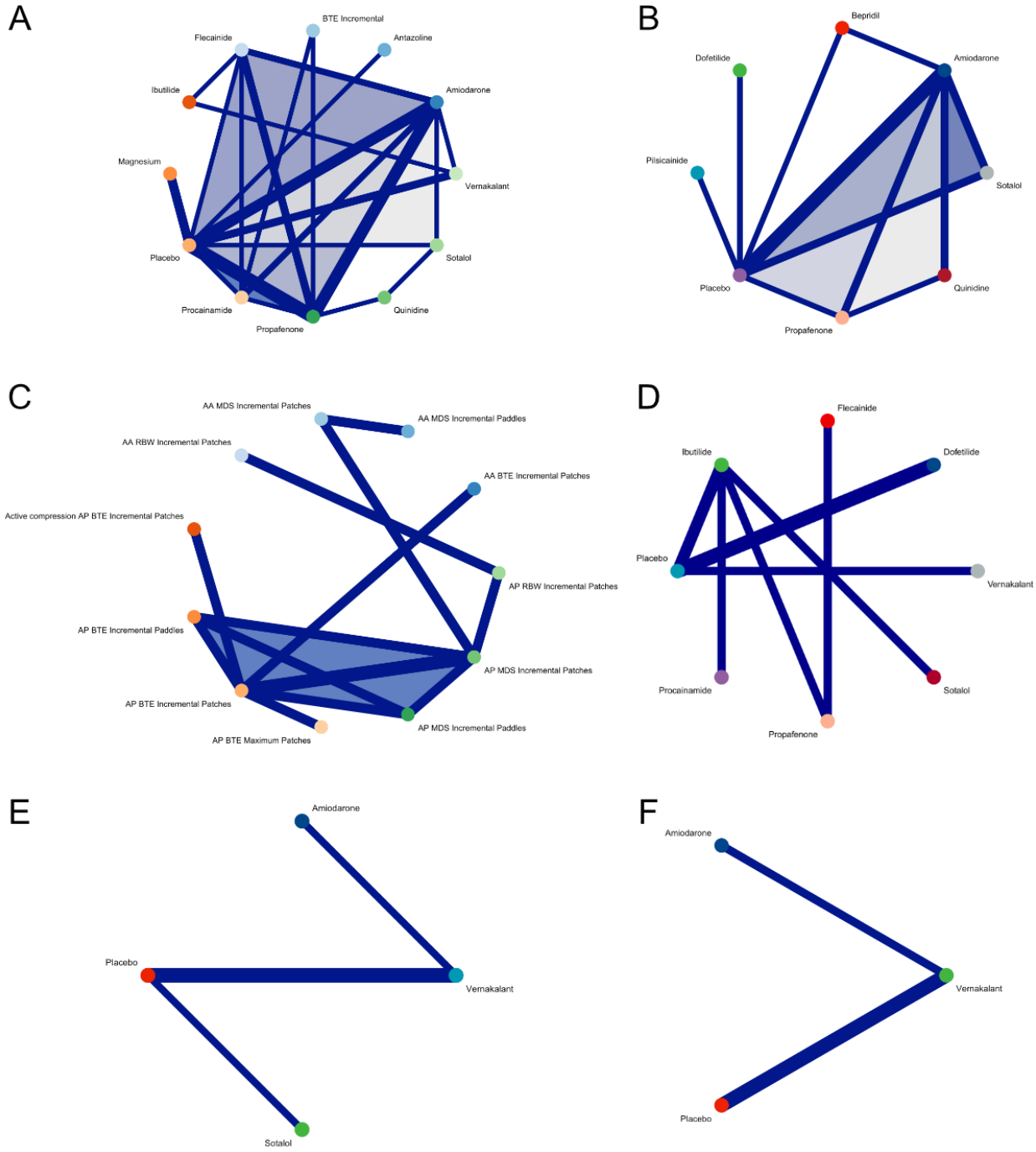


Figure 4: Network Graphs

Shaded areas indicate mulitple arm trials, Thickness of bar corresponds to total amount of patients in that direct comparison.

A - Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF) and Acute procedural success (Paroxysmal AF)

B - Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF: Drugs)

C - Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF: Electrical Cardioversion) and Acute procedural success (Persistent AF: Electrical Cardioversion)

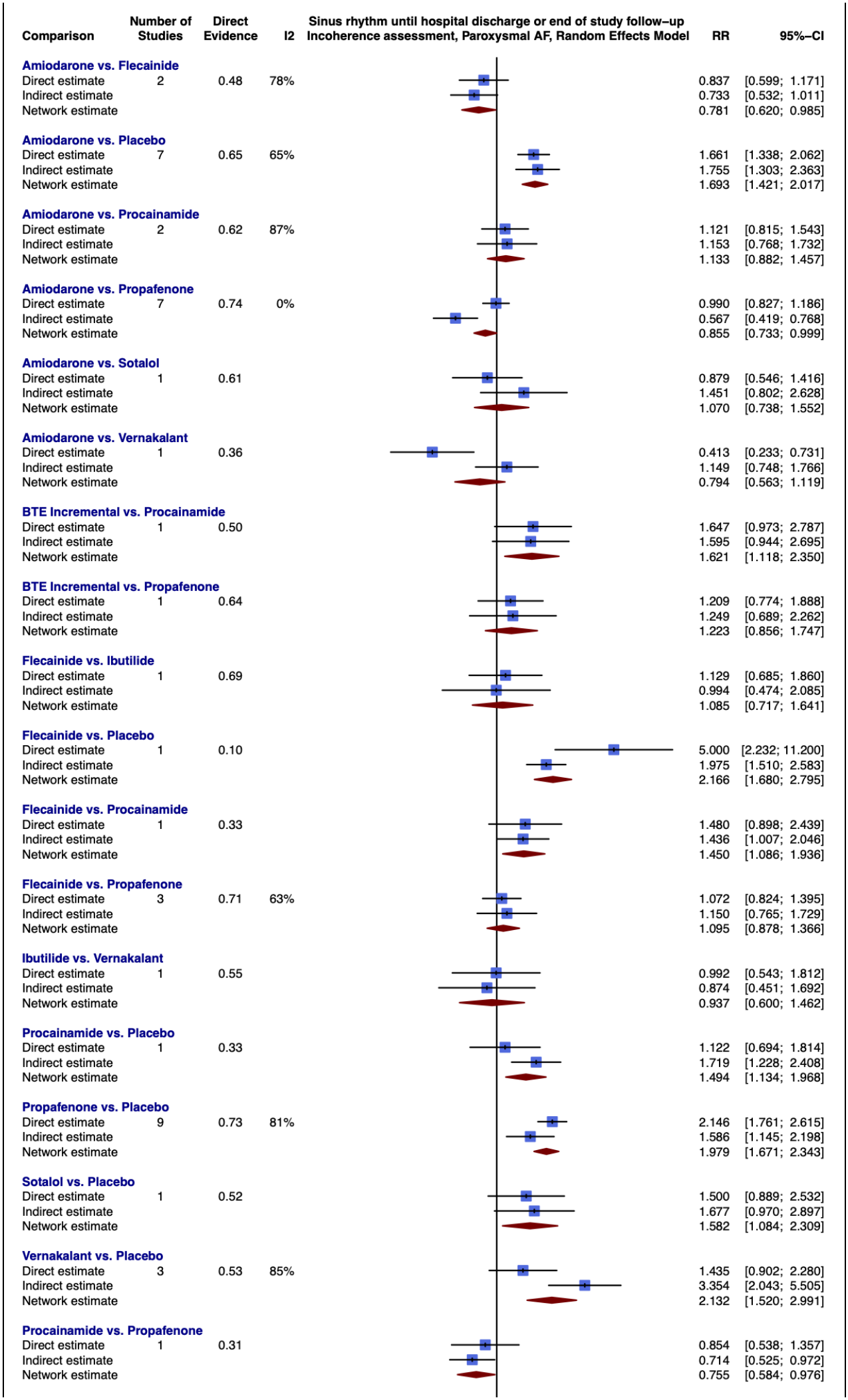
D - Sinus rhythm until hospital discharge or end of study follow-up (Atrial Flutter) and Acute procedural success (Atrial Flutter)

E - 30 day all cause mortality

F - 30 day cardiovascular mortality

AP = Anteroposterior, AA = Anteroapical, BTE = Biphasic Truncated Exponential, RBW = Rectilinear Biphasic Waveform, MDS = Monophasic Damped Sinewave

Figure 5


Comparison
Number of Studies
Direct Evidence
I2
Sinus rhythm until hospital discharge or end of study follow−up
Incoherence assessment, Paroxysmal AF, Random Effects Model
RR
95%−CI
Amiodarone vs. Flecainide
Direct estimate 2 0.48 78% 0.837 [0.599; 1.171]
Indirect estimate 0.733 [0.532; 1.011]
Network estimate 0.781 [0.620; 0.985]
Amiodarone vs. Placebo
Direct estimate 7 0.65 65% 1.661 [1.338; 2.062]
Indirect estimate 1.755 [1.303; 2.363]
Network estimate 1.693 [1.421; 2.017]
Amiodarone vs. Procainamide
Direct estimate 2 0.62 87% 1.121 [0.815; 1.543]
Indirect estimate 1.153 [0.768; 1.732]
Network estimate 1.133 [0.882; 1.457]
Amiodarone vs. Propafenone
Direct estimate 7 0.74 0% 0.990 [0.827; 1.186]
Indirect estimate 0.567 [0.419; 0.768]
Network estimate 0.855 [0.733; 0.999]
Amiodarone vs. Sotalol
Direct estimate 1 0.61 0.879 [0.546; 1.416]
Indirect estimate 1.451 [0.802; 2.628]
Network estimate 1.070 [0.738; 1.552]
Amiodarone vs. Vernakalant
Direct estimate 1 0.36 0.413 [0.233; 0.731]
Indirect estimate 1.149 [0.748; 1.766]
Network estimate 0.794 [0.563; 1.119]
BTE Incremental vs. Procainamide
Direct estimate 1 0.50 1.647 [0.973; 2.787]
Indirect estimate 1.595 [0.944; 2.695]
Network estimate 1.621 [1.118; 2.350]
BTE Incremental vs. Propafenone
Direct estimate 1 0.64 1.209 [0.774; 1.888]
Indirect estimate 1.249 [0.689; 2.262]
Network estimate 1.223 [0.856; 1.747]
Flecainide vs. Ibutilide
Direct estimate 1 0.69 1.129 [0.685; 1.860]
Indirect estimate 0.994 [0.474; 2.085]
Network estimate 1.085 [0.717; 1.641]
Flecainide vs. Placebo
Direct estimate 1 0.10 5.000 [2.232; 11.200]
Indirect estimate 1.975 [1.510; 2.583]
Network estimate 2.166 [1.680; 2.795]
Flecainide vs. Procainamide
Direct estimate 1 0.33 1.480 [0.898; 2.439]
Indirect estimate 1.436 [1.007; 2.046]
Network estimate 1.450 [1.086; 1.936]
Flecainide vs. Propafenone
Direct estimate 3 0.71 63% 1.072 [0.824; 1.395]
Indirect estimate 1.150 [0.765; 1.729]
Network estimate 1.095 [0.878; 1.366]
Ibutilide vs. Vernakalant
Direct estimate 1 0.55 0.992 [0.543; 1.812]
Indirect estimate 0.874 [0.451; 1.692]
Network estimate 0.937 [0.600; 1.462]
Procainamide vs. Placebo
Direct estimate 1 0.33 1.122 [0.694; 1.814]
Indirect estimate 1.719 [1.228; 2.408]
Network estimate 1.494 [1.134; 1.968]
Propafenone vs. Placebo
Direct estimate 9 0.73 81% 2.146 [1.761; 2.615]
Indirect estimate 1.586 [1.145; 2.198]
Network estimate 1.979 [1.671; 2.343]
Sotalol vs. Placebo
Direct estimate 1 0.52 1.500 [0.889; 2.532]
Indirect estimate 1.677 [0.970; 2.897]
Network estimate 1.582 [1.084; 2.309]
Vernakalant vs. Placebo
Direct estimate 3 0.53 85% 1.435 [0.902; 2.280]
Indirect estimate 3.354 [2.043; 5.505]
Network estimate 2.132 [1.520; 2.991]
Procainamide vs. Propafenone
Direct estimate 1 0.31 0.854 [0.538; 1.357]
Indirect estimate 0.714 [0.525; 0.972]
Network estimate 0.755 [0.584; 0.976]

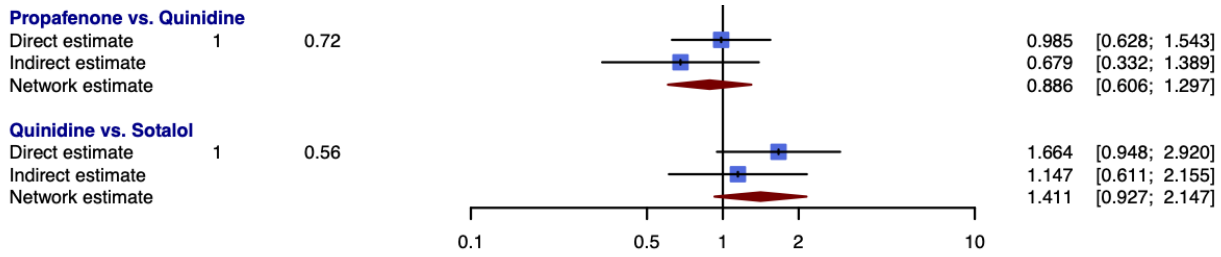


Figure 5: Forest plot assessing incoherence (local inconsistency) in network meta-analysis for sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF. BTE = Biphasic Truncated Exponential

Figure 6

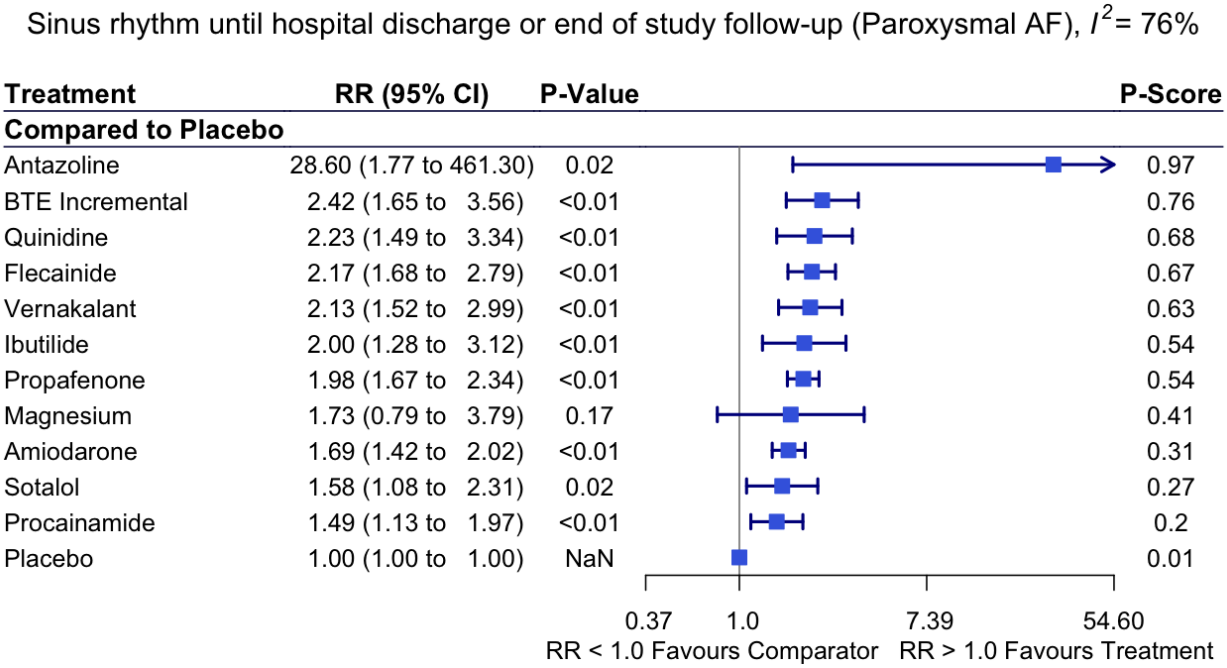


Figure 6: Forest plot for sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF, 34 trials, Random effects model

Figure 7

Frequentist NMA-SoF table

EFFECTS

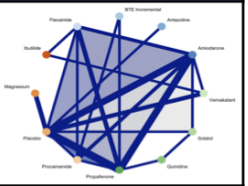
Patient or population: Patients with Paroxysmal Atrial Fibrillation

Interventions: Antazoline, Vernakalant, Ibutilide, Quinidine, Flecainide, Amiodarone, Propafenone, Magnesium, Procainamide, Sotalol, BTE Incremental, Placebo

Comparator (reference): Placebo

Outcome: Sinus rhythm until hospital discharge or end of study follow-up

Setting: Emergency Department, Elective Admission or Inpatient



Total studies, participants (34, 4467)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference			
	Antazoline (1, 22)	28.60 (1.77 to 461.30)	350 per 1000	10006 per 1000	9656 more per 1000 (270 more to 161035 more)	Low ⊕⊕◯◯ (1)	0.97	May result in a large increase in outcome
	BTE Incremental (2, 164)	2.42 (1.65 to 3.56)	350 per 1000	847 per 1000	497 more per 1000 (227 more to 895 more)	Moderate ⊕⊕⊕◯ (2)	0.76	Probably results in a large increase in outcome
	Quinidine (2, 66)	2.23 (1.49 to 3.34)	350 per 1000	781 per 1000	431 more per 1000 (172 more to 819 more)	Moderate ⊕⊕⊕◯ (3)	0.68	Probably results in a large increase in outcome
	Flecainide (5, 369)	2.17 (1.68 to 2.79)	350 per 1000	758 per 1000	408 more per 1000 (238 more to 628 more)	Low ⊕⊕◯◯ (4)	0.67	May result in a large increase in outcome
	Vernakalant (5, 372)	2.13 (1.52 to 2.99)	350 per 1000	746 per 1000	396 more per 1000 (182 more to 697 more)	Low ⊕⊕◯◯ (5)	0.63	May result in a large increase in outcome
	Ibutilide (2, 148)	2.00 (1.28 to 3.12)	350 per 1000	699 per 1000	349 more per 1000 (98 more to 741 more)	Moderate ⊕⊕⊕◯ (6)	0.54	Probably results in a large increase in outcome
	Propafenone (16, 1123)	1.98 (1.67 to 2.34)	350 per 1000	692 per 1000	342 more per 1000 (235 more to 470 more)	Moderate ⊕⊕⊕◯ (7)	0.54	Probably results in a large increase in outcome
	Magnesium (3, 57)	1.73 (0.79 to 3.79)	350 per 1000	606 per 1000	256 more per 1000 (72 fewer to 975 more)	Low ⊕⊕◯◯ (8)	0.41	May result in a large increase in outcome
	Amiodarone (13, 824)	1.69 (1.42 to 2.02)	350 per 1000	592 per 1000	242 more per 1000 (147 more to 356 more)	Moderate ⊕⊕⊕◯ (9)	0.31	Probably results in a large increase in outcome
	Sotalol (2, 73)	1.58 (1.08 to 2.31)	350 per 1000	553 per 1000	204 more per 1000 (29 more to 458 more)	Moderate ⊕⊕⊕◯ (10)	0.27	Probably results in a large increase in outcome
	Procainamide (4, 280)	1.49 (1.13 to 1.97)	350 per 1000	523 per 1000	173 more per 1000 (47 more to 339 more)	Moderate ⊕⊕⊕◯ (11)	0.2	Probably results in a large increase in outcome
	Placebo (20, 969)	1.00 (1.00 to 1.00)	350 per 1000				0.01	

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

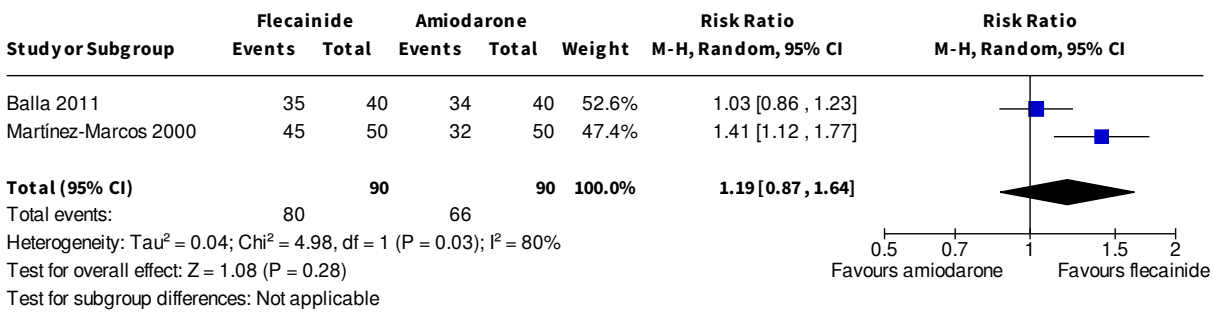
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. High global inconsistency. Imprecision present (Confidence interval many magnitudes larger than next highest)
2. High risk of bias from indirect estimate (Lack of information on randomisation and allocation concealment, selective outcome reporting).
3. High risk of bias from indirect estimate (Lack of information on randomisation and allocation concealment, selective outcome reporting).
4. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, selective outcome reporting). Incoherence present.
5. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, incomplete outcome reporting, selective outcome reporting). Incoherence present.
6. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, selective outcome reporting).
7. High risk of bias from indirect estimate (Lack of information on randomisation and allocation concealment, incomplete outcome reporting, selective outcome reporting).
8. High risk of bias from direct estimate (Lack of information on randomisation and allocation concealment, selective outcome reporting). Imprecision present.
9. High risk of bias from direct and indirect estimates (Lack of information on randomisation and selective outcome reporting, no allocation concealment, incomplete outcome reporting).
10. High risk of bias from direct and indirect estimates (Lack of information on randomisation and selective outcome reporting, no allocation concealment, incomplete outcome reporting).
11. High risk of bias from direct and indirect estimates (Lack of information on randomisation, and selective outcome reporting, no allocation concealment, incomplete outcome reporting).

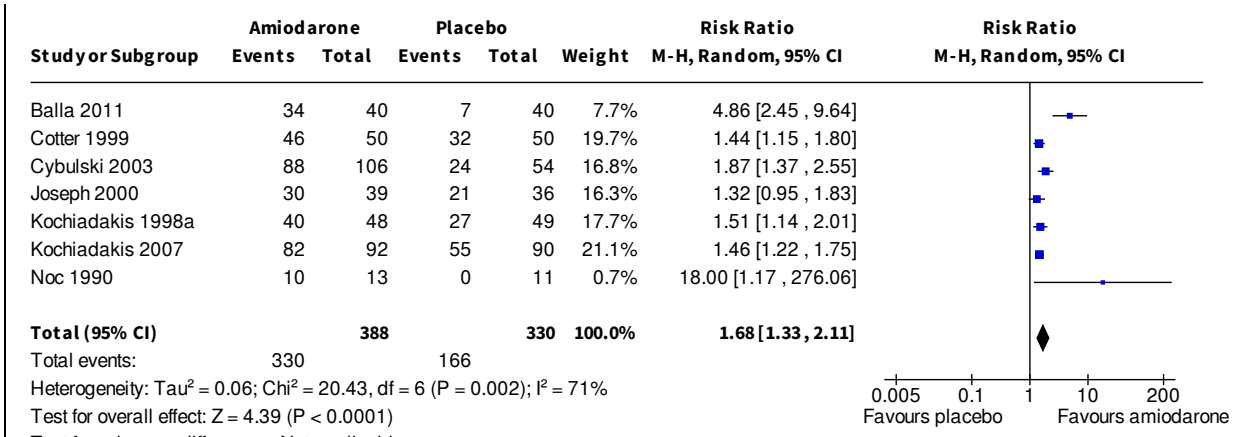
Summary of Findings Table: Sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF

Figure 8



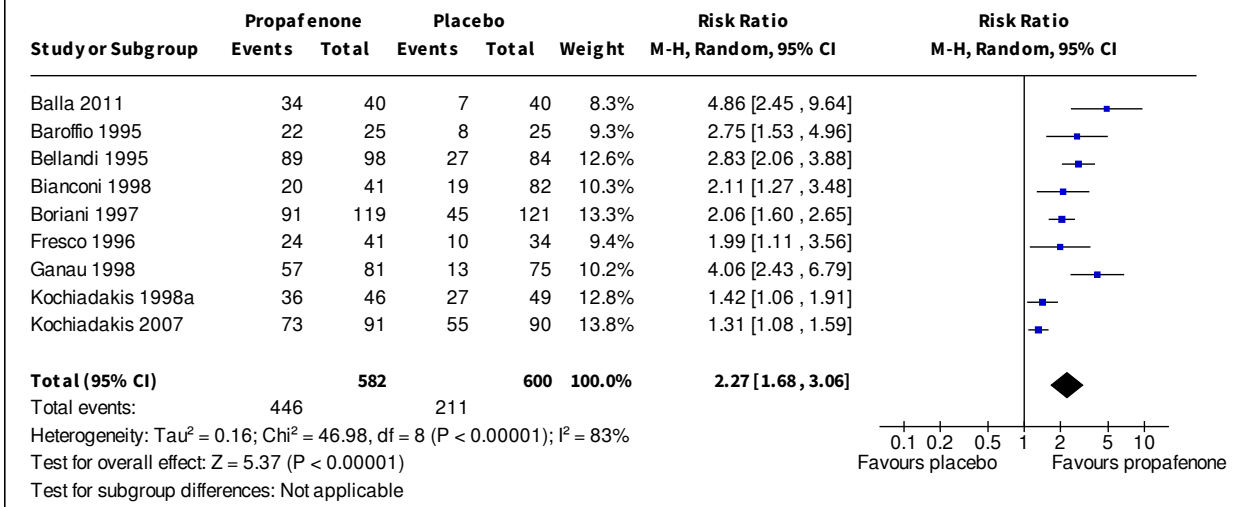
Pairwise analysis

Figure 9



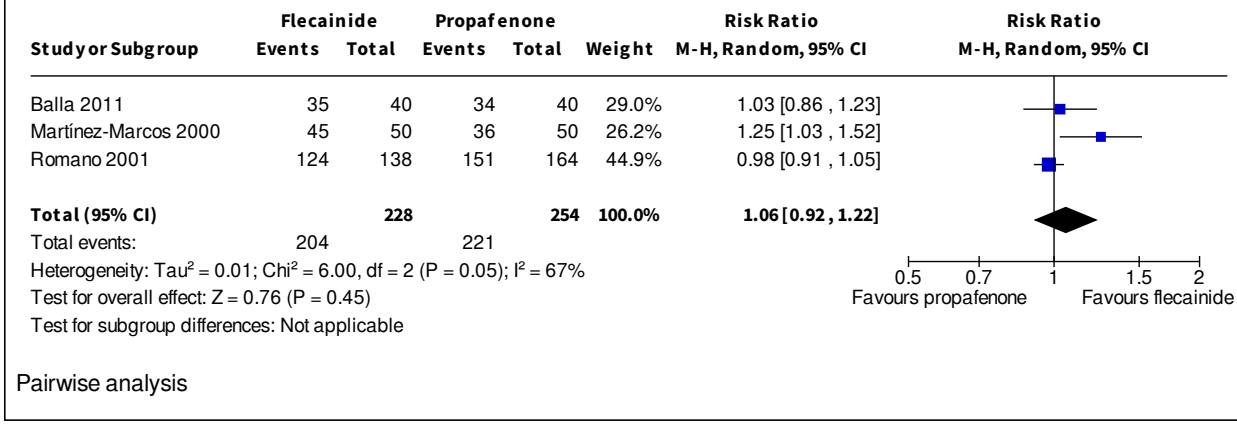
Pairwise analysis

Figure 10



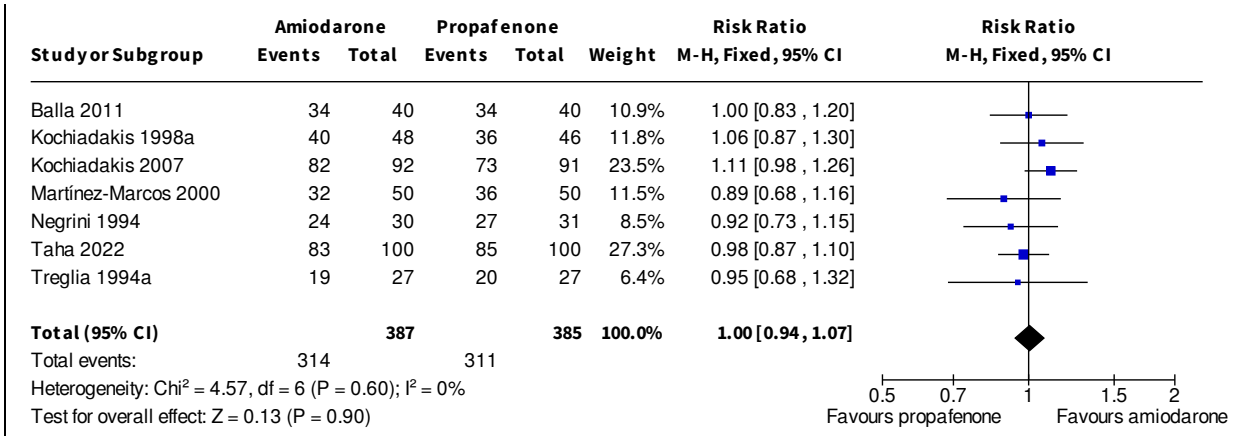
Pairwise analysis

Figure 11



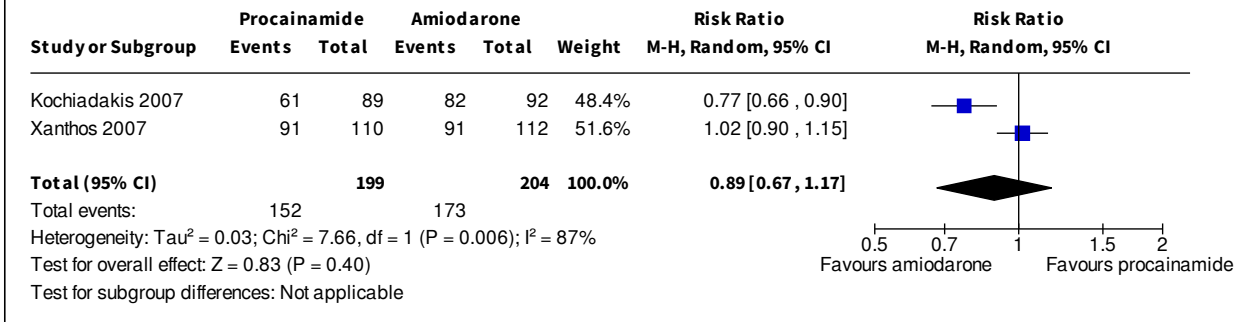
Pairwise analysis

Figure 12



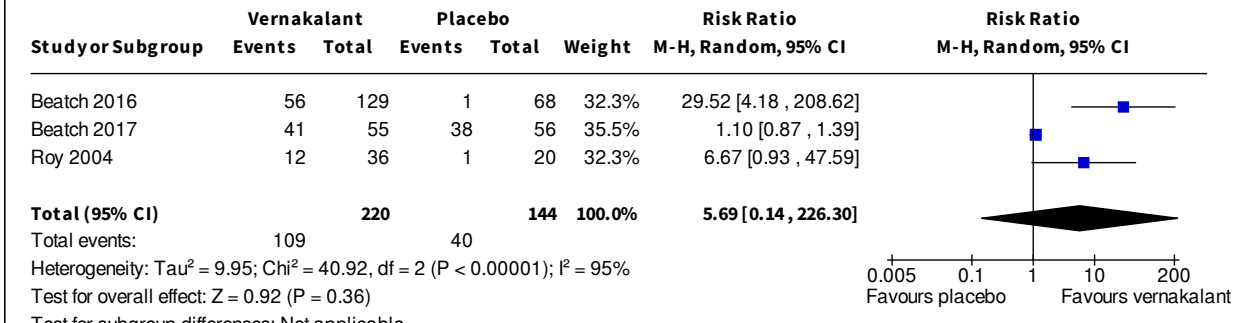
Pairwise analysis

Figure 13



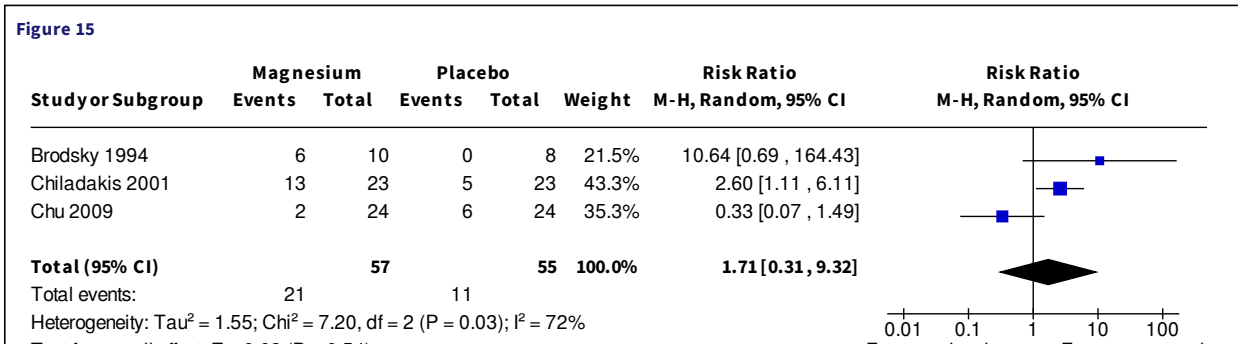
Pairwise analysis

Figure 14



Pairwise analysis

Figure 15



Pairwise analysis

Figure 16

Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF: DCCV), I^2 = 14%

Treatment	RR (95% CI)	P-Value	P-Score
Compared to AP BTE Incremental Patches			
AP BTE Maximum Patches	1.35 (1.17 to 1.55)	<0.01	0.99
Active compression AP BTE Incremental Patches	1.14 (1.00 to 1.31)	0.05	0.88
AP BTE Incremental Paddles	1.03 (0.98 to 1.09)	0.24	0.77
AP BTE Incremental Patches	1.00 (1.00 to 1.00)	NaN	0.67
AP MDS Incremental Paddles	0.95 (0.86 to 1.05)	0.31	0.58
AP MDS Incremental Patches	0.78 (0.70 to 0.87)	<0.01	0.37
AA RBW Incremental Patches	0.76 (0.66 to 0.88)	<0.01	0.25
AP RBW Incremental Patches	0.76 (0.68 to 0.86)	<0.01	0.23
AA MDS Incremental Patches	0.76 (0.67 to 0.86)	<0.01	0.23
AA MDS Incremental Paddles	0.66 (0.53 to 0.83)	<0.01	0.04

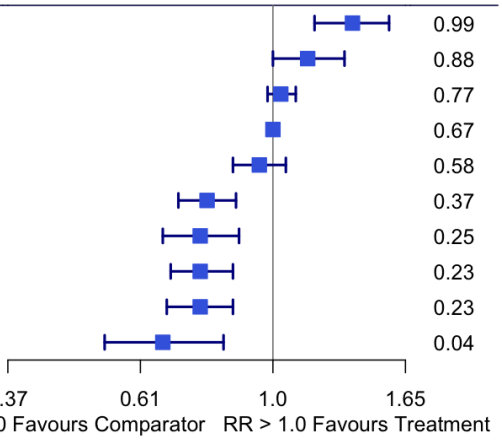


Figure 16: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Electrical Cardioversion, Persistent AF, 8 Trials, Fixed Effects Model.

AP = Anteroposterior, AA = Anteroapical, BTE = Biphasic Truncated Exponential, RBW = Rectilinear Biphasic Waveform, MDS = Monophasic Damped Sinewave, DCCV = Direct Current Cardioversion

Figure 17

Frequentist NMA-SoF table

EFFECTS

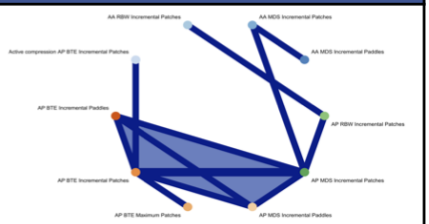
Patient or population: Patients with Persistent Atrial Fibrillation

Interventions: AP BTE Maximum Patches, AP BTE Incremental Patches, AP BTE Incremental Paddles, Active compression AP BTE Incremental Patches, AP MDS Incremental Patches, AP MDS Incremental Paddles, AA RBW Incremental Patches, AP RBW Incremental Patches, AA MDS Incremental Patches, AA MDS Incremental Paddles

Comparator (reference): AP BTE Incremental Patches

Outcome: Sinus rhythm until hospital discharge or end of study follow-up

Setting: Emergency Department, Elective Admission or Inpatient



Total studies, Participants (8, 1122)	Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
		Without intervention	*With* intervention	Difference to AP BTE Incremental Patches			
AP BTE Maximum Patches (1, 129)	1.35 (1.17 to 1.55)	N/A	1066 per 1000	275 more per 1000 (122 more to 454 more)	High ⊕⊕⊕⊕ (1)	0.99	Likely results in a large increase in outcome
Active compression AP BTE Incremental Patches (1, 50)	1.14 (1.00 to 1.31)	N/A	904 per 1000	113 more per 1000 (10 fewer to 256 more)	High ⊕⊕⊕⊕ (2)	0.88	Likely results in a large increase in outcome
AP BTE Incremental Paddles (1, 56)	1.03 (0.98 to 1.09)	N/A	815 per 1000	25 more per 1000 (40 fewer to 94 more)	Low ⊕⊕◯◯ (3)	0.76	May result in little or no increase in outcome
AP BTE Incremental Patches (4, 306)	1.00 (1.00 to 1.00)	N/A	791 per 1000			0.68	
AP MDS Incremental Paddles (1, 48)	0.95 (0.86 to 1.05)	N/A	748 per 1000	43 fewer per 1000 (126 fewer to 51 more)	Low ⊕⊕◯◯ (4)	0.58	May result in little or no decrease in outcome
AP MDS Incremental Patches (4, 244)	0.78 (0.70 to 0.87)	N/A	621 per 1000	170 fewer per 1000 (238 fewer to 93 fewer)	Moderate ⊕⊕⊕◯ (5)	0.35	Probably results in a large decrease in outcome
AA RBW Incremental Patches (1, 63)	0.76 (0.66 to 0.88)	N/A	604 per 1000	187 fewer per 1000 (283 fewer to 71 fewer)	Moderate ⊕⊕⊕◯ (6)	0.25	Probably results in a large decrease in outcome
AP RBW Incremental Patches (2, 168)	0.76 (0.68 to 0.86)	N/A	603 per 1000	188 fewer per 1000 (268 fewer to 96 fewer)	Moderate ⊕⊕⊕◯ (7)	0.24	Probably results in a large decrease in outcome
AA MDS Incremental Patches (2 ,43)	0.76 (0.67 to 0.86)	N/A	602 per 1000	189 fewer per 1000 (270 fewer to 96 fewer)	Moderate ⊕⊕⊕◯ (8)	0.24	Probably results in a large decrease in outcome
AA MDS Incremental Paddles (1, 15)	0.66 (0.53 to 0.83)	N/A	524 per 1000	267 fewer per 1000 (382 fewer to 119 fewer)	Moderate ⊕⊕⊕◯ (9)	0.05	Probably results in a large decrease in outcome

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

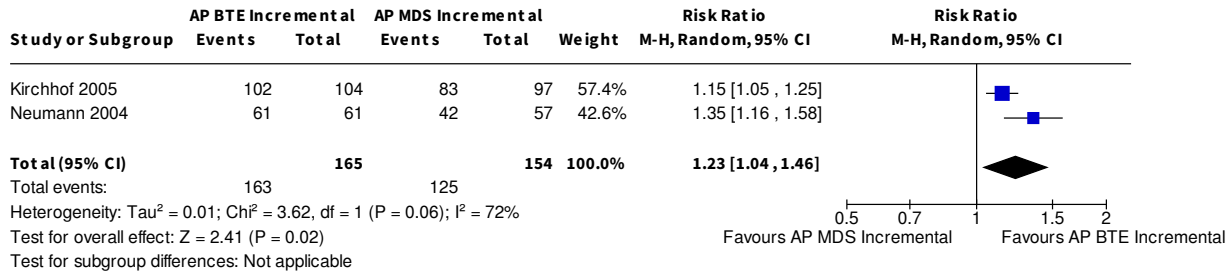
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. Low risk of bias
2. Moderate risk of bias (Lack of information on selective outcome reporting)
3. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting). Imprecision present.
4. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting). Imprecision present.
5. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting).
6. High risk of bias from direct estimate (Lack of information on randomisation, allocation concealment and selective outcome reporting).
7. High risk of bias from indirect estimate (Lack of information on randomisation, allocation concealment and selective outcome reporting).
8. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, selective outcome reporting).
9. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting).

Summary of Findings: Sinus rhythm until hospital discharge or end of study follow-up, Persistent AF for Electrical Cardioversion

Figure 18



Pairwise analysis

Figure 19

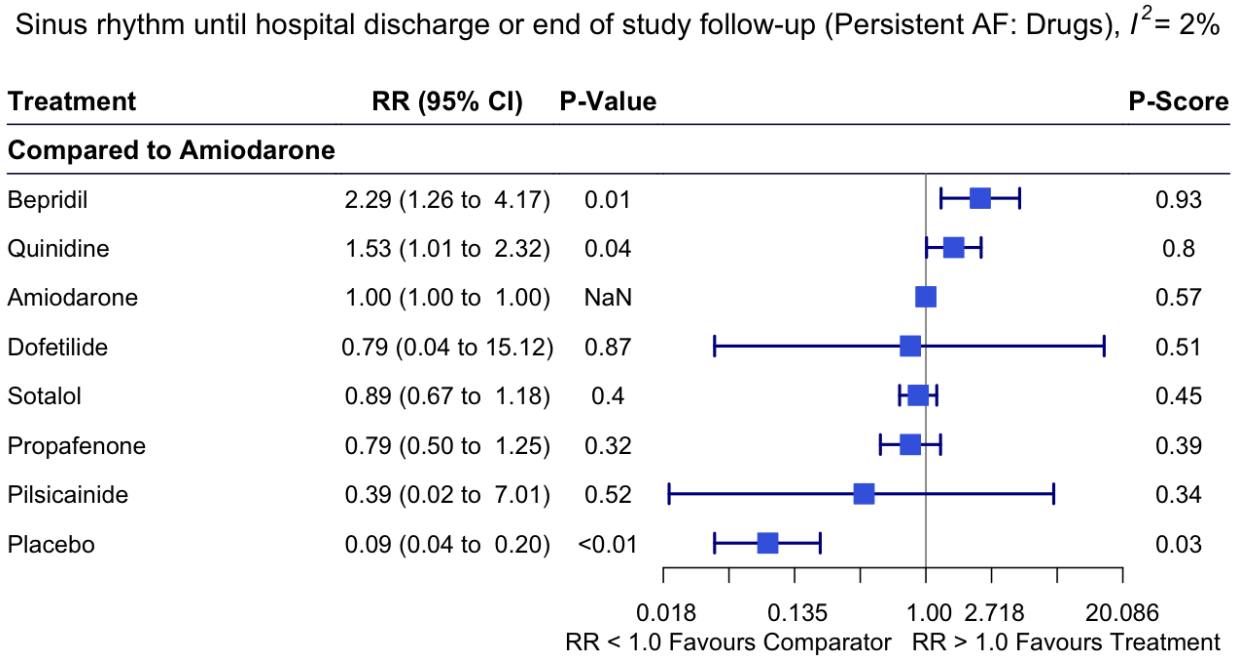


Figure 19: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Persistent AF, 12 Trials, Fixed Effects Model

Figure 20

Frequentist NMA-SoF table

EFFECTS

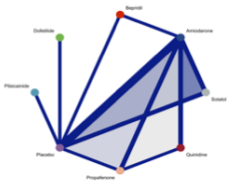
Patient or population: Patients with Persistent Atrial Fibrillation

Interventions: Bepridil, Quinidine, Amiodarone, Propafenone, Pilsicainide, Dofetilide, Placebo

Comparator (reference): Amiodarone

Outcome: Sinus rhythm until hospital discharge or end of study follow-up

Setting: Emergency Department, Elective Admission or Inpatient



Total studies, Participants (12, 1615)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference to Amiodarone			
●	Bepridil (2, 81)	2.29 (1.26 to 4.17)	23 per 1000	611 per 1000	344 more per 1000 (68 more to 847 more)	Moderate ⊕⊕⊕◯ (1)	0.93	Probably results in a large increase in outcome
●	Quinidine (2, 50)	1.53 (1.01 to 2.32)	23 per 1000	409 per 1000	142 more per 1000 (4 more to 351 more)	Moderate ⊕⊕⊕◯ (2)	0.8	Probably results in a large increase in outcome
●	Amiodarone (9, 607)	1.00 (1.00 to 1.00)	23 per 1000	267 per 1000			0.57	
●	Dofetilide (1, 49)	0.79 (0.04 to 15.12)	23 per 1000	210 per 1000	57 fewer per 1000 (256 fewer to 3770 more)	Low⊕⊕◯◯ (3)	0.51	May result in a slight decrease in outcome
●	Sotalol (2, 280)	0.89 (0.67 to 1.18)	23 per 1000	236 per 1000	30 fewer per 1000 (89 fewer to 47 more)	Low⊕⊕◯◯ (4)	0.45	May result in a slight decrease in outcome
●	Propafenone (2, 62)	0.79 (0.50 to 1.25)	23 per 1000	212 per 1000	55 fewer per 1000 (132 fewer to 67 more)	Low⊕⊕◯◯ (5)	0.39	May result in a slight decrease in outcome
●	Pilsicainide (1, 52)	0.39 (0.02 to 7.01)	23 per 1000	105 per 1000	162 fewer per 1000 (261 fewer to 1605 more)	Low⊕⊕◯◯ (6)	0.34	May result in a large decrease in outcome
●	Placebo (9, 434)	0.09 (0.04 to 0.20)	23 per 1000	23 per 1000	244 fewer per 1000 (257 fewer to 213 fewer)	Moderate ⊕⊕⊕◯ (7)	0.03	Probably results in a large decrease in outcome

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

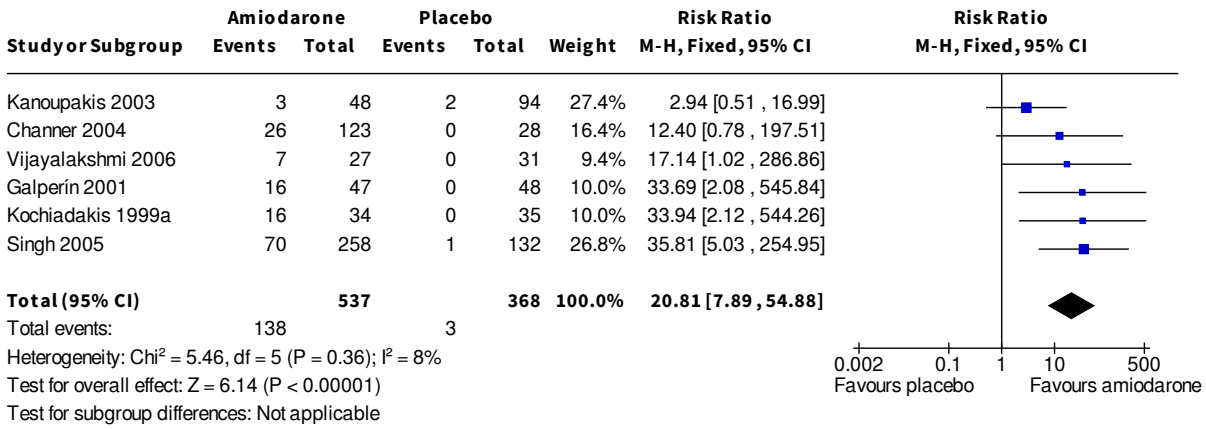
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. High risk of bias from direct and indirect estimates (lack of information on randomisation, allocation concealment and selective outcome reporting).
2. High risk of bias from direct and indirect estimates (lack of information on randomisation, allocation concealment and selective outcome reporting).
3. High risk of bias from indirect estimate (lack of information on randomisation and allocation concealment, selective outcome reporting). Imprecision present.
4. High risk of bias from direct and indirect estimates (lack of information on randomisation, allocation concealment and selective outcome reporting). Imprecision present.
5. High risk of bias from direct and indirect estimates (lack of information on randomisation, allocation concealment and selective outcome reporting). Imprecision present
6. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment and selective outcome reporting). Imprecision present.
7. High risk of bias from direct and indirect estimates (lack of information on randomisation and allocation concealment, selective outcome reporting).

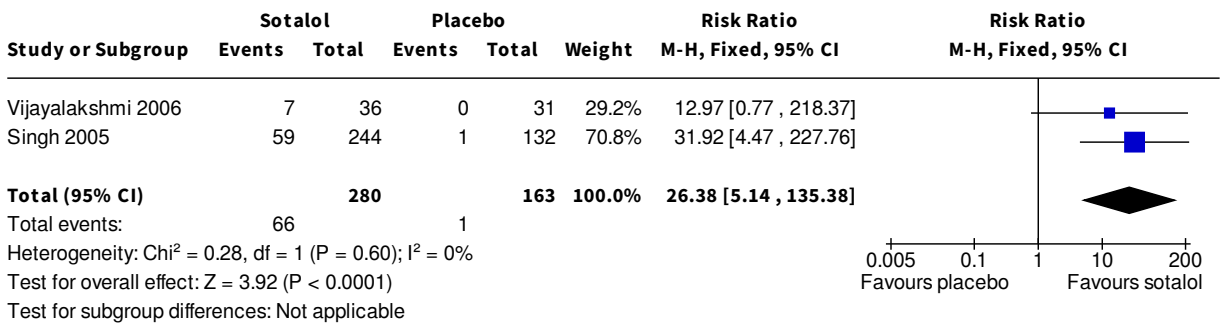
Summary of Findings Table: Sinus rhythm until hospital discharge or end of study follow-up, Persistent AF

Figure 21



Pairwise analysis

Figure 22

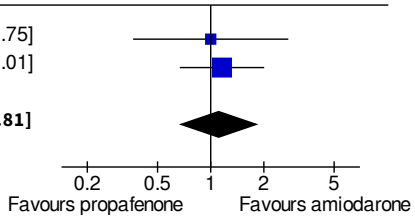


Pairwise analysis

Figure 23

Study or Subgroup	Amiodarone Events	Amiodarone Total	Propafenone Events	Propafenone Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baroni 2011	6	30	6	30	30.9%	1.00 [0.36 , 2.75]
Kochiadakis 1999a	16	34	13	32	69.1%	1.16 [0.67 , 2.01]
Total (95% CI)		**64**		**62**	**100.0%**	**1.11 [0.68 , 1.81]**
Total events:	22		19			

Heterogeneity: Chi² = 0.06, df = 1 (P = 0.80); I² = 0%
Test for overall effect: Z = 0.42 (P = 0.68)
Test for subgroup differences: Not applicable



Pairwise analysis

Figure 24

Study or Subgroup	Amiodarone Events	Amiodarone Total	Sotalol Events	Sotalol Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 2005	70	258	59	244	91.0%	1.12 [0.83 , 1.51]
Vijayalakshmi 2006	7	27	7	36	9.0%	1.33 [0.53 , 3.35]
Total (95% CI)		**285**		**280**	**100.0%**	**1.14 [0.86 , 1.52]**
Total events:	77		66			

Heterogeneity: Chi² = 0.12, df = 1 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.91 (P = 0.36)
Test for subgroup differences: Not applicable

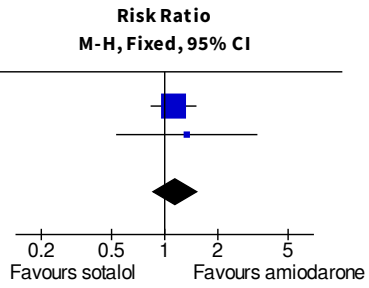
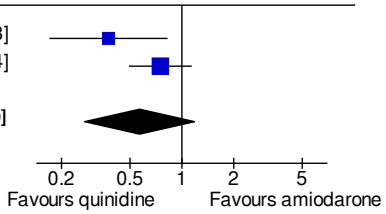


Figure 25

Study or Subgroup	Amiodarone Events	Amiodarone Total	Quinidine Events	Quinidine Total	Weight	Risk Ratio M-H, Random, 95% CI
Baroni 2011	6	30	16	30	40.1%	0.38 [0.17 , 0.83]
Zehender 1994	12	20	16	20	59.9%	0.75 [0.49 , 1.14]
Total (95% CI)		**50**		**50**	**100.0%**	**0.57 [0.27 , 1.19]**
Total events:	18		32			

Heterogeneity: Tau² = 0.19; Chi² = 2.82, df = 1 (P = 0.09); I² = 65%
Test for overall effect: Z = 1.51 (P = 0.13)
Test for subgroup differences: Not applicable



Pairwise analysis

Figure 26

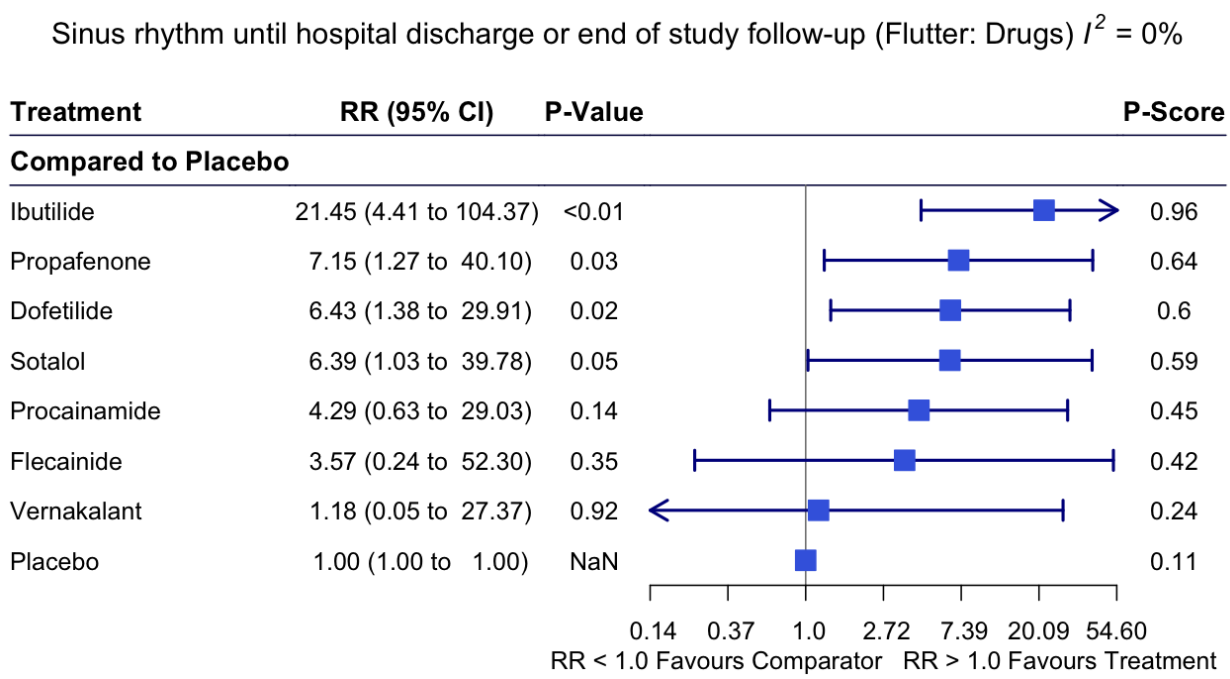


Figure 26: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Atrial Flutter, 10 trials, Fixed Effects Model

Figure 27

Frequentist NMA-SoF table

EFFECTS

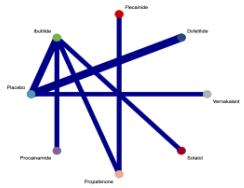
Patient or population: Patients with Atrial Flutter

Interventions: Vernakalant, Dofetilide, Flecainide, Ibutilide, Propafenone, Sotalol, Procainamide, Placebo

Comparator (reference): Placebo

Outcome: Sinus rhythm until hospital discharge or end of study follow-up

Setting: Emergency Department, Elective Admission or Inpatient



Total studies, Participants (10, 422)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference			
●	Ibutilide (5, 201)	21.45 (4.41 to 104.37)	12 per 1000	262 per 1000	249 more per 1000 (42 more to 1261 more)	Moderate ⊕⊕⊕◯ (1)	0.96	Probably results in a large increase in outcome
●	Propafenone (2, 25)	7.15 (1.27 to 40.10)	12 per 1000	87 per 1000	75 more per 1000 (3 more to 477 more)	Moderate ⊕⊕⊕◯ (2)	0.64	Probably results in a slight increase in outcome
●	Dofetilide (3, 29)	6.43 (1.38 to 29.91)	12 per 1000	78 per 1000	66 more per 1000 (5 more to 353 more)	Moderate ⊕⊕⊕◯ (3)	0.6	Probably results in a slight increase in outcome
●	Sotalol (1, 21)	6.39 (1.03 to 39.78)	12 per 1000	78 per 1000	66 more per 1000 (0 more to 473 more)	Moderate ⊕⊕⊕◯ (4)	0.59	Probably results in a slight increase in outcome
●	Procainamide (1, 20)	4.29 (0.63 to 29.03)	12 per 1000	52 per 1000	40 more per 1000 (4 fewer to 342 more)	Low ⊕⊕◯◯ (5)	0.45	May result in a slight increase in outcome
●	Flecainide (1, 5)	3.57 (0.24 to 52.30)	12 per 1000	44 per 1000	31 more per 1000 (9 fewer to 626 more)	Low ⊕⊕◯◯ (6)	0.42	May result in a slight increase in outcome
●	Vernakalant (1, 39)	1.18 (0.05 to 27.37)	12 per 1000	14 per 1000	2 more per 1000 (12 fewer to 322 more)	Low ⊕⊕◯◯ (7)	0.24	May result in a slight increase in outcome
●	Placebo (6, 82)	1.00 (1.00 to 1.00)	12 per 1000	12 per 1000			0.11	

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

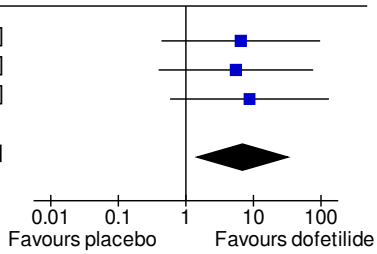
1. High risk of bias from direct estimate (lack of information on randomisation, allocation concealment and selective outcome reporting).
2. High risk of bias from direct estimate (lack of information on randomisation and allocation concealment, selective outcome reporting).
3. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting).
4. High risk of bias from direct estimate (lack of information on randomisation, allocation concealment and selective outcome reporting).
5. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting). Imprecision present.
6. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting). Imprecision present.
7. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting). Imprecision present.

Summary of Findings Table: Sinus until hospital discharge or end of study follow-up, Atrial Flutter

Figure 28

Study or Subgroup	Dofetilide Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Falk 1997	6	11	0	5	33.9%	6.50 [0.43 , 97.14]
Lindeboom 2000	5	7	0	3	33.9%	5.50 [0.39 , 76.65]
Norgaard 1999	7	11	0	6	32.1%	8.75 [0.58 , 131.07]
Total (95% CI)		**29**		**14**	**100.0%**	**6.88 [1.46 , 32.36]**
Total events:	18		0			

Heterogeneity: Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.44 (P = 0.01)
Test for subgroup differences: Not applicable

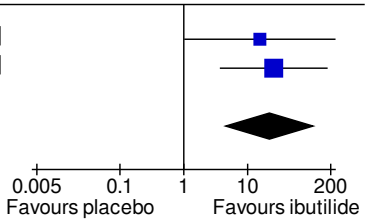


Pairwise analysis

Figure 29

Study or Subgroup	Ibutilide Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abi Mansour 1998	27	45	0	12	37.1%	15.54 [1.02 , 237.92]
Stambler 1996	50	80	1	41	62.9%	25.63 [3.67 , 178.91]
Total (95% CI)		**125**		**53**	**100.0%**	**21.89 [4.54 , 105.61]**
Total events:	77		1			

Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 3.84 (P = 0.0001)
Test for subgroup differences: Not applicable



Pairwise analysis

Figure 30

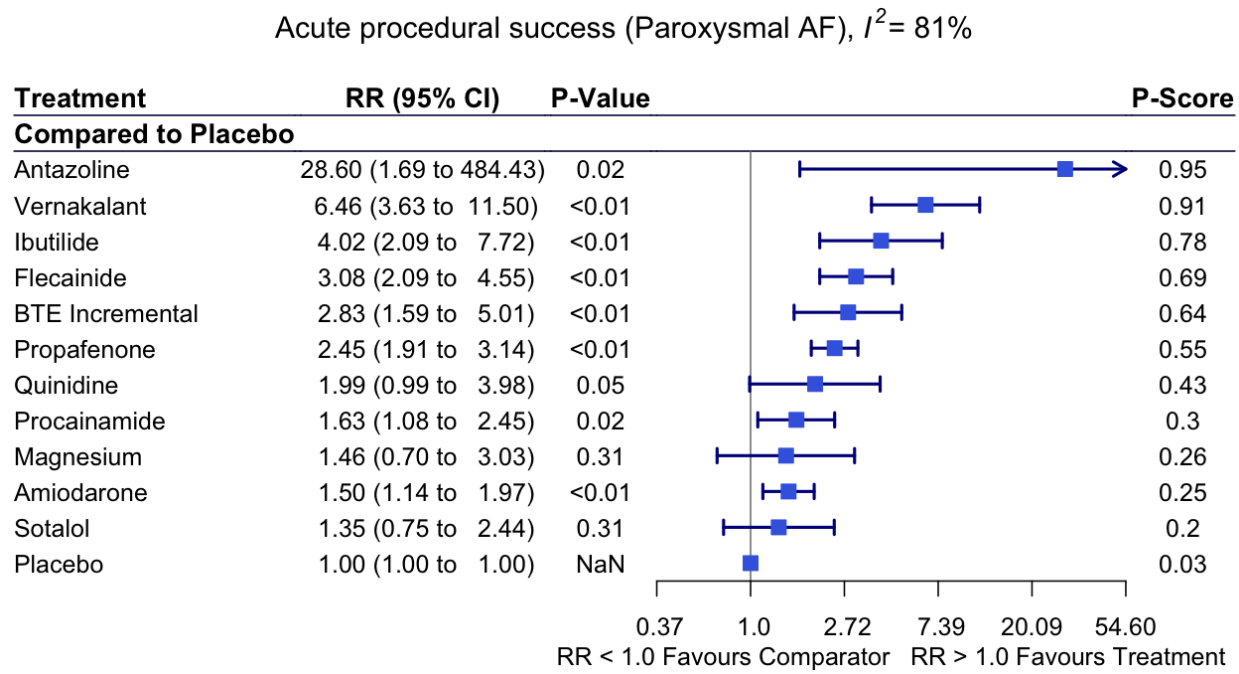
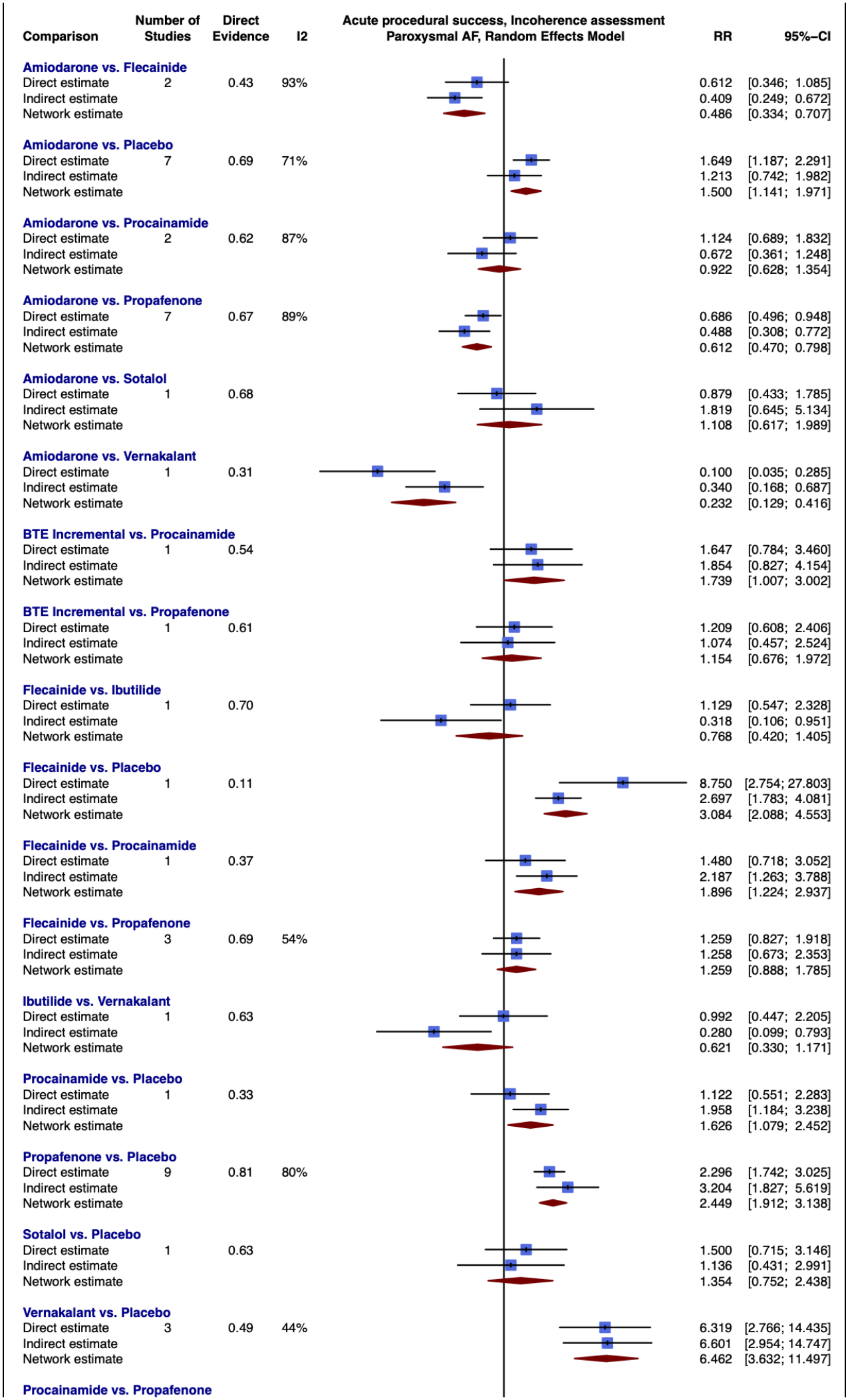


Figure 30: Forestplot for acute procedural success, Paroxysmal AF, 34 trials, Random effects model.
BTE = Biphasic Truncated Exponential

Figure 31


Comparison
Number of Studies
Direct Evidence
I2
Acute procedural success, Incoherence assessment
Paroxysmal AF, Random Effects Model
RR
95%–CI
Amiodarone vs. Flecainide
Direct estimate 2 0.43 93% 0.612 [0.346; 1.085]
Indirect estimate 0.409 [0.249; 0.672]
Network estimate 0.486 [0.334; 0.707]
Amiodarone vs. Placebo
Direct estimate 7 0.69 71% 1.649 [1.187; 2.291]
Indirect estimate 1.213 [0.742; 1.982]
Network estimate 1.500 [1.141; 1.971]
Amiodarone vs. Procainamide
Direct estimate 2 0.62 87% 1.124 [0.689; 1.832]
Indirect estimate 0.672 [0.361; 1.248]
Network estimate 0.922 [0.628; 1.354]
Amiodarone vs. Propafenone
Direct estimate 7 0.67 89% 0.686 [0.496; 0.948]
Indirect estimate 0.488 [0.308; 0.772]
Network estimate 0.612 [0.470; 0.798]
Amiodarone vs. Sotalol
Direct estimate 1 0.68 0.879 [0.433; 1.785]
Indirect estimate 1.819 [0.645; 5.134]
Network estimate 1.108 [0.617; 1.989]
Amiodarone vs. Vernakalant
Direct estimate 1 0.31 0.100 [0.035; 0.285]
Indirect estimate 0.340 [0.168; 0.687]
Network estimate 0.232 [0.129; 0.416]
BTE Incremental vs. Procainamide
Direct estimate 1 0.54 1.647 [0.784; 3.460]
Indirect estimate 1.854 [0.827; 4.154]
Network estimate 1.739 [1.007; 3.002]
BTE Incremental vs. Propafenone
Direct estimate 1 0.61 1.209 [0.608; 2.406]
Indirect estimate 1.074 [0.457; 2.524]
Network estimate 1.154 [0.676; 1.972]
Flecainide vs. Ibutilide
Direct estimate 1 0.70 1.129 [0.547; 2.328]
Indirect estimate 0.318 [0.106; 0.951]
Network estimate 0.768 [0.420; 1.405]
Flecainide vs. Placebo
Direct estimate 1 0.11 8.750 [2.754; 27.803]
Indirect estimate 2.697 [1.783; 4.081]
Network estimate 3.084 [2.088; 4.553]
Flecainide vs. Procainamide
Direct estimate 1 0.37 1.480 [0.718; 3.052]
Indirect estimate 2.187 [1.263; 3.788]
Network estimate 1.896 [1.224; 2.937]
Flecainide vs. Propafenone
Direct estimate 3 0.69 54% 1.259 [0.827; 1.918]
Indirect estimate 1.258 [0.673; 2.353]
Network estimate 1.259 [0.888; 1.785]
Ibutilide vs. Vernakalant
Direct estimate 1 0.63 0.992 [0.447; 2.205]
Indirect estimate 0.280 [0.099; 0.793]
Network estimate 0.621 [0.330; 1.171]
Procainamide vs. Placebo
Direct estimate 1 0.33 1.122 [0.551; 2.283]
Indirect estimate 1.958 [1.184; 3.238]
Network estimate 1.626 [1.079; 2.452]
Propafenone vs. Placebo
Direct estimate 9 0.81 80% 2.296 [1.742; 3.025]
Indirect estimate 3.204 [1.827; 5.619]
Network estimate 2.449 [1.912; 3.138]
Sotalol vs. Placebo
Direct estimate 1 0.63 1.500 [0.715; 3.146]
Indirect estimate 1.136 [0.431; 2.991]
Network estimate 1.354 [0.752; 2.438]
Vernakalant vs. Placebo
Direct estimate 3 0.49 44% 6.319 [2.766; 14.435]
Indirect estimate 6.601 [2.954; 14.747]
Network estimate 6.462 [3.632; 11.497]
Procainamide vs. Propafenone

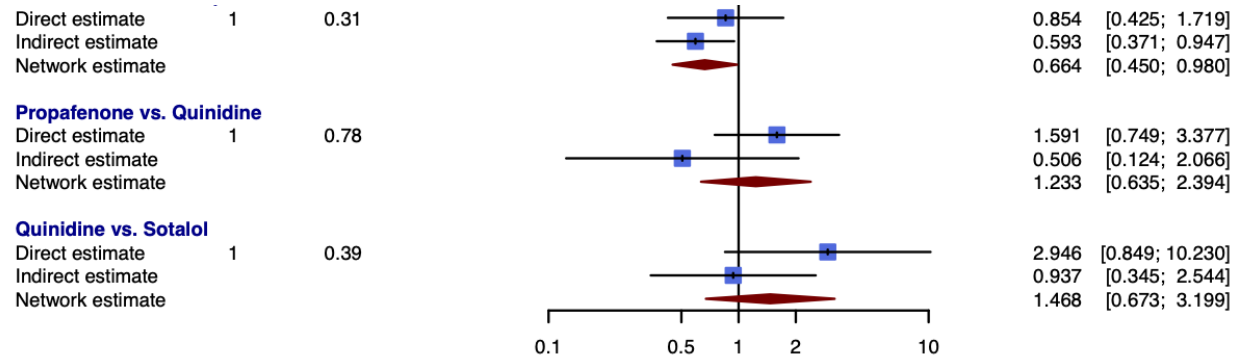


Figure 31: Forest plot assessing incoherence (local inconsistency) in network meta-analysis for acute procedural success, Paroxysmal AF. BTE = Biphasic Truncated Exponential

Figure 32

Frequentist NMA-SoF table

EFFECTS

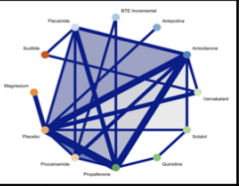
Patient or population: Patients with Paroxysmal Atrial Fibrillation

Interventions: Vernakalant, Antazoline, Ibutilide, Quinidine, Flecainide, Amiodarone, Propafenone, Magnesium, Procainamide, Sotalol, BTE Incremental, Placebo

Comparator (reference): Placebo

Outcome: Acute procedural success

Setting: Emergency Department, Elective Admission or Inpatient



Total studies, participants (34, 4467)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference			
	Antazoline (1, 22)	28.60 (1.69 to 484.43)	272 per 1000	7792 per 1000	7520 more per 1000 (187 more to 131709 more)	Very Low ⊕◯◯◯ (1)	0.95	The evidence is very uncertain about the effect on the outcome
	Vernakalant (5, 372)	6.46 (3.63 to 11.50)	272 per 1000	1761 per 1000	1488 more per 1000 (717 more to 2860 more)	Low ⊕⊕◯◯ (2)	0.91	May result in a large increase in outcome
	Ibutilide (2, 148)	4.02 (2.09 to 7.72)	272 per 1000	1094 per 1000	822 more per 1000 (297 more to 1830 more)	Low ⊕⊕◯◯ (3)	0.78	May result in a large increase in outcome
	Flecainide (5, 369)	3.08 (2.09 to 4.55)	272 per 1000	840 per 1000	568 more per 1000 (296 more to 968 more)	Very Low ⊕◯◯◯ (4)	0.69	The evidence is very uncertain about the effect on the outcome
	BTE Incremental (2, 164)	2.83 (1.59 to 5.01)	272 per 1000	770 per 1000	498 more per 1000 (162 more to 1093 more)	Low ⊕⊕◯◯ (5)	0.64	May result in a large increase in outcome
	Propafenone (16, 1123)	2.45 (1.91 to 3.14)	272 per 1000	667 per 1000	395 more per 1000 (248 more to 582 more)	Low ⊕⊕◯◯ (6)	0.55	May result in a large increase in outcome
	Quinidine (2, 66)	1.99 (0.99 to 3.98)	272 per 1000	541 per 1000	269 more per 1000 (2 fewer to 812 more)	Very Low ⊕◯◯◯ (7)	0.43	The evidence is very uncertain about the effect on the outcome
	Procainamide (4, 280)	1.63 (1.08 to 2.45)	272 per 1000	443 per 1000	171 more per 1000 (22 more to 396 more)	Very Low ⊕◯◯◯ (8)	0.3	The evidence is very uncertain about the effect on the outcome
	Magnesium (3, 57)	1.46 (0.70 to 3.03)	272 per 1000	397 per 1000	125 more per 1000 (81 fewer to 553 more)	Very Low ⊕◯◯◯ (9)	0.26	The evidence is very uncertain about the effect on the outcome
	Amiodarone (13, 824)	1.50 (1.14 to 1.97)	272 per 1000	409 per 1000	136 more per 1000 (38 more to 265 more)	Low ⊕⊕◯◯ (10)	0.25	May result in a large increase in outcome
	Sotalol (2, 73)	1.35 (0.75 to 2.44)	272 per 1000	369 per 1000	96 more per 1000 (68 fewer to 392 more)	Very Low ⊕◯◯◯ (11)	0.2	The evidence is very uncertain about the effect on the outcome
	Placebo (20, 969)	1.00 (1.00 to 1.00)	272 per 1000				0.03	

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

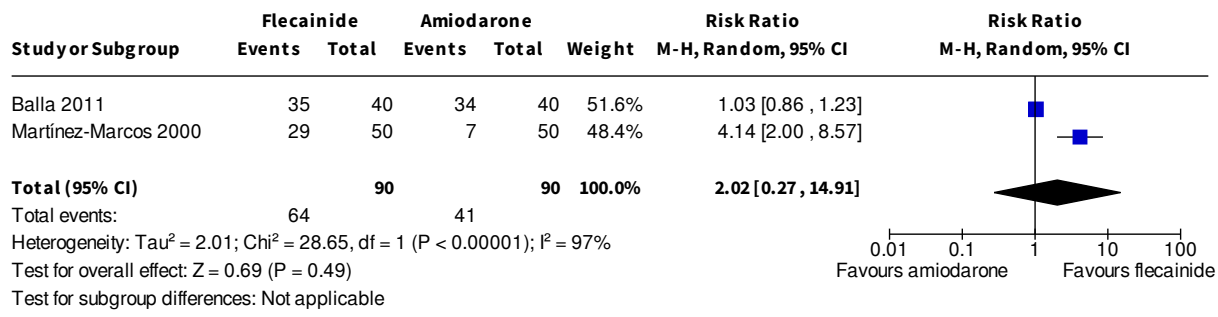
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. Imprecision present (Confidence interval many magnitudes larger than next highest). High global inconsistency.
2. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, incomplete outcome reporting, selective outcome reporting). High global inconsistency.
3. High risk of bias from indirect estimate (Lack of information on randomisation and allocation concealment, incomplete outcome reporting, selective outcome reporting). High global inconsistency.
4. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, selective outcome reporting). High global inconsistency.
5. High risk of bias from indirect estimate (Lack of information on randomisation and allocation concealment, selective outcome reporting). High global inconsistency.
6. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, selective outcome reporting). High global inconsistency.
7. High risk of bias from indirect estimate (Lack of information on randomisation and allocation concealment, selective outcome reporting). Imprecision present. High global inconsistency.
8. High risk of bias from direct and indirect estimates(Lack of information on randomisation, and selective outcome reporting, no allocation concealment, incomplete outcome reporting). High global inconsistency.
9. High risk of bias from direct estimate (Lack of information on randomisation and allocation concealment, selective outcome reporting). Imprecision present. High global inconsistency.
10. High risk of bias from direct and indirect estimates (Lack of information on randomisation and selective outcome reporting, no allocation concealment, incomplete outcome reporting). High global inconsistency.
11. High risk of bias from direct and indirect estimates (Lack of information on randomisation and selective outcome reporting, no allocation concealment, incomplete outcome reporting). Imprecision present. High global inconsistency.

Summary of Findings: Acute procedural success, Paroxysmal Atrial Fibrillation.

Figure 33

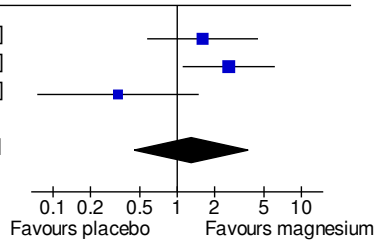


Pairwise analysis

Figure 34

Study or Subgroup	Magnesium Events	Magnesium Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brodsky 1994	6	10	3	8	35.2%	1.60 [0.57 , 4.47]
Chiladakis 2001	13	23	5	23	39.2%	2.60 [1.11 , 6.11]
Chu 2009	2	24	6	24	25.6%	0.33 [0.07 , 1.49]
Total (95% CI)		**57**		**55**	**100.0%**	**1.29 [0.45 , 3.73]**
Total events:	21		14			

Heterogeneity: Tau² = 0.55; Chi² = 5.58, df = 2 (P = 0.06); I² = 64%
Test for overall effect: Z = 0.48 (P = 0.63)
Test for subgroup differences: Not applicable

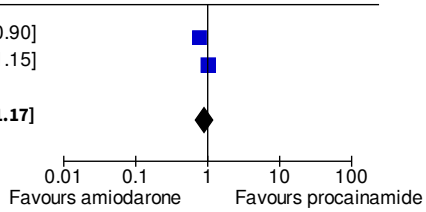


Pairwise analysis

Figure 35

Study or Subgroup	Procainamide Events	Procainamide Total	Amiodarone Events	Amiodarone Total	Weight	Risk Ratio M-H, Random, 95% CI
Kochiadakis 2007	61	89	82	92	48.4%	0.77 [0.66 , 0.90]
Xanthos 2007	91	110	91	112	51.6%	1.02 [0.90 , 1.15]
Total (95% CI)		**199**		**204**	**100.0%**	**0.89 [0.67 , 1.17]**
Total events:	152		173			

Heterogeneity: Tau² = 0.03; Chi² = 7.66, df = 1 (P = 0.006); I² = 87%
Test for overall effect: Z = 0.83 (P = 0.40)
Test for subgroup differences: Not applicable

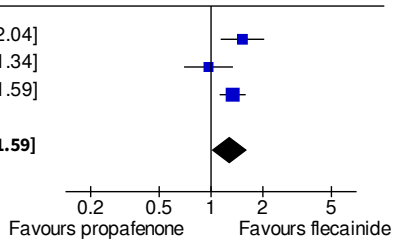


Pairwise analysis

Figure 36

Study or Subgroup	Flecainide Events	Flecainide Total	Propafenone Events	Propafenone Total	Weight	Risk Ratio M-H, Random, 95% CI
Balla 2011	35	40	23	40	29.6%	1.52 [1.14 , 2.04]
Martínez-Marcos 2000	29	50	30	50	26.1%	0.97 [0.70 , 1.34]
Romano 2001	100	138	89	164	44.2%	1.34 [1.12 , 1.59]
Total (95% CI)		**228**		**254**	**100.0%**	**1.28 [1.02 , 1.59]**
Total events:	164		142			

Heterogeneity: Tau² = 0.02; Chi² = 4.40, df = 2 (P = 0.11); I² = 55%
Test for overall effect: Z = 2.16 (P = 0.03)
Test for subgroup differences: Not applicable

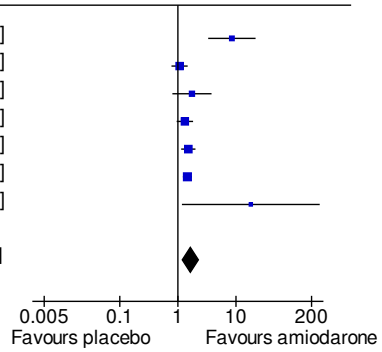


Pairwise analysis

Figure 37

Study or Subgroup	Amiodarone Events	Amiodarone Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Balla 2011	34	40	4	40	7.8%	8.50 [3.32 , 21.73]
Cotter 1999	31	50	29	50	19.3%	1.07 [0.78 , 1.47]
Cybulski 2003	24	106	7	54	9.9%	1.75 [0.80 , 3.79]
Joseph 2000	30	39	21	36	19.2%	1.32 [0.95 , 1.83]
Kochiadakis 1998a	40	48	27	49	20.2%	1.51 [1.14 , 2.01]
Kochiadakis 2007	82	92	55	90	22.3%	1.46 [1.22 , 1.75]
Noc 1990	10	13	0	11	1.3%	18.00 [1.17 , 276.06]
Total (95% CI)		**388**		**330**	**100.0%**	**1.64 [1.19 , 2.25]**
Total events:	251		143			

Heterogeneity: Tau² = 0.11; Chi² = 25.36, df = 6 (P = 0.0003); I² = 76%
Test for overall effect: Z = 3.03 (P = 0.002)
Test for subgroup differences: Not applicable

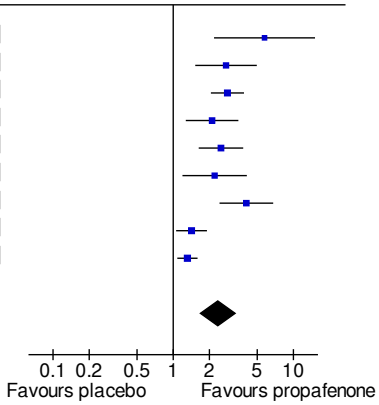


Pairwise analysis

Figure 38

Study or Subgroup	Propafenone Events	Propafenone Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Balla 2011	23	40	4	40	6.5%	5.75 [2.19 , 15.12]
Baroffio 1995	22	25	8	25	10.0%	2.75 [1.53 , 4.96]
Bellandi 1995	89	98	27	84	12.9%	2.83 [2.06 , 3.88]
Bianconi 1998	20	41	19	82	11.0%	2.11 [1.27 , 3.48]
Boriani 1997	54	119	22	121	11.8%	2.50 [1.63 , 3.82]
Fresco 1996	24	41	9	34	9.7%	2.21 [1.19 , 4.10]
Ganau 1998	57	81	13	75	10.9%	4.06 [2.43 , 6.79]
Kochiadakis 1998a	36	46	27	49	13.1%	1.42 [1.06 , 1.91]
Kochiadakis 2007	73	91	55	90	14.0%	1.31 [1.08 , 1.59]
Total (95% CI)		**582**		**600**	**100.0%**	**2.35 [1.68 , 3.27]**
Total events:	398		184			

Heterogeneity: Tau² = 0.20; Chi² = 47.77, df = 8 (P < 0.00001); I² = 83%
Test for overall effect: Z = 5.04 (P < 0.00001)
Test for subgroup differences: Not applicable

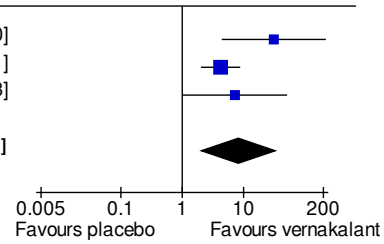


Pairwise analysis

Figure 39

Study or Subgroup	Vernakalant Events	Vernakalant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Beatch 2016	59	129	1	68	26.2%	31.10 [4.40 , 219.60]
Beatch 2017	29	55	7	56	47.6%	4.22 [2.02 , 8.81]
Roy 2004	13	36	1	20	26.2%	7.22 [1.02 , 51.23]
Total (95% CI)		**220**		**144**	**100.0%**	**8.20 [2.06 , 32.71]**
Total events:	101		9			

Heterogeneity: Tau² = 0.91; Chi² = 5.03, df = 2 (P = 0.08); I² = 60%
Test for overall effect: Z = 2.98 (P = 0.003)
Test for subgroup differences: Not applicable

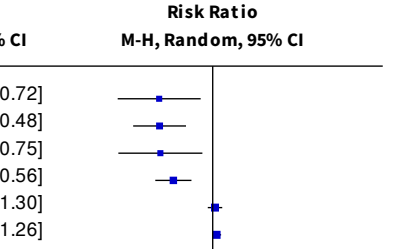


Pairwise analysis

Figure 40

Study or Subgroup	Amiodarone Events	Amiodarone Total	Propafenone Events	Propafenone Total	Weight	Risk Ratio M-H, Random, 95% CI
Treglia 1994a	3	27	13	27	9.2%	0.23 [0.07 , 0.72]
Martínez-Marcos 2000	7	50	30	50	13.1%	0.23 [0.11 , 0.48]
Negrini 1994	3	30	13	31	9.1%	0.24 [0.08 , 0.75]
Taha 2022	16	100	47	100	15.4%	0.34 [0.21 , 0.56]
Kochiadakis 1998a	40	48	36	46	17.8%	1.06 [0.87 , 1.30]
Kochiadakis 2007	82	92	73	91	18.1%	1.11 [0.98 , 1.26]
Balla 2011	34	40	23	40	17.2%	1.48 [1.10 , 1.99]
Total (95% CI)		**387**		**385**	**100.0%**	**0.59 [0.36 , 0.96]**
Total events:	185		235			

Heterogeneity: Tau² = 0.34; Chi² = 88.70, df = 6 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.10 (P = 0.04)
Test for subgroup differences: Not applicable



Pairwise analysis

Figure 41

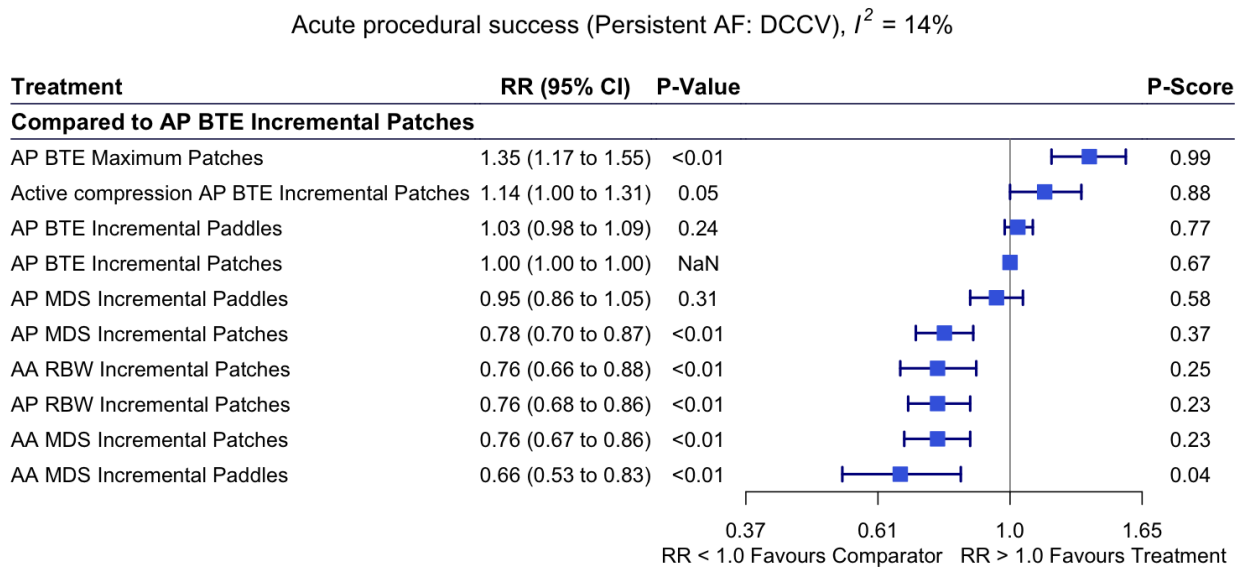


Figure 41: Forestplot for acute procedural success, Electrical cardioversion, Persistent AF, 8 trials, Fixed effects model.

AP = Anteroposterior, AA = Anteroapical, BTE = Biphasic Truncated Exponential, RBW = Rectilinear Biphasic Waveform, MDS = Monophasic Damped Sinewave, DCCV = Direct Current Cardioversion

Figure 42

Frequentist NMA-SoF table

EFFECTS

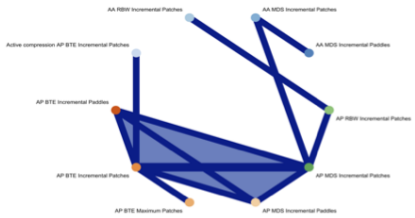
Patient or population: Patients with Persistent Atrial Fibrillation

Interventions: AP BTE Maximum Patches, AP BTE Incremental Patches, AP BTE Incremental Paddles, Active compression AP BTE Incremental Patches, AP MDS Incremental Patches, AP MDS Incremental Paddles, AA RBW Incremental Patches, AP RBW Incremental Patches, AA MDS Incremental Patches, AA MDS Incremental Paddles

Comparator (reference): AP BTE Incremental Patches

Outcome: Acute procedural success

Setting: Emergency Department, Elective Admission or Inpatient



Total studies, Participants (8, 1122)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference to AP BTE Incremental Patches			
●	AP BTE Maximum Patches (1, 129)	1.35 (1.17 to 1.55)	N/A	1066 per 1000	275 more per 1000 (122 more to 454 more)	High ⊕⊕⊕⊕ (1)	0.99	Likely results in a large increase in outcome
●	Active compression AP BTE Incremental Patches (1, 50)	1.14 (1.00 to 1.31)	N/A	904 per 1000	113 more per 1000 (10 fewer to 256 more)	High ⊕⊕⊕⊕ (2)	0.88	Likely results in a large increase in outcome
●	AP BTE Incremental Paddles (1, 56)	1.03 (0.98 to 1.09)	N/A	815 per 1000	25 more per 1000 (40 fewer to 94 more)	Low ⊕⊕◯◯ (3)	0.76	May result in little or no increase in outcome
●	AP BTE Incremental Patches (4, 306)	1.00 (1.00 to 1.00)	N/A	791 per 1000			0.68	
●	AP MDS Incremental Paddles (1, 48)	0.95 (0.86 to 1.05)	N/A	748 per 1000	43 fewer per 1000 (126 fewer to 51 more)	Low ⊕⊕◯◯ (4)	0.58	May result in little or no decrease in outcome
●	AP MDS Incremental Patches (4, 244)	0.78 (0.70 to 0.87)	N/A	621 per 1000	170 fewer per 1000 (238 fewer to 93 fewer)	Moderate ⊕⊕⊕◯ (5)	0.35	Probably results in a large decrease in outcome
●	AA RBW Incremental Patches (1, 63)	0.76 (0.66 to 0.88)	N/A	604 per 1000	187 fewer per 1000 (283 fewer to 71 fewer)	Moderate ⊕⊕⊕◯ (6)	0.25	Probably results in a large decrease in outcome
●	AP RBW Incremental Patches (2, 168)	0.76 (0.68 to 0.86)	N/A	603 per 1000	188 fewer per 1000 (268 fewer to 96 fewer)	Moderate ⊕⊕⊕◯ (7)	0.24	Probably results in a large decrease in outcome
●	AA MDS Incremental Patches (2 ,43)	0.76 (0.67 to 0.86)	N/A	602 per 1000	189 fewer per 1000 (270 fewer to 96 fewer)	Moderate ⊕⊕⊕◯ (8)	0.24	Probably results in a large decrease in outcome
●	AA MDS Incremental Paddles (1, 15)	0.66 (0.53 to 0.83)	N/A	524 per 1000	267 fewer per 1000 (382 fewer to 119 fewer)	Moderate ⊕⊕⊕◯ (9)	0.05	Probably results in a large decrease in outcome

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates mutiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

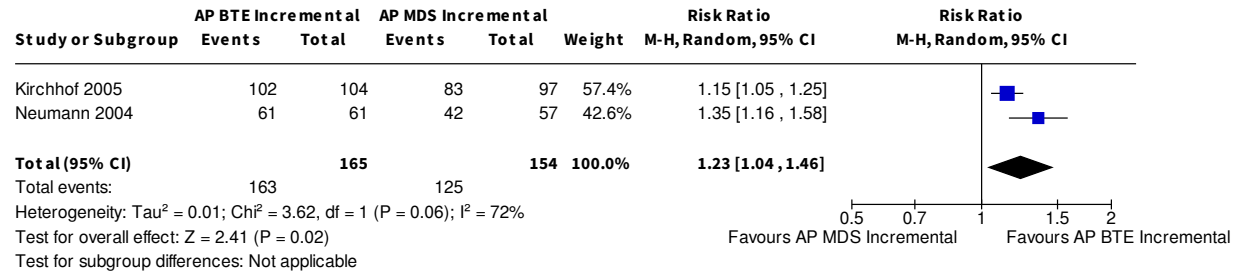
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. Low risk of bias
2. Moderate risk of bias (Lack of information on selective outcome reporting)
3. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting). Imprecision present.
4. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting). Imprecision present.
5. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting).
6. High risk of bias from direct estimate (Lack of information on randomisation, allocation concealment and selective outcome reporting).
7. High risk of bias from indirect estimate (Lack of information on randomisation, allocation concealment and selective outcome reporting).
8. High risk of bias from direct and indirect estimates (Lack of information on randomisation and allocation concealment, selective outcome reporting).
9. High risk of bias from direct and indirect estimates (Poor randomisation, allocation concealment and lack of information on selective outcome reporting).

Summary of Findings Table: Acute procedural success, Electrical Cardioversion, Persistent AF

Figure 43



Pairwise analysis

Figure 44

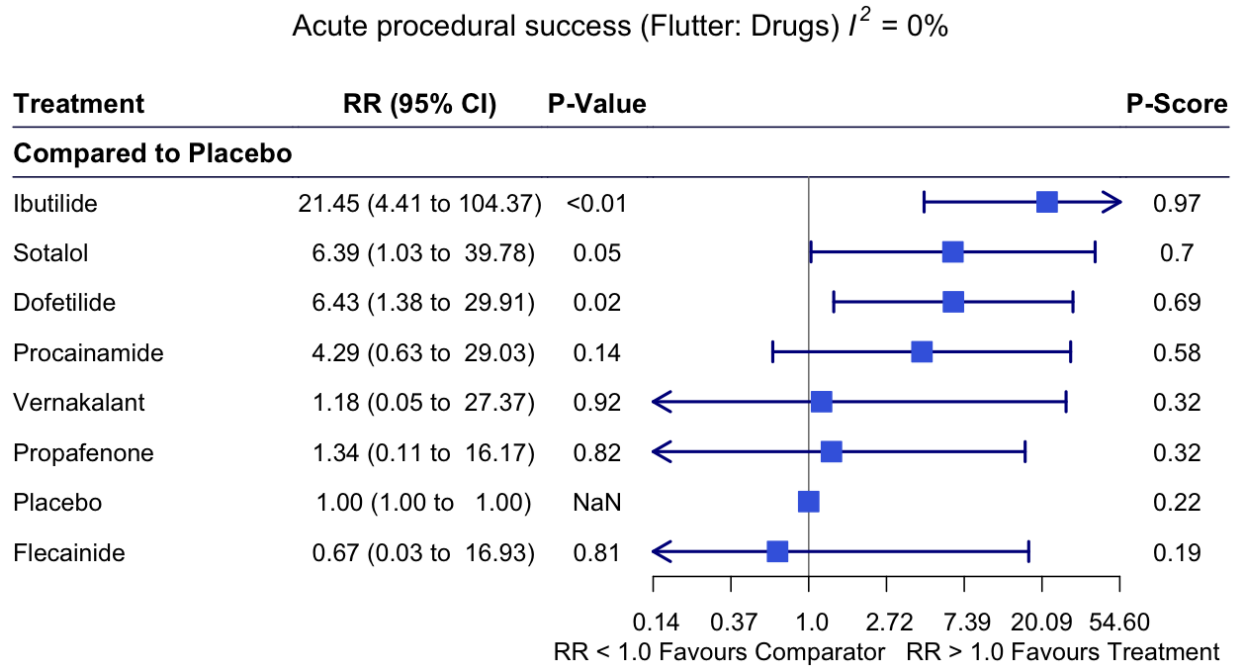


Figure 44: Forestplot for acute procedural success, Atrial Flutter, 10 trials, Fixed Effects Model

Figure 45

Frequentist NMA-SoF table

EFFECTS

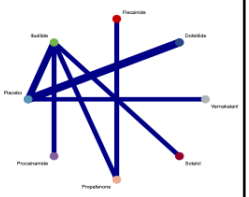
Patient or population: Patients with Atrial Flutter

Interventions: Vernakalant, Dofetilide, Flecainide, Ibutilide, Propafenone, Sotalol, Procainamide, Placebo

Comparator (reference): Placebo

Outcome: Acute procedural success

Setting: Emergency Department, Elective Admission or Inpatient



Total studies, Participants (10, 422)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference			
●	Ibutilide (5, 201)	21.45 (4.41 to 104.37)	12 per 1000	262 per 1000	249 more per 1000 (42 more to 1261 more)	Moderate ⊕⊕⊕◯ (1)	0.97	Probably results in a large increase in outcome
●	Sotalol (1, 21)	6.39 (1.03 to 39.78)	12 per 1000	78 per 1000	66 more per 1000 (0 more to 473 more)	Moderate ⊕⊕⊕◯ (2)	0.7	Probably results in a slight increase in outcome
●	Dofetilide (3, 29)	6.43 (1.38 to 29.91)	12 per 1000	78 per 1000	66 more per 1000 (5 more to 353 more)	Moderate ⊕⊕⊕◯ (3)	0.69	Probably results in a slight increase in outcome
●	Procainamide (1, 20)	4.29 (0.63 to 29.03)	12 per 1000	52 per 1000	40 more per 1000 (4 fewer to 342 more)	Low ⊕⊕◯◯ (4)	0.58	May result in a slight increase in outcome
●	Vernakalant (1, 39)	1.18 (0.05 to 27.37)	12 per 1000	14 per 1000	2 more per 1000 (12 fewer to 322 more)	Low ⊕⊕◯◯ (5)	0.32	May result in a slight increase in outcome
●	Propafenone (2, 25)	1.34 (0.11 to 16.17)	12 per 1000	16 per 1000	4 more per 1000 (11 fewer to 185 more)	Low ⊕⊕◯◯ (6)	0.32	May result in a slight increase in outcome
●	Placebo (6, 82)	1.00 (1.00 to 1.00)	12 per 1000				0.22	
●	Flecainide (1, 5)	0.67 (0.03 to 16.93)	12 per 1000	8 per 1000	4 fewer per 1000 (12 fewer to 194 more)	Low ⊕⊕◯◯ (7)	0.19	May result in a slight decrease in outcome

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

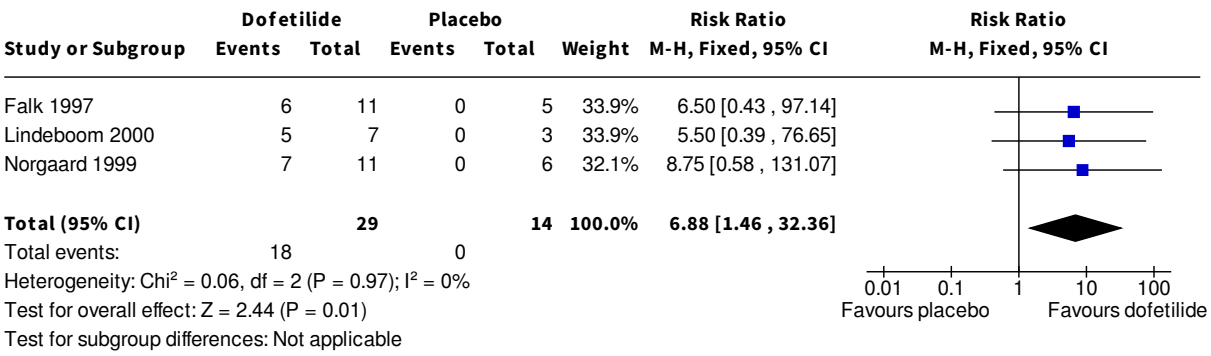
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. High risk of bias from direct estimate (lack of information on randomisation, allocation concealment and selective outcome reporting).
2. High risk of bias from direct estimate (lack of information on randomisation, allocation concealment and selective outcome reporting).
3. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting).
4. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting). Imprecision present.
5. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting). Imprecision present.
6. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting). Imprecision present.
7. High risk of bias from indirect estimate (lack of information on randomisation, allocation concealment, and selective outcome reporting). Imprecision present.

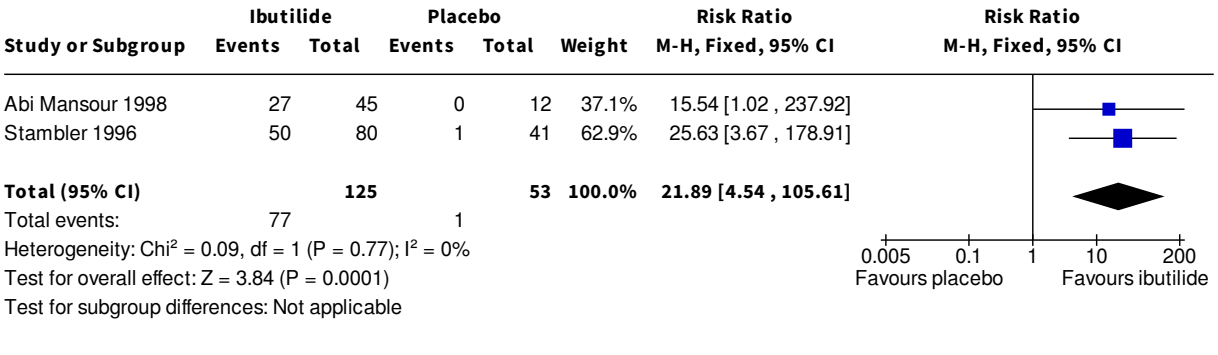
Summary of Findings Table: Acute procedural success, Atrial Flutter

Figure 46



Pairwise analysis

Figure 47



Pairwise analysis

Figure 48

Frequentist NMA-SoF table

HARMS

Patient or population: Patients with Atrial Fibrillation or Flutter eligible for electrical or pharmacological cardioversion

Interventions: -

Comparator (reference): -

Outcome: Stroke or systemic embolism occurring within the first 30 days following cardioversion

Setting: Emergency Department, Elective Admission or Inpatient

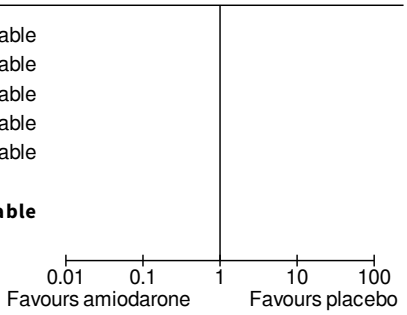
Most studies reported only acute (<24h) results, and provided no follow-up data for the first 30 days. Two ischemic stroke events were reported, hence incidence of stroke was extremely low: 0% across all electrical cardioversion studies, less than 0.1% in patients receiving antiarrhythmic drugs and 0.1% in patients recieving placebo. Similarly, a very low incidence of potential systemic embolism events (n=2) was observed. Due to the low incidence of this adverse event it was not possible to do a meta-analysis to compare multiple therapies.

Summary of Findings Table: Stroke, Systemic embolism or TIA in first 30 days following cardioversion.

Figure 49

Study or Subgroup	Amiodarone Events	Amiodarone Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Galperín 2001	0	47	0	48		Not estimable
Kochiadakis 1999	0	33	0	34		Not estimable
Kochiadakis 1999a	0	34	0	35		Not estimable
Singh 2005	0	258	0	132		Not estimable
Vardas 2000	0	108	0	100		Not estimable
Total (95% CI)		**480**		**349**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

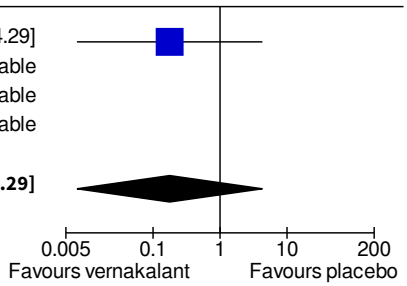


Pairwise analysis

Figure 50

Study or Subgroup	Vernakalant Events	Vernakalant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Beatch 2016	0	129	1	68	100.0%	0.18 [0.01 , 4.29]
Camm 2012	0	39	0	15		Not estimable
Pratt 2010	0	134	0	131		Not estimable
Roy 2008	0	221	0	115		Not estimable
Total (95% CI)		**523**		**329**	**100.0%**	**0.18 [0.01 , 4.29]**
Total events:	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.29)
Test for subgroup differences: Not applicable



Pairwise analysis

Figure 51

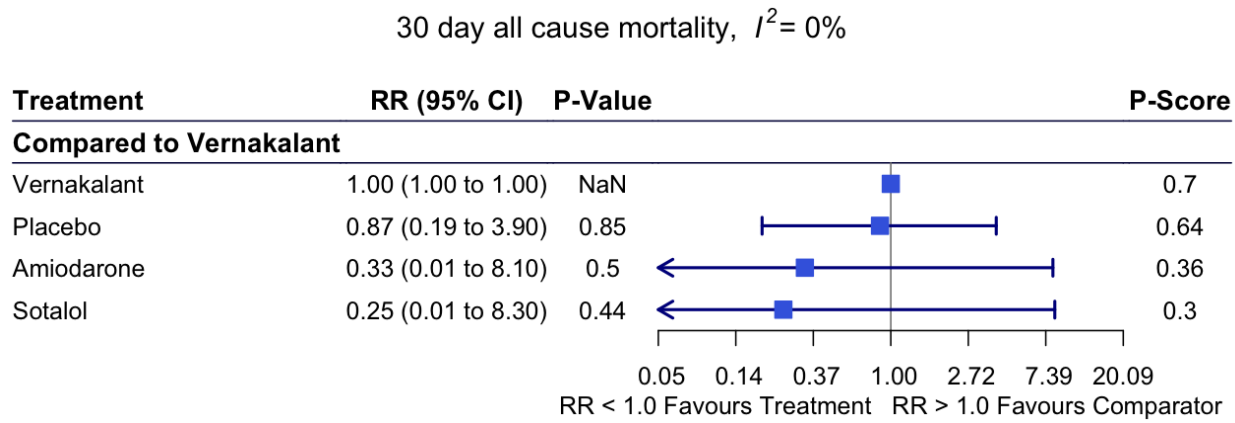
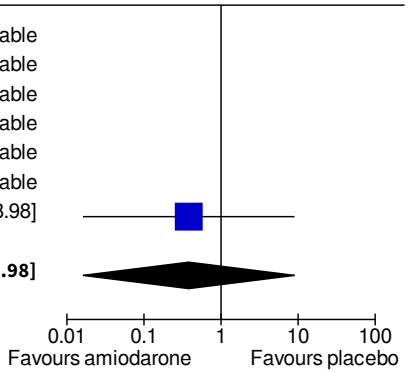


Figure 12: Forestplot for 30 day all cause mortality, 6 trials, Fixed effects model

Figure 52

Study or Subgroup	Amiodarone Events	Amiodarone Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Channer 2004	0	123	0	38		Not estimable
Galperín 2001	0	47	0	48		Not estimable
Kochiadakis 1999	0	33	0	34		Not estimable
Kochiadakis 1999a	0	34	0	35		Not estimable
Singh 2005	0	258	0	132		Not estimable
Vardas 2000	0	108	0	100		Not estimable
Vijayalakshmi 2006	0	27	1	31	100.0%	0.38 [0.02 , 8.98]
Total (95% CI)		**630**		**418**	**100.0%**	**0.38 [0.02 , 8.98]**
Total events:	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable

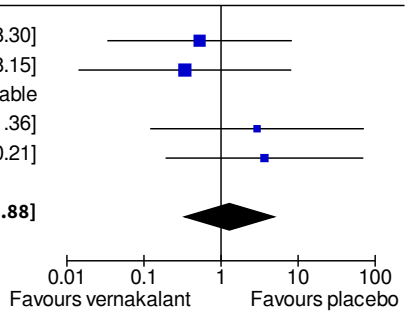


Pairwise analysis

Figure 53

Study or Subgroup	Vernakalant Events	Vernakalant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Beatch 2016	1	129	1	68	33.1%	0.53 [0.03 , 8.30]
Beatch 2017	0	55	1	56	37.6%	0.34 [0.01 , 8.15]
Camm 2012	0	39	0	15		Not estimable
Pratt 2010	1	134	0	131	12.8%	2.93 [0.12 , 71.36]
Roy 2008	3	221	0	115	16.6%	3.66 [0.19 , 70.21]
Total (95% CI)		**578**		**385**	**100.0%**	**1.28 [0.34 , 4.88]**
Total events:	5		2			

Heterogeneity: Chi^2 = 1.81, df = 3 (P = 0.61); I^2 = 0%
Test for overall effect: Z = 0.37 (P = 0.71)
Test for subgroup differences: Not applicable

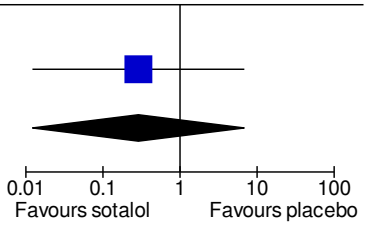


Pairwise analysis

Figure 54

Study or Subgroup	Sotalol Events	Sotalol Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 2005	0	244	0	132		Not estimable
Vijayalakshmi 2006	0	36	1	31	100.0%	0.29 [0.01 , 6.83]
Total (95% CI)		**280**		**163**	**100.0%**	**0.29 [0.01 , 6.83]**
Total events:	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)
Test for subgroup differences: Not applicable



Pairwise analysis

Figure 55

Frequentist NMA-SoF table

HARMS

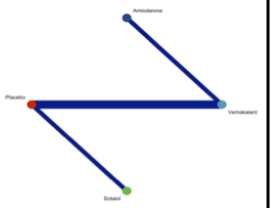
Patient or population: Patients with Atrial Fibrillation or Flutter eligible for electrical or pharmacological cardioversion

Interventions: Vernakalant, Amiodarone, Sotalol, Placebo

Comparator (reference): Vernakalant

Outcome: 30 day all cause mortality

Setting: Emergency Department, Elective Admission, Inpatient or Outpatient



Total studies, Participants (6, 1026)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference to Vernakalant			
●	Vernakalant (5, 655)	1.00 (1.00 to 1.00)	8 per 1000	9 per 1000			0.7	
●	Placebo (5, 401)	0.87 (0.19 to 3.90)	8 per 1000		1 fewer per 1000 (7 fewer to 27 more)	Low ⨁⨁◯◯ (1)	0.64	May result in a slight increase in outcome
●	Amiodarone (1, 116)	0.33 (0.01 to 8.10)	8 per 1000	3 per 1000	6 fewer per 1000 (9 fewer to 65 more)	Low ⨁⨁◯◯ (2)	0.36	May result in a large reduction in outcome
●	Sotalol (1, 36)	0.25 (0.01 to 8.30)	8 per 1000	2 per 1000	7 fewer per 1000 (9 fewer to 67 more)	Low ⨁⨁◯◯ (3)	0.3	May result in a large reduction in outcome

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. High risk of bias from direct estimate (Lack of information on randomisation and allocation concealment, incomplete outcome reporting). Imprecision present.
2. High risk of bias from direct estimate (Lack of information on allocation concealment and randomisation). Imprecision present.
3. High risk of bias from indirect estimate (Lack of information on allocation concealment, randomisation and selection bias). Imprecision present.

Summary of Findings Table: 30 day mortality, All AF/Atrial Flutter patients.

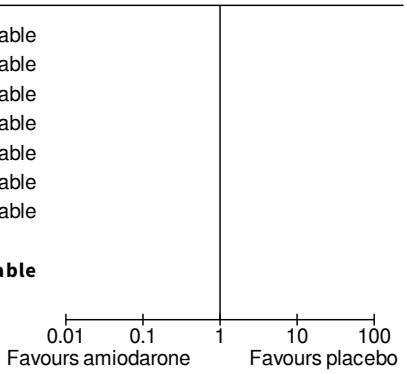
Figure 56

Study or Subgroup	Amiodarone Events	Amiodarone Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Channer 2004	0	123	0	38		Not estimable
Galperín 2001	0	47	0	48		Not estimable
Kochiadakis 1999	0	33	0	34		Not estimable
Kochiadakis 1999a	0	34	0	35		Not estimable
Singh 2005	0	258	0	132		Not estimable
Vardas 2000	0	108	0	100		Not estimable
Vijayalakshmi 2006	0	27	0	31		Not estimable
Total (95% CI)		**630**		**418**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable

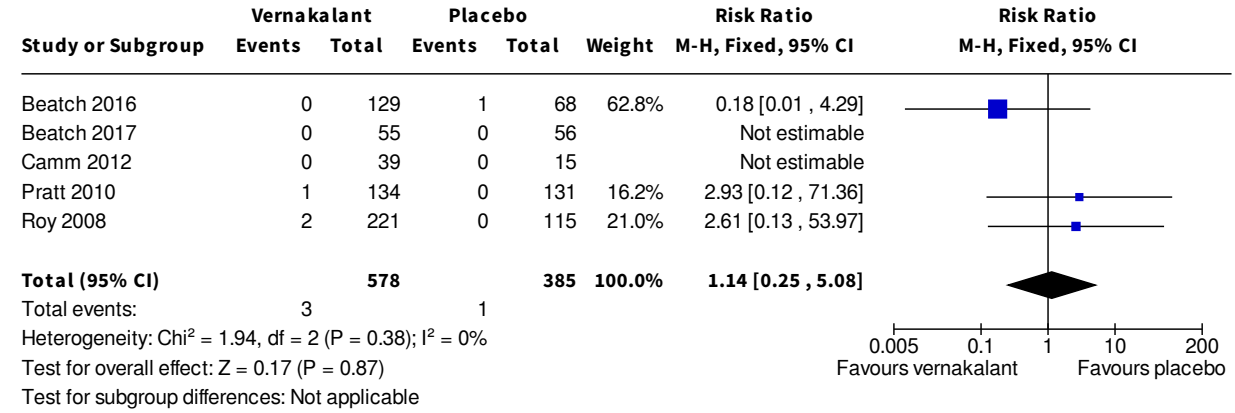
Test for overall effect: Not applicable

Test for subgroup differences: Not applicable



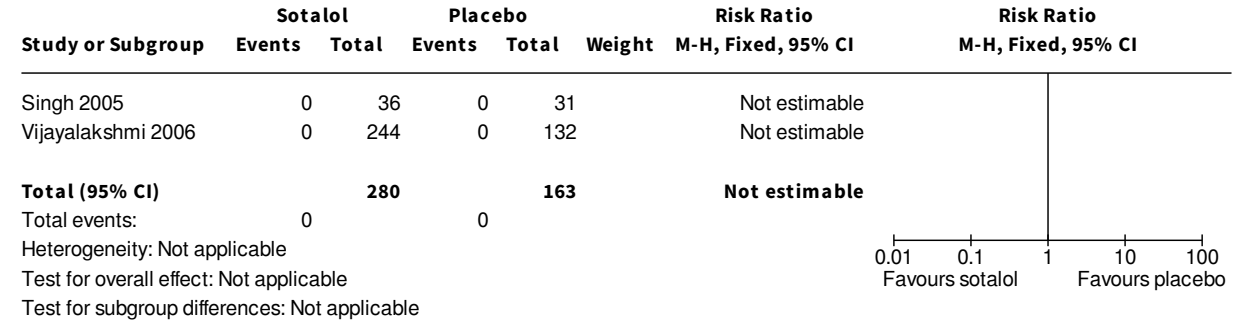
Pairwise analysis

Figure 57



Pairwise analysis

Figure 58



Pairwise analysis

Figure 59

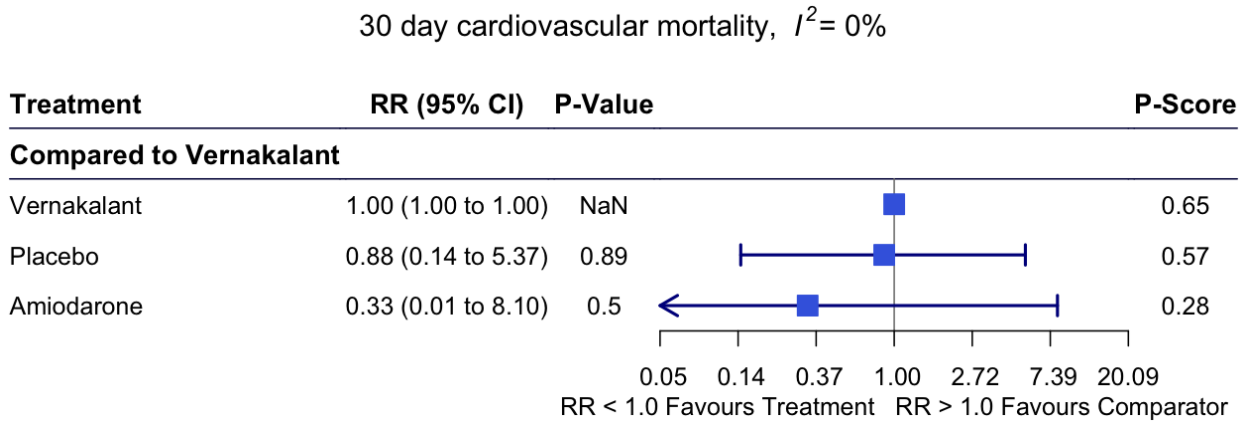


Figure 59: Forestplot for 30 day cardiovascular mortality, 4 trials, Fixed effects model

Figure 60

Frequentist NMA-SoF table

HARMS

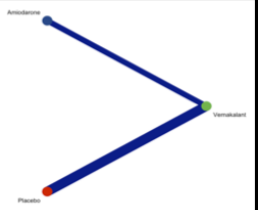
Patient or population: Patients with Atrial Fibrillation or Flutter eligible for electrical or pharmacological cardioversion

Interventions: Vernakalant, Amiodarone, Placebo

Comparator (reference): Vernakalant

Outcome: 30 day cardiovascular mortality

Setting: Emergency Department, Elective Admission, Inpatient or Outpatient



Total studies, Particpiants (4, 694)		Risk Ratio* (95% CI)	Anticipated absolute effect** (95% CrI)			Certainty of the evidence	Ranking***	Interpretation of Findings
			Without intervention	*With* intervention	Difference to Vernakalant			
●	Vernakalant (4, 600)	1.00 (1.00 to 1.00)	5 per 1000	5 per 1000			0.65	
●	Placebo (3, 314)	0.88 (0.14 to 5.37)	5 per 1000		1 fewer per 1000 (5 fewer to 23 more)	Low ⊕⊕◯◯ (1)	0.57	May result in a large reduction in outcome
●	Amiodarone (1, 116)	0.33 (0.01 to 8.10)	5 per 1000	2 per 1000	4 fewer per 1000 (5 fewer to 37 more)	Low ⊕⊕◯◯ (2)	0.28	May result in a large reduction in outcome

NMA-SoF table definitions

Number of trials and total observations for each treatment in network model given as such: Treatment (number of trials, total observations)

Network Graph: Lines represent direct comparisons. Thickness indicates total observations for comparison. Shading indicates multiple arm trials.

* Estimates are reported as Risk Ratio. CI: Confidence Interval.

** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.

*** P-Score. Relative effects are in descending order.

GRADE Working Group grades of evidence (or certainty in the evidence)

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanatory Footnotes:

1. High risk of bias from direct estimate (Lack of information on randomisation and allocation concealment, incomplete outcome reporting). Imprecision present.
2. High risk of bias from direct estimate (Lack of information on allocation concealment and randomisation). Imprecision present.

Summary of Findings Table: 30 day cardiovascular mortality, All AF/Atrial Flutter patients.

Figure 61

Frequentist NMA-SoF table

HARMS

Patient or population: Patients with Atrial Fibrillation or Flutter eligible for electrical or pharmacological cardioversion

Interventions: -

Comparator (reference): -

Outcome: Duration of hospital stay

Setting: Emergency Department, Elective Admission or Inpatient

Only two trials reported on this outcome and hospitalization was measured in different ways: from hospital admission in one trial and following cardioversion in the other trial. Furthermore, no common comparator was present across the two trials. Hence, it was not possible to do a meta-analysis to compare multiple therapies.

Summary of Findings Table: Duration of Hospital Stay

Figure 62

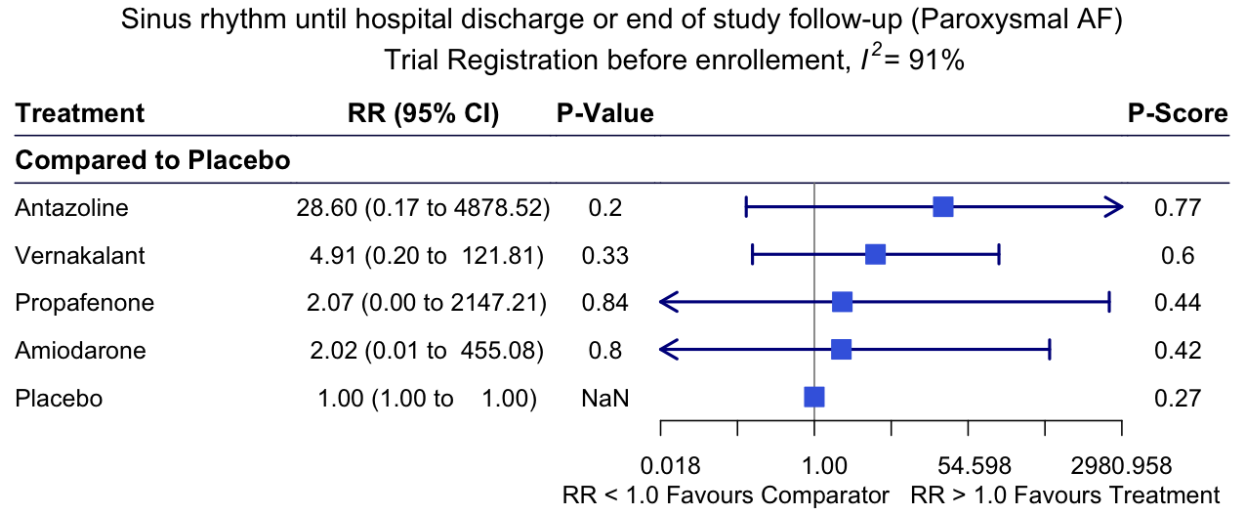


Figure 62: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF, sensitivity analysis for evidence of trial registration before enrollment. 5 Trials.

Figure 63

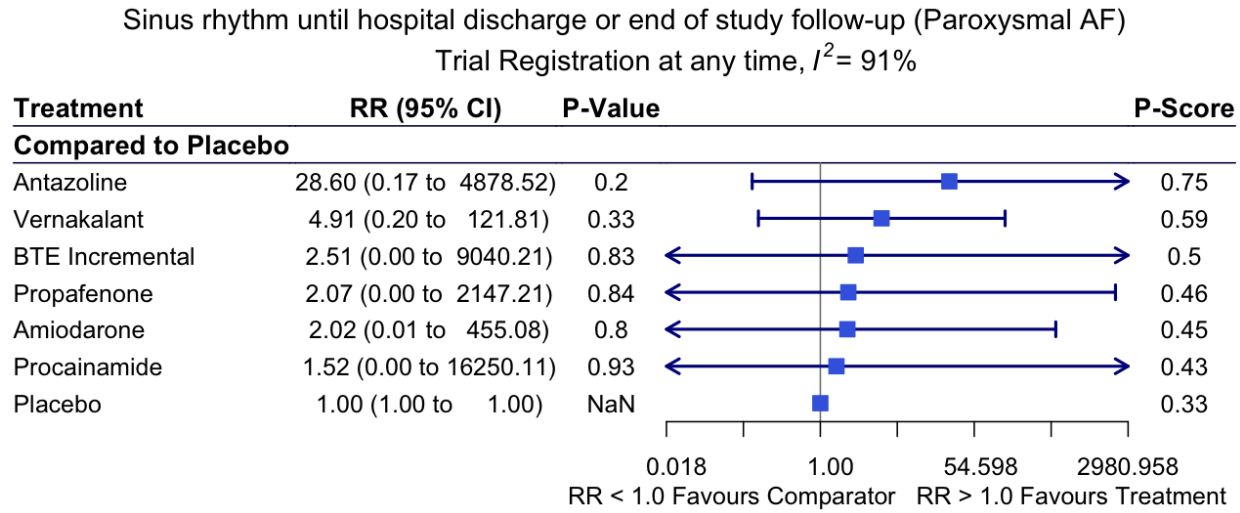


Figure 63: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF, sensitivity analysis for evidence of trial registration before, during or after enrollment. 7 Trials.

Figure 64

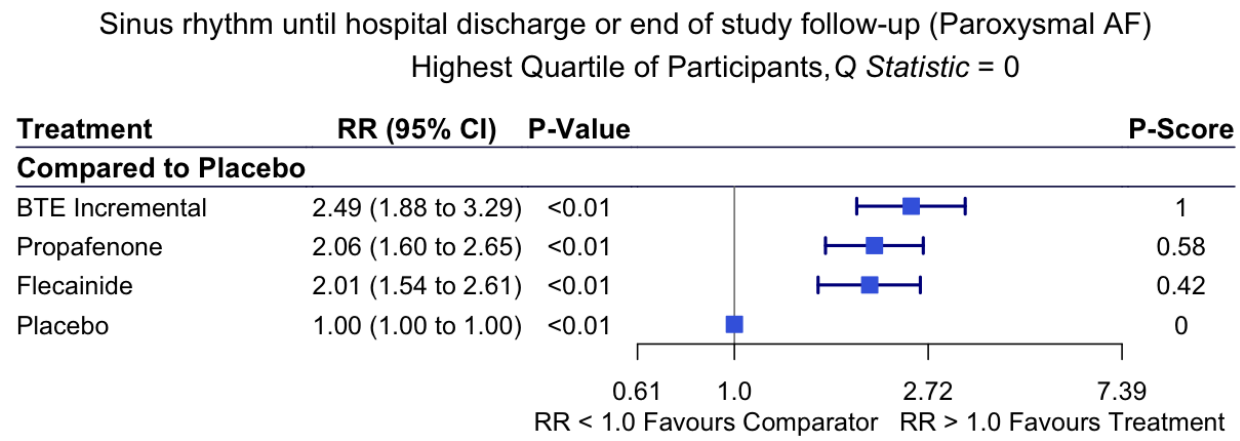


Figure 64: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, paroxysmal AF, sensitivity analysis for highest quartile of participants. 3 Trials.

Figure 65

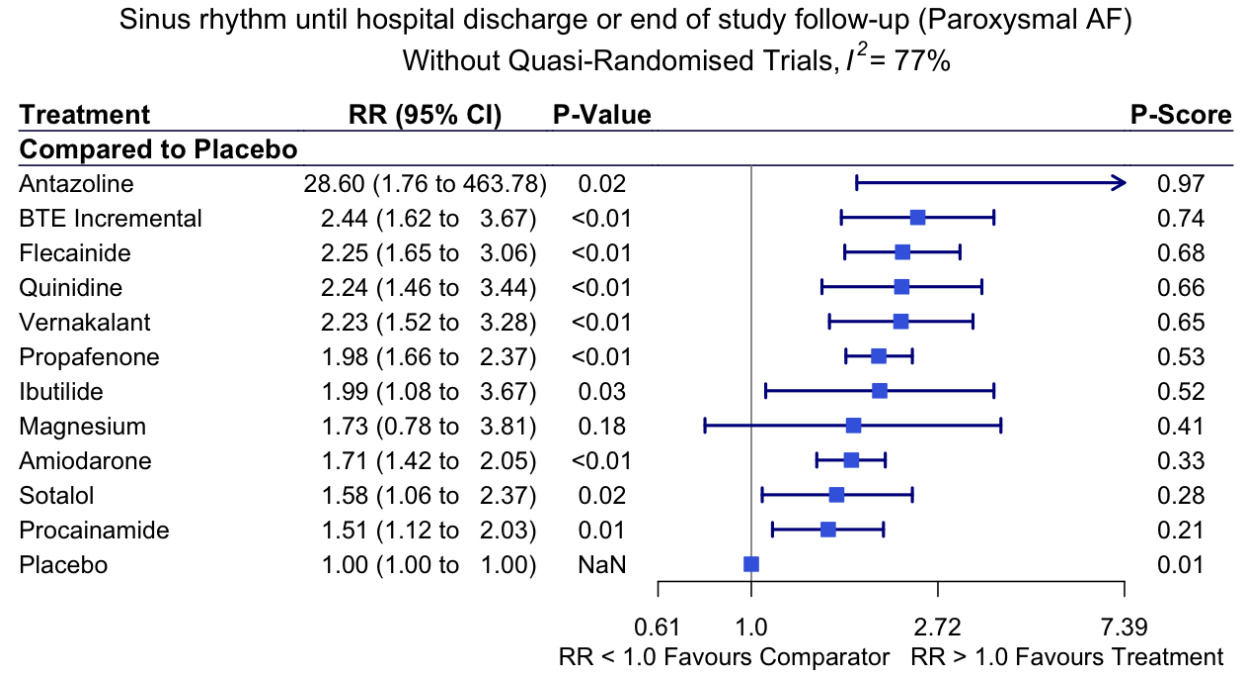


Figure 65: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF, sensitivity analysis without quasi-randomised trials. 32 trials.

Figure 66

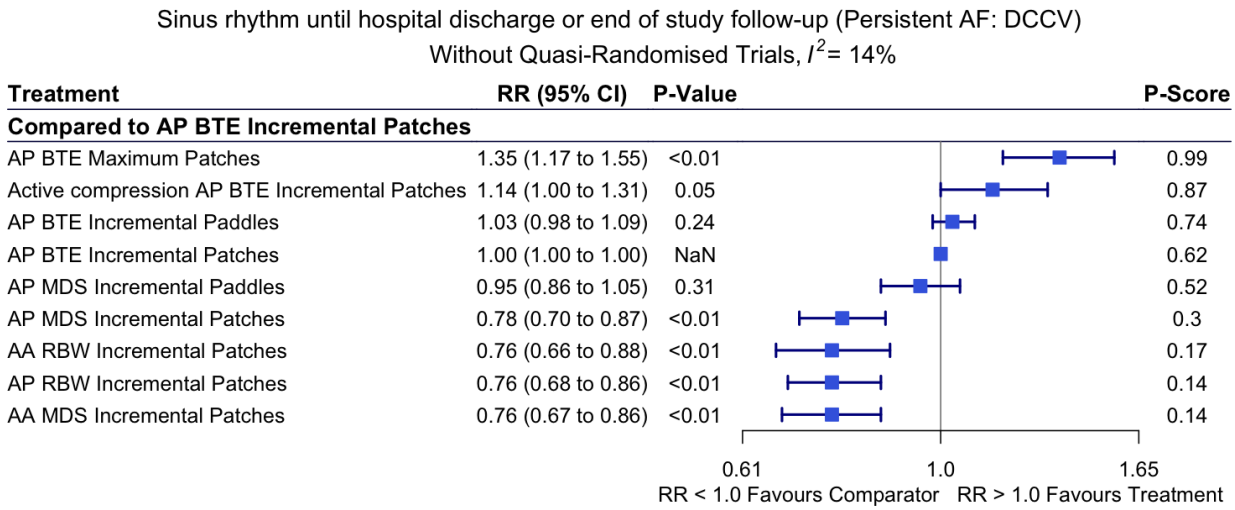


Figure 66: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Electrical Cardioversion, Persistent AF, sensitivity analysis without quasi-randomised trials. 7 Trials.

AP = Anteroposterior, AA = Anteroapical, BTE = Biphasic Truncated Exponential, RBW = Rectilinear Biphasic Waveform, MDS = Monophasic Damped Sinewave, DCCV = Direct Current Cardioversion

Figure 67

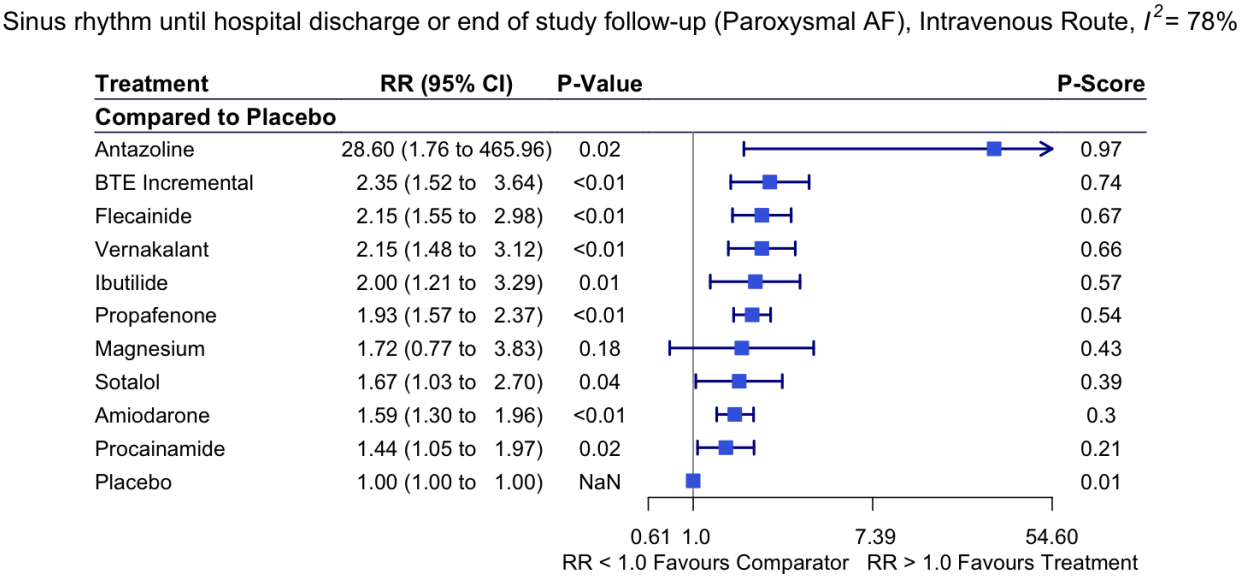


Figure 67: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF, subgroup analysis for intravenous route only. 29 Trials.

Figure 68

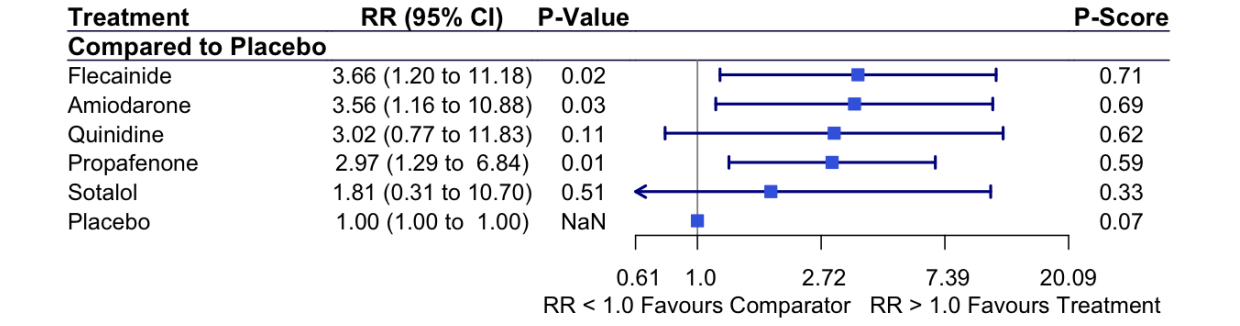


Figure 68: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, Paroxysmal AF, subgroup analysis for oral route only. 4 Trials.

Figure 69

Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF: Drugs), Intravenous Route, I^2= 0%

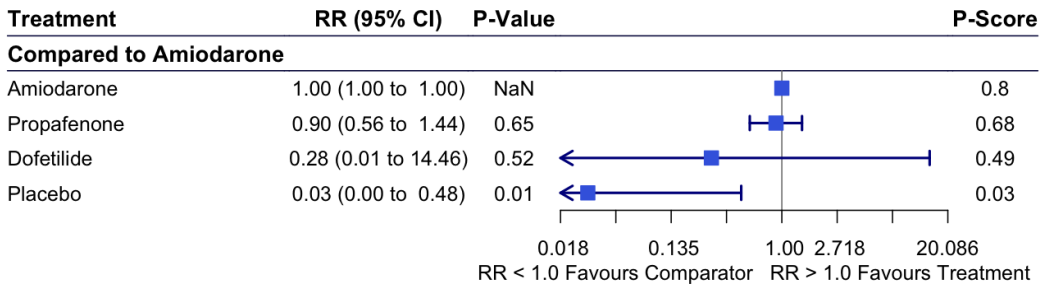


Figure 69: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, persistent AF, sensitivity analysis for intravenous route only. 3 Trials.

Figure 70

Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF: Drugs), Oral Route, I^2= 0%

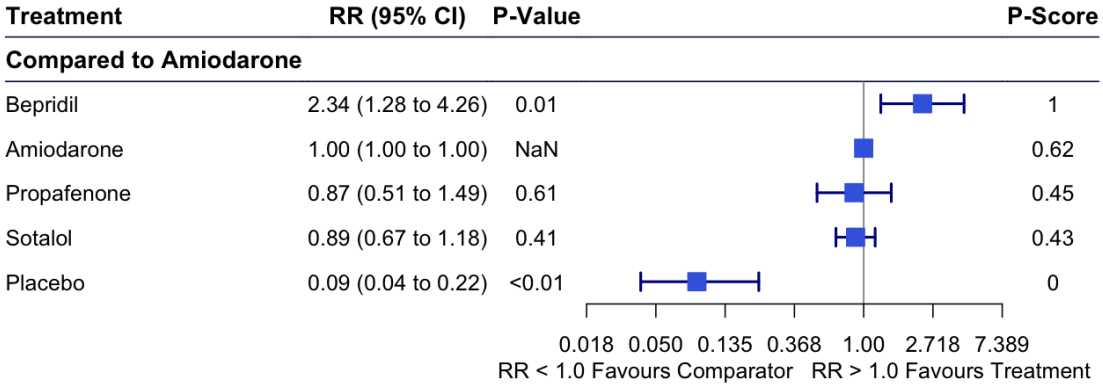
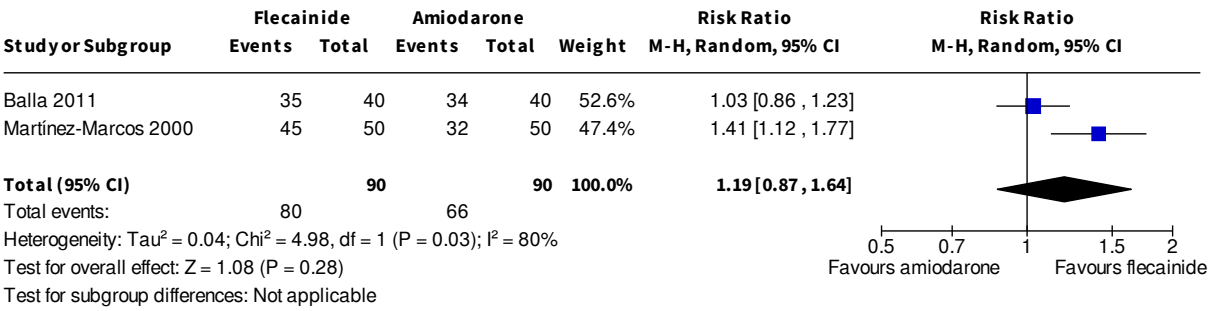


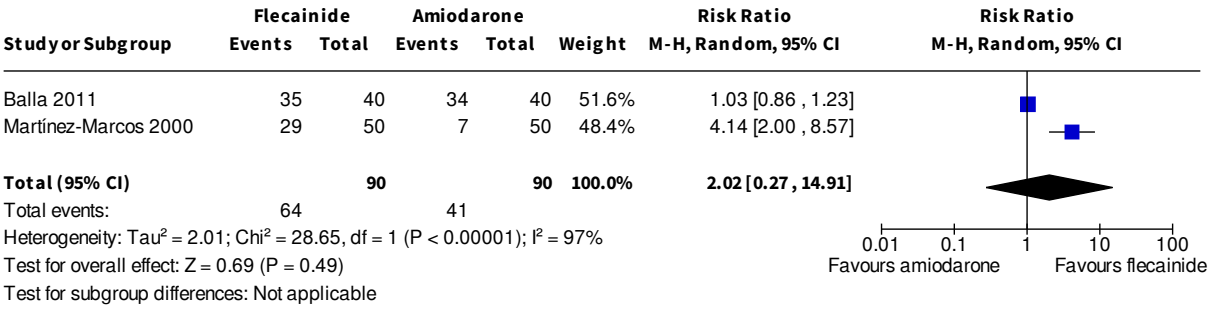
Figure 70: Forestplot for sinus rhythm until hospital discharge or end of study follow-up, persistent AF, subgroup analysis for oral route only. 8 Trials.

Analysis 1.1



Comparison 1: Flecainide vs Amiodarone, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 1.2

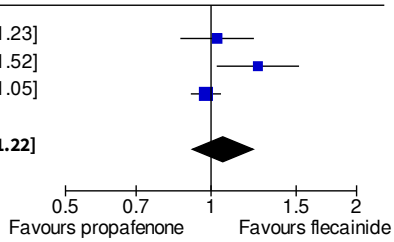


Comparison 1: Flecainide vs Amiodarone, Outcome 2: Acute procedural success (Paroxysmal AF)

Analysis 2.1

Study or Subgroup	Flecainide Events	Total	Propafenone Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Balla 2011	35	40	34	40	29.0%	1.03 [0.86 , 1.23]
Martínez-Marcos 2000	45	50	36	50	26.2%	1.25 [1.03 , 1.52]
Romano 2001	124	138	151	164	44.9%	0.98 [0.91 , 1.05]
Total (95% CI)		**228**		**254**	**100.0%**	**1.06 [0.92 , 1.22]**
Total events:	204		221			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.00$, df = 2 (P = 0.05); $I^2 = 67\%$
Test for overall effect: Z = 0.76 (P = 0.45)
Test for subgroup differences: Not applicable

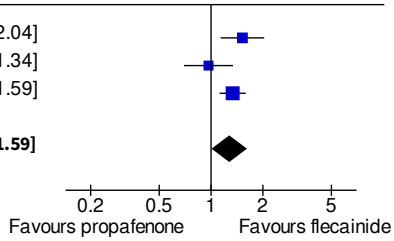


Comparison 2: Flecainide vs Propafenone, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 2.2

Study or Subgroup	Flecainide Events	Total	Propafenone Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Balla 2011	35	40	23	40	29.6%	1.52 [1.14 , 2.04]
Martínez-Marcos 2000	29	50	30	50	26.1%	0.97 [0.70 , 1.34]
Romano 2001	100	138	89	164	44.2%	1.34 [1.12 , 1.59]
Total (95% CI)		**228**		**254**	**100.0%**	**1.28 [1.02 , 1.59]**
Total events:	164		142			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 4.40$, df = 2 (P = 0.11); $I^2 = 55\%$
Test for overall effect: Z = 2.16 (P = 0.03)
Test for subgroup differences: Not applicable

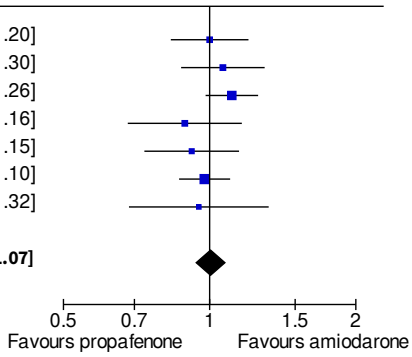


Comparison 2: Flecainide vs Propafenone, Outcome 2: Acute procedural success (Paroxysmal AF)

Analysis 3.1

Study or Subgroup	Amiodarone Events	Total	Propafenone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Balla 2011	34	40	34	40	10.9%	1.00 [0.83 , 1.20]
Kochiadakis 1998a	40	48	36	46	11.8%	1.06 [0.87 , 1.30]
Kochiadakis 2007	82	92	73	91	23.5%	1.11 [0.98 , 1.26]
Martínez-Marcos 2000	32	50	36	50	11.5%	0.89 [0.68 , 1.16]
Negrini 1994	24	30	27	31	8.5%	0.92 [0.73 , 1.15]
Taha 2022	83	100	85	100	27.3%	0.98 [0.87 , 1.10]
Treglia 1994a	19	27	20	27	6.4%	0.95 [0.68 , 1.32]
Total (95% CI)		**387**		**385**	**100.0%**	**1.00 [0.94 , 1.07]**
Total events:	314		311			

Heterogeneity: $Chi^2 = 4.57$, df = 6 (P = 0.60); $I^2 = 0\%$
Test for overall effect: Z = 0.13 (P = 0.90)
Test for subgroup differences: Not applicable

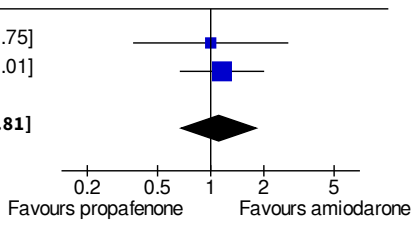


Comparison 3: Amiodarone vs Propafenone, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 3.2

Study or Subgroup	Amiodarone Events	Total	Propafenone Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baroni 2011	6	30	6	30	30.9%	1.00 [0.36 , 2.75]
Kochiadakis 1999a	16	34	13	32	69.1%	1.16 [0.67 , 2.01]
Total (95% CI)		**64**		**62**	**100.0%**	**1.11 [0.68 , 1.81]**
Total events:	22		19			

Heterogeneity: $Chi^2 = 0.06$, df = 1 (P = 0.80); $I^2 = 0\%$
Test for overall effect: Z = 0.42 (P = 0.68)
Test for subgroup differences: Not applicable

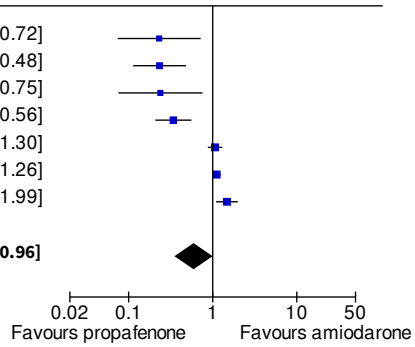


Comparison 3: Amiodarone vs Propafenone, Outcome 2: Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)

Analysis 3.3

Study or Subgroup	Amiodarone Events	Total	Propafenone Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Treglia 1994a	3	27	13	27	9.2%	0.23 [0.07 , 0.72]
Martínez-Marcos 2000	7	50	30	50	13.1%	0.23 [0.11 , 0.48]
Negrini 1994	3	30	13	31	9.1%	0.24 [0.08 , 0.75]
Taha 2022	16	100	47	100	15.4%	0.34 [0.21 , 0.56]
Kochiadakis 1998a	40	48	36	46	17.8%	1.06 [0.87 , 1.30]
Kochiadakis 2007	82	92	73	91	18.1%	1.11 [0.98 , 1.26]
Balla 2011	34	40	23	40	17.2%	1.48 [1.10 , 1.99]
Total (95% CI)		**387**		**385**	**100.0%**	**0.59 [0.36 , 0.96]**
Total events:	185		235			

Heterogeneity: Tau² = 0.34; Chi² = 88.70, df = 6 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.10 (P = 0.04)
Test for subgroup differences: Not applicable

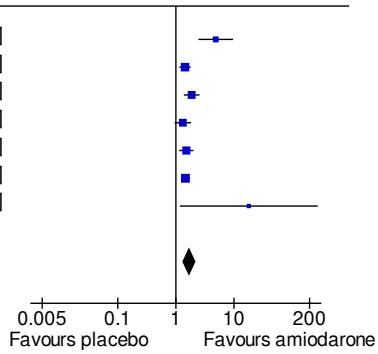


Comparison 3: Amiodarone vs Propafenone, Outcome 3: Acute procedural success (Paroxysmal AF)

Analysis 4.1

Study or Subgroup	Amiodarone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Balla 2011	34	40	7	40	7.7%	4.86 [2.45 , 9.64]
Cotter 1999	46	50	32	50	19.7%	1.44 [1.15 , 1.80]
Cybulski 2003	88	106	24	54	16.8%	1.87 [1.37 , 2.55]
Joseph 2000	30	39	21	36	16.3%	1.32 [0.95 , 1.83]
Kochiadakis 1998a	40	48	27	49	17.7%	1.51 [1.14 , 2.01]
Kochiadakis 2007	82	92	55	90	21.1%	1.46 [1.22 , 1.75]
Noc 1990	10	13	0	11	0.7%	18.00 [1.17 , 276.06]
Total (95% CI)		**388**		**330**	**100.0%**	**1.68 [1.33 , 2.11]**
Total events:	330		166			

Heterogeneity: Tau² = 0.06; Chi² = 20.43, df = 6 (P = 0.002); I² = 71%
Test for overall effect: Z = 4.39 (P < 0.0001)
Test for subgroup differences: Not applicable

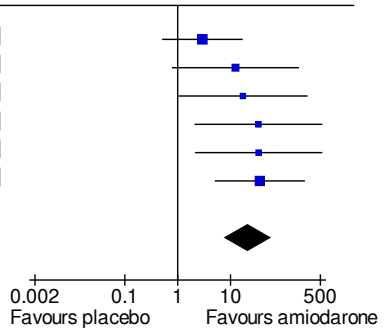


Comparison 4: Amiodarone vs Placebo, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 4.2

Study or Subgroup	Amiodarone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kanoupakis 2003	3	48	2	94	27.4%	2.94 [0.51 , 16.99]
Channer 2004	26	123	0	28	16.4%	12.40 [0.78 , 197.51]
Vijayalakshmi 2006	7	27	0	31	9.4%	17.14 [1.02 , 286.86]
Galperín 2001	16	47	0	48	10.0%	33.69 [2.08 , 545.84]
Kochiadakis 1999a	16	34	0	35	10.0%	33.94 [2.12 , 544.26]
Singh 2005	70	258	1	132	26.8%	35.81 [5.03 , 254.95]
Total (95% CI)		**537**		**368**	**100.0%**	**20.81 [7.89 , 54.88]**
Total events:	138		3			

Heterogeneity: Chi² = 5.46, df = 5 (P = 0.36); I² = 8%
Test for overall effect: Z = 6.14 (P < 0.00001)
Test for subgroup differences: Not applicable

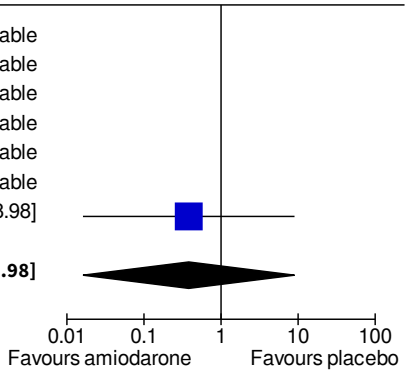


Comparison 4: Amiodarone vs Placebo, Outcome 2: Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)

Analysis 4.3

Study or Subgroup	Amiodarone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Channer 2004	0	123	0	38		Not estimable
Galperín 2001	0	47	0	48		Not estimable
Kochiadakis 1999	0	33	0	34		Not estimable
Kochiadakis 1999a	0	34	0	35		Not estimable
Singh 2005	0	258	0	132		Not estimable
Vardas 2000	0	108	0	100		Not estimable
Vijayalakshmi 2006	0	27	1	31	100.0%	0.38 [0.02 , 8.98]
Total (95% CI)		**630**		**418**	**100.0%**	**0.38 [0.02 , 8.98]**
Total events:	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable

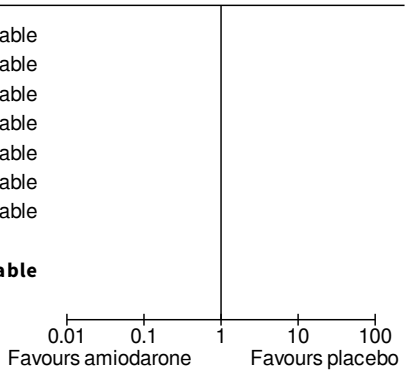


Comparison 4: Amiodarone vs Placebo, Outcome 3: 30 day all-cause mortality

Analysis 4.4

Study or Subgroup	Amiodarone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Channer 2004	0	123	0	38		Not estimable
Galperín 2001	0	47	0	48		Not estimable
Kochiadakis 1999	0	33	0	34		Not estimable
Kochiadakis 1999a	0	34	0	35		Not estimable
Singh 2005	0	258	0	132		Not estimable
Vardas 2000	0	108	0	100		Not estimable
Vijayalakshmi 2006	0	27	0	31		Not estimable
Total (95% CI)		**630**		**418**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

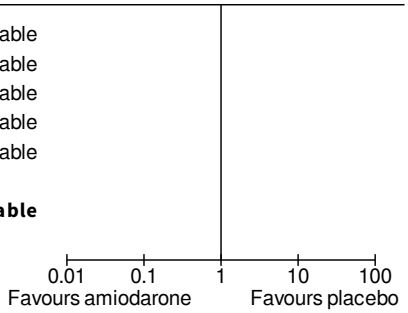


Comparison 4: Amiodarone vs Placebo, Outcome 4: 30 day cardiovascular mortality

Analysis 4.5

Study or Subgroup	Amiodarone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Galperín 2001	0	47	0	48		Not estimable
Kochiadakis 1999	0	33	0	34		Not estimable
Kochiadakis 1999a	0	34	0	35		Not estimable
Singh 2005	0	258	0	132		Not estimable
Vardas 2000	0	108	0	100		Not estimable
Total (95% CI)		**480**		**349**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

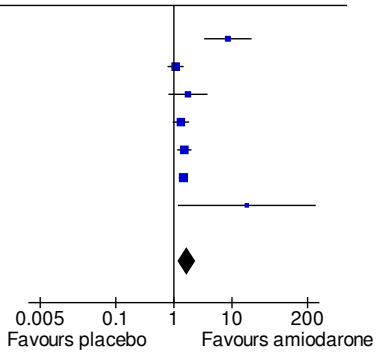


Comparison 4: Amiodarone vs Placebo, Outcome 5: Stroke or Systemic Embolism at 30 days

Analysis 4.6

Study or Subgroup	Amiodarone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Balla 2011	34	40	4	40	7.8%	8.50 [3.32 , 21.73]
Cotter 1999	31	50	29	50	19.3%	1.07 [0.78 , 1.47]
Cybulski 2003	24	106	7	54	9.9%	1.75 [0.80 , 3.79]
Joseph 2000	30	39	21	36	19.2%	1.32 [0.95 , 1.83]
Kochiadakis 1998a	40	48	27	49	20.2%	1.51 [1.14 , 2.01]
Kochiadakis 2007	82	92	55	90	22.3%	1.46 [1.22 , 1.75]
Noc 1990	10	13	0	11	1.3%	18.00 [1.17 , 276.06]
Total (95% CI)		**388**		**330**	**100.0%**	**1.64 [1.19 , 2.25]**
Total events:	251		143			

Heterogeneity: Tau² = 0.11; Chi² = 25.36, df = 6 (P = 0.0003); I² = 76%
Test for overall effect: Z = 3.03 (P = 0.002)
Test for subgroup differences: Not applicable

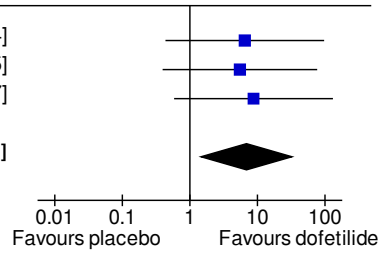


Comparison 4: Amiodarone vs Placebo, Outcome 6: Acute procedural success (Paroxysmal AF)

Analysis 5.1

Study or Subgroup	Dofetilide Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Falk 1997	6	11	0	5	33.9%	6.50 [0.43 , 97.14]
Lindeboom 2000	5	7	0	3	33.9%	5.50 [0.39 , 76.65]
Norgaard 1999	7	11	0	6	32.1%	8.75 [0.58 , 131.07]
Total (95% CI)		**29**		**14**	**100.0%**	**6.88 [1.46 , 32.36]**
Total events:	18		0			

Heterogeneity: Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.44 (P = 0.01)
Test for subgroup differences: Not applicable

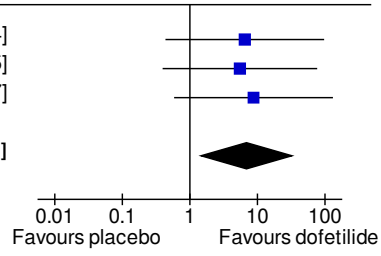


Comparison 5: Dofetilide vs Placebo, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Atrial Flutter)

Analysis 5.2

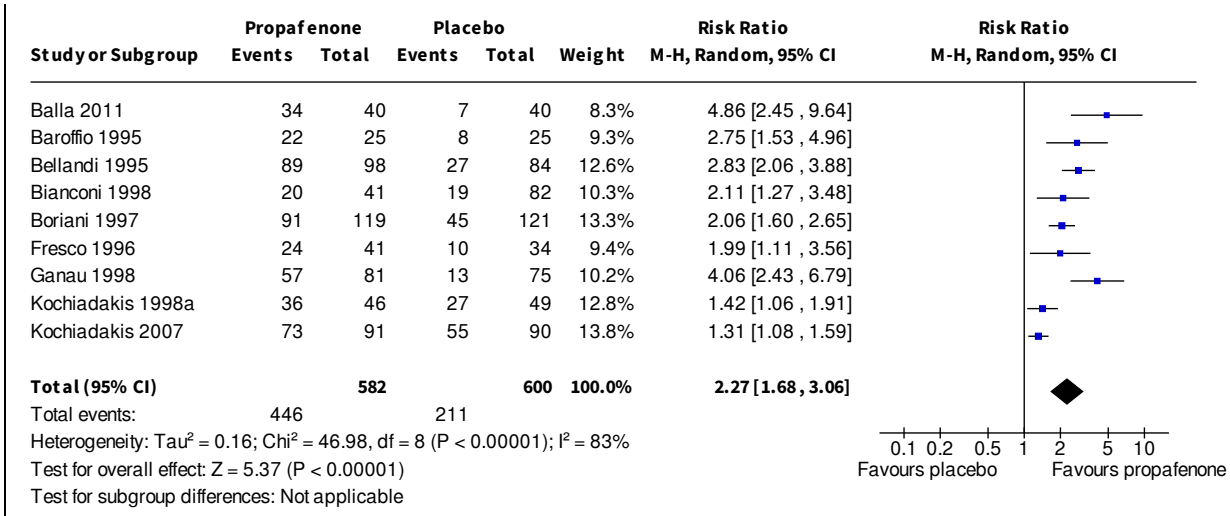
Study or Subgroup	Dofetilide Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Falk 1997	6	11	0	5	33.9%	6.50 [0.43 , 97.14]
Lindeboom 2000	5	7	0	3	33.9%	5.50 [0.39 , 76.65]
Norgaard 1999	7	11	0	6	32.1%	8.75 [0.58 , 131.07]
Total (95% CI)		**29**		**14**	**100.0%**	**6.88 [1.46 , 32.36]**
Total events:	18		0			

Heterogeneity: Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.44 (P = 0.01)
Test for subgroup differences: Not applicable



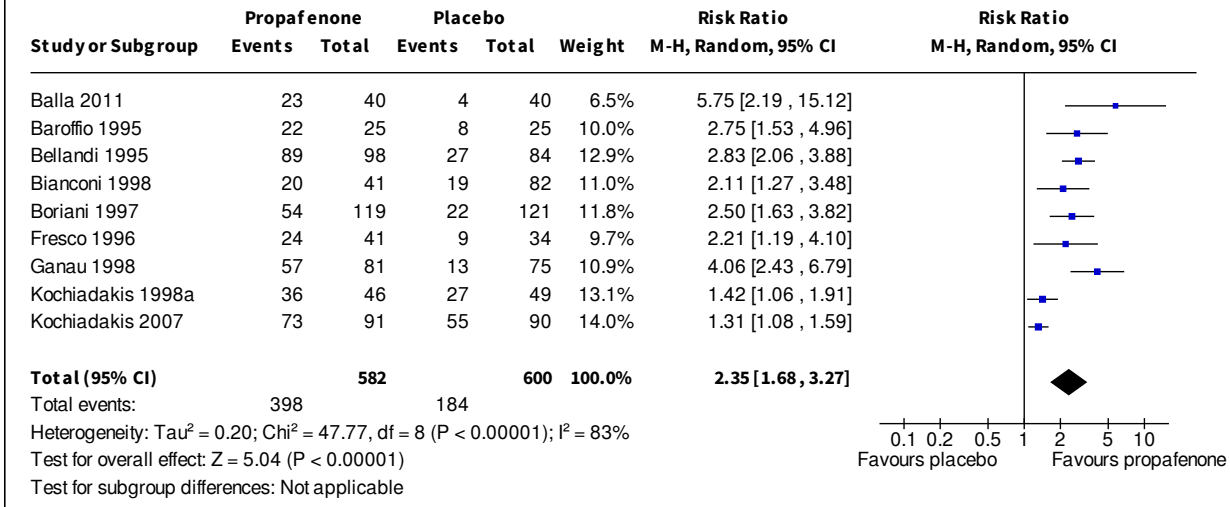
Comparison 5: Dofetilide vs Placebo, Outcome 2: Acute procedural success (Atrial Flutter)

Analysis 6.1



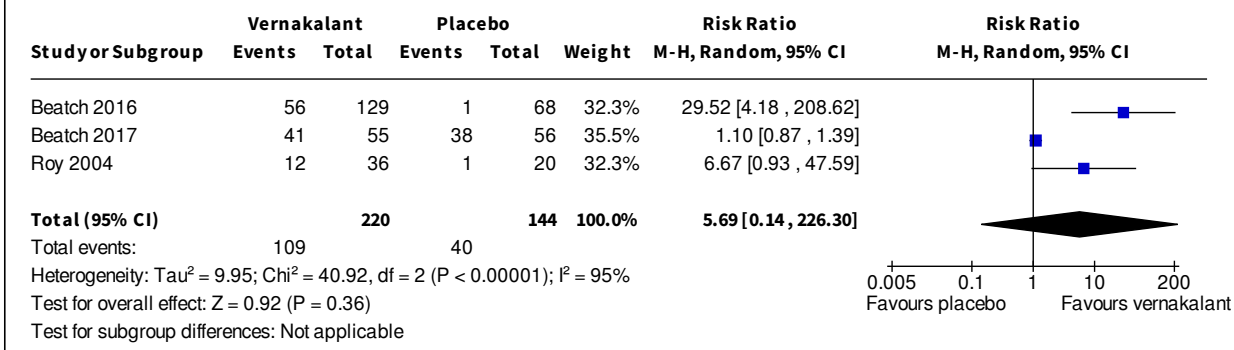
Comparison 6: Propafenone vs Placebo, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 6.2



Comparison 6: Propafenone vs Placebo, Outcome 2: Acute procedural success (Paroxysmal AF)

Analysis 7.1

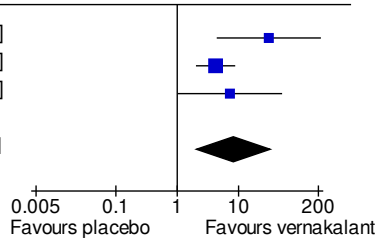


Comparison 7: Vernakalant vs Placebo, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 7.2

Study or Subgroup	Vernakalant Events	Vernakalant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Beatch 2016	59	129	1	68	26.2%	31.10 [4.40 , 219.60]
Beatch 2017	29	55	7	56	47.6%	4.22 [2.02 , 8.81]
Roy 2004	13	36	1	20	26.2%	7.22 [1.02 , 51.23]
Total (95% CI)		**220**		**144**	**100.0%**	**8.20 [2.06 , 32.71]**
Total events:	101		9			

Heterogeneity: Tau² = 0.91; Chi² = 5.03, df = 2 (P = 0.08); I² = 60%
Test for overall effect: Z = 2.98 (P = 0.003)
Test for subgroup differences: Not applicable

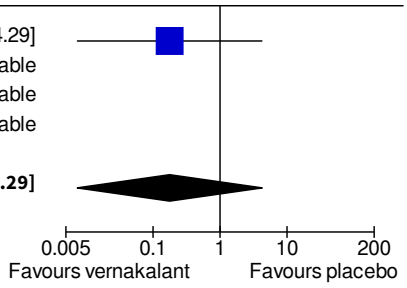


Comparison 7: Vernakalant vs Placebo, Outcome 2: Acute procedural success (Paroxysmal AF)

Analysis 7.3

Study or Subgroup	Vernakalant Events	Vernakalant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Beatch 2016	0	129	1	68	100.0%	0.18 [0.01 , 4.29]
Camm 2012	0	39	0	15		Not estimable
Pratt 2010	0	134	0	131		Not estimable
Roy 2008	0	221	0	115		Not estimable
Total (95% CI)		**523**		**329**	**100.0%**	**0.18 [0.01 , 4.29]**
Total events:	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.29)
Test for subgroup differences: Not applicable

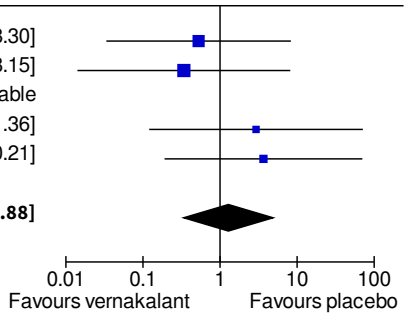


Comparison 7: Vernakalant vs Placebo, Outcome 3: Stroke or Systemic Embolism at 30 days

Analysis 7.4

Study or Subgroup	Vernakalant Events	Vernakalant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Beatch 2016	1	129	1	68	33.1%	0.53 [0.03 , 8.30]
Beatch 2017	0	55	1	56	37.6%	0.34 [0.01 , 8.15]
Camm 2012	0	39	0	15		Not estimable
Pratt 2010	1	134	0	131	12.8%	2.93 [0.12 , 71.36]
Roy 2008	3	221	0	115	16.6%	3.66 [0.19 , 70.21]
Total (95% CI)		**578**		**385**	**100.0%**	**1.28 [0.34 , 4.88]**
Total events:	5		2			

Heterogeneity: Chi² = 1.81, df = 3 (P = 0.61); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)
Test for subgroup differences: Not applicable

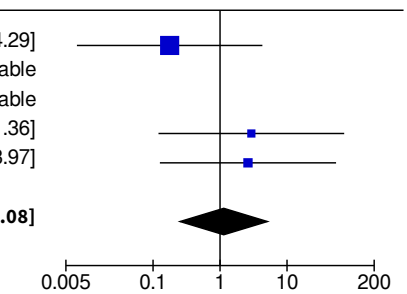


Comparison 7: Vernakalant vs Placebo, Outcome 4: 30 day all-cause mortality

Analysis 7.5

Study or Subgroup	Vernakalant Events	Vernakalant Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Beatch 2016	0	129	1	68	62.8%	0.18 [0.01 , 4.29]
Beatch 2017	0	55	0	56		Not estimable
Camm 2012	0	39	0	15		Not estimable
Pratt 2010	1	134	0	131	16.2%	2.93 [0.12 , 71.36]
Roy 2008	2	221	0	115	21.0%	2.61 [0.13 , 53.97]
Total (95% CI)		**578**		**385**	**100.0%**	**1.14 [0.25 , 5.08]**
Total events:	3		1			

Heterogeneity: Chi² = 1.94, df = 2 (P = 0.38); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.87)
Test for subgroup differences: Not applicable

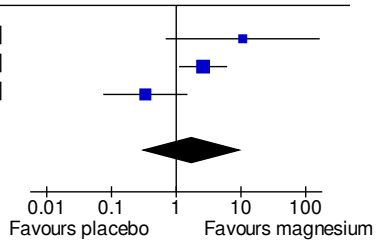


Comparison 7: Vernakalant vs Placebo, Outcome 5: 30 day cardiovascular mortality

Analysis 8.1

Study or Subgroup	Magnesium Events	Magnesium Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brodsky 1994	6	10	0	8	21.5%	10.64 [0.69 , 164.43]
Chiladakis 2001	13	23	5	23	43.3%	2.60 [1.11 , 6.11]
Chu 2009	2	24	6	24	35.3%	0.33 [0.07 , 1.49]
Total (95% CI)		**57**		**55**	**100.0%**	**1.71 [0.31 , 9.32]**
Total events:	21		11			

Heterogeneity: Tau² = 1.55; Chi² = 7.20, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 0.62 (P = 0.54)
Test for subgroup differences: Not applicable

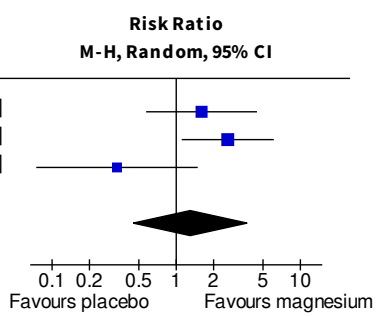


Comparison 8: Magnesium vs Placebo, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 8.2

Study or Subgroup	Magnesium Events	Magnesium Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Brodsky 1994	6	10	3	8	35.2%	1.60 [0.57 , 4.47]
Chiladakis 2001	13	23	5	23	39.2%	2.60 [1.11 , 6.11]
Chu 2009	2	24	6	24	25.6%	0.33 [0.07 , 1.49]
Total (95% CI)		**57**		**55**	**100.0%**	**1.29 [0.45 , 3.73]**
Total events:	21		14			

Heterogeneity: Tau² = 0.55; Chi² = 5.58, df = 2 (P = 0.06); I² = 64%
Test for overall effect: Z = 0.48 (P = 0.63)
Test for subgroup differences: Not applicable

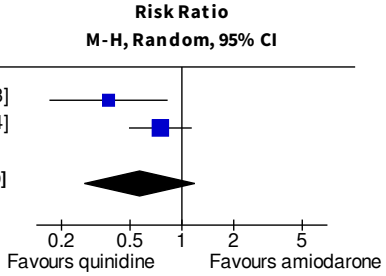


Comparison 8: Magnesium vs Placebo, Outcome 2: Acute procedural success (Paroxysmal AF)

Analysis 9.1

Study or Subgroup	Amiodarone Events	Amiodarone Total	Quinidine Events	Quinidine Total	Weight	Risk Ratio M-H, Random, 95% CI
Baroni 2011	6	30	16	30	40.1%	0.38 [0.17 , 0.83]
Zehender 1994	12	20	16	20	59.9%	0.75 [0.49 , 1.14]
Total (95% CI)		**50**		**50**	**100.0%**	**0.57 [0.27 , 1.19]**
Total events:	18		32			

Heterogeneity: Tau² = 0.19; Chi² = 2.82, df = 1 (P = 0.09); I² = 65%
Test for overall effect: Z = 1.51 (P = 0.13)
Test for subgroup differences: Not applicable

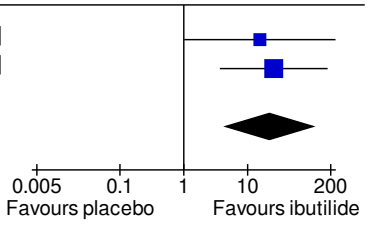


Comparison 9: Amiodarone vs Quinidine, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)

Analysis 10.1

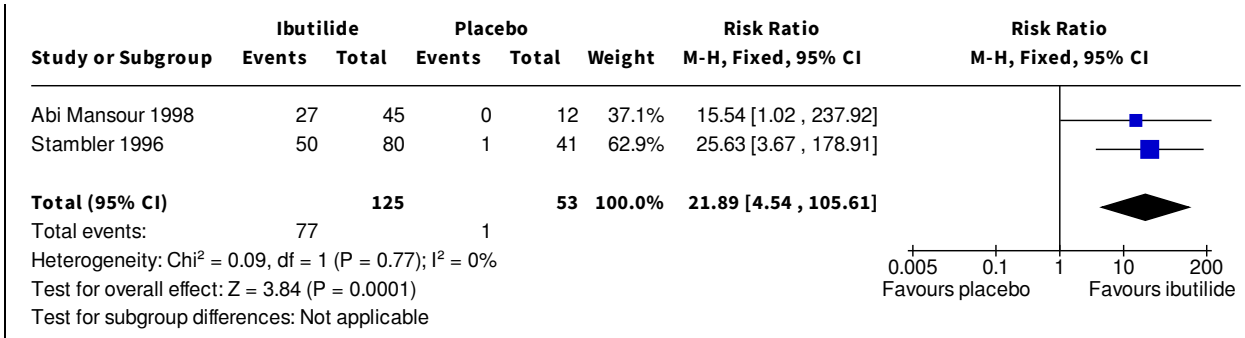
Study or Subgroup	Ibutilide Events	Ibutilide Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abi Mansour 1998	27	45	0	12	37.1%	15.54 [1.02 , 237.92]
Stambler 1996	50	80	1	41	62.9%	25.63 [3.67 , 178.91]
Total (95% CI)		**125**		**53**	**100.0%**	**21.89 [4.54 , 105.61]**
Total events:	77		1			

Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 3.84 (P = 0.0001)
Test for subgroup differences: Not applicable



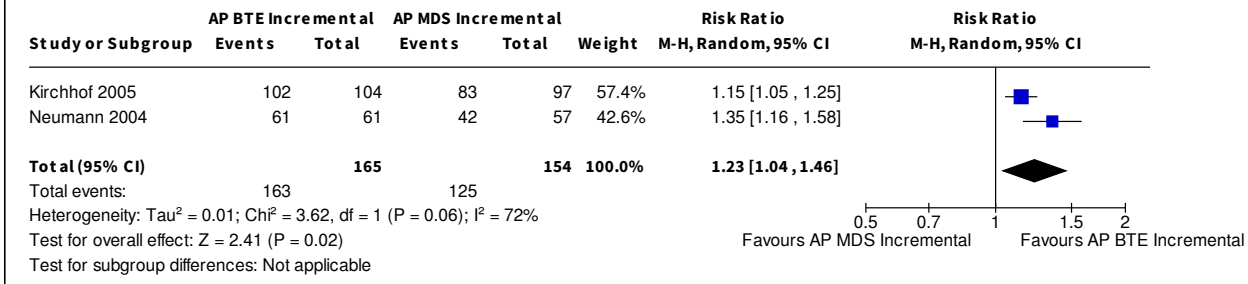
Comparison 10: Ibutilide vs Placebo, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Atrial Flutter)

Analysis 10.2



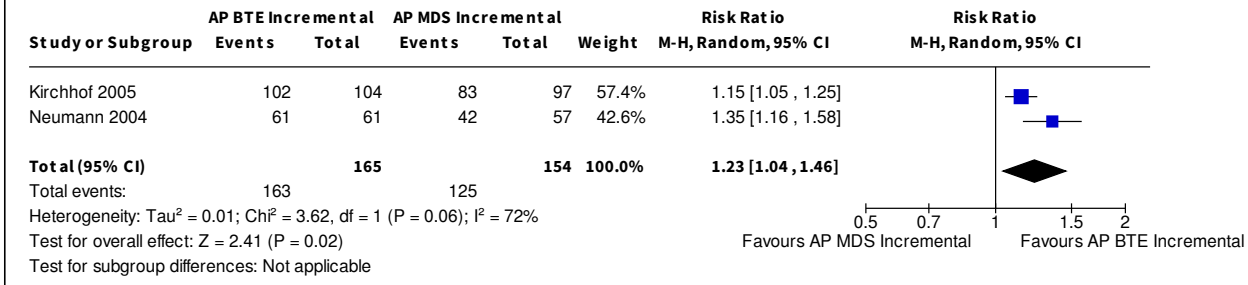
Comparison 10: Ibutilide vs Placebo, Outcome 2: Acute procedural success (Atrial Flutter)

Analysis 11.1



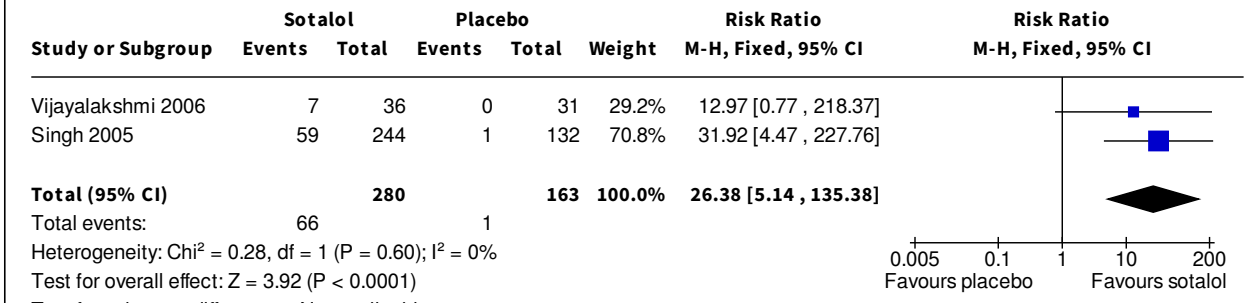
Comparison 11: AP BTE Incremental vs AP MDS Incremental, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)

Analysis 11.2



Comparison 11: AP BTE Incremental vs AP MDS Incremental, Outcome 2: Acute procedural success (Persistent AF)

Analysis 12.1

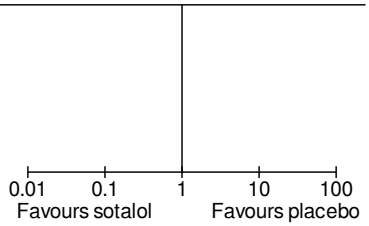


Comparison 12: Sotalol vs Placebo, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)

Analysis 12.2

Study or Subgroup	Sotalol Events	Sotalol Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 2005	0	36	0	31		Not estimable
Vijayalakshmi 2006	0	244	0	132		Not estimable
Total (95% CI)		**280**		**163**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

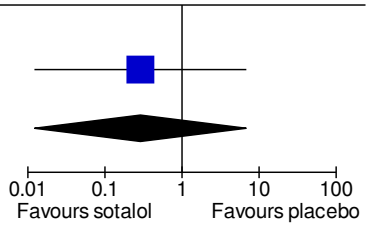


Comparison 12: Sotalol vs Placebo, Outcome 2: 30 day cardiovascular mortality

Analysis 12.3

Study or Subgroup	Sotalol Events	Sotalol Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 2005	0	244	0	132		Not estimable
Vijayalakshmi 2006	0	36	1	31	100.0%	0.29 [0.01 , 6.83]
Total (95% CI)		**280**		**163**	**100.0%**	**0.29 [0.01 , 6.83]**
Total events:	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)
Test for subgroup differences: Not applicable

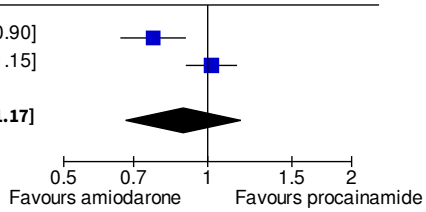


Comparison 12: Sotalol vs Placebo, Outcome 3: 30 day all cause mortality

Analysis 13.1

Study or Subgroup	Procainamide Events	Procainamide Total	Amiodarone Events	Amiodarone Total	Weight	Risk Ratio M-H, Random, 95% CI
Kochiadakis 2007	61	89	82	92	48.4%	0.77 [0.66 , 0.90]
Xanthos 2007	91	110	91	112	51.6%	1.02 [0.90 , 1.15]
Total (95% CI)		**199**		**204**	**100.0%**	**0.89 [0.67 , 1.17]**
Total events:	152		173			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 7.66$, df = 1 (P = 0.006); $I^2 = 87\%$
Test for overall effect: Z = 0.83 (P = 0.40)
Test for subgroup differences: Not applicable

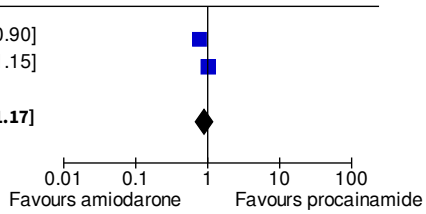


Comparison 13: Procainamide vs Amiodarone, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Paroxysmal AF)

Analysis 13.2

Study or Subgroup	Procainamide Events	Procainamide Total	Amiodarone Events	Amiodarone Total	Weight	Risk Ratio M-H, Random, 95% CI
Kochiadakis 2007	61	89	82	92	48.4%	0.77 [0.66 , 0.90]
Xanthos 2007	91	110	91	112	51.6%	1.02 [0.90 , 1.15]
Total (95% CI)		**199**		**204**	**100.0%**	**0.89 [0.67 , 1.17]**
Total events:	152		173			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 7.66$, df = 1 (P = 0.006); $I^2 = 87\%$
Test for overall effect: Z = 0.83 (P = 0.40)
Test for subgroup differences: Not applicable

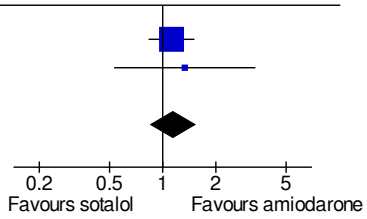


Comparison 13: Procainamide vs Amiodarone, Outcome 2: Acute procedural success (Paroxysmal AF)

Analysis 14.1

Study or Subgroup	Amiodarone Events	Total	Sotalol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 2005	70	258	59	244	91.0%	1.12 [0.83 , 1.51]
Vijayalakshmi 2006	7	27	7	36	9.0%	1.33 [0.53 , 3.35]
Total (95% CI)		**285**		**280**	**100.0%**	**1.14 [0.86 , 1.52]**
Total events:	77		66			

Heterogeneity: Chi² = 0.12, df = 1 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.91 (P = 0.36)
Test for subgroup differences: Not applicable

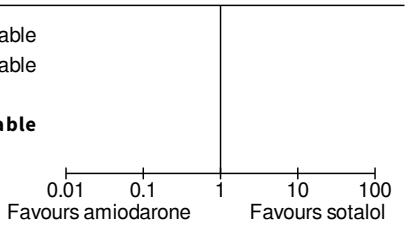


Comparison 14: Amiodarone vs Sotalol, Outcome 1: Sinus rhythm until hospital discharge or end of study follow-up (Persistent AF)

Analysis 14.2

Study or Subgroup	Amiodarone Events	Total	Sotalol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 2005	0	258	0	244		Not estimable
Vijayalakshmi 2006	0	27	0	36		Not estimable
Total (95% CI)		**285**		**280**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

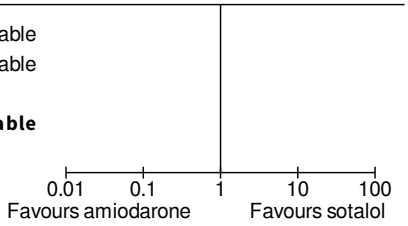


Comparison 14: Amiodarone vs Sotalol, Outcome 2: 30 day cardiovascular mortality

Analysis 14.3

Study or Subgroup	Amiodarone Events	Total	Sotalol Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Singh 2005	0	258	0	244		Not estimable
Vijayalakshmi 2006	0	27	0	36		Not estimable
Total (95% CI)		**285**		**280**		**Not estimable**
Total events:	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Comparison 14: Amiodarone vs Sotalol, Outcome 3: 30 day all cause mortality