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Antihypertensive treatment for kidney transplant recipients (Review)

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Antihypertensive treatment for kidney transplant recipients.
Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD003598.
DOI: 10.1002/14651858.CD003598.pub2.

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[Intervention Review]

Antihypertensive treatment for kidney transplant recipients

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Editorial group: Cochrane Kidney and Transplant Group.
Publication status and date: Edited (no change to conclusions), published in Issue 2, 2010.

Citation: Cross NB, Webster AC, Masson P, O'Connell PJ, Craig JC. Antihypertensive treatment for kidney transplant recipients. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD003598. DOI: 10.1002/14651858.CD003598.pub2.

ABSTRACT

Background

In some nontransplant populations, effects of different antihypertensive drug classes vary. Relative effects in kidney transplant recipients are uncertain.

Objectives

To assess comparative effects of different classes of antihypertensive agents in kidney transplant recipients.

Search methods

MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, conference proceedings and reference lists of identified studies were searched.

Selection criteria

Randomised controlled trials of any antihypertensive agent applied to kidney transplant recipients for at least two weeks were included.

Data collection and analysis

Data was extracted by two investigators independently. Study quality, transplant outcomes and other patient centred outcomes were assessed using random effects meta-analysis. Risk ratios (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes, both with 95% confidence intervals (CI) were calculated. Stratified analyses and meta-regression were used to investigate heterogeneity.

Main results

We identified 60 studies, enrolling 3802 recipients. Twenty-nine studies (2262 participants) compared calcium channel blockers (CCB) to placebo/no treatment, 10 studies (445 participants) compared angiotensin converting enzyme inhibitors (ACEi) to placebo/no treatment and seven studies (405 participants) compared CCB to ACEi. CCB compared to placebo/no treatment (plus additional agents in either arm as required) reduced graft loss (RR 0.75, 95% CI 0.57 to 0.99) and improved glomerular filtration rate (GFR), (MD, 4.45 mL/min, 95% CI 2.22 to 6.68). Data on ACEi versus placebo/no treatment were inconclusive for GFR (MD -8.07 mL/min, 95% CI -18.57 to 2.43), and variable for graft loss, precluding meta-analysis. In direct comparison with CCB, ACEi decreased GFR (MD -11.48 mL/min, 95% CI -5.75 to -7.21), proteinuria

(MD -0.28 g/24 h, 95% CI -0.47 to -0.10), haemoglobin (MD -12.96 g/L, 95% CI -5.72 to -10.21) and increased hyperkalaemia (RR 3.74, 95% CI 1.89 to 7.43). Graft loss data were inconclusive (RR 7.37, 95% CI 0.39 to 140.35). Other drug comparisons were compared in small numbers of participants and studies.

Authors' conclusions

These data suggest that CCB may be preferred as first line agents for hypertensive kidney transplant recipients. ACEi have some detrimental effects in kidney transplant recipients. More high quality studies reporting patient centred outcomes are required.

PLAIN LANGUAGE SUMMARY

Blood pressure medication for kidney transplant recipients

In some patient groups, different blood pressure lowering drugs have differing relative beneficial and harmful effects in addition to their blood pressure lowering action. We investigated whether different classes of drugs might have different relative effects in kidney transplant patients. We found that calcium channel blockers (CCB) reduced the risk of graft loss by about 25% in randomised studies, compared to placebo or no treatment. CCB also improved the function of grafts, as measured by glomerular filtration rate (GFR) with GFR 4.5 mL/min higher on average in patients receiving CCB compared to placebo. There were fewer studies comparing angiotensin converting enzyme inhibitors (ACEi) to placebo and their results were inconclusive. In studies that compared ACEi to CCB, ACEi worsened GFR by about 11.5 mL/min on average. ACEi also lowered haemoglobin and increased the risk of elevated blood potassium compared to CCB. There were not enough studies of other classes of drugs to draw conclusions about their relative effects. On current evidence CCB might therefore be the best agents for kidney transplant patients.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Calcium channel blockers versus placebo/no treatment for kidney transplant recipients

Calcium channel blockers versus placebo/no treatment for kidney transplant recipients

Patient or population: kidney transplant recipients
Settings:
Intervention: Calcium channel blockers
Comparison: Placebo/no treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo/no treatment	Calcium channel blockers				
Death Follow-up: median 12 months[1]	**Medium risk population**		**RR 0.82** (0.37 to 1.82)	792 (12 studies)	⊕⊕⊝⊝ **low** [2,3]	
	60 per 1000	**49 per 1000** (22 to 109)				
Graft loss Follow-up: median 12 months[4]	**Medium risk population**		**RR 0.75** (0.57 to 0.99)	1255 (17 studies)	⊕⊕⊝⊝ **low** [2,5]	
	90 per 1000	**68 per 1000** (51 to 89)				
GFR (measured or estimated) mL/min Follow-up: median 3 months[6]		The mean GFR (measured or estimated) in the intervention groups was **4.45 higher** (2.22 to 6.68 higher)		1119 (18 studies)	⊕⊕⊕⊝ **moderate** [2]	
Acute rejection Follow-up: median 12 months[7]	**Medium risk population**		**RR 1.02** (0.85 to 1.23)	771 (11 studies)	⊕⊕⊝⊝ **low** [2,5]	
	200 per 1000	**204 per 1000** (170 to 246)				
Withdrawal due to side effects Follow-up: median 3 months	**Medium risk population**		**RR 0.99** (0.53 to 1.87)	156 (2 studies)	⊕⊕⊝⊝ **low** [2,5]	
	140 per 1000	**139 per 1000** (74 to 262)				

Proteinuria g/24 h Follow-up: median 18.5 months		The mean Proteinuria in the intervention groups was **0.03 higher** (0.25 lower to 0.32 higher)		90 (2 studies)	⊕⊕⊝⊝ **low** [2,5]
Blood pressure mm Hg Follow-up: median 4.5 months[8]	See comment	See comment	Not estimable	590 (10 studies)	⊕⊝⊝⊝ **very low** [2,9]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] IQR 4.5 to 18 months
[2] More than 50% of studies rated as allocation concealment unclear or high risk of causing bias
[3] Based on few events across all studies
[4] IQR 12 to 24 months
[5] Confidence interval includes range of plausible values below clinical significance or including harm
[6] IQR 1 to 12 months
[7] IQR 3 to 12 months
[8] IQR 1 to 24 months
[9] Significant heterogeneity in effect precluded meta-analysis

Summary of findings 2. ACE inhibitors versus placebo/no treatment for kidney transplant recipients

ACE inhibitors versus placebo/no treatment for kidney transplant recipients

Patient or population: kidney transplant recipients
Settings:
Intervention: ACE inhibitors
Comparison: Placebo/no treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				

	Placebo/no treatment	ACE inhibitors			
Death Follow-up: 3 months	**Medium risk population**		**RR 1** (0.07 to 14.55)	30 (1 study)	⊕⊕⊝⊝ **low** [1,2]
	60 per 1000	**60 per 1000** (4 to 873)			
Graft loss	See comment	See comment	Not estimable	93 (2 studies)	⊕⊕⊝⊝ **low** [1,3]
GFR (measured or estimated) mL/min Follow-up: median 3 months[4]		The mean GFR (measured or estimated) in the intervention groups was **8.07 lower** (18.57 lower to 2.43 higher)		77 (3 studies)	⊕⊕⊝⊝ **low** [1,2]
Proteinuria g/24 h Follow-up: median 18 months[5]		The mean Proteinuria in the intervention groups was **0.08 lower** (0.23 lower to 0.06 higher)		175 (3 studies)	⊕⊕⊕⊝ **moderate** [6]
Serum creatinine umol/L Follow-up: median 3 months[7]		The mean Serum creatinine in the intervention groups was **7.55 higher** (2.1 lower to 17.2 higher)		272 (7 studies)	⊕⊕⊝⊝ **low** [1,2]
Haemoglobin g/L Follow-up: median 4 months[8]		The mean Haemoglobin in the intervention groups was **11.7 lower** (19.96 to 3.44 lower)		191 (5 studies)	⊕⊕⊕⊝ **moderate** [1]
Blood pressure mmHg Follow-up: median 4 months[9]	See comment	See comment	Not estimable	392 (9 studies)	⊕⊝⊝⊝ **very low** [1,3]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[1] Allocation concealment rated at unclear or high risk of bias in > 50% of included studies
[2] CI includes beneficial effect and no clinically relevant effect or harm
[3] Heterogeneity in treatment effect precluded meta-analysis
[4] IQR 1 to 4 months
[5] IQR 1 to 23 months
[6] No explanation was provided
[7] IQR 2 to 18 months
[8] IQR 3 to 12 months
[9] IQR 3 to 12 months

Summary of findings 3. ACE Inhibitors versus calcium channel blockers for kidney transplant recipients

ACE Inhibitors versus calcium channel blockers for kidney transplant recipients

Patient or population: kidney transplant recipients
Settings:
Intervention: ACE Inhibitors
Comparison: Calcium channel blockers

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Calcium channel blockers	ACE Inhibitors				
Death Follow-up: 6 to 24 months	**Medium risk population**		**RR 4.03** (0.45 to 35.82)	221 (2 studies)	⊕⊕⊝⊝ **low** [1,2]	
	49 per 1000	**198 per 1000** (22 to 1000)				
Graft loss Follow-up: 24 months	**Medium risk population**		**RR 7.37** (0.39 to 140.35)	152 (1 study)	⊕⊕⊝⊝ **low** [1,2]	
	68 per 1000	**497 per 1000** (26 to 1000)				
GFR (measured or estimated) Follow-up: median 6 months[3]		The mean GFR (measured or estimated) in the intervention groups was **11.48 lower**		296 (6 studies)	⊕⊕⊕⊝ **moderate** [1]	

		(15.75 to 7.21 lower)			
Acute rejection	**Medium risk population**		**RR 1.54** (1.14 to 2.07)	221 (2 studies)	⊕⊝⊝⊝ **very low** [1,4,5]
	204 per 1000	**314 per 1000** (233 to 422)			
Proteinuria g/24 h Follow-up: 1-12 months		The mean Proteinuria in the intervention groups was **0.28 lower** (0.47 to 0.1 lower)		142 (2 studies)	⊕⊕⊕⊝ **moderate** [1]
Haemoglobin g/L Follow-up: median 6 months[6]		The mean Haemoglobin in the intervention groups was **12.96 lower** (15.72 to 10.21 lower)		332 (5 studies)	⊕⊕⊕⊝ **moderate** [1]
Haematocrit % Follow-up: 6 to 30 months		The mean Haematocrit in the intervention groups was **4.33 lower** (5.45 to 3.2 lower)		153 (4 studies)	⊕⊕⊕⊝ **moderate** [1]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Allocation concealment rated at unclear or high risk of bias in > 50% of included studies
[2] CI includes beneficial effect and no clinically relevant effect or harm
[3] IQR 2 to 24 months
[4] High variability in background event rates between studies
[5] Study with events had very high rejection rate amongst both arms compared to current norms
[6] IQR 6 to 12 months

BACKGROUND

Hypertension affects up to 75% of kidney transplant recipients (Kasiske 1996; Kasiske 2000) and is associated with premature death (El-Agroudy 2003) and graft loss (Opelz 1998). Other conditions for which antihypertensive drugs have been shown to be of benefit in nontransplant patients are also common in kidney recipients, such as ischaemic heart disease, diabetes mellitus and proteinuria (Barama 2008; Kasiske 2000; Kasiske 2003).

Choice of antihypertensive agent is likely to be important in kidney transplant recipients (Curtis 1997; Kendrick 2001). In other patient populations, specific classes of antihypertensive agent offer benefits beyond their ability to control blood pressure alone. For example, angiotensin-converting enzyme inhibitors (ACEi) slow the progression of diabetic kidney disease, and reduce risk of end-stage kidney disease (ESKD) and death (Strippoli 2006) and are recommended for all patients with diabetic kidney disease, irrespective of blood pressure (K/DOQI 2004; Nicholls 2006). There are biological reasons why benefits and harms may differ between kidney recipients and other populations. For example, calcium channel blockers (CCB) promote vasodilation of afferent arterioles which may counteract calcineurin inhibitor induced afferent arteriolar vasoconstriction (Baroletti 2003).

OBJECTIVES

1. To compare relative benefits and harms of different classes or combinations of antihypertensive drugs (e.g. ACEi, angiotensin receptor blockers (ARBs), CCBs, beta-blockers, alpha-blockers, diuretics) in kidney transplant recipients.
2. To assess any variation in effects by study, intervention and patient characteristics, including differences in achieved blood pressure.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and quasi-RCTs of pharmaceutical antihypertensive agents used for at least two weeks in kidney transplant recipients. Where studies did not explicitly include the word “randomly” (or a derivation) but it appeared likely that random allocation had occurred, author contact was sought for clarification before inclusion of the study. There were no restrictions by language or publication type.

Types of participants

Hypertensive and non-hypertensive kidney transplant recipients with a functioning kidney transplant. All studies enrolling patients with functioning kidney transplants were eligible, irrespective of any other selection criteria. For example, studies enrolling only hypertensive recipients and studies enrolling unselected kidney transplant recipients at the time of transplant were eligible. We excluded studies where the intervention was only applied to the donor, or to the graft *ex vivo*.

Types of interventions

Treatment group must have received at least one pharmacologic antihypertensive agent. Studies in which the randomised comparator was placebo, no intervention, another class of antihypertensive agent, or non-antihypertensive agent were eligible. Because we were interested in class effects of antihypertensive agents on clinical outcomes, we excluded studies comparing two agents from the same class of antihypertensive drug, or the same compound tested at different doses.

Types of outcome measures

1. Death
2. Graft loss (death censored)
3. Blood pressure, any of:
   a. Systolic (SBP), mean arterial (MAP), and/or diastolic (DBP)
   b. Proportion of patients achieving blood pressure control (author defined)
4. Kidney function, any of:
   a. Glomerular filtration rate (GFR) (measured or estimated using equations (e.g. Cockcroft-Gault, MDRD, Schwartz, Nankivell) or creatinine clearance (CrCl))
   b. Serum creatinine (SCr) (continuous measure, or change beyond a threshold as defined by study authors)
5. Acute rejection (proportion of patients affected with at least one episode, or rates of rejection (number of episodes/patient/unit time)), any of:
   a. Any rejection
   b. Rejection by subcategory, as reported (e.g. vascular, cellular, humoral)
6. Proteinuria (as continuous measure (g/24 h or creatinine/protein ratio), or proportion of patients with proteinuria above author specified thresholds
7. Cardiovascular disease events, any of:
   a. Fatal and nonfatal stroke
   b. Fatal and non-fatal coronary heart disease (myocardial infarction, sudden death)
   c. Other cardiovascular events (congestive heart failure, transient ischaemic attacks, revascularisation)
   d. Composite measures, as reported
8. Haemoglobin (Hb)/haematocrit (HCT)
9. Serum potassium and/or hyperkalaemia
10. Other adverse effects, as defined by authors (for example, peripheral oedema, cough), with or without leading to interruption of therapy

Continuous outcomes were recorded as mean and standard deviation (SD), with numbers of individual observed. Where study authors provided the mean and SD of the change in the outcome this is favoured, otherwise mean and SD at the follow-up time point was used. Dichotomous outcomes were recorded as number of patients in whom the event occurred/number of patients observed. For dichotomous outcomes where more than one event/patient possible (e.g. acute rejection), count data were also collected where published (e.g. number of rejection episodes/month). Where individuals were followed for different durations, time at risk was estimated from data provided.

Where studies report outcomes at several time points, all time points reported were collected.

Search methods for identification of studies

Electronic databases were searched for relevant studies, reviews and meta-analyses:

- MEDLINE
- EMBASE
- Cochrane Renal Group Specialised Register
- Cochrane Central Register of Controlled Trials (CENTRAL)

Search strategies, designed and undertaken by Cochrane Renal Group Trial Search Coordinators, are available in Appendix 1. Reference lists of included studies and conference proceedings (the International Society of Nephrology, American Society of Nephrology, European Dialysis and Transplantation Association, and Transplantation Society) were searched for unpublished studies.

Data collection and analysis

Titles and abstracts of all identified papers were reviewed by two authors (NC, AW), and any titles deemed eligible or possibly eligible by either author were retrieved in full. Where more than one report from a single study was identified, all reports were assessed for eligible data, but each study was included only once. Where it was unclear if reports were of the same study, authors were contacted for clarification.

Data was extracted by two authors (NC and PM or AW) working independently, using a preformatted purpose designed data recording sheet. Consensus was used to resolve disagreements with another author (AW or JC) arbitrating any that remained unresolved. Data were then entered into Review Manager. Microsoft ® Excel 2002, SAS version 9.1 (SAS Institute Inc, Cary, NC, USA) and Intercooled Stata 8.2 for Windows (TX, USA) were used for additional analyses.

Data were extracted on study and sample characteristics (study inclusion and exclusion criteria, setting, mean age, male:female ratio, donor source, immunosuppression) randomised intervention(s) and control(s) (name, class, dose, frequency, route, duration of administration), non-randomised antihypertensive cointerventions (allowed or not, class(es) permitted), and publication type (journal article, letter, abstract or unpublished). Where studies reported outcomes separately for groups by patient characteristics data was entered separately into analyses, designated by a suffix after the study name to identify the subgroup (for example, in patients receiving cyclosporin (CSA) (Wilkie 1993 CSA) and not receiving calcineurin inhibitors (CNI) (Wilkie 1993 No CNI).

Included studies were assessed for quality using the following six domains:

- method of random sequence generation;
- allocation concealment;
- blinding (effect on objective outcomes and partially subjective outcomes (e.g. bedside blood pressure measurement, side effect reporting, clinical rejection rates) considered separately);
- intention to treat analysis and loss to follow-up;
- selective outcome reporting and;
- other sources of bias.

Items were assessed according to the method described in the Cochrane Collaboration Handbook (Higgins 2008), and risk of bias tables created.

Quantitative data synthesis

Dichotomous outcomes were reported as risk ratio (RR) and continuous outcomes as mean difference (MD), both with 95% confidence intervals (CI). Mean change in continuous outcomes was used where possible, otherwise mean results at final follow-up were used. Studies reporting change differences and end of treatment differences were entered into the same analyses. Interventions were compared on the basis of drug class, so where studies randomised recipients across three or more arms, involving comparisons of members of the same drug class, the data for arms comparing the same drug class were combined.

Heterogeneity in treatment effects across studies was assessed using inspection of forest plots, was assessed using the Cochran Q test and I^2 statistic ($P < 0.05$ and $> 50\%$ respectively considered evidence of significant heterogeneity). Where there was no significant heterogeneity, the random effects method of DerSimonian and Laird was used to combine study results (DerSimonian 1986). Where significant heterogeneity was evident summary estimates were not calculated but investigated further using stratified analyses and random effects meta-regression (Thompson 2002). Potential factors that might contribute to heterogeneity were defined *a-priori*, and included specific immunosuppression regimen used, participant selection criteria (for example, hypertension, erythrocytosis), and subgroup of CCB, dihydropyridine versus non-dihydropyridine. To investigate the potential effect of differences in blood pressure control across randomised comparisons on outcomes, we assessed differences in achieved blood pressure (where reported) and performed sensitivity analyses by eliminating studies which reported significant differences in blood pressure across arms. Funnel plots were generated and inspected for evidence of publication or other bias.

Interventions were compared on the basis of drug class. Individual classes were compared to placebo, to other individual classes, (e.g. CCB versus ACEi). Studies that randomised patients to more than two eligible interventions were used in each available pair wise comparison. To enable this within Review Manager, entries were made for each comparison identifiable by the final part of the name (e.g. Sperschneider 1997 Dilt / Sperschneider 1997 Nifed identifies the comparisons diltiazem versus no treatment and nifedipine versus no treatment respectively). Where studies enrolled patients to more than two arms eligible for inclusion in a single comparison, the total number of patients and outcomes is divided equally for the arm that appears twice within the comparison for dichotomous outcomes (e.g. for a study of 50 patients in each arm of diltiazem versus nifedipine versus placebo for CCB versus placebo, with 10 deaths in each arm, becomes 10/50 deaths in diltiazem versus 5/25 deaths in placebo AND 10/50 deaths in nifedipine versus 5/25 deaths in placebo, each entered into the CCB versus placebo/no treatment comparison). For continuous outcomes, the number of individuals is divided equally across comparisons half in the arm to be included twice (mean and SD are unchanged). In this way, each individual patient appears no more than once in any single analysis.

Heterogeneity of intervention effects is further investigated using stratified analyses and random effects meta-regression (Thompson 2002). It was expected *a-priori* that important causes of difference in outcome could include immunosuppression regimen used (especially for outcomes such as rejection, which tend to occur less frequently with newer immunosuppressive agents),

indication for selection for treatment (for example, patients with established hypertension would be likely to have poorer clinical outcomes overall than unselected kidney transplants, and might have stronger beneficial effects of some classes of agent, or be insensitive to the benefits of some classes of agents), and subgroups of medication within classes (for example, dihydropyridine versus non-dihydropyridine CCB). In addition, differences in blood pressure in different groups could account for differences in outcomes, should the effect of the intervention be due to non-specific blood pressure reduction. Study quality factors could affect outcomes, for example blinding in semi-subjective outcomes such as clinic recorded blood pressure. Stratified analyses and meta-regression were performed where sufficient numbers of trails were available, and where there was sufficient between study heterogeneity in outcome and predictor variables.

RESULTS

Description of studies

We identified 150 reports from 66 studies, with 4516 participants (Figure 1). Six studies (714 participants) could not be included because relevant outcome data were not available in published reports and could not be obtained from study authors (Almeshari 2000; Aros 2005; Calo 2002; Cartier 1978; Riggio 1992; SECRET 2004), so 60 studies (3802 participants) contributed to data summary. Studies enrolled kidney recipients with hypertension (21 studies, 1370 participants), erythrocytosis (6 studies, 111 participants), chronic allograft nephropathy (CAN; 2 studies, 93 participants), left ventricular hypertrophy (LVH; 2 studies, 131 participants), and no specific indication for therapy (30 studies, 2099 participants).

Figure 1. Search strategy, study inclusion and outcomes reported

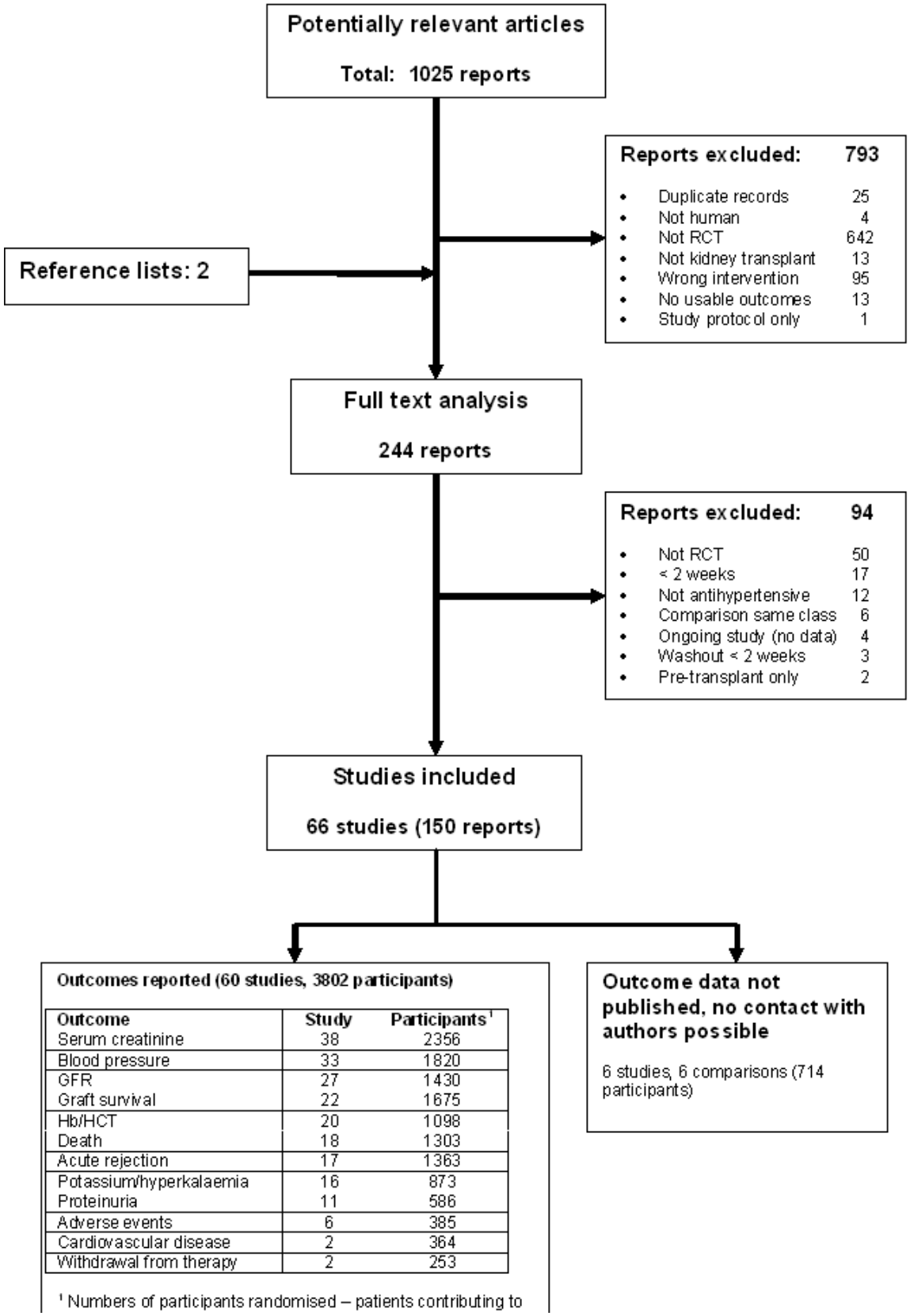
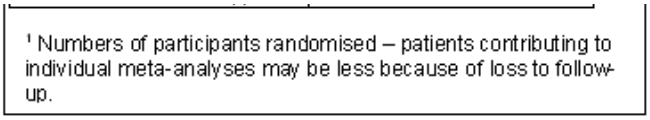


Figure 1. (Continued)



Median study duration was six months (IQR 3 to 12 months). In 56/60 studies, patients were still receiving the randomised intervention at the time of the final outcome recording. In four studies, outcomes were reported while on treatment, and then also after a period without treatment (Dawidson 1991, Lehtonen 2000, Morales 1989 and Hausberg 1999).

Patients generally received cyclosporin (all patients in 47 studies, and the majority of patients in a further five studies). In three studies, separate outcome data were available for patients receiving no CNI. Tacrolimus (TAC) was used in only a proportion of patients in at least three studies (it was unclear in a further seven studies), but no study reported effects in TAC patients separately.

Risk of bias in included studies

No study included all outcomes of interest in this review (Figure 1). For example, participant death was only reported in 18/60 included studies. Most studies did not report methodology in sufficient detail to allow assessment of all potential sources bias, leading to a high proportion of 'unclear' classifications (Figure 2; Figure 3).

Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

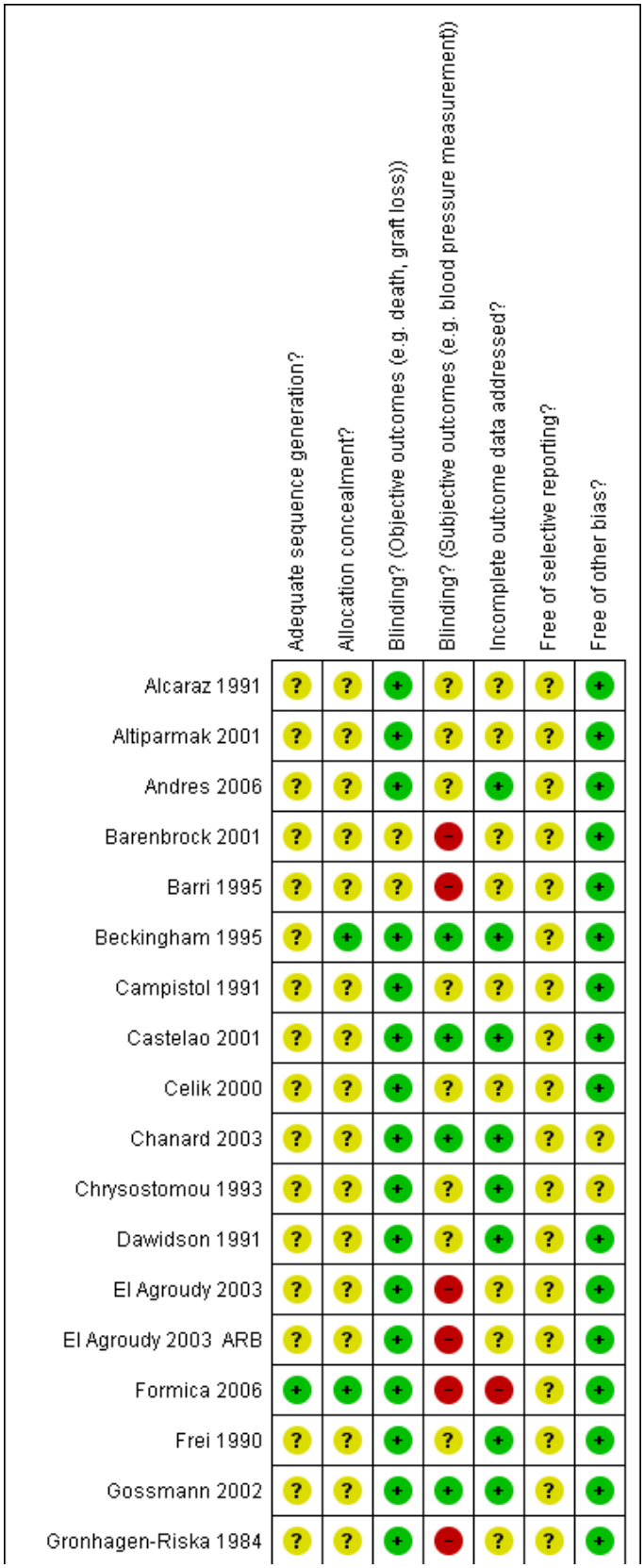


Figure 2. (Continued)

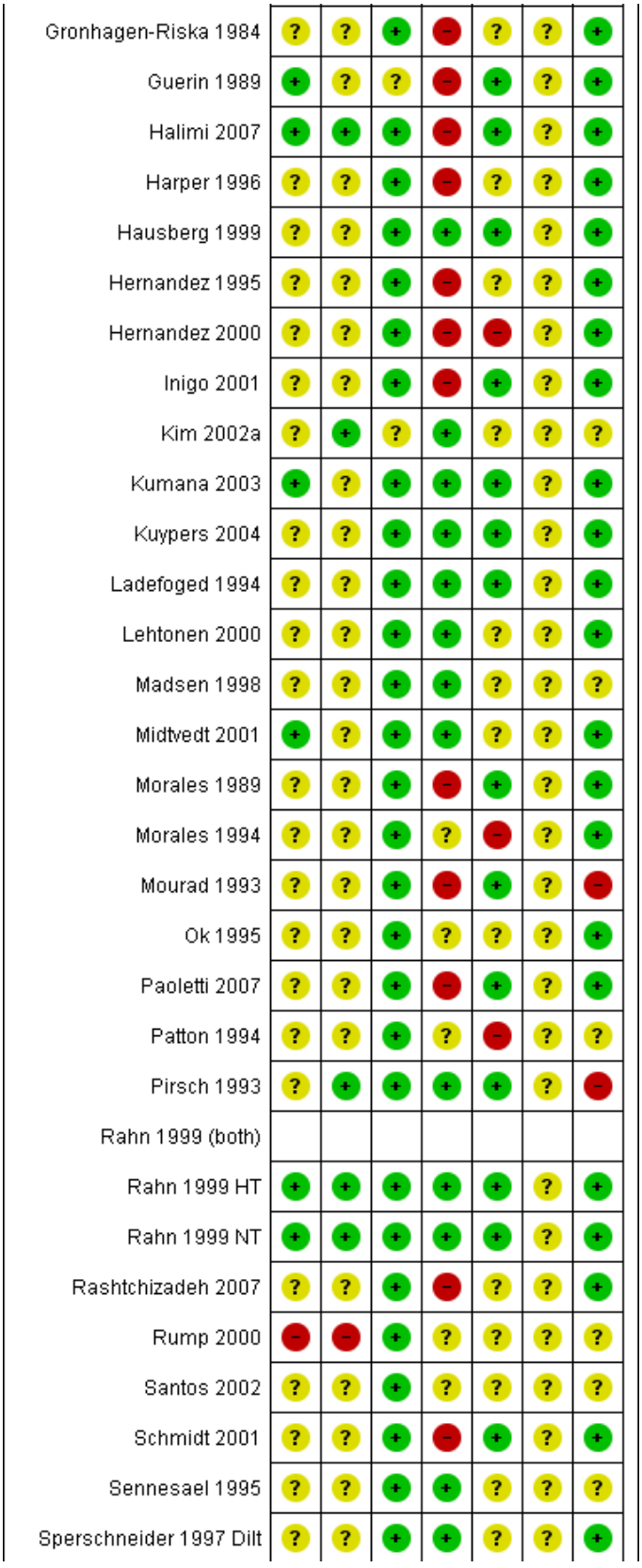


Figure 2. (Continued)

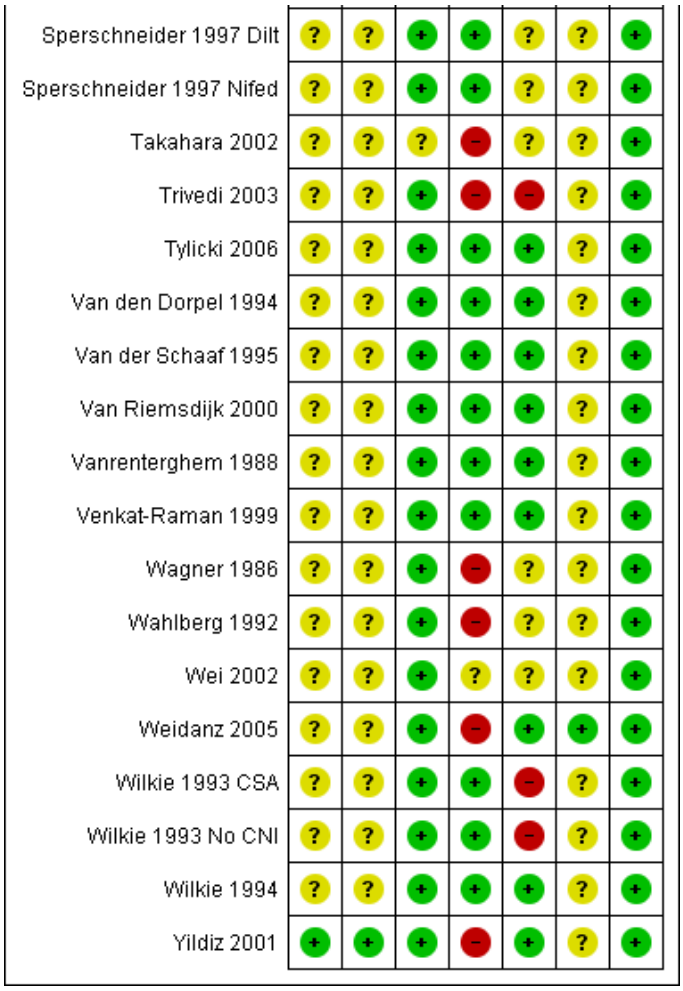
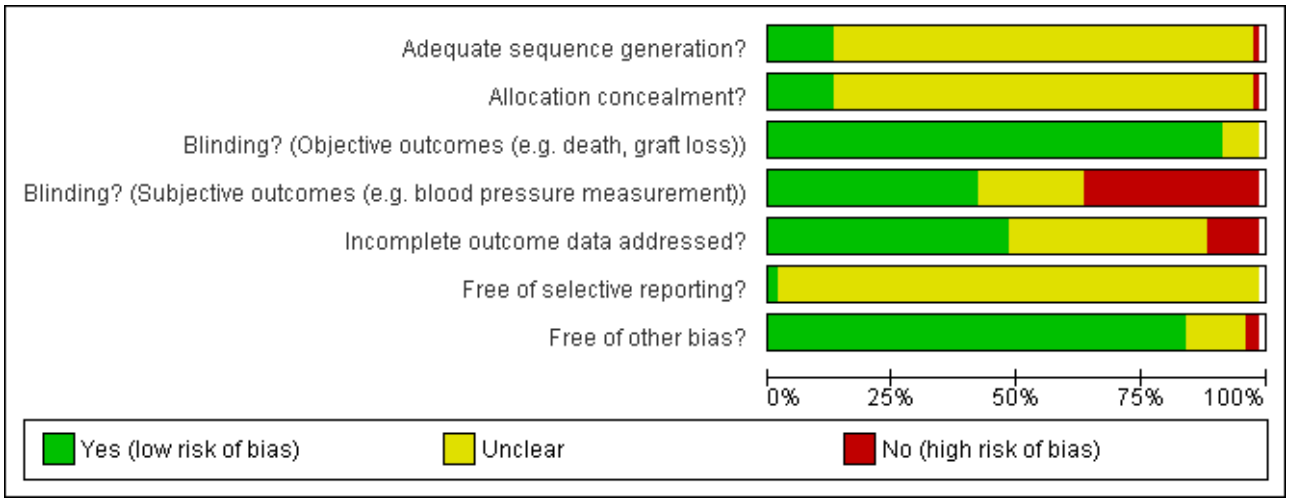


Figure 3. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

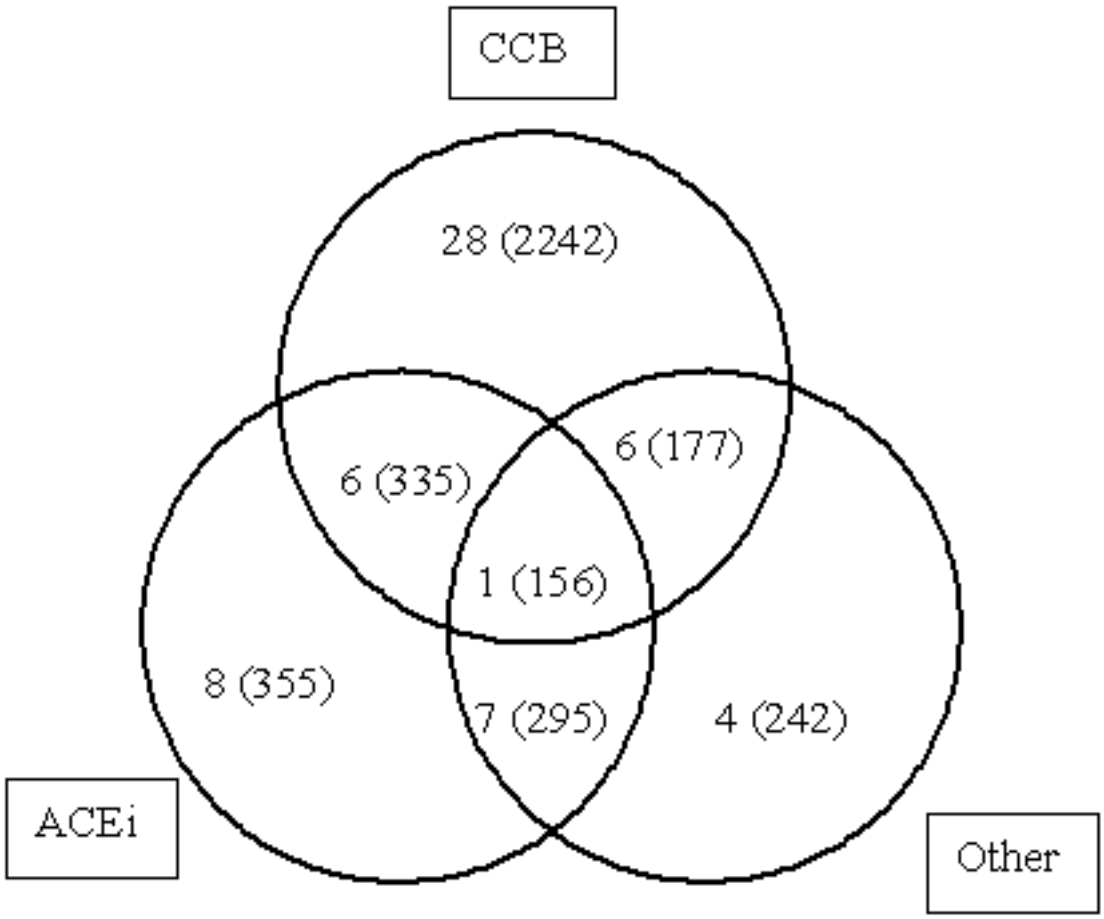


Effects of interventions

See: **Summary of findings for the main comparison** Calcium channel blockers versus placebo/no treatment for kidney transplant recipients; **Summary of findings 2** ACE inhibitors versus placebo/no treatment for kidney transplant recipients; **Summary of findings 3** ACE Inhibitors versus calcium channel blockers for kidney transplant recipients

There were 17 pair wise comparisons available across all included studies (Table 1). Most studies involved CCB and/or ACEi (Figure 4). Most studies assessed single agents versus placebo or no treatment, or single agents versus another active comparator. Four studies included three intervention arms and a single study included four arms. ACEi and ARB were considered separate drug classes, although reanalysis of data combining these drug classes together for the comparisons ACEi or ARB versus no treatment and ACEi or ARB versus CCB made no difference to any conclusion (comparisons 21 and 22 respectively).

Figure 4. Numbers of studies (participants) by class of randomised antihypertensive agent(s) compared (CCB = calcium channel blocker, ACEi = angiotensin converting enzyme inhibitor, other = other class)



The most important outcomes from comparisons with sufficient data to enable conclusions to be drawn are summarised in Summary of findings for the main comparison (CCB versus placebo/no treatment), Summary of findings 2 (ACEi versus placebo/no treatment) and Summary of findings 3 (ACEi versus CCB).

Blood pressure cointerventions and differences in achieved blood pressure among interventions

In addition to the randomised intervention, 31 studies permitted additional treatment for hypertension control if required and 17 studies reported explicit protocols for use of additional agents (see Table 1 for allowable cointerventions for included studies). Only one two-month duration crossover study comparing two active agents in 10 individuals explicitly prohibited additional cointerventions (Sennesael 1995). In the remaining studies, antihypertensive cointerventions were not mentioned. There were no systematic differences in blood pressure noted in any comparison where two active agents were compared, including the six studies of CCB versus ACEi (Analysis 18.16.2: MD -0.81 mm Hg, 95% CI -3.89 to 2.88 mm Hg, P = 0.61). Where an active agent was compared to placebo, effects varied. Blood pressure was reported

in eight studies comparing CCB with placebo/no treatment (590 patients), and in some studies there was no difference in blood pressure (Guerin 1989; Harper 1996; Rahn 1999 HT/Rahn 1999 NT; Venkat-Raman 1999, Wilkie 1994; Wilkie 1993 CSA/Wilkie 1993 No CNI), while in others blood pressure was significantly lower in the CCB arm (Madsen 1998; Van der Schaaf 1995). In studies of ACEi compared to placebo/no treatment, blood pressure was reported in nine studies (392 patients), and was lower in patients randomised to ACEi in some studies (Beckingham 1995; Hernandez 2000; Kim 2002a; Trivedi 2003; Van der Schaaf 1995) but not others (Gronhagen-Riska 1984; Paoletti 2007; Rashtchizadeh 2007; Takahara 2002).

CCB versus placebo/no treatment

Twenty-nine studies (2262 participants) evaluated CCBs versus placebo/no treatment. Twenty-five studies (1951 participants) enrolled kidney transplant recipients irrespective of blood pressure. In 18 (1500 participants) of these studies enrolment was within the first month after transplantation. In the remaining four (311 participants) of the 29 studies, patients were enrolled after the first post transplant month and were hypertensive.

Blood pressure at the end of follow-up was reported in eight studies (590 participants). Significant heterogeneity precluded meta-analysis (Analysis 1.1).

There was no effect of CCB on risk of death at 12 months (Analysis 1.2 (12 studies, 792 patients): RR 0.82, 95% CI 0.37 to 1.82). This result did not change after eliminating the study which showed lower blood pressure (favouring CCB) at the end of follow-up (Madsen 1998) (leaving 11 studies, 693 patients: RR 0.96, 95% CI 0.42 to 2.21).

CCB reduced the risk of graft loss at 12 months (Analysis 1.3 (17 studies 1255 participants): RR 0.75, 95% CI 0.57 to 0.99). There was no difference in this result if the study in which a blood pressure difference at the end of follow-up favouring CCB was eliminated (Rahn 1999 HT/Rahn 1999 NT; leaving 16 studies, 1002 participants: RR 0.76, 95% CI 0.57 to 1.02).

CCB had no effect on the risk of acute rejection, either reported as risk of any episode (as defined by individual study authors; Analysis 1.4 (10 studies, 771 participants): RR 1.02, 95% CI 0.85 to 1.23), or as rejection rates (i.e. number of episodes of any proven or suspected rejection/person/unit time) (Analysis 1.5.1: RR 0.88 95% CI 0.64 to 1.20, P = 0.4). A single study (Chrysostomou 1993, 113 participants) reported rejection by histological subtypes and found lower biopsy proven vascular rejection rates in patients exposed to CCB (Analysis 1.5.3: RR 0.27, 95% CI 0.08 to 0.96). No study with a reported difference in final blood pressure reported rejection outcomes.

Patients treated with CCB had higher estimated or measured GFR (Analysis 1.6 (16 studies, 1119 participants): MD 4.45 mL/min, 95% CI 2.22 to 6.68). Excluding estimated CrCl studies (leaving 11 studies, 533 participants: MD 4.77 mL/min, 95% CI 1.92 to 7.63), or excluding the data from three studies with differences in end of follow-up blood pressure did not alter this summary estimate (Madsen 1998; Rahn 1999 NT; Van der Schaaf 1995, leaving 14 studies, 919 participants, MD 4.29 mL/min, 95% CI 1.18 to 7.40 mL/min).

Serum creatinine was reported in 17 studies (1174 participants). There was significant heterogeneity, accounted for by a study that allowed CCB intervention in the control arm if required (Pirsch 1993). Serum creatinine in the remaining 16 studies (1140 participants) was lower in patients allocated to CCB (Analysis 1.7, MD -10.13 µmol/L, 95% CI -17.32 to -2.93 µmol/L). This result did not alter if the two studies with lower blood pressure in the CCB arm at follow-up were also removed (Van der Schaaf 1995; Rahn 1999 NT; leaving 15 studies, 991 participants: MD -10.01 µmol/L, 95% CI -18.24 to 1.77 µmol/L).

Other outcomes with no difference between groups were HCT (Analysis 1.8: 1 study, 40 participants), withdrawal due to side effects (Analysis 1.9: 2 studies, 156 participants), proteinuria (Analysis 1.10: 2 studies, 90 participants), incidence of myocardial infarction (Analysis 1.11: 1 study, 210 participants) and incidence of hypertension (Analysis 1.12: 4 studies, 241 participants).

Additional time points for reporting outcomes are contained in Analyses 1.13 to 1.21. The most important outcomes for this comparison are contained in Summary of findings for the main comparison.

ACEi versus placebo/no treatment

There were 10 studies assessing this comparison (445 participants). Studies enrolled participants with erythrocytosis (3 studies, 53 participants), hypertension (2 studies, 77 participants), left ventricular hypertrophy (LVH) (2 studies, 131 participants), hypertension and LVH (1 study, 52 participants), CAN (1 study, 65 participants) and transplant recipients without other criteria in two studies (67 participants). In one study, selection criteria were unclear (Takahara 2002).

Blood pressure (either SBP or MAP) was reported in nine studies (392 participants). Although in all studies patients were allowed to be treated if they developed hypertension in either arm, there was significant heterogeneity, with blood pressure lower in patients randomised to ACEi in some studies but not in others (Analysis 2.1). There was no apparent association with baseline blood pressure or allowable cointerventions.

Patient death was reported in only one study (30 participants) with a single death in both arms (Analysis 2.2, RR 1.0, 95% CI 0.07 to 14.55).

Graft loss was reported in only two studies (93 participants). Heterogeneity precluded meta-analysis (Analysis 2.3). In one study, performed in patients not receiving CNI, two grafts were lost from each arm at three months follow-up (Gronhagen-Riska 1984). In Kim 2002a 65 patients with CAN were treated for a mean of 23 months and graft losses were significantly fewer in patients treated with ACEi (RR 0.35, 95% CI 0.14 to 0.85).

A single study (19 participants) reported acute rejection risk, there was no difference between ACEi and no treatment (Analysis 2.4, RR 0.90, 95% CI 0.52 to 1.55).

GFR was measured in two studies and estimated by CrCl in a third (77 participants in total). In all studies, mean GFR was lower in ACEi arms, although the results were consistent with no difference in effect on GFR (Analysis 2.5, MD -8.07 mL/min, 95% CI -18.57 to 2.43).

Seven studies (282 participants) reported SCr. There was significant heterogeneity, accounted for by the study undertaken in patients with CAN (Kim 2002a). In this study, SCr was significantly lower

in patients treated with enalapril (Analysis 2.6: MD -100 µmol/L, 95% CI -112 to -88). In the remaining six studies (236 participants), SCr was no different with ACEi treatment (Analysis 2.6, MD 7.55 µmol/L, 95% CI -2.10 to 17.20). This finding was not affected if the two studies with significantly lower blood pressures in the ACEi arms were removed (Van der Schaaf 1995; Hernandez 2000; leaving 4 studies, 144 participants: MD 7.50 µmol/L, 95% CI -9.74 to 24.74). In no study was presence of proteinuria a selection criterion. Proteinuria was reported in three studies (175 participants), and showed no difference with ACEi treatment (Analysis 2.7, MD -0.08 g/24 h, 95% CI -0.23 to 0.06). This finding was similar in the two studies with lower blood pressure in the ACEi arm.

For the effects of ACEi on HCT (Analysis 2.8, 5 studies, 103 participants) and Hb (Analysis 2.9, 5 studies, 191 participants) there was significant heterogeneity, related to patient selection and intervention dose. In studies of treatment of erythrocytosis, compared to no treatment or placebo, ACEi reduced HCT (3 studies, 53 participants) by MD -7.29% (95% CI -10.34 to -4.24). The effect was smaller in the study that used enalapril 2.5 mg as the intervention (Beckingham 1995), and greatest in one that used fosinopril 10-20 mg (Trivedi 2003). The effect was not seen in studies in patients without erythrocytosis (two studies, 50 participants: MD -1.29%, 95% CI -2.93 to 0.35). Similar effects were seen in studies reporting the effect on Hb concentration.

Serum potassium was higher in patients randomised to ACEi, by between 0.2 and 0.7 mmol/L (3 studies, 59 participants). Significant heterogeneity precluded obtaining summary estimates of effect (Analysis 2.10).

No study reported cardiovascular outcomes.

Additional time points for reported outcomes across all studies can be found in Analyses 2.11 to 2.19. The most important outcomes for this comparison are contained in Summary of findings 2.

ACEi versus CCB

ACEi and CCB were compared head to head in seven studies (405 participants). All studies selected hypertensive kidney transplant recipients for enrolment, and in one study patients also had to have dipstick detectable proteinuria (Halimi 2007). One study enrolled patients within the first month after transplantation (Midtvedt 2001), the remainder were at least five months after transplant.

Blood pressure at the end of follow-up was reported in six studies (275 participants). There was no difference in blood pressure at the end of follow-up (Analysis 3.1: MD 0.58 mm Hg, 95% CI -2.02 to 3.18).

Death was reported in two studies (221 participants) with no difference in risk (Analysis 3.2: RR 4.03, 95% CI 0.45 to 35.82). Graft loss was only reported in one study (157 participants) with no difference in risk (Analysis 3.3: RR 7.37, 95% CI 0.39 to 140.35).

GFR was assessed in six studies, by measured GFR in four (208 participants) and CrCl in two (88 participants). Patients receiving ACEi had lower GFR (Analysis 3.4: MD -11.48 mL/min, 95% CI -15.75 to -7.21).This difference was consistent across all studies, including the study of transplant recipients with proteinuria on dipstick (Halimi 2007).

SCr was higher in patients randomised to ACEi (Analysis 3.5: MD 12.88 µmol/L, 95% CI 8.14 to 17.62).

Acute rejection was reported in three studies, with inconsistent results which may be due to study era or selection criteria. In one 2007 study which enrolled 67 patients at least 12 months post-transplant, no patient in either arm had an episode of acute rejection (Halimi 2007). In a 2001 study that enrolled patients within the first three weeks after transplantation (Midtvedt 2001), 85/154 patients had at least one episode of acute rejection and risk of rejection was higher in patients on ACEi (Analysis 3.6, RR 1.54, 95% CI 1.14 to 2.07). In one study of 102 patients, the rate of rejection episodes was not increased in patients receiving ACEi (Analysis 3.7: RR 0.92, 95% CI 0.65 to 1.31).

Cardiovascular disease outcomes after 12 months were reported in one study (123 participants). No patient suffered myocardial infarction (Analysis 3.8). Three patients on ACEi and one on CCB developed new onset angina pectoris, consistent with no difference in risk (Analysis 3.9, RR 3.83, 95% CI 0.41 to 35.83). Ankle oedema was also consistent with no difference in risk (Analysis 3.10: RR 0.25, 95% CI 0.01 to 5.19).

ACEi, compared to CCB, increased serum potassium (Analysis 3.11 (4 studies, 189 participants): MD 0.27 mmol/L, 95% CI 0.14 to 0.41) and risk of hyperkalaemia (Analysis 3.12 (3 studies, 211 participants): RR 3.74, 95% CI 1.89 to 7.43). ACEi reduced proteinuria (Analysis 3.13 (2 studies, 142 participants): MD -0.28 g/d, 95% CI -0.47 to -0.10) and Hb (Analysis 3.14 (5 studies, 332 participants): MD -12.96 g/L, 95% CI -15.72 to -10.21). HCT outcomes exhibited significant heterogeneity. This was accounted for by one crossover study of one month duration, which showed no difference between ACEi and CCB (Van der Schaaf 1995). In the remaining three longer studies (all more than six months, 153 participants), HCT was lower in ACEi recipients (Analysis 3.15, MD -4.33%, 95% CI -5.45 to -3.20).

The most important outcomes for this comparison are contained in Summary of findings 3.

ARB versus CCB

Five studies compared ARB to CCB (216 participants). No study reported death, graft loss or cardiovascular disease outcomes. There were no significant differences in any of the following outcomes: MAP achieved with treatment (Analysis 4.1 (3 studies, 149 participants): MD -1.98 mm Hg, 95% CI -9.37 to 5.41), GFR (Analysis 4.2 (1 study, 148 participants): MD -10.0 mL/min/1.73 m^2, 95% CI -31.2 to 11.2), SCr (Analysis 4.3 (4 studies 193 participants): MD -2.36 µmol/L, 95% CI -18.16 to 13.43), hyperkalaemia (Analysis 4.4 (1 study, 56 participants): RR 5.6, 95% CI 0.7 to 43), rejection rates (Analysis 4.5 (1 study, 102 participants): RR 0.92, 95% CI 0.65 to 1.31), Hb (Analysis 4.6 (2 studies 129 participants): MD -8.51 g/L, 95% CI -23.08 to 6.06), proteinuria (Analysis 4.7 (2 studies, 136 participants): MD -0.20 g/24 h, 95% CI -0.55 to 0.15). Serum potassium was higher in patients allocated to ARB (Analysis 4.8 (3 studies, 163 participants): MD 0.31 mmol/L, 95% CI 0.06 to 0.56). Additional time points for reported outcomes may be found in Analysis 4.9 and Analysis 4.10.

ACEi versus ARB

ACEi were compared to ARB in six studies (230 participants). Death, graft loss, GFR and cardiovascular disease outcomes were not reported in any study in this comparison. There was no significant difference in any of the following outcomes: BP (Analysis 5.1 (5 studies, 201 participants): MD -1.82 mm Hg, 95% CI -4.67 to 1.04), rejection rates (Analysis 5.2 (1 study, 108 participants): RR 1.00, 95%

CI 0.71 to 1.41), SCr (Analysis 5.3 (4 studies, 187 participants): MD -2.21 µmol/L, 95% CI -8.94 to 4.51), serum potassium (Analysis 5.4 (4 studies, 187 participants): MD 0.07 mmol/L, 95% CI -0.03 to 0.18), risk of hyperkalaemia (Analysis 5.5 (1 study, 37 participants): RR 0.96 95% CI 0.10 to 9.57), proteinuria (Analysis 5.6 (2 studies, 130 participants): MD 0.04 g/24 h, 95% CI -0.06 to 0.14) or probability of remission of proteinuria (Analysis 5.7 (1 study, 37 participants): RR 1.32 95% CI 0.53 to 3.29).

HCT was lower in patients allocated to ACEi compared to ARB, including the two studies which enrolled recipients with erythrocytosis (Analysis 5.8: MD -1.14%, 95% CI -1.89 to -0.39). Hb was reported in three studies (165 participants), and in only 1/2 studies enrolling recipients with erythrocytosis. Patients receiving ACEi had lower Hb although the difference could have been due to chance (Analysis 5.9: MD -4.62 g/L, 95% CI -10.02 to 0.78).

Additional time points for reported outcomes may be found in Analyses 5.10 to 5.13.

ARB versus placebo/no treatment

Four studies (185 participants) compared ARB to placebo/no treatment. Two studies were in transplant recipients without further restrictions, and two in hypertensive recipients. Three studies used losartan 25-100 mg and one used valsartan 80 mg (Andres 2006).

Blood pressure was no different at the end of follow-up except in Andres 2006 where blood pressure was significantly lower in the patients randomised to receive valsartan (Analysis 6.1). This study enrolled hypertensive recipients and allowed diuretics in either arm if blood pressure was uncontrolled.

One study reported death and graft loss (Weidanz 2005) – there were no deaths or graft losses in either arm at 12 months.

There was no difference in estimated GFR (Analysis 6.4 (2 studies, 49 participants): MD 0.65 mL/min, 95% CI -5.58 to 6.89) or SCr, (Analysis 6.5 (3 studies, 170 participants): MD 7.77 µmol/L, 95% CI -3.01 to 18.54). ARB lowered Hb significantly in the study using valsartan (Andres 2006) but not in the other two studies - heterogeneity precluded meta-analysis (Analysis 6.6). HCT was only reported in one study and was no different between arms (Analysis 6.7). Serum potassium was reported in three studies, and was higher in each case in patients allocated to ARB. Mean differences in individual studies ranged from 0.1 to 0.6 mmol/L, but heterogeneity precluded meta-analysis (Analysis 6.8).

Additional time points for reported outcomes may be found in Analyses 6.10 to 6.15.

Other agents and combinations

Other intervention combinations were considered in small numbers of studies. Generally, differences in effects were not apparent. Important differences in effect are not excluded, due to small numbers of participants.

ACEi were also compared to beta-blockers (1 study, 96 participants, Analysis 7.1 to Analysis 7.8), alpha-blockers (1 study, 42 participants, Analysis 8.1 to Analysis 8.8). There were no significant differences in reported outcomes.

CCB compared to beta-blockers was associated with higher measured GFR (Analysis 9.1 (1 study, 48 participants): MD 16.50 mL/min, 95% CI 3.21 to 29.79). SBP was significantly lower in CCB patients in this single study (Analysis 9.2: MD -16.9 mm Hg, 95% CI -25.46 to -8.34). There was no difference in adverse events (Analysis 9.3: RR 0.92, 95% CI 0.54 to 1.59). No other outcomes were reported.

A small, three arm crossover study comparing ARB, beta-blockers and placebo (14 participants) provided data for the comparison of beta-blocker and placebo (Analysis 10.1 to Analysis 10.9) and ARB versus beta-blocker (Analysis 11.1 to Analysis 11.8). There were no significant differences in any reported outcome.

A single study assessed the affects of alpha-blocker to placebo (93 participants) and found no difference in any outcome including: SBP (Analysis 12.1: MD 1.0 mm Hg, 95% CI -11.38 to 13.38), death (Analysis 12.2: RR 1.98, 95% CI 0.06 to 15.19), graft loss (Analysis 12.3: RR 0.98, 95% CI 0.26 to 3.68) or rejection rates (Analysis 12.4: RR 0.89, 95% CI 0.43 to 1.81).

Two studies provided information on the relative effects of combination treatment to single agents and no treatment. The first compared ACEi, CCB and ACEi/CCB combination.

ACEi/CCB was compared to ACEi alone (1 study, 65 participants). DBP (Analysis 13.2: MD -6.00 mm Hg, 95% CI -10.00 to -2.00) and MAP (Analysis 13.3: MD -6.0 mm Hg, 95% CI -11.23 to -0.77), but not SBP (Analysis 13.1: MD -5.00 mm Hg, 95% CI -13.10 to 3.10) were lower on combination treatment. ACEi/CCB compared to ACEi alone had no apparent effect on participant death (Analysis 13.4: RR 1.03, 95% CI 0.07 to 15.79), acute rejection (Analysis 13.5: no events in either arm), GFR (Analysis 13.6: MD 7.00 mL/min, 95% CI -4.80 to 18.80), Hb (Analysis 13.8: MD 4.00 g/L, 95% CI -1.27 to 9.27), HCT (Analysis 13.9 MD 1.10%, 95% CI -0.62 to 2.82), serum potassium (Analysis 13.10: MD -0.20 mmol/L, 95% CI -0.39 to -0.01) or risk of hyperkalaemia (Analysis 13.11: RR 0.69, 95% CI 0.12 to 3.85). Combination ACEi/CCB compared to ACEi was associated with lower SCr (Analysis 13.7: MD -6.00 µmol/L, 95% CI -11.84 to -0.16).

ACEi/CCB combination compared to CCB alone had no significant effect on SBP (Analysis 14.1: MD -4.00 mm Hg, 95% CI -11.50 to 3.50) or death (Analysis 14.2: RR 3.18, 95% CI 0.13 to 75.38). There were no episodes of acute rejection in either arm. Graft function was worse in patients receiving ACEi/CCB compared to CCB, as indicated by CrCl (Analysis 14.4: MD -16.00 mL/min, 95% CI -28.51 to -3.49) and SCr (Analysis 14.5: MD 800 µmol/L, 95% CI 1.97 to 14.03). There were two episodes of hyperkalaemia in the combination arm and none in the CCB alone arm (Analysis 14.7: RR 5.30, 95% CI 0.26 to 106.40). Combination therapy also lead to lower Hb (Analysis 14.8: MD -10 g/L, 95% -15.08 to -4.92) and HCT (Analysis 14.9: MD -3.00%, 95% CI -4.65 to -1.35).

Data was also available from a single four arm study (ACEi versus ARB versus ACEi/ARB versus no treatment).

ACEi/ARB compared to ACEi (25 participants), reduced Hb (Analysis 15.2: MD -8.10 g/L, 95% CI -15.69 to -0.51), increased serum potassium (Analysis 15.4: MD 0.22 mmol/L, 95% CI -0.03 to 0.47) but had no effect on MAP (Analysis 15.5: MD 0.40 mm Hg, 95% CI -11.19 to 11.99), HCT (Analysis 15.1: MD -1.10%, 95% CI -3.22 to 1.02) or SCr (Analysis 15.3: MD -1.00 µmol/L, 95% CI -14.13 to 12.13).

ACEi/ARB combination compared ARB (31 participants) alone to no treatment MAP (Analysis 16.5: MD -6.30 mm Hg, 95% CI -17.64 to 5.04), HCT (Analysis 16.1: MD -1.30%, 95% CI -3.19 to 0.59), HB (Analysis 16.2: MD -8.80 g/L, 95% CI -14.96 to -2.64), SCr (Analysis 16.3: MD -2.0 µmol/L, -13.22 to 9.22), serum potassium (Analysis 16.4: MD 0.29 mmol/L, 95% CI 0.07 to 0.51).

ACEi/ARB combination compared to placebo (31 participants) had no effect on MAP (Analysis 17.1: MD -3.00 mm Hg, 95% CI -14.82 to 8.82) but increased SCr (Analysis 17.2: MD 14.00 µmol/L, 95% CI 2.97 to 25.03) and serum potassium (Analysis 17.5: MD 0.90 mmol/L, 95% CI 0.68 to 1.12) and lowered Hb (Analysis 17.3: MD -10.00 g/L, 95% CI -16.11 to -3.89) and HCT (Analysis 17.4: MD -2.50%, 95% CI -4.30 to -0.70).

Stratified analyses and meta-regression

Heterogeneity in treatment effect was investigated in CCB versus placebo or no treatment studies, using stratified analyses and random effects meta-regression. One study that allowed CCB in the placebo arm if required is excluded from this analysis (Pirsch 1993) because in the earlier meta-analysis it was responsible for heterogeneity of effect. Other comparisons either had insufficient studies or insufficient variability in effect on the outcome of interest to allow informative stratified analyses or meta-regression. Six outcomes were reported sufficiently frequently across CCB versus placebo/no treatment studies to be investigated – death, graft loss (death censored), acute rejection (proportion with at least one episode of rejection), GFR, SCr, and blood pressure.

Prespecified confounders largely did not alter the effect of CCB relative to placebo or no treatment, with the exception of CCB subtype on SCr outcomes and follow-up time on graft loss (Table 2 - *Calcium channel blocker (CCB) versus placebo/no treatment: meta-regression of potential confounding factors*). Compared to non-dihydropyridine CCB (DHPCCB) studies (n = 7), studies using DHPCCB (such as amlodipine, n = 12) resulted in increasingly favourable SCr in the treated arms (MD -13.1 µmol/L, 95% CI -24.3 to -2.0). There was a commensurate, but not statistically significant, relative beneficial association between GFR and CCB subtype favouring DHPCCB (4.4 mL/min, 95% CI -1.3 to 10.1, P = 0.13). Graft loss was reduced by CCB across all studies, but the effect was more marked in studies that followed patients for at least 12 months (RR compared to studies < 12 months 0.2, 95% CI 0.09 to 0.7, P = 0.006).

DISCUSSION

Summary of main results

Data from 17 studies involving 1255 kidney transplant recipients suggest that the routine administration of CCB reduces the risk of graft loss by about 25%, and improves GFR and SCr (surrogate outcomes for graft survival). These findings suggest that CCB should be the first line treatment for hypertensive kidney transplant recipients, although there are limited data on side effects and cardiovascular outcomes. This is contrary to published guidelines which do not select any class for first-line status for the treatment of kidney recipients (K/DOQI 2004). As improvements in outcomes were seen irrespective of the presence of hypertension, and because hypertension is extremely common after transplantation (Kasiske 1996; Kasiske 2000), CCB may be indicated for all patients from the time of transplantation.

CCB have been evaluated in more participants and in more studies than other agents and were significantly superior to placebo and ACEi for most outcomes. In head to head studies, CCB significantly improved GFR compared to ACEi by about 12 mL/min. While reduction in GFR may be observed acutely following introduction of ACEi, reduced GFR in ACEi compared to CCB was observed in all six studies, including three which measured GFR at least six months after treatment initiation. Effects on outcomes were inconclusive due to sparse data, but the point estimates favoured CCB (for example, less graft loss). In studies comparing CCB to placebo or no treatment, in addition to a significant reduction in risk of graft loss, CCB improved graft function. Beneficial effects of CCB were not accounted for by differences in blood pressure. The effects of CCB were consistent across studies with different enrolment characteristics, treatment doses, and allowable additional interventions.

We used meta-regression to explore potential differences in outcomes by enrolment and intervention characteristics in studies of CCB versus placebo/no treatment. The beneficial effects of CCB on graft loss did not vary by indication for therapy (patients selected for enrolment with any blood pressure versus hypertensive patients), suggesting that these medications could benefit patients irrespective of baseline hypertension. Reduction in graft loss was more apparent in studies with longer follow-up. There was heterogeneity in SCr outcomes which was explained by choice of CCB. Non-dihydropyridine CCB (e.g. verapamil, diltiazem) cause important impairment in CYP3A4 and p-glycoprotein, necessitating dose reductions of calcineurin inhibitors (CNI) (Page 2005). Dihydropyridine CCB cause less impact on CNI metabolism and generally do not lead to dose reduction (Ciclosporin DRUGDEX(R) Evaluation; Tacrolimus DRUGDEX(R) Evaluation). Dihydropyridine CCB studies reported greater differences in SCr, favouring CCB. There was a commensurate effect seen on GFR outcomes, although this did not reach statistical significance. These findings suggest that dihydropyridine CCB, which may be simpler to administer to patients receiving CNI because of lack of interaction, might be favoured over non-dihydropyridine CCB.

ACEi (and ARB) are recommended for use preferentially in non-transplant patients with diabetic kidney disease and in other patients with chronic kidney disease and proteinuria, based on evidence that they slow decline in GFR and progression to ESKD (K/DOQI 2004; Taal 2007). However, as these additional benefits are not shown to extend to transplant recipients based on currently available RCTs, ACEi should not be preferred to CCB in this patient population. Outcomes are generally less favourable than with CCB (both in the indirect comparison with placebo or no treatment as the common comparator, and in the direct comparison) and there are considerably less data for ACEi used in transplant patients. Compared to CCB, ACEi reduced GFR. While poorer graft function is associated with an increased risk of graft loss in registry based observational studies (Hariharan 2002; Lenihan 2008), it is uncertain whether ACEi induced reduction in GFR leads to increased graft loss. In the only head to head comparison of ACEi versus CCB study in which graft loss was reported, three patients in the ACEi arm lost their grafts compared to no patient in the CCB arm (P= 0.18) (Midtvedt 2001). Hyperkalaemia was more common in patients randomised to receive ACEi compared to CCB (RR 3.7). In studies of ACEi compared to placebo or no treatment, ACEi reduced GFR in two small studies (MD -5.4 mL/min). Graft loss outcomes were heterogeneous. In a single study undertaken in 65 patients

with CAN, enalapril compared to placebo reduced graft loss (RR 0.35). In the only other study, 28 kidney recipients treated from the time of transplant for three months, there was no effect on graft loss (RR 1.0). ACEi use was also associated with reduction in Hb, compared to CCB or placebo or no treatment. While this may be a therapeutic goal of therapy in some post-transplant patients with erythrocytosis, this effect was also observed in studies where hypertensive and unselected patients were enrolled. Anaemia is associated with increased risk of poor outcomes including rejection and graft loss in cohort studies (Chhabra 2008).

There may still be a role for ACEi in kidney transplant recipients. Beneficial effects may not have been seen in this review due to a lack of reported data, leading to inability to detect clinically relevant benefits, particularly in subgroups of transplant patients (for example, recipients with proteinuria). In our review, proteinuria was reduced by ACEi relative to CCB by 0.28 g/24 h (although not significantly in the few studies comparing ACEi to placebo or no treatment and reporting this outcome). In the non-transplant setting, proteinuria reduction of approximately 0.3 g/24 h was associated with reduced risk of ESKD in a patient-level data meta-analysis of ACEi in patients with proteinuria, although the beneficial effect was restricted to patients with proteinuria at least 0.5 g/24 h (Jafar 2001). Reduction of proteinuria as a therapeutic goal is not necessarily associated with improved kidney outcomes in all settings. For example, although combination ACE/ARB therapy reduces proteinuria over either treatment alone (Kunz 2008; Mann 2008), combination therapy increased adverse kidney outcomes in patients with atherosclerosis or diabetes with end-organ damage compared to either agent alone (Mann 2008).Whether ACEi cause net benefit or harm to proteinuric kidney transplant patients is unresolved, although a study in progress in proteinuric transplants with reduced GFR will address this group (Knoll 2008). Whether ACEi are beneficial overall for an individual patient may be a balance of competing harms (e.g. increased risk of anaemia, hyperkalaemia, reduction in GFR) and benefits (e.g. reduction in proteinuria, treatment of LVH) (Cruzado 2008). Observational registry based data suggest that there is no associated patient or graft survival benefit associated with ACEi or ARB prescription in kidney transplant recipients (Opelz 2006).

Potential biases in the review process

There are potential caveats that may affect the validity of these findings. Firstly, the quality of available studies is moderate only, with many included studies judged to have a risk of bias on at least some domains assessed. Despite this, there was limited heterogeneity in outcomes, suggesting that no important bias was present. Secondly, publication bias can not be excluded (i.e. bias caused by lack of publication of studies with neutral or negative effects), although funnel plots do not suggest significant publication bias is present (Figure 5; Figure 6; Figure 7; Figure 8; Figure 9; Figure 10; Figure 11).Thirdly, highly relevant clinical outcomes were not reported in the majority of studies (e.g. patient death, cardiovascular disease events). We cannot be sure that outcomes in these studies were the same as in the studies which did report, or that differences in patient death or cardiovascular outcomes favouring other agents and outweighing the demonstrated graft survival and GFR benefit of CCB do not exist. Finally, few patients enrolled were receiving TAC as immunosuppression. If there are differences in effects of antihypertensive agents in patients receiving TAC then these findings may not apply.

Figure 5. Funnel plot of comparison: 1 CCB versus placebo/no treatment, outcome: 1.2 Death at last follow-up.

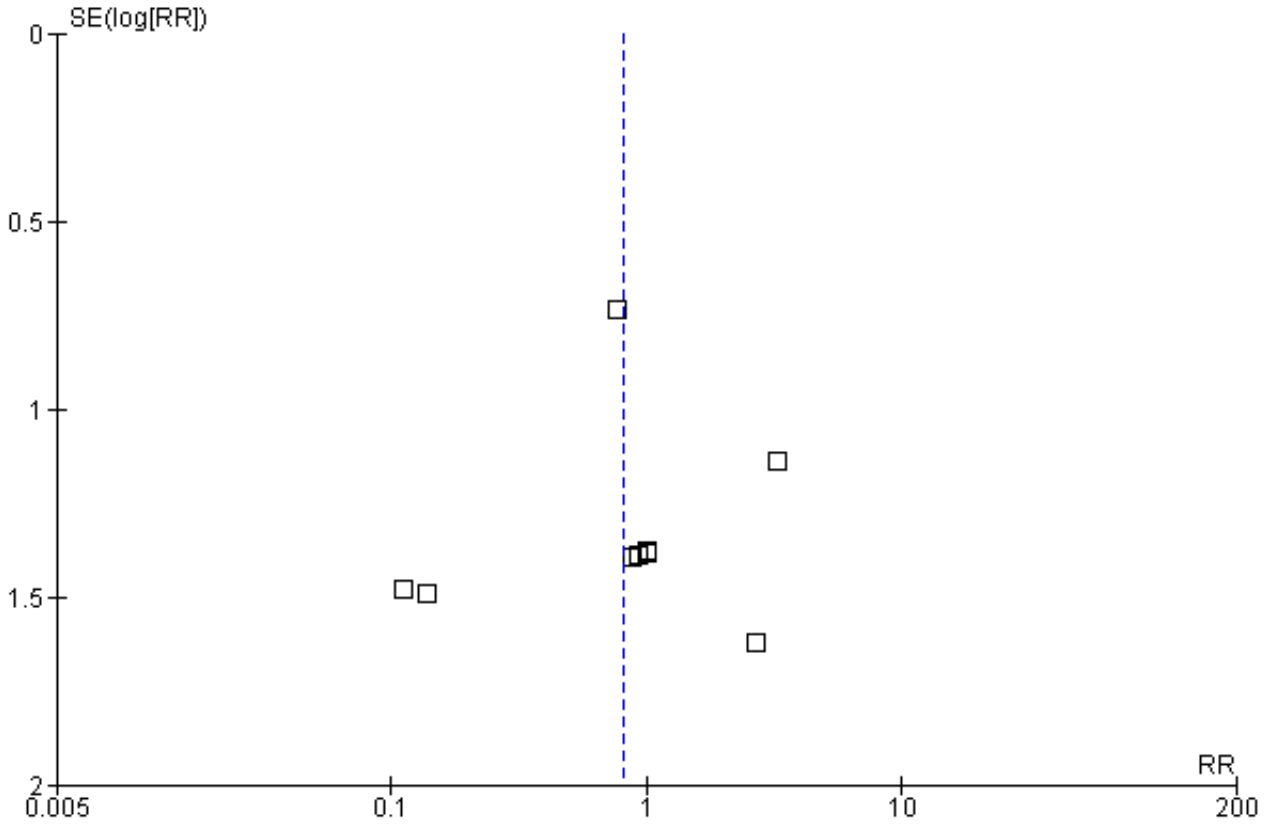


Figure 6. Funnel plot of comparison: 1 CCB versus placebo/no treatment, outcome: 1.3 Graft loss at last follow-up

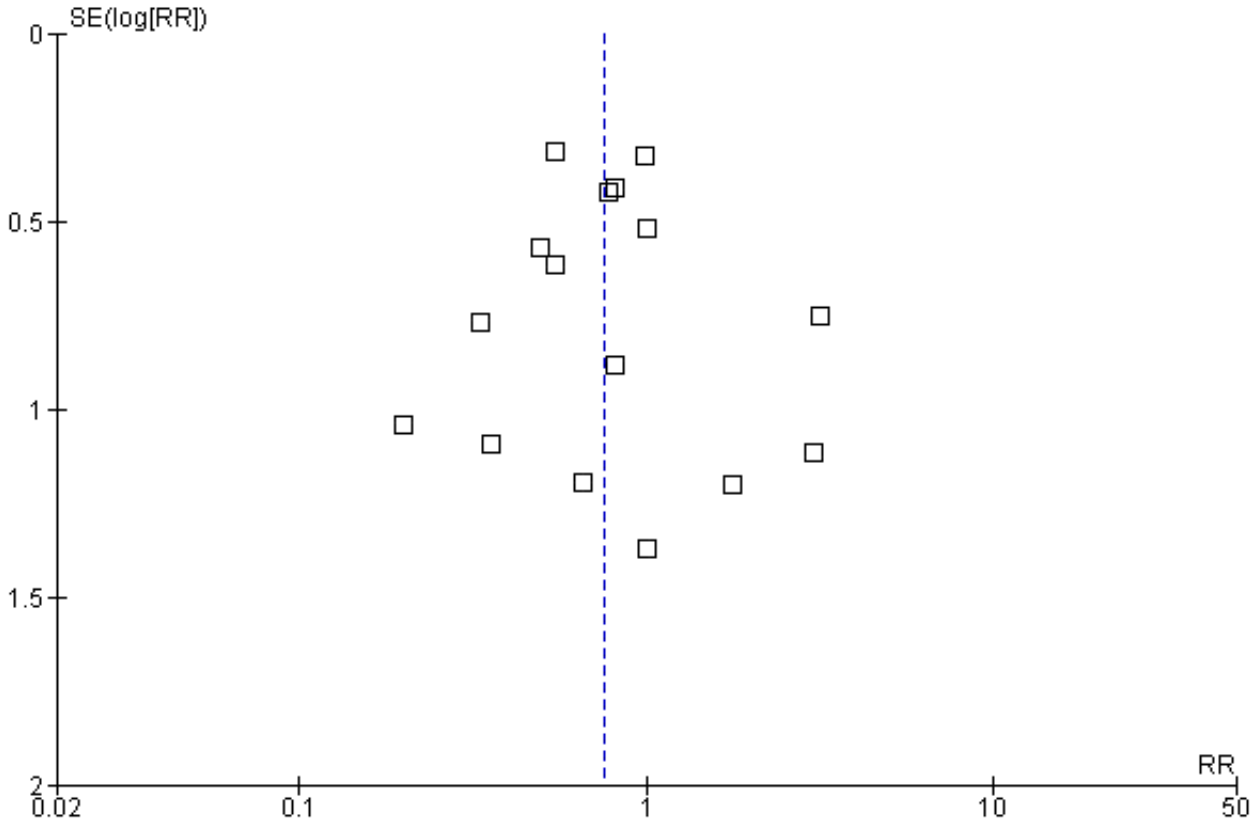


Figure 7. Funnel plot of comparison: 1 CCB versus placebo/no treatment, outcome: 1.6 Any GFR measure at last follow-up.

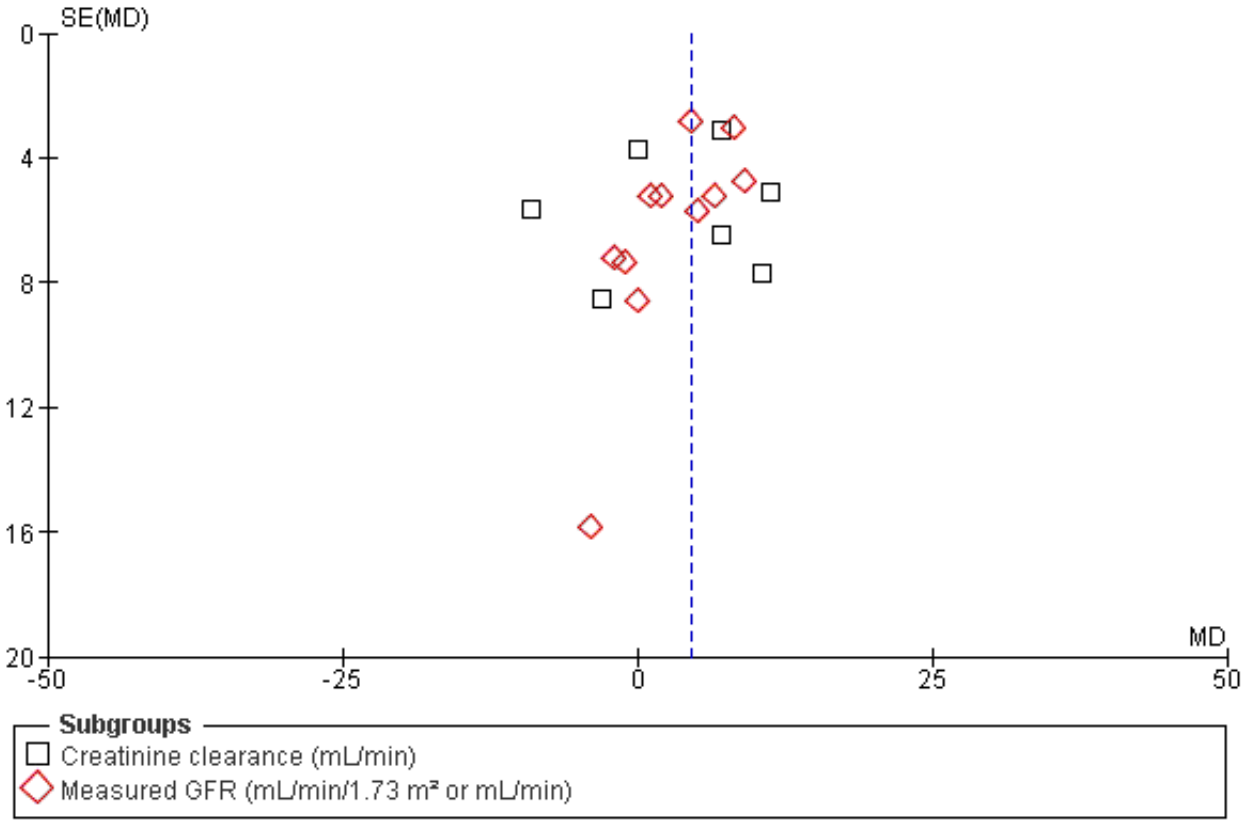


Figure 8. Funnel plot of comparison: 1 CCB versus placebo/no treatment, outcome: 1.7 Serum creatinine (mmol/L) at last follow-up

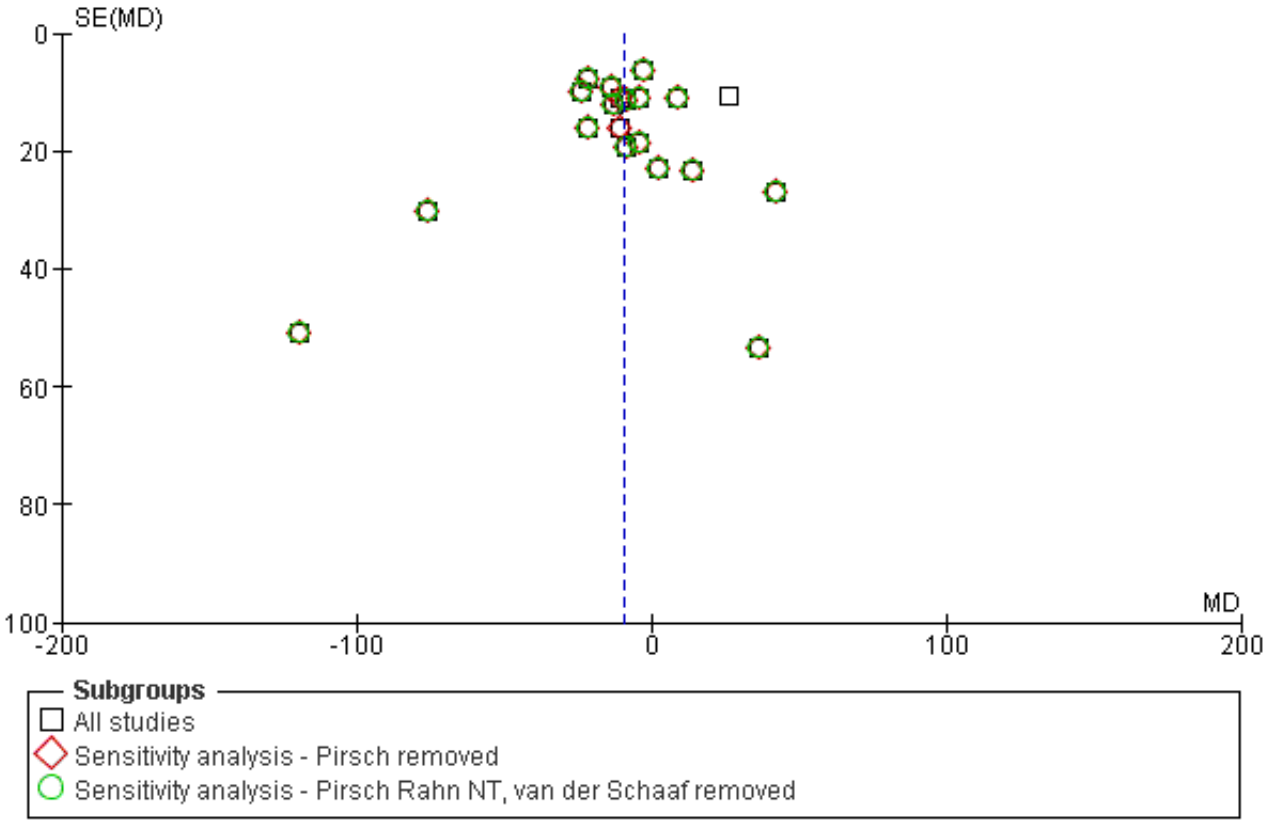


Figure 9. Funnel plot of comparison: 3 ACEi versus CCB, outcome: 3.1 Any blood pressure measure (mm Hg) at last follow-up.

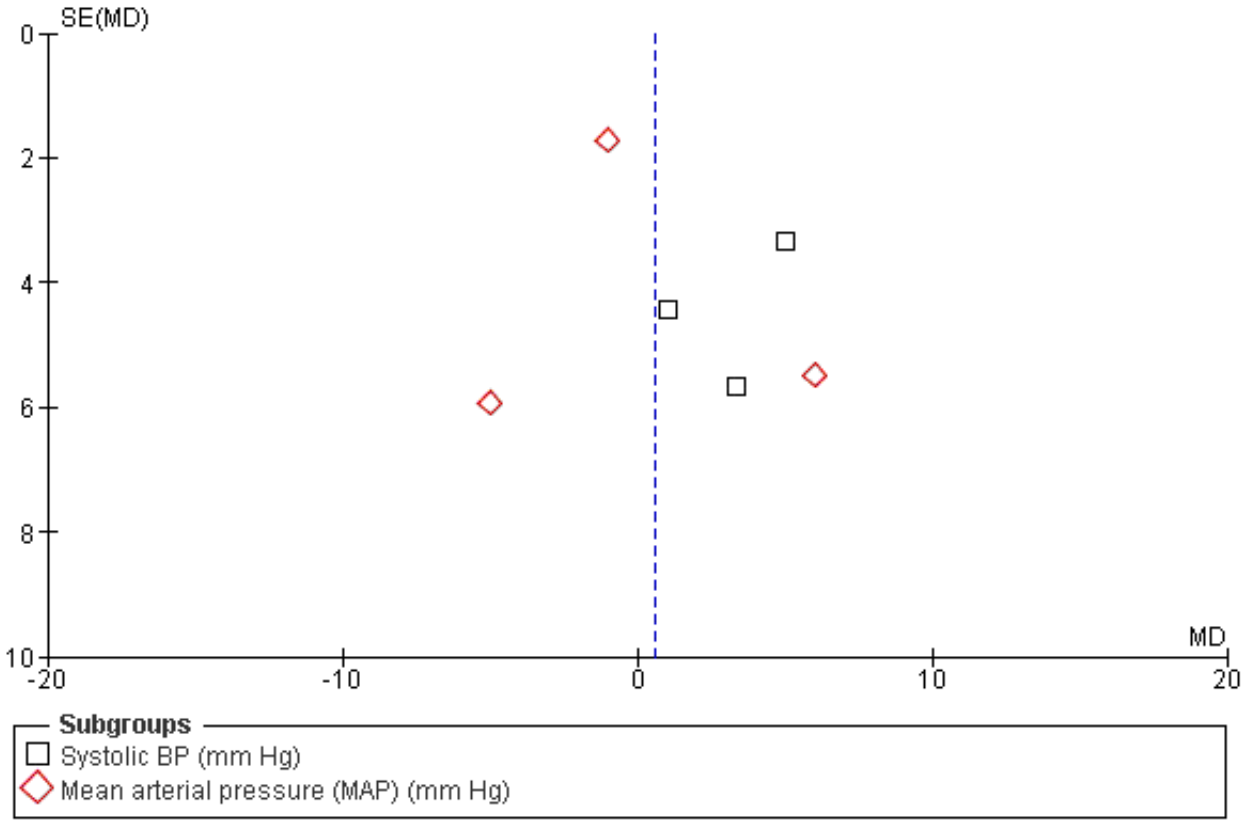


Figure 10. Funnel plot of comparison: 3 ACEi versus CCB, outcome: 3.4 Any GFR measure (mL/min or mL/min/1.73 m²) at last follow-up.

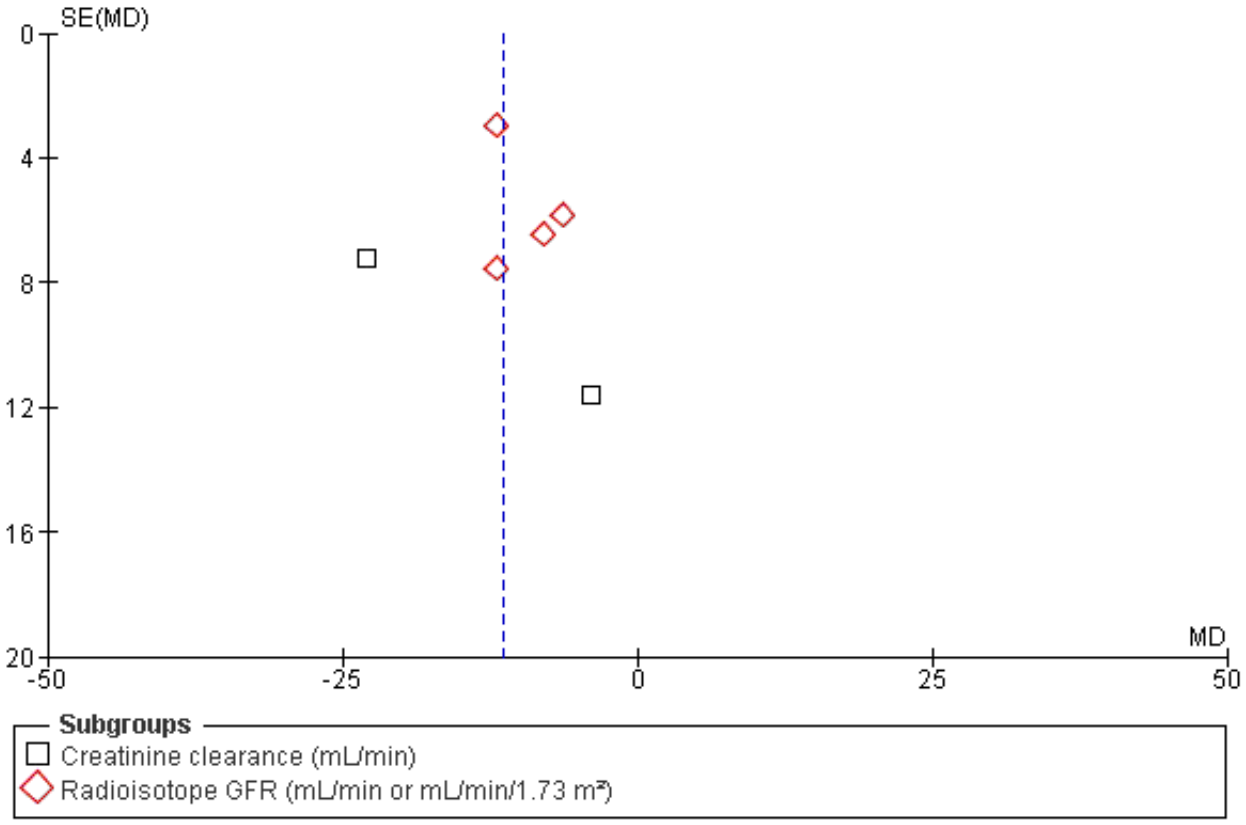
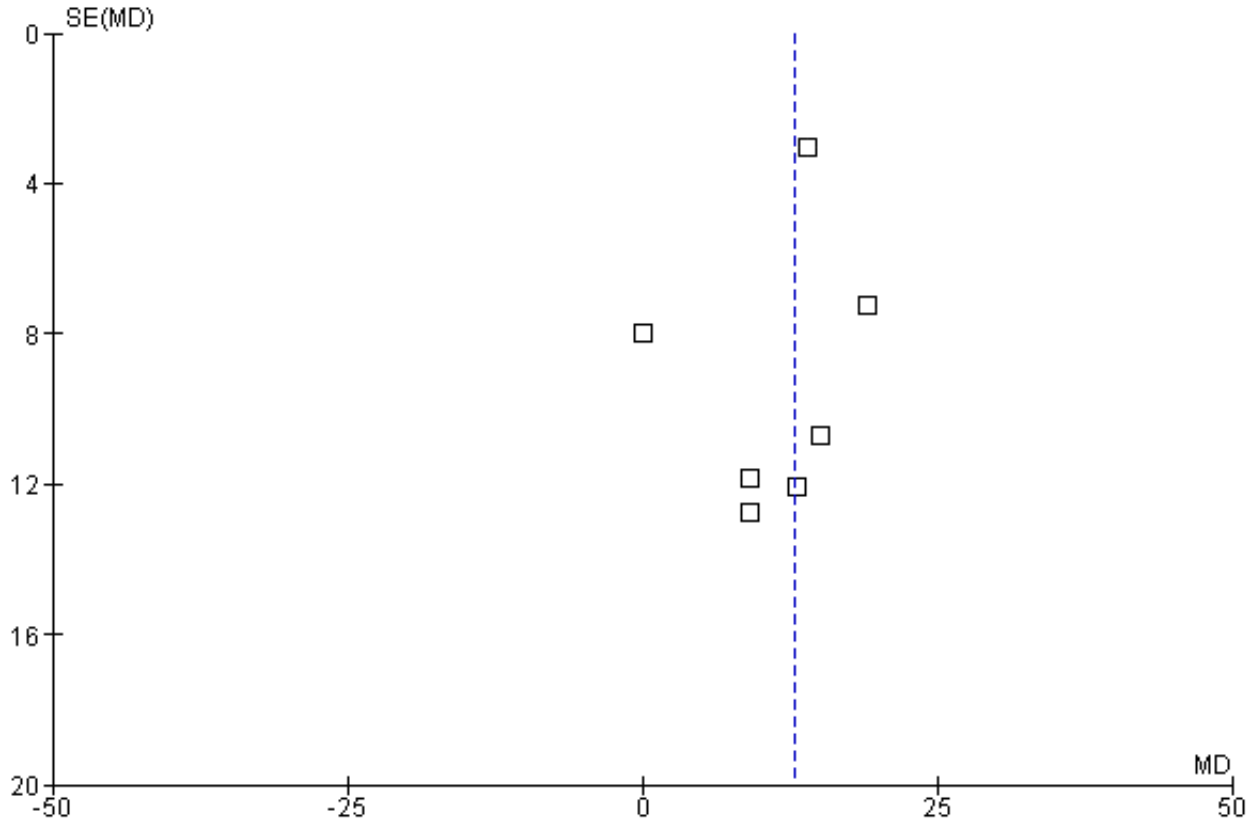


Figure 11. Funnel plot of comparison: 3 ACEi versus CCB, outcome: 3.5 Serum creatinine (µmol/L) at last follow-up.



Agreements and disagreements with other studies or reviews

An earlier systematic review and meta-analysis assessed the effects of ACEi or ARB in kidney transplant recipients (Hiremath 2007), and concluded that ACEi or ARB lead to clinically important reductions proteinuria, HCT and GFR, consistent with our work . We have shown that at least some of this detrimental effect of ACEi on GFR is likely to be due to the beneficial effect of the CCB, which were the comparator agent in approximately half of the included studies in that review (Hiremath 2007).

AUTHORS' CONCLUSIONS

Implications for practice

Currently available data suggest that CCB should be first line antihypertensive agents in kidney transplant patients, because they improve graft function and reduce graft loss. On the basis of the findings from this review, treating 100 patients with average risk of graft loss over the first year (˜10%) with CCB, compared to no treatment, would prevent three patients from losing their grafts over this period. This effect does not appear to be modified by the presence of hypertension or confined to any identifiable subgroup of patients, suggesting that these drugs should be considered for all patients after kidney transplantation. ACEi have detrimental effects on clinically relevant transplant outcomes such as graft function, and have fewer studies investigating their effects in kidney recipients. They should be reserved for situations where any potential advantage to the patient for the treatment of other conditions outweighs demonstrated detrimental effects. Other agents have limited data in kidney transplant patients.

Implications for research

Few studies reported cardiovascular disease outcomes. This is particularly important, given evidence from observational studies suggesting that the use of dihydropyridine CCB (but not non-dihydropyridine CCB) are associated with an increased risk of cardiovascular disease events in the first year after transplantation (Kasiske 2000). Additional studies of CCB reporting cardiovascular outcomes are needed or meta-analysis of existing study data if cardiovascular outcomes were collected but not yet reported. Studies of kidney transplant recipients with specific indications for other therapies (e.g. diabetic recipients, recipients with proteinuria) are needed to establish whether specific benefits of these agents apply to kidney transplant recipients with these conditions.

Available studies were also of short duration (median six months). This is important as it is possible that relative beneficial effects of CCB over other agents may not persist in the medium to long term. For example, in non-transplant patients, ACEi are recognised to cause reduction in GFR in the short term (weeks) after initiation, yet are recommended over other agents because ACEi reduce risk of long-term adverse renal events (K/DOQI 2004). To clarify remaining uncertainty in the transplant population, longer term outcomes where collected but not yet published, or meta-analysis of individual patient data would be informative, followed by additional studies if required.

ACKNOWLEDGEMENTS

This review has been co-published with *Transplantation* July 2009 (Cross 2009)

The authors would like thank the authors of individual studies who very kindly responded to requests for further information about their studies, including Dr Amir Ghorbanihaghjo and Professor Bryan Becker. We also acknowledge the work of Prof Teut Risler, Dr Friederike Bachmann and Dr Norbert Braun who developed the initial protocol for this review, and Dr Angie Morrow, who provided translated papers published in Spanish.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Alcaraz 1991

Methods	• Unblinded • Parallel study • No placebo • ITT Unclear • Compliance not assessed

Alcaraz 1991 *(Continued)*

	• Good group similarity
Participants	• Cadaveric transplant • Mean age: 45.2 years • Sex M/F: 33/20 • Enrolled: At time of transplant • Immunosuppression: All CSA
Interventions	**Treatment group 1** • Diltiazem IV + 60 mg orally twice daily **Treatment group 2** • IV dopamine
Outcomes	• Graft survival (1 year) • Acute rejection-free (6 months) • SCr (30 days) • SCr (60 days)
Notes	• 2 SPK recipients included • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"A prospective randomised study was made" Unclear randomisation method
Allocation concealment?	Unclear risk	Not described
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, depending on how assessed rejection proportion could be affected
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear if ITT, or if any loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Altiparmak 2001

Methods	• Single centre • Randomisation method unclear

Altiparmak 2001 *(Continued)*

- Parallel study
- Blinding unclear
- ITT unclear
- Unclear % followed-up
- Compliance not assessed
- Good group similarity

Participants	• Proteinuric kidney transplant recipients > 1g/d (not diabetics) • SCr < 177 • Mean age: 35.7 • Sex M/F: 27/10 • Immunosuppression: Not stated • Enrolled: Range 3-61 months post-transplant
Interventions	**Treatment group 1** • Enalapril 5-10 mg **Treatment group 2** • Losartan 25-50 mg
Outcomes	• BP • Proteinuria (remission and concentration) • CrCl • HCT • SK All outcomes measured at 1 year
Notes	• Uneven treatment allocation (25 on enalapril, 12 on losartan) • Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No description of method
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Blinding unclear, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Blinding unclear, no subjective outcomes reported
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear if ITT or proportion lost to follow-up - NOTE uneven group numbers uneven loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes were prespecified if any

Altiparmak 2001 *(Continued)*

Free of other bias?	Low risk	No evidence of other sources of bias

Andres 2006

Methods	• Parallel study • Double blind • Randomisation method: Not stated • Not ITT • Compliance not assessed • Good group similarity
Participants	• Age: 18-75 years (mean 49.0) • Sex M/F: 65/41 • Enrolled: 6 months post-transplant • Immunosuppression: All CSA • BP: SBP 140-165 and/or DBP 90-105
Interventions	**Treatment group** • Valsartan 80 mg ± frusemide **Control group** • Placebo ± frusemide
Outcomes	• BP (automated Omron HEM705CP) • SCr • SK+ • Hb All outcomes measured at 8 weeks
Notes	• Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No description of method
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	No subjective outcomes
Incomplete outcome data addressed?	Low risk	Excluded from analysis if side effects, but similar proportion from each arm and small numbers excluded (n = 4 and n = 5)

Andres 2006 *(Continued)*

All outcomes

Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Barenbrock 2001

Methods	• Unblinded • Parallel • Open • Not ITT "per protocol" performed on 13/21 • Compliance not assessed • Good group similarity
Participants	• Hypertensive • Stable • Mean age: 51 years • Number: 21 • Sex M/F: unclear • Immunosuppression: Not stated
Interventions	**Treatment group 1** • Candesartan **Treatment group 2** • Amlodipine Use of other antihypertensive agents and dose unclear
Outcomes	• MAP (6 months)
Notes	• Only abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Not described
Allocation concealment?	Unclear risk	Not described
Blinding? Objective outcomes (e.g. death, graft loss)	Unclear risk	Unblinded, no objective outcomes
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, BP measurement could be biased

Barenbrock 2001 *(Continued)*

Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear ITT and loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Barri 1995

Methods	• Unblinded • Crossover • Open • ITT unclear • Compliance not assessed • Group similarity unclear
Participants	• Mild-moderate hypertension • Enrolled: 3-18 months post-transplant • Immunosuppression: All CSA
Interventions	**Treatment group 1** • Israpidine 5-20 mg **Treatment group 2** • Metoprolol 50-200 mg + hydrochlorothiazide 25-50 mg
Outcomes	• SBP (3 months) • DBP (3 months)
Notes	• Only abstract • SCr outcome data collected but not available

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Unclear randomisation method
Allocation concealment?	Unclear risk	Unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Unclear risk	Unblinded, no objective outcomes
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, BP measurement could be biased

Barri 1995 *(Continued)*

Incomplete outcome data addressed? All outcomes	Unclear risk	ITT and follow-up unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Beckingham 1995

Methods	• Double blind • Parallel • ITT • Compliance not assessed • Group similarity unclear
Participants	• Enrolled: > 1 year post-transplant • HCT ≥ 50% 3 consecutive measures over 3 months • Stable kidney function • Number: 25 • Sex M/F: Not stated • Immunosuppression: Not stated Exclusion criteria: RAS, hydronephrosis, already on ACEi
Interventions	**Treatment group** • Enalapril 2.5 mg **Control group** • Placebo Cointerventions: Diuretics continued in those already taking them, no others started. Other antihypertensives not stated
Outcomes	• SBP • DBP • HCT • Hb • Cr-EDTA GFR All outcomes measured at 4 months
Notes	• Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Low risk	"Patients were randomised by the hospital pharmacy [...]"

Beckingham 1995 *(Continued)*

Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	ITT, no loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Campistol 1991

Methods	• Randomisation method unclear • Not blinded • ITT unclear • Follow-up proportion unclear • Compliance not assessed • No placebo • Parallel • Group similarity unclear
Participants	• Enrolled: < 3 months post-transplant • Immunosuppression: All CSA Exclusion criteria: Post-transplant ATN, use of rifampicin, cimetidine or erythromicin
Interventions	**Treatment group** • Diltiazem (dose unknown) **Control group** • No treatment Coninterventions: Not stated
Outcomes	• Graft survival (1 year) • Rejection (1 year)
Notes	• Unclear when treatment commenced in relation to transplant • Letter only • Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement

Campistol 1991 *(Continued)*

Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Unclear, uneven groups suggests problems with any allocation concealment, randomisation method or loss to follow-up
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, rejection rates could be biased, depending on method of diagnosis (unclear)
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Castelao 2001

Methods	• Double blind • Crossover study • ITT unclear • Compliance not assessed • Good group similarity
Participants	• Enrolled: mean 61/12 post-transplant • Immunosuppression: All CSA • SCr < 350 • All hypertensive (SBP > 140 or DBP > 90) • Sex M/F: 20/17 • Mean age: 43 years
Interventions	**Treatment group 1** • Doxazosin 1-8 mg/d **Treatment group 2** • Enalapril 2.5-20 mg/d Cointerventions: Unclear
Outcomes	• BP: 24 h ambulatory • GFR (method unclear) • SCr • Proteinuria (g/d) • Hb • SK+

Castelao 2001 *(Continued)*

	All outcomes measured at 11 weeks
Notes	• 37/42 patients reported on (2 retracted consent, 2 violated protocol and 1 non-compliant) • Table states 12 months follow-up but methods suggest 11 weeks (entered as 3 months) • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No comments from authors
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	37/42 randomised patients analysed - probably not informative reasons or sufficient to cause bias
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Celik 2000

Methods	• Unclear blind • Crossover • ITT Unclear • Compliance not assessed • Good group similarity
Participants	• Enrolled: > 6 months post-transplant • HCT > 0.51 on > 3 occasions • Stable CrCr < 177 • Immunosuppression: Not stated
Interventions	**Treatment group 1** • Enalapril 10 mg/d **Treatment group 2** • Losartan 50 mg/d
Outcomes	• HCT (4 weeks)

Celik 2000 *(Continued)*

Notes	• Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No comments from authors
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, but no subjective outcomes
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear but probably no loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

Chanard 2003

Methods	• Double blind • Parallel • Multicentre • Not ITT - 53 randomised, 48 analysed (3 not treated, 2 adverse events, unclear what allocation) • Different time since transplant in treatment groups (amlodipine longer) • Compliance not assessed
Participants	• Enrolled: > 6 months post-transplant • Age: > 18 years (mean 46.7) • Sex M/F: 33/15 • Immunosuppression: All CSA • BP: DBP 90-100 and/or SBP 140-180 Exclusion criteria: Comorbidities, drugs
Interventions	**Treatment group 1** • Amlodipine 5-10 mg/d **Treatment group 2** • Tertatolol 5-10 mg/d Cointerventions: Unclear

Chanard 2003 *(Continued)*

Outcomes	• Serum urate • Inulin GFR (mL/min) • Any adverse event All outcomes measured at 2 months
Notes	• Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	2/52 patients had side effects and not analysed - not clear which allocation group, but unlikely to affect outcomes due to small numbers
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Unclear risk	Different time since transplantation (amlodipine group later)

Chrysostomou 1993

Methods	• Unblinded (except Pathologists) • Parallel • Mulitcentre • Non-ITT • Compliance not assessed • Good group similarity
Participants	• Consecutive first cadaveric kidney transplant • Enrolled: Time of transplant (once oral CSA commenced) • Sex M/F: 72/41 • Mean age: 44.8 years • Immunosuppression: All CAP Exclusion criteria: DM; Echo/ECG abnormal
Interventions	**Treatment group** • Diltiazem 60 mg thrice daily

Chrysostomou 1993 *(Continued)*

	Control group • Nothing
Outcomes	• Graft loss (1 year) • Rejection (1 year) • Requirement for antihypertensive treatment at 3 months
Notes	• Industry funding • Problematic data - unclear denominators

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No comments from authors
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Pathologists blinded to allocation but decision to biopsy made by unblinded clinicians, may lead to bias
Incomplete outcome data addressed? All outcomes	Low risk	Small numbers withdrawn, non-differential
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Unclear risk	No evidence of other sources of bias

Dawidson 1991

Methods	• Unblinded • Parallel • Single centre • ITT • Compliance not assessed • Good group similarity
Participants	• All cadaveric transplant recipients • Enrolled: At time of transplant (intraoperatively) • Mean age: 38.7 years • Sex M/F: 32/27 • Immunosuppression: All CAP
Interventions	**Treatment group**

Dawidson 1991 *(Continued)*

	• Verapamil 2.5-10 mg IV intraoperatively + 120 mg twice daily **Control group** • No treatment Duration: 2 weeks
Outcomes	• Graft loss at 1 year • Death at 1 year
Notes	• Non CCB antihypertensives allowed • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No comments from authors
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	No subjective outcomes assessed
Incomplete outcome data addressed? All outcomes	Low risk	Intention to treat analysis with no loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

El Agroudy 2003

Methods	• Unblinded • Parallel • Single centre • Not ITT • Compliance not assessed • Good group similarity
Participants	• Age: > 18 years • Enrolled: Mean 39 months post-transplant • All living donor recipients • Mean age: 29.9 years • Sex M/F: 111/51

El Agroudy 2003 *(Continued)*

	• Immunosuppression: CSA • SBP 140-170/DBP 85-100 twice over 3 days Exclusion criteria: RAS, prior ARB
Interventions	**Treatment group 1** • Losartan 50 mg/d **Treatment group 2** • Captopril 50 mg/d **Treatment group 3** • Amlodipine 5 mg/d Cointerventions: Diuretic/AB/BB allowed Duration: 12 months
Outcomes	• SBP/DBP • Hb • SCr • Proteinuria • SK+ All outcomes measure at 1, 2 and 12 months
Notes	• Three active arms - this entry for ACEi versus CCB comparison • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No comments from authors
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, BP measurement at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Six patients in amlodipine group withdrew because they "stopped all antihypertensive drugs" - unclear if this was due to side effects or other reason, not analysed
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other sources of bias

El Agroudy 2003 ARB

Methods	• Unblinded • Parallel • Single centre • Not ITT • Compliance not assessed • Good group similarity
Participants	• Age: >18 years • Enrolled: Mean 39 months post-transplant • All living donor recipients • Mean age: 29.9 years • Sex M/F: 111/51 • Immunosuppression: CSA • SBP 140-170/DBP 85-100 twice over 3 days Exclusion criteria: RAS, prior ARB
Interventions	**Treatment group 1** • Losartan 50 mg/d **Treatment group 2** • Captopril 50 mg/d **Treatment group 3** • Amlodipine 5 mg/d Cointerventions: Diuretic/AB/BB allowed Duration: 12 months
Outcomes	• SBP/DBP • Hb • SCr • Proteinuria • SK+ All outcomes measured at 1, 2 and 12 months
Notes	• Three active arms - this entry for ARB versus CCB comparison • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	No comments from authors
Blinding?	Low risk	Unblinded, but objective measures unlikely to be biased

El Agroudy 2003 ARB *(Continued)*

Objective outcomes (e.g. death, graft loss)		
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, BP measurement at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Six patients in amlodipine group withdrew because they "stopped all antihypertensive drugs" - unclear if this was due to side effects or other reason, not analysed
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No evidence of other bias

Formica 2006

Methods	• Unblinded • Parallel • Not ITT • Compliance not assessed • Differential stopping rules and withdrawal rates
Participants	• Consecutive patients, any donor (60% agreed) • Hypertension in first 30 days • SK < 5.5 • SCr < 265 or falling > 88/d • Sex M/F: 34/23 • Mean age: 48.0 years • Immunosuppression: Not stated
Interventions	**Treatment group 1** • Losartan up to 100 mg/d **Treatment group 2** • Amlodipine up to 20 mg/d Cointerventions: BB/AB/diuretic allowed as required (no protocol)
Outcomes	• SCr • Hb • Proportion withdrawing • Proportion hyperkalaemia > 6 mmol/L All outcomes measured at 3, 6 and 12 months
Notes	• Random number allocation • Different stopping rules by treatment allocation - refractory oedema, HCT > 0.5 in CCB, K > 5.5 in ARB • ARB 41% and CCB 63% withdrew before 1 year • Funding not reported

Formica 2006 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Random number tables (block of 5)
Allocation concealment?	Low risk	'Sealed envelopes'
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective measures unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, and subjective measures (e.g. withdrawal due to side effects) may at risk of bias
Incomplete outcome data addressed? All outcomes	High risk	Not ITT - different stopping rules by allocation, with different rates of withdrawal (12/29 in ARB, 4/27 in CCB)
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other cause of bias apparent

Frei 1990

Methods	• Unblinded • Parallel • ITT unclear • Compliance not assessed • Good group similarity
Participants	• Enrolled: At time of transplant • SCr < 194 • Immunosuppression: CAP or CMP • Sex M/F:37/27 • Mean age: 36.5 years Exclusion criteria: RAS, second transplant, DM, diuretics, BB
Interventions	**Treatment group** • Diltiazem intraoperatively IV + 90 mg twice daily **Control group** • No treatment
Outcomes	• Graft loss (1 year) • Death (1 year) • GFR (CrCl) (1 year)

Frei 1990 *(Continued)*

Notes	• 129/134 reported • Rejection data quoted as episodes of rejection, not per patient, so unusable • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be affected by bias
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, but no subjective outcomes
Incomplete outcome data addressed? All outcomes	Low risk	Only 5/134 lost to follow-up, reasons unclear, from both groups
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other cause of bias apparent

Gossmann 2002

Methods	• Double blind • ITT unclear • Parallel • Blood testing to detect active intervention (compliance monitoring) • Good group similarity
Participants	• Age: > 18 years • Enrolled: > 6 months post-transplant • SCr < 221 • Immunosuppression: CSA (Sandimmune) Exclusion criteria: ACEi, BB, CHF, MI, arrhythmia
Interventions	**Treatment group** • Gallopamil 200 mg/d **Control group** • Placebo Cointerventions: Unclear if other antihypertensives used

Gossmann 2002 *(Continued)*

Outcomes	• SCr • GFR (Inulin, not BSA adjusted) All outcomes measured at 3 months
Notes	• Industry funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	Only one patient withdrew secondary to heart block (so not ITT, but unlikely to affect outcome)
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent cause of bias

Gronhagen-Riska 1984

Methods	• Unblinded • ITT unclear • Parallel • Single centre • Compliance not assessed • Good group similarity
Participants	• Enrolled: At time of transplant (postoperative oral medication) • Mean age: 38.9 years • Sex M/F: 22/8 • Similar disease/age/sex in groups • Immunosuppression: AZA/Pred
Interventions	**Treatment group** • Captopril 12.5 thrice daily and as required **Control group**

Gronhagen-Riska 1984 *(Continued)*

	• No treatment Cointerventions: Other antihypertensives allowed
Outcomes	• At 3 months * Death * Graft loss * Rejection • At 3 weeks and 3 months * BP * SCr * CrCl * SK+
Notes	• 3/52 outcomes included in 1 month tables • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Comment: Unblinded, but objective outcomes unlikely to be affected by bias
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Comment: Unblinded, which places partially subjective outcomes (e.g. blood pressure, rejection) at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear if ITT (unclear if withdrawals from treatment included in outcome measurement)
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent cause of bias

Guerin 1989

Methods	• Parallel • Unblinded • Not ITT - one patients excluded after randomisation (diabetes) from control arm • Block of 4 randomisation • Good group similarity • Compliance not assessed
Participants	• Consecutive cadaveric kidney transplant recipients

Guerin 1989 *(Continued)*

	• Enrolled: At time of transplant • Immunosuppression: AZA/Pred + antibody Exclusion criteria: Living donor, previous diltiazem, conduction deficit
Interventions	**Treatment group** • Diltiazem IV then 120-180 mg/d **Control group** • No treatment
Outcomes	• BP >160/95 (= hypertension) at 1 year
Notes	• No funding comment

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Block of four randomisation
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Unclear risk	Unblinded, no objective outcomes
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, so subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Low risk	One patient withdrawn after randomisation from control arm due to diabetes - unlikely to bias outcomes
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent bias

Halimi 2007

Methods	• Unblinded • Permuted block randomisation • ITT • Parallel • Compliance not assessed • 100% follow-up • Last observation carried forward if missing data • Good group similarity
Participants	• Enrolled: > 12 months post-transplant

Halimi 2007 *(Continued)*

	• Stable SCr: < 300 • Cadaveric transplant • Sex M/F:66/35 • Mean age: 36.3 years • Immunosuppression: CNI/MMF or AZA/ATG/Pred • Hypertension: > 140/90 and proteinuria on dipstick
Interventions	**Treatment group 1** • Amlodipine 5 mg **treatment group 2** • Enalapril 5 mg **Treatment group 3** • Amlodipine and enalapril (all titrated to BP) Cointerventions: Diuretic/atenolol added as required
Outcomes	• Achieving BP control (SBP/DBP) • Hyperkalaemic (> 5.5) • Acute rejection • Death • Graft loss • Change CrCl • Change Hb • Change HCT • Change SK • Change SCr All outcomes measured at 6 months
Notes	• Skewed data for proteinuria - medians/IQR presented not used here • Local university funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Permuted block randomisation
Allocation concealment?	Low risk	Statistician not involved with study otherwise; sealed envelopes
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Comment: Unblinded, but objective outcomes unlikely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Comment: Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Low risk	Similar numbers withdrawn due to side effects, but all analysed

Halimi 2007 *(Continued)*

Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent cause of bias

Harper 1996

Methods	• Unblinded • ITT unclear • Three centres • Parallel • Compliance not assessed • Good group similarity
Participants	• Enrolled: At time of transplant (commenced pre-operatively) • Mean age: 45.6 years • Sex M/ F: Unknown • Immunosuppression: All CSA/Pred Exclusion criteria: > 3 grafts; PRA > 50%; enzyme inducing drugs
Interventions	**Treatment group** • Nifedipine 10 - 40 thrice daily **Control group** • No treatment Cointerventions: Other antihypertensives allowed
Outcomes	• GFR (EDTA) • Death • MAP All outcomes measured at 24 months

Notes	• Three arms in initial study - two different CSA doses and one arm with nifedipine - here only CSA standard dose with and without nifedipine considered.
	  * High dose CSA used (17 mg/kg commenced)
	• Inconsistency exists in the reporting of death-censored and non censored graft losses
	  * Censored losses have larger number at risk, so data not usable.
	• Industry and scholarship funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding?	Low risk	Unblinded, but objective outcomes unlikely to be affected

Harper 1996 *(Continued)*

Objective outcomes (e.g. death, graft loss)		
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear if patient lost
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent bias

Hausberg 1999

Methods	• Double blind (including outcome assessors) • Parallel • Randomisation method unclear • ITT (mostly) • Medication count • 100% follow-up • Good group similarity
Participants	• Salt restricted • Hypertension: BP >140/90 on 3 occasions over 1 month • Enrolled: 6-12 weeks post transplant • Mean age: 43 years • Sex M/F: 68/28 • Immunosuppression: All CSA Exclusion criteria: SCr > 265, MI/CVA 6/12 prior, DM, RAS
Interventions	**Treatment group 1** • Quinapril 5-40 mg **Treatment group 2** • Atenolol 12.5-100 mg titrated to DBP < 90 Cointerventions: Frusemide 40-80; nifedipine 5-60; clonidine 75-150 (diuretics first then the others if required) Duration: 2 years intervention
Outcomes	• BP • SCr • CGGFR • Proteinuria • Death • Hb

Hausberg 1999 *(Continued)*

	Outcomes measured to 5 years Intervention was for 2 years, last available value used was for reported 2 year outcomes
Notes	• Industry funding • Earlier papers subset of the later papers in term of numbers - unclear if all were enrolled and partially report

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	ITT analysis
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent cause of bias

Hernandez 1995

Methods	• Unblinded • ITT unclear • Parallel • Single centre • Compliance not assessed • Good group similarity
Participants	• Enrolled: Unclear, but > 6 months post-transplant • HCT > 0.5 for > 6 months with no secondary cause • BP controlled with nifedipine (MAP < 106) • Immunosuppression: All CSA • Sex M/F: 20/1 • Mean age: 43.0 years
Interventions	**Treatment group 1** • Captopril replacing nifedipine (dose unknown)

Hernandez 1995 *(Continued)*

	Treatment group 2 • Nifedipine continued (dose unknown)
Outcomes	• Inulin GFR (mL/min) • SCr • MAP • Any adverse event All outcomes measured at 2 months
Notes	• Outcomes measured monthly and mean for each individual provided • Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear if all patients enrolled had outcomes reported
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other bias apparent

Hernandez 2000

Methods	• Single blind • Non ITT • Single centre • Parallel • Compliance not assessed • Imbalance in groups - placebo longer post-transplant
Participants	• Enrolled: Mean 69.5 months post-transplant • Hypertension: >150/90 (both) on 2 antihypertensives and LVH on echo • SCr < 220, stable • Sex M/F: 34/18 • Immunosuppression: All CSA

Hernandez 2000 *(Continued)*

	• Mean age: 48.7 years Exclusion criteria: RAS, DM, MI, CHF, proteinuria
Interventions	**Treatment group** • Lisinopril 10 mg **Control group** • Placebo Cointerventions: Other nonACEi/nonARB antihypertensives allowed
Outcomes	• BP (6 and 12 months (no method)) • SCr (6 and 12 months) • Hb (6 and 12 months)
Notes	• Informative withdrawals (5/29 from active arm because of increased creatinine on treatment) • Appearance drugs similar • Government sponsorship

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Outcome assessors not blinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Outcome assessors not blinded, BP outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	High risk	Informative withdrawals from active treatment arm due to increased creatinine may lead to bias (in favour of active agent)
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent source of bias

Inigo 2001

Methods	• Unblinded • Crossover, adequate washout • Single centre • ITT • Compliance not assessed

Inigo 2001 *(Continued)*

	• Good group similarity
Participants	• Enrolled: Mean 90 months post-transplant • Hypertension: 140-170/85-100 • Sex M/F: 11/6 • Immunosuppression: All CSA • SCr < 141 • Proteinuria < 300 mg/d • Mean age: 53 years
Interventions	**Treatment group 1** • Losartan 50 mg/d **Treatment group 2** • Amlodipine 5 mg/d Doxazosin given as required to achieve BP 130/80
Outcomes	• BP • SCr • CrCl • SK All outcomes measured at 6 weeks
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes not at risk of bias
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, blood pressure outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Low risk	ITT, no loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other sources of bias apparent

Kim 2002a

Methods	• Randomisation method unclear • Single blind (participants only) • ITT • Completeness unclear • Group similarity unclear
Participants	• Kidney transplant with CAN on histology • Immunosuppression: All CAP
Interventions	**Treatment group** • Enalapril 5-10 mg **Control group** • Placebo
Outcomes	• Graft loss • MAP • Proteinuria • SCr Mean follow-up at 2 years
Notes	• Abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Low risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Unclear risk	Participants only blinded, objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Outcome assessors not blinded, outcomes with subjective element (e.g. MAP) at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear what proportion lost to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Unclear risk	No group baseline data

Kumana 2003

Methods	• Double blind • Parallel • Block randomisation • Not ITT (110/114 followed) • Compliance not assessed • DM: Diltiazem (10) placebo (1), otherwise balanced groups
Participants	• Immunosuppression: All CSA • Enrolled: Unclear when post -transplant (probably at start) • Sex M/F: 80/54 • Mean age: 42 years Exclusion criteria: Hypotension, indication for diltiazem
Interventions	**Treatment group** • Diltiazem 30 mg or 60 mg/d (if < or > 60 kg) **Control group** • Placebo Cointerventions: Other antihypertensives except diltiazem/verapamil allowed
Outcomes	• SCr (3 and 6 months) • Rejection (6 months)
Notes	• One withdrawal due to rejection in diltiazem group added as event in outcome rejection • Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Block randomisation
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	Small numbers only lost, unclear why, but unlikely to bias outcomes
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias apparent

Kuypers 2004

Methods	• Double blind • Parallel • ITT • Compliance not assessed • Good group similarity
Participants	• First kidney transplant • Enrolled: At time of transplant • Age: 18-65 years (mean 47.4) • Immunosuppression: All CSA
Interventions	**Treatment group** • Lacidipine 2-6 mg/d **Control group** • Placebo Cointerventions: Other antihypertensives allowed - atenolol, enalapril and frusemide in that order
Outcomes	• BP • SCr • CrCl All outcomes measured at 6 weeks
Notes	• 118/131 initially enrolled available for analysis (need to have a creatinine measured at 1 month to be included) • Industry funding (GSK)

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	Reasons for withdrawals in each group tabulated, similar proportions of adverse events in each arm
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any

Kuypers 2004 *(Continued)*

Free of other bias?	Low risk	No other sources of bias apparent

Ladefoged 1994

Methods	• Double blind • ITT • Parallel • Single centre • Compliance not assessed • Good group similarity
Participants	• Cadaveric kidney transplant • Enrolled: At time of transplant • Immunosuppression: All CSA • Mean age: 43.5 years • Sex M/F: 27/12
Interventions	**Treatment group** • IV then oral diltiazem 60-120 mg thrice daily (unclear why) **Control group** • Placebo
Outcomes	• SCr • CrCl • Graft survival at 3 months
Notes	• Industry funding • Rates for rejection calculated based on patients at risk provided in figure 1 (patients available for creatinine observation)

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	All withdrawals accounted for, ITT analysis

Ladefoged 1994 *(Continued)*

Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other cause for bias identified

Lehtonen 2000

Methods	• Double blind • Parallel • Randomisation method unclear • Unclear ITT • Compliance not assessed • Group similarity unclear
Participants	• Immunosuppression: All CSA • Enrolled: At time of transplant
Interventions	**Treatment group** • IV israpidine then oral israpidine 10 mg/d **Control group** • Placebo Duration: 3 weeks
Outcomes	• SCr (3 weeks, 3 months, 1, 3 and 5 years - no variance measure) • CrCl (1 year - no variance measure) • Graft survival (1, 3 and 5 years) Median follow-up: 4.7 years
Notes	• Abstract publication only • Note 3 week intervention then long term follow-up • Standard deviations not provided for SCr/CrCl outcomes • Unclear denominator for numbers at risk • No funding statement

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding?	Low risk	Double blind

Lehtonen 2000 *(Continued)*

Subjective outcomes (e.g. blood pressure measurement)		
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear loss to follow-up and numbers at risk
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other cause of bias apparent

Madsen 1998

Methods	• Parallel • Double blind • Randomisation method not stated • Not ITT • Tablet count for compliance • Different time since transplant in treatment groups (amlodipine longer)
Participants	• Immunosuppression: All CSA • Enrolled: At time of transplant • Mean age: 42.1 years • Sex M/F: 54/25 • Number: 79 patients included, 99 were enrolled and randomised Exclusion criteria: CHF, prior CVA
Interventions	**Treatment group** • Felodipine ER 10 mg **Control group** • Placebo Cointerventions: Diuretics/BB/pinacidil allowed but no protocol
Outcomes	• Iothalamate GFR (6 and 12 weeks) • Death (12 weeks) • Withdrawal due to side effects (12 weeks) • SBP (6 and 12 weeks) • DBP (6 and 12 weeks)
Notes	• Funding not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear

Madsen 1998 *(Continued)*

Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Unclear risk	Significant numbers removed from analysis due to side effects and not analysed (in both arms)
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Unclear risk	Different time from transplant for each group (amlodipine longer)

Midtvedt 2001

Methods	• Double blind • Parallel • Randomisation method not stated • Not ITT (some outcomes) • Compliance not studied • Good group similarity
Participants	• Immunosuppression: CSA • Enrolled: < 3 weeks post-transplant • Age: > 18 years (mean 44.4) • Hypertension: DBP > 95 • Sex M/F: 116/38 Exclusion criteria: Hypersensitivity
Interventions	**Treatment group 1** • Lisinopril 10-20 mg/d **Treatment group 2** • Nifedipine CR 30-60 mg/d Cointerventions: Other non CCB/ACEi/ARB allowed duration: 1 year and extended to 2 years in patients who agreed
Outcomes	• Graft loss (1 year) • Death (1 year) • Hyperkalaemia leading to stopping treatment (1 year) • Hyperkalaemia, unspecified (1 year) • Ankle oedema leading to withdrawal (1 year) • New angina (1 year)

Midtvedt 2001 *(Continued)*

	• MI (1 year) • Rejection, any (to 2 years) • SCr (1 month, 1 and 2 years) • GFR (1 year) • Hb (1 year)
Notes	• Funding not disclosed • Proteinuria outcome reported as mg/L - not usable

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Block randomisation
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Unclear risk	All accounted for at early time points, large numbers at later time points unaccounted for
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other potential source of bias

Morales 1989

Methods	• Blinding unclear • Parallel • Randomisation method not stated • ITT unclear • 100% follow-up • Compliance not studied • Good group similarity
Participants	• All cadaveric transplants • Immunosuppression: All CSA • Enrolled: At time of transplant • Mean age: 42.9 years • Sex M/F: 33/21
Interventions	**Treatment group**

Morales 1989 *(Continued)*

	• Nifedipine SR 40 mg/d **Control group** • Placebo Duration: 15 days
Outcomes	• SCr • Acute rejection • Graft loss • Death All outcomes measured at 1 month
Notes	• Unclear withdrawals

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Blinding unclear, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Blinding unclear, somewhat subjective outcomes including acute rejection at risk of bias
Incomplete outcome data addressed? All outcomes	Low risk	No loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No additional cause of bias identified

Morales 1994

Methods	• Unblinded (different treatment allocation no placebo) • Parallel • Randomisation method unclear • ITT unclear • Compliance not assessed • Good group similarity
Participants	• All hypertensive (DBP ≥ 95) • Immunosuppression: All CSA/Pred • Enrolled: 1 month post-transplant

Morales 1994 *(Continued)*

	• Sex M/F: 57/40 • Mean age: 41.1 years
Interventions	**Treatment group 1** • Nifedipine SR 40-80 mg/d **Treatment group 2** • Non-CCB antihypertensive
Outcomes	• SCr (to 5 years) • Graft survival (to 5 years)
Notes	• Unclear withdrawals

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, but no subjective outcomes
Incomplete outcome data addressed? All outcomes	High risk	Withdrawal reasons and numbers unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other causes of bias apparent

Mourad 1993

Methods	• Unblinded • Parallel • Not ITT • Single centre • Randomisation method unclear • Compliance not assessed • Follow-up: 25/31
Participants	• Donors: 27 deceased, 4 living related (haplo-identical) • Immunosuppression: All CAP

Mourad 1993 *(Continued)*

- All hypertensive (DBP > 95 mm Hg on 3 occasions)
- All SCr < 200 and stable for 3 months
- Enrolled: Mean 5 months post-transplant
- Mean age: 44.4 years
- Sex M/F: 18/7

Interventions	**Treatment group 1** • Lisinopril 5-15 mg ± frusemide **Treatment group 2** • Nivedipine SR 20-60 mg ± BB
Outcomes	• SCr • SK • DTPA GFR • HCT • Change in MAP Outcomes measured at 1 and 2.5 years
Notes	• Exclusions included 2 in ACEi group (one pregnancy and one severe acute rejection) and 4 in CCB group (one aldosterone-secreting tumour, one RAS and two chronic rejection) • Different cointerventions in each group • Funding source not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Low risk	All exclusions addressed, not ITT but unlikely to bias results
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	High risk	Different cointerventions - lisinopril patients given diuretics, nifedipine given beta-blockers if additional treatment needed - could bias outcomes

Ok 1995

Methods	• Unblinded • Parallel • ITT unclear • Randomisation method unclear • Single centre • Compliance not assessed • Good group similarity
Participants	• HCT > 0.51 on three consecutive occasions • First kidney transplant • Enrolled: Mean 6 months post-transplant • Immunosuppression: AZA/Pred P(4), CAP (15) • Mean age: 34.4 years • Sex: M/F: 14/5
Interventions	**Treatment group** • Enalapril 10 mg/d **Control group** • No treatment
Outcomes	• HCT at 2 months
Notes	• Funding not stated • Third arm given theophylline, patients reallocated after 3 months if persistent increase in HCT to enalapril, also patients on enalapril who relapsed after 1 month, restarted at half dose - this second phase not included, also theophylline patients not included. • Additional outcomes only reported for enalapril group (not control) including SCr and SK

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, but no subjective outcomes reported
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear if ITT but likely
Free of selective reporting?	Unclear risk	SCr and SK data reported for intervention group but not controls

Ok 1995 *(Continued)*

Free of other bias?	Low risk	No other cause of bias identified

Paoletti 2007

Methods	• Unblinded • Parallel • Not ITT • Randomisation method unclear • Compliance not assessed • Good group similarity
Participants	• Enrolled: 3-6 months post-transplant • LVH on echo 3 months post-transplant • Stable SCr < 221 • Urinary protein < 1g/d Exclusion criteria: Living donor, preemptive transplant, rejection in last 3 months, RAS Randomised previously to TAC/CSA
Interventions	**Treatment group** • Lisinopril 2.5-20 mg/d **Control group** • No treatment Cointerventions: Both arms allowed non-renin-angiotensin system active antihypertensives to treat BP to < 130/80

Outcomes	• Change in
	  * SBP
	  * DBP
	  * SCr
	  * Hb
	  * Urinary protein
	
	All outcomes measured at 18 months

Notes	• Described as ITT but excluded 3 patients with worsening kidney function and one with severe infection from analysis • No funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding?	Low risk	Unblinded, but objective outcomes unlikely to be biased

Paoletti 2007 *(Continued)*

Objective outcomes (e.g. death, graft loss)		
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Low risk	Described as ITT but 3 patients with worsening kidney function excluded from analysis - informative censoring, BUT one from ACEi arm, two from control, unlikely to affect outcomes differentially
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other

Patton 1994

Methods	• Unblinded • Parallel • Single centre • Randomisation method not stated • Not ITT • Compliance not assessed
Participants	• Enrolled: < 1 week post-transplant • Immunosuppression: All CSA • Sex M/F: 53/23 • Mean age: 44.6 years
Interventions	**Treatment group** • Diltiazem 60 mg twice daily **Control group** • No treatment
Outcomes	• Death (1 year)
Notes	• 68/76 followed (exclusions included erratic CSA concentrations, hypotension in diltiazem arm, diltiazem commencement in control arm • Funding not reported • Third arm of patients on ketoconazole also included, not used here • Reporting of rejection poor not able to attribute proportions to groups. • No SD on SCr data so not able to be included

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear

Patton 1994 *(Continued)*

Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, no subjective outcomes
Incomplete outcome data addressed? All outcomes	High risk	Not ITT, patients removed if had side effect from analysis (greater numbers in diltiazem arm)
Free of selective reporting?	Unclear risk	Rejection events, side effects reported across study, not by intervention; SCr outcome not usable as no SD - unclear if this a source of bias
Free of other bias?	Unclear risk	No other sources of bias apparent

Pirsch 1993

Methods	• Double blind • Randomisation method unclear • Central drug distribution • Not ITT (4 randomised to placebo withdrawn before treatment for medical indications) • Parallel • Compliance not assessed • Imbalance in M/F in groups (placebo 9/19, verapamil 22/10)
Participants	• Sex M/F: 31/29 (see above) • All adult cadaveric donors • Immunosuppression: CAP and ALG • Enrolled: Prior to discharge when CSA commenced
Interventions	**Treatment group** • Verapamil 80 mg twice daily **Control group** • Placebo Cointerventions: Sublingual nifedipine allowed to control BP
Outcomes	• Death • Graft survival • Rejection • CSA toxicity • New hypertension by 12 months • SCR (1, 3, 6 and 12 months)
Notes	• Identical appearance

Pirsch 1993 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Low risk	Sequence generated by investigational pharmacy service
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	Four patients withdrew from placebo arm after randomisation because of contraindications for treatment - unlikely to bias results
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	High risk	More M/F on verapamil (32/22) compared to placebo (9/28), will tend to bias creatinine values (males have higher values) - bias creatinine results in favour of placebo

Rahn 1999 (both)

Methods	
Participants	
Interventions	
Outcomes	
Notes	Used for Rahn 1999 HT and Rahn 1999 NT, where outcomes reported together for both groups and unable to be disaggregated.

Rahn 1999 HT

Methods	• Double blind • Parallel • Placebo used • Mulitcentre • ITT • Compliance not assessed • Good group similarity

Rahn 1999 HT *(Continued)*

Participants	• SCr < 265, variation < 22 over 2 weeks • Enrolled: 6-12 weeks post-transplant • DBP 90-115 OR antihypertensive treatment • All cadaveric donors • Number: 144 • Sex M/F: Unclear • Mean age: 43 years • Immunosuppression: All CSA Exclusion criteria: Malignancy, RAS, MI previous 6 months, > 2 kidney transplants, CCB indicated
Interventions	**Treatment group** • Nitrendipine 10-20 mg twice daily **Control group** • Placebo Coninterventions: Frusemide then propanolol then captopril then prazosin
Outcomes	• SCr • Graft failure • SBP • DBP • MAP All outcomes measure at 2 years
Notes	• Author contacted 11/10/07 for information about graft failure by treatment allocation and hypertensive status • Industry funding • 2 year outcomes include last known values for withdrawals

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Computer generated
Allocation concealment?	Low risk	Geographical separation, opaque packaging
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	ITT, similar numbers of withdrawals per arm and reasons documented

Rahn 1999 HT *(Continued)*

Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent cause of bias

Rahn 1999 NT

Methods	• Double blind • Parallel • Placebo used • Mulitcentre • ITT • Compliance not assessed • Good group similarity
Participants	• SCr < 265, variation < 22 over 2 weeks • Enrolled: 6-12 weeks post-transplant • DBP 90-115 OR antihypertensive treatment • All cadaveric donors • Number: 144 • Sex M/F: Unclear • Mean age: 43 years • Immunosuppression: All CSA Exclusion criteria: Malignancy, RAS, MI previous 6 months, > second transplant, CCB indicated
Interventions	**Treatment group** • Nitrendipine 5-10 mg twice daily **Control group** • Placebo Coninterventions: Frusemide then propanolol then captopril then prazosin
Outcomes	• SCr • Graft failure • SBP • DBP • MAP All outcomes measure at 2 years
Notes	• Author contacted 11/10/07 for information about graft failure by treatment allocation and hypertensive status • Industry funding • 2 year outcomes include last known values for withdrawals

Risk of bias

Bias	Authors' judgement	Support for judgement

Rahn 1999 NT *(Continued)*

Adequate sequence generation?	Low risk	Computer generated
Allocation concealment?	Low risk	Geographical separation, opaque packaging
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	ITT, similar numbers of withdrawals per arm and reasons documented
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent cause of bias

Rashtchizadeh 2007

Methods	• Unblinded • Parallel (for the data recorded here) • Randomisation method unclear • Single centre • ITT unclear • Compliance not assessed • Good group similarity
Participants	• Enrolled: > 6 months post-transplant • SCr < 194 • Immunosuppression: CAP or CMP • Sex M/F: 37/27 • Mean age: 36.5 years Exclusion criteria: RAS, second transplant, DM, diuretics, BB
Interventions	**Treatment group 1** • Enalapril 10 mg/d **Treatment group 2** • Losartan 50 mg/d **Treatment group 3** • Enalapril (10 mg/d) + losartan (50 mg/d) **Control group** • No treatment

Rashtchizadeh 2007 *(Continued)*

	Duration: 8 weeks
Outcomes	• Hb • HCT • SCr • SK • MAP All outcomes measured at 2 months
Notes	• Note that there was additional data provided for a further 2 months treatment with enalapril and losartan groups swapping to other treatment after 2/52 washout - this data not included • No mention of cointerventions for control of BP • University based funding • Continuous measures the SDs seem small - checked with authors confirm are SDs not SEs (reply from Dr Ghorbanihaghio 29 Sep 08)

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	ITT and completeness of follow-up unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other causes of bias apparent

Rump 2000

Methods	• Parallel • Unblinded • Unclear ITT • Quasi-RCT by year of birth • Compliance not assessed • Group similarity unclear
Participants	• Enrolled: 3 months post-transplant

Rump 2000 *(Continued)*

	• Immunosuppression: All CAP • 'Stable function' not defined • BP > 140/90 or antihypertensive treatment Exclusion criteria: RAS
Interventions	**Treatment group** • Nitrendipine or nifedipine 10-60 mg/d **Control group** • No treatment Coninterventions: BB, then diuretics, then AB to control BP
Outcomes	• EDTA GFR (2 years) • Proteinuria (2 years) • Death (2 years) Follow-up: 3 years
Notes	• Further control arm of non-hypertensive patients not given any treatment in study not included here (not the same as those randomised) • Funding source not stated • No table 1 data for group comparisons

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	High risk	Allocation by year of birth
Allocation concealment?	High risk	Allocation by year of birth
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	Unblinded, but no subjective outcomes reported
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear ITT and loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Unclear risk	No baseline data for the two groups compared provided

Santos 2002

Methods	• Unblinded

Santos 2002 *(Continued)*

	• Parallel • Randomisation method not stated • ITT unclear • Compliance not assessed • Group similarity unclear
Participants	• Immunosuppression: All CAP • Enrolled: Not clear
Interventions	**Treatment group** • Diltiazem 90 mg/d **Control group** • No treatment Conninterventions: Not stated
Outcomes	• Graft survival (1 month, 1 and 5 years) • SCr (1 month, 1 and 5 years)
Notes	• Only abstract available • No table 1 data • Unclear denominators • No funding statement

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	No subjective outcomes reported
Incomplete outcome data addressed? All outcomes	Unclear risk	ITT and follow-up unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Unclear risk	No baseline data available for each group

Schmidt 2001

Methods	• Crossover, 2 weeks washout • Single centre • Blinding not stated • ITT • 100% follow-up (except 3 SK results excluded because of haemolysis) • Compliance not assessed • Good group similarity
Participants	• Immunosuppression: All CSA • Enrolled: >1 year post-transplant • SCr stable < 177 • Proteinuria < 1 g/d • Hypertension: SBP 140-159, DBP 90-99 • Mean age: 58 years • Sex M/F: 12/1
Interventions	**Treatment group 1** • Losartan 50 mg **Treatment group 2** • Enalapril 10 mg Cointerventions: CCB/BB/AB/diuretics allowed but schedule not mandated Duration: 3 weeks
Outcomes	• SCr • SBP/DBP • SK • Proteinuria • MAP • SK > 5.5 All outcomes measured at 3 weeks
Notes	• Industry funding (MSD) • No side effects on losartan, 4/13 patients required dose reduction on enalapril because of postural hypotension • Abstract seems to be the same study but only 11 patients included (one additional result from abstract).

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Blinding unclear, but objective outcomes unlikely to be biased
Blinding?	High risk	Blinding unclear, subjective outcomes at risk of bias

Schmidt 2001 *(Continued)*

Subjective outcomes (e.g. blood pressure measurement)		
Incomplete outcome data addressed? All outcomes	Low risk	ITT, withdrawals accounted for and non-informative
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other sources of bias identified

Sennesael 1995

Methods	• Crossover, 2 weeks washout • Double blind, double placebo • Randomisation method not stated • Initial placebo run-in • ITT unclear • Compliance not assessed • Good group similarity
Participants	• Cadaveric transplant • Enrolled: Mean 29.7 months post-transplant • Immunosuppression: CSA • DBP 95-115 • Stable SCr 80-168 • No proteinuria • Sex M/F: 7/3 • Age: Range 36-71 years Exclusions: RAS, CHF, recent MI (< 6 months)
Interventions	**Treatment group 1** • Perindopril 2-4 mg (kidney function-dependent) **Treatment group 2** • Amlodipine 5 mg Initial doses doubled if BP not controlled at 4 weeks Cointerventions: None for BP
Outcomes	• EDTA GFR • Hb • K • SCr • Ambulatory BP • Number BP controlled (undefined) All outcomes measure at 2 months

Sennesael 1995 *(Continued)*

Notes	• Industry funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Unclear risk	Loss to follow-up or withdrawals unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Unclear risk	No other cause of bias apparent

Sperschneider 1997 Dilt

Methods	• Parallel • Double blind • Randomisation method unclear • ITT unclear • Completeness of follow-up unclear • Compliance not assessed • Good group similarity
Participants	• First kidney transplant • Immunosuppression: All CSA • Mean age: 46.6 years • Sex M/F: 32/19 Exclusion criteria: Drugs that interfere with CSA metabolism (except diltiazem)
Interventions	**Treatment group** • Diltiazem (dose unknown) **Control group** • No treatment Duration: 12 weeks

Sperschneider 1997 Dilt *(Continued)*

Outcomes	• Any rejection (3 months)
Notes	• Funding source unclear

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Unclear risk	ITT and any loss to follow-up unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias identified

Sperschneider 1997 Nifed

Methods	• Parallel • Double blind • Randomisation method unclear • ITT unclear • Completeness of follow-up unclear • Compliance not assessed • Good group similarity
Participants	• First kidney transplant • Immunosuppression: All CSA • Mean age: 46.6 years • Sex M/F: 32/19 Exclusion criteria: Drugs that interfere with CSA metabolism
Interventions	**Treatment group** • Nifedipine (dose unknown) **Control group** • No treatment

Sperschneider 1997 Nifed *(Continued)*

	Duration: 12 weeks
Outcomes	• Any rejection (3 months)
Notes	• Funding source unclear

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Unclear risk	ITT and any loss to follow-up unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias identified

Takahara 2002

Methods	• Randomisation with envelopes • Unblinded • Parallel • Unclear ITT • Percent lost to follow-up unclear • Compliance not assessed • Good group similarity
Participants	• Enrolled: Mean 8 years post-transplant • Immunosuppression: CSA (58), TAC (16), other (2) Exclusion criteria: RAS
Interventions	**Treatment group** • Benazepril (dose unknown) **Control group** • No treatment

Takahara 2002 *(Continued)*

	Cointerventions: CCB/AB/BB/other allowed, not protocolised
Outcomes	• MAP (12 months)
Notes	• Unclear if selected as hypertensive or not

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	'the envelope method' - unclear what this means exactly
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Unclear risk	No objective outcomes collected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	ITT and any loss to follow-up unclear
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias identified

Trivedi 2003

Methods	• Crossover, 3 weeks washout • Randomisation method not stated • Unblinded • Not ITT (4 patients failed to complete theophylline arm and were excluded) • Compliance not assessed • Good group similarity
Participants	• HCT > 50% on 2 occasions • 'Stable' transplant recipients • Enrolled: Mean 3 years post-transplant • Immunosuppression: CAP or CSA/Pred • Mean age: 54.9 years • Ethnicity: Caucasian (8); African American (1) Exclusion criteria: Pregnancy, COPD
Interventions	**Treatment group 1** • Fosinopril 10-20 mg/d

Trivedi 2003 *(Continued)*

	Treatment group 2 • Theophylline up to 8mg/kg/d as tolerated Duration: 3 weeks
Outcomes	• Hb • HCT • SCr • SK • MAP All outcomes measure at 3 months
Notes	• Phlebotomy also used if patients HCT became > 0.58 • Funding not mentioned

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	High risk	4/9 patients on theophylline withdrew due to intolerance and were not assessed - large enough to cause bias
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other causes of bias identified

Tylicki 2006

Methods	• Crossover, 8 weeks washout • Randomisation method unclear • Double blind • Not ITT 14/16 included (2 withdrawals due to side effects) • Compliance not assessed • Good group similarity
Participants	• Enrolled: > 6 months post-transplant • Immunosuppression: All CSA (stable levels for 6 months)

Tylicki 2006 *(Continued)*

	• SCr < 155 and stable • Hypertensive on 1 or 2 agents • Mean age: 45.4 years • Sex M/F: 5/9 Exclusion criteria: Proteinuria > 300 mg/g, RAS, CHF, CVA
Interventions	**Treatment group 1** • Losartan 50-100 mg/d **Treatment group 2** • Carvedilol 12.5-25 mg/d **Control group** • Placebo Cointerventions: Doxazosin used as required to achieve comparable BP Target BP < 130/80
Outcomes	• SK > 5.0 • BP (SBP, DBP) • Albuminuria • SCr • CrCl • Hb All outcomes measured at 2 months
Notes	• Placebo arm is following 8 week washout period • No funding statement

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	Two withdrawals for non-informative reasons, balanced, and crossover study mean bias unlikely
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any

Tylicki 2006 *(Continued)*

Free of other bias?	Low risk	No other source of bias identified

Van den Dorpel 1994

Methods	• Double blind • Placebo • Parallel • Not ITT - graft function analysis only performed in patients with immediate graft function (18/25 in each group) • Compliance not assessed • Good group similarity
Participants	• Consecutive non-diabetic first kidney transplants • Enrolled: At time of transplant • Immunosuppression: All ATG/CSA • Mean age: 48.9 years • Sex M/F: 36/14
Interventions	**Treatment group** • Israpidine IV then 2.5 mg twice daily **control group** • Placebo Cointerventions: Labetalol up to 400 mg thrice daily and guanfacine 1-2 mg twice daily allowed to control BP Duration: 3 months
Outcomes	• Graft loss (1 year) • SCr (3 months) • CrCl (3 months)
Notes	• Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind

Van den Dorpel 1994 *(Continued)*

Incomplete outcome data addressed? All outcomes	Low risk	Patients with delayed graft function not analysed, but equal numbers in each group
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias identified

Van der Schaaf 1995

Methods	• Crossover, 4 weeks washout • Randomisation method unclear • Double blind • ITT • 100% follow-up • Compliance not assessed • Good group similarity
Participants	• SCr < 250 • No graft bruit • Enrolled: 1-8 years post-transplant • DBP 95-125 • 2 weeks after stopping any antihypertensive medication • Sex M/F: 12/8 • mean age: 42.9 years • Immunosuppression: All CSA + steroids
Interventions	**Treatment group 1** • Lisinopril 5-10 mg (titrated to BP < 150/95) **Treatment group 2** • Amlodipine 5-10 mg (titrated to BP < 150/95) **Control group** • Placebo Duration: 4 weeks
Outcomes	• BP (MAP, SBP, DNP) • SCr • HCT • GFR • Proteinuria All outcomes at 4 weeks
Notes	• Funding source not stated
Risk of bias	

Van der Schaaf 1995 *(Continued)*

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	ITT, 100% follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias apparent

Van Riemsdijk 2000

Methods	• Randomisation method not stated • Parallel • Double blind • ITT • 100% follow-up • Compliance not assessed • Good group similarity
Participants	• Age: > 18 years • Enrolled: At time of transplant • immunosuppression: CSA/Pred
Interventions	**Treatment group** • Israpidine IV then oral 2.5 mg twice daily **Control group** • Placebo Coninterventions: Unclear Duration: 12 months
Outcomes	• MI (12 months) • Rejection (12 months)
Notes	• SCr data only provided as medians - not available

Van Riemsdijk 2000 *(Continued)*

- Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	ITT, 100% follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias identified

Vanrenterghem 1988

Methods	• Randomisation method not stated • Parallel • Double blind • Not ITT • Compliance not assessed • Good group similarity
Participants	• Cadaveric transplants • Enrolled: At time of transplant • Immunosuppression: All CSA • Mean age: 43.5 years
Interventions	**Treatment group** • IV Hydergine 0.6 mg thrice daily then oral 4.5 mg thrice daily **Control group** • Placebo
Outcomes	• Death • Graft loss • Rejection • SBP

Vanrenterghem 1988 *(Continued)*

	• DBP All outcomes measure at 6 months
Notes	• Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	Withdrawals due to side effects similar numbers in each arm
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other cause of bias apparent

Venkat-Raman 1999

Methods	• Crossover, 8 weeks washout • Randomisation method not stated • Double blind • Not ITT (1 patient allocated to placebo and 2 to amlodipine (as first treatment) excluded for unclear reasons) • Compliance not assessed • Matching appearance of placebo and active arms • Good group similarity
Participants	• Age: 18-70 years • Enrolled: 3 months post-transplant • Stable SCr 2-7 µmol/L/kg • Sex M/F: 21/9 • Immunosuppression: All CSA Exclusion criteria: "clinically significant" disease, acute rejection previous 3 months
Interventions	**Treatment group** • Amlodipine 5 mg once daily

Venkat-Raman 1999 *(Continued)*

	Control group • Placebo
Outcomes	• DTPA GFR • Treatment withdrawal due to adverse events All outcomes measured at 2 months
Notes	• Funding source not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	Small numbers only withdrawn from each arms unlikely to bias outcome
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other apparent source of bias

Wagner 1986

Methods	• Parallel • Method of randomisation unclear • Unblinded • Good group similarity • ITT Unclear • 100% follow-up • Compliance not assessed
Participants	• Immunosuppression: All CSA • Number: Study 1(42), study 2 (21) • Mean age: 42.5 years • Enrolled: At time of transplant
Interventions	**Study 1**

Wagner 1986 *(Continued)*

	• IV Diltiazem pre-operatively • IV Diltiazem postoperatively, then oral 60 mg twice daily **Study 2** • IV Diltiazem postoperatively, then oral 60 mg twice daily **Control group (both studies)** • No treatment
Outcomes	• Graft loss (1, 2, 3, 4 years) • Rejection (first month)
Notes	• Three studies reported. Studies 1 and 2 are acceptable for this SR, study 3 is RCT of kidneys treated ex vivo only (with diltiazem and iloprost) and is excluded • The outcomes for study 1 and 2 are reported together so are entered here together • No funding statement

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear reasons for withdrawal
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias apparent

Wahlberg 1992

Methods	• Parallel • Randomisation method not mentioned • Unblinded • Unclear ITT • Follow-up unclear • Compliance not assessed • Group similarity good

Wahlberg 1992 *(Continued)*

Participants	• Cadaveric transplants • Immunosuppression: CAP • Mean age: 46 years • Enrolled: At time of transplant
Interventions	**Treatment group** • Preoperative IV diltiazem • Postoperative IV diltiazem then oral diltiazem 120 mg twice daily **Control group** • No treatment Cointerventions: CCB not allowed in control arm, otherwise cointerventions not mentioned Duration: 3 months
Outcomes	• Death • SCr • Rejection All outcomes measured at 3 months
Notes	• No funding statement

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Randomisation method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear ITT and loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias apparent

Wei 2002

Methods	• Parallel

Wei 2002 *(Continued)*

- Randomisation method unclear
- Blinding not stated
- ITT Unclear
- Follow-up unclear
- Compliance not assessed
- Group similarity unclear

Participants	• All CAN • enrolled: 2.8 years post-transplant • Mean SCr 309
Interventions	**Treatment group 1** • Candesartan 16-32 mg/d **Treatment group 2** • Amlodipine 5-10 mg/d Cointerventions: Non-ACEi antihypertensives used
Outcomes	• SCr (mean 13.6 months)
Notes	• Only published in abstract form (4 abstracts) • Different N in each abstract - seems to have only provided data on a subset in earlier abstracts, largest N taken for the results • Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Blinding unclear, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Unclear risk	No subjective outcomes
Incomplete outcome data addressed? All outcomes	Unclear risk	Unclear ITT and loss to follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other cause of bias identified

Weidanz 2005

Methods	• Parallel • Randomisation method unclear • Not blinded • ITT • 100% follow-up • Compliance not assessed • Group similarity good
Participants	• SCr > 27 µmol/L above baseline • Enrolled: 6 months post-transplant • Immunosuppression: CNI (14), sirolimus and CNI free (7)
Interventions	**Treatment group 1** • Losartan 25-100 mg/d twice daily **Treatment group 2** • Non-ARB antihypertensive
Outcomes	• Death • Graft loss • eGFR • BP All measured at 12 months
Notes	• Additional data supplied from author contact (B Becker, 4 August 2008) • Funding not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes not likely to be affected
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	BP observation could be confounded due to lack of blinding
Incomplete outcome data addressed? All outcomes	Low risk	100% follow-up
Free of selective reporting?	Low risk	
Free of other bias?	Low risk	

Wilkie 1993 CSA

Methods	• Crossover, 2 weeks washout • Double blind placebo • Randomisation method unclear • Not ITT 22/28 completed
Participants	• Stable function • Enrolled: > 1 year post-transplant • No CCB in prior 3 months • Immunosuppression: All CAP • Sex M/F: 9/6 • Age: 30-65 years • SCr 92-204
Interventions	**Treatment group** • Nifedipine SR 10 mg twice daily **Control group** • Placebo Duration: 4 weeks
Outcomes	• EDTA GFR • CrCl • SCr • BP (SBP, DBP, MAP) All outcomes measured at 4 weeks
Notes	• Two parallel groups reported for this study - those treated with CAP and those with AZA/Pred. As all data provided for both groups, two entries in RevMan • Industry funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	High risk	6/28 withdrew for reasons of side effects (4 in treatment arm), potential source of bias (unclear whether in CSA or non CSA strata)

Wilkie 1993 CSA *(Continued)*

Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other cause of bias identified

Wilkie 1993 No CNI

Methods	• Crossover, 2 weeks washout • Double blind placebo • Randomisation method unclear • Not ITT 22/28 completed
Participants	• Stable function • Enrolled: > 1 year post-transplant • No CCB in prior 3 months • Immunosuppression: All AZA/Pred • Sex M/F: 9/6 • Age: 30-65 years • SCr 92-204
Interventions	**Treatment group** • Nifedipine SR 10 mg twice daily **Control group** • Placebo Duration: 4 weeks
Outcomes	• EDTA GFR • CrCl • SCr • BP (SBP, DBP, MAP) All outcomes measured at 4 weeks
Notes	• Two parallel groups reported for this study - those treated with CAP and those with AZA/Pred. As all data provided for both groups, two entries in RevMan • Industry funding

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding?	Low risk	Double blind

Wilkie 1993 No CNI *(Continued)*

Subjective outcomes (e.g. blood pressure measurement)		
Incomplete outcome data addressed? All outcomes	High risk	6/28 withdrew for reasons of side effects (4 in treatment arm), potential source of bias (unclear whether in CSA or non CSA strata)
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias identified

Wilkie 1994

Methods	• Parallel • Double blind • Computer minimisation randomisation • Placebo • ITT • 100% follow-up • Compliance check with tablet count • Good group similarity
Participants	• Age: 16-65 years • Immunosuppression: All CAP • Enrolled: At time of transplant • All cadaveric • Mean age: 44 years • Sex M/F: 18/16 Exclusion criteria: Intolerance or prior CCB use, PRA > 90%, BP < 100/60
Interventions	**Treatment group** • Nifedipine SR 20 mg twice daily **Control group** • Placebo Cointerventions: No CCB allowed for BP Duration: 3 months
Outcomes	• CrCl • MAP • GFR • Graft loss • Death Outcomes measured at 3 and 6 months (intervention only given for 3 months)
Notes	• 3rd arm not included as 48 hours only nifedipine exposure (numbers and mean age refer to two included arm only)

Wilkie 1994 *(Continued)*

- Industry funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Randomisation method unclear
Allocation concealment?	Unclear risk	Concealment method unclear
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Double blind
Blinding? Subjective outcomes (e.g. blood pressure measurement)	Low risk	Double blind
Incomplete outcome data addressed? All outcomes	Low risk	ITT and 100% follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias apparent

Yildiz 2001

Methods	• Parallel • Not blinded • Opaque envelope randomisation • ITT • 100% follow-up • Compliance not assessed • Good group similarity
Participants	• HCT > 50% • Enrolled: Mean 12.5 months post-transplant • Immunosuppression: CSA (25/27), AZA/Pred (2/27) Exclusion criteria: Heavy smokers, APKD, RAS
Interventions	**Treatment group 1** • Enalapril 10 mg/d **Treatment group 2** • Losartan 50 mg/d
Outcomes	• Effective reduction in Hb (decrease at least 10 g/L) • SBP • SCr

Yildiz 2001 *(Continued)*

	• SK • HCT • Change in Hb All outcomes measured at 8 weeks
Notes	• Funding by Turkish Kidney Foundation

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Random envelope selection
Allocation concealment?	Low risk	Opaque envelopes
Blinding? Objective outcomes (e.g. death, graft loss)	Low risk	Unblinded, but objective outcomes unlikely to be biased
Blinding? Subjective outcomes (e.g. blood pressure measurement)	High risk	Unblinded, subjective outcomes at risk of bias
Incomplete outcome data addressed? All outcomes	Low risk	ITT, 100% follow-up
Free of selective reporting?	Unclear risk	No protocol available, unclear what outcomes prespecified if any
Free of other bias?	Low risk	No other source of bias apparent

AB - alpha-blocker; ACEi - angiotensin-converting enzyme inhibitors; APKD- autosomal polycystic kidney disease; ALG - antilymphocyte globulin; AP - azathioprine and prednisone; ARB - angiotensin receptor blockers; ATG - antithymocyte globulin; ATN - acute tubular necrosis; AZA - azathioprine; BB - beta-blocker; BP - blood pressure; CAN - chronic allograft nephropathy; CAP - CSA, AZA and Pred; CCB - calcium channel blockers; CHF - chronic heart failure; CMP - CSA, methylprednisolone; CNI - calcineurin inhibitor; COPD - chronic obstructive pulmonary disease; CR - controlled release; CrCl - creatinine clearance; CSA - cyclosporin A; CVA - cerebrovascular accident; DBP - diastolic BP; DM - diabetes mellitus; ER - extended release; GFR - glomerular filtration rate; Hb - haemoglobin; HCT - haematocrit; LVH - left ventricular hypertrophy; MI - myocardial infarction; MMF - mycophenolate mofetil; PRA - panel reactive antibodies; Pred - prednisone; RAS - renal artery stenosis; SBP - systolic BP; SCr - serum creatinine; SK - serum potassium; SPK - simultaneous pancreas-kidney; SR - sustained release; TAC - tacrolimus

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Alexander 2005	Wrong intervention
Almeshari 2000	No usable outcomes (no SD reported for continuous outcomes) - author contact failed
Aros 2005	No usable outcomes (mentions "no difference" in outcomes but doesn't provide them) - author contact failed

Study	Reason for exclusion
Bailey 1982	Not RCT
Bewick 1974	Not RCT
Borchhardt 1997	Not RCT
Bourbigot 1990	Wrong intervention, same class both arms
Branten 1998	Not RCT
Calo 2002	No relevant outcomes reported
Carozzi 1995	Not RCT
Cartier 1978	No relevant outcomes reported
Castelao 1993 HT ACE	Not RCT. Patients with proteinuria allocated to ACEi arm
Christians 1996	Wrong intervention, intervention < 2 weeks (1 week)
Cieciura 2000	Not RCT
Citterio 1996	Wrong intervention, intervention < 2 weeks (10 days)
Colak 2001	Not RCT
Curtis 1993	Wrong Intervention, intervention < 2 weeks
D'Amelio 1997	Not RCT
Dawidson 1989	Intervention < 2 weeks
Dawidson 1994	Not RCT
Dominguez-Gil 2002	Not RCT
Donmez 1999	Intervention < 2 weeks
Duggan 1985	Wrong population (intervention applied only to donor pretransplant)
Erken 1993	Not RCT
Ferguson 1994	Not RCT
Hadjigavriel 1999	Not RCT
Hetzel 2004	Not RCT
Hortal 1998	Not RCT
Inigo 1999	Not RCT
Ishikawa 2003	Not RCT (unclear in publication, authors not contactable)
Ishikawa 2005	Not RCT

Study	Reason for exclusion
Javid 1999	Not RCT
Kamper 2001	Crossover study, inadequate washout (control observations include data from 1 week after stopping treatment)
Kauffman 1980	Wrong intervention (not antihypertensive agent)
Kim 2002b	Not RCT (appears not, author contact failed)
Koller 1988	Wrong population (donor intervention)
Konstadinidou 1997	Two ACEi compared, therefore same intervention to both arms. No doses provided.
Kunzendorf 1987	Not RCT
Kupin 1997	Not RCT
Lal 1995	Not RCT
Leeman 1993	Both arms included only beta-blockers
Logan 2005	Not RCT
MacKinnon 2005	Not RCT
Madsen 1995a	Two studies reported: first study intervention < 2 weeks, second study wrong population (dermatology patients)
Markell 1990	Not RCT
McCune 2005	Wrong intervention
Mezzano 1998	Not RCT
Montanaro 2000	Not RCT
Montanaro 2005	Not RCT
Mourad 1997	Not RCT
Nanni 2000	Wrong intervention, intervention < 2 weeks (10 days)
Neumayer 1988	Wrong intervention, kidneys treated ex vivo prior to transplantation only
Niyamathullah 1989	Wrong intervention, not antihypertensive agent
Noel 1997	Wrong intervention, not antihypertensive agent
Ogborn 1989	Not RCT
Okuno 1997	Wrong intervention, not antihypertensive agent
Opelz 1996	Not RCT
Oppenheimer 1995	Not RCT

Study	Reason for exclusion
Orlic 2006	Not RCT
Paczek 1995	Not RCT
Pisani 1994	Not RCT
Ploeg 1990	Wrong intervention, not antihypertensive agent
Po 1993	Not RCT, both arms ACEi at differing doses
Po 1994	Not RCT
Podobinska 1995	Not RCT
Polyak 1998	Wrong intervention, not antihypertensive agent
Porras 1992	Wrong intervention, not antihypertensive agent
Puig 1991	Wrong intervention, intervention < 2 weeks
Rhee 1996	Not RCT
Richards 1989	Wrong intervention, not antihypertensive agent
Riggio 1992	No useable outcomes
Rogan 2000 HT	Both interventions the same drug class
Roy 1989	Wrong intervention, intervention < 2 weeks
Ruggenenti 1993	Not RCT
SECRET 2004	Terminated early, outcomes not adequately reported (unclear numbers in each group). No response from authors after emailing
Shin 1996	Not RCT
Sobh 1989	Wrong intervention, treated donor and one dose to recipient
Sorensen 1991	Wrong intervention, intervention < 2 weeks
Spieker 1991	Wrong intervention, intervention < 2 weeks
Spieker 1993	Wrong population, not kidney transplant recipients
Stempel 1993	Not RCT
Suh 1996	Not RCT
Tenschert 1991	Wrong intervention, intervention < 2 weeks
Tsang 1998	Not RCT
Venkat-Raman 1998	Wrong intervention, both arms same class of antihypertensive

Study	Reason for exclusion
Wlodarczyk 2000	Wrong intervention, not antihypertensive agent
Zhang 2005	Wrong intervention, not antihypertensive agent

DATA AND ANALYSES

Comparison 1. CCB versus placebo/no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any blood pressure (BP) measure at last follow-up	10		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Systolic BP (mm Hg)	8	478	Mean Difference (IV, Random, 95% CI)	-6.56 [-11.20, -1.92]
1.2 Mean arterial pressure (MAP) (mm Hg)	2	112	Mean Difference (IV, Random, 95% CI)	0.28 [-4.61, 5.18]
2 Death at last follow-up	12	792	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.37, 1.82]
3 Graft loss at last follow-up	17	1255	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.57, 0.99]
4 Any rejection at last follow-up	11	771	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.85, 1.23]
5 Rejection rate	4		Rate Ratio (Random, 95% CI)	Subtotals only
5.1 Proven or suspected	4		Rate Ratio (Random, 95% CI)	0.88 [0.64, 1.20]
5.2 Cellular: interstitial	1		Rate Ratio (Random, 95% CI)	1.02 [0.64, 1.63]
5.3 Cellular: vascular	1		Rate Ratio (Random, 95% CI)	0.27 [0.08, 0.96]
6 Any GFR measure at last follow-up	18	1119	Mean Difference (IV, Random, 95% CI)	4.45 [2.22, 6.68]
6.1 Creatinine clearance (mL/min)	7	586	Mean Difference (IV, Random, 95% CI)	3.62 [-1.63, 8.88]
6.2 Measured GFR (mL/min/1.73 m^2 or mL/min)	11	533	Mean Difference (IV, Random, 95% CI)	4.77 [1.92, 7.63]
7 Serum creatinine (µmol/L) at last follow-up	20		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 All studies	20	1174	Mean Difference (IV, Random, 95% CI)	-7.58 [-15.79, 0.63]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Sensitivity analysis - Pirsch removed	19	1140	Mean Difference (IV, Random, 95% CI)	-10.13 [-17.32, -2.93]
7.3 Sensitivity analysis - Pirsch Rahn NT, van der Schaaf removed	17	991	Mean Difference (IV, Random, 95% CI)	-10.01 [-18.24, -1.77]
8 Haematocrit (%) at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9 Withdrawal due to side effects	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 Withdrawal by 2-3 months	2	156	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.53, 1.87]
10 Proteinuria (g/24 h) at last follow-up	2	90	Mean Difference (IV, Random, 95% CI)	0.03 [-0.25, 0.32]
11 Myocardial infarction at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12 New onset hypertension	4	241	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.65, 1.01]
12.1 At 1 month	1	54	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.51, 2.48]
12.2 At 3 months	1	97	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.59, 1.03]
12.3 At 1 year	2	90	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.55, 1.19]
13 Systolic blood pressure (mm Hg)	8	478	Mean Difference (IV, Random, 95% CI)	-6.56 [-11.20, -1.92]
13.1 At 1-3 months	6	225	Mean Difference (IV, Random, 95% CI)	-7.14 [-13.76, -0.52]
13.2 At 2 years	2	253	Mean Difference (IV, Random, 95% CI)	-4.93 [-10.81, 0.94]
14 Diastolic blood pressure (mm Hg)	8		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 At 1-3 months	6	225	Std. Mean Difference (IV, Random, 95% CI)	-0.38 [-0.76, 0.00]
14.2 At 2 years	2	253	Std. Mean Difference (IV, Random, 95% CI)	-0.38 [-0.75, -0.02]
15 Mean arterial pressure (mm Hg)	7	483	Mean Difference (IV, Random, 95% CI)	-2.48 [-6.01, 1.04]
15.1 At 1-3 months	4	118	Mean Difference (IV, Random, 95% CI)	-1.70 [-10.52, 7.11]
15.2 At 6-12 months	1	34	Mean Difference (IV, Random, 95% CI)	-3.0 [-12.41, 6.41]

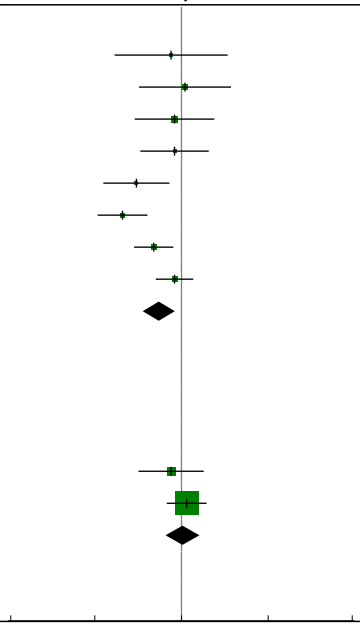
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
15.3 At 2 years	3	331	Mean Difference (IV, Random, 95% CI)	-2.61 [-6.41, 1.20]
16 Death	12		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
16.1 At 1 month	1	30	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
16.2 At 3 months	4	202	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.11, 2.54]
16.3 At 1 year	5	413	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.12, 3.51]
16.4 At 2 years	1	97	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.18, 3.24]
16.5 At 3 years	2	147	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.06, 13.95]
16.6 At 5 years	1	97	Risk Ratio (M-H, Random, 95% CI)	3.19 [0.34, 29.62]
17 Graft loss	17		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
17.1 At 1 month	2	84	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.07, 15.18]
17.2 At 3-4 months	5	192	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.18, 2.87]
17.3 At 6 months	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
17.4 At 1 year	11	830	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.37, 0.87]
17.5 At 2 years	2	316	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.17, 1.11]
17.6 At 3 years	3	344	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.45, 1.15]
17.7 At 4 years	1	63	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.34, 1.77]
17.8 At 5 years	3	311	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.50, 1.16]
18 Any rejection	11		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 At 1 month	2	83	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.43, 1.42]
18.2 At 2 months	1	53	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.50, 1.43]
18.3 At 3-4 months	5	189	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.76, 1.35]
18.4 At 6 months	1	111	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.26, 3.73]
18.5 At 1 year	2	270	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.80, 1.41]
18.6 At 2 years	1	118	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.61, 2.92]
19 GFR (mL/min or mL/min/1.73 m^2)	18		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
19.1 Cockcroft-Gault: 1-3 months	1	118	Mean Difference (IV, Random, 95% CI)	6.0 [-0.14, 12.14]
19.2 Creatinine clearance: 1-3 months	8	400	Mean Difference (IV, Random, 95% CI)	4.17 [-2.20, 10.54]
19.3 Measured GFR: 1-3 months	9	405	Mean Difference (IV, Random, 95% CI)	4.04 [0.69, 7.38]
19.4 Cockcroft-Gault: 6-12 months	1	118	Mean Difference (IV, Random, 95% CI)	9.30 [1.94, 16.66]
19.5 Creatinine clearance: 6-12 months	4	378	Mean Difference (IV, Random, 95% CI)	10.52 [4.60, 16.44]
19.6 Measured GFR: 6-12 months	2	140	Mean Difference (IV, Random, 95% CI)	6.64 [1.27, 12.02]
19.7 Cockcroft-Gault: 2 years	1	118	Mean Difference (IV, Random, 95% CI)	8.40 [0.84, 15.96]
19.8 Creatinine clearance: 2 years	4	468	Mean Difference (IV, Random, 95% CI)	6.97 [-0.02, 13.95]
19.9 Measured GFR: 2 years	3	234	Mean Difference (IV, Random, 95% CI)	5.53 [1.61, 9.45]
19.10 Creatinine clearance: 5 years	1	97	Mean Difference (IV, Random, 95% CI)	11.30 [1.32, 21.28]
20 Serum creatinine (µmol/L)	20		Mean Difference (IV, Random, 95% CI)	Subtotals only
20.1 At 1-3 months	17	852	Mean Difference (IV, Random, 95% CI)	-6.35 [-15.49, 2.80]
20.2 At 6-12 months	5	389	Mean Difference (IV, Random, 95% CI)	-11.07 [-32.17, 10.03]
20.3 At 2 years	5	546	Mean Difference (IV, Random, 95% CI)	-24.19 [-30.80, -17.57]
20.4 At 3 years	1	97	Mean Difference (IV, Random, 95% CI)	-35.0 [-48.45, -21.55]
20.5 At 5 years	2	127	Mean Difference (IV, Random, 95% CI)	-17.44 [-32.23, -2.65]
21 Proteinuria (g/24 h)	2	90	Mean Difference (IV, Random, 95% CI)	0.03 [-0.25, 0.32]
21.1 At 1 month	1	40	Mean Difference (IV, Random, 95% CI)	0.05 [-0.32, 0.42]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
21.2 At 3 years	1	50	Mean Difference (IV, Random, 95% CI)	0.01 [-0.43, 0.45]

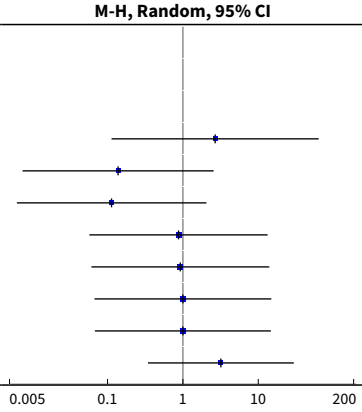
Analysis 1.1. Comparison 1 CCB versus placebo/no treatment, Outcome 1 Any blood pressure (BP) measure at last follow-up.

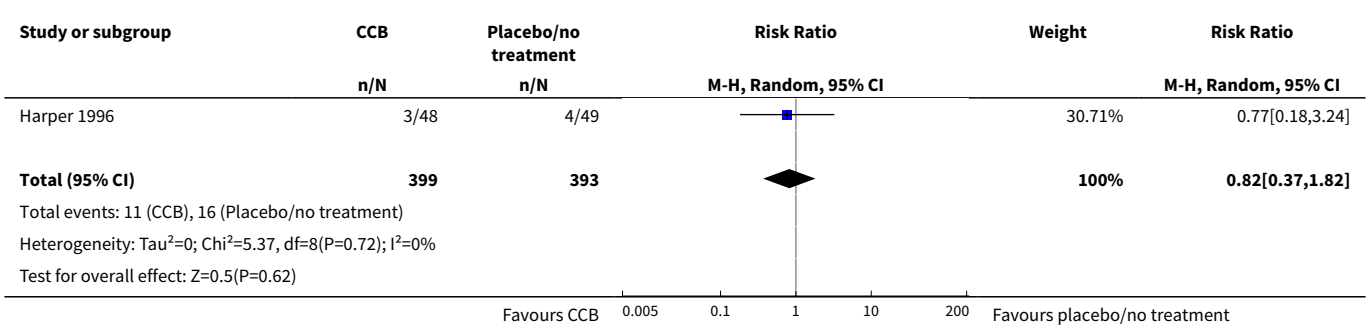
Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 Systolic BP (mm Hg)							
Wilkie 1993 No CNI	7	131 (17)	7	134 (14)		6.09%	-3[-19.31,13.31]
Wilkie 1993 CSA	15	152 (17)	15	151 (20)		8.17%	1[-12.28,14.28]
Guerin 1989	13	136 (17)	12	138 (12)		9.85%	-2[-13.47,9.47]
Venkat-Raman 1999	27	139 (18)	27	141 (19)		11.67%	-2[-11.87,7.87]
Madsen 1998	30	131 (16)	32	144 (22)		12.1%	-13[-22.53,-3.47]
Van der Schaaf 1995	20	148 (10)	20	165 (13)		15.52%	-17[-24.19,-9.81]
Rahn 1999 NT	57	133 (14)	52	141 (16)		18.07%	-8[-13.67,-2.33]
Rahn 1999 HT	73	142 (16)	71	144 (17)		18.54%	-2[-7.4,3.4]
Subtotal ***	**242**		**236**			**100%**	**-6.56[-11.2,-1.92]**
Heterogeneity: Tau²=22.62; Chi²=15.69, df=7(P=0.03); I²=55.37%							
Test for overall effect: Z=2.77(P=0.01)							
1.1.2 Mean arterial pressure (MAP) (mm Hg)							
Wilkie 1994	17	110 (14)	17	113 (14)		27.05%	-3[-12.41,6.41]
Harper 1996	42	103.9 (11.7)	36	102.4 (13.8)		72.95%	1.5[-4.23,7.23]
Subtotal ***	**59**		**53**			**100%**	**0.28[-4.61,5.18]**
Heterogeneity: Tau²=0; Chi²=0.64, df=1(P=0.42); I²=0%							
Test for overall effect: Z=0.11(P=0.91)							



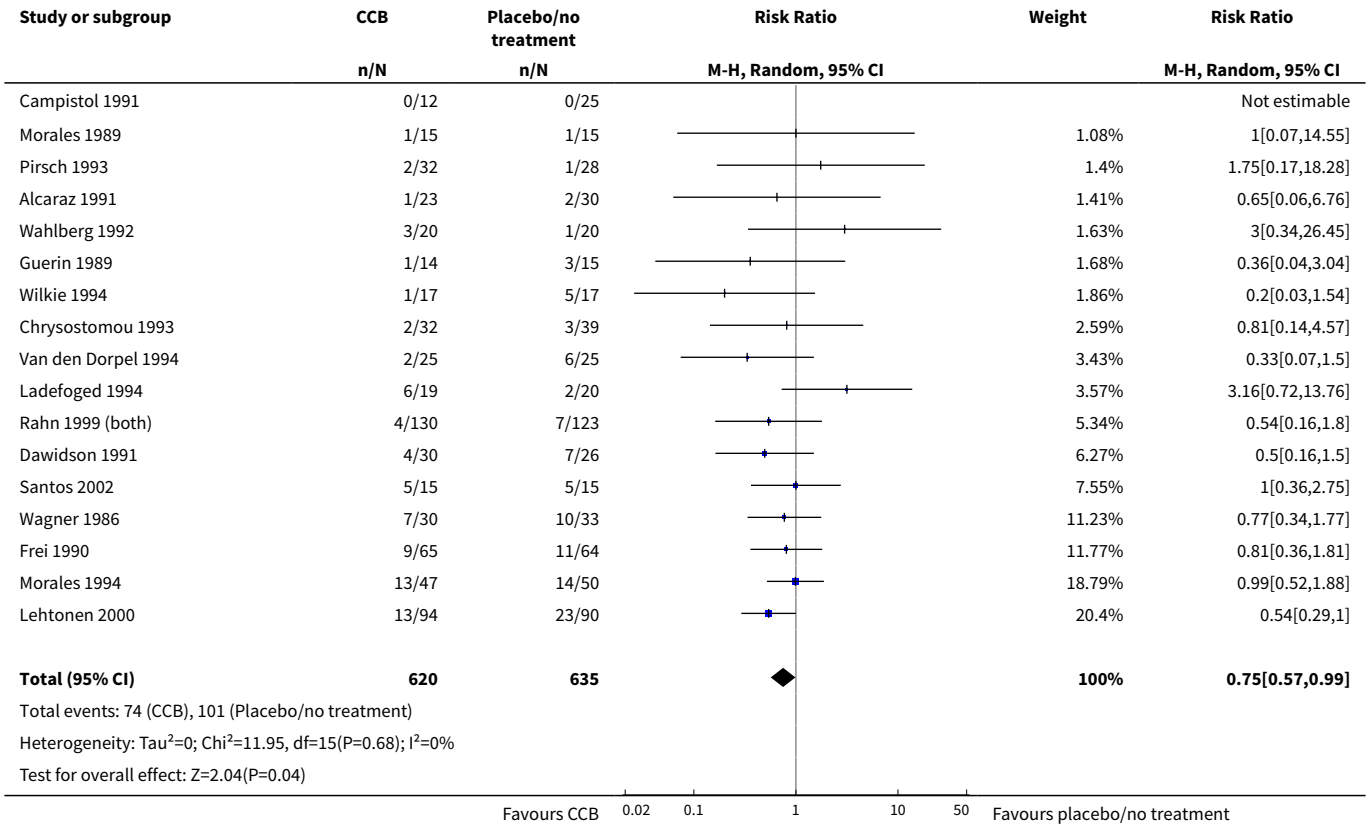
Analysis 1.2. Comparison 1 CCB versus placebo/no treatment, Outcome 2 Death at last follow-up.

Study or subgroup	CCB n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Morales 1989	0/15	0/15			Not estimable
Guerin 1989	0/14	0/15			Not estimable
Frei 1990	0/65	0/64			Not estimable
Patton 1994	1/36	0/32		6.38%	2.68[0.11,63.45]
Dawidson 1991	0/30	3/29		7.5%	0.14[0.01,2.56]
Madsen 1998	0/49	4/50		7.63%	0.11[0.01,2.05]
Pirsch 1993	1/32	1/28		8.61%	0.88[0.06,13.35]
Rump 2000	1/26	1/24		8.67%	0.92[0.06,13.95]
Wahlberg 1992	1/20	1/20		8.76%	1[0.07,14.9]
Wilkie 1994	1/17	1/17		8.84%	1[0.07,14.72]
Morales 1994	3/47	1/50		12.89%	3.19[0.34,29.62]

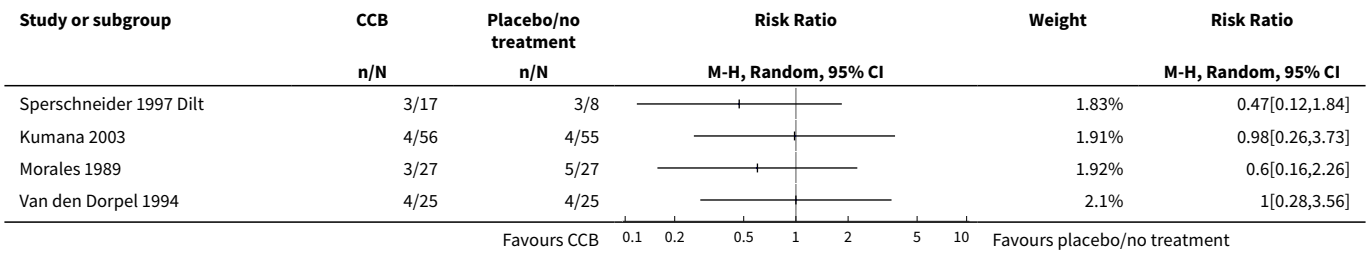




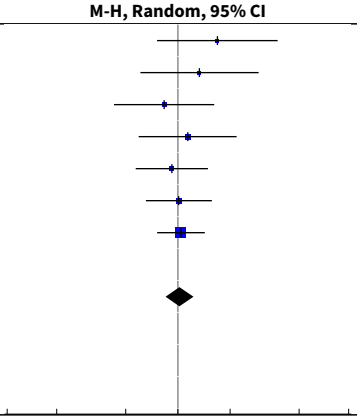
Analysis 1.3. Comparison 1 CCB versus placebo/no treatment, Outcome 3 Graft loss at last follow-up.



Analysis 1.4. Comparison 1 CCB versus placebo/no treatment, Outcome 4 Any rejection at last follow-up.



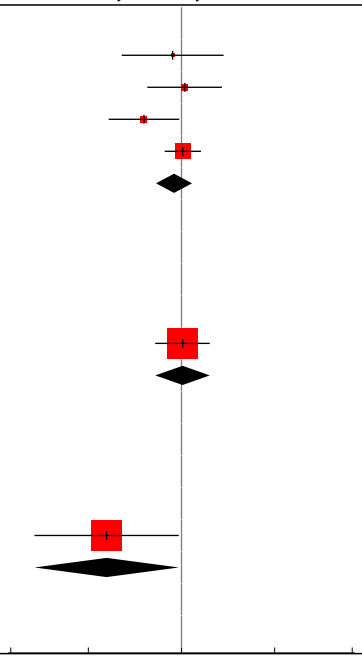
Study or subgroup	CCB	Placebo/no treatment	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Sperschneider 1997 Nifed	9/12	4/9		5.3%	1.69[0.76,3.76]
Kuypers 2004	12/59	9/59		5.51%	1.33[0.61,2.92]
Guerin 1989	7/14	9/15		7.63%	0.83[0.43,1.62]
Pirsch 1993	13/32	10/28		8.04%	1.14[0.59,2.18]
Wahlberg 1992	12/20	13/20		14.67%	0.92[0.57,1.49]
Alcaraz 1991	14/23	18/30		17.62%	1.01[0.65,1.57]
Van Riemsdijk 2000	42/98	46/112		33.46%	1.04[0.76,1.43]
Total (95% CI)	**383**	**388**		**100%**	**1.02[0.85,1.23]**
Total events: 123 (CCB), 125 (Placebo/no treatment)					
Heterogeneity: Tau^2=0; Chi^2=4.47, df=10(P=0.92); I^2=0%					
Test for overall effect: Z=0.22(P=0.82)					



Favours CCB — Favours placebo/no treatment

Analysis 1.5. Comparison 1 CCB versus placebo/no treatment, Outcome 5 Rejection rate.

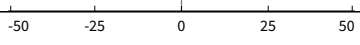
Study or subgroup	CCB	Placebo/no treatment	log[Rate Ratio]	Rate Ratio	Weight	Rate Ratio
	N	N	(SE)	IV, Random, 95% CI		IV, Random, 95% CI
1.5.1 Proven or suspected						
Campistol 1991	1	1	-0.2 (0.449)		11.08%	0.86[0.36,2.07]
Wahlberg 1992	1	1	0.1 (0.329)		18.83%	1.06[0.55,2.01]
Wagner 1986	1	1	-0.6 (0.311)		20.55%	0.52[0.28,0.96]
Chrysostomou 1993	1	1	0 (0.159)		49.55%	1.02[0.75,1.4]
Subtotal (95% CI)					**100%**	**0.88[0.64,1.2]**
Heterogeneity: Tau^2=0.03; Chi^2=3.92, df=3(P=0.27); I^2=23.54%						
Test for overall effect: Z=0.82(P=0.41)						
1.5.2 Cellular: interstitial						
Chrysostomou 1993	1	1	0 (0.241)		100%	1.02[0.64,1.63]
Subtotal (95% CI)					**100%**	**1.02[0.64,1.63]**
Heterogeneity: Not applicable						
Test for overall effect: Z=0.07(P=0.94)						
1.5.3 Cellular: vascular						
Chrysostomou 1993	1	1	-1.3 (0.636)		100%	0.27[0.08,0.96]
Subtotal (95% CI)					**100%**	**0.27[0.08,0.96]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.03(P=0.04)						



Favours CCB — Favours placebo/no treatment

Analysis 1.6. Comparison 1 CCB versus placebo/no treatment, Outcome 6 Any GFR measure at last follow-up.

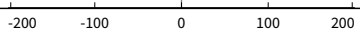
Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.6.1 Creatinine clearance (mL/min)							
Ladefoged 1994	13	43 (21.6)	18	46 (25.5)		1.8%	-3[-19.63,13.63]
Van den Dorpel 1994	18	66.1 (19.1)	18	55.6 (26.3)		2.21%	10.5[-4.52,25.52]
Frei 1990	65	71 (37)	64	64 (36)		3.14%	7[-5.6,19.6]
Wahlberg 1992	20	36.6 (12.3)	20	45.6 (22)		4.08%	-9[-20.05,2.05]
Morales 1994	47	79.2 (27)	50	67.9 (22.8)		5.01%	11.3[1.32,21.28]
Rahn 1999 NT	57	-1.4 (20.4)	52	-1.4 (18.7)		9.25%	0[-7.34,7.34]
Rahn 1999 HT	73	1 (19.7)	71	-6 (17.7)		13.33%	7[0.89,13.11]
Subtotal ***	**293**		**293**			**38.81%**	**3.62[-1.63,8.88]**
Heterogeneity: Tau^2=21.52; Chi^2=11.06, df=6(P=0.09); I^2=45.75%							
Test for overall effect: Z=1.35(P=0.18)							
1.6.2 Measured GFR (mL/min/1.73 m² or mL/min)							
Wilkie 1993 No CNI	7	85 (27)	7	89 (32)		0.52%	-4[-35.02,27.02]
Wilkie 1994	17	64 (25)	17	64 (25)		1.76%	0[-16.81,16.81]
Wilkie 1993 CSA	15	64 (19)	15	65 (21)		2.43%	-1[-15.33,13.33]
Rump 2000	24	47 (19.6)	26	49 (30.6)		2.49%	-2[-16.14,12.14]
Van der Schaaf 1995	20	54 (20)	20	49 (16)		3.95%	5[-6.22,16.22]
Venkat-Raman 1999	23	49 (20)	23	47 (15)		4.77%	2[-8.22,12.22]
Guerin 1989	12	34 (15)	12	33 (10)		4.79%	1[-9.2,11.2]
Gossmann 2002	31	54.9 (21.5)	29	48.3 (18.7)		4.81%	6.6[-3.58,16.78]
Madsen 1998	27	49 (18)	24	40 (16)		5.72%	9[-0.33,18.33]
Kuypers 2004	53	50.1 (16.2)	53	42 (15.4)		13.76%	8.1[2.08,14.12]
Harper 1996	42	43.9 (12.3)	36	39.4 (12.6)		16.19%	4.5[-1.05,10.05]
Subtotal ***	**271**		**262**			**61.19%**	**4.77[1.92,7.63]**
Heterogeneity: Tau^2=0; Chi^2=5.03, df=10(P=0.89); I^2=0%							
Test for overall effect: Z=3.28(P=0)							
Total ***	**564**		**555**			**100%**	**4.45[2.22,6.68]**
Heterogeneity: Tau^2=0; Chi^2=16.22, df=17(P=0.51); I^2=0%							
Test for overall effect: Z=3.91(P<0.0001)							
Test for subgroup differences: Chi^2=0.13, df=1 (P=0.72), I^2=0%							



Favours placebo/no treatment — Favours CCB

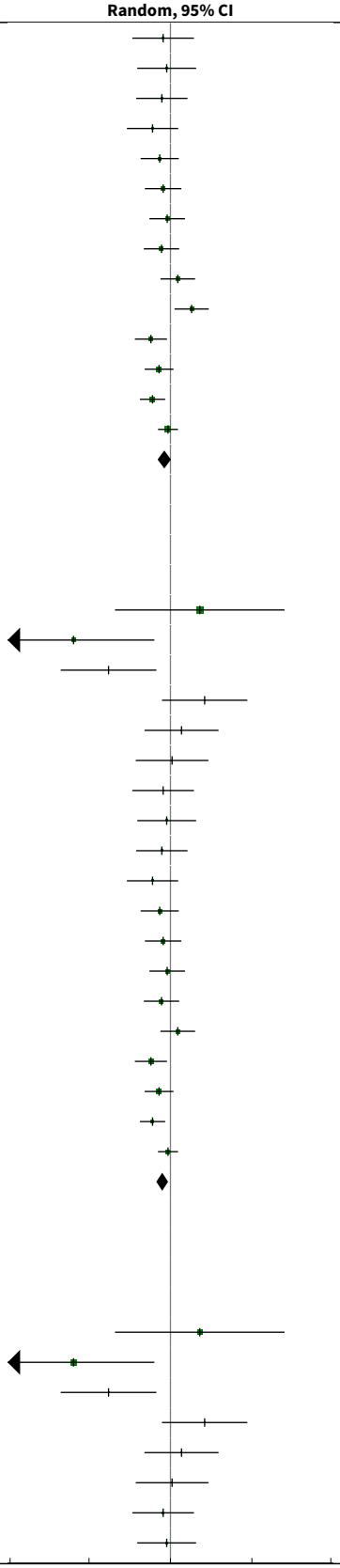
Analysis 1.7. Comparison 1 CCB versus placebo/no treatment, Outcome 7 Serum creatinine (µmol/L) at last follow-up.

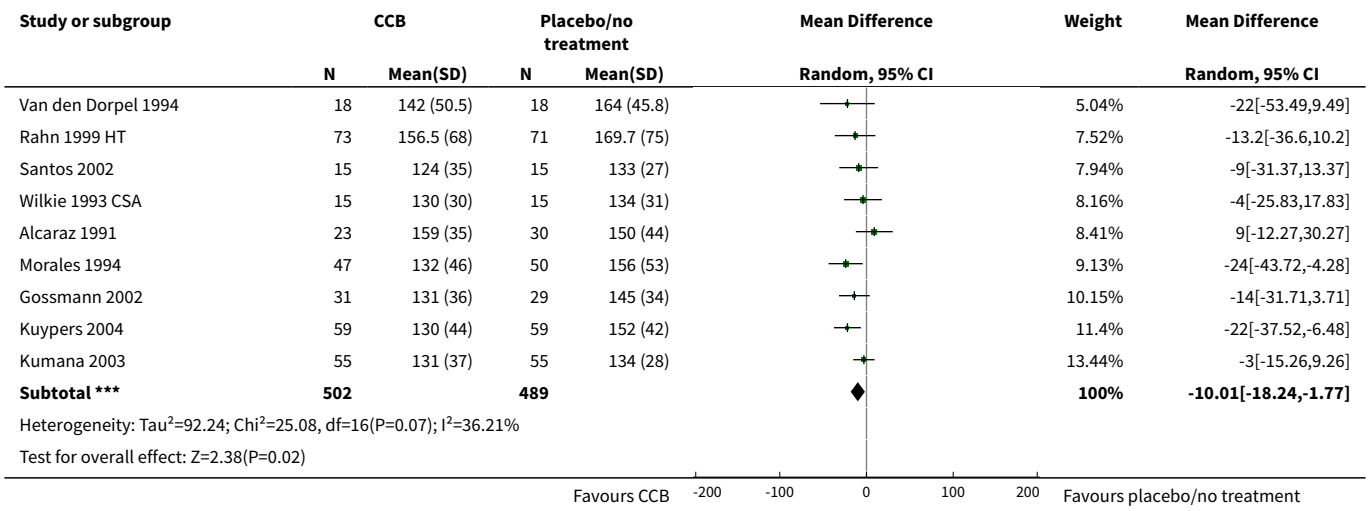
Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.7.1 All studies							
Ladefoged 1994	13	225 (169)	18	189 (106)		0.59%	36[-68.1,140.1]
Morales 1989	27	150 (88)	27	269 (248)		0.65%	-119[-218.26,-19.74]
Harper 1996	42	191 (104)	36	267 (152)		1.69%	-76[-134.78,-17.22]
Wahlberg 1992	20	192 (104)	20	150 (59)		2.06%	42[-10.4,94.4]
Sperschneider 1997 Nifed	17	153.4 (73.4)	8	139.8 (42.1)		2.59%	13.6[-31.88,59.08]
Wilkie 1993 No CNI	7	104 (45)	7	102 (40)		2.67%	2[-42.6,46.6]



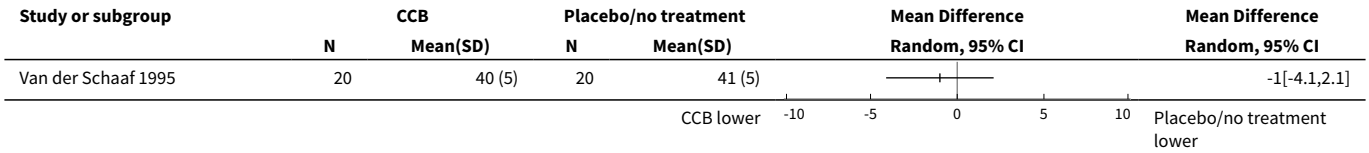
Favours CCB — Favours placebo/no treatment

Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Venkat-Raman 1999	23	168 (65)	23	177 (66)		3.43%	-9[-46.86,28.86]
Sperschneider 1997 Dilt	17	135.2 (44.9)	8	139.8 (42.1)		3.67%	-4.6[-40.75,31.55]
Rahn 1999 NT	57	137.9 (58)	52	148.5 (102)		4.41%	-10.6[-42.15,20.95]
Van den Dorpel 1994	18	142 (50.5)	18	164 (45.8)		4.42%	-22[-53.49,9.49]
Rahn 1999 HT	73	156.5 (68)	71	169.7 (75)		6.24%	-13.2[-36.6,10.2]
Santos 2002	15	124 (35)	15	133 (27)		6.53%	-9[-31.37,13.37]
Wilkie 1993 CSA	15	130 (30)	15	134 (31)		6.68%	-4[-25.83,17.83]
Van der Schaaf 1995	20	139 (35)	20	150 (35)		6.72%	-11[-32.69,10.69]
Alcaraz 1991	23	159 (35)	30	150 (44)		6.84%	9[-12.27,30.27]
Pirsch 1993	17	150 (27)	17	124 (35)		6.92%	26[4.99,47.01]
Morales 1994	47	132 (46)	50	156 (53)		7.32%	-24[-43.72,-4.28]
Gossmann 2002	31	131 (36)	29	145 (34)		7.97%	-14[-31.71,3.71]
Kuypers 2004	59	130 (44)	59	152 (42)		8.72%	-22[-37.52,-6.48]
Kumana 2003	55	131 (37)	55	134 (28)		9.87%	-3[-15.26,9.26]
Subtotal * **	**596**		**578**			**100%**	**-7.58[-15.79,0.63]**
Heterogeneity: Tau²=138.64; Chi²=35.64, df=19(P=0.01); I²=46.69%							
Test for overall effect: Z=1.81(P=0.07)							
1.7.2 Sensitivity analysis - Pirsch removed							
Ladefoged 1994	13	225 (169)	18	189 (106)		0.47%	36[-68.1,140.1]
Morales 1989	27	150 (88)	27	269 (248)		0.51%	-119[-218.26,-19.74]
Harper 1996	42	191 (104)	36	267 (152)		1.4%	-76[-134.78,-17.22]
Wahlberg 1992	20	192 (104)	20	150 (59)		1.73%	42[-10.4,94.4]
Sperschneider 1997 Nifed	17	153.4 (73.4)	8	139.8 (42.1)		2.24%	13.6[-31.88,59.08]
Wilkie 1993 No CNI	7	104 (45)	7	102 (40)		2.32%	2[-42.6,46.6]
Venkat-Raman 1999	23	168 (65)	23	177 (66)		3.09%	-9[-46.86,28.86]
Sperschneider 1997 Dilt	17	135.2 (44.9)	8	139.8 (42.1)		3.34%	-4.6[-40.75,31.55]
Rahn 1999 NT	57	137.9 (58)	52	148.5 (102)		4.18%	-10.6[-42.15,20.95]
Van den Dorpel 1994	18	142 (50.5)	18	164 (45.8)		4.19%	-22[-53.49,9.49]
Rahn 1999 HT	73	156.5 (68)	71	169.7 (75)		6.54%	-13.2[-36.6,10.2]
Santos 2002	15	124 (35)	15	133 (27)		6.95%	-9[-31.37,13.37]
Wilkie 1993 CSA	15	130 (30)	15	134 (31)		7.18%	-4[-25.83,17.83]
Van der Schaaf 1995	20	139 (35)	20	150 (35)		7.24%	-11[-32.69,10.69]
Alcaraz 1991	23	159 (35)	30	150 (44)		7.43%	9[-12.27,30.27]
Morales 1994	47	132 (46)	50	156 (53)		8.17%	-24[-43.72,-4.28]
Gossmann 2002	31	131 (36)	29	145 (34)		9.27%	-14[-31.71,3.71]
Kuypers 2004	59	130 (44)	59	152 (42)		10.66%	-22[-37.52,-6.48]
Kumana 2003	55	131 (37)	55	134 (28)		13.1%	-3[-15.26,9.26]
Subtotal * **	**579**		**561**			**100%**	**-10.13[-17.32,-2.93]**
Heterogeneity: Tau²=63.84; Chi²=25.09, df=18(P=0.12); I²=28.26%							
Test for overall effect: Z=2.76(P=0.01)							
1.7.3 Sensitivity analysis - Pirsch Rahn NT, van der Schaaf removed							
Ladefoged 1994	13	225 (169)	18	189 (106)		0.61%	36[-68.1,140.1]
Morales 1989	27	150 (88)	27	269 (248)		0.66%	-119[-218.26,-19.74]
Harper 1996	42	191 (104)	36	267 (152)		1.78%	-76[-134.78,-17.22]
Wahlberg 1992	20	192 (104)	20	150 (59)		2.19%	42[-10.4,94.4]
Sperschneider 1997 Nifed	17	153.4 (73.4)	8	139.8 (42.1)		2.8%	13.6[-31.88,59.08]
Wilkie 1993 No CNI	7	104 (45)	7	102 (40)		2.89%	2[-42.6,46.6]
Venkat-Raman 1999	23	168 (65)	23	177 (66)		3.79%	-9[-46.86,28.86]
Sperschneider 1997 Dilt	17	135.2 (44.9)	8	139.8 (42.1)		4.08%	-4.6[-40.75,31.55]

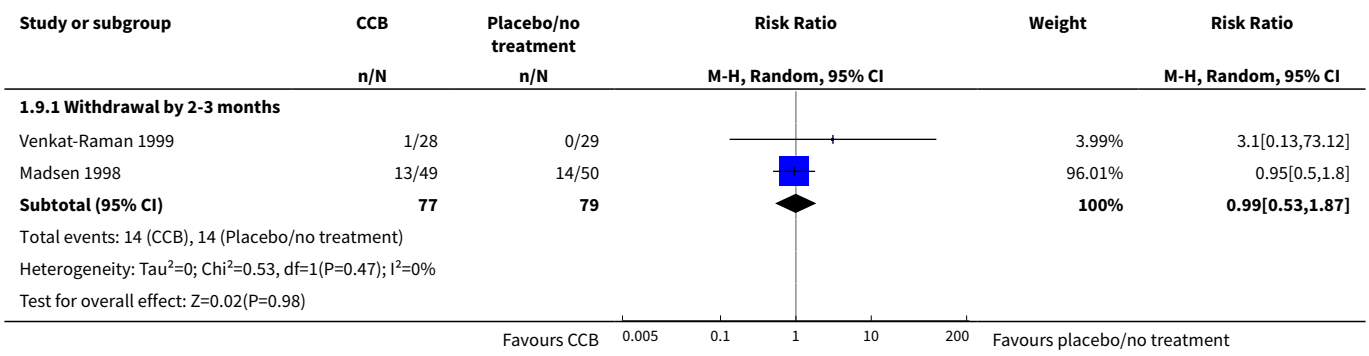




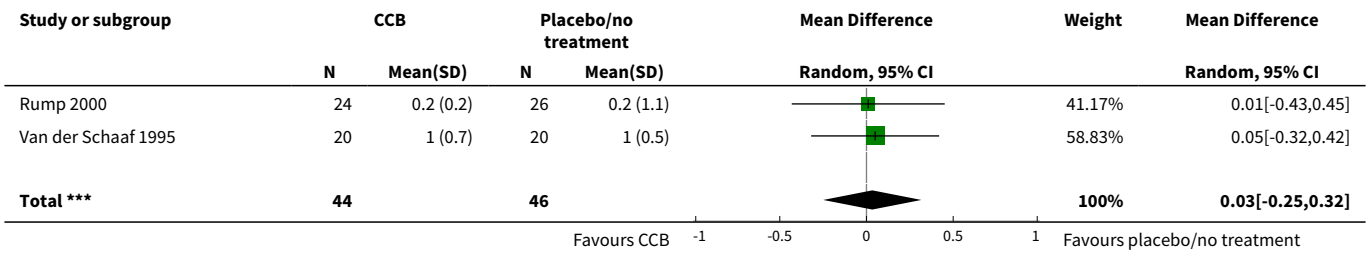
Analysis 1.8. Comparison 1 CCB versus placebo/no treatment, Outcome 8 Haematocrit (%) at last follow-up.

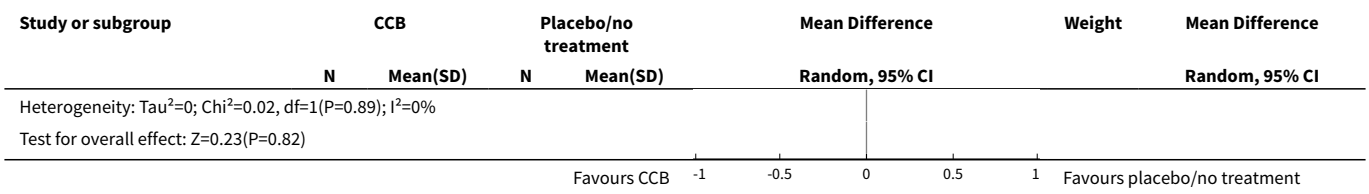


Analysis 1.9. Comparison 1 CCB versus placebo/no treatment, Outcome 9 Withdrawal due to side effects.

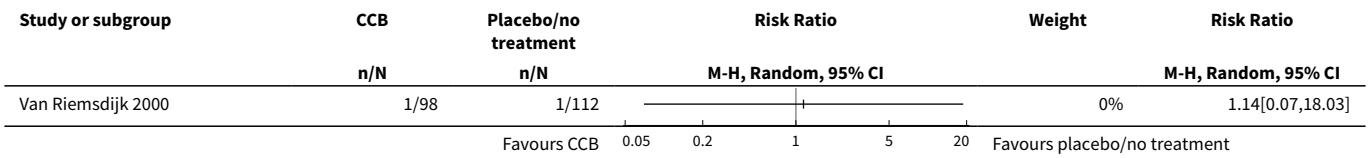


Analysis 1.10. Comparison 1 CCB versus placebo/no treatment, Outcome 10 Proteinuria (g/24 h) at last follow-up.

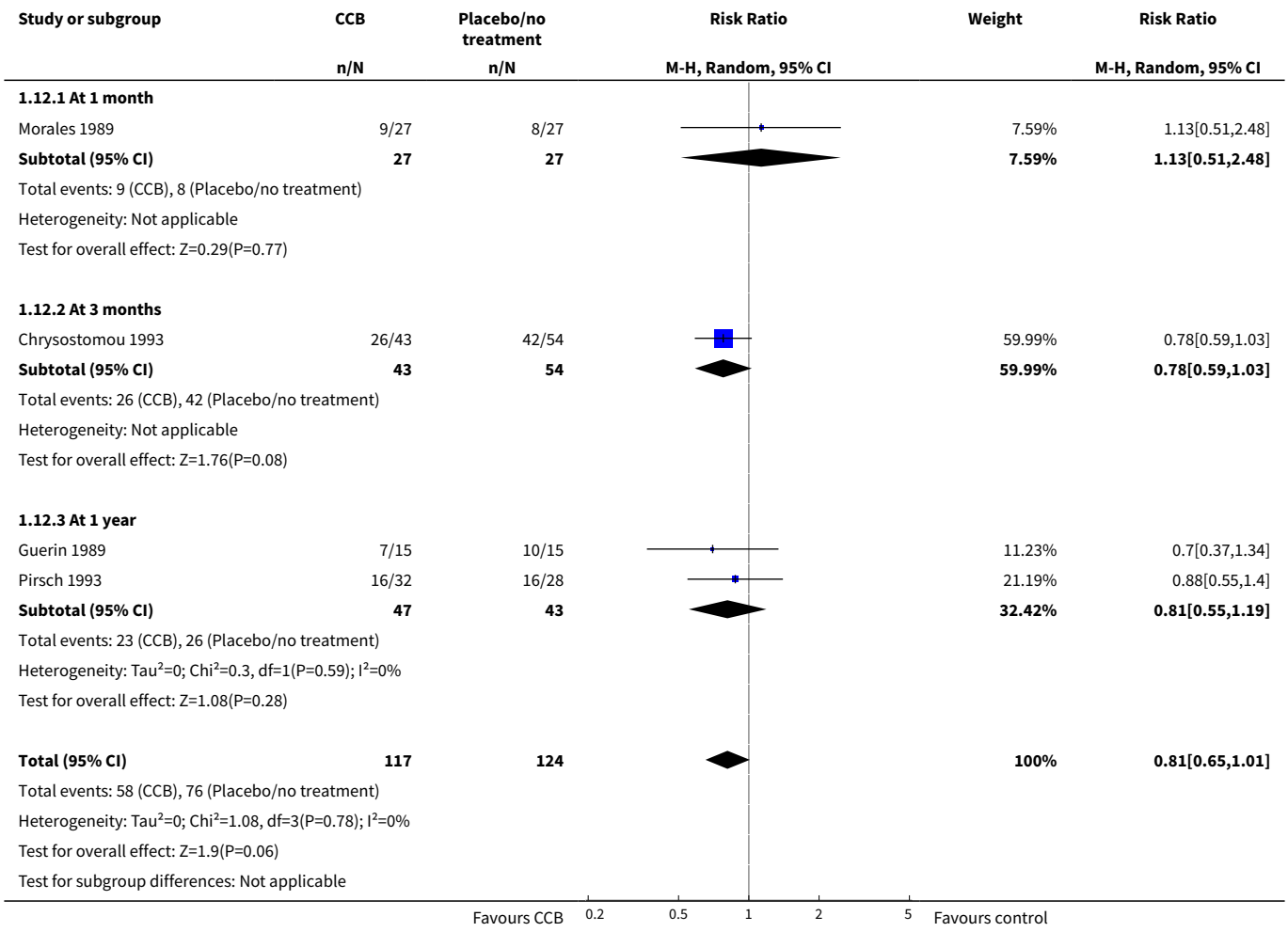




Analysis 1.11. Comparison 1 CCB versus placebo/no treatment, Outcome 11 Myocardial infarction at last follow-up.

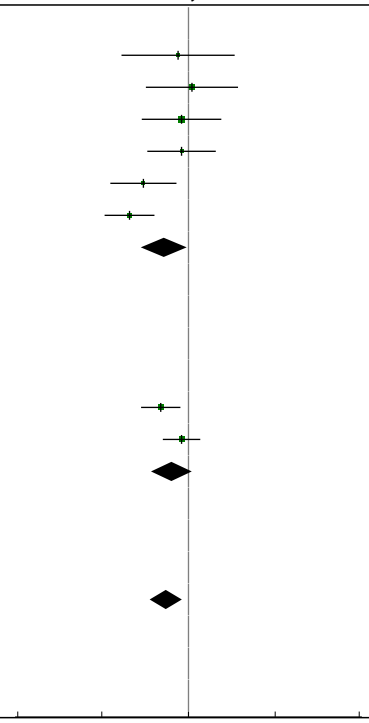


Analysis 1.12. Comparison 1 CCB versus placebo/no treatment, Outcome 12 New onset hypertension.



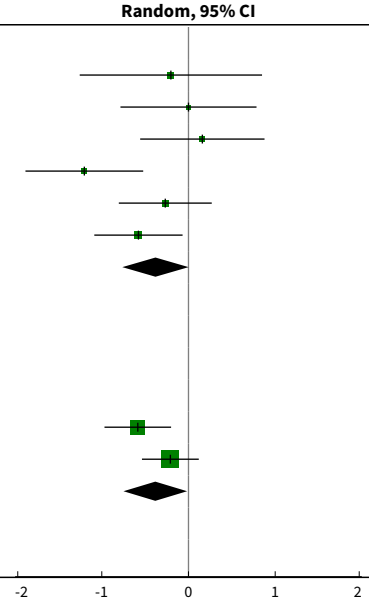
Analysis 1.13. Comparison 1 CCB versus placebo/no treatment, Outcome 13 Systolic blood pressure (mm Hg).

Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.13.1 At 1-3 months							
Wilkie 1993 No CNI	7	131 (17)	7	134 (14)		6.09%	-3[-19.31,13.31]
Wilkie 1993 CSA	15	152 (17)	15	151 (20)		8.17%	1[-12.28,14.28]
Guerin 1989	13	136 (17)	12	138 (12)		9.85%	-2[-13.47,9.47]
Venkat-Raman 1999	27	139 (18)	27	141 (19)		11.67%	-2[-11.87,7.87]
Madsen 1998	30	131 (16)	32	144 (22)		12.1%	-13[-22.53,-3.47]
Van der Schaaf 1995	20	148 (10)	20	165 (13)		15.52%	-17[-24.19,-9.81]
Subtotal ***	**112**		**113**			**63.39%**	**-7.14[-13.76,-0.52]**
Heterogeneity: Tau^2=37.21; Chi^2=11.49, df=5(P=0.04); I^2=56.49%							
Test for overall effect: Z=2.11(P=0.03)							
1.13.2 At 2 years							
Rahn 1999 NT	57	133 (14)	52	141 (16)		18.07%	-8[-13.67,-2.33]
Rahn 1999 HT	73	142 (16)	71	144 (17)		18.54%	-2[-7.4,3.4]
Subtotal ***	**130**		**123**			**36.61%**	**-4.93[-10.81,0.94]**
Heterogeneity: Tau^2=10.03; Chi^2=2.26, df=1(P=0.13); I^2=55.73%							
Test for overall effect: Z=1.65(P=0.1)							
Total ***	**242**		**236**			**100%**	**-6.56[-11.2,-1.92]**
Heterogeneity: Tau^2=22.62; Chi^2=15.69, df=7(P=0.03); I^2=55.37%							
Test for overall effect: Z=2.77(P=0.01)							
Test for subgroup differences: Chi^2=1.94, df=1 (P=0.16), I^2=48.32%							



Analysis 1.14. Comparison 1 CCB versus placebo/no treatment, Outcome 14 Diastolic blood pressure (mm Hg).

Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.14.1 At 1-3 months							
Wilkie 1993 No CNI	7	79 (7)	7	81 (11)		9.68%	-0.2[-1.25,0.85]
Guerin 1989	13	80 (7)	12	80 (12)		14.33%	0[-0.78,0.78]
Wilkie 1993 CSA	15	89 (14)	15	87 (10)		15.92%	0.16[-0.56,0.88]
Van der Schaaf 1995	20	92 (9)	20	105 (12)		16.89%	-1.2[-1.88,-0.52]
Venkat-Raman 1999	27	81 (12)	27	84 (10)		21.14%	-0.27[-0.8,0.27]
Madsen 1998	30	78 (8)	32	84 (12)		22.04%	-0.58[-1.09,-0.07]
Subtotal ***	**112**		**113**			**100%**	**-0.38[-0.76,0]**
Heterogeneity: Tau^2=0.11; Chi^2=9.53, df=5(P=0.09); I^2=47.51%							
Test for overall effect: Z=1.95(P=0.05)							
1.14.2 At 2 years							
Rahn 1999 NT	57	83 (8)	52	88 (9)		46.29%	-0.58[-0.97,-0.2]
Rahn 1999 HT	73	89 (10)	71	91 (9)		53.71%	-0.21[-0.54,0.12]
Subtotal ***	**130**		**123**			**100%**	**-0.38[-0.75,-0.02]**
Heterogeneity: Tau^2=0.04; Chi^2=2.13, df=1(P=0.14); I^2=53.01%							
Test for overall effect: Z=2.04(P=0.04)							

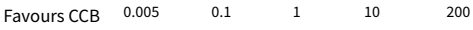


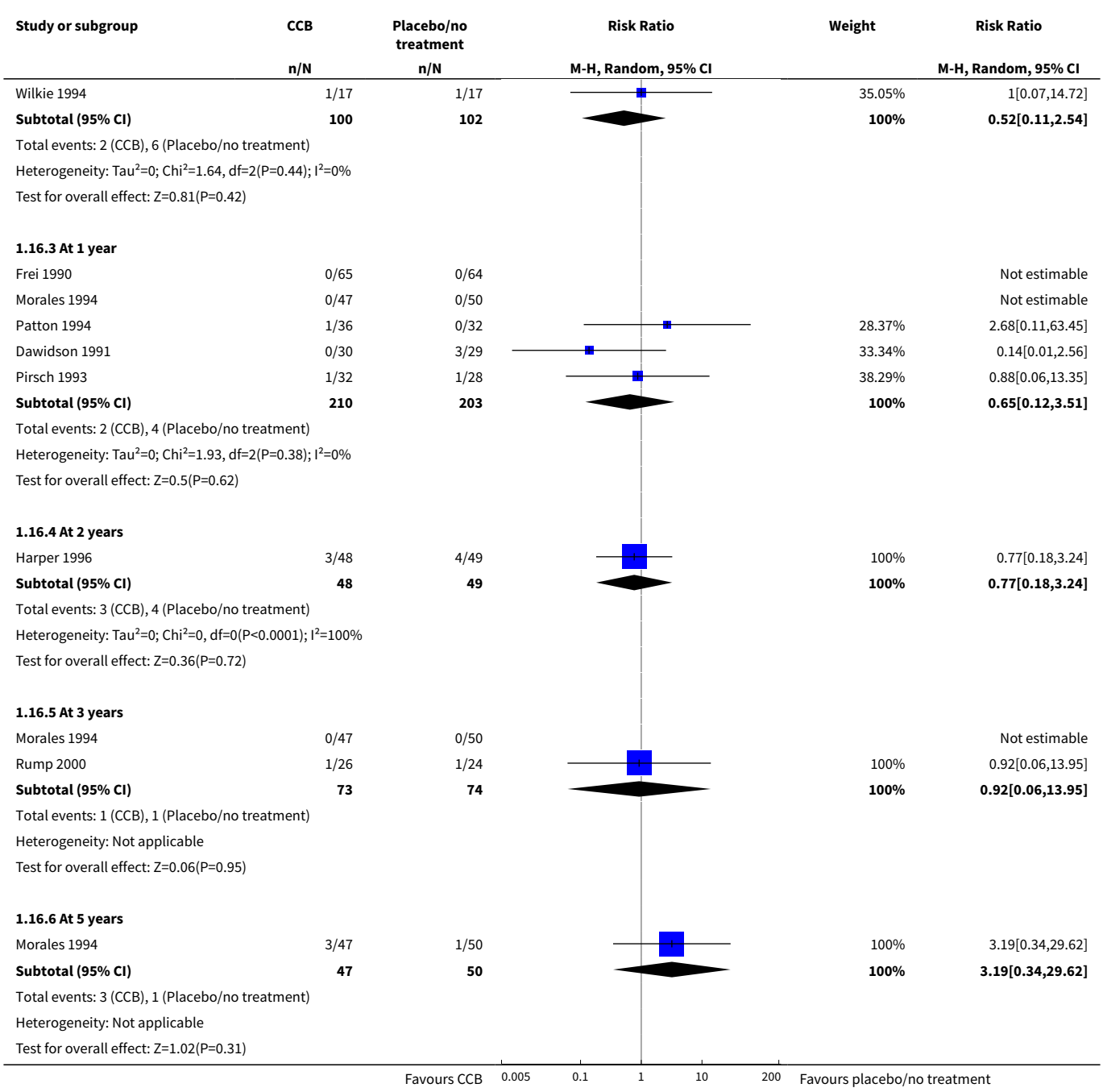
Analysis 1.15. Comparison 1 CCB versus placebo/no treatment, Outcome 15 Mean arterial pressure (mm Hg).

Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.15.1 At 1-3 months							
Wilkie 1993 No CNI	7	97 (8)	7	91 (11)		7.92%	6[-4.08,16.08]
Wilkie 1994	17	109 (13)	17	108 (14)		9.01%	1[-8.08,10.08]
Wilkie 1993 CSA	15	109 (11)	15	108 (11)		10.58%	1[-6.87,8.87]
Van der Schaaf 1995	20	111 (9)	20	124 (12)		12.59%	-13[-19.57,-6.43]
Subtotal ***	**59**		**59**			**40.1%**	**-1.7[-10.52,7.11]**
Heterogeneity: Tau²=62.53; Chi²=13.64, df=3(P=0); I²=78%							
Test for overall effect: Z=0.38(P=0.71)							
1.15.2 At 6-12 months							
Wilkie 1994	17	110 (14)	17	113 (14)		8.63%	-3[-12.41,6.41]
Subtotal ***	**17**		**17**			**8.63%**	**-3[-12.41,6.41]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.62(P=0.53)							
1.15.3 At 2 years							
Harper 1996	42	103.9 (11.7)	36	102.4 (13.8)		14.06%	1.5[-4.23,7.23]
Rahn 1999 NT	57	100 (9)	52	106 (10)		18.16%	-6[-9.58,-2.42]
Rahn 1999 HT	73	106 (9)	71	108 (10)		19.04%	-2[-5.11,1.11]
Subtotal ***	**172**		**159**			**51.27%**	**-2.61[-6.41,1.2]**
Heterogeneity: Tau²=7.02; Chi²=5.46, df=2(P=0.07); I²=63.34%							
Test for overall effect: Z=1.34(P=0.18)							
Total ***	**248**		**235**			**100%**	**-2.48[-6.01,1.04]**
Heterogeneity: Tau²=14.5; Chi²=19.14, df=7(P=0.01); I²=63.43%							
Test for overall effect: Z=1.38(P=0.17)							
Test for subgroup differences: Chi²=0.05, df=1 (P=0.98), I²=0%							

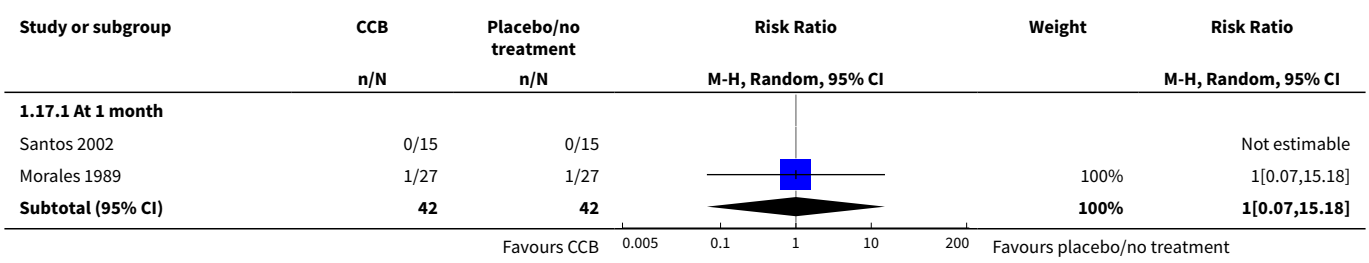
Analysis 1.16. Comparison 1 CCB versus placebo/no treatment, Outcome 16 Death.

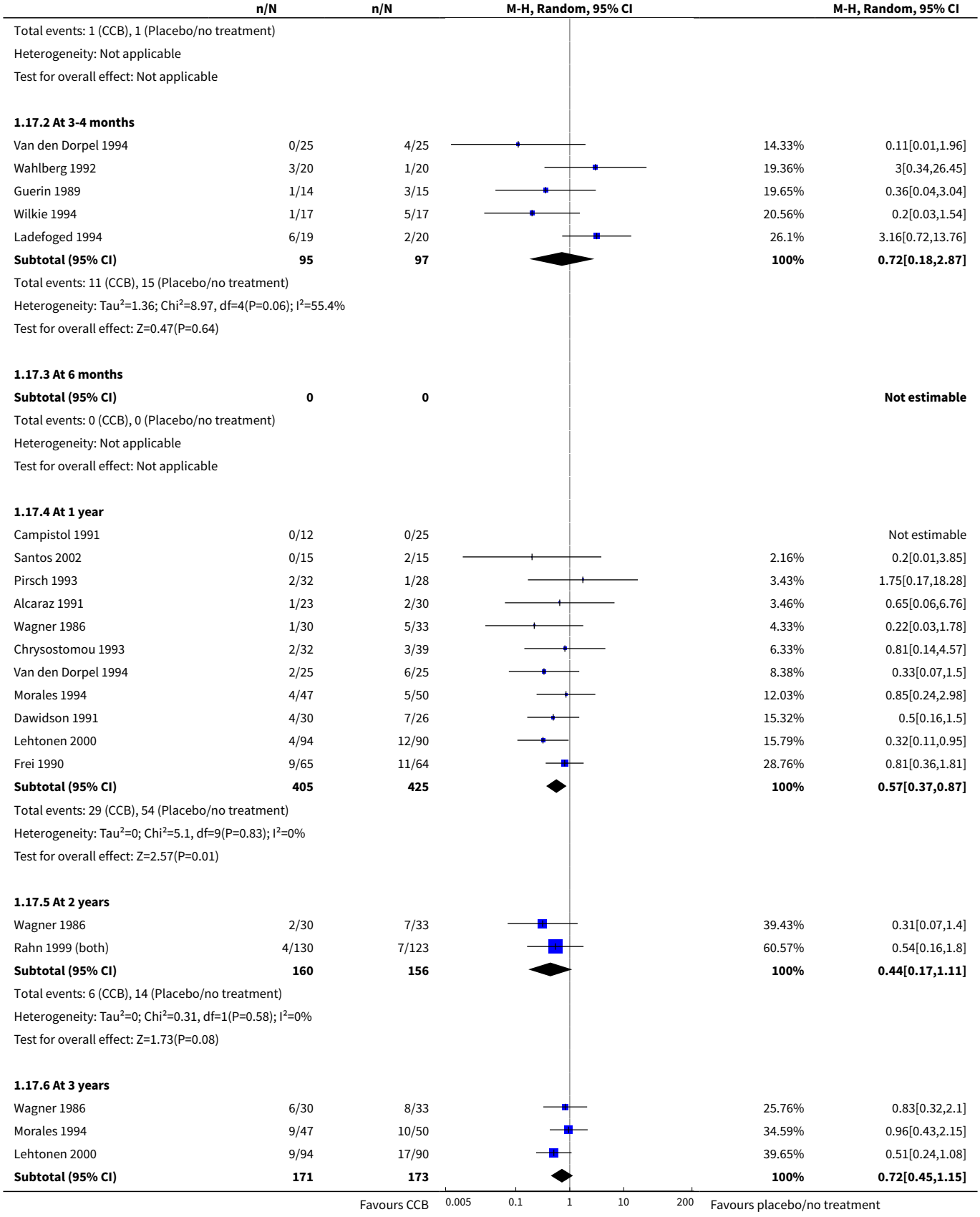
Study or subgroup	CCB n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.16.1 At 1 month					
Morales 1989	0/15	0/15			Not estimable
Subtotal (95% CI)	**15**	**15**			**Not estimable**
Total events: 0 (CCB), 0 (Placebo/no treatment)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.16.2 At 3 months					
Guerin 1989	0/14	0/15			Not estimable
Madsen 1998	0/49	4/50		30.23%	0.11[0.01,2.05]
Wahlberg 1992	1/20	1/20		34.72%	1[0.07,14.9]

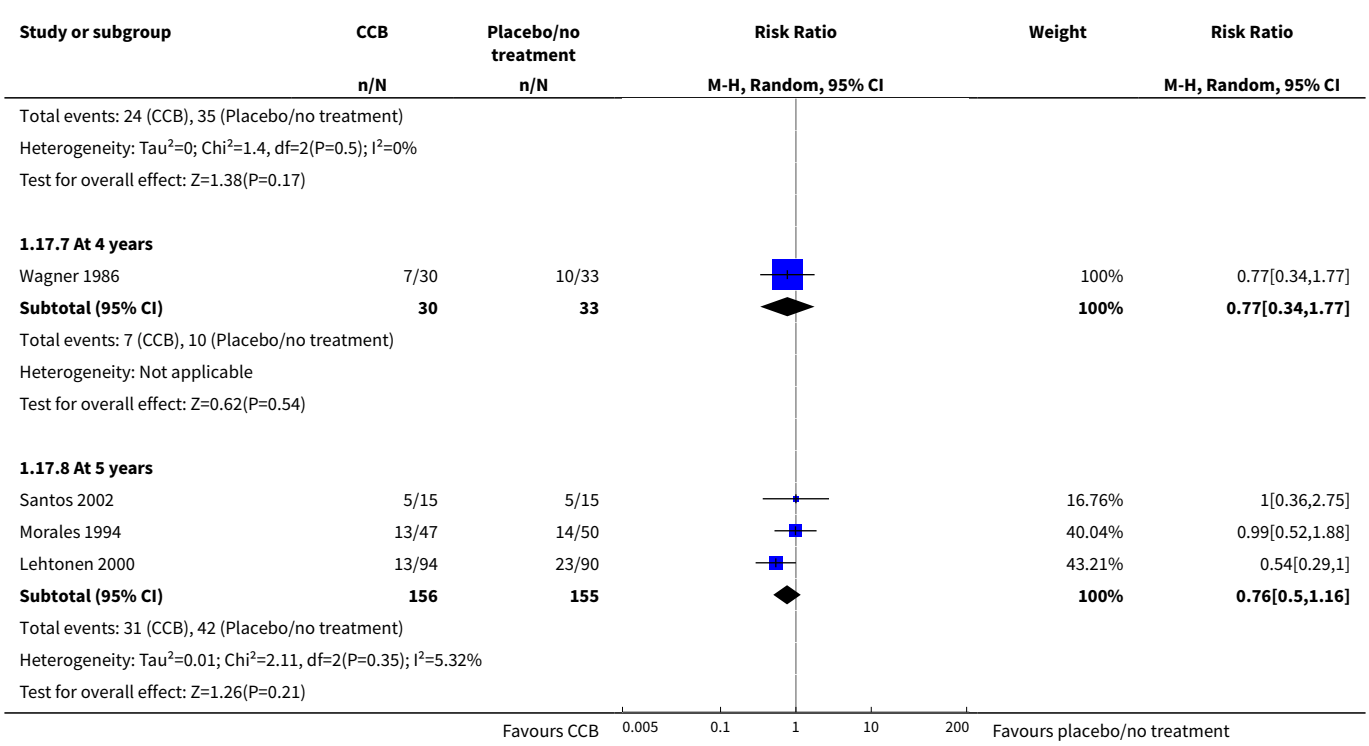




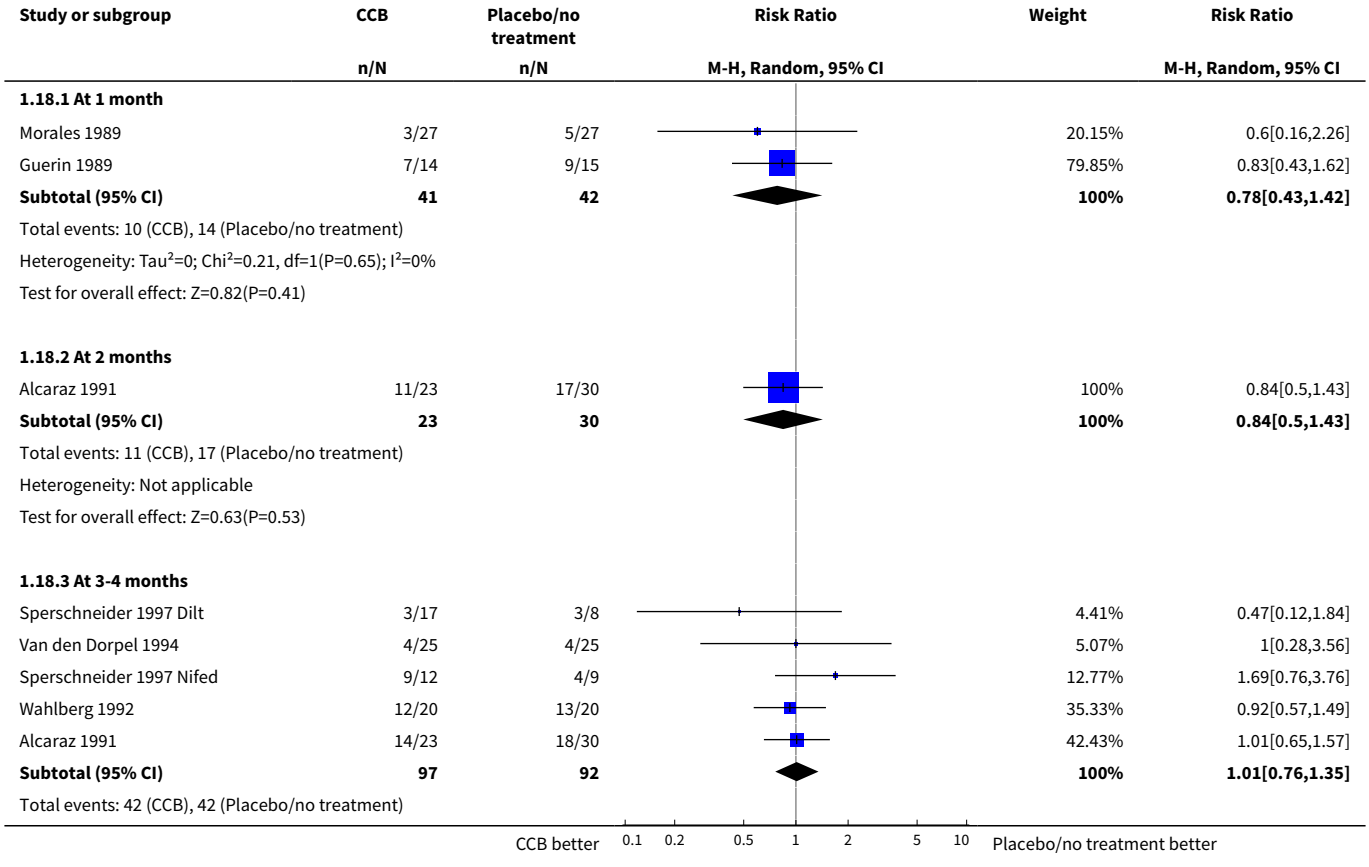
Analysis 1.17. Comparison 1 CCB versus placebo/no treatment, Outcome 17 Graft loss.

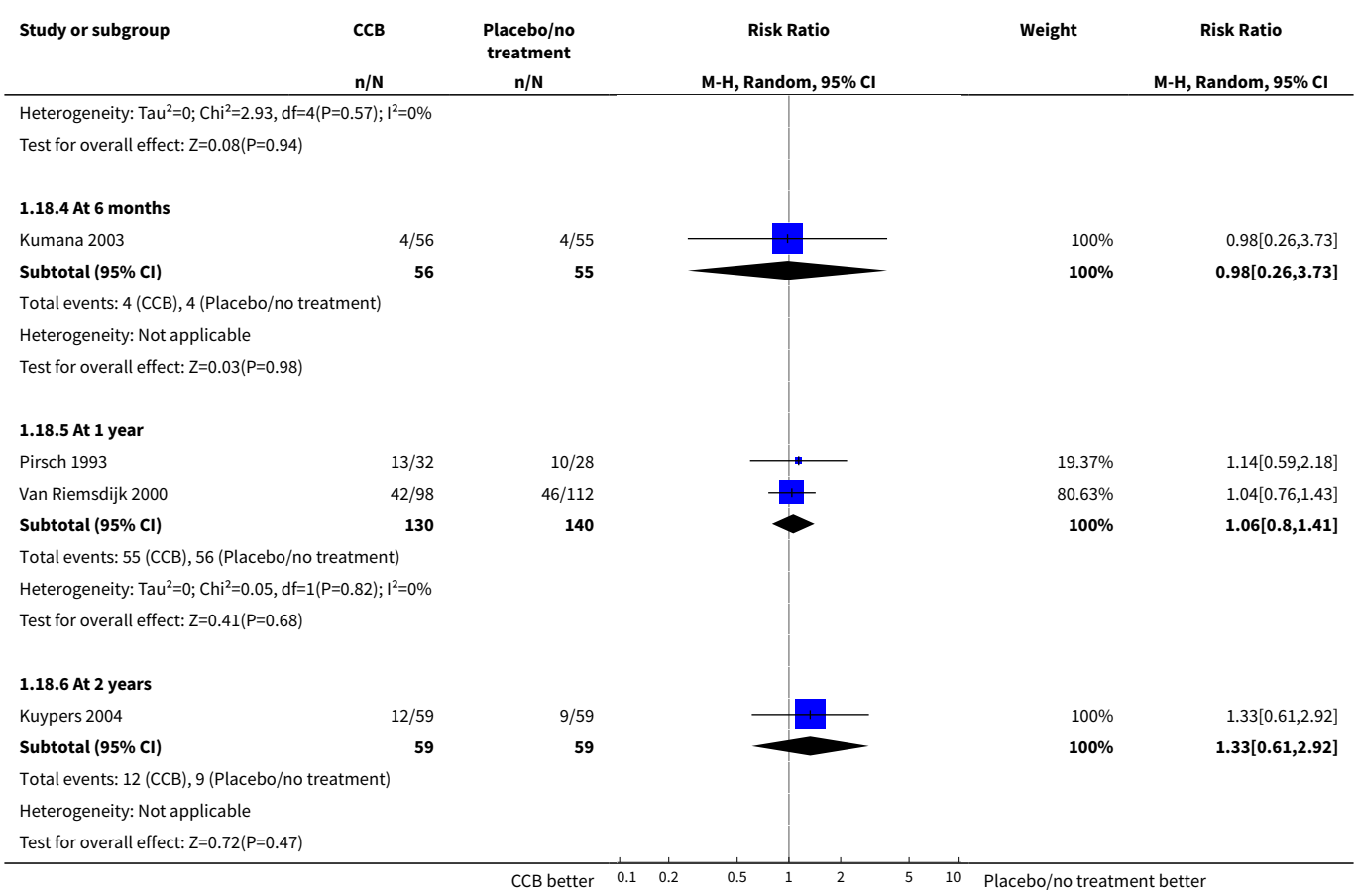




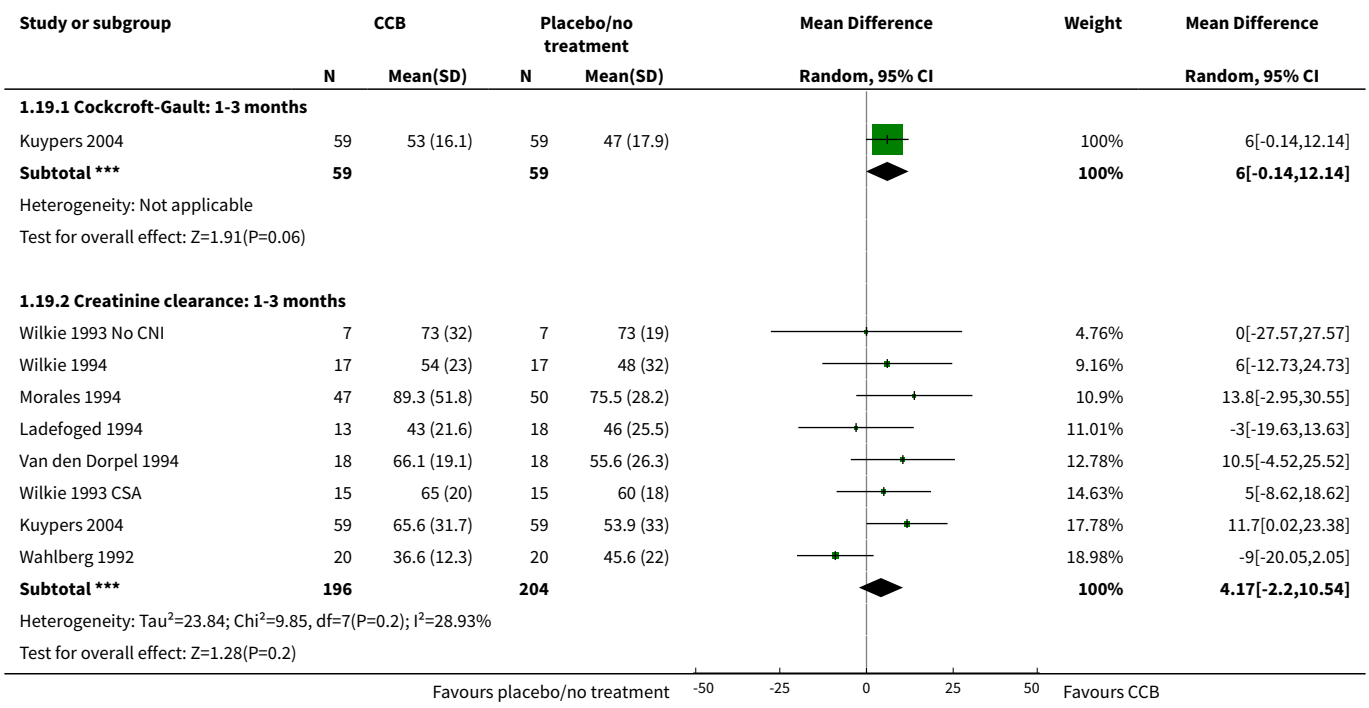


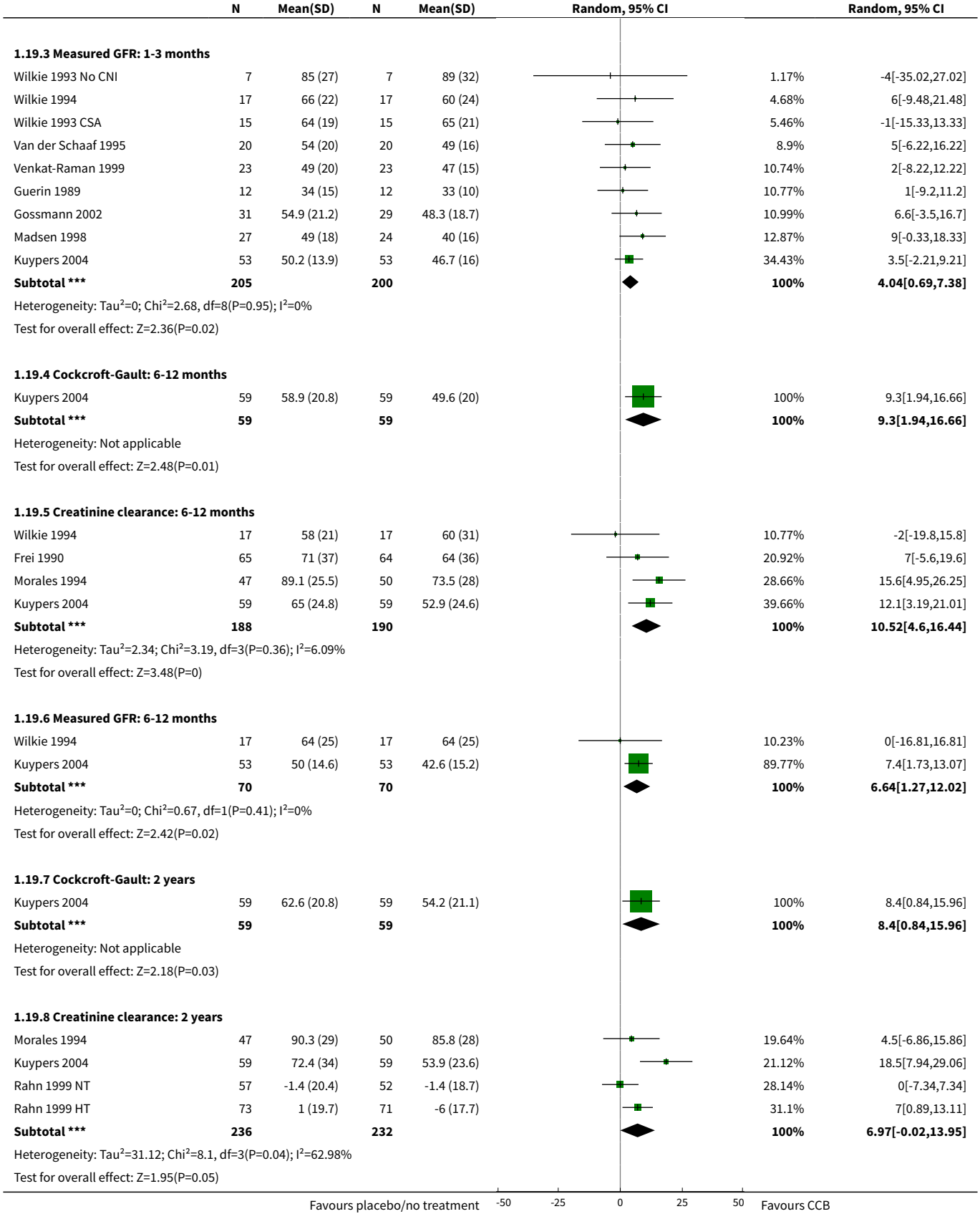
Analysis 1.18. Comparison 1 CCB versus placebo/no treatment, Outcome 18 Any rejection.

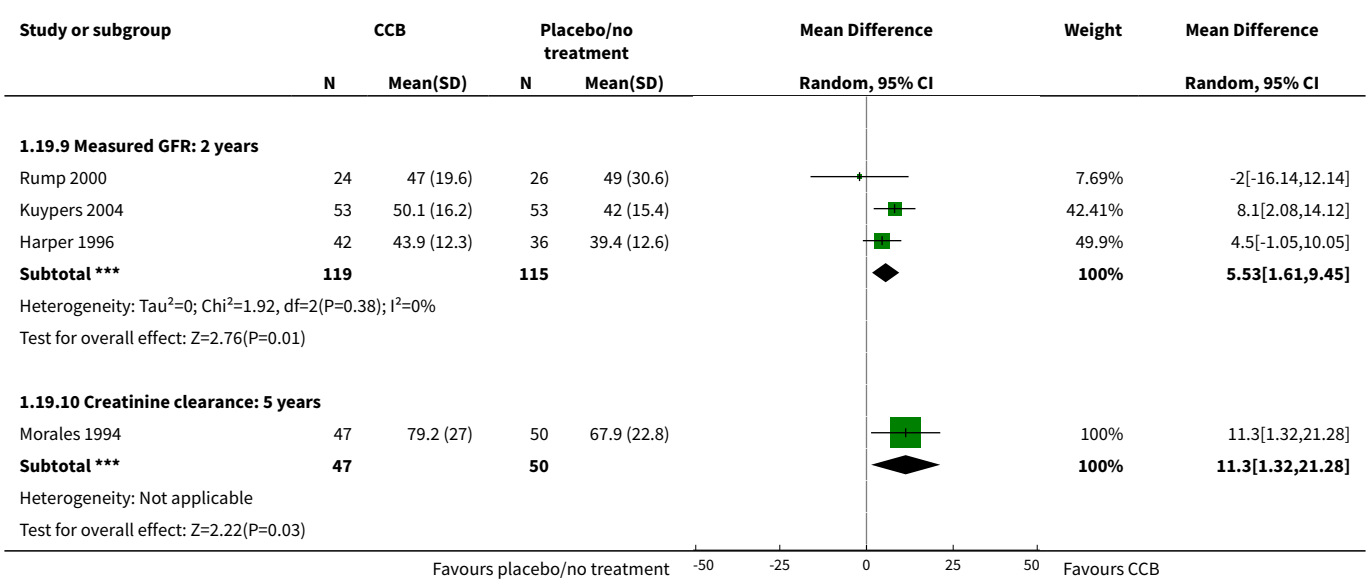




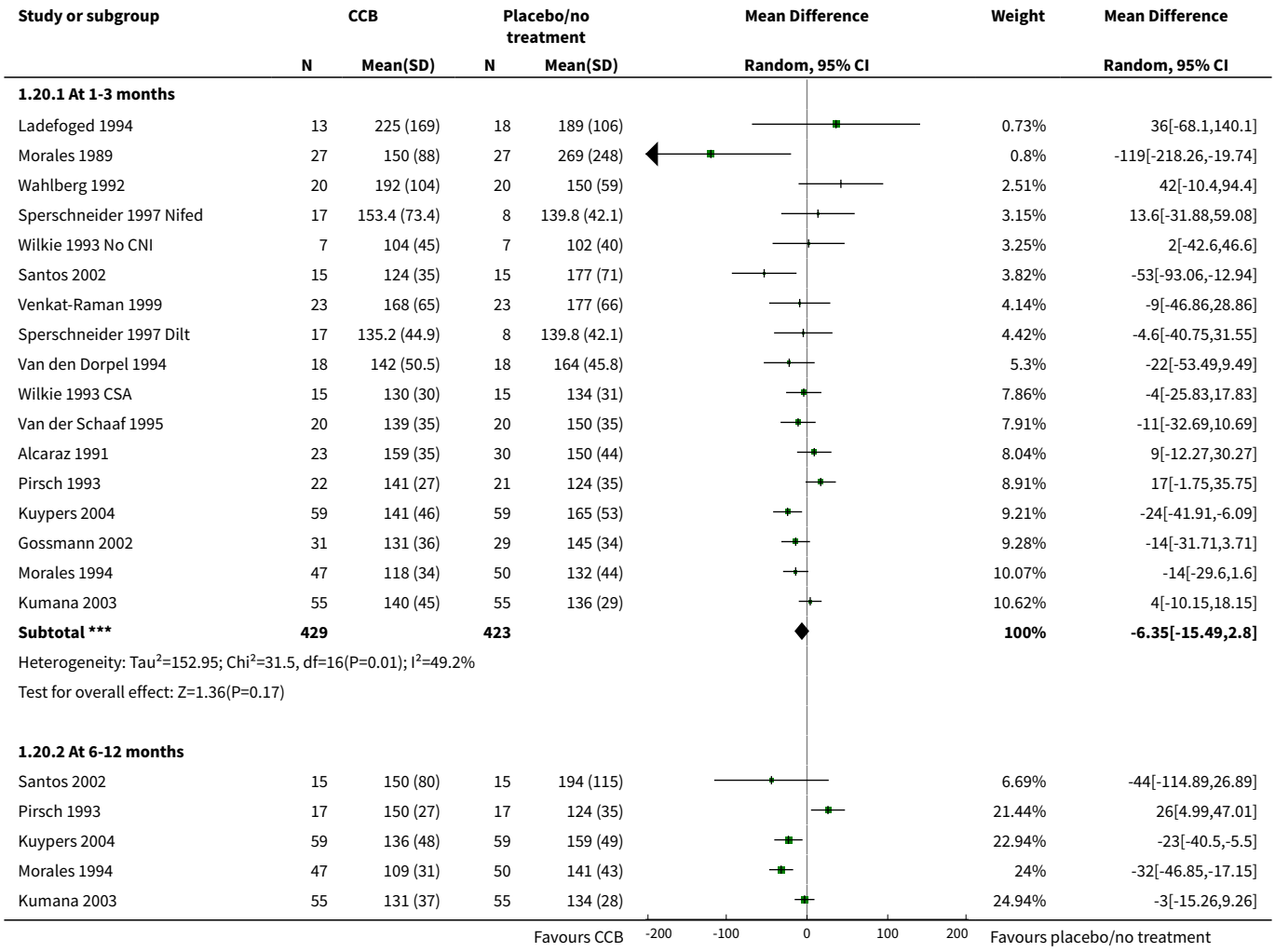
Analysis 1.19. Comparison 1 CCB versus placebo/no treatment, Outcome 19 GFR (mL/min or mL/min/1.73 m²).

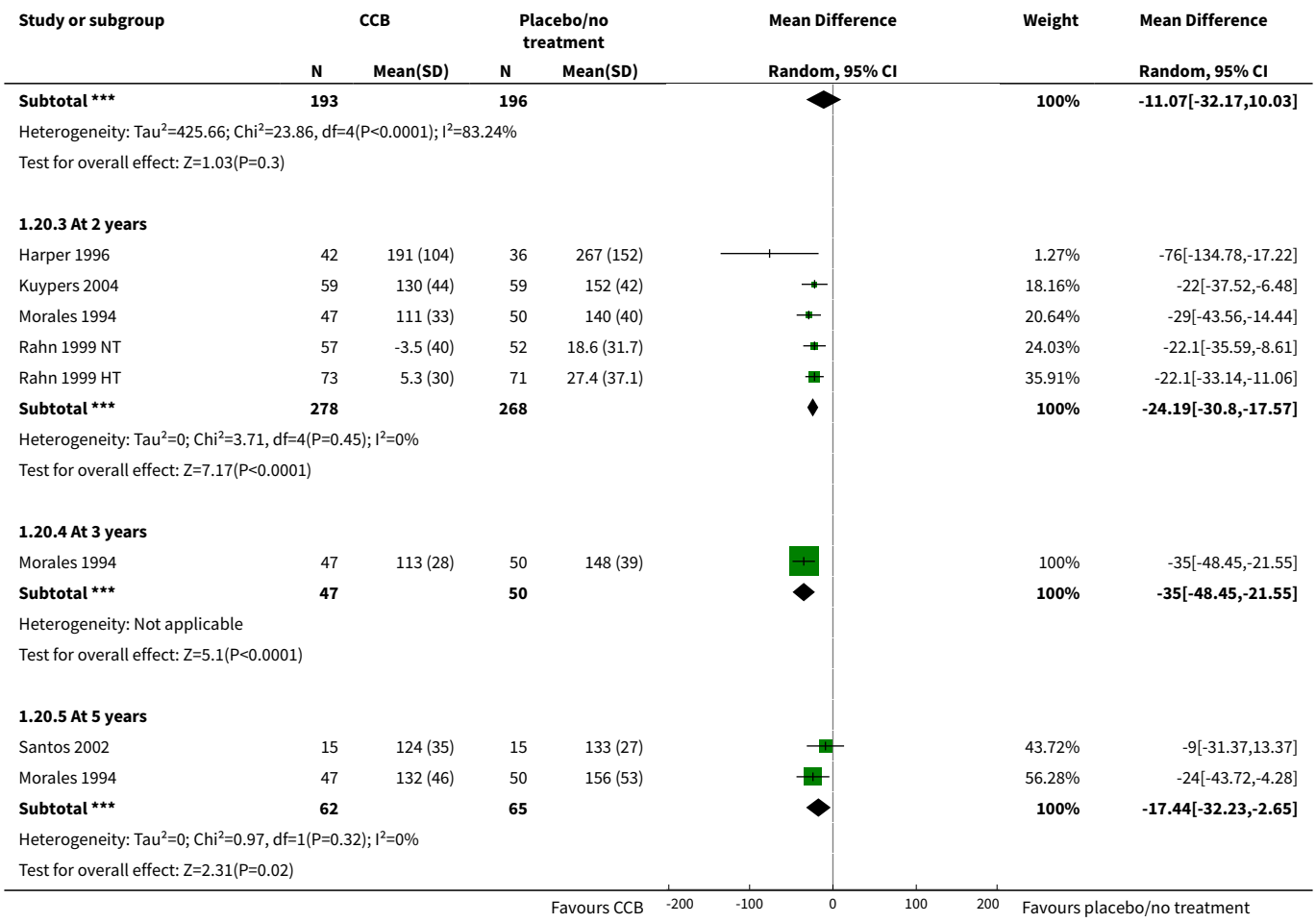




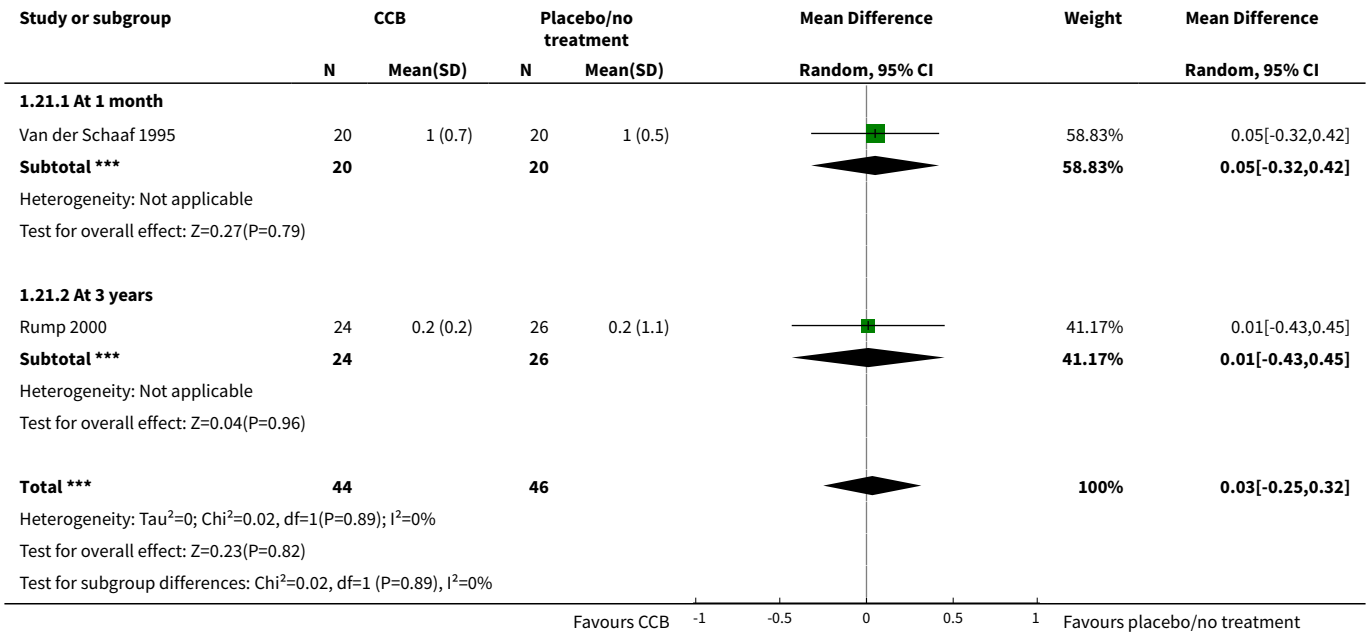


Analysis 1.20. Comparison 1 CCB versus placebo/no treatment, Outcome 20 Serum creatinine (µmol/L).





Analysis 1.21. Comparison 1 CCB versus placebo/no treatment, Outcome 21 Proteinuria (g/24 h).



Comparison 2. ACEi versus placebo/no treatment/non-antihypertensive

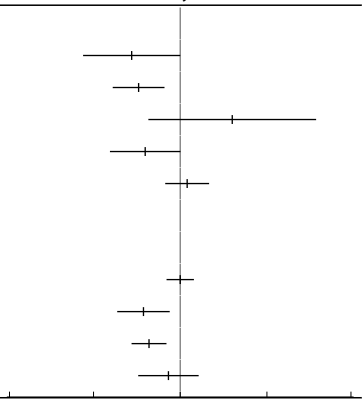
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any blood pressure (BP) measure at last follow-up	9		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Systolic BP (mm Hg)	5		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Mean arterial pressure (MAP) (mm Hg)	4		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Death	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 At 3 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Graft loss at last follow-up	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Any rejection	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 At 3 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Any GFR measure at last follow-up	3	77	Mean Difference (IV, Random, 95% CI)	-8.07 [-18.57, 2.43]
5.1 Creatinine clearance (mL/min)	1	12	Mean Difference (IV, Random, 95% CI)	-27.0 [-58.55, 4.55]
5.2 Measured GFR (mL/min/1.73 m^2 or mL/min)	2	65	Mean Difference (IV, Random, 95% CI)	-5.51 [-15.31, 4.30]
6 Serum creatinine (µmol/L) at last follow-up	7	272	Mean Difference (IV, Random, 95% CI)	-6.97 [-49.72, 35.79]
7 Proteinuria (g/24 h) at last follow-up	3	175	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.23, 0.06]
8 Haematocrit (%) at last follow-up (by selection criteria)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 Erythrocytosis	3	58	Mean Difference (IV, Random, 95% CI)	-7.29 [-10.34, -4.24]
8.2 Unselected or hypertensive	2	70	Mean Difference (IV, Random, 95% CI)	-1.29 [-2.93, 0.35]
9 Haemoglobin (g/L) at last follow-up (by selection criteria)	5	191	Mean Difference (IV, Random, 95% CI)	-11.70 [-19.96, -3.44]
9.1 Erythrocytosis	2	39	Mean Difference (IV, Random, 95% CI)	-21.46 [-46.92, 4.00]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.2 Unselected or hypertensive	3	152	Mean Difference (IV, Random, 95% CI)	-6.40 [-12.13, -0.68]
10 Serum potassium (mmol/L) at last follow-up	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
11 Systolic blood pressure (mm Hg)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 At 1 month	2	70	Mean Difference (IV, Random, 95% CI)	-7.38 [-19.57, 4.82]
11.2 At 3-4 months	2	45	Mean Difference (IV, Random, 95% CI)	-1.24 [-29.46, 26.97]
11.3 At 6 months	1	52	Mean Difference (IV, Random, 95% CI)	-8.10 [-17.77, 1.57]
11.4 At 1 year	1	52	Mean Difference (IV, Random, 95% CI)	-10.10 [-20.27, 0.07]
12 Diastolic blood pressure (mm Hg)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 At 1 month	2	70	Mean Difference (IV, Random, 95% CI)	-4.12 [-12.86, 4.61]
12.2 At 3-4 months	2	45	Mean Difference (IV, Random, 95% CI)	-0.50 [-13.09, 12.08]
12.3 At 6 months	1	52	Mean Difference (IV, Random, 95% CI)	-0.90 [-7.58, 5.78]
12.4 At 12-18 months	2	122	Mean Difference (IV, Random, 95% CI)	-2.13 [-7.22, 2.96]
13 Mean arterial pressure (mm Hg)	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.1 At 1-3 months	4	103	Mean Difference (IV, Random, 95% CI)	-7.82 [-11.46, -4.18]
13.2 At 6 months	1	52	Mean Difference (IV, Random, 95% CI)	-3.20 [-9.70, 3.30]
13.3 At 1 year	2	128	Mean Difference (IV, Random, 95% CI)	-2.94 [-9.70, 3.83]
13.4 At 2 years	1	65	Mean Difference (IV, Random, 95% CI)	-9.0 [-14.03, -3.97]
14 Any GFR measure	3		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Creatinine clearance (mL/min): 1 month	1	30	Mean Difference (IV, Random, 95% CI)	0.0 [-18.73, 18.73]
14.2 GFR (mL/min/1.73 m^2): 1 month	1	40	Mean Difference (IV, Random, 95% CI)	-3.00 [-14.57, 8.57]
14.3 Creatinine clearance (mL/min): 3 months	1	12	Mean Difference (IV, Random, 95% CI)	-27.0 [-58.55, 4.55]
14.4 GFR (mL/min/1.73 m^2): 4 months	1	25	Mean Difference (IV, Random, 95% CI)	-6.0 [-13.12, 1.12]
15 Serum creatinine (µmol/L)	6	226	Mean Difference (IV, Random, 95% CI)	7.55 [-2.10, 17.20]
15.1 At 1-3 months	4	104	Mean Difference (IV, Random, 95% CI)	13.90 [6.76, 21.04]
15.2 At 6-24 months	2	122	Mean Difference (IV, Random, 95% CI)	1.01 [-13.66, 15.67]
16 Serum potassium (mmol/L)	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
16.1 At 1-3 months	3		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
17 Haematocrit (%)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
17.1 At 1 month	2	59	Mean Difference (IV, Random, 95% CI)	-2.69 [-5.61, 0.22]
17.2 At 2-4 months	4	88	Mean Difference (IV, Random, 95% CI)	-5.82 [-9.56, -2.08]
18 Haemoglobin (g/L)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
18.1 At 1-4 months	3	69	Mean Difference (IV, Random, 95% CI)	-14.33 [-29.90, 1.23]
18.2 At 6-18 months	2	122	Mean Difference (IV, Random, 95% CI)	-8.78 [-15.50, -2.07]
19 Proteinuria (g/24 h)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
19.1 At 1 month	1	40	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.47, 0.07]
19.2 At 6-24 months	2	135	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.20, 0.14]

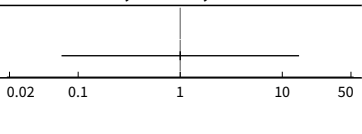
Analysis 2.1. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 1 Any blood pressure (BP) measure at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
2.1.1 Systolic BP (mm Hg)						
Beckingham 1995	15	131 (15)	10	145 (19)		-14[-28.01,0.01]
Van der Schaaf 1995	20	153 (11)	20	165 (13)		-12[-19.46,-4.54]
Gronhagen-Riska 1984	9	160 (27)	11	145 (28)		15[-9.19,39.19]
Hernandez 2000	24	140.6 (19.1)	28	150.7 (18.1)		-10.1[-20.27,0.07]
Paoletti 2007	36	-5 (14)	34	-7 (13)		2[-4.33,8.33]
2.1.2 Mean arterial pressure (MAP) (mm Hg)						
Takahara 2002	41	94 (7)	35	94 (10)		0[-3.95,3.95]
Trivedi 2003	9	100.4 (8.2)	5	111 (6.1)		-10.6[-18.17,-3.03]
Kim 2002a	33	107 (10.7)	32	116 (10)		-9[-14.03,-3.97]
Rashtchizadeh 2007	12	93.6 (10.5)	18	97 (13.8)		-3.4[-12.11,5.31]



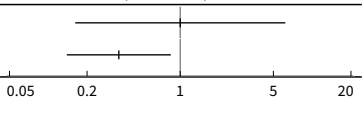
Analysis 2.2. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 2 Death.

Study or subgroup	ACEi n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
2.2.1 At 3 months				
Gronhagen-Riska 1984	1/15	1/15		1[0.07,14.55]



Analysis 2.3. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 3 Graft loss at last follow-up.

Study or subgroup	ACEi n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Gronhagen-Riska 1984	2/14	2/14		1[0.16,6.14]
Kim 2002a	5/33	14/32		0.35[0.14,0.85]

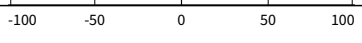


Analysis 2.4. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 4 Any rejection.

Study or subgroup	ACEi n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
2.4.1 At 3 months				
Gronhagen-Riska 1984	9/15	10/15		0.9[0.52,1.55]

Analysis 2.5. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 5 Any GFR measure at last follow-up.

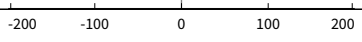
Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.5.1 Creatinine clearance (mL/min)							
Gronhagen-Riska 1984	7	31 (14)	5	58 (34)		10.58%	-27[-58.55,4.55]
Subtotal ***	**7**		**5**			**10.58%**	**-27[-58.55,4.55]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.68(P=0.09)							
2.5.2 Measured GFR (mL/min/1.73 m² or mL/min)							
Beckingham 1995	15	54.9 (17.4)	10	66.8 (26.2)		28.41%	-11.9[-30.37,6.57]
Van der Schaaf 1995	20	46 (21)	20	49 (16)		61.01%	-3[-14.57,8.57]
Subtotal ***	**35**		**30**			**89.42%**	**-5.51[-15.31,4.3]**
Heterogeneity: Tau^2=0; Chi^2=0.64, df=1(P=0.42); I^2=0%							
Test for overall effect: Z=1.1(P=0.27)							
Total ***	**42**		**35**			**100%**	**-8.07[-18.57,2.43]**
Heterogeneity: Tau^2=12.19; Chi^2=2.27, df=2(P=0.32); I^2=11.72%							
Test for overall effect: Z=1.51(P=0.13)							
Test for subgroup differences: Chi^2=1.63, df=1 (P=0.2), I^2=38.47%							



Favours placebo/no treatment — Favours ACEi

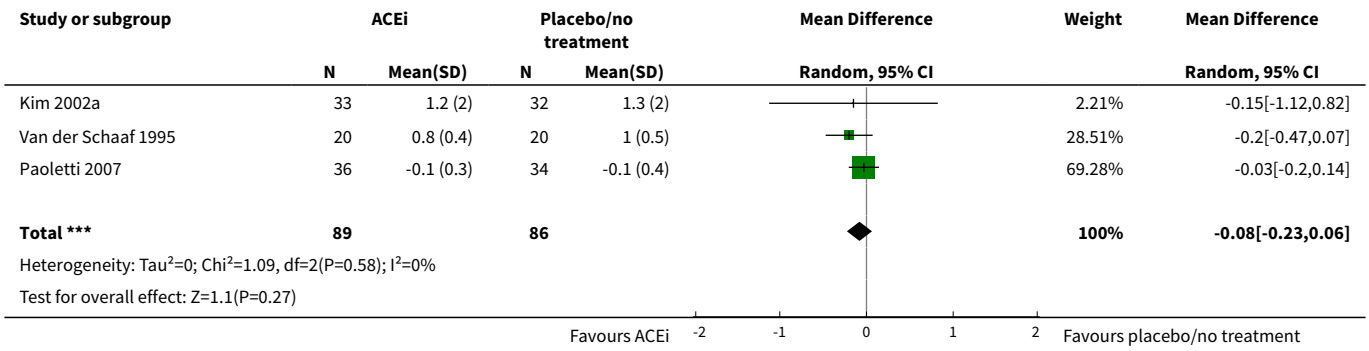
Analysis 2.6. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 6 Serum creatinine (µmol/L) at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Gronhagen-Riska 1984	9	192 (101)	11	136 (83)		10.01%	56[-26.22,138.22]
Trivedi 2003	9	141 (35)	5	141 (62)		12.21%	0[-58.96,58.96]
Van der Schaaf 1995	20	152 (41)	20	150 (35)		15.17%	2[-21.63,25.63]
Hernandez 2000	24	133 (26)	28	124 (37)		15.5%	9[-8.21,26.21]
Paoletti 2007	36	-4 (34)	34	2 (32)		15.58%	-6[-21.46,9.46]
Kim 2002a	28	260 (20)	18	360 (20)		15.71%	-100[-111.84,-88.16]
Rashtchizadeh 2007	12	130 (13)	18	115 (4)		15.82%	15[7.42,22.58]
Total ***	**138**		**134**			**100%**	**-6.97[-49.72,35.79]**
Heterogeneity: Tau^2=2991.98; Chi^2=271.18, df=6(P<0.0001); I^2=97.79%							
Test for overall effect: Z=0.32(P=0.75)							

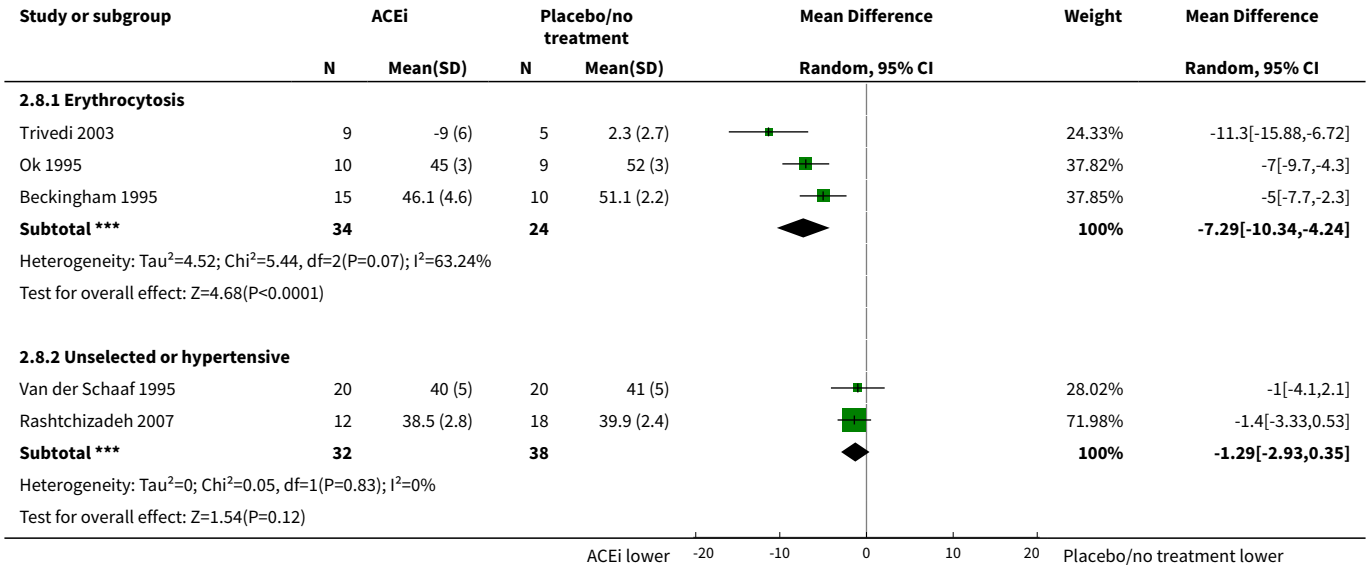


Favours ACEi — Favours placebo/no treatment

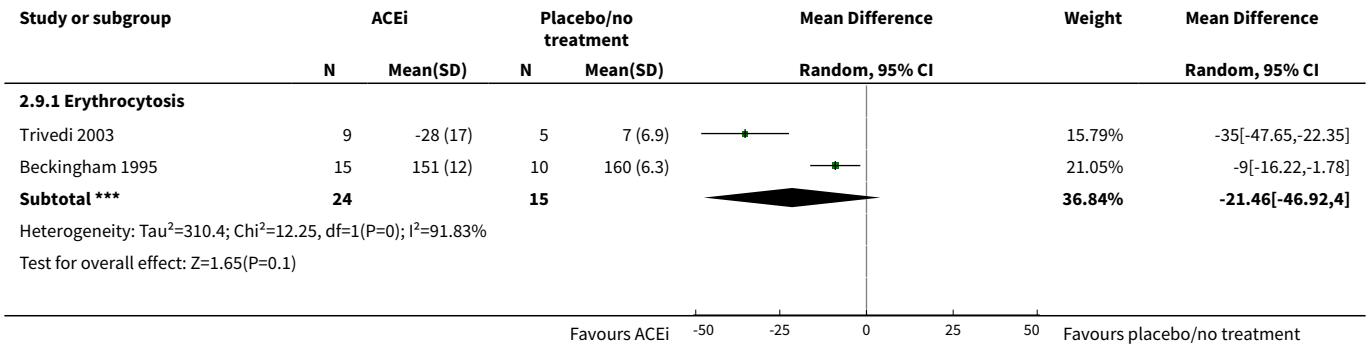
Analysis 2.7. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 7 Proteinuria (g/24 h) at last follow-up.



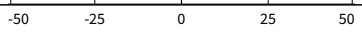
Analysis 2.8. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 8 Haematocrit (%) at last follow-up (by selection criteria).



Analysis 2.9. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 9 Haemoglobin (g/L) at last follow-up (by selection criteria).



Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.9.2 Unselected or hypertensive							
Hernandez 2000	24	124 (16)	28	137 (16)		19.6%	-13[-21.72,-4.28]
Rashtchizadeh 2007	12	132 (10.1)	18	133.9 (7.6)		21.52%	-1.9[-8.61,4.81]
Paoletti 2007	36	-3 (12)	34	3 (14)		22.04%	-6[-12.12,0.12]
Subtotal ***	**72**		**80**			**63.16%**	**-6.4[-12.13,-0.68]**
Heterogeneity: Tau^2=12.48; Chi^2=3.91, df=2(P=0.14); I^2=48.84%							
Test for overall effect: Z=2.19(P=0.03)							
Total ***	**96**		**95**			**100%**	**-11.7[-19.96,-3.44]**
Heterogeneity: Tau^2=70.84; Chi^2=22.25, df=4(P=0); I^2=82.02%							
Test for overall effect: Z=2.78(P=0.01)							
Test for subgroup differences: Chi^2=6.09, df=1 (P=0.01), I^2=83.59%							



Favours ACEi | Favours placebo/no treatment

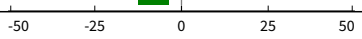
Analysis 2.10. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 10 Serum potassium (mmol/L) at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Rashtchizadeh 2007	12	4.6 (0.2)	18	3.9 (0.1)		0.68[0.56,0.8]
Gronhagen-Riska 1984	9	4.3 (0.2)	11	4 (0.3)		0.3[0.08,0.52]
Trivedi 2003	9	4.4 (0.6)	5	4.2 (0.2)		0.2[-0.23,0.63]

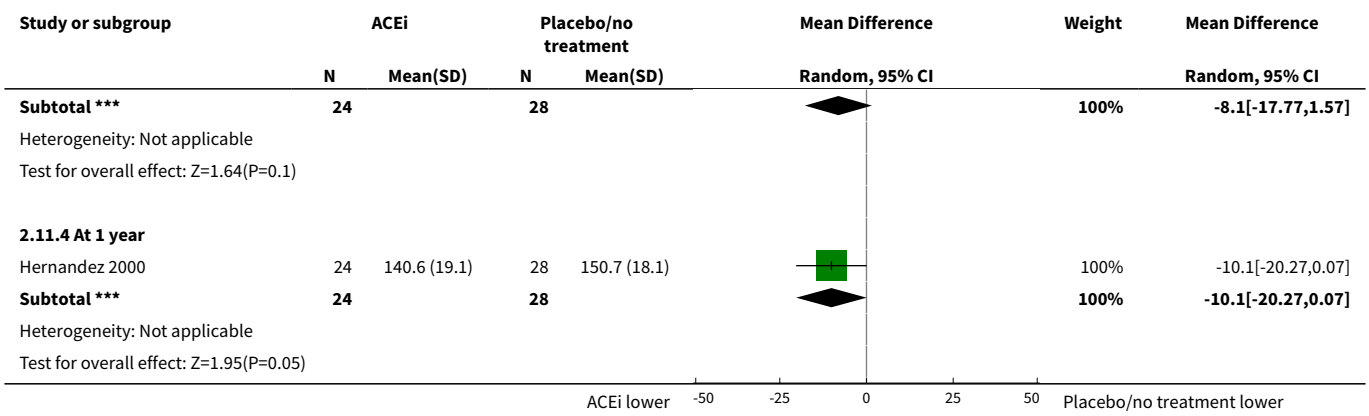
Favours ACEi | Favours placebo/no treatment

Analysis 2.11. Comparison 2 ACEi versus placebo/no treatment/non-antihypertensive, Outcome 11 Systolic blood pressure (mm Hg).

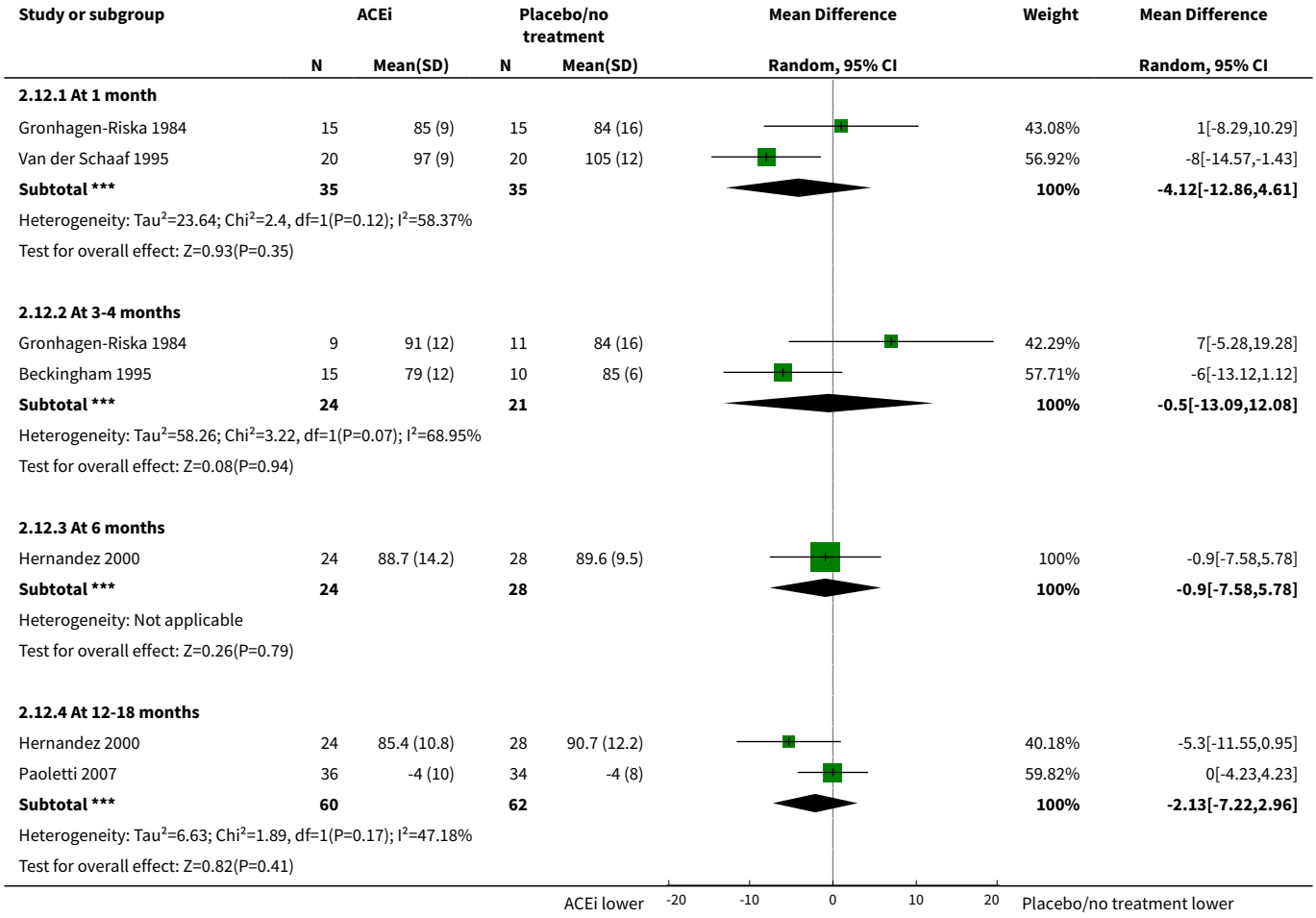
Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.11.1 At 1 month							
Gronhagen-Riska 1984	15	142 (18)	15	141 (25)		35.57%	1[-14.59,16.59]
Van der Schaaf 1995	20	153 (11)	20	165 (13)		64.43%	-12[-19.46,-4.54]
Subtotal ***	**35**		**35**			**100%**	**-7.38[-19.57,4.82]**
Heterogeneity: Tau^2=45.62; Chi^2=2.17, df=1(P=0.14); I^2=53.98%							
Test for overall effect: Z=1.19(P=0.24)							
2.11.2 At 3-4 months							
Gronhagen-Riska 1984	9	160 (27)	11	145 (28)		43.98%	15[-9.19,39.19]
Beckingham 1995	15	131 (15)	10	145 (19)		56.02%	-14[-28.01,0.01]
Subtotal ***	**24**		**21**			**100%**	**-1.24[-29.46,26.97]**
Heterogeneity: Tau^2=318.81; Chi^2=4.14, df=1(P=0.04); I^2=75.82%							
Test for overall effect: Z=0.09(P=0.93)							
2.11.3 At 6 months							
Hernandez 2000	24	145.5 (19.6)	28	153.6 (15.3)		100%	-8.1[-17.77,1.57]



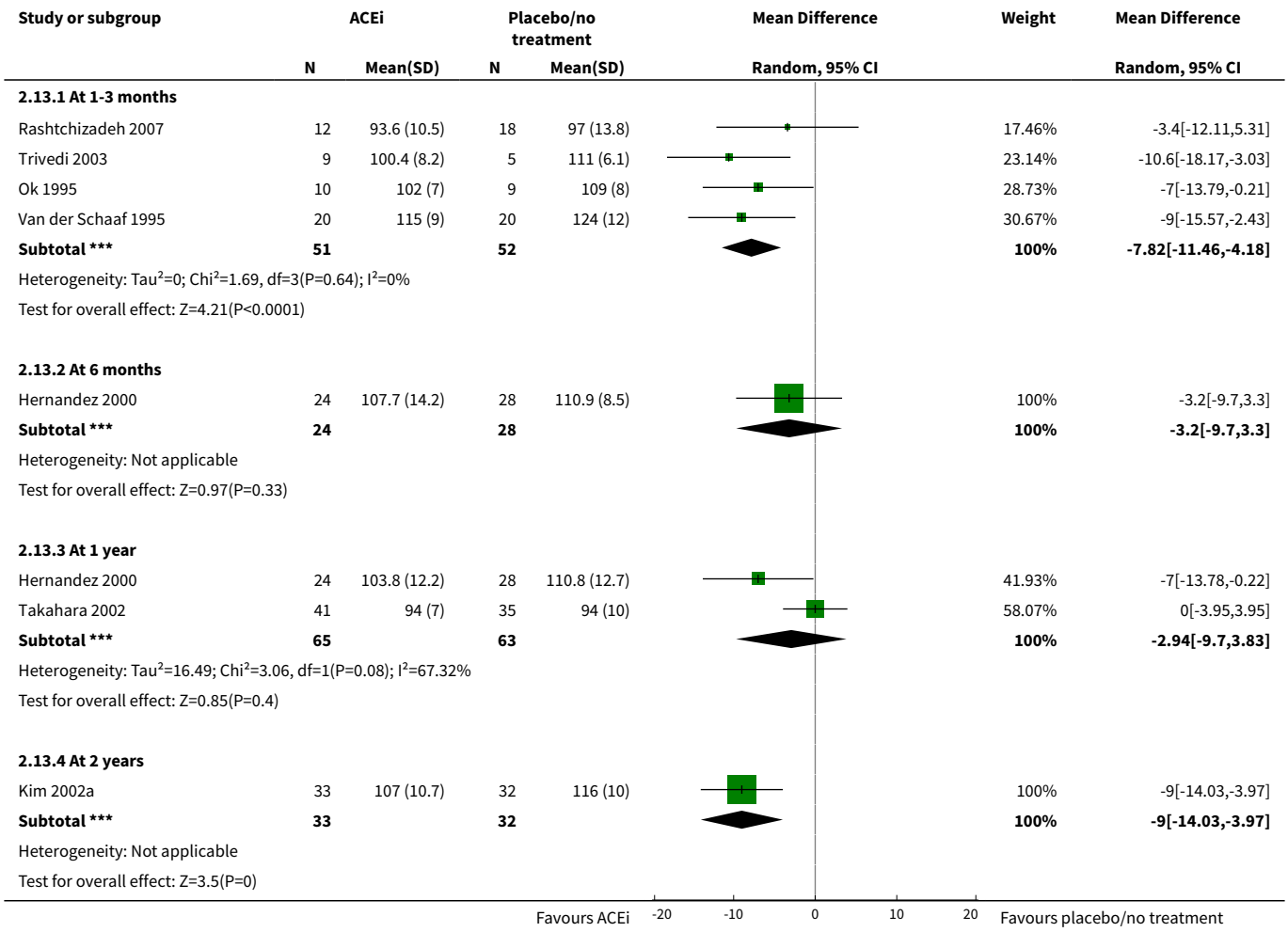
ACEi lower | Placebo/no treatment lower



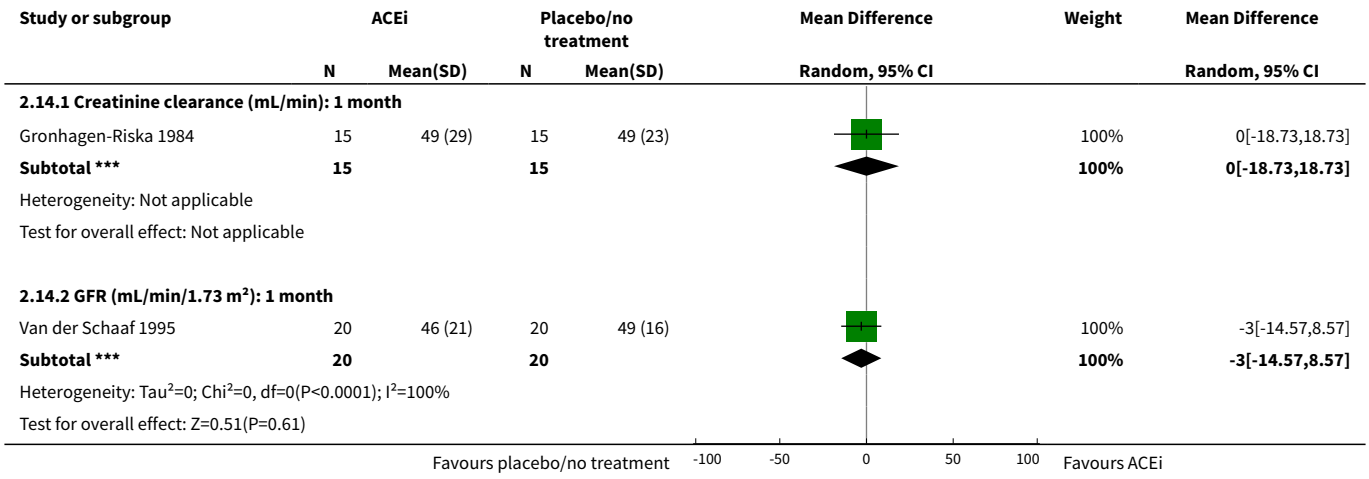
Analysis 2.12. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 12 Diastolic blood pressure (mm Hg).

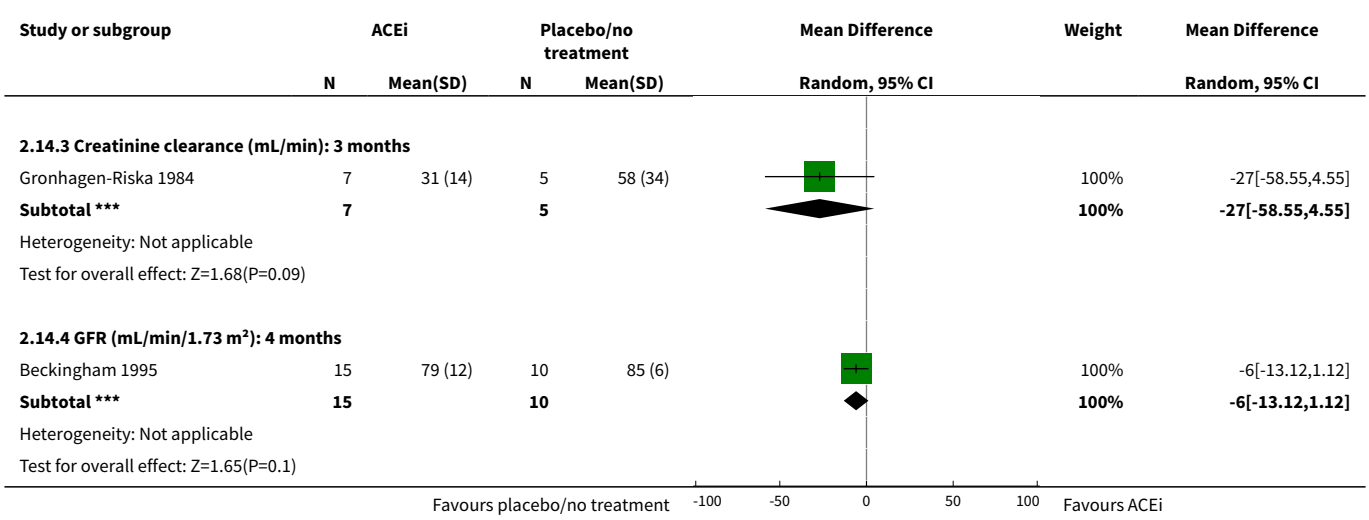


Analysis 2.13. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 13 Mean arterial pressure (mm Hg).

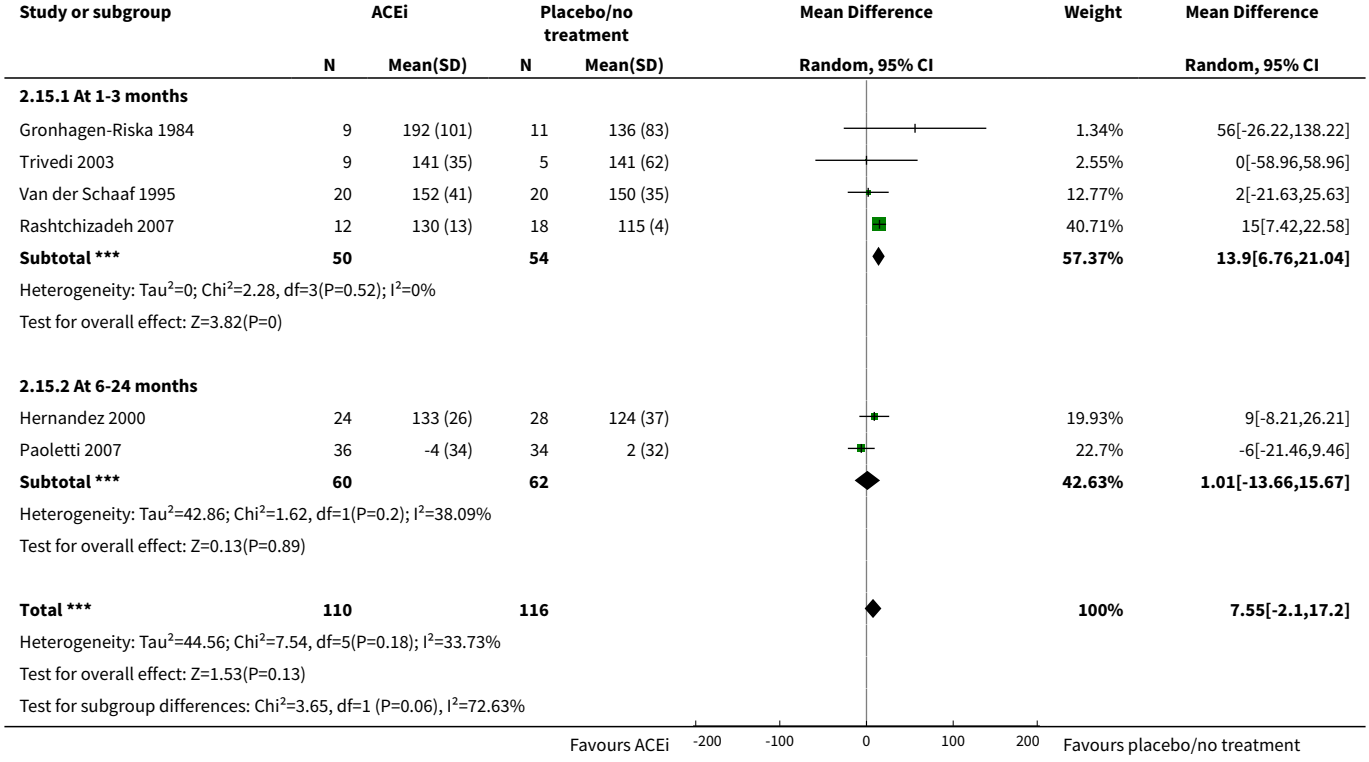


Analysis 2.14. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 14 Any GFR measure.



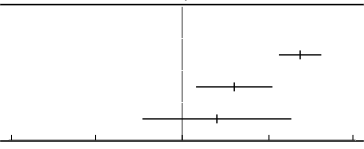


Analysis 2.15. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 15 Serum creatinine (µmol/L).



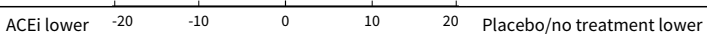
Analysis 2.16. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 16 Serum potassium (mmol/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
2.16.1 At 1-3 months						
Rashtchizadeh 2007	12	4.6 (0.2)	18	3.9 (0.1)		0.68[0.56,0.8]
Gronhagen-Riska 1984	9	4.3 (0.2)	11	4 (0.3)		0.3[0.08,0.52]
Trivedi 2003	9	4.4 (0.6)	5	4.2 (0.2)		0.2[-0.23,0.63]



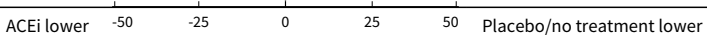
Analysis 2.17. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 17 Haematocrit (%).

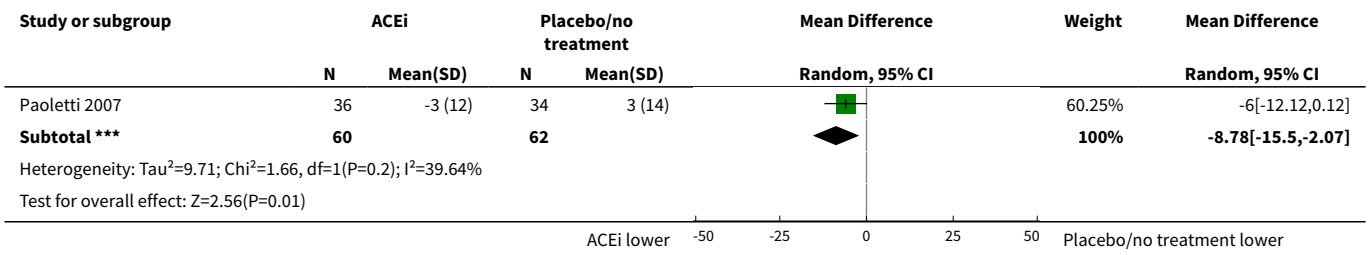
Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.17.1 At 1 month							
Ok 1995	10	51 (3)	9	55 (2)		56.42%	-4[-6.27,-1.73]
Van der Schaaf 1995	20	40 (5)	20	41 (5)		43.58%	-1[-4.1,2.1]
Subtotal ***	**30**		**29**			**100%**	**-2.69[-5.61,0.22]**
Heterogeneity: Tau^2=2.58; Chi^2=2.34, df=1(P=0.13); I^2=57.28%							
Test for overall effect: Z=1.81(P=0.07)							
2.17.2 At 2-4 months							
Beckingham 1995	15	46.1 (4.6)	10	51.1 (2.2)		25.86%	-5[-7.7,-2.3]
Ok 1995	10	45 (3)	9	52 (3)		25.85%	-7[-9.7,-4.3]
Rashtchizadeh 2007	12	38.5 (2.8)	18	39.9 (2.4)		27.67%	-1.4[-3.33,0.53]
Trivedi 2003	9	-9 (6)	5	2.3 (2.7)		20.63%	-11.3[-15.88,-6.72]
Subtotal ***	**46**		**42**			**100%**	**-5.82[-9.56,-2.08]**
Heterogeneity: Tau^2=12.16; Chi^2=21.71, df=3(P<0.0001); I^2=86.18%							
Test for overall effect: Z=3.05(P=0)							



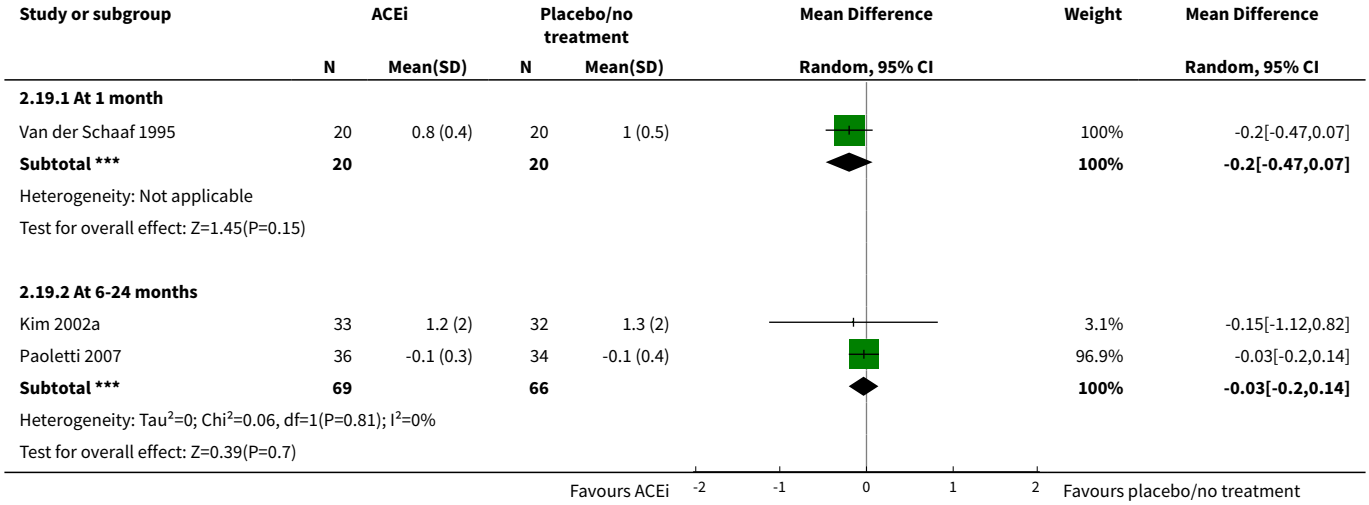
Analysis 2.18. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 18 Haemoglobin (g/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.18.1 At 1-4 months							
Beckingham 1995	15	151 (12)	10	160 (6.3)		34.77%	-9[-16.22,-1.78]
Rashtchizadeh 2007	12	132 (10.1)	18	133.9 (7.6)		35.13%	-1.9[-8.61,4.81]
Trivedi 2003	9	-28 (17)	5	7 (6.9)		30.11%	-35[-47.65,-22.35]
Subtotal ***	**36**		**33**			**100%**	**-14.33[-29.9,1.23]**
Heterogeneity: Tau^2=167.82; Chi^2=20.54, df=2(P<0.0001); I^2=90.26%							
Test for overall effect: Z=1.81(P=0.07)							
2.18.2 At 6-18 months							
Hernandez 2000	24	124 (16)	28	137 (16)		39.75%	-13[-21.72,-4.28]





Analysis 2.19. Comparison 2 ACEi versus placebo/no treatment/ non-antihypertensive, Outcome 19 Proteinuria (g/24 h).



Comparison 3. ACEi versus CCB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any blood pressure (BP) measure at last follow-up	6	275	Mean Difference (IV, Random, 95% CI)	0.58 [-2.02, 3.18]
1.1 Systolic BP (mm Hg)	3	127	Mean Difference (IV, Random, 95% CI)	3.51 [-1.21, 8.22]
1.2 Mean arterial pressure (MAP) (mm Hg)	3	148	Mean Difference (IV, Random, 95% CI)	-0.66 [-3.99, 2.67]
2 Death at last follow-up	2	221	Risk Ratio (M-H, Random, 95% CI)	4.03 [0.45, 35.82]
2.1 At 6 months	1	67	Risk Ratio (M-H, Random, 95% CI)	3.09 [0.13, 73.20]
2.2 At 1 year	1	154	Risk Ratio (M-H, Random, 95% CI)	5.13 [0.25, 105.13]

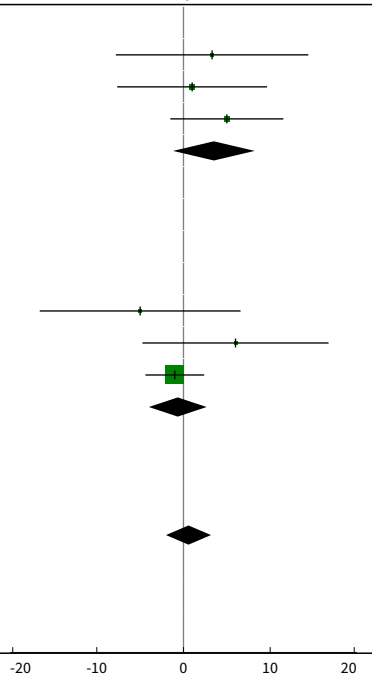
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Graft loss at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Any GFR measure at last follow-up	6	296	Mean Difference (IV, Random, 95% CI)	-11.48 [-15.75, -7.21]
4.1 Creatinine clearance (mL/min)	2	88	Mean Difference (IV, Random, 95% CI)	-15.66 [-33.79, 2.47]
4.2 Radioisotope GFR (mL/min or mL/min/1.73 m^2)	4	208	Mean Difference (IV, Random, 95% CI)	-10.58 [-15.15, -6.01]
5 Serum creatinine (µmol/L) at last follow-up	7	397	Mean Difference (IV, Random, 95% CI)	12.88 [8.14, 17.62]
6 Any rejection at last follow-up	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
7 Rejection rate at last follow-up	1		Rate ratio (Random, 95% CI)	Totals not selected
8 Myocardial infarction	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9 New onset angina	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
10 Ankle oedema	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11 Serum potassium (mmol/L) at last follow-up	4	189	Mean Difference (IV, Random, 95% CI)	0.27 [0.14, 0.41]
12 Hyperkalaemia	3	211	Risk Ratio (M-H, Random, 95% CI)	3.74 [1.89, 7.43]
12.1 'Transient' hyperkalaemia	1	123	Risk Ratio (M-H, Random, 95% CI)	3.51 [1.70, 7.27]
12.2 > 5.5 mmol/L	2	88	Risk Ratio (M-H, Random, 95% CI)	6.27 [0.79, 49.59]
13 Proteinuria (g/24 h) at last follow-up	2	142	Mean Difference (IV, Random, 95% CI)	-0.28 [-0.47, -0.10]
14 Haemoglobin (g/L) at last follow-up`	5	332	Mean Difference (IV, Random, 95% CI)	-12.96 [-15.72, -10.21]
15 Haematocrit (%) at last follow-up	3	113	Mean Difference (IV, Random, 95% CI)	-4.33 [-5.45, -3.20]
16 Serum creatinine (µmol/L)	7		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
16.1 At 1-3 months	4	284	Mean Difference (IV, Random, 95% CI)	4.05 [-6.31, 14.41]
16.2 At 6-12 months	4	313	Mean Difference (IV, Random, 95% CI)	12.41 [5.97, 18.85]
16.3 At 2 years	1	25	Mean Difference (IV, Random, 95% CI)	15.0 [-5.98, 35.98]
17 Serum potassium (mmol/L)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
17.1 At 2 months	1	19	Mean Difference (IV, Random, 95% CI)	0.30 [0.03, 0.57]
17.2 At 6-12 months	2	145	Mean Difference (IV, Random, 95% CI)	0.27 [-0.03, 0.56]
17.3 At 2 years	1	25	Mean Difference (IV, Random, 95% CI)	0.20 [-0.07, 0.47]
18 Haemoglobin (g/L)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
18.1 At 1-3 months	2	121	Mean Difference (IV, Random, 95% CI)	-6.42 [-15.73, 2.88]
18.2 At 6-12 months	4	313	Mean Difference (IV, Random, 95% CI)	-12.96 [-15.78, -10.14]
19 Haematocrit (%)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
19.1 At 1 month	1	40	Mean Difference (IV, Random, 95% CI)	0.0 [-3.10, 3.10]
19.2 At 6-12 months	2	88	Mean Difference (IV, Random, 95% CI)	-4.25 [-5.40, -3.09]
19.3 At 2 years	1	25	Mean Difference (IV, Random, 95% CI)	-6.0 [-11.40, -0.60]
20 Diastolic blood pressure (mm Hg)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
20.1 At 1-2 months	2	60	Mean Difference (IV, Random, 95% CI)	4.34 [0.42, 8.27]
20.2 At 6-12 months	1	67	Mean Difference (IV, Random, 95% CI)	0.0 [-4.14, 4.14]
21 Mean arterial blood pressure (mm Hg)	6		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21.1 At 1-2 months	2	60	Mean Difference (IV, Random, 95% CI)	3.42 [-1.28, 8.13]
21.2 At 6-12 months	4	215	Mean Difference (IV, Random, 95% CI)	0.06 [-2.58, 2.71]
21.3 At 2 years	1	25	Mean Difference (IV, Random, 95% CI)	-5.0 [-16.58, 6.58]
22 Systolic blood pressure (mm Hg)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
22.1 At 1-2 months	2	60	Mean Difference (IV, Random, 95% CI)	4.56 [-1.05, 10.18]
22.2 At 6-12 months	1	67	Mean Difference (IV, Random, 95% CI)	1.0 [-7.64, 9.64]
23 Any GFR measure	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
23.1 Measured GFR (mL/min/1.73 m^2): 1-2 months	2	60	Mean Difference (IV, Random, 95% CI)	-7.11 [-15.60, 1.37]
23.2 Creatinine clearance (mL/min): 6 months	2	88	Mean Difference (IV, Random, 95% CI)	-19.92 [-31.92, -7.93]
23.3 Creatinine clearance (mL/min): 6-12 months	2	88	Mean Difference (IV, Random, 95% CI)	-19.92 [-31.92, -7.93]
23.4 Measured GFR (mL/min/1.73 m^2): 6-12 months	2	148	Mean Difference (IV, Random, 95% CI)	-10.46 [-17.10, -3.82]
23.5 Measured GFR (mL/min/1.73 m^2): 2 years	1	25	Mean Difference (IV, Random, 95% CI)	-12.0 [-26.76, 2.76]
24 Proteinuria (g/24 h)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
24.1 At 1 month	2	142	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.37, 0.12]
24.2 At 3 months	1	102	Mean Difference (IV, Random, 95% CI)	-0.40 [-0.68, -0.12]
24.3 At 12 months	1	102	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.52, -0.08]

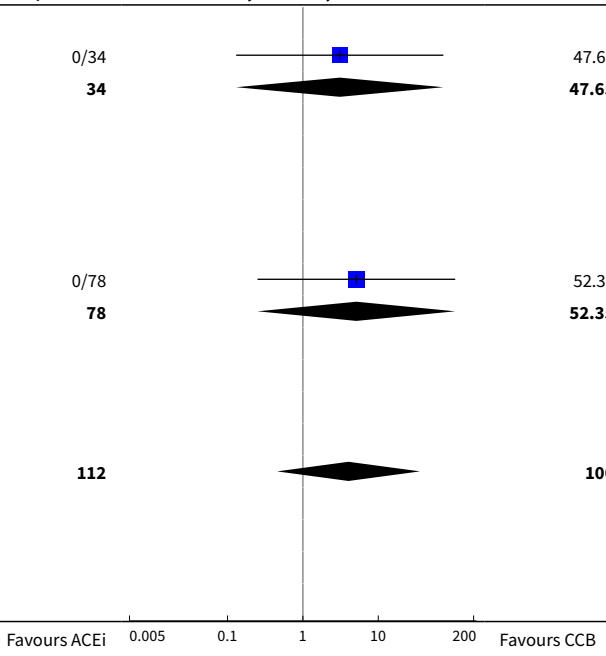
Analysis 3.1. Comparison 3 ACEi versus CCB, Outcome 1 Any blood pressure (BP) measure at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.1.1 Systolic BP (mm Hg)							
Sennesael 1995	10	159.7 (13.3)	10	156.4 (12)		5.47%	3.3[-7.8,14.4]
Halimi 2007	33	140 (19)	34	139 (17)		9.03%	1[-7.64,9.64]
Van der Schaaf 1995	20	153 (11)	20	148 (10)		15.89%	5[-1.52,11.52]
Subtotal ***	**63**		**64**			**30.4%**	**3.51[-1.21,8.22]**
Heterogeneity: Tau²=0; Chi²=0.53, df=2(P=0.77); I²=0%							
Test for overall effect: Z=1.46(P=0.14)							
3.1.2 Mean arterial pressure (MAP) (mm Hg)							
Mourad 1993	14	-18 (11)	11	-13 (17)		5.03%	-5[-16.58,6.58]
Hernandez 1995	10	105 (13)	11	99 (12)		5.86%	6[-4.73,16.73]
El Agroudy 2003	54	94 (7)	48	95 (10)		58.72%	-1[-4.39,2.39]
Subtotal ***	**78**		**70**			**69.6%**	**-0.66[-3.99,2.67]**
Heterogeneity: Tau²=0.52; Chi²=2.06, df=2(P=0.36); I²=2.74%							
Test for overall effect: Z=0.39(P=0.7)							
Total ***	**141**		**134**			**100%**	**0.58[-2.02,3.18]**
Heterogeneity: Tau²=0; Chi²=4.71, df=5(P=0.45); I²=0%							
Test for overall effect: Z=0.44(P=0.66)							
Test for subgroup differences: Chi²=2.13, df=1 (P=0.14), I²=53.07%							

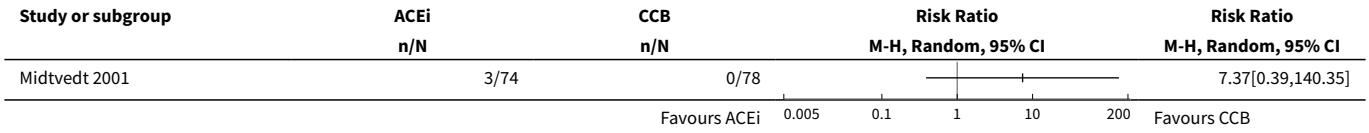


Analysis 3.2. Comparison 3 ACEi versus CCB, Outcome 2 Death at last follow-up.

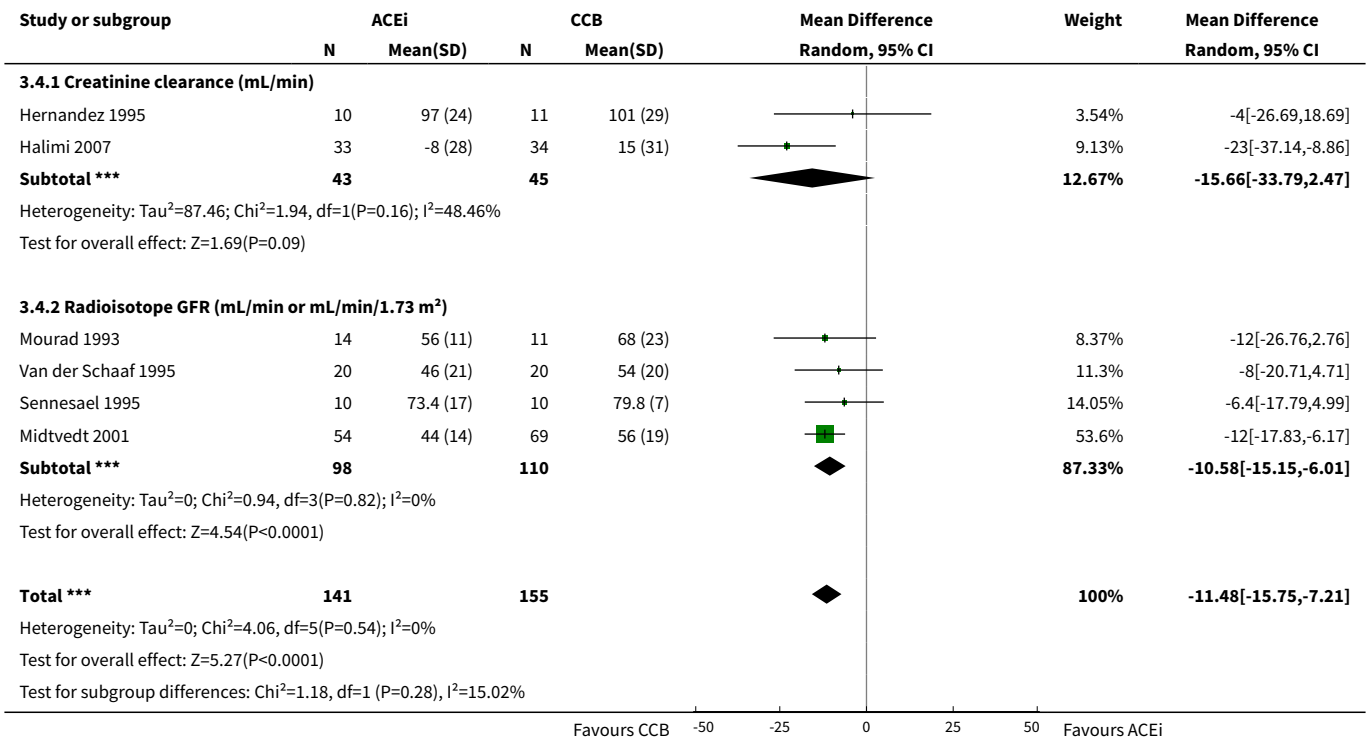
Study or subgroup	ACEi n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
3.2.1 At 6 months					
Halimi 2007	1/33	0/34		47.65%	3.09[0.13,73.2]
Subtotal (95% CI)	**33**	**34**		**47.65%**	**3.09[0.13,73.2]**
Total events: 1 (ACEi), 0 (CCB)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.7(P=0.49)					
3.2.2 At 1 year					
Midtvedt 2001	2/76	0/78		52.35%	5.13[0.25,105.13]
Subtotal (95% CI)	**76**	**78**		**52.35%**	**5.13[0.25,105.13]**
Total events: 2 (ACEi), 0 (CCB)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.06(P=0.29)					
Total (95% CI)	**109**	**112**		**100%**	**4.03[0.45,35.82]**
Total events: 3 (ACEi), 0 (CCB)					
Heterogeneity: Tau²=0; Chi²=0.05, df=1(P=0.82); I²=0%					
Test for overall effect: Z=1.25(P=0.21)					
Test for subgroup differences: Not applicable					



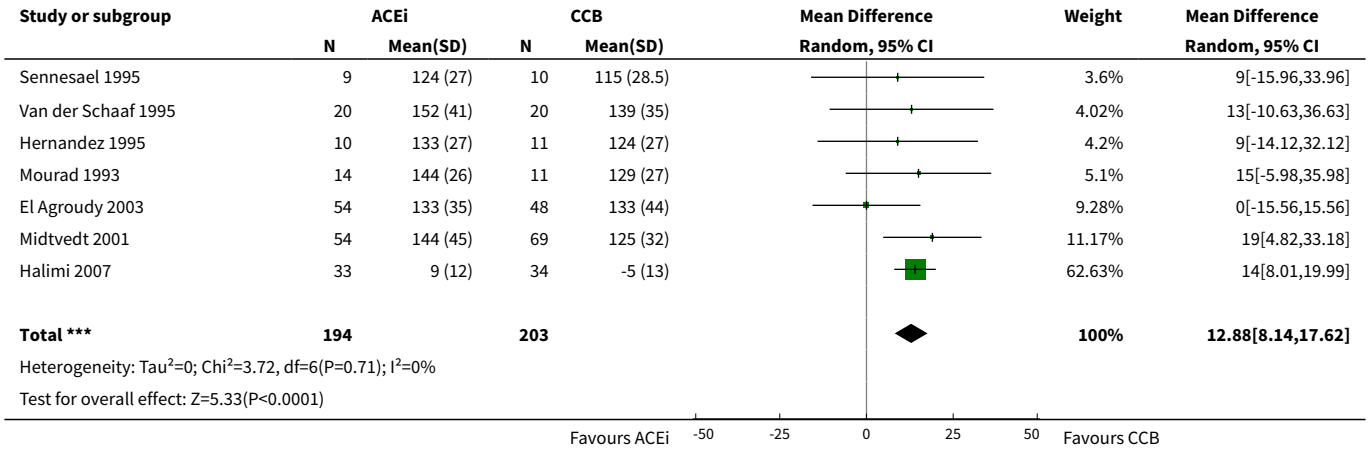
Analysis 3.3. Comparison 3 ACEi versus CCB, Outcome 3 Graft loss at last follow-up.



Analysis 3.4. Comparison 3 ACEi versus CCB, Outcome 4 Any GFR measure at last follow-up.

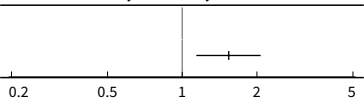


Analysis 3.5. Comparison 3 ACEi versus CCB, Outcome 5 Serum creatinine (µmol/L) at last follow-up.



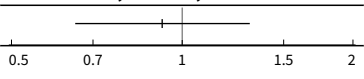
Analysis 3.6. Comparison 3 ACEi versus CCB, Outcome 6 Any rejection at last follow-up.

Study or subgroup	ACEi n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Halimi 2007	0/33	0/34		Not estimable
Midtvedt 2001	51/76	34/78		1.54[1.14,2.07]



Analysis 3.7. Comparison 3 ACEi versus CCB, Outcome 7 Rejection rate at last follow-up.

Study or subgroup	ACEi N	CCB N	log[Rate ratio] (SE)	Rate ratio IV, Random, 95% CI	Rate ratio IV, Random, 95% CI
El Agroudy 2003	54	48	-0.1 (0.177)		0.92[0.65,1.31]

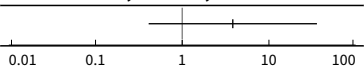


Analysis 3.8. Comparison 3 ACEi versus CCB, Outcome 8 Myocardial infarction.

Study or subgroup	ACEi n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Midtvedt 2001	0/54	0/69		Not estimable

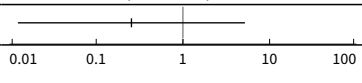
Analysis 3.9. Comparison 3 ACEi versus CCB, Outcome 9 New onset angina.

Study or subgroup	ACEi n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Midtvedt 2001	3/54	1/69		3.83[0.41,35.83]



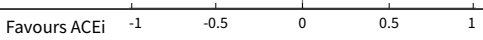
Analysis 3.10. Comparison 3 ACEi versus CCB, Outcome 10 Ankle oedema.

Study or subgroup	ACEi n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Midtvedt 2001	0/54	2/69		0%	0.25[0.01,5.19]



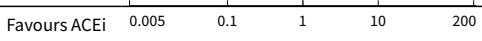
Analysis 3.11. Comparison 3 ACEi versus CCB, Outcome 11 Serum potassium (mmol/L) at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Mourad 1993	14	3.9 (0.4)	11	3.7 (0.3)		19.75%	0.2[-0.07,0.47]
Sennesael 1995	9	3.9 (0.3)	10	3.6 (0.3)		20.24%	0.3[0.03,0.57]
El Agroudy 2003	54	4.3 (0.6)	24	4.2 (0.5)		21.95%	0.1[-0.16,0.36]
Halimi 2007	33	0.2 (0.4)	34	-0.2 (0.3)		38.06%	0.4[0.23,0.57]
Total ***	**110**		**79**			**100%**	**0.27[0.14,0.41]**
Heterogeneity: Tau^2=0.01; Chi^2=4.14, df=3(P=0.25); I^2=27.62%							
Test for overall effect: Z=3.89(P<0.0001)							



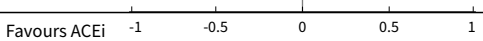
Analysis 3.12. Comparison 3 ACEi versus CCB, Outcome 12 Hyperkalaemia.

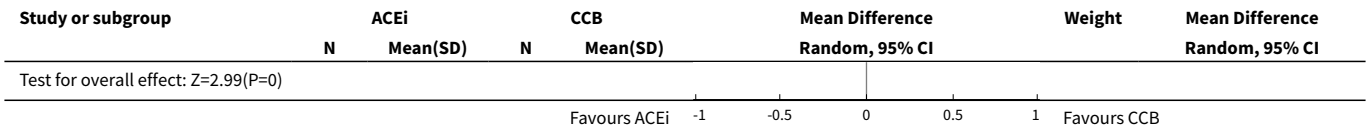
Study or subgroup	ACEi n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
3.12.1 'Transient' hyperkalaemia					
Midtvedt 2001	22/54	8/69		89.01%	3.51[1.7,7.27]
Subtotal (95% CI)	**54**	**69**		**89.01%**	**3.51[1.7,7.27]**
Total events: 22 (ACEi), 8 (CCB)					
Heterogeneity: Not applicable					
Test for overall effect: Z=3.39(P=0)					
3.12.2 > 5.5 mmol/L					
Halimi 2007	3/33	0/34		5.49%	7.21[0.39,134.32]
Hernandez 1995	2/10	0/11		5.5%	5.45[0.29,101.55]
Subtotal (95% CI)	**43**	**45**		**10.99%**	**6.27[0.79,49.59]**
Total events: 5 (ACEi), 0 (CCB)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.89); I^2=0%					
Test for overall effect: Z=1.74(P=0.08)					
Total (95% CI)	**97**	**114**		**100%**	**3.74[1.89,7.43]**
Total events: 27 (ACEi), 8 (CCB)					
Heterogeneity: Tau^2=0; Chi^2=0.29, df=2(P=0.86); I^2=0%					
Test for overall effect: Z=3.77(P=0)					
Test for subgroup differences: Not applicable					



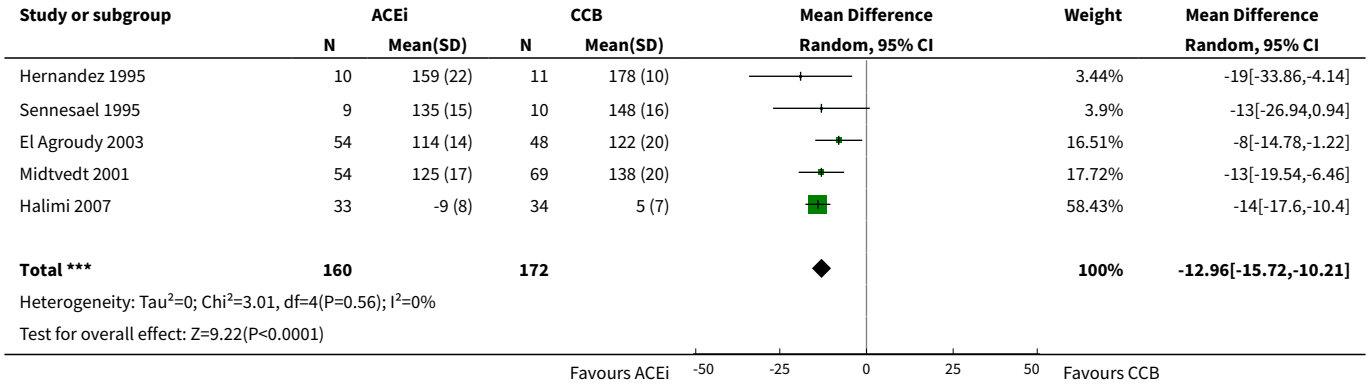
Analysis 3.13. Comparison 3 ACEi versus CCB, Outcome 13 Proteinuria (g/24 h) at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Van der Schaaf 1995	20	0.8 (0.4)	20	1 (0.7)		31.55%	-0.25[-0.58,0.08]
El Agroudy 2003	54	0.5 (0.4)	48	0.8 (0.7)		68.45%	-0.3[-0.52,-0.08]
Total ***	**74**		**68**			**100%**	**-0.28[-0.47,-0.1]**
Heterogeneity: Tau^2=0; Chi^2=0.06, df=1(P=0.81); I^2=0%							

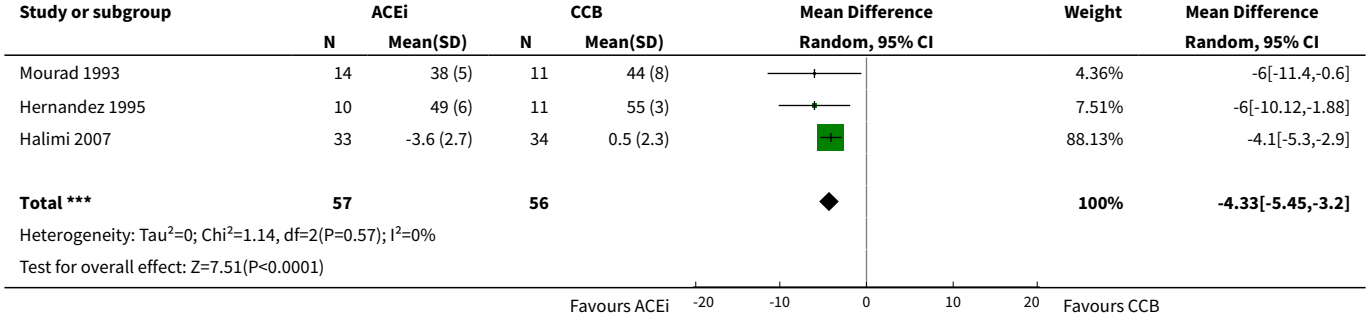




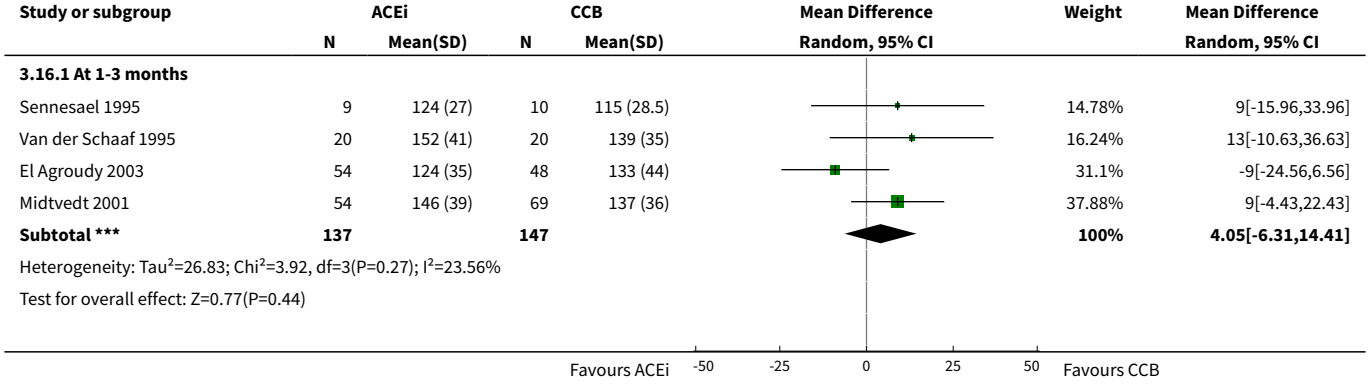
Analysis 3.14. Comparison 3 ACEi versus CCB, Outcome 14 Haemoglobin (g/L) at last follow-up`.

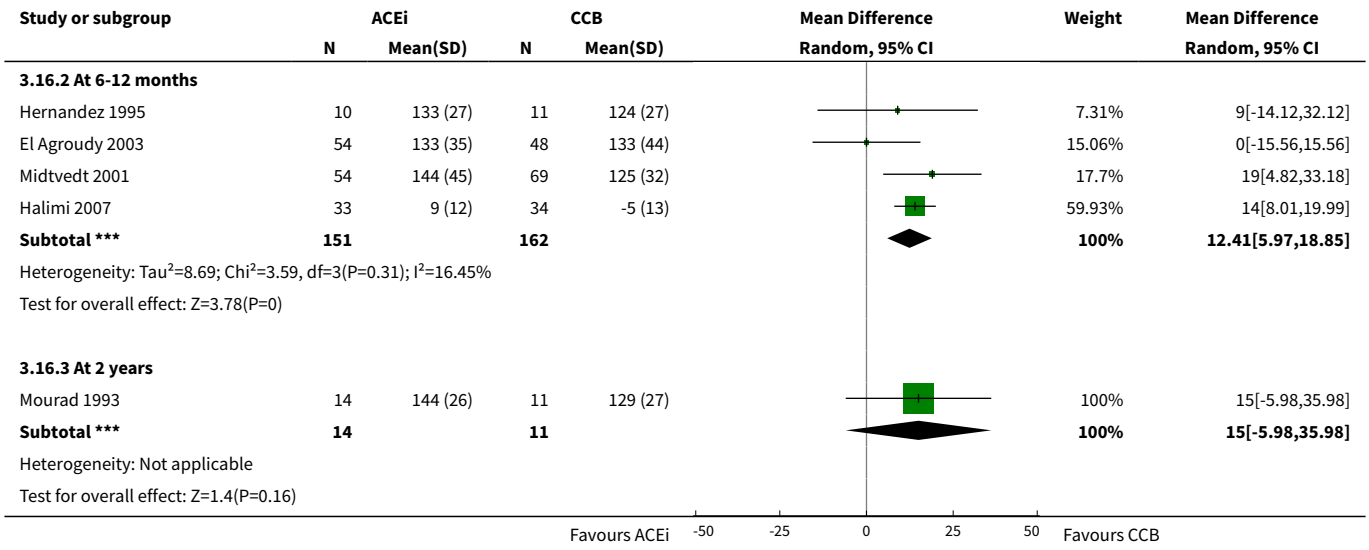


Analysis 3.15. Comparison 3 ACEi versus CCB, Outcome 15 Haematocrit (%) at last follow-up.

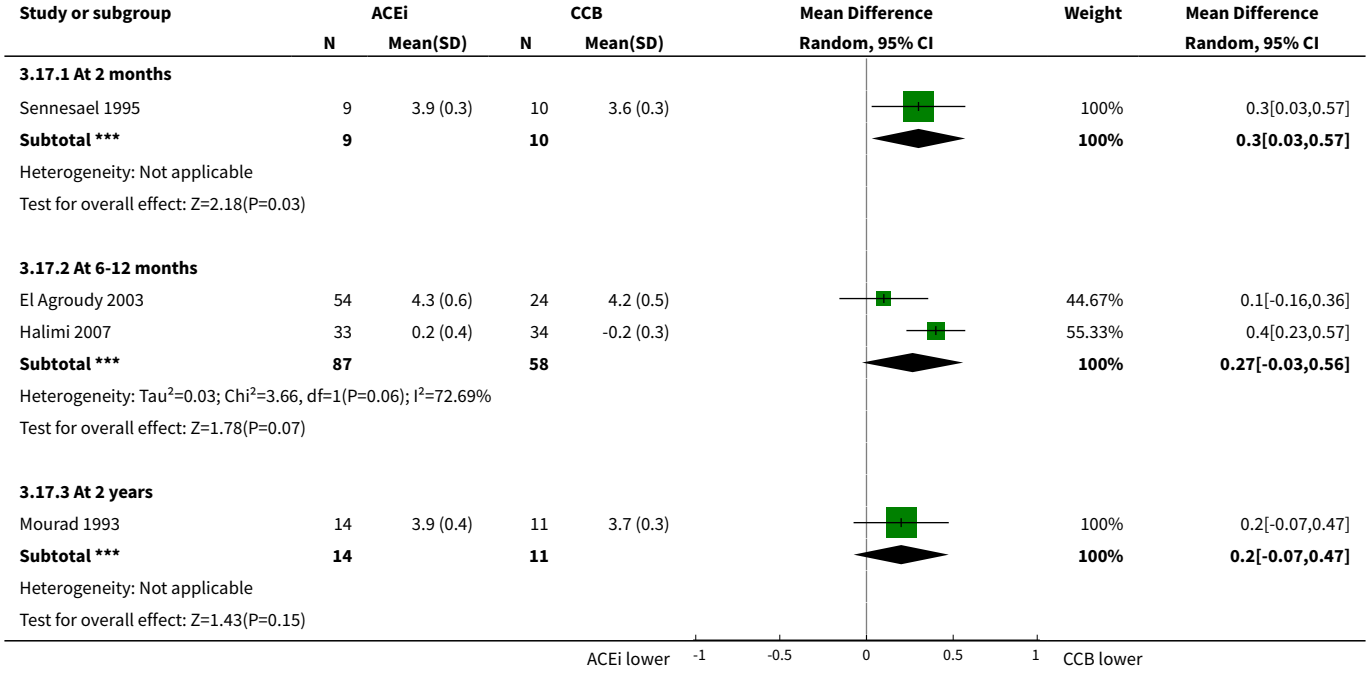


Analysis 3.16. Comparison 3 ACEi versus CCB, Outcome 16 Serum creatinine (µmol/L).

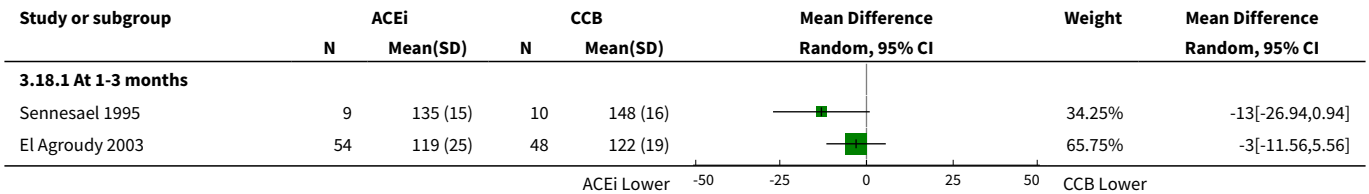


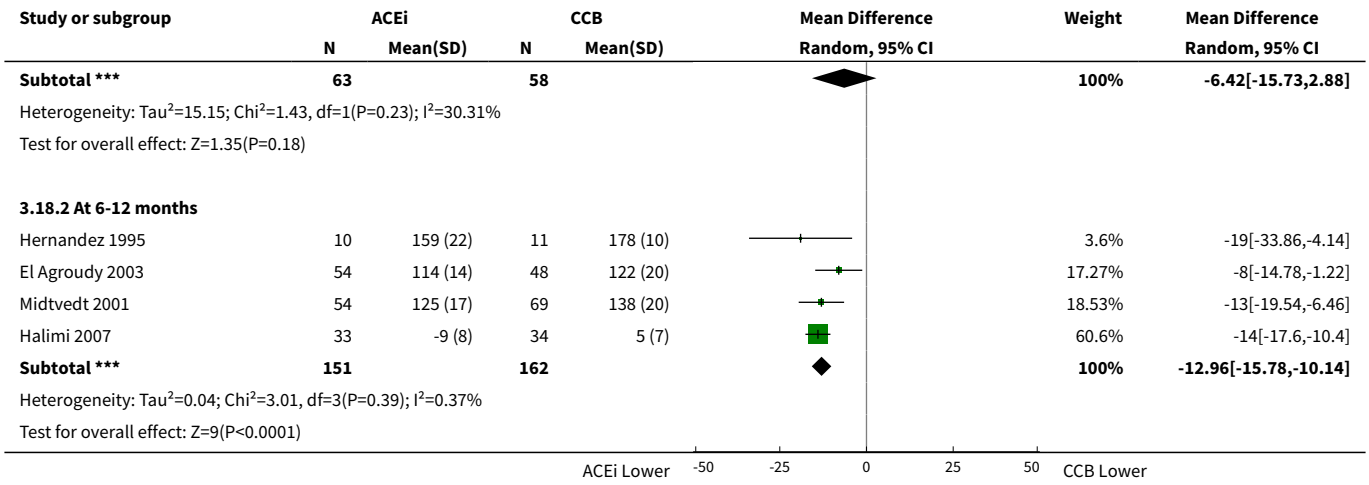


Analysis 3.17. Comparison 3 ACEi versus CCB, Outcome 17 Serum potassium (mmol/L).

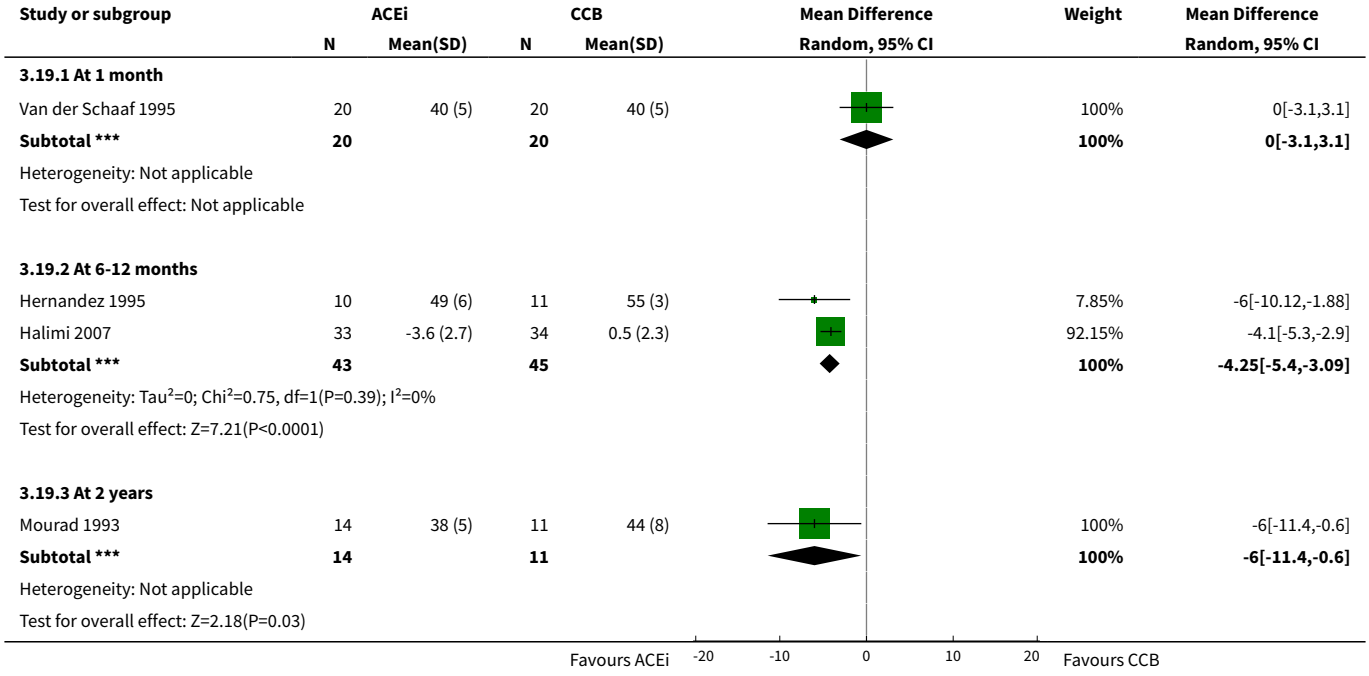


Analysis 3.18. Comparison 3 ACEi versus CCB, Outcome 18 Haemoglobin (g/L).

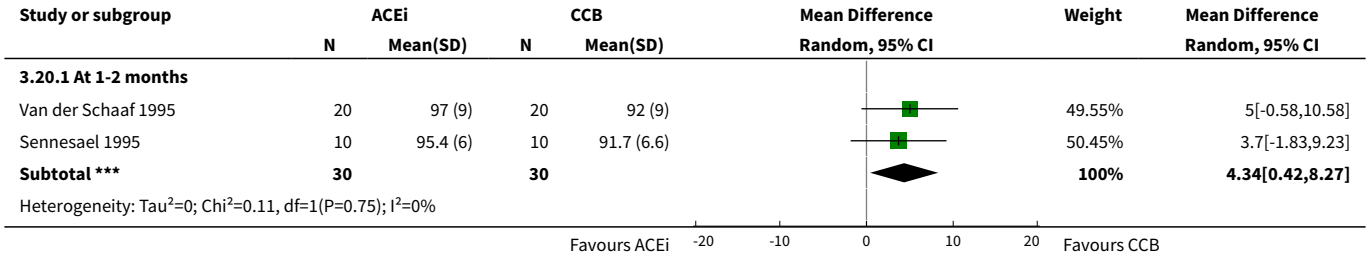


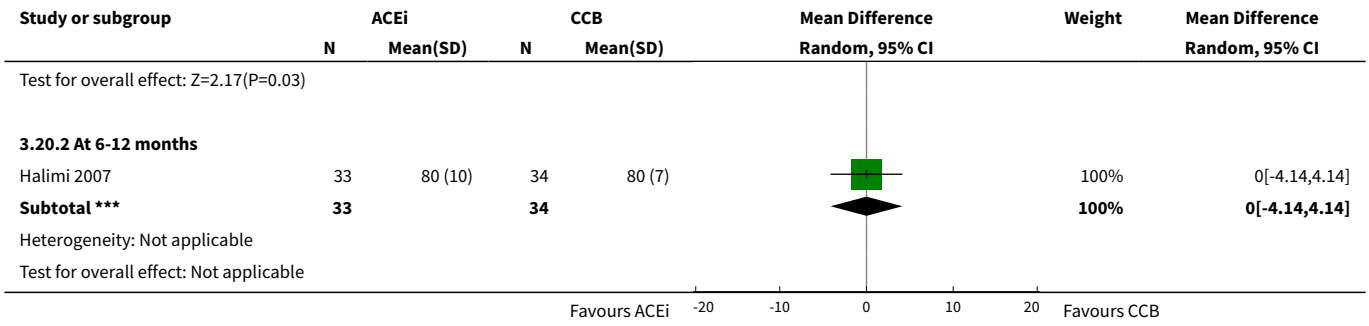


Analysis 3.19. Comparison 3 ACEi versus CCB, Outcome 19 Haematocrit (%).

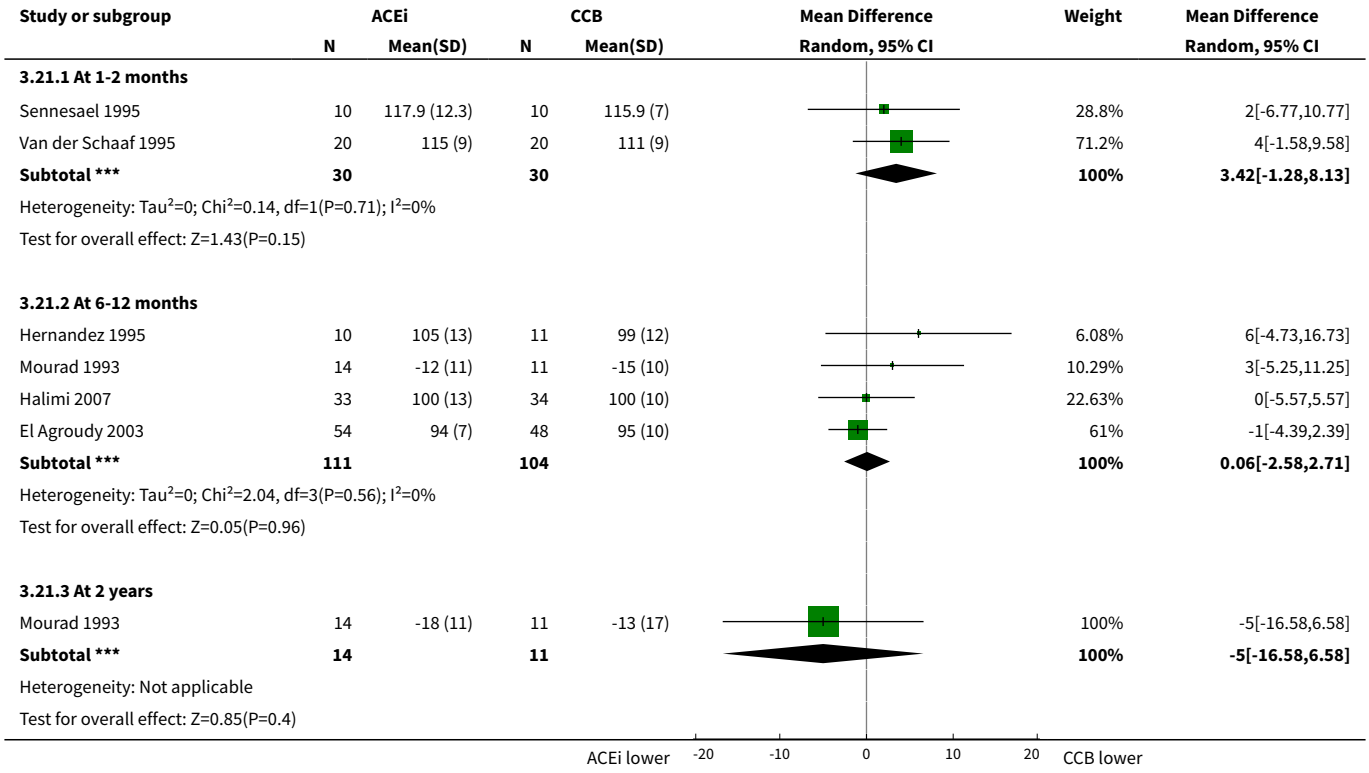


Analysis 3.20. Comparison 3 ACEi versus CCB, Outcome 20 Diastolic blood pressure (mm Hg).

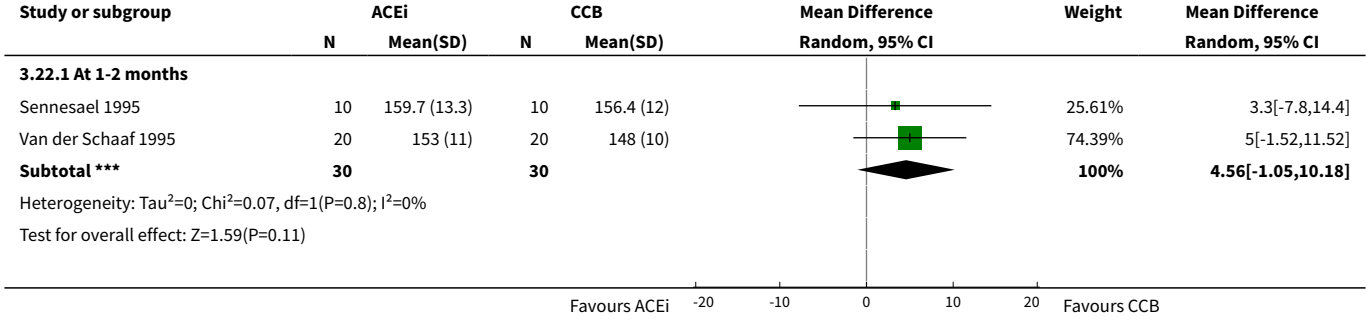




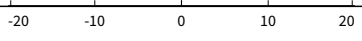
Analysis 3.21. Comparison 3 ACEi versus CCB, Outcome 21 Mean arterial blood pressure (mm Hg).



Analysis 3.22. Comparison 3 ACEi versus CCB, Outcome 22 Systolic blood pressure (mm Hg).

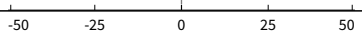


Study or subgroup	ACEi N	ACEi Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.22.2 At 6-12 months							
Halimi 2007	33	140 (19)	34	139 (17)		100%	1[-7.64,9.64]
Subtotal ***	**33**		**34**			**100%**	**1[-7.64,9.64]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.23(P=0.82)							

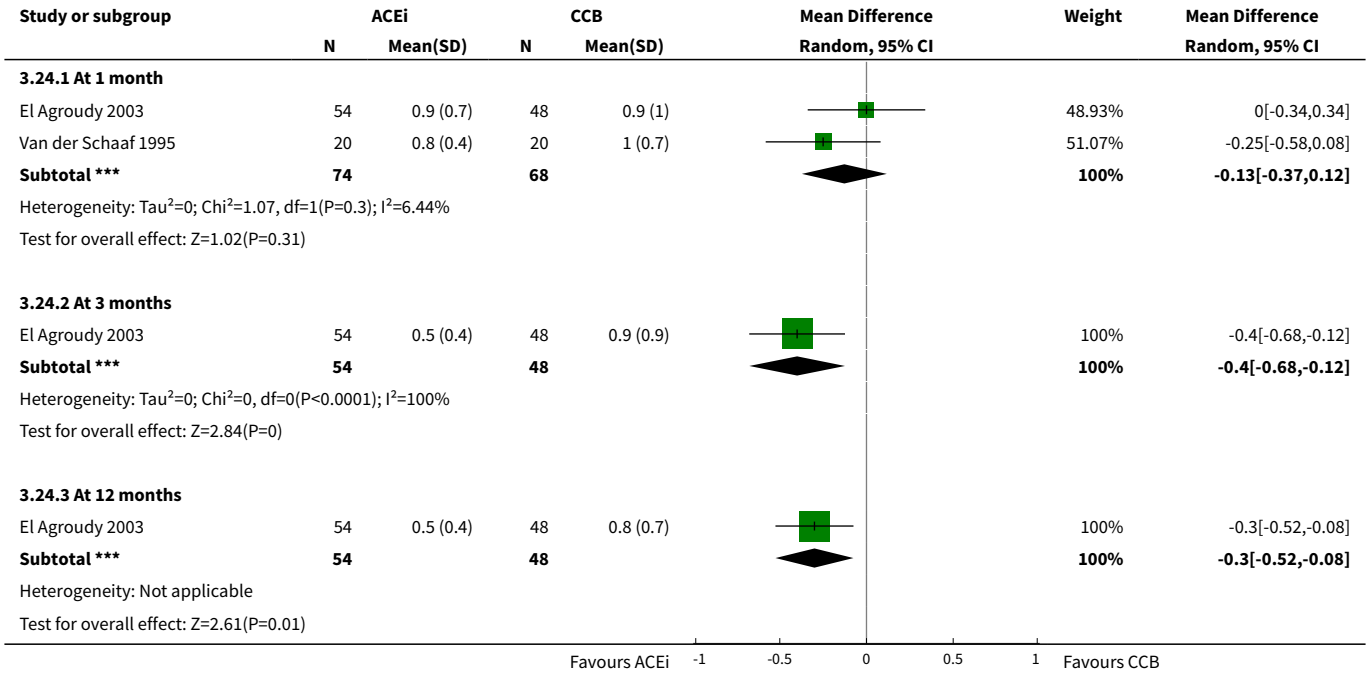


Analysis 3.23. Comparison 3 ACEi versus CCB, Outcome 23 Any GFR measure.

Study or subgroup	ACEi N	ACEi Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.23.1 Measured GFR (mL/min/1.73 m²): 1-2 months							
Van der Schaaf 1995	20	46 (21)	20	54 (20)		44.56%	-8[-20.71,4.71]
Sennesael 1995	10	73.4 (17)	10	79.8 (7)		55.44%	-6.4[-17.79,4.99]
Subtotal ***	**30**		**30**			**100%**	**-7.11[-15.6,1.37]**
Heterogeneity: Tau^2=0; Chi^2=0.03, df=1(P=0.85); I^2=0%							
Test for overall effect: Z=1.64(P=0.1)							
3.23.2 Creatinine clearance (mL/min): 6 months							
Hernandez 1995	10	97 (24)	11	109 (29)		27.96%	-12[-34.69,10.69]
Halimi 2007	33	-8 (28)	34	15 (31)		72.04%	-23[-37.14,-8.86]
Subtotal ***	**43**		**45**			**100%**	**-19.92[-31.92,-7.93]**
Heterogeneity: Tau^2=0; Chi^2=0.65, df=1(P=0.42); I^2=0%							
Test for overall effect: Z=3.25(P=0)							
3.23.3 Creatinine clearance (mL/min): 6-12 months							
Hernandez 1995	10	97 (24)	11	109 (29)		27.96%	-12[-34.69,10.69]
Halimi 2007	33	-8 (28)	34	15 (31)		72.04%	-23[-37.14,-8.86]
Subtotal ***	**43**		**45**			**100%**	**-19.92[-31.92,-7.93]**
Heterogeneity: Tau^2=0; Chi^2=0.65, df=1(P=0.42); I^2=0%							
Test for overall effect: Z=3.25(P=0)							
3.23.4 Measured GFR (mL/min/1.73 m²): 6-12 months							
Mourad 1993	14	59 (19)	11	62 (20)		17.11%	-3[-18.45,12.45]
Midtvedt 2001	54	44 (14)	69	56 (19)		82.89%	-12[-17.83,-6.17]
Subtotal ***	**68**		**80**			**100%**	**-10.46[-17.1,-3.82]**
Heterogeneity: Tau^2=4.99; Chi^2=1.14, df=1(P=0.29); I^2=12.33%							
Test for overall effect: Z=3.09(P=0)							
3.23.5 Measured GFR (mL/min/1.73 m²): 2 years							
Mourad 1993	14	56 (11)	11	68 (23)		100%	-12[-26.76,2.76]
Subtotal ***	**14**		**11**			**100%**	**-12[-26.76,2.76]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.59(P=0.11)							



Analysis 3.24. Comparison 3 ACEi versus CCB, Outcome 24 Proteinuria (g/24 h).



Comparison 4. ARB versus CCB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean arterial blood pressure (mm Hg) at last follow-up	3	149	Mean Difference (IV, Random, 95% CI)	-1.98 [-9.37, 5.41]
2 Any GFR measure at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Serum creatinine (µmol/L) at last follow-up	4	193	Mean Difference (IV, Random, 95% CI)	-2.36 [-18.16, 13.43]
4 Hyperkalaemia at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4.1 > 6.0 mmol/L	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Rejection rate	1		Rate ratio (Random, 95% CI)	Totals not selected
6 Haemoglobin (g/L) at last follow-up	2	129	Mean Difference (IV, Random, 95% CI)	-8.51 [-23.08, 6.06]
7 Proteinuria (g/24 h) at last follow-up	2	136	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.55, 0.15]

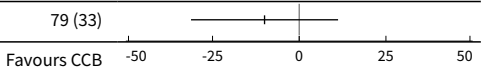
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8 Serum potassium (mmol/L) at last follow-up	3	163	Mean Difference (IV, Random, 95% CI)	0.31 [0.06, 0.56]
9 Serum creatinine (µmol/L)	4	335	Mean Difference (IV, Random, 95% CI)	-1.46 [-11.90, 8.99]
9.1 At 1-3 months	3	176	Mean Difference (IV, Random, 95% CI)	3.41 [-11.16, 17.99]
9.2 At 6-12 months	3	159	Mean Difference (IV, Random, 95% CI)	-8.11 [-24.75, 8.54]
10 Proteinuria (g/24 h)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 At 1 month	2	136	Mean Difference (IV, Random, 95% CI)	-0.18 [-0.52, 0.17]
10.2 At 3 months	1	102	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.62, 0.02]
10.3 At 1 year	1	102	Mean Difference (IV, Random, 95% CI)	-0.4 [-0.62, -0.18]

Analysis 4.1. Comparison 4 ARB versus CCB, Outcome 1 Mean arterial blood pressure (mm Hg) at last follow-up.

Study or subgroup	ARB N	ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Inigo 2001	17	96 (10)	17	92 (7)		31.7%	4[-1.8,9.8]
Barenbrock 2001	6	89 (5)	7	99 (5)		32.45%	-10[-15.45,-4.55]
El Agroudy 2003 ARB	54	95 (9)	48	95 (10)		35.85%	0[-3.71,3.71]
Total ***	**77**		**72**			**100%**	**-1.98[-9.37,5.41]**
Heterogeneity: Tau²=36.06; Chi²=13.41, df=2(P=0); I²=85.09%							
Test for overall effect: Z=0.52(P=0.6)							

Analysis 4.2. Comparison 4 ARB versus CCB, Outcome 2 Any GFR measure at last follow-up.

Study or subgroup	ARB N	ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Inigo 2001	17	69 (30)	17	79 (33)		-10[-31.2,11.2]

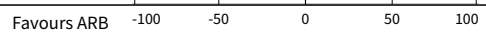


Analysis 4.3. Comparison 4 ARB versus CCB, Outcome 3 Serum creatinine (µmol/L) at last follow-up.

Study or subgroup	ARB N	ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Wei 2002	16	256 (72)	14	292 (34)		12.58%	-36[-75.52,3.52]
Formica 2006	17	133 (53)	10	141 (3)		23.55%	-8[-33.26,17.26]
Inigo 2001	17	122 (35)	17	108 (27)		28.92%	14[-7.01,35.01]
El Agroudy 2003 ARB	54	133 (44)	48	133 (44)		34.95%	0[-17.11,17.11]
Total ***	**104**		**89**			**100%**	**-2.36[-18.16,13.43]**

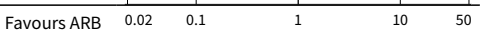
Heterogeneity: Tau²=109.56; Chi²=5.27, df=3(P=0.15); I²=43.08%

Test for overall effect: Z=0.29(P=0.77)



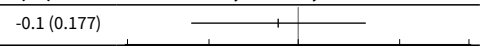
Analysis 4.4. Comparison 4 ARB versus CCB, Outcome 4 Hyperkalaemia at last follow-up.

Study or subgroup	ARB n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
4.4.1 > 6.0 mmol/L				
Formica 2006	6/29	1/27		5.59[0.72,43.44]



Analysis 4.5. Comparison 4 ARB versus CCB, Outcome 5 Rejection rate.

Study or subgroup	ARB N	CCB N	log[Rate ratio] (SE)	Rate ratio IV, Random, 95% CI	Rate ratio IV, Random, 95% CI
El Agroudy 2003	54	48	-0.1 (0.177)		0.92[0.65,1.31]

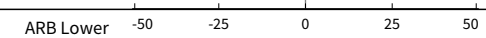


Analysis 4.6. Comparison 4 ARB versus CCB, Outcome 6 Haemoglobin (g/L) at last follow-up.

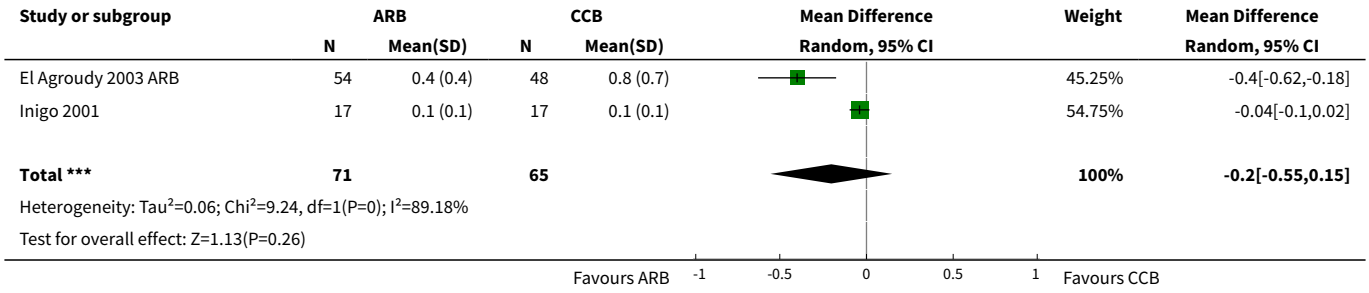
Study or subgroup	ARB N	ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Formica 2006	17	122 (22)	10	139 (13)		43.42%	-17[-30.2,-3.8]
El Agroudy 2003 ARB	54	120 (20)	48	122 (20)		56.58%	-2[-9.78,5.78]
Total ***	**71**		**58**			**100%**	**-8.51[-23.08,6.06]**

Heterogeneity: Tau²=81.94; Chi²=3.68, df=1(P=0.06); I²=72.84%

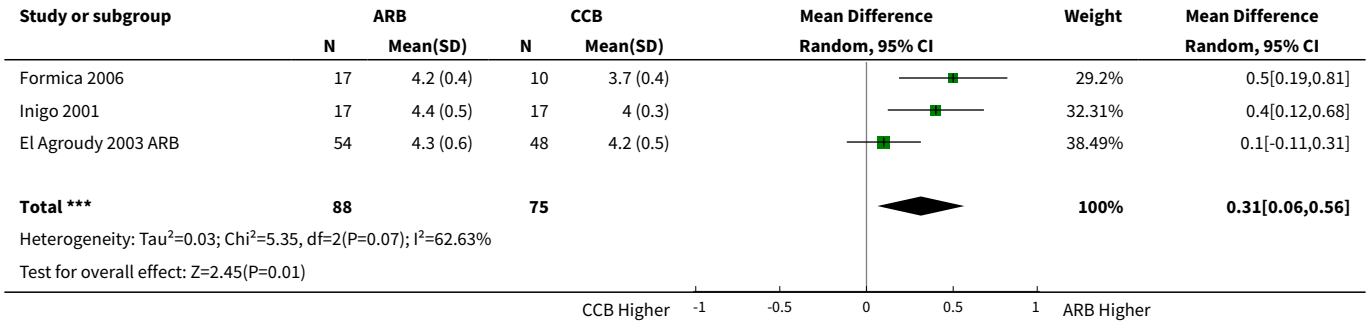
Test for overall effect: Z=1.14(P=0.25)



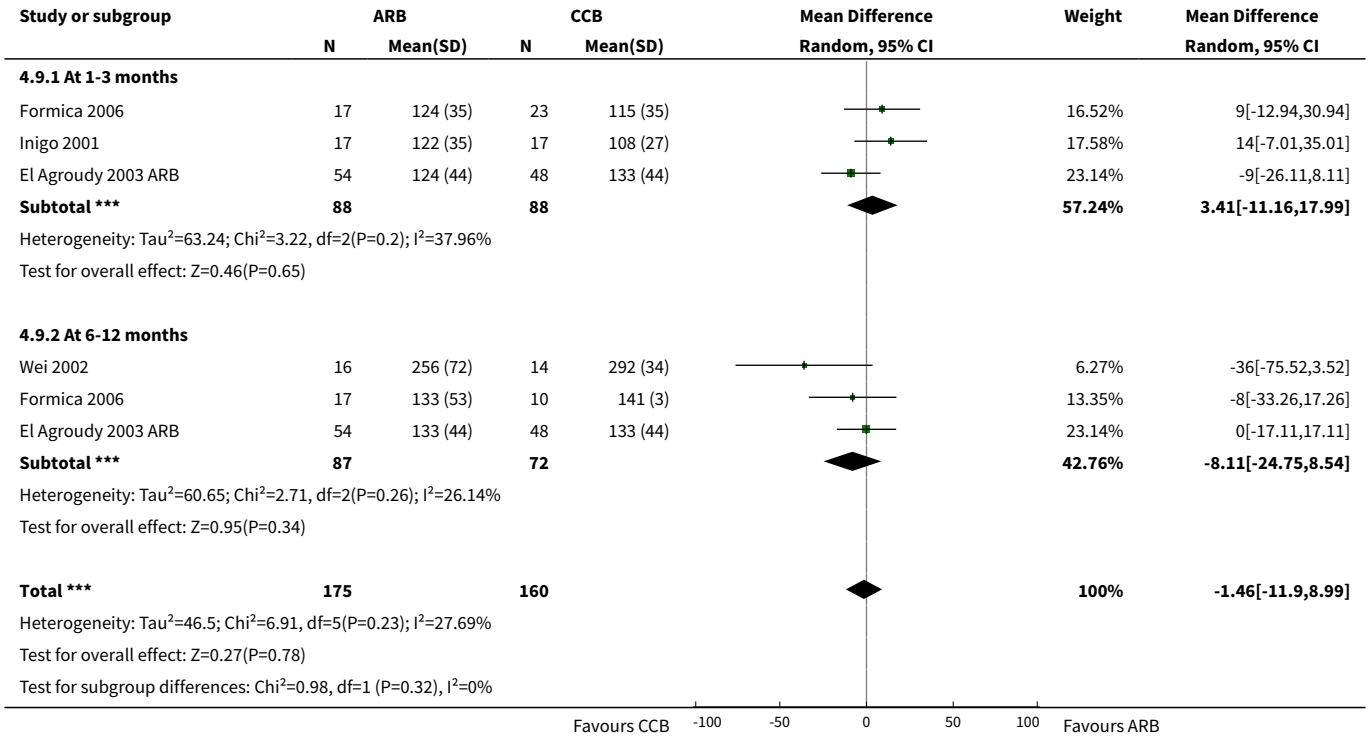
Analysis 4.7. Comparison 4 ARB versus CCB, Outcome 7 Proteinuria (g/24 h) at last follow-up.



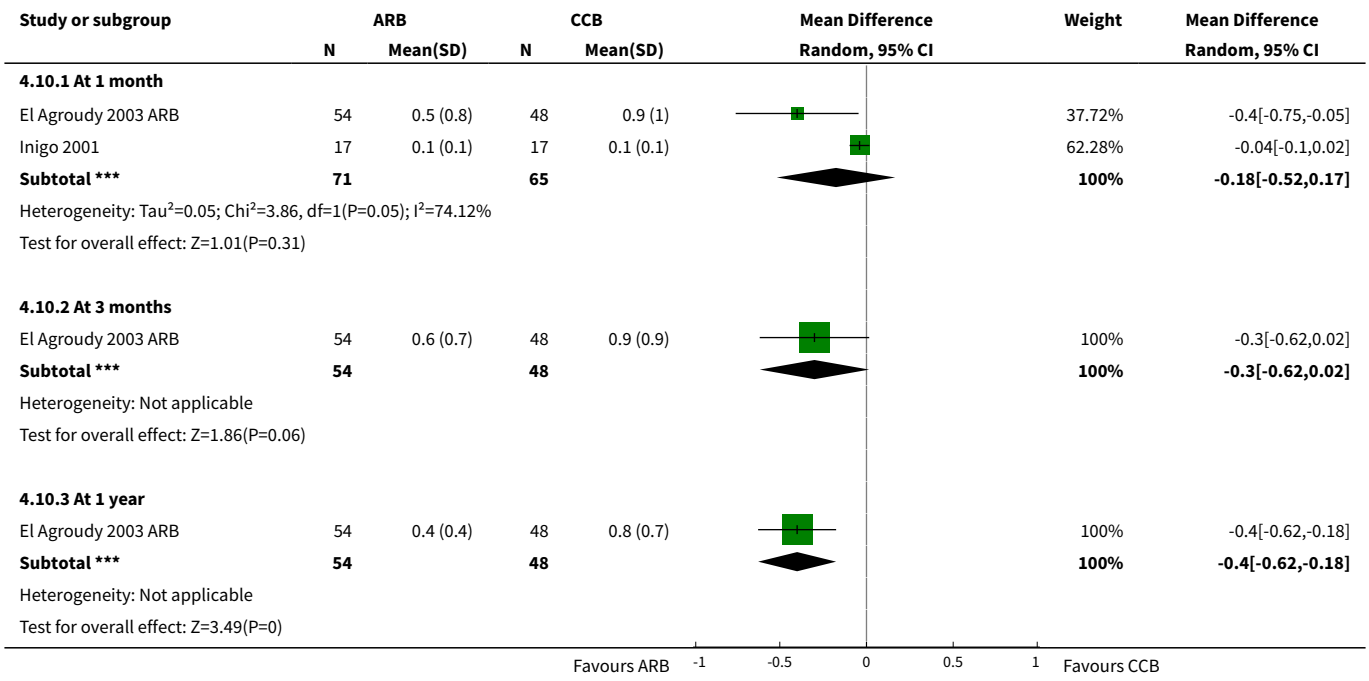
Analysis 4.8. Comparison 4 ARB versus CCB, Outcome 8 Serum potassium (mmol/L) at last follow-up.



Analysis 4.9. Comparison 4 ARB versus CCB, Outcome 9 Serum creatinine (µmol/L).



Analysis 4.10. Comparison 4 ARB versus CCB, Outcome 10 Proteinuria (g/24 h).



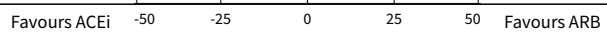
Comparison 5. ACEi versus ARB

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Any blood pressure (BP) measure at last follow-up	5	201	Mean Difference (IV, Random, 95% CI)	-1.82 [-4.67, 1.04]
1.1 Systolic BP (mm Hg)	2	49	Mean Difference (IV, Random, 95% CI)	-2.74 [-11.13, 5.65]
1.2 Mean arterial pressure (mm Hg)	3	152	Mean Difference (IV, Random, 95% CI)	-1.69 [-4.73, 1.34]
2 Rejection rate	1		Rate ratio (Random, 95% CI)	Totals not selected
3 Serum creatinine (µmol/L) at last follow-up	4	187	Mean Difference (IV, Random, 95% CI)	-2.21 [-8.94, 4.51]
4 Serum potassium (mmol/L) at last follow-up	4	187	Mean Difference (IV, Random, 95% CI)	0.07 [-0.03, 0.18]
5 Hyperkalaemia at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6 Proteinuria (g/24 h) at last follow-up	2	130	Mean Difference (IV, Random, 95% CI)	0.04 [-0.06, 0.14]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
7 Proteinuria remission	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
7.1 < 0.5 g/24 h at follow-up	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Haematocrit (%) at last follow-up	3	77	Mean Difference (IV, Random, 95% CI)	-1.14 [-1.89, -0.39]
9 Haemoglobin (g/L) at last follow-up	3	165	Mean Difference (IV, Random, 95% CI)	-4.62 [-10.02, 0.78]
10 Haemoglobin (g/L)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 At 1-3 months	3	165	Mean Difference (IV, Random, 95% CI)	-3.12 [-8.43, 2.18]
10.2 At 1 years	1	108	Mean Difference (IV, Random, 95% CI)	-6.0 [-12.51, 0.51]
11 Serum creatinine (µmol/L)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 At 1-3 months	5	207	Mean Difference (IV, Random, 95% CI)	0.19 [-7.66, 8.05]
11.2 At 6-12 months	1	108	Mean Difference (IV, Random, 95% CI)	0.0 [-13.00, 15.00]
12 Serum potassium (mmol/L)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 At 1-3 months	4	99	Mean Difference (IV, Random, 95% CI)	0.09 [-0.01, 0.20]
12.2 At 6-12 months	1	108	Mean Difference (IV, Random, 95% CI)	0.0 [-0.23, 0.23]
13 Proteinuria (g/24 h)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.1 At 1-3 months	2	130	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.14, 0.09]
13.2 At 6-12 months	1	108	Mean Difference (IV, Random, 95% CI)	0.10 [-0.05, 0.25]

Analysis 5.1. Comparison 5 ACEi versus ARB, Outcome 1 Any blood pressure (BP) measure at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.1.1 Systolic BP (mm Hg)							
Yildiz 2001	15	121 (11)	12	130 (25)		3.53%	-9[-24.2,6.2]
Schmidt 2001	11	127 (13)	11	127 (11)		8.04%	0[-10.06,10.06]
Subtotal ***	**26**		**23**			**11.57%**	**-2.74[-11.13,5.65]**
Heterogeneity: Tau²=0; Chi²=0.94, df=1(P=0.33); I²=0%							
Test for overall effect: Z=0.64(P=0.52)							
5.1.2 Mean arterial pressure (mm Hg)							
Celik 2000	10	97 (10)	10	96 (18)		5%	1[-11.76,13.76]
Rashtchizadeh 2007	12	93.6 (10.5)	18	100.3 (11.8)		12.53%	-6.7[-14.76,1.36]
El Agroudy 2003	54	94 (7)	48	95 (10)		70.9%	-1[-4.39,2.39]
Subtotal ***	**76**		**76**			**88.43%**	**-1.69[-4.73,1.34]**
Heterogeneity: Tau²=0; Chi²=1.81, df=2(P=0.4); I²=0%							
Test for overall effect: Z=1.09(P=0.27)							
Total ***	**102**		**99**			**100%**	**-1.82[-4.67,1.04]**
Heterogeneity: Tau²=0; Chi²=2.8, df=4(P=0.59); I²=0%							
Test for overall effect: Z=1.25(P=0.21)							
Test for subgroup differences: Chi²=0.05, df=1 (P=0.82), I²=0%							



Analysis 5.2. Comparison 5 ACEi versus ARB, Outcome 2 Rejection rate.

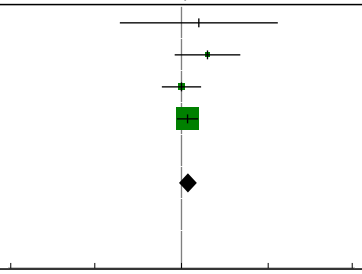
Study or subgroup	ACEi N	ARB N	log[Rate ratio] (SE)	Rate ratio IV, Random, 95% CI	Rate ratio IV, Random, 95% CI
El Agroudy 2003	54	54	0 (0.176)		1[0.71,1.41]

Analysis 5.3. Comparison 5 ACEi versus ARB, Outcome 3 Serum creatinine (µmol/L) at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Schmidt 2001	11	141 (35)	11	133 (27)		6.52%	8[-18.12,34.12]
Yildiz 2001	15	109 (23)	12	126 (26)		12.45%	-17[-35.76,1.76]
El Agroudy 2003	54	133 (35)	54	133 (44)		19.14%	0[-15,15]
Rashtchizadeh 2007	12	130 (13)	18	131 (6)		61.9%	-1[-8.86,6.86]
Total ***	**92**		**95**			**100%**	**-2.21[-8.94,4.51]**
Heterogeneity: Tau²=2.92; Chi²=3.15, df=3(P=0.37); I²=4.72%							
Test for overall effect: Z=0.65(P=0.52)							

Analysis 5.4. Comparison 5 ACEi versus ARB, Outcome 4 Serum potassium (mmol/L) at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Yildiz 2001	15	4.6 (1.2)	12	4.4 (1.2)		1.27%	0.2[-0.71,1.11]
Schmidt 2001	11	4.8 (0.4)	11	4.5 (0.5)		7.38%	0.3[-0.08,0.68]
El Agroudy 2003	54	4.3 (0.6)	54	4.3 (0.6)		20.63%	0[-0.23,0.23]
Rashtchizadeh 2007	12	4.6 (0.2)	18	4.5 (0.1)		70.72%	0.07[-0.05,0.19]
Total ***	**92**		**95**			**100%**	**0.07[-0.03,0.18]**
Heterogeneity: Tau²=0; Chi²=1.86, df=3(P=0.6); I²=0%							
Test for overall effect: Z=1.41(P=0.16)							

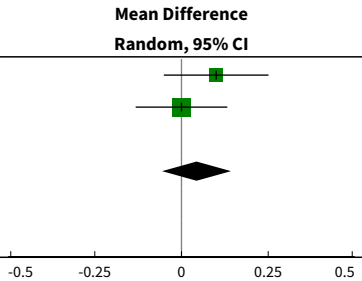


Analysis 5.5. Comparison 5 ACEi versus ARB, Outcome 5 Hyperkalaemia at last follow-up.

Study or subgroup	ACEi n/N	ARB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Altiparmak 2001	2/25	1/12		0.96[0.1,9.57]

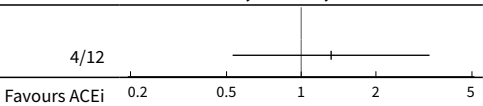
Analysis 5.6. Comparison 5 ACEi versus ARB, Outcome 6 Proteinuria (g/24 h) at last follow-up.

Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
El Agroudy 2003	54	0.5 (0.4)	54	0.4 (0.4)		43.41%	0.1[-0.05,0.25]
Schmidt 2001	11	0.1 (0.2)	11	0.1 (0.1)		56.59%	0[-0.13,0.13]
Total ***	**65**		**65**			**100%**	**0.04[-0.06,0.14]**
Heterogeneity: Tau²=0; Chi²=0.95, df=1(P=0.33); I²=0%							
Test for overall effect: Z=0.86(P=0.39)							

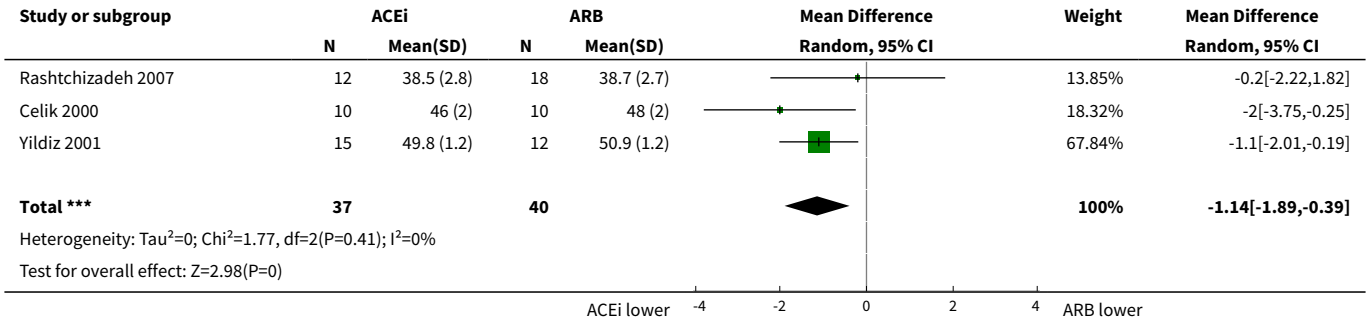


Analysis 5.7. Comparison 5 ACEi versus ARB, Outcome 7 Proteinuria remission.

Study or subgroup	ACEi n/N	ARB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
5.7.1 < 0.5 g/24 h at follow-up				
Altiparmak 2001	11/25	4/12		1.32[0.53,3.29]

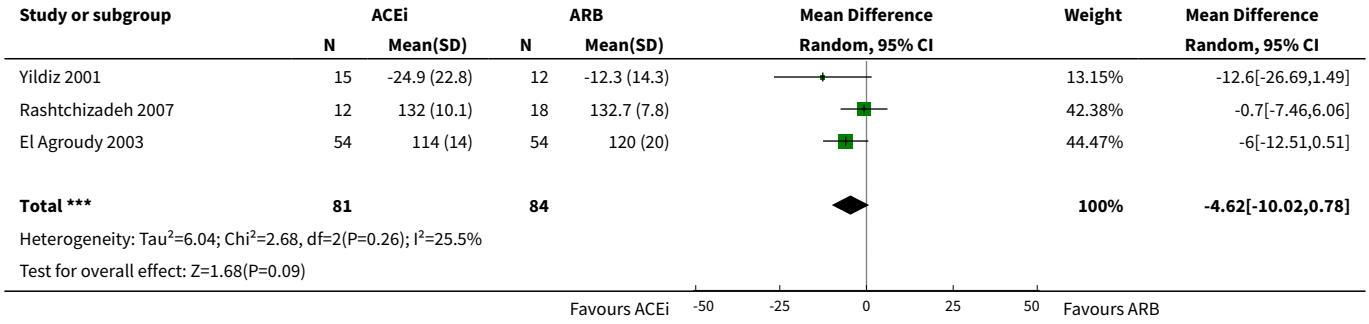


Analysis 5.8. Comparison 5 ACEi versus ARB, Outcome 8 Haematocrit (%) at last follow-up.



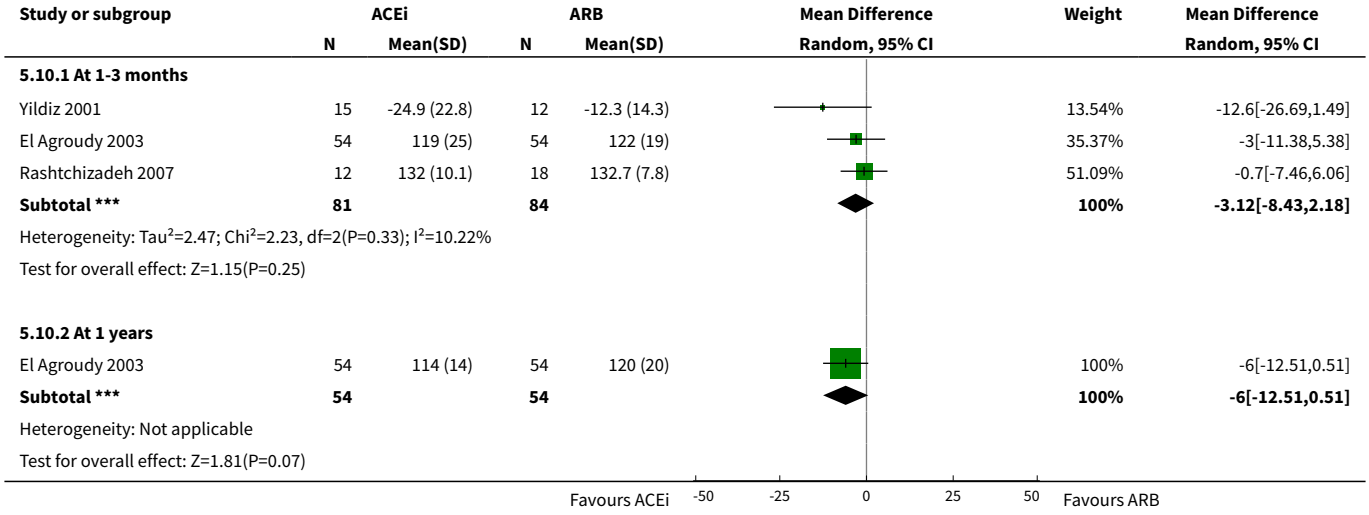
Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Rashtchizadeh 2007	12	38.5 (2.8)	18	38.7 (2.7)		13.85%	-0.2[-2.22,1.82]
Celik 2000	10	46 (2)	10	48 (2)		18.32%	-2[-3.75,-0.25]
Yildiz 2001	15	49.8 (1.2)	12	50.9 (1.2)		67.84%	-1.1[-2.01,-0.19]
Total ***	**37**		**40**			**100%**	**-1.14[-1.89,-0.39]**
Heterogeneity: Tau²=0; Chi²=1.77, df=2(P=0.41); I²=0%							
Test for overall effect: Z=2.98(P=0)							

Analysis 5.9. Comparison 5 ACEi versus ARB, Outcome 9 Haemoglobin (g/L) at last follow-up.



Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Yildiz 2001	15	-24.9 (22.8)	12	-12.3 (14.3)		13.15%	-12.6[-26.69,1.49]
Rashtchizadeh 2007	12	132 (10.1)	18	132.7 (7.8)		42.38%	-0.7[-7.46,6.06]
El Agroudy 2003	54	114 (14)	54	120 (20)		44.47%	-6[-12.51,0.51]
Total ***	**81**		**84**			**100%**	**-4.62[-10.02,0.78]**
Heterogeneity: Tau²=6.04; Chi²=2.68, df=2(P=0.26); I²=25.5%							
Test for overall effect: Z=1.68(P=0.09)							

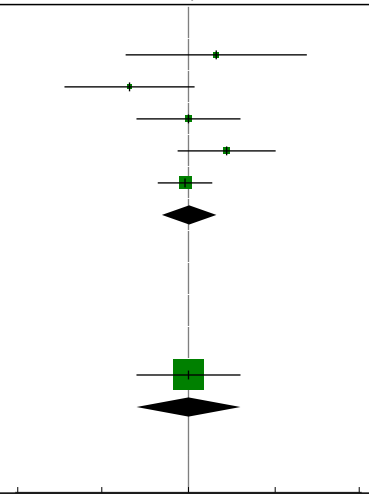
Analysis 5.10. Comparison 5 ACEi versus ARB, Outcome 10 Haemoglobin (g/L).



Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.10.1 At 1-3 months							
Yildiz 2001	15	-24.9 (22.8)	12	-12.3 (14.3)		13.54%	-12.6[-26.69,1.49]
El Agroudy 2003	54	119 (25)	54	122 (19)		35.37%	-3[-11.38,5.38]
Rashtchizadeh 2007	12	132 (10.1)	18	132.7 (7.8)		51.09%	-0.7[-7.46,6.06]
Subtotal ***	**81**		**84**			**100%**	**-3.12[-8.43,2.18]**
Heterogeneity: Tau²=2.47; Chi²=2.23, df=2(P=0.33); I²=10.22%							
Test for overall effect: Z=1.15(P=0.25)							
5.10.2 At 1 years							
El Agroudy 2003	54	114 (14)	54	120 (20)		100%	-6[-12.51,0.51]
Subtotal ***	**54**		**54**			**100%**	**-6[-12.51,0.51]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.81(P=0.07)							

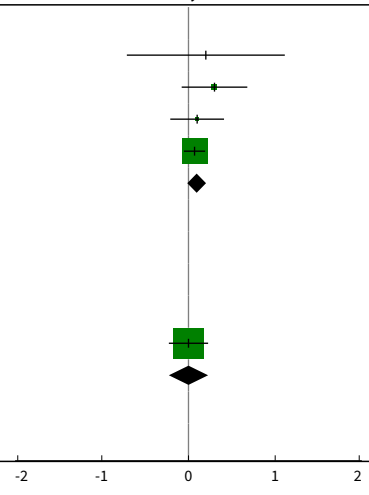
Analysis 5.11. Comparison 5 ACEi versus ARB, Outcome 11 Serum creatinine (µmol/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.11.1 At 1-3 months							
Schmidt 2001	11	141 (35)	11	133 (27)		7.91%	8[-18.12,34.12]
Yildiz 2001	15	109 (23)	12	126 (26)		13.71%	-17[-35.76,1.76]
El Agroudy 2003	54	124 (35)	54	124 (44)		19.1%	0[-15,15]
Celik 2000	10	126 (14)	10	115 (18)		20.71%	11[-3.13,25.13]
Rashtchizadeh 2007	12	130 (13)	18	131 (6)		38.56%	-1[-8.86,6.86]
Subtotal ***	**102**		**105**			**100%**	**0.19[-7.66,8.05]**
Heterogeneity: Tau^2=25.6; Chi^2=5.9, df=4(P=0.21); I^2=32.25%							
Test for overall effect: Z=0.05(P=0.96)							
5.11.2 At 6-12 months							
El Agroudy 2003	54	133 (35)	54	133 (44)		100%	0[-15,15]
Subtotal ***	**54**		**54**			**100%**	**0[-15,15]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



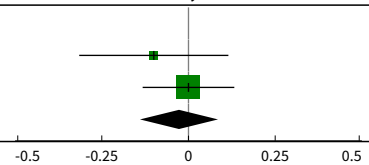
Analysis 5.12. Comparison 5 ACEi versus ARB, Outcome 12 Serum potassium (mmol/L).

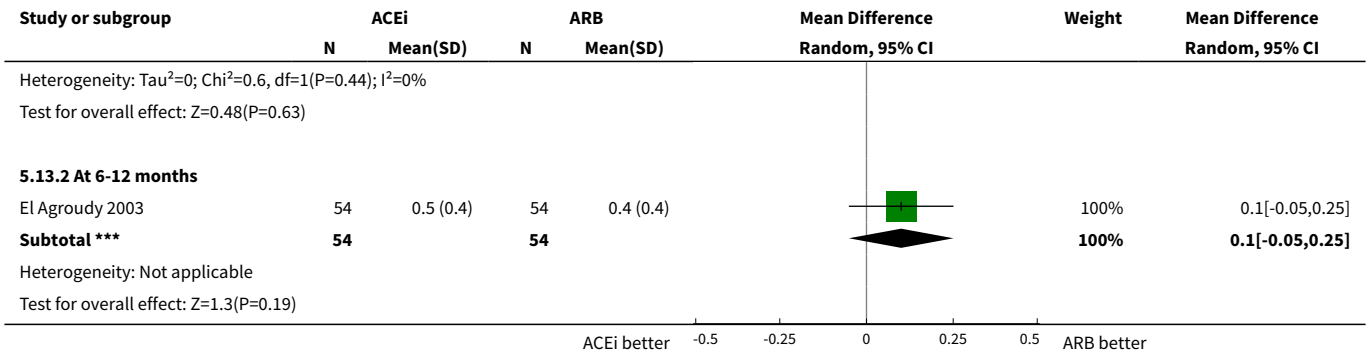
Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.12.1 At 1-3 months							
Yildiz 2001	15	4.6 (1.2)	12	4.4 (1.2)		1.41%	0.2[-0.71,1.11]
Schmidt 2001	11	4.8 (0.4)	11	4.5 (0.5)		8.16%	0.3[-0.08,0.68]
Celik 2000	10	4.3 (0.4)	10	4.2 (0.3)		12.17%	0.1[-0.21,0.41]
Rashtchizadeh 2007	12	4.6 (0.2)	18	4.5 (0.1)		78.25%	0.07[-0.05,0.19]
Subtotal ***	**48**		**51**			**100%**	**0.09[-0.01,0.2]**
Heterogeneity: Tau^2=0; Chi^2=1.34, df=3(P=0.72); I^2=0%							
Test for overall effect: Z=1.71(P=0.09)							
5.12.2 At 6-12 months							
El Agroudy 2003	54	4.3 (0.6)	54	4.3 (0.6)		100%	0[-0.23,0.23]
Subtotal ***	**54**		**54**			**100%**	**0[-0.23,0.23]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



Analysis 5.13. Comparison 5 ACEi versus ARB, Outcome 13 Proteinuria (g/24 h).

Study or subgroup	ACEi N	ACEi Mean(SD)	ARB N	ARB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.13.1 At 1-3 months							
El Agroudy 2003	54	0.5 (0.4)	54	0.6 (0.7)		27.41%	-0.1[-0.32,0.12]
Schmidt 2001	11	0.1 (0.2)	11	0.1 (0.1)		72.59%	0[-0.13,0.13]
Subtotal ***	**65**		**65**			**100%**	**-0.03[-0.14,0.09]**





Comparison 6. ARB versus placebo/no treatment

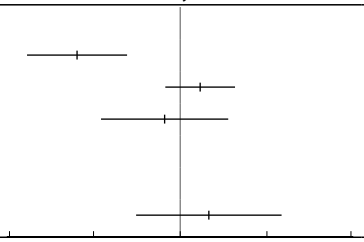
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Any blood pressure (BP) measure at last follow-up	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Systolic BP (mm Hg)	3		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Death	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 At 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Graft loss (censored for death)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.1 At 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Any GFR measure at last follow-up	2	49	Mean Difference (IV, Random, 95% CI)	0.65 [-5.58, 6.89]
4.1 Creatinine clearance (mL/min)	1	28	Mean Difference (IV, Random, 95% CI)	-1.08 [-9.66, 7.50]
4.2 Nankivell eGFR (mL/min/1.73 m^2)	1	21	Mean Difference (IV, Random, 95% CI)	2.60 [-6.49, 11.69]
5 Serum creatinine (µmol/L) at last follow-up	3	170	Mean Difference (IV, Random, 95% CI)	7.77 [-3.01, 18.54]
6 Haemoglobin (g/L) at last follow-up	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
7 Haematocrit (%)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Serum potassium (mmol/L) at last follow-up	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
9 Hyperkalaemia at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9.1 > 5.0 mmol/L	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
10 Systolic blood pressure (mm Hg)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 At 1 month	1	106	Mean Difference (IV, Random, 95% CI)	-9.30 [-16.10, -2.50]
10.2 At 2 months	2	134	Mean Difference (IV, Random, 95% CI)	-7.11 [-15.00, 2.77]
10.3 At 1 year	1	21	Mean Difference (IV, Random, 95% CI)	2.30 [-1.72, 6.32]
11 Diastolic blood pressure (mm Hg)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 At 1 month	1	106	Mean Difference (IV, Random, 95% CI)	-4.80 [-8.94, -0.66]
11.2 At 2 months	2	134	Mean Difference (IV, Random, 95% CI)	-5.09 [-8.68, -1.49]
11.3 At 1 year	1	21	Mean Difference (IV, Random, 95% CI)	-3.10 [-6.78, 0.58]
12 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
12.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13 Serum potassium (mmol/L)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.1 At 1 month	1	106	Mean Difference (IV, Random, 95% CI)	0.30 [0.13, 0.47]
13.2 At 2 months	3	170	Mean Difference (IV, Random, 95% CI)	0.31 [0.03, 0.59]
14 Serum creatinine (µmol/L)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 At 1 month	1	106	Mean Difference (IV, Random, 95% CI)	-5.20 [-21.92, 11.52]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
14.2 At 2 months	3	170	Mean Difference (IV, Random, 95% CI)	7.19 [-2.87, 17.25]
15 Haemoglobin (g/L)	3	276	Mean Difference (IV, Random, 95% CI)	-7.56 [-13.90, -1.22]
15.1 At 1 month	1	106	Mean Difference (IV, Random, 95% CI)	-9.0 [-15.09, -2.91]
15.2 At 2 months	3	170	Mean Difference (IV, Random, 95% CI)	-7.09 [-16.09, 1.90]

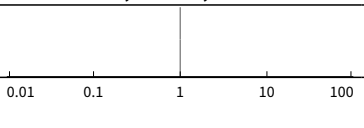
Analysis 6.1. Comparison 6 ARB versus placebo/no treatment, Outcome 1 Any blood pressure (BP) measure at last follow-up.

Study or subgroup	ARB N	ARB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
6.1.1 Systolic BP (mm Hg)						
Andres 2006	52	136.5 (15)	54	148.4 (15.3)		-11.9[-17.67,-6.13]
Weidanz 2005	11	138 (4.2)	10	135.7 (5.1)		2.3[-1.72,6.32]
Tylicki 2006	14	118.6 (10.1)	14	120.4 (9.7)		-1.8[-9.14,5.54]
6.1.2 Mean arterial pressure (mm Hg)						
Rashtchizadeh 2007	18	100.3 (11.8)	18	97 (13.8)		3.3[-5.09,11.69]



Analysis 6.2. Comparison 6 ARB versus placebo/no treatment, Outcome 2 Death.

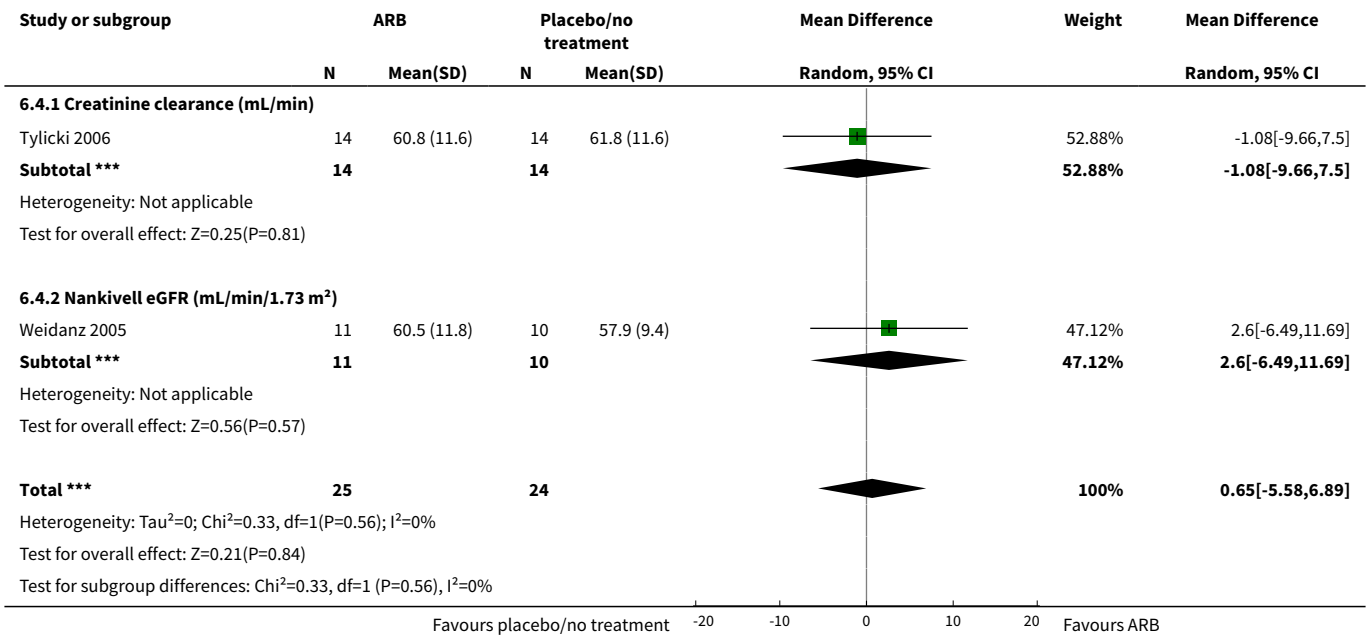
Study or subgroup	ARB n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.2.1 At 1 year				
Weidanz 2005	0/11	0/10		Not estimable



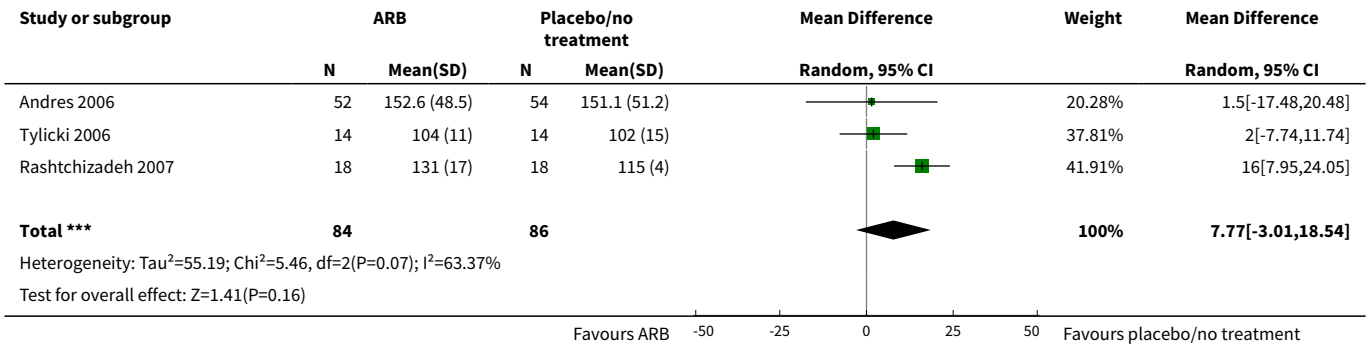
Analysis 6.3. Comparison 6 ARB versus placebo/no treatment, Outcome 3 Graft loss (censored for death).

Study or subgroup	ARB n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.3.1 At 1 year				
Weidanz 2005	0/11	0/10		Not estimable

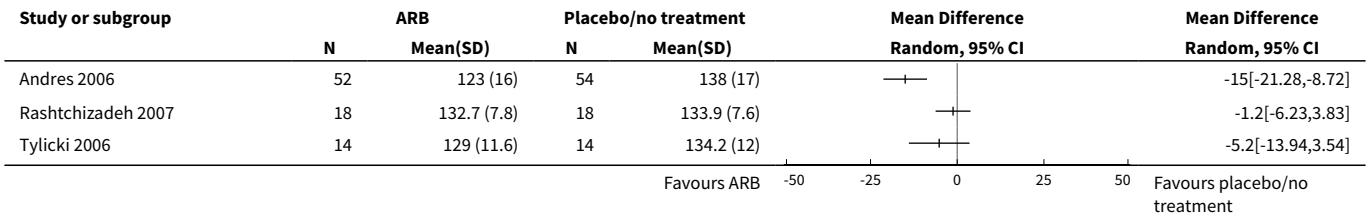
Analysis 6.4. Comparison 6 ARB versus placebo/no treatment, Outcome 4 Any GFR measure at last follow-up.



Analysis 6.5. Comparison 6 ARB versus placebo/no treatment, Outcome 5 Serum creatinine (µmol/L) at last follow-up.



Analysis 6.6. Comparison 6 ARB versus placebo/no treatment, Outcome 6 Haemoglobin (g/L) at last follow-up.

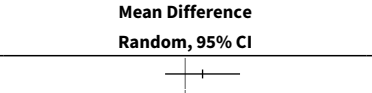


Analysis 6.7. Comparison 6 ARB versus placebo/no treatment, Outcome 7 Haematocrit (%).

Study or subgroup	ARB N	ARB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
6.7.1 At 2 months						
Rashtchizadeh 2007	18	38.7 (2.7)	18	39.9 (2.4)		-1.2[-2.87,0.47]

Analysis 6.8. Comparison 6 ARB versus placebo/no treatment, Outcome 8 Serum potassium (mmol/L) at last follow-up.

Study or subgroup	ARB N	ARB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Andres 2006	52	4.3 (0.4)	54	4.2 (0.7)		0.1[-0.12,0.32]
Rashtchizadeh 2007	18	4.5 (0.4)	18	3.9 (0.4)		0.61[0.34,0.88]
Tylicki 2006	14	4.4 (0.3)	14	4.1 (0.3)		0.26[0.04,0.48]

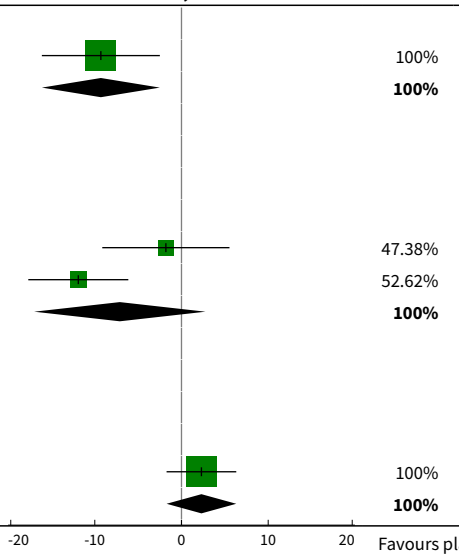


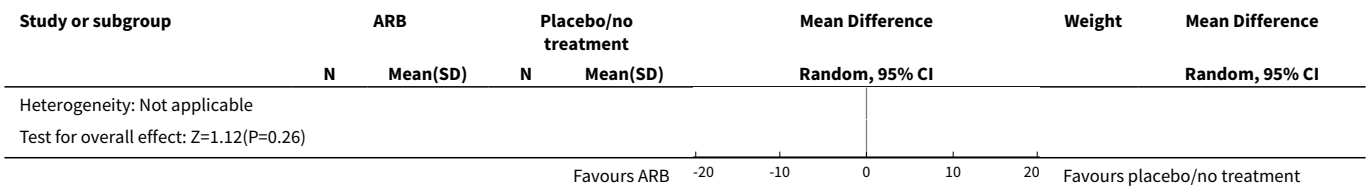
Analysis 6.9. Comparison 6 ARB versus placebo/no treatment, Outcome 9 Hyperkalaemia at last follow-up.

Study or subgroup	ARB n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
6.9.1 > 5.0 mmol/L				
Tylicki 2006	0/14	0/14		Not estimable

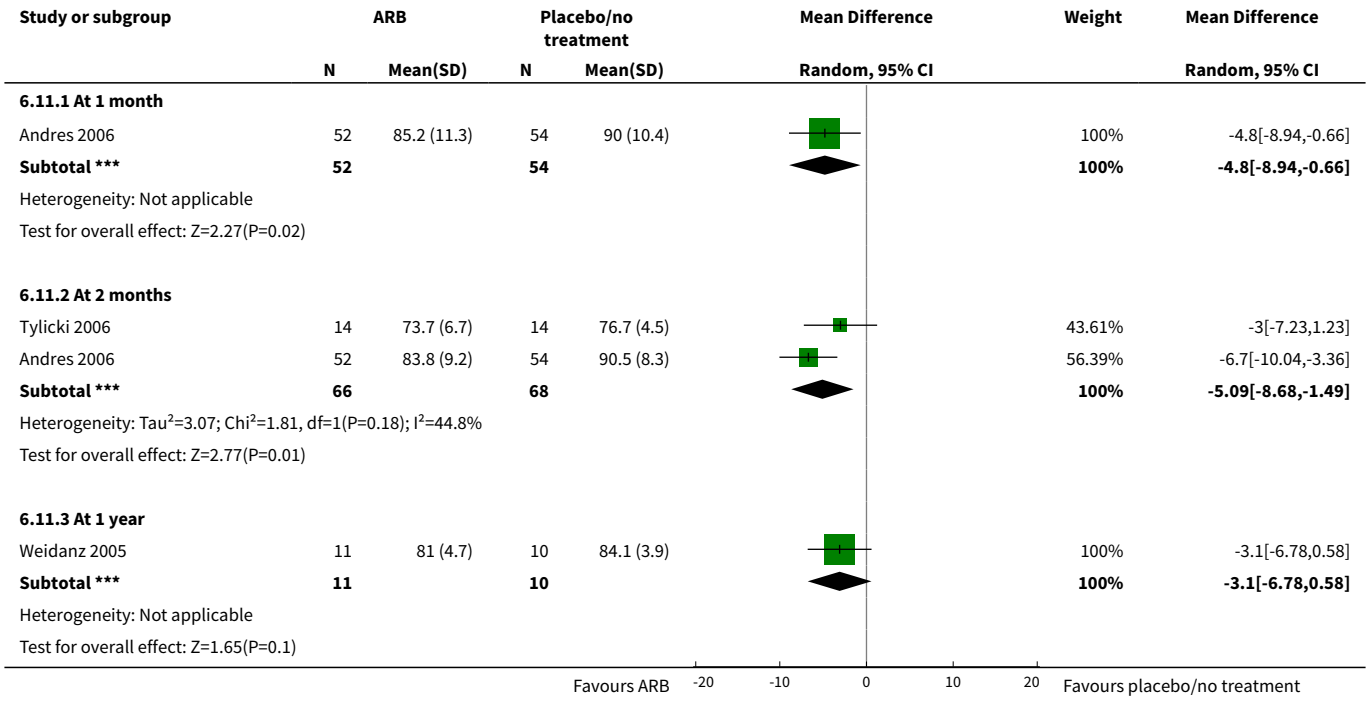
Analysis 6.10. Comparison 6 ARB versus placebo/no treatment, Outcome 10 Systolic blood pressure (mm Hg).

Study or subgroup	ARB N	ARB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
6.10.1 At 1 month							
Andres 2006	52	140.9 (18.4)	54	150.2 (17.3)		100%	-9.3[-16.1,-2.5]
Subtotal ***	**52**		**54**			**100%**	**-9.3[-16.1,-2.5]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.68(P=0.01)							
6.10.2 At 2 months							
Tylicki 2006	14	118.6 (10.1)	14	120.4 (9.7)		47.38%	-1.8[-9.14,5.54]
Andres 2006	52	136.5 (15)	54	148.4 (15.3)		52.62%	-11.9[-17.67,-6.13]
Subtotal ***	**66**		**68**			**100%**	**-7.11[-17,2.77]**
Heterogeneity: Tau²=39.67; Chi²=4.5, df=1(P=0.03); I²=77.78%							
Test for overall effect: Z=1.41(P=0.16)							
6.10.3 At 1 year							
Weidanz 2005	11	138 (4.2)	10	135.7 (5.1)		100%	2.3[-1.72,6.32]
Subtotal ***	**11**		**10**			**100%**	**2.3[-1.72,6.32]**

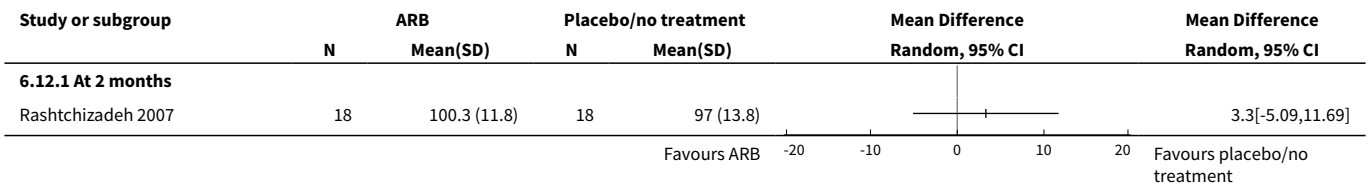




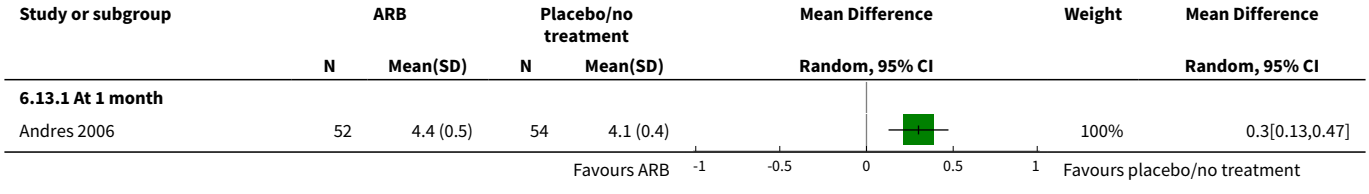
Analysis 6.11. Comparison 6 ARB versus placebo/no treatment, Outcome 11 Diastolic blood pressure (mm Hg).

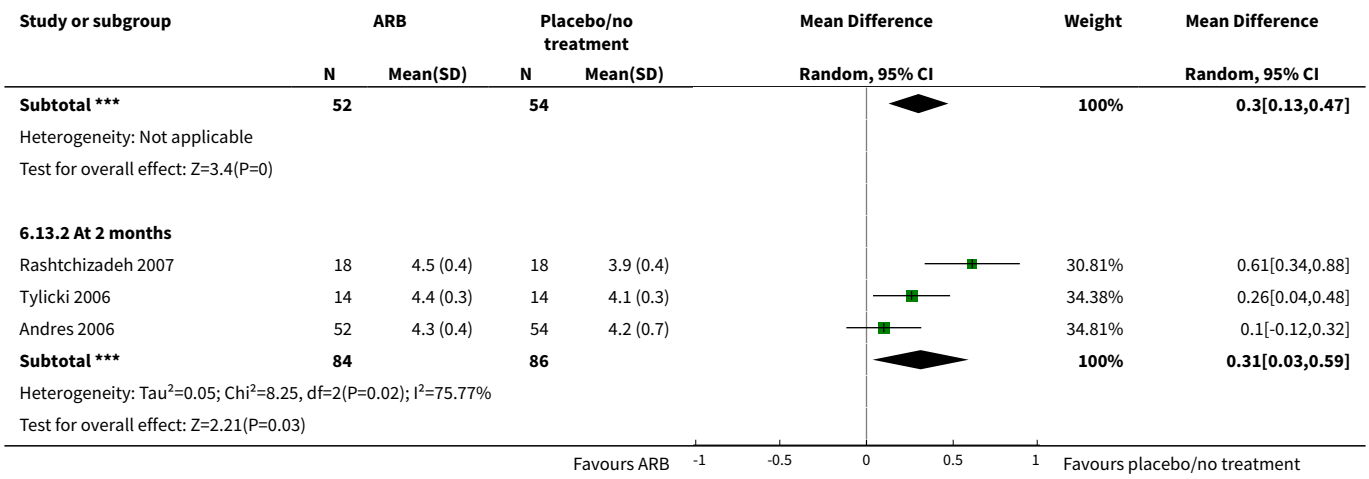


Analysis 6.12. Comparison 6 ARB versus placebo/no treatment, Outcome 12 Mean arterial pressure (mm Hg).

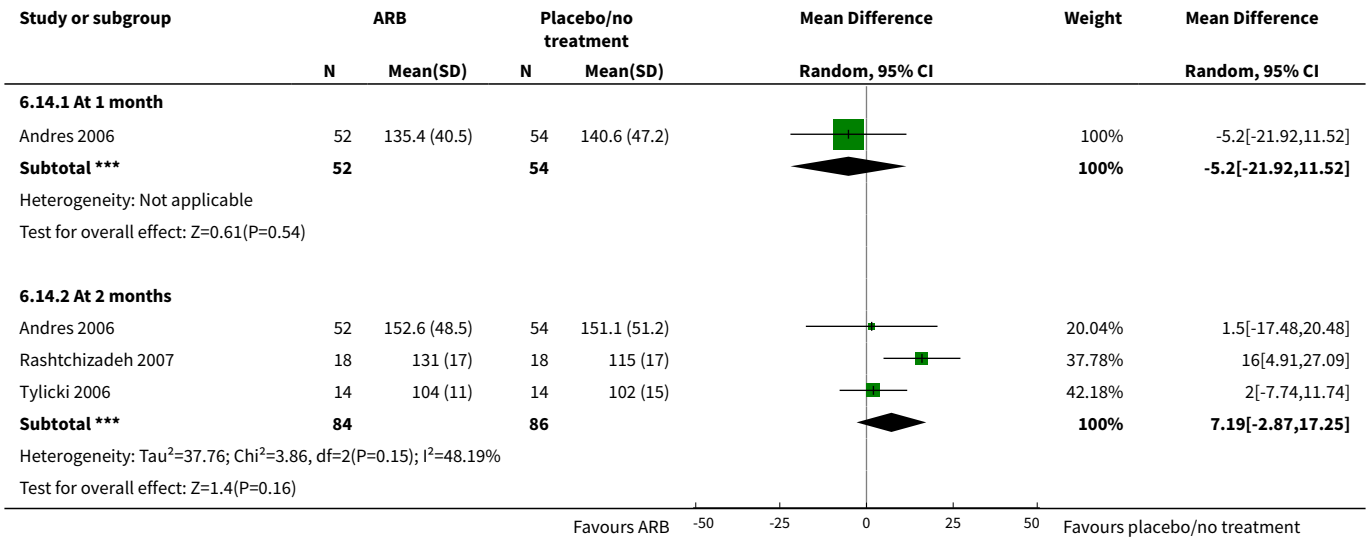


Analysis 6.13. Comparison 6 ARB versus placebo/no treatment, Outcome 13 Serum potassium (mmol/L).

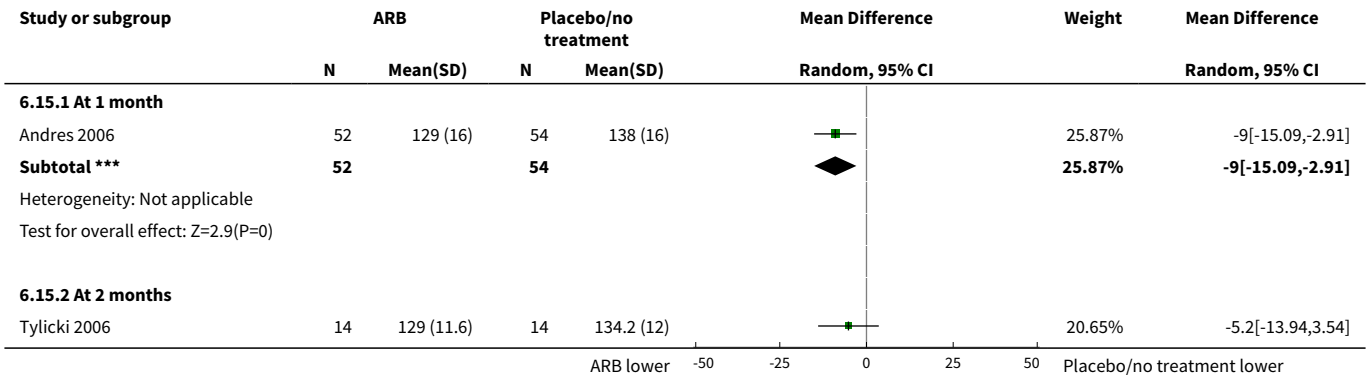


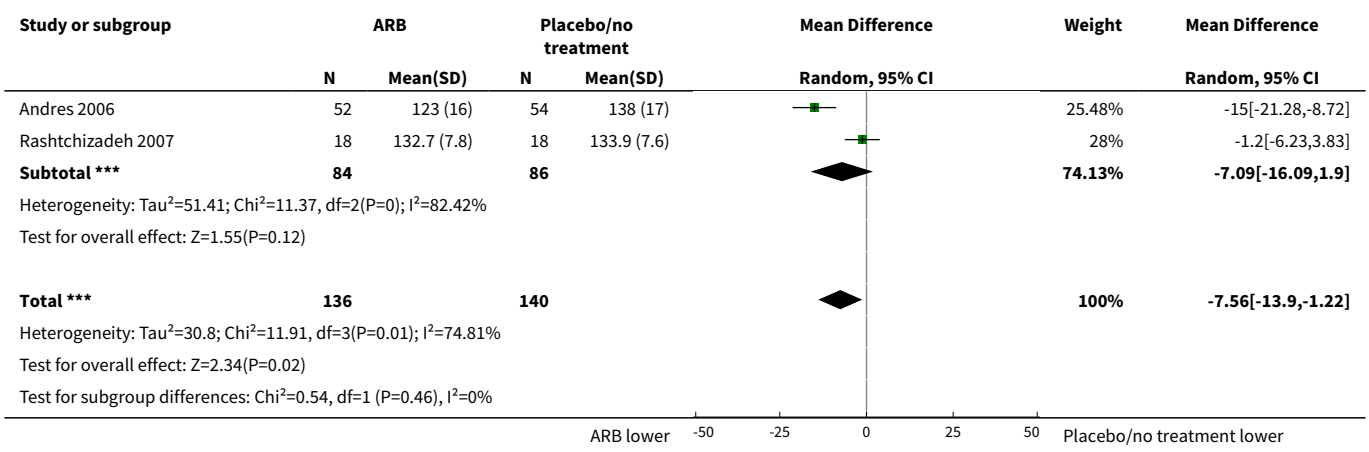


Analysis 6.14. Comparison 6 ARB versus placebo/no treatment, Outcome 14 Serum creatinine (µmol/L).



Analysis 6.15. Comparison 6 ARB versus placebo/no treatment, Outcome 15 Haemoglobin (g/L).





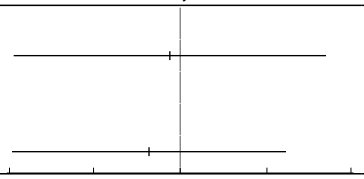
Comparison 7. ACEi versus beta-blocker

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 2 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 At 5 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Any GFR measure	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 Creatinine clearance (mL/min): 2 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Systolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 At 2 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 At 5 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Diastolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 At 2 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 At 5 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 At 5 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Death	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6.1 At 2 years	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.2 At 5 years	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Increased creatinine (> 45 µmol/L)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
7.1 At 2 years	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8.1 At 5 years	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

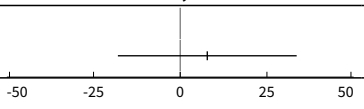
Analysis 7.1. Comparison 7 ACEi versus beta-blocker, Outcome 1 Serum creatinine (µmol/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
7.1.1 At 2 years						
Hausberg 1999	35	24 (112)	35	27 (77)		-3[-48.03,42.03]
7.1.2 At 5 years						
Hausberg 1999	40	9 (57)	40	18 (114)		-9[-48.5,30.5]



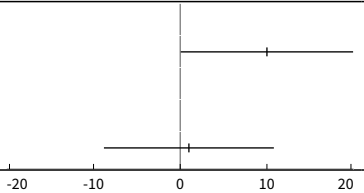
Analysis 7.2. Comparison 7 ACEi versus beta-blocker, Outcome 2 Any GFR measure.

Study or subgroup	ACE Inhibitor N	ACE Inhibitor Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
7.2.1 Creatinine clearance (mL/min): 2 years						
Hausberg 1999	35	8 (47)	35	0.2 (62)		7.8[-17.98,33.58]



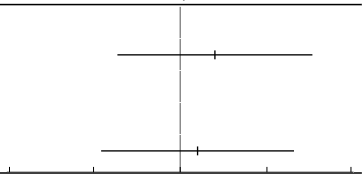
Analysis 7.3. Comparison 7 ACEi versus beta-blocker, Outcome 3 Systolic blood pressure (mm Hg).

Study or subgroup	ACEi N	ACEi Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
7.3.1 At 2 years						
Hausberg 1999	35	-3 (18)	35	-13 (24)		10[0.06,19.94]
7.3.2 At 5 years						
Hausberg 1999	48	-8 (27.7)	48	-9 (20.8)		1[-8.8,10.8]



Analysis 7.4. Comparison 7 ACEi versus beta-blocker, Outcome 4 Diastolic blood pressure (mm Hg).

Study or subgroup	ACEi N	ACEi Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
7.4.1 At 2 years						
Hausberg 1999	35	-10 (12)	35	-12 (12)		2[-3.62,7.62]
7.4.2 At 5 years						
Hausberg 1999	48	-5 (13.9)	48	-6 (13.9)		1[-4.56,6.56]

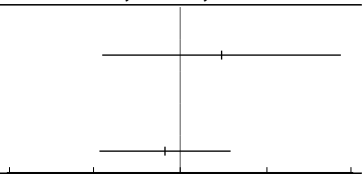


Analysis 7.5. Comparison 7 ACEi versus beta-blocker, Outcome 5 Mean arterial pressure (mm Hg).

Study or subgroup	ACEi N	ACEi Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
7.5.1 At 5 years						
Hausberg 1999	48	-6 (20.8)	48	-7 (13.9)		1[-6.08,8.08]

Analysis 7.6. Comparison 7 ACEi versus beta-blocker, Outcome 6 Death.

Study or subgroup	ACEi n/N	Beta-blocker n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
7.6.1 At 2 years				
Hausberg 1999	1/35	0/35		3[0.13,71.22]
7.6.2 At 5 years				
Hausberg 1999	2/48	3/48		0.67[0.12,3.81]

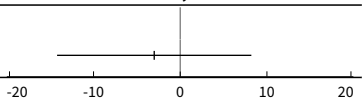


Analysis 7.7. Comparison 7 ACEi versus beta-blocker, Outcome 7 Increased creatinine (> 45 µmol/L).

Study or subgroup	ACEi n/N	Beta-blocker n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
7.7.1 At 2 years				
Hausberg 1999	4/35	6/35		0.67[0.21,2.16]

Analysis 7.8. Comparison 7 ACEi versus beta-blocker, Outcome 8 Haemoglobin (g/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	Beta-blockers N	Beta-blockers Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
7.8.1 At 5 years						
Hausberg 1999	48	129 (28)	48	132 (28)		-3[-14.2,8.2]



Comparison 8. ACEi versus alpha-blocker

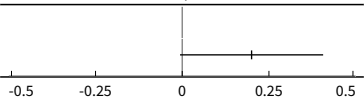
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Serum potassium (mmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Diastolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Any GFR measure	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 Measured GFR (mL/min/1.73 m^2): 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Systolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Proteinuria (g/24 h)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 8.1. Comparison 8 ACEi versus alpha-blocker, Outcome 1 Serum creatinine (µmol/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.1.1 At 3 months						
Castelao 2001	37	150 (36)	37	147 (42)		3[-14.82,20.82]

Analysis 8.2. Comparison 8 ACEi versus alpha-blocker, Outcome 2 Serum potassium (mmol/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.2.1 At 3 months						
Castelao 2001	37	4.9 (0.4)	37	4.7 (0.5)		0.2[-0.01,0.41]

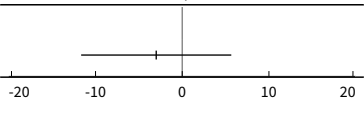


Analysis 8.3. Comparison 8 ACEi versus alpha-blocker, Outcome 3 Diastolic blood pressure (mm Hg).

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.3.1 At 3 months						
Castelao 2001	37	82 (8)	37	83 (7)		-1[-4.43,2.43]

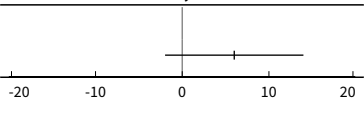
Analysis 8.4. Comparison 8 ACEi versus alpha-blocker, Outcome 4 Any GFR measure.

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.4.1 Measured GFR (mL/min/1.73 m²): 3 months						
Castelao 2001	37	46.5 (19)	37	49.5 (19)		-3[-11.66,5.66]



Analysis 8.5. Comparison 8 ACEi versus alpha-blocker, Outcome 5 Haemoglobin (g/L).

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.5.1 At 3 months						
Castelao 2001	37	139 (18)	37	133 (17)		6[-1.98,13.98]



Analysis 8.6. Comparison 8 ACEi versus alpha-blocker, Outcome 6 Systolic blood pressure (mm Hg).

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.6.1 At 3 months						
Castelao 2001	37	140 (14)	37	142 (15)		-2[-8.61,4.61]

Analysis 8.7. Comparison 8 ACEi versus alpha-blocker, Outcome 7 Mean arterial pressure (mm Hg).

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.7.1 At 3 months						
Castelao 2001	37	101 (8)	37	103 (8)		-2[-5.65,1.65]

Favours ACEi -10 -5 0 5 10 Favours alpha-blocker

Analysis 8.8. Comparison 8 ACEi versus alpha-blocker, Outcome 8 Proteinuria (g/24 h).

Study or subgroup	ACEi N	ACEi Mean(SD)	Alpha-blocker N	Alpha-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.8.1 At 3 months						
Castelao 2001	37	0.3 (0.3)	37	0.4 (0.4)		-0.03[-0.2,0.14]

Favours ACEi -0.5 -0.25 0 0.25 0.5 Favours alpha-blocker

Comparison 9. CCB versus beta-blocker

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any GFR measure	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 mL/min: At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Systolic blood pressure (mm Hg)	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 At 2-3 months	2		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Any adverse event	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.1 At 2 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

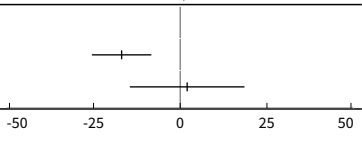
Analysis 9.1. Comparison 9 CCB versus beta-blocker, Outcome 1 Any GFR measure.

Study or subgroup	CCB N	CCB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
9.1.1 mL/min: At 2 months						
Chanard 2003	24	70.5 (25.9)	24	54 (20.8)		16.5[3.21,29.79]

Beta-blocker better -50 -25 0 25 50 CCB better

Analysis 9.2. Comparison 9 CCB versus beta-blocker, Outcome 2 Systolic blood pressure (mm Hg).

Study or subgroup	CCB N	CCB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
9.2.1 At 2-3 months						
Chanard 2003	24	131.5 (10.4)	24	148.4 (18.7)		-16.9[-25.46,-8.34]
Barri 1995	15	141 (25)	15	139 (21)		2[-14.52,18.52]



Analysis 9.3. Comparison 9 CCB versus beta-blocker, Outcome 3 Any adverse event.

Study or subgroup	CCB n/N	Beta-blocker n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
9.3.1 At 2 months				
Chanard 2003	12/24	13/24		0.92[0.54,1.59]

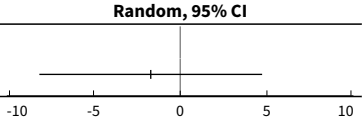
Comparison 10. Beta-blocker versus placebo/no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Systolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Diastolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Albumin:creatinine ratio (mg/g)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Creatinine clearance (mL/min)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Serum potassium (mmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Hyperkalaemia	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
8.1 > 5.0 mmol/L: At 2 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9 Controlled blood pressure	0		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9.1 < 150/90: At 2 months	0		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

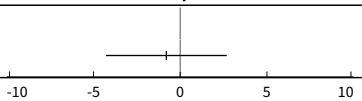
Analysis 10.1. Comparison 10 Beta-blocker versus placebo/ no treatment, Outcome 1 Systolic blood pressure (mm Hg).

Study or subgroup	Beta-blocker N	Beta-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.1.1 At 2 months						
Tylicki 2006	14	118.7 (7.5)	14	120.4 (9.7)		-1.7[-8.12,4.72]



Analysis 10.2. Comparison 10 Beta-blocker versus placebo/ no treatment, Outcome 2 Diastolic blood pressure (mm Hg).

Study or subgroup	Beta-blocker N	Beta-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.2.1 At 2 months						
Tylicki 2006	14	75.9 (4.9)	14	76.7 (4.5)		-0.8[-4.28,2.68]



Analysis 10.3. Comparison 10 Beta-blocker versus placebo/no treatment, Outcome 3 Albumin:creatinine ratio (mg/g).

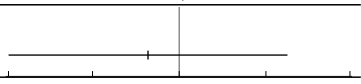
Study or subgroup	Beta-blocker N	Beta-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.3.1 At 2 months						
Tylicki 2006	14	44.8 (81.9)	14	49.6 (94.8)		-4.78[-70.42,60.86]

Analysis 10.4. Comparison 10 Beta-blocker versus placebo/no treatment, Outcome 4 Serum creatinine (µmol/L).

Study or subgroup	Beta-blocker N	Beta-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.4.1 At 2 months						
Tylicki 2006	14	105 (19)	14	102 (15)		3[-9.68,15.68]

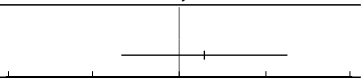
Analysis 10.5. Comparison 10 Beta-blocker versus placebo/no treatment, Outcome 5 Creatinine clearance (mL/min).

Study or subgroup	Beta-blocker N	Beta-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.5.1 At 2 months						
Tylicki 2006	14	60 (10.1)	14	61.8 (11.6)		-1.8[-9.84,6.24]



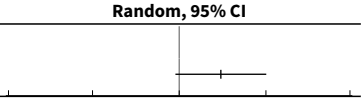
Analysis 10.6. Comparison 10 Beta-blocker versus placebo/no treatment, Outcome 6 Haemoglobin (g/L).

Study or subgroup	Beta-blocker N	Beta-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.6.1 At 2 months						
Tylicki 2006	14	137.1 (13.8)	14	134.2 (12)		2.9[-6.68,12.48]



Analysis 10.7. Comparison 10 Beta-blocker versus placebo/no treatment, Outcome 7 Serum potassium (mmol/L).

Study or subgroup	Beta-blocker N	Beta-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.7.1 At 2 months						
Tylicki 2006	14	4.4 (0.4)	14	4.1 (0.3)		0.24[-0.02,0.5]



Analysis 10.8. Comparison 10 Beta-blocker versus placebo/no treatment, Outcome 8 Hyperkalaemia.

Study or subgroup	Beta-blocker n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
10.8.1 > 5.0 mmol/L: At 2 months				
Tylicki 2006	0/14	0/14		Not estimable

Favours beta-blocker 0.1 0.2 0.5 1 2 5 10 Favours placebo/no treatment

Comparison 11. ARB versus beta-blocker

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Systolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Diastolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Albumin:creatinine ratio (mg/g)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Creatinine clearance (mL/min)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Serum potassium (mmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Hyperkalaemia	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
8.1 > 5.0 mmol/L: At 2 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 11.1. Comparison 11 ARB versus beta-blocker, Outcome 1 Systolic blood pressure (mm Hg).

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.1.1 At 2 months						

Favours ARB -10 -5 0 5 10 Favours beta-blocker

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Tylicki 2006	14	118.4 (10.1)	14	118.7 (7.5)		-0.34[-6.93,6.25]

Favours ARB -10 -5 0 5 10 Favours beta-blocker

Analysis 11.2. Comparison 11 ARB versus beta-blocker, Outcome 2 Diastolic blood pressure (mm Hg).

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.2.1 At 2 months						
Tylicki 2006	14	73.7 (6.7)	14	75.9 (4.9)		-2.2[-6.55,2.15]

Favours ARB -10 -5 0 5 10 Favours beta-blocker

Analysis 11.3. Comparison 11 ARB versus beta-blocker, Outcome 3 Albumin:creatinine ratio (mg/g).

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.3.1 At 2 months						
Tylicki 2006	14	27.6 (65.8)	14	44.8 (81.9)		-17.15[-72.2,37.9]

Favours ARB -100 -50 0 50 100 Favours beta-blocker

Analysis 11.4. Comparison 11 ARB versus beta-blocker, Outcome 4 Serum creatinine (µmol/L).

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.4.1 At 2 months						
Tylicki 2006	14	104 (11)	14	105 (19)		-1[-12.5,10.5]

Favours ARB -20 -10 0 10 20 Favours beta-blocker

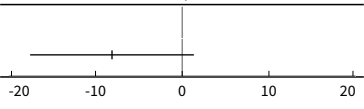
Analysis 11.5. Comparison 11 ARB versus beta-blocker, Outcome 5 Creatinine clearance (mL/min).

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.5.1 At 2 months						
Tylicki 2006	14	60.8 (11.6)	14	60 (10.1)		0.72[-7.34,8.78]

Favours beta-blocker -10 -5 0 5 10 Favours ARB

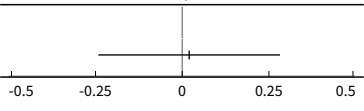
Analysis 11.6. Comparison 11 ARB versus beta-blocker, Outcome 6 Haemoglobin (g/L).

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.6.1 At 2 months						
Tylicki 2006	14	129 (11.6)	14	137.1 (13.8)		-8.1[-17.54,1.34]



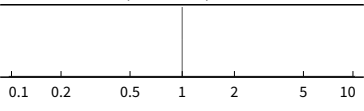
Analysis 11.7. Comparison 11 ARB versus beta-blocker, Outcome 7 Serum potassium (mmol/L).

Study or subgroup	ARB N	ARB Mean(SD)	Beta-blocker N	Beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.7.1 At 2 months						
Tylicki 2006	14	4.4 (0.3)	14	4.4 (0.4)		0.02[-0.24,0.28]



Analysis 11.8. Comparison 11 ARB versus beta-blocker, Outcome 8 Hyperkalaemia.

Study or subgroup	ARB n/N	Beta-blocker n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
11.8.1 > 5.0 mmol/L: At 2 months				
Tylicki 2006	0/14	0/14		Not estimable



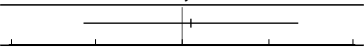
Comparison 12. Alpha-blocker versus placebo/no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Systolic blood pressure (mm Hg) at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Death	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 At 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Graft loss	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.1 At 6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Rejection rate	1		Rate Ratio (Random, 95% CI)	Totals not selected
4.1 At 6 months	1		Rate Ratio (Random, 95% CI)	0.0 [0.0, 0.0]
5 Systolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 At 1 month	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.2 At 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 12.1. Comparison 12 Alpha-blocker versus placebo/no treatment, Outcome 1 Systolic blood pressure (mm Hg) at last follow-up.

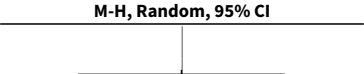
Study or subgroup	Alpha-blocker N	Alpha-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Vanrenterghem 1988	46	150 (33.2)	45	149 (26.8)		1[-11.38,13.38]



Favours alpha-blocker — Favours placebo/no treatment

Analysis 12.2. Comparison 12 Alpha-blocker versus placebo/no treatment, Outcome 2 Death.

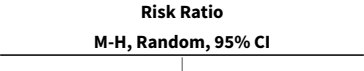
Study or subgroup	Alpha-blockers n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
12.2.1 At 6 months				
Vanrenterghem 1988	1/47	1/46		0.98[0.06,15.19]



Favours alpha-blocker — Favours placebo/no treatment

Analysis 12.3. Comparison 12 Alpha-blocker versus placebo/no treatment, Outcome 3 Graft loss.

Study or subgroup	Alpha-blocker n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
12.3.1 At 6 months				
Vanrenterghem 1988	4/46	4/45		0.98[0.26,3.68]



Favours alpha-blocker — Favours placebo/no treatment

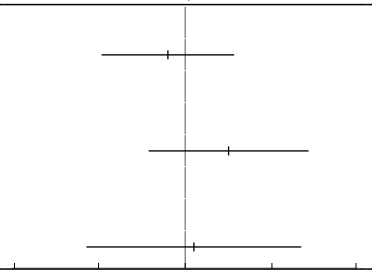
Analysis 12.4. Comparison 12 Alpha-blocker versus placebo/no treatment, Outcome 4 Rejection rate.

Study or subgroup	Alpha-blocker N	Placebo/no treatment N	log[Rate Ratio] (SE)	Rate Ratio IV, Random, 95% CI	Rate Ratio IV, Random, 95% CI
12.4.1 At 6 months					
Vanrenterghem 1988	46	45	-0.1 (0.366)		0.89[0.43,1.81]

Favours alpha-blocker — Favours placebo/no treatment

Analysis 12.5. Comparison 12 Alpha-blocker versus placebo/ no treatment, Outcome 5 Systolic blood pressure (mm Hg).

Study or subgroup	Alpha-blocker N	Alpha-blocker Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
12.5.1 At 1 month						
Vanrenterghem 1988	46	142 (20.3)	45	144 (16.8)		-2[-9.65,5.65]
12.5.2 At 3 months						
Vanrenterghem 1988	46	152 (25.1)	45	147 (19.5)		5[-4.22,14.22]
12.5.3 At 6 months						
Vanrenterghem 1988	46	150 (33.2)	45	149 (26.8)		1[-11.38,13.38]



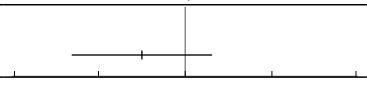
Comparison 13. ACEi plus CCB versus ACEi alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Systolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Diastolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Death at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Acute rejection at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6 Any GFR measure	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 CrCl (mL/min): At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
8 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
9 Haematocrit (%)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
10 Serum potassium (mmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11 Hyperkalaemia at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
11.1 > 5.5 mmol/L	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

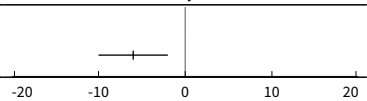
Analysis 13.1. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 1 Systolic blood pressure (mm Hg).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.1.1 At 6 months						
Halimi 2007	32	135 (14)	33	140 (19)		-5[-13.1,3.1]



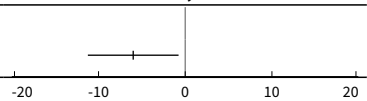
Analysis 13.2. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 2 Diastolic blood pressure (mm Hg).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.2.1 At 6 months						
Halimi 2007	32	74 (6)	33	80 (10)		-6[-10,-2]



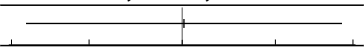
Analysis 13.3. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 3 Mean arterial pressure (mm Hg).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.3.1 At 6 months						
Halimi 2007	32	94 (8)	33	100 (13)		-6[-11.23,-0.77]



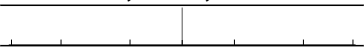
Analysis 13.4. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 4 Death at last follow-up.

Study or subgroup	ACEi + CCB n/N	ACEi alone n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Halimi 2007	1/32	1/33		1.03[0.07,15.79]



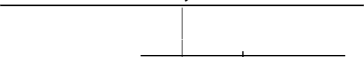
Analysis 13.5. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 5 Acute rejection at last follow-up.

Study or subgroup	ACEi + CCB n/N	ACEi alone n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Halimi 2007	0/32	0/33		Not estimable



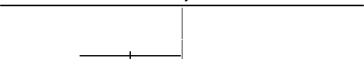
Analysis 13.6. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 6 Any GFR measure.

Study or subgroup	ACEi + CA N	ACEi + CA Mean(SD)	ACEi Alone N	ACEi Alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.6.1 CrCl (mL/min): At 6 months						
Halimi 2007	32	-1 (20)	33	-8 (28)		7[-4.8,18.8]



Analysis 13.7. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 7 Serum creatinine (µmol/L).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.7.1 Change: At 6 months						
Halimi 2007	32	3 (12)	33	9 (12)		-6[-11.84,-0.16]

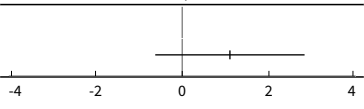


Analysis 13.8. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 8 Haemoglobin (g/L).

Study or subgroup	ACE-I + CA N	ACE-I + CA Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.8.1 Change: At 6 months						
Halimi 2007	32	-5 (13)	33	-9 (8)		4[-1.27,9.27]

Analysis 13.9. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 9 Haematocrit (%).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.9.1 Change: At 6 months						
Halimi 2007	32	-2.5 (4.2)	33	-3.6 (2.7)		1.1[-0.62,2.82]

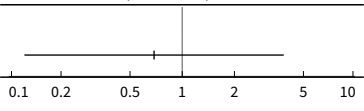


Analysis 13.10. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 10 Serum potassium (mmol/L).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.10.1 Change: At 6 months						
Halimi 2007	32	0 (0.4)	33	0.2 (0.4)		-0.2[-0.39,-0.01]

Analysis 13.11. Comparison 13 ACEi plus CCB versus ACEi alone, Outcome 11 Hyperkalaemia at last follow-up.

Study or subgroup	ACEi + CCB n/N	ACEi alone n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
13.11.1 > 5.5 mmol/L				
Halimi 2007	2/32	3/33		0.69[0.12,3.85]



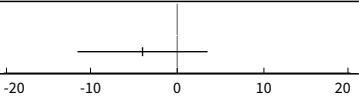
Comparison 14. ACEi plus CCB versus CCB alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Systolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Death at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3 Acute rejection at last follow-up	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Creatinine clearance (mL/min)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
5.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Serum potassium (mmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Hyperkalaemia	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
7.1 > 5.5 mmol/L	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
9 Haematocrit (%)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.1 Change: At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
10 Diastolic blood pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10.1 At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
11.1 At 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 14.1. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 1 Systolic blood pressure (mm Hg).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	CCB alone N	CCB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.1.1 At 6 months						
Halimi 2007	32	135 (14)	34	139 (17)		-4[-11.5,3.5]



Analysis 14.2. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 2 Death at last follow-up.

Study or subgroup	ACEi + CCB n/N	CCB alone n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Halimi 2007	1/32	0/34		0%	3.18[0.13,75.38]

ACEi + CCB better 0.01 0.1 1 10 100 CCB alone better

Analysis 14.3. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 3 Acute rejection at last follow-up.

Study or subgroup	ACEi + CCB n/N	CCB alone n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Halimi 2007	0/32	0/34		Not estimable

Favours ACEi + CCB 0.1 0.2 0.5 1 2 5 10 Favours CCB alone

Analysis 14.4. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 4 Creatinine clearance (mL/min).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	CCB only N	CCB only Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.4.1 Change: At 6 months						
Halimi 2007	32	-1 (20)	34	15 (31)		-16[-28.51,-3.49]

CCB alone better -50 -25 0 25 50 ACEi + CCB better

Analysis 14.5. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 5 Serum creatinine (µmol/L).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	CCB alone N	CCB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.5.1 Change: At 6 months						
Halimi 2007	32	3 (12)	34	-5 (13)		8[1.97,14.03]

ACEi + CCB better -20 -10 0 10 20 CCB alone bBetter

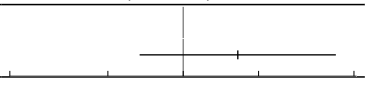
Analysis 14.6. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 6 Serum potassium (mmol/L).

Study or subgroup	ACEi + CCB N	ACEi + CCB Mean(SD)	CCB alone N	CCB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.6.1 Change: At 6 months						
Halimi 2007	32	0 (0.4)	34	-0.2 (0.3)		0.2[0.03,0.37]

ACEi + CCB lower -0.5 -0.25 0 0.25 0.5 CCB alone lower

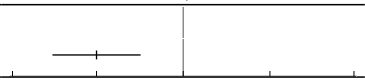
Analysis 14.7. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 7 Hyperkalaemia.

Study or subgroup	ACEi + CCB n/N	CCB alone n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
14.7.1 > 5.5 mmol/L				
Halimi 2007	2/32	0/34		5.3[0.26,106.4]



Analysis 14.8. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 8 Haemoglobin (g/L).

Study or subgroup	ACEi + CCB N	Mean(SD)	CCB alone N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.8.1 Change: At 6 months						
Halimi 2007	32	-5 (13)	34	5 (7)		-10[-15.08,-4.92]

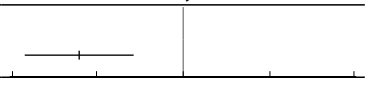


Analysis 14.9. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 9 Haematocrit (%).

Study or subgroup	ACEi + CCB N	Mean(SD)	CCB alone N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.9.1 Change: At 6 months						
Halimi 2007	32	-2.5 (4.2)	34	0.5 (2.3)		-3[-4.65,-1.35]

Analysis 14.10. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 10 Diastolic blood pressure (mm Hg).

Study or subgroup	ACEi + CCB N	Mean(SD)	CCB alone N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.10.1 At 6 months						
Halimi 2007	32	74 (6)	34	80 (7)		-6[-9.14,-2.86]



Analysis 14.11. Comparison 14 ACEi plus CCB versus CCB alone, Outcome 11 Mean arterial pressure (mm Hg).

Study or subgroup	ACEi + CCB N	Mean(SD)	CCB alone N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.11.1 At 6 months						
Halimi 2007	32	94 (8)	34	100 (10)		-6[-10.36,-1.64]

Comparison 15. ACEi plus ARB versus ACEi alone

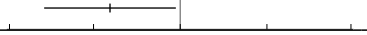
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Haematocrit (%)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Serum potassium (mmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 15.1. Comparison 15 ACEi plus ARB versus ACEi alone, Outcome 1 Haematocrit (%).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
15.1.1 At 1-3 months						
Rashtchizadeh 2007	13	37.4 (2.6)	12	38.5 (2.8)		-1.1[-3.22,1.02]

Analysis 15.2. Comparison 15 ACEi plus ARB versus ACEi alone, Outcome 2 Haemoglobin (g/L).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
15.2.1 At 1-3 months						
Rashtchizadeh 2007	13	123.9 (9.2)	12	132 (10.1)		-8.1[-15.69,-0.51]

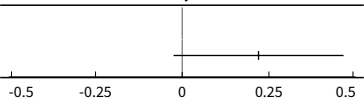


Analysis 15.3. Comparison 15 ACEi plus ARB versus ACEi alone, Outcome 3 Serum creatinine (µmol/L).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
15.3.1 At 1-3 months						
Rashtchizadeh 2007	13	129 (20)	12	130 (13)		-1[-14.13,12.13]

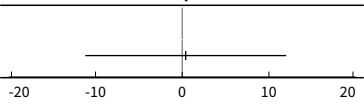
Analysis 15.4. Comparison 15 ACEi plus ARB versus ACEi alone, Outcome 4 Serum potassium (mmol/L).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
15.4.1 At 1-3 months						
Rashtchizadeh 2007	13	4.8 (0.4)	12	4.6 (0.2)		0.22[-0.03,0.47]



Analysis 15.5. Comparison 15 ACEi plus ARB versus ACEi alone, Outcome 5 Mean arterial pressure (mm Hg).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ACEi alone N	ACEi alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
15.5.1 At 1-3 months						
Rashtchizadeh 2007	13	94 (18.3)	12	93.6 (10.5)		0.4[-11.19,11.99]



Comparison 16. ACEi plus ARB versus ARB alone

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Haematocrit (%)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Haemoglobin (g/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 At 2 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Serum creatinine (µmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4 Serum potassium (mmol/L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Mean arterial pressure (mm Hg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 At 1-3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 16.1. Comparison 16 ACEi plus ARB versus ARB alone, Outcome 1 Haematocrit (%).

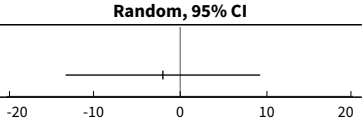
Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ARB alone N	ARB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
16.1.1 At 1-3 months						
Rashtchizadeh 2007	13	37.4 (2.6)	18	38.7 (2.7)		-1.3[-3.19,0.59]

Analysis 16.2. Comparison 16 ACEi plus ARB versus ARB alone, Outcome 2 Haemoglobin (g/L).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ARB alone N	ARB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
16.2.1 At 2 months						
Rashtchizadeh 2007	13	123.9 (9.2)	18	132.7 (7.8)		-8.8[-14.96,-2.64]

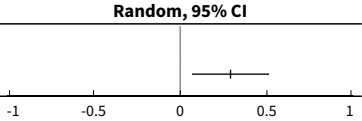
Analysis 16.3. Comparison 16 ACEi plus ARB versus ARB alone, Outcome 3 Serum creatinine (µmol/L).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ARB alone N	ARB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
16.3.1 At 1-3 months						
Rashtchizadeh 2007	13	129 (20)	18	131 (6)		-2[-13.22,9.22]



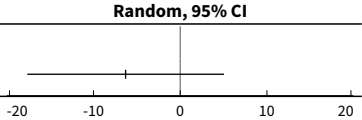
Analysis 16.4. Comparison 16 ACEi plus ARB versus ARB alone, Outcome 4 Serum potassium (mmol/L).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ARB alone N	ARB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
16.4.1 At 1-3 months						
Rashtchizadeh 2007	13	4.8 (0.4)	18	4.5 (0.1)		0.29[0.07,0.51]



Analysis 16.5. Comparison 16 ACEi plus ARB versus ARB alone, Outcome 5 Mean arterial pressure (mm Hg).

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	ARB alone N	ARB alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
16.5.1 At 1-3 months						
Rashtchizadeh 2007	13	94 (18.3)	18	100.3 (11.8)		-6.3[-17.64,5.04]

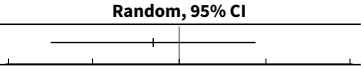


Comparison 17. ACEi plus ARB versus placebo/no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean arterial pressure (mm Hg) at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Serum creatinine (µmol/L) at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Haemoglobin (g/L) at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Haematocrit (%) at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Serum potassium (mmol/L) at last follow-up	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

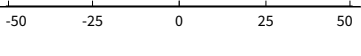
Analysis 17.1. Comparison 17 ACEi plus ARB versus placebo/no treatment, Outcome 1 Mean arterial pressure (mm Hg) at last follow-up.

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Rashtchizadeh 2007	13	94 (18.3)	18	97 (13.8)		-3[-14.82,8.82]



Analysis 17.2. Comparison 17 ACEi plus ARB versus placebo/no treatment, Outcome 2 Serum creatinine (µmol/L) at last follow-up.

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Rashtchizadeh 2007	13	129 (20)	18	115 (4)		14[2.97,25.03]

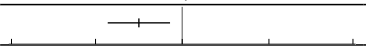


Analysis 17.3. Comparison 17 ACEi plus ARB versus placebo/no treatment, Outcome 3 Haemoglobin (g/L) at last follow-up.

Study or subgroup	ACEi + ARB N	ACEi + ARB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Rashtchizadeh 2007	13	123.9 (9.2)	18	133.9 (7.6)		-10[-16.11,-3.89]

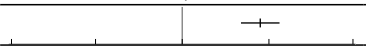
Analysis 17.4. Comparison 17 ACEi plus ARB versus placebo/no treatment, Outcome 4 Haematocrit (%) at last follow-up.

Study or subgroup	ACEi + ARB		Placebo/no treatment		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Rashtchizadeh 2007	13	37.4 (2.6)	18	39.9 (2.4)		-2.5[-4.3,-0.7]



Analysis 17.5. Comparison 17 ACEi plus ARB versus placebo/no treatment, Outcome 5 Serum potassium (mmol/L) at last follow-up.

Study or subgroup	ACEi + ARB		Placebo/no treatment		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Rashtchizadeh 2007	13	4.8 (0.4)	18	3.9 (0.1)		0.9[0.68,1.12]



Comparison 18. CCB versus any other intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum creatinine (6 months to 2 years of treatment)	16		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 CCB versus placebo/no treatment	8	720	Mean Difference (IV, Random, 95% CI)	-16.55 [-29.56, -3.54]
1.2 CCB versus ACEi	4	247	Mean Difference (IV, Random, 95% CI)	-12.50 [-21.77, -3.23]
1.3 CCB versus ACEi (change)	1	67	Mean Difference (IV, Random, 95% CI)	-14.00 [-20.24, -7.76]
1.4 CCB versus ARB	3	135	Mean Difference (IV, Random, 95% CI)	8.98 [-8.19, 26.14]
2 Serum creatinine (µmol/L) at last follow-up	29		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 CCB versus placebo/no treatment	19	1130	Mean Difference (IV, Random, 95% CI)	-12.50 [-19.71, -5.28]
2.2 CCB versus ACEi	6	296	Mean Difference (IV, Random, 95% CI)	-12.15 [-20.46, -3.85]
2.3 CCB versus ACEi (change)	1	67	Mean Difference (IV, Random, 95% CI)	-14.00 [-20.24, -7.76]
2.4 CCB versus ARB	4	169	Mean Difference (IV, Random, 95% CI)	2.69 [-14.06, 19.45]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3 Any GFR measure (6 months to 2 years of treatment)	13		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 CCB versus placebo/no treatment	9	749	Mean Difference (IV, Random, 95% CI)	4.89 [2.10, 7.69]
3.2 CCB versus ACEi	4	236	Mean Difference (IV, Random, 95% CI)	12.93 [8.00, 17.87]
4 Any GFR measure at last follow-up	25		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 CCB versus placebo/no treatment	18	1109	Mean Difference (IV, Random, 95% CI)	4.44 [2.20, 6.69]
4.2 CCB versus ACEi	6	286	Mean Difference (IV, Random, 95% CI)	11.61 [7.26, 15.97]
4.3 CCB versus beta-blocker	1	48	Mean Difference (IV, Random, 95% CI)	16.5 [3.21, 29.79]
4.4 CCB versus ARB	1	34	Mean Difference (IV, Random, 95% CI)	10.0 [-11.20, 31.20]
5 Measured GFR at last follow-up	16		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 CCB versus placebo/no treatment	11	523	Mean Difference (IV, Random, 95% CI)	4.77 [1.88, 7.66]
5.2 CCB versus ACEi	4	198	Mean Difference (IV, Random, 95% CI)	10.69 [6.02, 15.36]
5.3 CCB versus beta-blocker	1	48	Mean Difference (IV, Random, 95% CI)	16.5 [3.21, 29.79]
5.4 CCB versus ARB	1	34	Mean Difference (IV, Random, 95% CI)	10.0 [-11.20, 31.20]
6 Death at last follow-up	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 CCB versus placebo/no treatment	12	792	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.37, 1.82]
6.2 CCB versus ACEi	2	221	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.03, 2.21]
7 Acute rejection at last follow-up	13		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 CCB versus placebo/no treatment	11	771	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.85, 1.23]

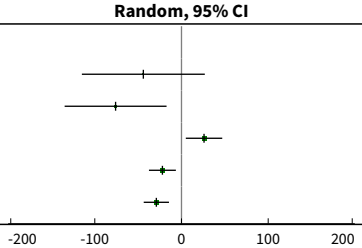
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
7.2 CCB versus ACEi	2	221	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.48, 0.87]
8 Graft loss at last follow-up	18		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 CCB versus placebo/no treatment	17	1279	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.57, 0.99]
8.2 CCB versus ACEi	1	152	Risk Ratio (M-H, Random, 95% CI)	0.14 [0.01, 2.58]
9 Haemoglobin (g/L) (6 months to 2 years of treatment)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.1 CCB versus ACEi	3	222	Mean Difference (IV, Random, 95% CI)	12.09 [7.14, 17.05]
9.2 CCB versus ACEi (change)	1	67	Mean Difference (IV, Random, 95% CI)	14.0 [10.40, 17.60]
9.3 CCB versus ARB	2	105	Mean Difference (IV, Random, 95% CI)	8.79 [-5.84, 23.42]
10 Haemoglobin (g/L) at last follow-up	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 CCB versus ACEi	4	241	Mean Difference (IV, Random, 95% CI)	12.19 [7.52, 16.86]
10.2 CCB versus ACEi (change)	1	67	Mean Difference (IV, Random, 95% CI)	14.0 [10.40, 17.60]
10.3 CCB versus ARB	2	105	Mean Difference (IV, Random, 95% CI)	8.79 [-5.84, 23.42]
11 Haematocrit (%) (6 months to 2 years of treatment)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 CCB versus ACEi	2	46	Mean Difference (IV, Random, 95% CI)	6.00 [2.72, 9.28]
11.2 CCB versus ACEi (change)	1	67	Mean Difference (IV, Random, 95% CI)	4.1 [2.90, 5.30]
12 Haematocrit (%) at last follow-up	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 CCB versus placebo/no treatment	1	30	Mean Difference (IV, Random, 95% CI)	-1.0 [-4.80, 2.80]
12.2 CCB versus ACEi	3	76	Mean Difference (IV, Random, 95% CI)	3.79 [-0.42, 7.99]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.3 CCB versus ACEi (change)	1	67	Mean Difference (IV, Random, 95% CI)	4.1 [2.90, 5.30]
13 Proteinuria (6 months to 2 years of treatment)	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
13.1 CCB versus ACEi	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.2 CCB versus ARB	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Proteinuria (g/24 h) at last follow-up	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
14.1 CCB versus placebo/no treatment	2	80	Mean Difference (IV, Random, 95% CI)	0.03 [-0.29, 0.35]
14.2 CCB versus ACEi	2	108	Mean Difference (IV, Random, 95% CI)	0.28 [0.04, 0.53]
14.3 CCB versus ARB	2	112	Mean Difference (IV, Random, 95% CI)	0.19 [-0.16, 0.54]
15 Blood pressure (systolic/mean arterial/diastolic) (6 months to 2 years of treatment)	10		Mean Difference (IV, Random, 95% CI)	Subtotals only
15.1 CCB versus placebo/no treatment	4	365	Mean Difference (IV, Random, 95% CI)	-2.86 [-7.10, 1.38]
15.2 CCB versus ACEi	4	215	Mean Difference (IV, Random, 95% CI)	0.50 [-2.42, 3.43]
15.3 CCB versus ARB	2	91	Mean Difference (IV, Random, 95% CI)	4.90 [-4.90, 14.69]
16 Blood pressure at last follow-up (systolic/mean arterial/diastolic)	20		Mean Difference (IV, Random, 95% CI)	Subtotals only
16.1 CCB versus placebo/no treatment	10	580	Mean Difference (IV, Random, 95% CI)	-4.93 [-8.86, 1.00]
16.2 CCB versus ACEi	6	241	Mean Difference (IV, Random, 95% CI)	-0.81 [-3.89, 2.28]
16.3 CCB versus beta-blocker	2	78	Mean Difference (IV, Random, 95% CI)	-8.83 [-27.15, 9.50]
16.4 CCB versus ARB	3	125	Mean Difference (IV, Random, 95% CI)	2.01 [-5.80, 9.83]
17 Systolic blood pressure (mm Hg) at last follow-up	10		Mean Difference (IV, Random, 95% CI)	Subtotals only

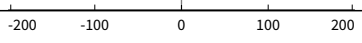
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.1 CCB versus placebo/no treatment	8	468	Mean Difference (IV, Random, 95% CI)	-6.39 [-10.78, 0.00]
17.2 CCB versus ACEi	3	117	Mean Difference (IV, Random, 95% CI)	-3.21 [-8.36, 1.93]
18 Withdrawal due to side effects at last follow-up	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 CCB versus placebo/no treatment	2	156	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.53, 1.87]
19 Serum potassium (mmol/L) at last follow-up	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
19.1 CCB versus ACEi	4	189	Mean Difference (IV, Random, 95% CI)	-0.27 [-0.41, -0.14]
19.2 CCB versus ARB	3	139	Mean Difference (IV, Random, 95% CI)	-0.32 [-0.56, -0.08]
20 Hyperkalaemia at last follow-up	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
20.1 CCB versus ACEi	3	211	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.13, 0.53]
20.2 CCB versus ARB	1	56	Risk Ratio (M-H, Random, 95% CI)	0.18 [0.02, 1.39]
21 Rejection rate	5		Rate Ratio (Random, 95% CI)	Subtotals only
21.1 CCB versus placebo/no treatment	4	8	Rate Ratio (Random, 95% CI)	0.88 [0.64, 1.20]
21.2 CCB versus ACEi	1	78	Rate Ratio (Random, 95% CI)	1.08 [0.77, 1.53]
21.3 CCB versus ARB	1	78	Rate Ratio (Random, 95% CI)	1.0 [0.71, 1.41]

Analysis 18.1. Comparison 18 CCB versus any other intervention, Outcome 1 Serum creatinine (6 months to 2 years of treatment).

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.1.1 CCB versus placebo/no treatment							
Santos 2002	15	150 (80)	15	194 (115)		2.87%	-44[-114.89,26.89]
Harper 1996	42	191 (104)	36	267 (152)		3.91%	-76[-134.78,-17.22]
Pirsch 1993	17	150 (27)	17	124 (35)		12.87%	26[4.99,47.01]
Kuypers 2004	59	130 (44)	59	152 (42)		15.19%	-22[-37.52,-6.48]
Morales 1994	47	111 (33)	50	140 (40)		15.59%	-29[-43.56,-14.44]

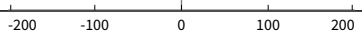


Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Rahn 1999 NT	57	-3.5 (40)	52	18.6 (31.7)		16.03%	-22.1[-35.59,-8.61]
Kumana 2003	55	131 (37)	55	134 (28)		16.53%	-3[-15.26,9.26]
Rahn 1999 HT	73	5.3 (30)	71	27.4 (37.1)		17%	-22.1[-33.14,-11.06]
Subtotal ***	**365**		**355**			**100%**	**-16.55[-29.56,-3.54]**
Heterogeneity: Tau^2=227.53; Chi^2=29.85, df=7(P=0); I^2=76.55%							
Test for overall effect: Z=2.49(P=0.01)							
18.1.2 CCB versus ACEi							
Hernandez 1995	11	124 (27)	10	133 (27)		16.08%	-9[-32.12,14.12]
Mourad 1993	11	129 (27)	14	144 (26)		19.53%	-15[-35.98,5.98]
El Agroudy 2003	24	133 (44)	54	133 (35)		21.65%	0[-19.93,19.93]
Midtvedt 2001	69	125 (32)	54	144 (45)		42.75%	-19[-33.18,-4.82]
Subtotal ***	**115**		**132**			**100%**	**-12.5[-21.77,-3.23]**
Heterogeneity: Tau^2=0; Chi^2=2.46, df=3(P=0.48); I^2=0%							
Test for overall effect: Z=2.64(P=0.01)							
18.1.3 CCB versus ACEi (change)							
Halimi 2007	34	-5 (14)	33	9 (12)		100%	-14[-20.24,-7.76]
Subtotal ***	**34**		**33**			**100%**	**-14[-20.24,-7.76]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=4.4(P<0.0001)							
18.1.4 CCB versus ARB							
Wei 2002	14	292 (34)	16	256 (72)		16.92%	36[-3.52,75.52]
Formica 2006	10	141 (3)	17	133 (53)		36.05%	8[-17.26,33.26]
El Agroudy 2003 ARB	24	133 (44)	54	133 (44)		47.03%	0[-21.16,21.16]
Subtotal ***	**48**		**87**			**100%**	**8.98[-8.19,26.14]**
Heterogeneity: Tau^2=46.52; Chi^2=2.48, df=2(P=0.29); I^2=19.28%							
Test for overall effect: Z=1.03(P=0.31)							

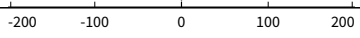


Analysis 18.2. Comparison 18 CCB versus any other intervention, Outcome 2 Serum creatinine (µmol/L) at last follow-up.

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.2.1 CCB versus placebo/no treatment							
Ladefoged 1994	13	225 (169)	18	189 (106)		0.47%	36[-68.1,140.1]
Morales 1989	27	150 (88)	27	269 (248)		0.51%	-119[-218.26,-19.74]
Harper 1996	42	191 (104)	36	267 (152)		1.38%	-76[-134.78,-17.22]
Wahlberg 1992	20	192 (104)	20	150 (59)		1.69%	42[-10.4,94.4]
Sperschneider 1997 Nifed	17	153.4 (73.4)	8	139.8 (42.1)		2.17%	13.6[-31.88,59.08]
Wilkie 1993 No CNI	7	104 (45)	7	102 (40)		2.24%	2[-42.6,46.6]
Venkat-Raman 1999	23	168 (65)	23	177 (66)		2.95%	-9[-46.86,28.86]
Sperschneider 1997 Dilt	17	135.2 (44.9)	8	139.8 (42.1)		3.18%	-4.6[-40.75,31.55]
Van den Dorpel 1994	18	142 (50.5)	18	164 (45.8)		3.94%	-22[-53.49,9.49]
Van der Schaaf 1995	10	139 (35)	20	150 (35)		5.03%	-11[-37.57,15.57]
Santos 2002	15	124 (35)	15	133 (27)		6.27%	-9[-31.37,13.37]
Wilkie 1993 CSA	15	130 (30)	15	134 (31)		6.46%	-4[-25.83,17.83]

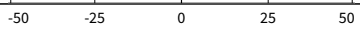


Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Alcaraz 1991	23	159 (35)	30	150 (44)		6.66%	9[-12.27,30.27]
Morales 1994	47	132 (46)	50	156 (53)		7.25%	-24[-43.72,-4.28]
Gossmann 2002	31	131 (36)	29	145 (34)		8.1%	-14[-31.71,3.71]
Kuypers 2004	59	130 (44)	59	152 (42)		9.13%	-22[-37.52,-6.48]
Rahn 1999 NT	57	-3.5 (40)	52	18.6 (31.7)		10.18%	-22.1[-35.59,-8.61]
Kumana 2003	55	131 (37)	55	134 (28)		10.85%	-3[-15.26,9.26]
Rahn 1999 HT	73	5.3 (30)	71	27.4 (37.1)		11.54%	-22.1[-33.14,-11.06]
Subtotal ***	**569**		**561**			**100%**	**-12.5[-19.71,-5.28]**
Heterogeneity: Tau^2=85.69; Chi^2=30.41, df=18(P=0.03); I^2=40.81%							
Test for overall effect: Z=3.4(P=0)							
18.2.2 CCB versus ACEi							
Van der Schaaf 1995	10	139 (35)	20	152 (41)		8.69%	-13[-41.17,15.17]
Sennesael 1995	10	115 (28.5)	9	124 (27)		11.07%	-9[-33.96,15.96]
Hernandez 1995	11	124 (27)	10	133 (27)		12.9%	-9[-32.12,14.12]
Mourad 1993	11	129 (27)	14	144 (26)		15.67%	-15[-35.98,5.98]
El Agroudy 2003	24	133 (44)	54	133 (35)		17.37%	0[-19.93,19.93]
Midtvedt 2001	69	125 (32)	54	144 (45)		34.3%	-19[-33.18,-4.82]
Subtotal ***	**135**		**161**			**100%**	**-12.15[-20.46,-3.85]**
Heterogeneity: Tau^2=0; Chi^2=2.53, df=5(P=0.77); I^2=0%							
Test for overall effect: Z=2.87(P=0)							
18.2.3 CCB versus ACEi (change)							
Halimi 2007	34	-5 (14)	33	9 (12)		100%	-14[-20.24,-7.76]
Subtotal ***	**34**		**33**			**100%**	**-14[-20.24,-7.76]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=4.4(P<0.0001)							
18.2.4 CCB versus ARB							
Wei 2002	14	292 (34)	16	256 (72)		13.78%	36[-3.52,75.52]
Formica 2006	10	141 (3)	17	133 (53)		25.2%	8[-17.26,33.26]
El Agroudy 2003 ARB	24	133 (44)	54	133 (44)		30.41%	0[-21.16,21.16]
Inigo 2001	17	108 (27)	17	122 (35)		30.61%	-14[-35.01,7.01]
Subtotal ***	**65**		**104**			**100%**	**2.69[-14.06,19.45]**
Heterogeneity: Tau^2=123.86; Chi^2=5.27, df=3(P=0.15); I^2=43.07%							
Test for overall effect: Z=0.31(P=0.75)							

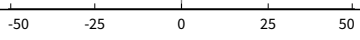


Analysis 18.3. Comparison 18 CCB versus any other intervention, Outcome 3 Any GFR measure (6 months to 2 years of treatment).

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.3.1 CCB versus placebo/no treatment							
Alcaraz 1991	1	0 (0)	1	0 (0)			Not estimable
Wilkie 1994	17	64 (25)	17	64 (25)		2.77%	0[-16.81,16.81]
Rump 2000	24	47 (19.6)	26	49 (30.6)		3.91%	-2[-16.14,12.14]
Frei 1990	65	71 (37)	64	64 (36)		4.92%	7[-5.6,19.6]
Morales 1994	47	90.3 (29)	50	85.8 (28)		6.06%	4.5[-6.86,15.86]



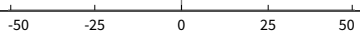
Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Rahn 1999 NT	57	-1.4 (20.4)	52	-1.4 (18.7)		14.5%	0[-7.34,7.34]
Rahn 1999 HT	73	1 (19.7)	71	-6 (17.7)		20.9%	7[0.89,13.11]
Kuypers 2004	53	50.1 (16.2)	53	42 (15.4)		21.57%	8.1[2.08,14.12]
Harper 1996	42	43.9 (12.3)	36	39.4 (12.6)		25.38%	4.5[-1.05,10.05]
Subtotal ***	**379**		**370**			**100%**	**4.89[2.1,7.69]**
Heterogeneity: Tau²=0; Chi²=4.62, df=7(P=0.71); I²=0%							
Test for overall effect: Z=3.43(P=0)							
18.3.2 CCB versus ACEi							
Hernandez 1995	11	101 (27)	10	97 (24)		5.12%	4[-17.81,25.81]
Mourad 1993	11	68 (23)	14	56 (11)		11.17%	12[-2.76,26.76]
Halimi 2007	34	15 (31)	33	-8 (28)		12.18%	23[8.86,37.14]
Midtvedt 2001	69	56 (19)	54	44 (14)		71.53%	12[6.17,17.83]
Subtotal ***	**125**		**111**			**100%**	**12.93[8,17.87]**
Heterogeneity: Tau²=0; Chi²=2.71, df=3(P=0.44); I²=0%							
Test for overall effect: Z=5.14(P<0.0001)							



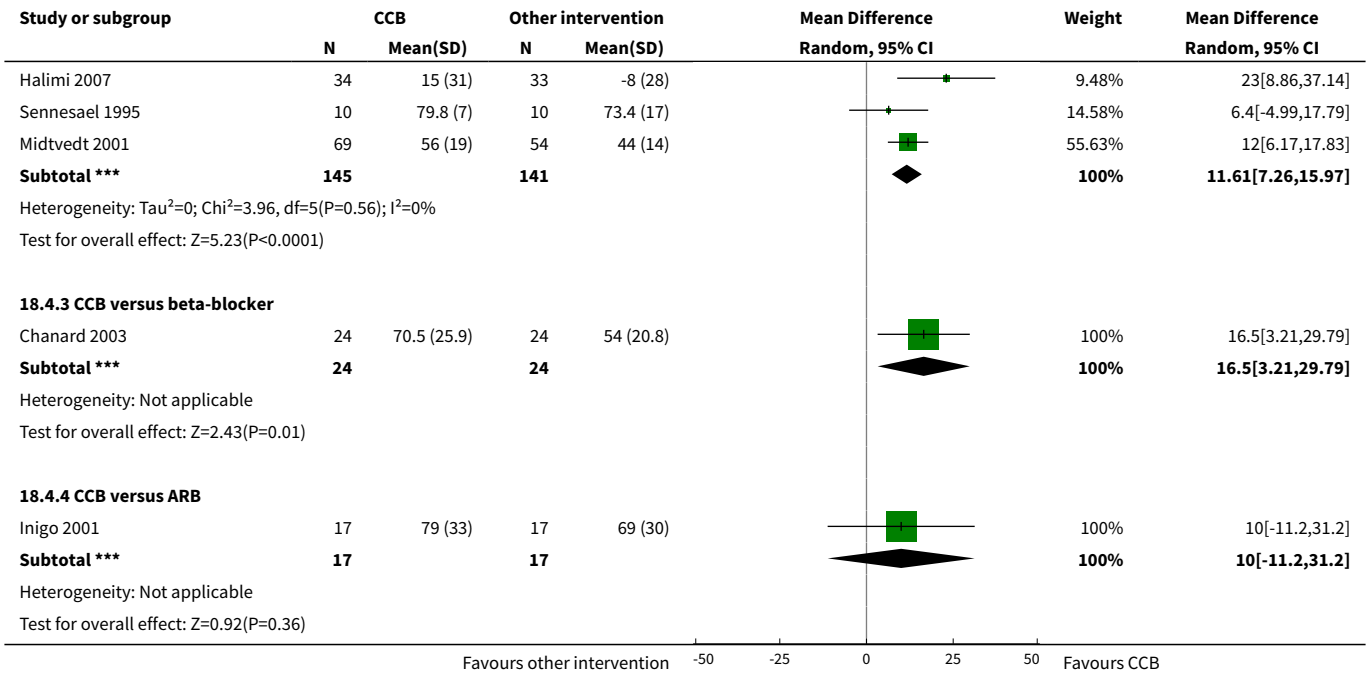
Favours other intervention — Favours CCB

Analysis 18.4. Comparison 18 CCB versus any other intervention, Outcome 4 Any GFR measure at last follow-up.

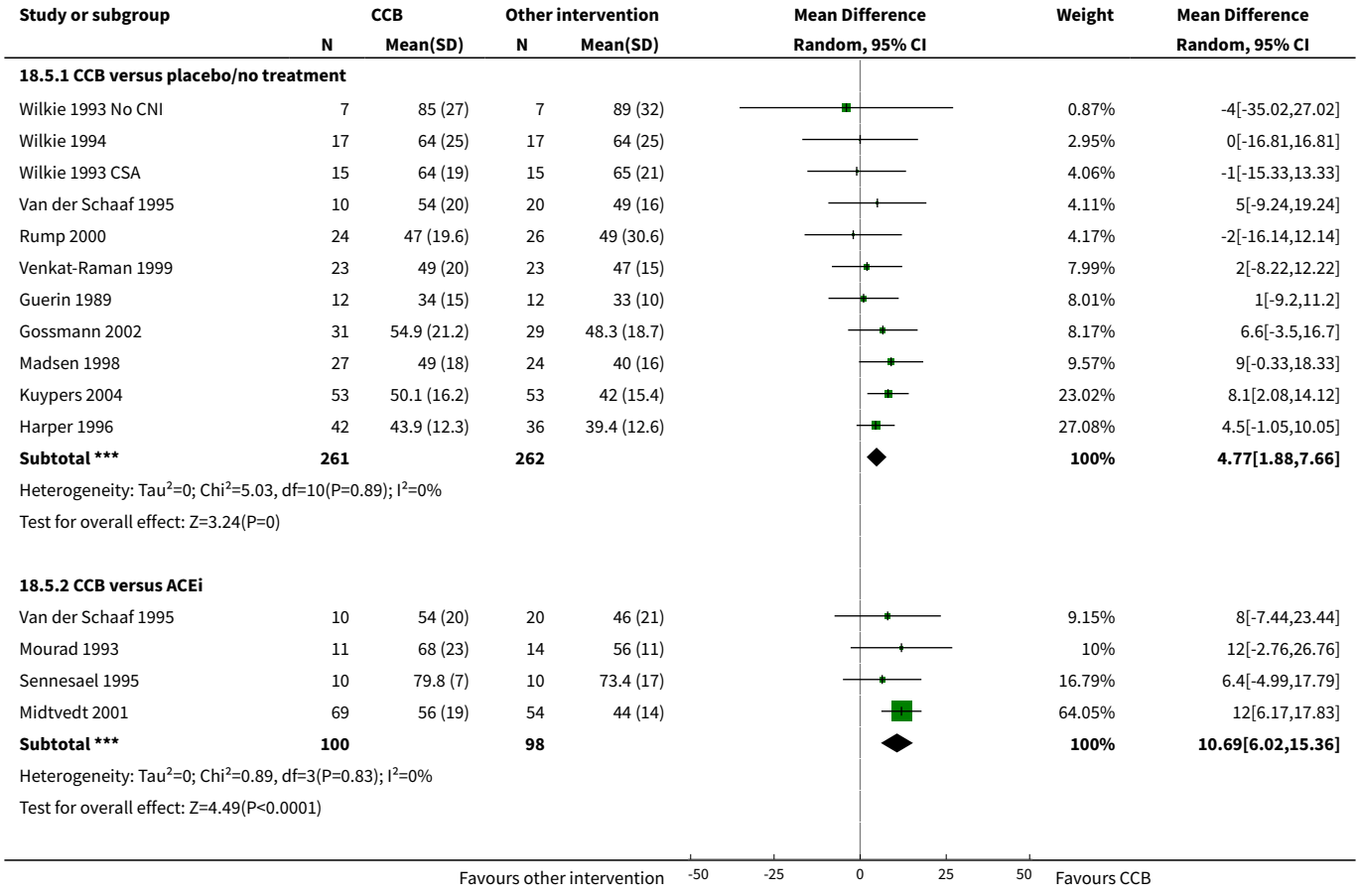
Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.4.1 CCB versus placebo/no treatment							
Wilkie 1993 No CNI	7	85 (27)	7	89 (32)		0.53%	-4[-35.02,27.02]
Wilkie 1994	17	64 (25)	17	64 (25)		1.79%	0[-16.81,16.81]
Ladefoged 1994	13	43 (21.6)	18	46 (25.5)		1.83%	-3[-19.63,13.63]
Van den Dorpel 1994	18	66.1 (19.1)	18	55.6 (26.3)		2.24%	10.5[-4.52,25.52]
Wilkie 1993 CSA	15	64 (19)	15	65 (21)		2.46%	-1[-15.33,13.33]
Van der Schaaf 1995	10	54 (20)	20	49 (16)		2.49%	5[-9.24,19.24]
Rump 2000	24	47 (19.6)	26	49 (30.6)		2.53%	-2[-16.14,12.14]
Frei 1990	65	71 (37)	64	64 (36)		3.18%	7[-5.6,19.6]
Wahlberg 1992	20	36.6 (12.3)	20	45.6 (22)		4.14%	-9[-20.05,2.05]
Venkat-Raman 1999	23	49 (20)	23	47 (15)		4.84%	2[-8.22,12.22]
Guerin 1989	12	34 (15)	12	33 (10)		4.86%	1[-9.2,11.2]
Gossmann 2002	31	54.9 (21.2)	29	48.3 (18.7)		4.95%	6.6[-3.5,16.7]
Morales 1994	47	79.2 (27)	50	67.9 (22.8)		5.08%	11.3[1.32,21.28]
Madsen 1998	27	49 (18)	24	40 (16)		5.8%	9[-0.33,18.33]
Rahn 1999 NT	57	-1.4 (20.4)	52	-1.4 (18.7)		9.38%	0[-7.34,7.34]
Rahn 1999 HT	73	1 (19.7)	71	-6 (17.7)		13.52%	7[0.89,13.11]
Kuypers 2004	53	50.1 (16.2)	53	42 (15.4)		13.96%	8.1[2.08,14.12]
Harper 1996	42	43.9 (12.3)	36	39.4 (12.6)		16.42%	4.5[-1.05,10.05]
Subtotal ***	**554**		**555**			**100%**	**4.44[2.2,6.69]**
Heterogeneity: Tau²=0; Chi²=16.22, df=17(P=0.51); I²=0%							
Test for overall effect: Z=3.87(P=0)							
18.4.2 CCB versus ACEi							
Hernandez 1995	11	101 (29)	10	97 (24)		3.68%	4[-18.69,26.69]
Van der Schaaf 1995	10	54 (20)	20	46 (21)		7.94%	8[-7.44,23.44]
Mourad 1993	11	68 (23)	14	56 (11)		8.69%	12[-2.76,26.76]

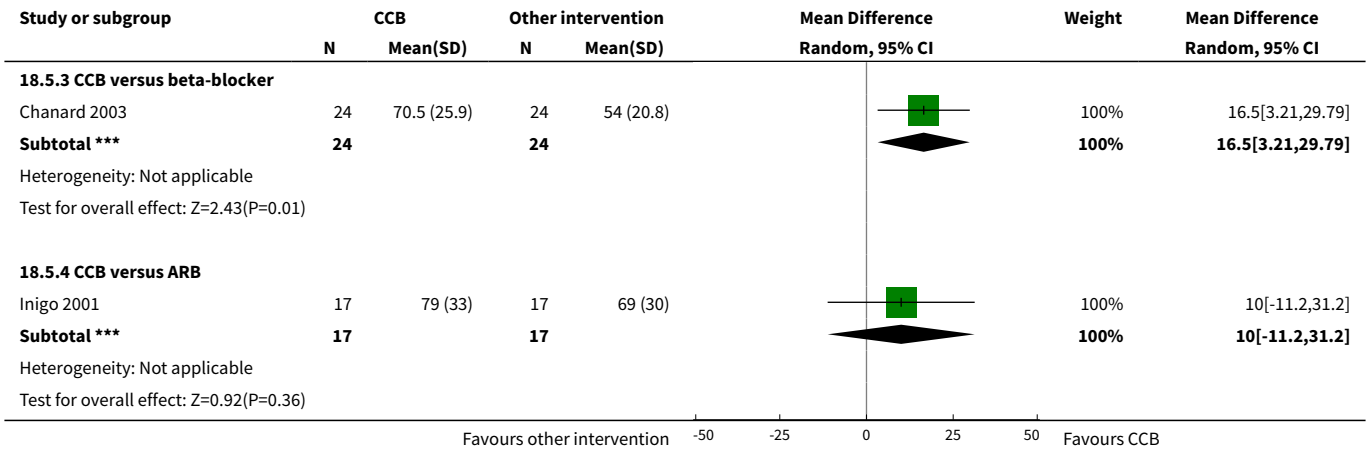


Favours other intervention — Favours CCB

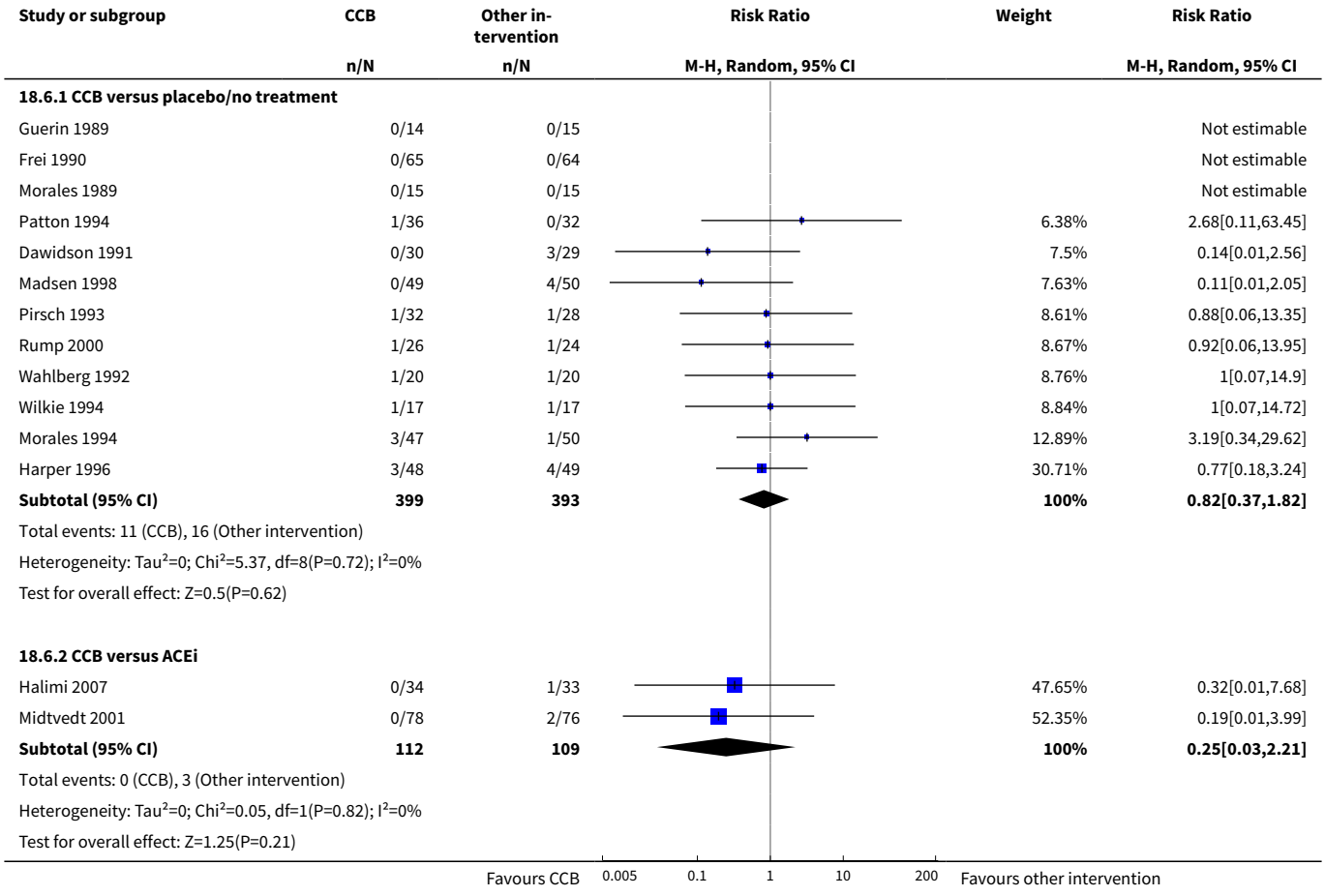


Analysis 18.5. Comparison 18 CCB versus any other intervention, Outcome 5 Measured GFR at last follow-up.



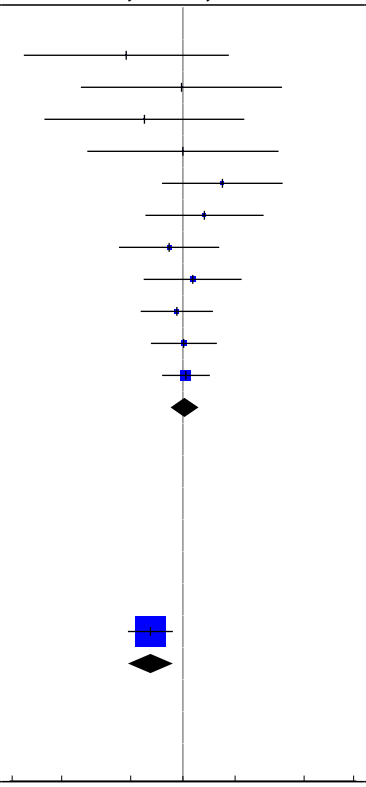


Analysis 18.6. Comparison 18 CCB versus any other intervention, Outcome 6 Death at last follow-up.



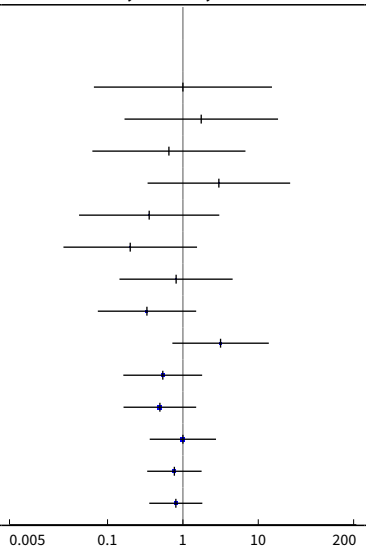
Analysis 18.7. Comparison 18 CCB versus any other intervention, Outcome 7 Acute rejection at last follow-up.

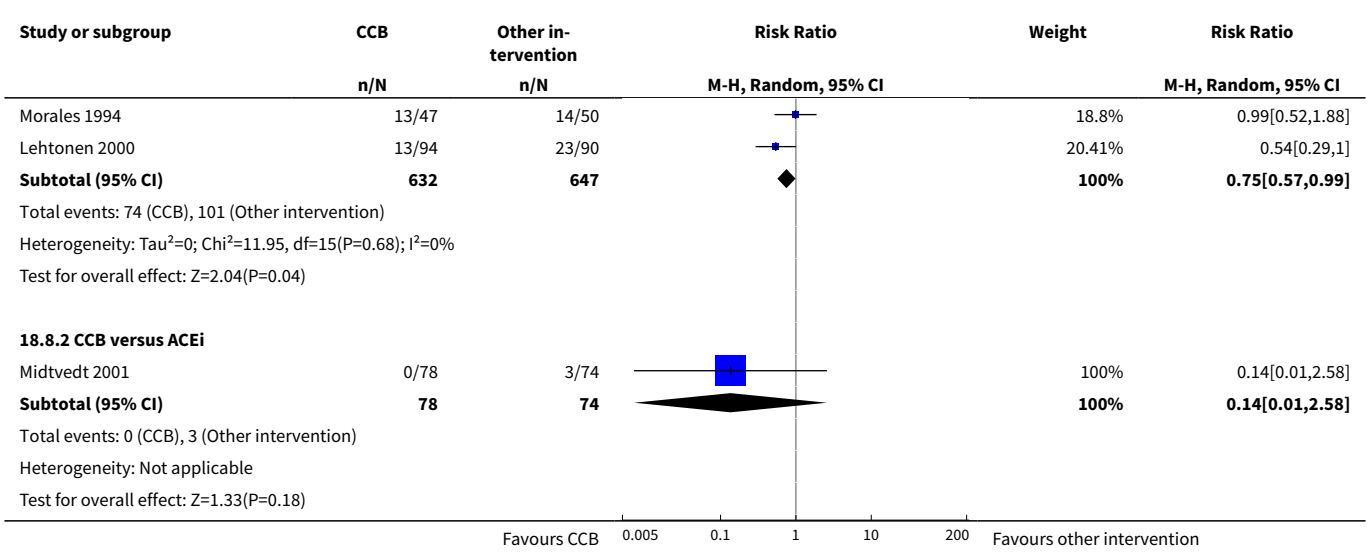
Study or subgroup	CCB n/N	Other intervention n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
18.7.1 CCB versus placebo/no treatment					
Sperschneider 1997 Dilt	3/17	3/8		1.83%	0.47[0.12,1.84]
Kumana 2003	4/56	4/55		1.91%	0.98[0.26,3.73]
Morales 1989	3/27	5/27		1.92%	0.6[0.16,2.26]
Van den Dorpel 1994	4/25	4/25		2.1%	1[0.28,3.56]
Sperschneider 1997 Nifed	9/12	4/9		5.3%	1.69[0.76,3.76]
Kuypers 2004	12/59	9/59		5.51%	1.33[0.61,2.92]
Guerin 1989	7/14	9/15		7.63%	0.83[0.43,1.62]
Pirsch 1993	13/32	10/28		8.04%	1.14[0.59,2.18]
Wahlberg 1992	12/20	13/20		14.67%	0.92[0.57,1.49]
Alcaraz 1991	14/23	18/30		17.62%	1.01[0.65,1.57]
Van Riemsdijk 2000	42/98	46/112		33.46%	1.04[0.76,1.43]
Subtotal (95% CI)	**383**	**388**		**100%**	**1.02[0.85,1.23]**
Total events: 123 (CCB), 125 (Other intervention)					
Heterogeneity: Tau^2=0; Chi^2=4.47, df=10(P=0.92); I^2=0%					
Test for overall effect: Z=0.22(P=0.82)					
18.7.2 CCB versus ACEi					
Halimi 2007	0/34	0/33			Not estimable
Midtvedt 2001	34/78	51/76		100%	0.65[0.48,0.87]
Subtotal (95% CI)	**112**	**109**		**100%**	**0.65[0.48,0.87]**
Total events: 34 (CCB), 51 (Other intervention)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.84(P=0)					



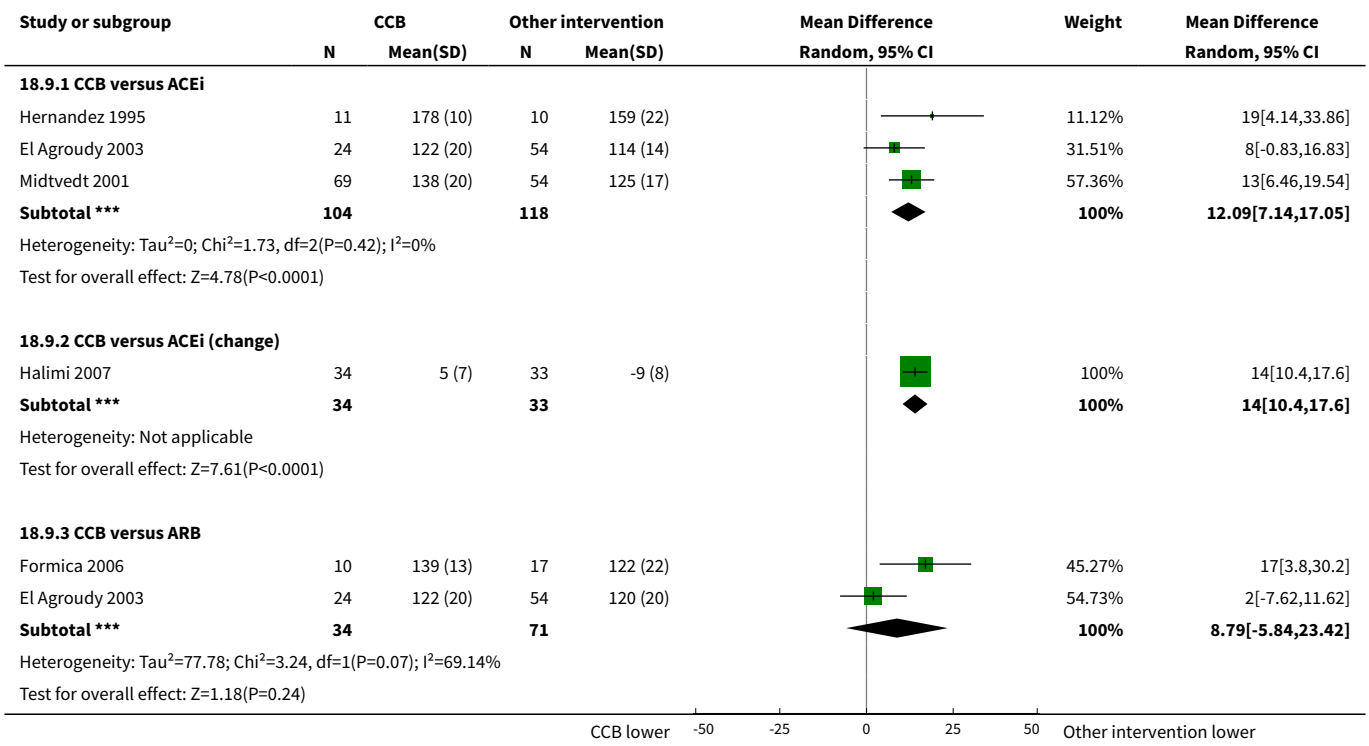
Analysis 18.8. Comparison 18 CCB versus any other intervention, Outcome 8 Graft loss at last follow-up.

Study or subgroup	CCB n/N	Other intervention n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
18.8.1 CCB versus placebo/no treatment					
Campistol 1991	0/12	0/25			Not estimable
Morales 1989	1/27	1/27		1.05%	1[0.07,15.18]
Pirsch 1993	2/32	1/28		1.4%	1.75[0.17,18.28]
Alcaraz 1991	1/23	2/30		1.41%	0.65[0.06,6.76]
Wahlberg 1992	3/20	1/20		1.63%	3[0.34,26.45]
Guerin 1989	1/14	3/15		1.68%	0.36[0.04,3.04]
Wilkie 1994	1/17	5/17		1.86%	0.2[0.03,1.54]
Chrysostomou 1993	2/32	3/39		2.59%	0.81[0.14,4.57]
Van den Dorpel 1994	2/25	6/25		3.43%	0.33[0.07,1.5]
Ladefoged 1994	6/19	2/20		3.57%	3.16[0.72,13.76]
Rahn 1999 (both)	4/130	7/123		5.34%	0.54[0.16,1.8]
Dawidson 1991	4/30	7/26		6.27%	0.5[0.16,1.5]
Santos 2002	5/15	5/15		7.55%	1[0.36,2.75]
Wagner 1986	7/30	10/33		11.23%	0.77[0.34,1.77]
Frei 1990	9/65	11/64		11.77%	0.81[0.36,1.81]



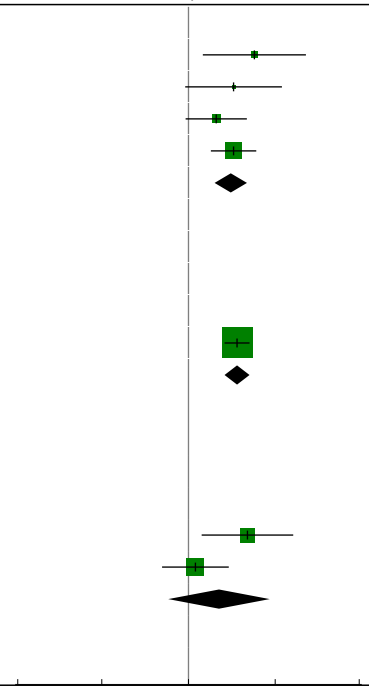


Analysis 18.9. Comparison 18 CCB versus any other intervention, Outcome 9 Haemoglobin (g/L) (6 months to 2 years of treatment).



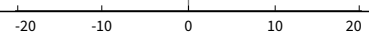
Analysis 18.10. Comparison 18 CCB versus any other intervention, Outcome 10 Haemoglobin (g/L) at last follow-up.

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.10.1 CCB versus ACEi							
Hernandez 1995	11	178 (10)	10	159 (22)		9.88%	19[4.14,33.86]
Sennesael 1995	10	148 (16)	9	135 (15)		11.22%	13[-0.94,26.94]
El Agroudy 2003	24	122 (20)	54	114 (14)		27.98%	8[-0.83,16.83]
Midtvedt 2001	69	138 (20)	54	125 (17)		50.93%	13[6.46,19.54]
Subtotal ***	**114**		**127**			**100%**	**12.19[7.52,16.86]**
Heterogeneity: Tau²=0; Chi²=1.74, df=3(P=0.63); I²=0%							
Test for overall effect: Z=5.12(P<0.0001)							
18.10.2 CCB versus ACEi (change)							
Halimi 2007	34	5 (7)	33	-9 (8)		100%	14[10.4,17.6]
Subtotal ***	**34**		**33**			**100%**	**14[10.4,17.6]**
Heterogeneity: Not applicable							
Test for overall effect: Z=7.61(P<0.0001)							
18.10.3 CCB versus ARB							
Formica 2006	10	139 (13)	17	122 (22)		45.27%	17[3.8,30.2]
El Agroudy 2003	24	122 (20)	54	120 (20)		54.73%	2[-7.62,11.62]
Subtotal ***	**34**		**71**			**100%**	**8.79[-5.84,23.42]**
Heterogeneity: Tau²=77.78; Chi²=3.24, df=1(P=0.07); I²=69.14%							
Test for overall effect: Z=1.18(P=0.24)							

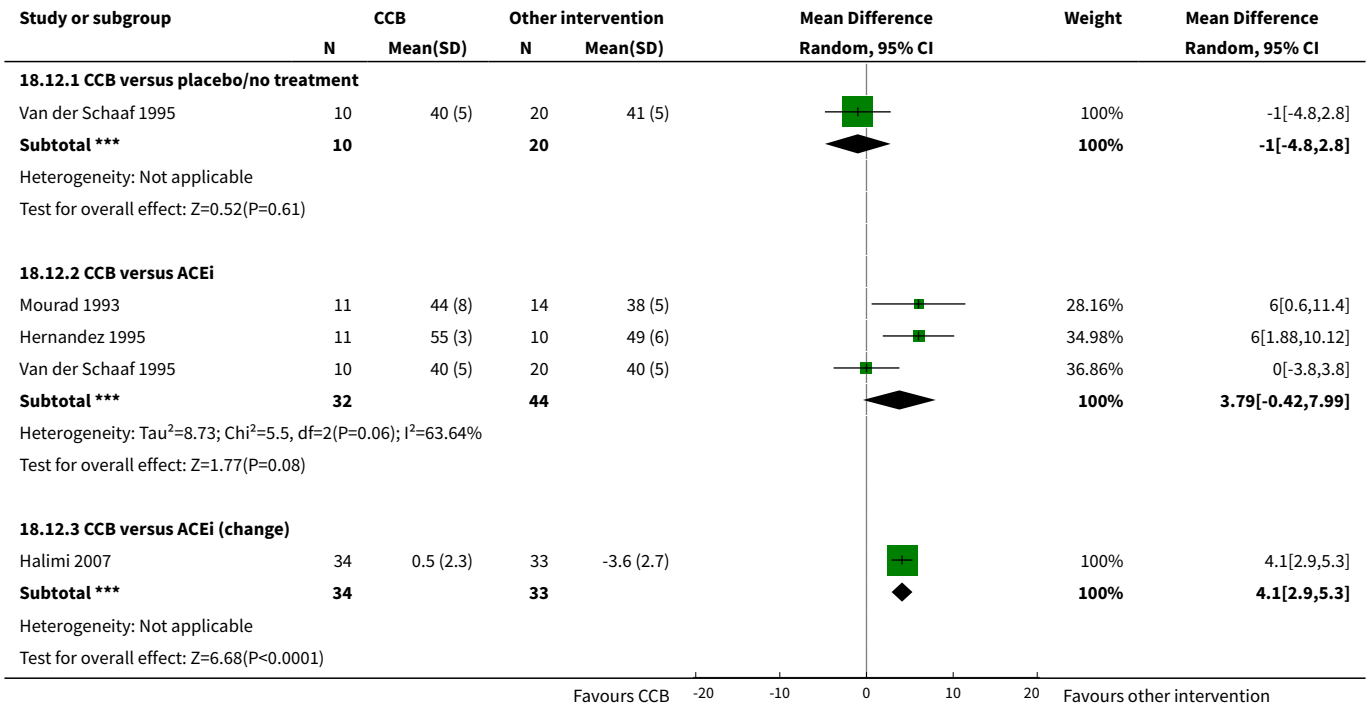


Analysis 18.11. Comparison 18 CCB versus any other intervention, Outcome 11 Haematocrit (%) (6 months to 2 years of treatment).

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.11.1 CCB versus ACEi							
Mourad 1993	11	44 (8)	14	38 (5)		36.75%	6[0.6,11.4]
Hernandez 1995	11	55 (3)	10	49 (6)		63.25%	6[1.88,10.12]
Subtotal ***	**22**		**24**			**100%**	**6[2.72,9.28]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=1); I²=0%							
Test for overall effect: Z=3.59(P=0)							
18.11.2 CCB versus ACEi (change)							
Halimi 2007	34	0.5 (2.3)	33	-3.6 (2.7)		100%	4.1[2.9,5.3]
Subtotal ***	**34**		**33**			**100%**	**4.1[2.9,5.3]**
Heterogeneity: Not applicable							
Test for overall effect: Z=6.68(P<0.0001)							

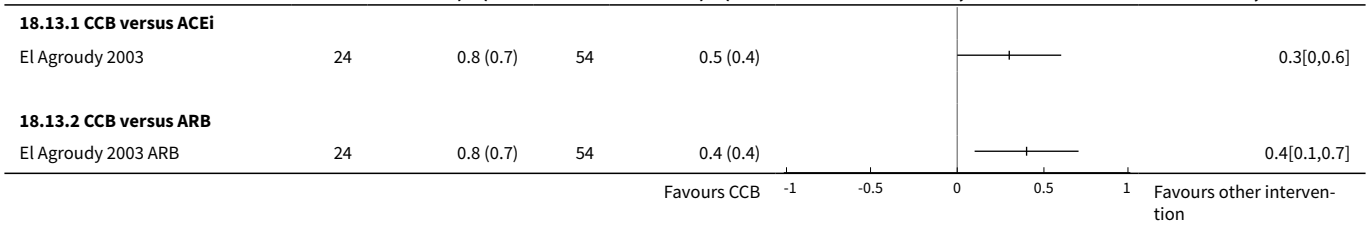


Analysis 18.12. Comparison 18 CCB versus any other intervention, Outcome 12 Haematocrit (%) at last follow-up.



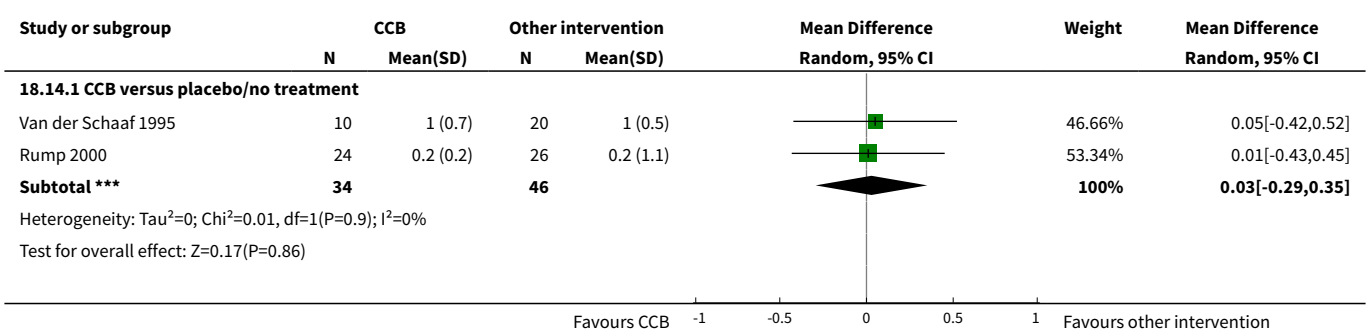
Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.12.1 CCB versus placebo/no treatment							
Van der Schaaf 1995	10	40 (5)	20	41 (5)		100%	-1[-4.8,2.8]
Subtotal ***	**10**		**20**			**100%**	**-1[-4.8,2.8]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.52(P=0.61)							
18.12.2 CCB versus ACEi							
Mourad 1993	11	44 (8)	14	38 (5)		28.16%	6[0.6,11.4]
Hernandez 1995	11	55 (3)	10	49 (6)		34.98%	6[1.88,10.12]
Van der Schaaf 1995	10	40 (5)	20	40 (5)		36.86%	0[-3.8,3.8]
Subtotal ***	**32**		**44**			**100%**	**3.79[-0.42,7.99]**
Heterogeneity: Tau^2=8.73; Chi^2=5.5, df=2(P=0.06); I^2=63.64%							
Test for overall effect: Z=1.77(P=0.08)							
18.12.3 CCB versus ACEi (change)							
Halimi 2007	34	0.5 (2.3)	33	-3.6 (2.7)		100%	4.1[2.9,5.3]
Subtotal ***	**34**		**33**			**100%**	**4.1[2.9,5.3]**
Heterogeneity: Not applicable							
Test for overall effect: Z=6.68(P<0.0001)							

Analysis 18.13. Comparison 18 CCB versus any other intervention, Outcome 13 Proteinuria (6 months to 2 years of treatment).

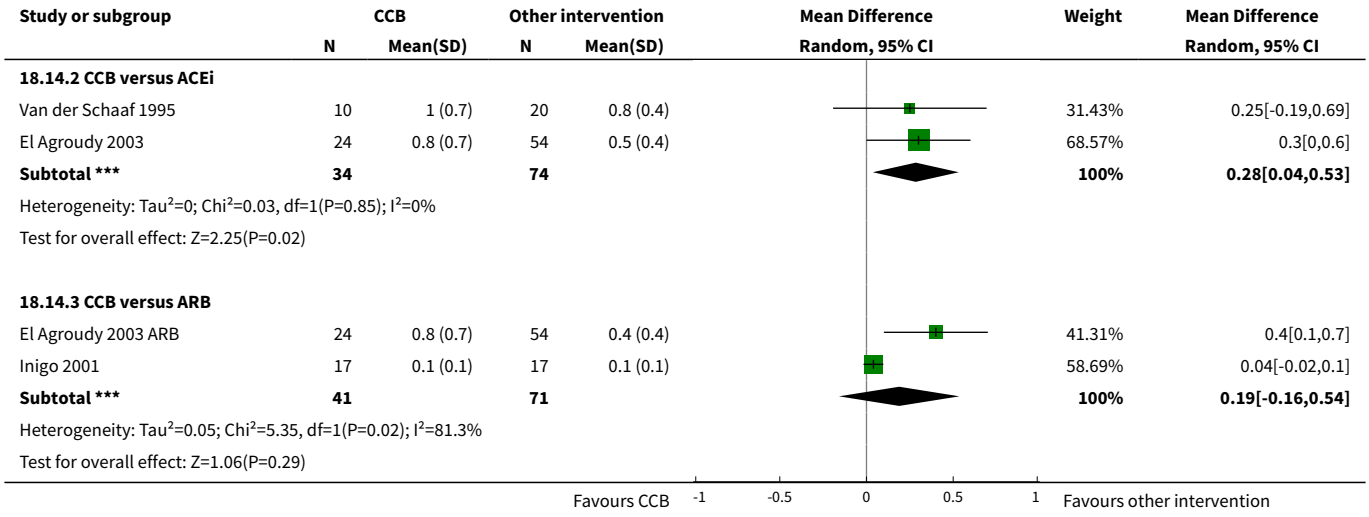


Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
18.13.1 CCB versus ACEi						
El Agroudy 2003	24	0.8 (0.7)	54	0.5 (0.4)		0.3[0,0.6]
18.13.2 CCB versus ARB						
El Agroudy 2003 ARB	24	0.8 (0.7)	54	0.4 (0.4)		0.4[0.1,0.7]

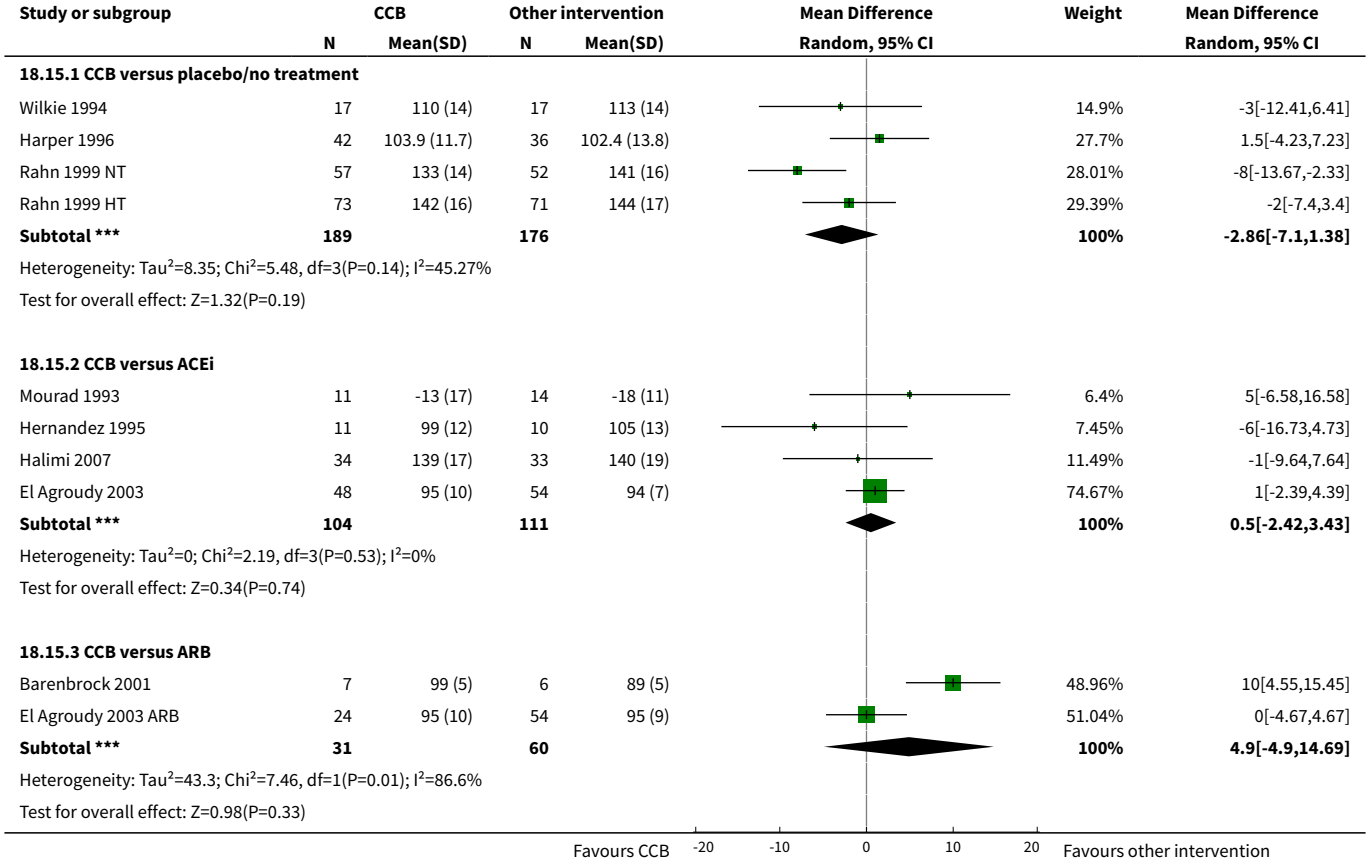
Analysis 18.14. Comparison 18 CCB versus any other intervention, Outcome 14 Proteinuria (g/24 h) at last follow-up.



Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.14.1 CCB versus placebo/no treatment							
Van der Schaaf 1995	10	1 (0.7)	20	1 (0.5)		46.66%	0.05[-0.42,0.52]
Rump 2000	24	0.2 (0.2)	26	0.2 (1.1)		53.34%	0.01[-0.43,0.45]
Subtotal ***	**34**		**46**			**100%**	**0.03[-0.29,0.35]**
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.9); I^2=0%							
Test for overall effect: Z=0.17(P=0.86)							

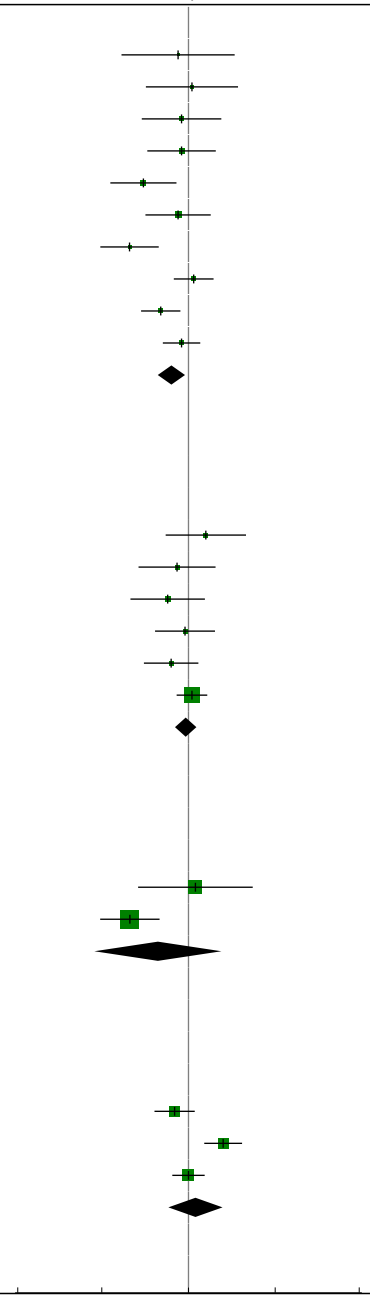


Analysis 18.15. Comparison 18 CCB versus any other intervention, Outcome 15 Blood pressure (systolic/mean arterial/diastolic) (6 months to 2 years of treatment).



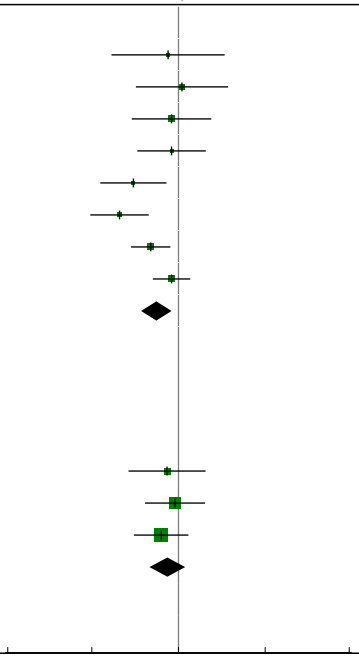
Analysis 18.16. Comparison 18 CCB versus any other intervention, Outcome 16 Blood pressure at last follow-up (systolic/mean arterial/diastolic).

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.16.1 CCB versus placebo/no treatment							
Wilkie 1993 No CNI	7	131 (17)	7	134 (14)		4.53%	-3[-19.31,13.31]
Wilkie 1993 CSA	15	152 (17)	15	151 (20)		6.14%	1[-12.28,14.28]
Guerin 1989	13	136 (17)	12	138 (12)		7.48%	-2[-13.47,9.47]
Venkat-Raman 1999	27	139 (18)	27	141 (19)		8.96%	-2[-11.87,7.87]
Madsen 1998	30	131 (16)	32	144 (22)		9.31%	-13[-22.53,-3.47]
Wilkie 1994	17	110 (14)	17	113 (14)		9.44%	-3[-12.41,6.41]
Van der Schaaf 1995	10	148 (10)	20	165 (13)		10.59%	-17[-25.42,-8.58]
Harper 1996	42	103.9 (11.7)	36	102.4 (13.8)		14.31%	1.5[-4.23,7.23]
Rahn 1999 NT	57	133 (14)	52	141 (16)		14.41%	-8[-13.67,-2.33]
Rahn 1999 HT	73	142 (16)	71	144 (17)		14.83%	-2[-7.4,3.4]
Subtotal ***	**291**		**289**			**100%**	**-4.93[-8.86,-1]**
Heterogeneity: Tau^2=19.56; Chi^2=19.24, df=9(P=0.02); I^2=53.22%							
Test for overall effect: Z=2.46(P=0.01)							
18.16.2 CCB versus ACEi							
Mourad 1993	11	-13 (17)	14	-18 (11)		7.09%	5[-6.58,16.58]
Sennesael 1995	10	156.4 (12)	10	159.7 (13.3)		7.71%	-3.3[-14.4,7.8]
Hernandez 1995	11	99 (12)	10	105 (13)		8.25%	-6[-16.73,4.73]
Halimi 2007	34	139 (17)	33	140 (19)		12.73%	-1[-9.64,7.64]
Van der Schaaf 1995	10	148 (10)	20	153 (11)		15.42%	-5[-12.85,2.85]
El Agroudy 2003	24	95 (10)	54	94 (7)		48.79%	1[-3.41,5.41]
Subtotal ***	**100**		**141**			**100%**	**-0.81[-3.89,2.28]**
Heterogeneity: Tau^2=0; Chi^2=3.8, df=5(P=0.58); I^2=0%							
Test for overall effect: Z=0.51(P=0.61)							
18.16.3 CCB versus beta-blocker							
Barri 1995	15	141 (25)	15	139 (21)		42.72%	2[-14.52,18.52]
Chanard 2003	24	131.5 (10.4)	24	148.4 (18.7)		57.28%	-16.9[-25.46,-8.34]
Subtotal ***	**39**		**39**			**100%**	**-8.83[-27.15,9.5]**
Heterogeneity: Tau^2=133.53; Chi^2=3.96, df=1(P=0.05); I^2=74.76%							
Test for overall effect: Z=0.94(P=0.35)							
18.16.4 CCB versus ARB							
Inigo 2001	17	92 (7)	17	96 (10)		32.38%	-4[-9.8,1.8]
Barenbrock 2001	7	99 (5)	6	89 (5)		33.07%	10[4.55,15.45]
El Agroudy 2003 ARB	24	95 (10)	54	95 (9)		34.56%	0[-4.67,4.67]
Subtotal ***	**48**		**77**			**100%**	**2.01[-5.8,9.83]**
Heterogeneity: Tau^2=40.33; Chi^2=13.08, df=2(P=0); I^2=84.71%							
Test for overall effect: Z=0.5(P=0.61)							



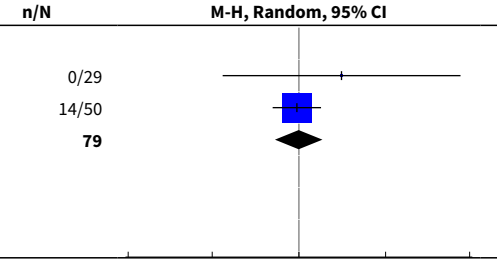
Analysis 18.17. Comparison 18 CCB versus any other intervention, Outcome 17 Systolic blood pressure (mm Hg) at last follow-up.

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.17.1 CCB versus placebo/no treatment							
Wilkie 1993 No CNI	7	131 (17)	7	134 (14)		5.76%	-3[-19.31,13.31]
Wilkie 1993 CSA	15	152 (17)	15	151 (20)		7.88%	1[-12.28,14.28]
Guerin 1989	13	136 (17)	12	138 (12)		9.66%	-2[-13.47,9.47]
Venkat-Raman 1999	27	139 (18)	27	141 (19)		11.64%	-2[-11.87,7.87]
Madsen 1998	30	131 (16)	32	144 (22)		12.12%	-13[-22.53,-3.47]
Van der Schaaf 1995	10	148 (10)	20	165 (13)		13.87%	-17[-25.42,-8.58]
Rahn 1999 NT	57	133 (14)	52	141 (16)		19.24%	-8[-13.67,-2.33]
Rahn 1999 HT	73	142 (16)	71	144 (17)		19.83%	-2[-7.4,3.4]
Subtotal ***	**232**		**236**			**100%**	**-6.39[-10.78,-2]**
Heterogeneity: Tau^2=17.71; Chi^2=13.47, df=7(P=0.06); I^2=48.05%							
Test for overall effect: Z=2.85(P=0)							
18.17.2 CCB versus ACEi							
Sennesael 1995	10	156.4 (12)	10	159.7 (13.3)		21.51%	-3.3[-14.4,7.8]
Halimi 2007	34	139 (17)	33	140 (19)		35.5%	-1[-9.64,7.64]
Van der Schaaf 1995	10	148 (10)	20	153 (11)		43%	-5[-12.85,2.85]
Subtotal ***	**54**		**63**			**100%**	**-3.21[-8.36,1.93]**
Heterogeneity: Tau^2=0; Chi^2=0.45, df=2(P=0.8); I^2=0%							
Test for overall effect: Z=1.22(P=0.22)							



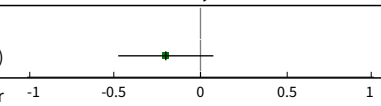
Analysis 18.18. Comparison 18 CCB versus any other intervention, Outcome 18 Withdrawal due to side effects at last follow-up.

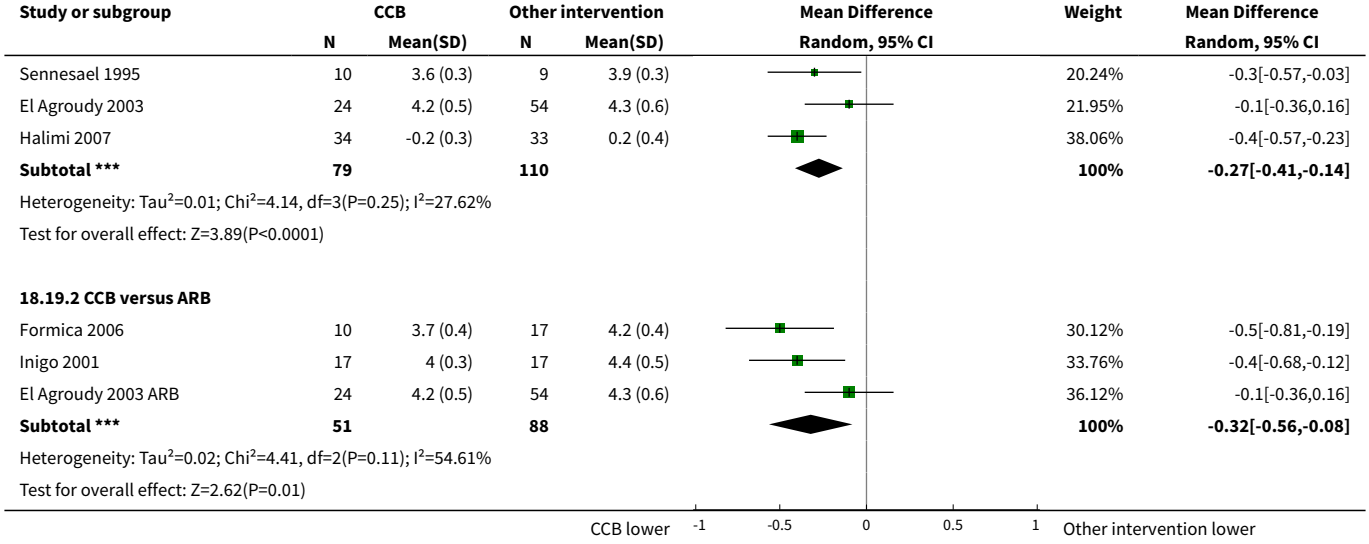
Study or subgroup	CCB n/N	Other intervention n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
18.18.1 CCB versus placebo/no treatment					
Venkat-Raman 1999	1/28	0/29		3.99%	3.1[0.13,73.12]
Madsen 1998	13/49	14/50		96.01%	0.95[0.5,1.8]
Subtotal (95% CI)	**77**	**79**		**100%**	**0.99[0.53,1.87]**
Total events: 14 (CCB), 14 (Other intervention)					
Heterogeneity: Tau^2=0; Chi^2=0.53, df=1(P=0.47); I^2=0%					
Test for overall effect: Z=0.02(P=0.98)					



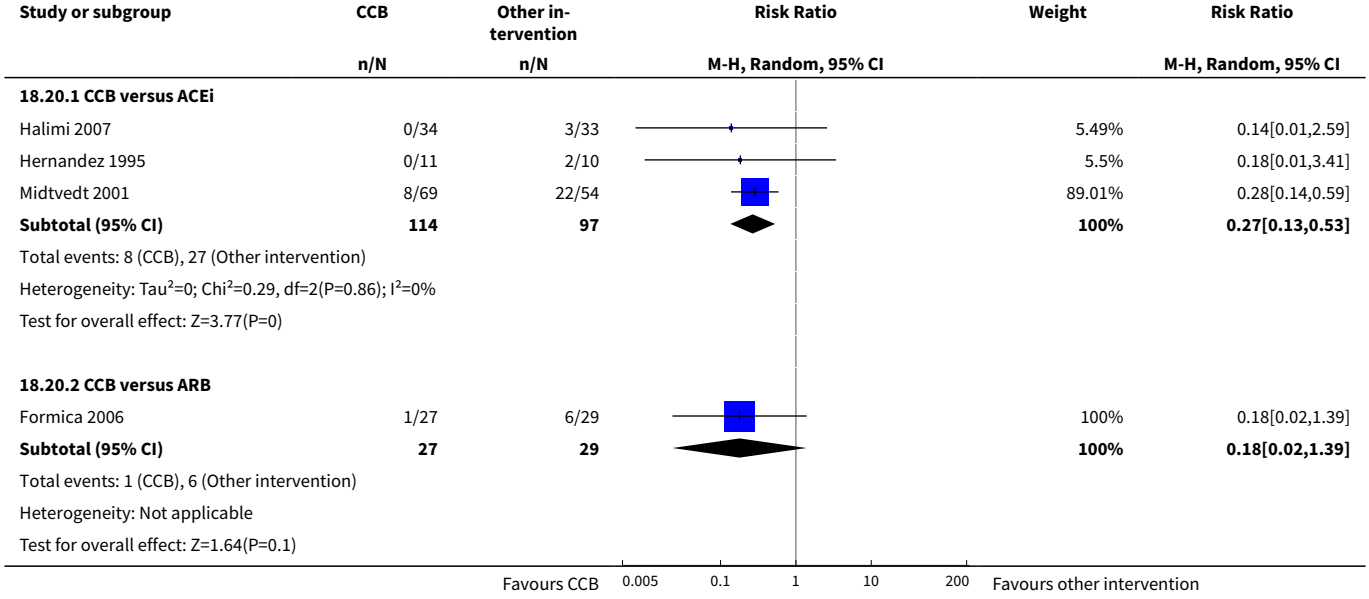
Analysis 18.19. Comparison 18 CCB versus any other intervention, Outcome 19 Serum potassium (mmol/L) at last follow-up.

Study or subgroup	CCB N	CCB Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
18.19.1 CCB versus ACEi							
Mourad 1993	11	3.7 (0.3)	14	3.9 (0.4)		19.75%	-0.2[-0.47,0.07]

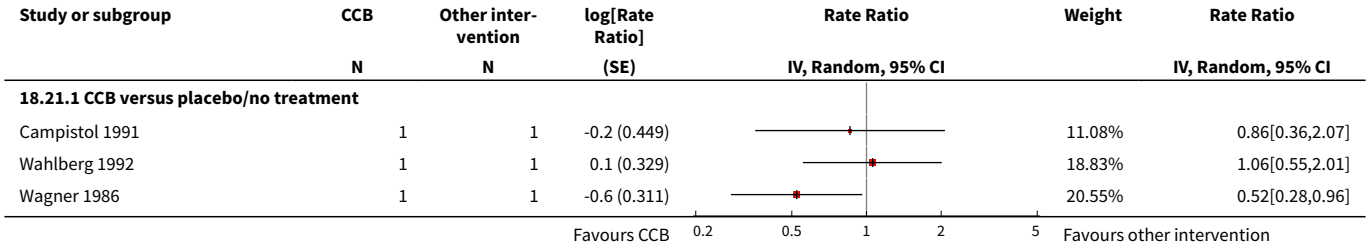


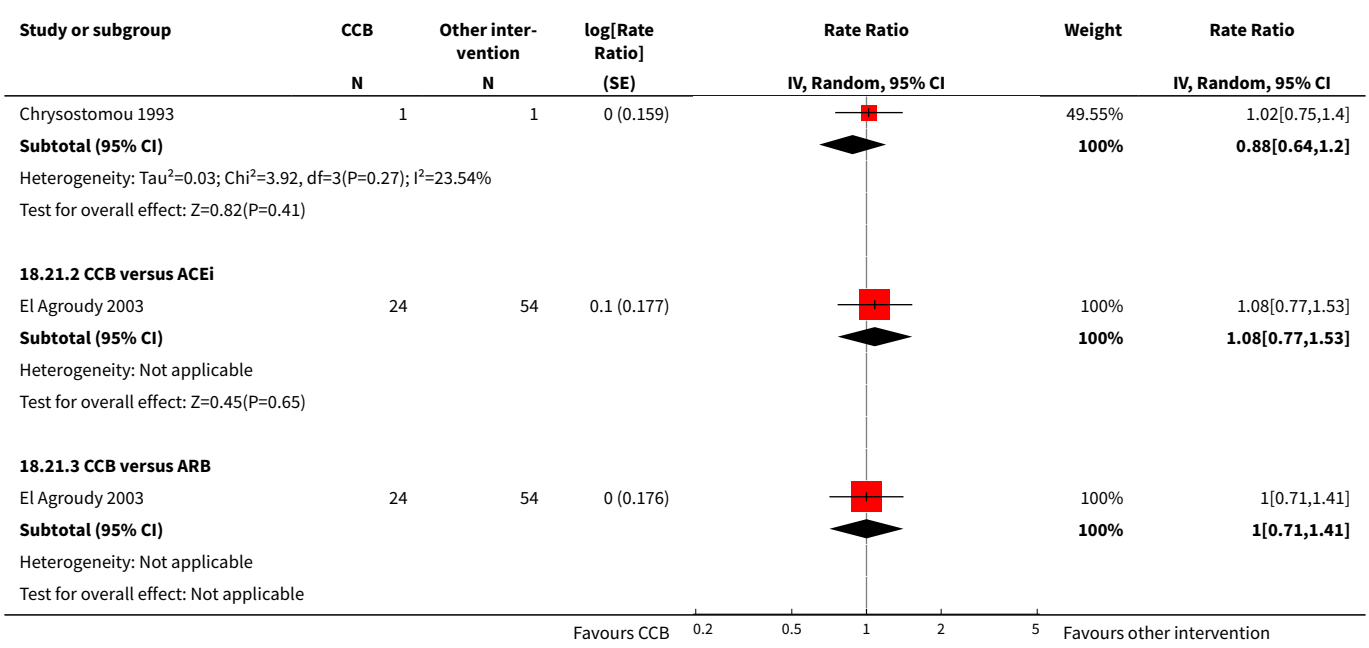


Analysis 18.20. Comparison 18 CCB versus any other intervention, Outcome 20 Hyperkalaemia at last follow-up.



Analysis 18.21. Comparison 18 CCB versus any other intervention, Outcome 21 Rejection rate.





Comparison 19. ACEi versus any other intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum creatinine (6 months to 2 years of treatment)	8		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 ACEi versus placebo/no treatment	2	122	Mean Difference (IV, Random, 95% CI)	1.01 [-13.66, 15.67]
1.2 ACEi versus CCB	5	311	Mean Difference (IV, Random, 95% CI)	13.38 [8.38, 18.38]
1.3 ACEi versus beta-blocker	1	70	Mean Difference (IV, Random, 95% CI)	-3.0 [-48.03, 42.03]
1.4 ACEi versus ARB	1	81	Mean Difference (IV, Random, 95% CI)	0.0 [-17.66, 17.66]
2 Serum creatinine (µmol/L) at last follow-up	16		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 ACEi versus placebo/no treatment	6	210	Mean Difference (IV, Random, 95% CI)	7.32 [-2.17, 16.82]
2.2 ACEi versus CCB	7	360	Mean Difference (IV, Random, 95% CI)	13.21 [8.37, 18.04]
2.3 ACEi versus alpha-blocker	1	74	Mean Difference (IV, Random, 95% CI)	3.0 [-14.82, 20.82]

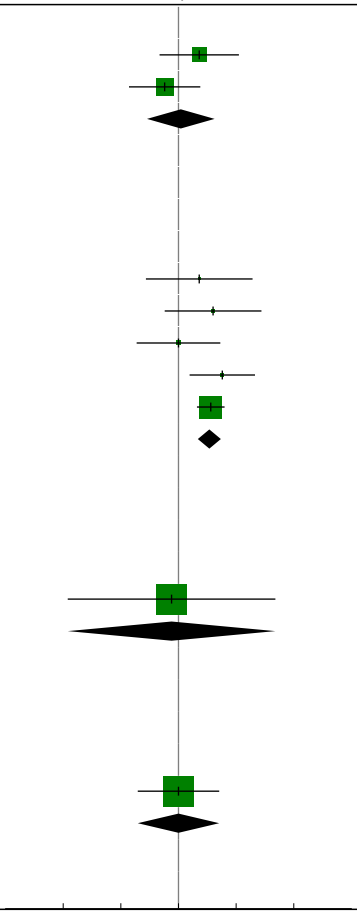
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2.4 ACEi versus beta-blocker	1	70	Mean Difference (IV, Random, 95% CI)	-3.0 [-48.03, 42.03]
2.5 ACEi versus ARB	4	154	Mean Difference (IV, Random, 95% CI)	-2.83 [-10.83, 5.18]
3 Any GFR measure (6 months to 2 years of treatment)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 ACEi versus CCB	4	236	Mean Difference (IV, Random, 95% CI)	-12.97 [-17.91, -8.02]
3.2 ACEi versus beta-blocker (change)	1	70	Mean Difference (IV, Random, 95% CI)	7.8 [-18.06, 33.66]
4 Any GFR measure at last follow-up	10		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 ACEi versus placebo/no treatment	3	67	Mean Difference (IV, Random, 95% CI)	-8.90 [-19.74, 1.94]
4.2 ACEi versus CCB	6	286	Mean Difference (IV, Random, 95% CI)	-11.62 [-15.98, -7.27]
4.3 ACEi versus alpha-blocker	1	74	Mean Difference (IV, Random, 95% CI)	-3.0 [-11.66, 5.66]
4.4 ACEi versus beta-blocker	1	70	Mean Difference (IV, Random, 95% CI)	7.8 [-18.06, 33.66]
5 Measured GFR at last follow-up	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 ACEi versus placebo/no treatment	2	55	Mean Difference (IV, Random, 95% CI)	-5.44 [-11.85, 0.98]
5.2 ACEi versus CCB	4	198	Mean Difference (IV, Random, 95% CI)	-10.70 [-15.38, -6.03]
5.3 ACEi versus alpha-blocker	1	74	Mean Difference (IV, Random, 95% CI)	-3.0 [-11.66, 5.66]
6 Death at last follow-up	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 ACEi versus placebo/no treatment	1	30	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.07, 14.55]
6.2 ACEi versus CCB	2	221	Risk Ratio (M-H, Random, 95% CI)	4.03 [0.45, 35.82]
6.3 ACEi versus beta-blocker	1	96	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.12, 3.81]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
7 Graft loss at last follow-up	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 ACEi versus placebo/no treatment	2	93	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.19, 1.01]
7.2 ACEi versus CCB	1	152	Risk Ratio (M-H, Random, 95% CI)	7.37 [0.39, 140.35]
8 Acute rejection at last follow-up	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
8.1 ACEi versus placebo/no treatment	1	30	Risk Ratio (M-H, Random, 95% CI)	0.9 [0.52, 1.55]
8.2 ACEi versus CCB	2	221	Risk Ratio (M-H, Random, 95% CI)	1.54 [1.14, 2.07]
9 Systolic blood pressure (mm Hg) at last follow-up	11		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.1 ACEi versus placebo/no treatment	5	197	Mean Difference (IV, Random, 95% CI)	-5.65 [-14.12, 2.82]
9.2 ACEi versus CCB	3	117	Mean Difference (IV, Random, 95% CI)	3.17 [-2.05, 8.38]
9.3 ACEi versus alpha-blocker	1	74	Mean Difference (IV, Random, 95% CI)	-2.0 [-8.61, 4.61]
9.4 ACEi versus beta-blocker	1	96	Mean Difference (IV, Random, 95% CI)	1.0 [-8.80, 10.80]
9.5 ACEi versus ARB	2	49	Mean Difference (IV, Random, 95% CI)	-2.74 [-11.13, 5.65]
10 Proteinuria (g/24 h) at last follow-up	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 ACEi versus placebo/no treatment	3	165	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.22, 0.08]
10.2 ACEi versus CCB	2	105	Mean Difference (IV, Random, 95% CI)	-0.28 [-0.49, -0.08]
10.3 ACEi versus alpha-blocker	1	74	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.20, 0.14]
10.4 ACEi versus ARB	2	103	Mean Difference (IV, Random, 95% CI)	0.03 [-0.07, 0.14]
11 Serum potassium (mmol/L) at last follow-up	10		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
11.1 ACEi versus placebo/no treatment	3	58	Mean Difference (IV, Random, 95% CI)	0.43 [0.11, 0.74]
11.2 ACEi versus CCB	4	162	Mean Difference (IV, Random, 95% CI)	0.29 [0.16, 0.42]
11.3 ACEi versus alpha-blocker	1	74	Mean Difference (IV, Random, 95% CI)	0.20 [-0.01, 0.41]
11.4 ACEi versus ARB	4	154	Mean Difference (IV, Random, 95% CI)	0.08 [-0.05, 0.22]
12 Hyperkalaemia at last follow-up	4	248	Risk Ratio (M-H, Random, 95% CI)	3.35 [1.74, 6.46]
12.1 ACEi versus CCB	3	211	Risk Ratio (M-H, Random, 95% CI)	3.74 [1.89, 7.43]
12.2 ACEi versus ARB	1	37	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.10, 9.57]
13 Haemoglobin (g/L) at last follow-up	13		Mean Difference (IV, Random, 95% CI)	Subtotals only
13.1 ACEi versus placebo/no treatment	5	185	Mean Difference (IV, Random, 95% CI)	-11.91 [-20.29, -3.53]
13.2 ACEi versus CCB	5	305	Mean Difference (IV, Random, 95% CI)	-13.16 [-15.97, -10.35]
13.3 ACEi versus alpha-blocker	1	74	Mean Difference (IV, Random, 95% CI)	6.00 [-1.98, 13.98]
13.4 ACEi versus ARB	3	132	Mean Difference (IV, Random, 95% CI)	-5.06 [-10.52, 0.41]
13.5 ACEi versus beta-blocker	1	96	Mean Difference (IV, Random, 95% CI)	-3.0 [-14.20, 8.20]
14 Rejection rate	1	156	Rate ratio (Random, 95% CI)	0.96 [0.75, 1.23]
14.1 ACEi versus CCB	1	75	Rate ratio (Random, 95% CI)	0.92 [0.65, 1.31]
14.2 ACEi versus ARB	1	81	Rate ratio (Random, 95% CI)	1.0 [0.71, 1.41]

Analysis 19.1. Comparison 19 ACEi versus any other intervention, Outcome 1 Serum creatinine (6 months to 2 years of treatment).

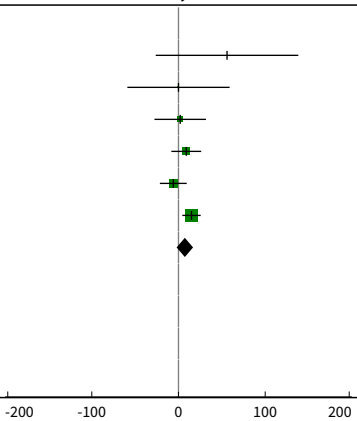
Study or subgroup	ACEi N	ACEi Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
19.1.1 ACEi versus placebo/no treatment							
Hernandez 2000	24	133 (26)	28	124 (37)		46.7%	9[-8.21,26.21]
Paoletti 2007	36	-4 (34)	34	2 (32)		53.3%	-6[-21.46,9.46]
Subtotal ***	**60**		**62**			**100%**	**1.01[-13.66,15.67]**
Heterogeneity: Tau^2=42.86; Chi^2=1.62, df=1(P=0.2); I^2=38.09%							
Test for overall effect: Z=0.13(P=0.89)							
19.1.2 ACEi versus CCB							
Hernandez 1995	10	133 (27)	11	124 (27)		4.67%	9[-14.12,32.12]
Mourad 1993	14	144 (26)	11	129 (27)		5.67%	15[-5.98,35.98]
El Agroudy 2003	27	133 (35)	48	133 (44)		7.59%	0[-18.14,18.14]
Midtvedt 2001	54	144 (45)	69	125 (32)		12.42%	19[4.82,33.18]
Halimi 2007	33	9 (12)	34	-5 (13)		69.65%	14[8.01,19.99]
Subtotal ***	**138**		**173**			**100%**	**13.38[8.38,18.38]**
Heterogeneity: Tau^2=0; Chi^2=2.89, df=4(P=0.58); I^2=0%							
Test for overall effect: Z=5.25(P<0.0001)							
19.1.3 ACEi versus beta-blocker							
Hausberg 1999	35	24 (112)	35	27 (77)		100%	-3[-48.03,42.03]
Subtotal ***	**35**		**35**			**100%**	**-3[-48.03,42.03]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.13(P=0.9)							
19.1.4 ACEi versus ARB							
El Agroudy 2003	27	133 (35)	54	133 (44)		100%	0[-17.66,17.66]
Subtotal ***	**27**		**54**			**100%**	**0[-17.66,17.66]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



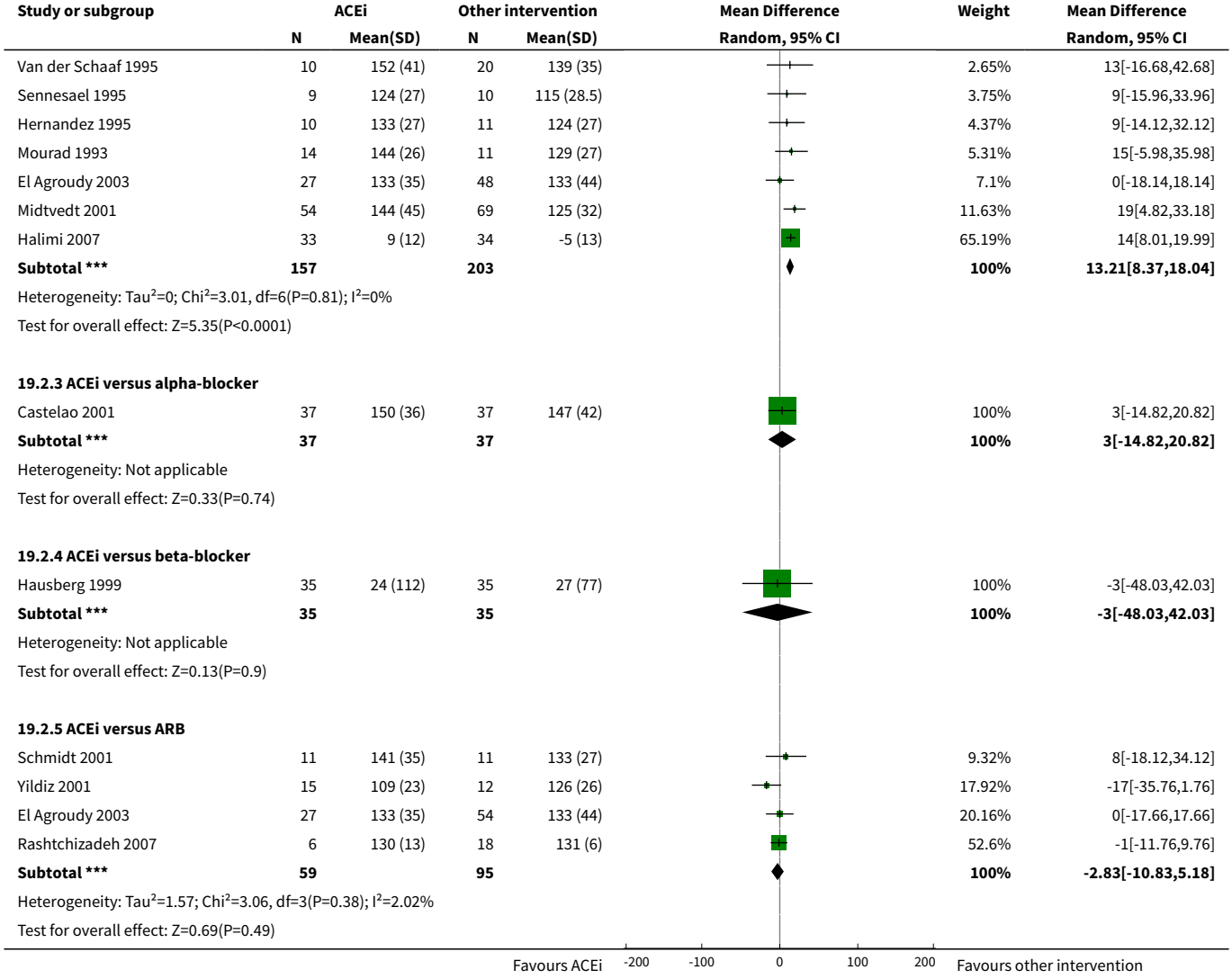
Favours ACEi — Favours other intervention

Analysis 19.2. Comparison 19 ACEi versus any other intervention, Outcome 2 Serum creatinine (µmol/L) at last follow-up.

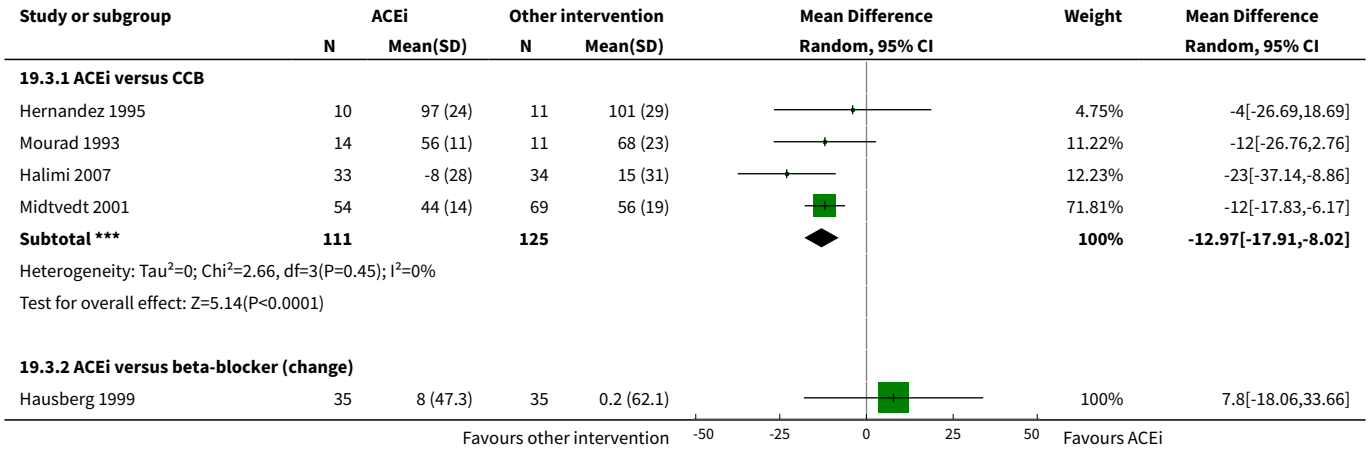
Study or subgroup	ACEi N	ACEi Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
19.2.1 ACEi versus placebo/no treatment							
Gronhagen-Riska 1984	9	192 (101)	11	136 (83)		1.31%	56[-26.22,138.22]
Trivedi 2003	9	141 (35)	5	141 (62)		2.51%	0[-58.96,58.96]
Van der Schaaf 1995	10	152 (41)	20	150 (35)		9.05%	2[-27.68,31.68]
Hernandez 2000	24	133 (26)	28	124 (37)		21.92%	9[-8.21,26.21]
Paoletti 2007	36	-4 (34)	34	2 (32)		25.45%	-6[-21.46,9.46]
Rashtchizadeh 2007	6	130 (13)	18	115 (4)		39.75%	15[4.44,25.56]
Subtotal ***	**94**		**116**			**100%**	**7.32[-2.17,16.82]**
Heterogeneity: Tau^2=29.98; Chi^2=6.38, df=5(P=0.27); I^2=21.63%							
Test for overall effect: Z=1.51(P=0.13)							
19.2.2 ACEi versus CCB							

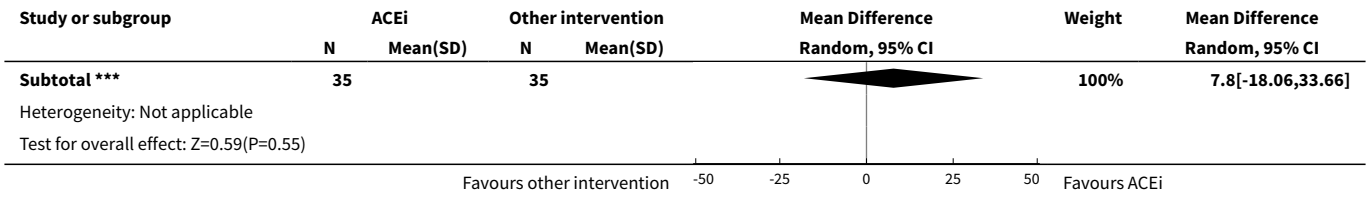


Favours ACEi — Favours other intervention

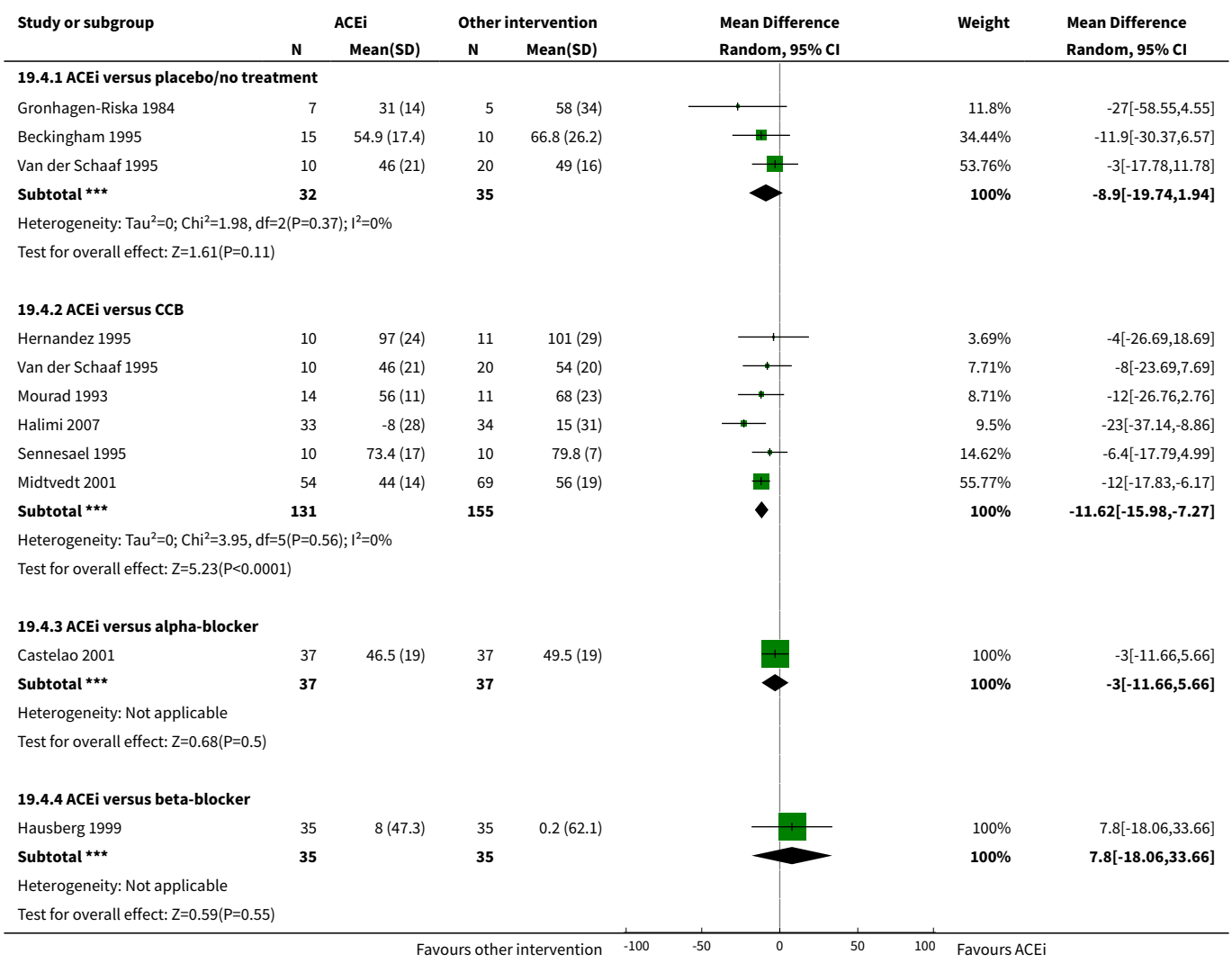


Analysis 19.3. Comparison 19 ACEi versus any other intervention, Outcome 3 Any GFR measure (6 months to 2 years of treatment).

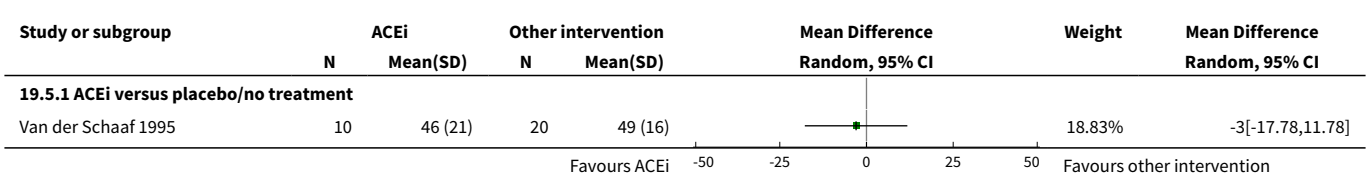


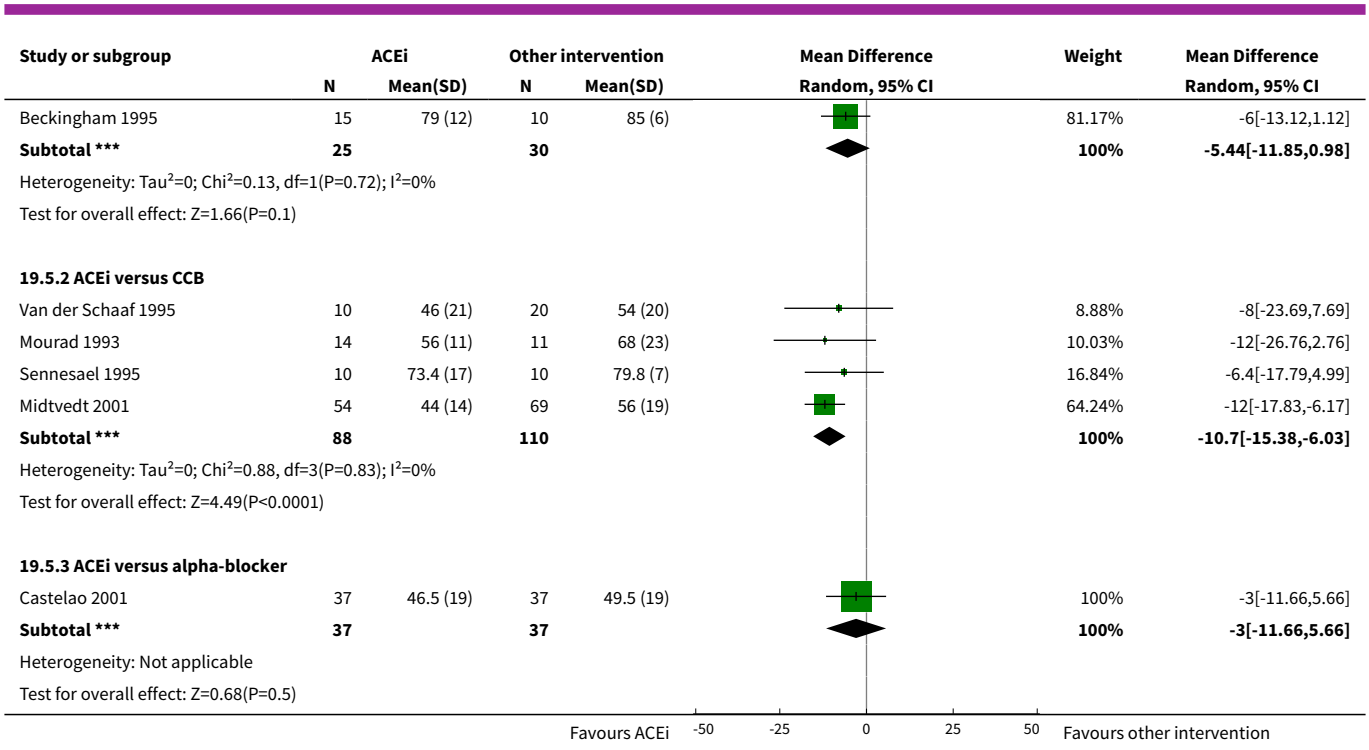


Analysis 19.4. Comparison 19 ACEi versus any other intervention, Outcome 4 Any GFR measure at last follow-up.

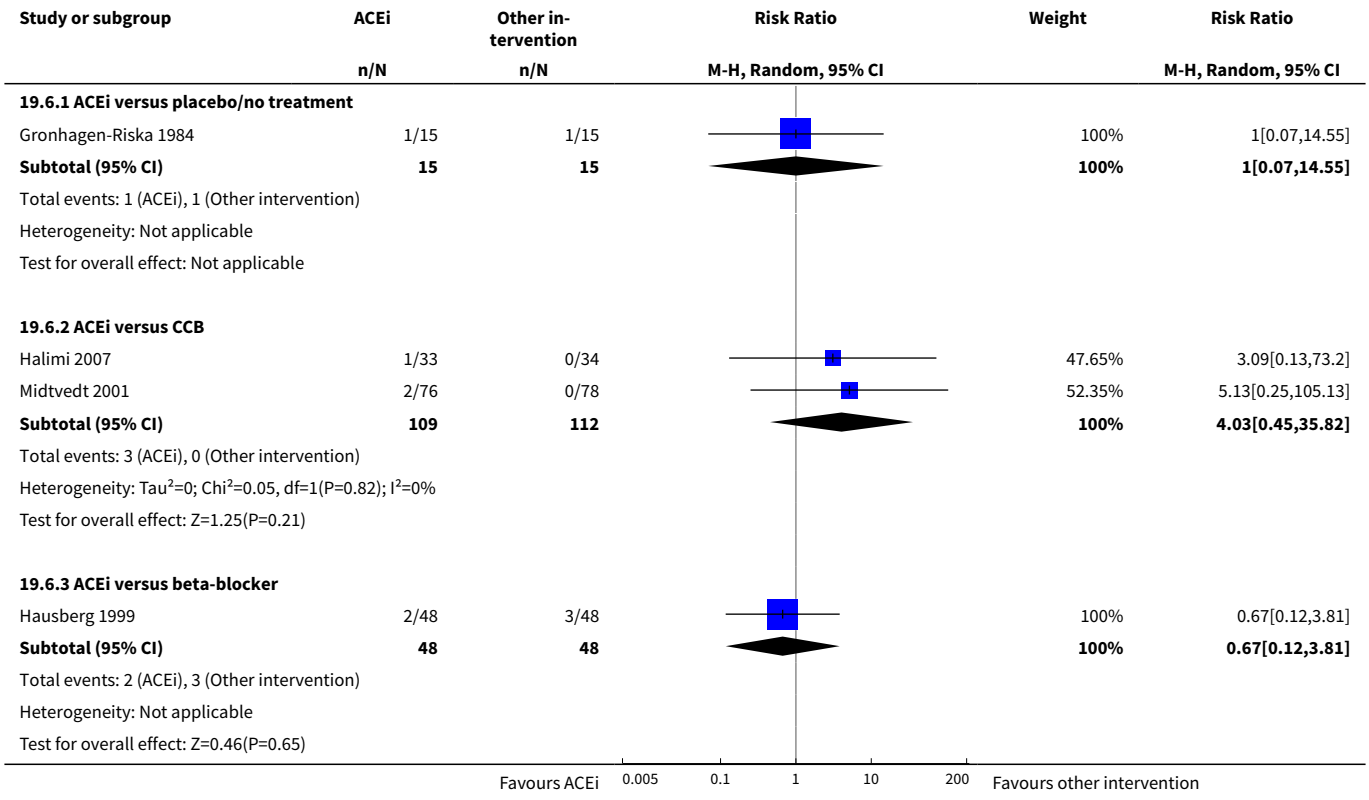


Analysis 19.5. Comparison 19 ACEi versus any other intervention, Outcome 5 Measured GFR at last follow-up.

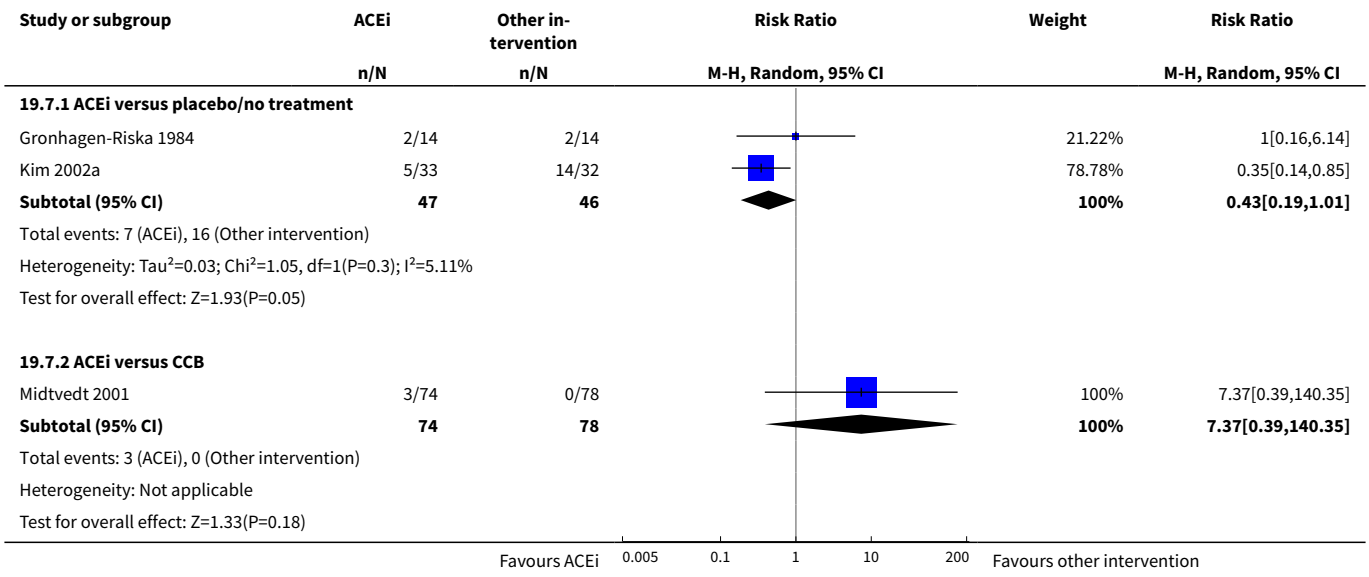




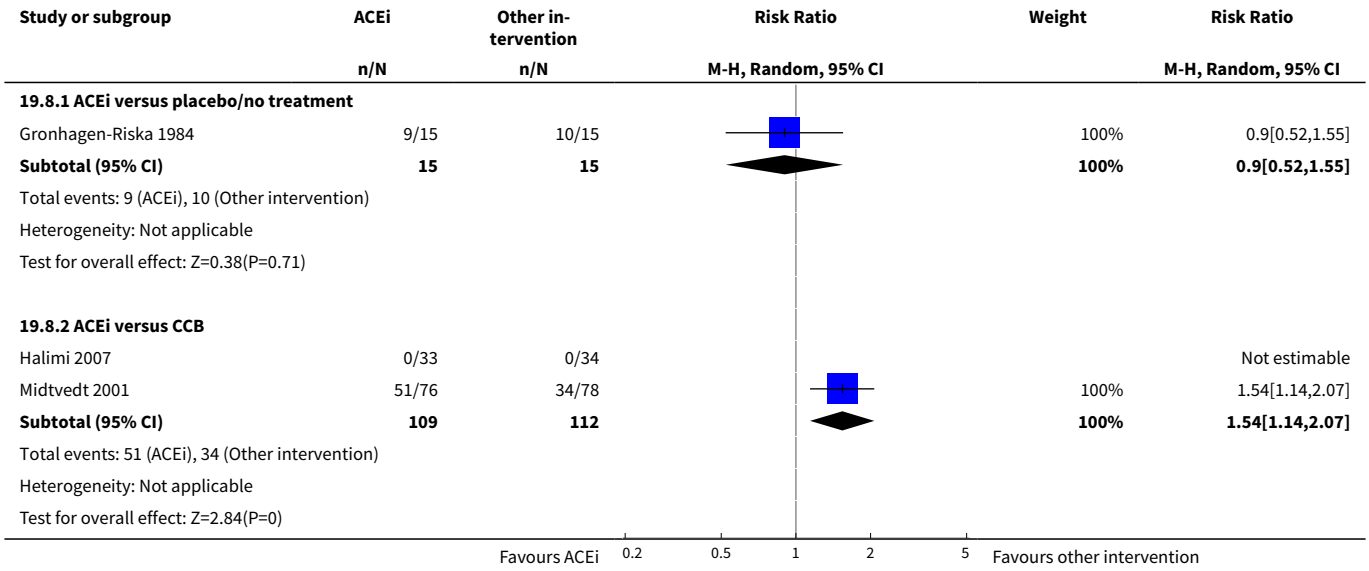
Analysis 19.6. Comparison 19 ACEi versus any other intervention, Outcome 6 Death at last follow-up.



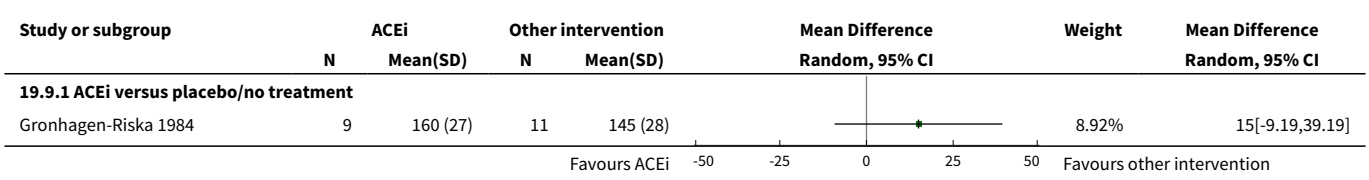
Analysis 19.7. Comparison 19 ACEi versus any other intervention, Outcome 7 Graft loss at last follow-up.

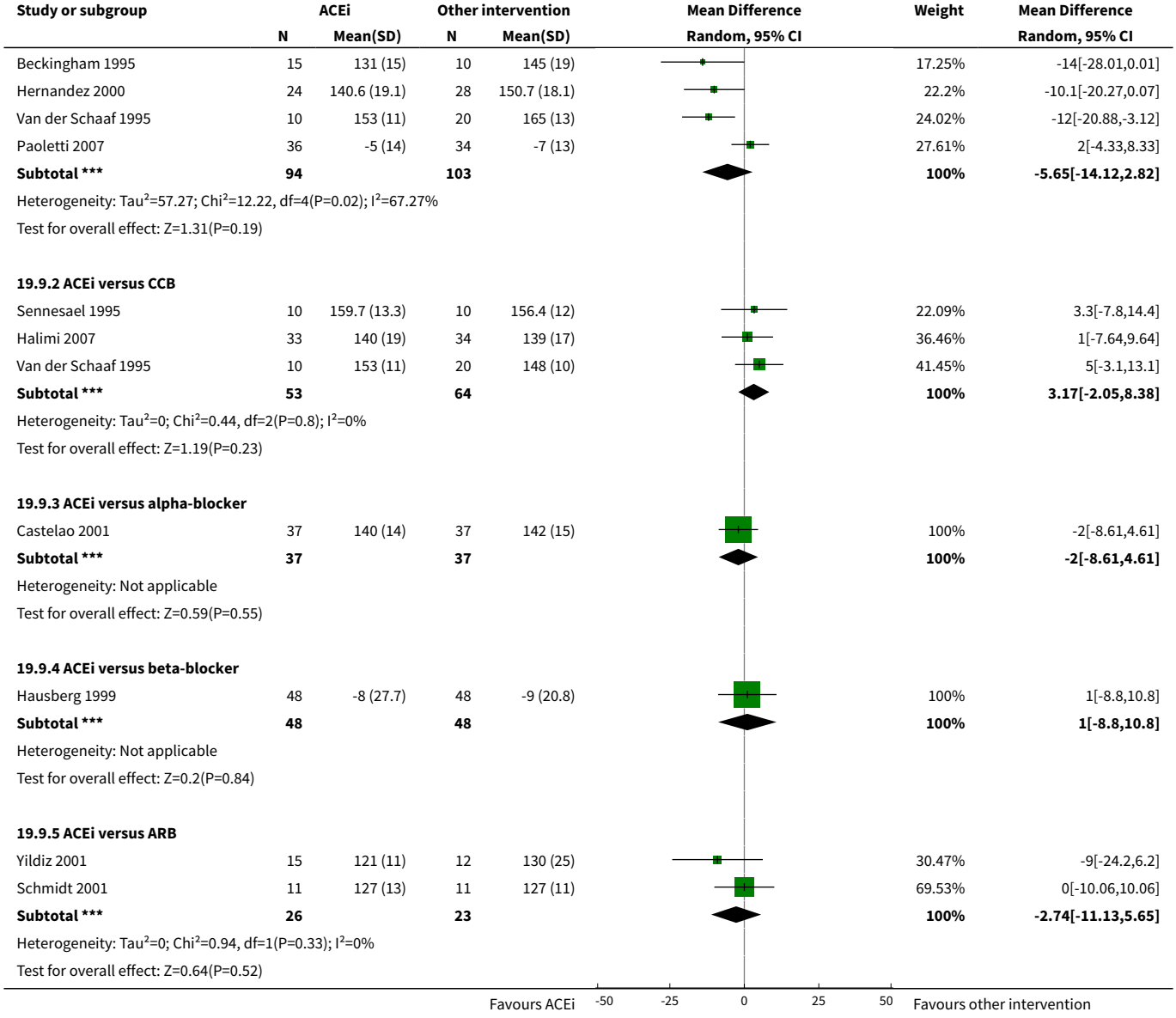


Analysis 19.8. Comparison 19 ACEi versus any other intervention, Outcome 8 Acute rejection at last follow-up.



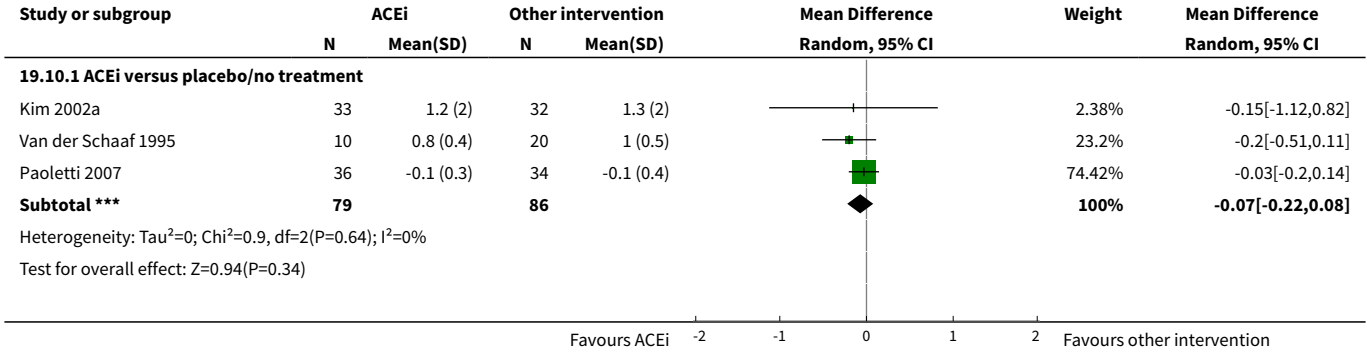
Analysis 19.9. Comparison 19 ACEi versus any other intervention, Outcome 9 Systolic blood pressure (mm Hg) at last follow-up.



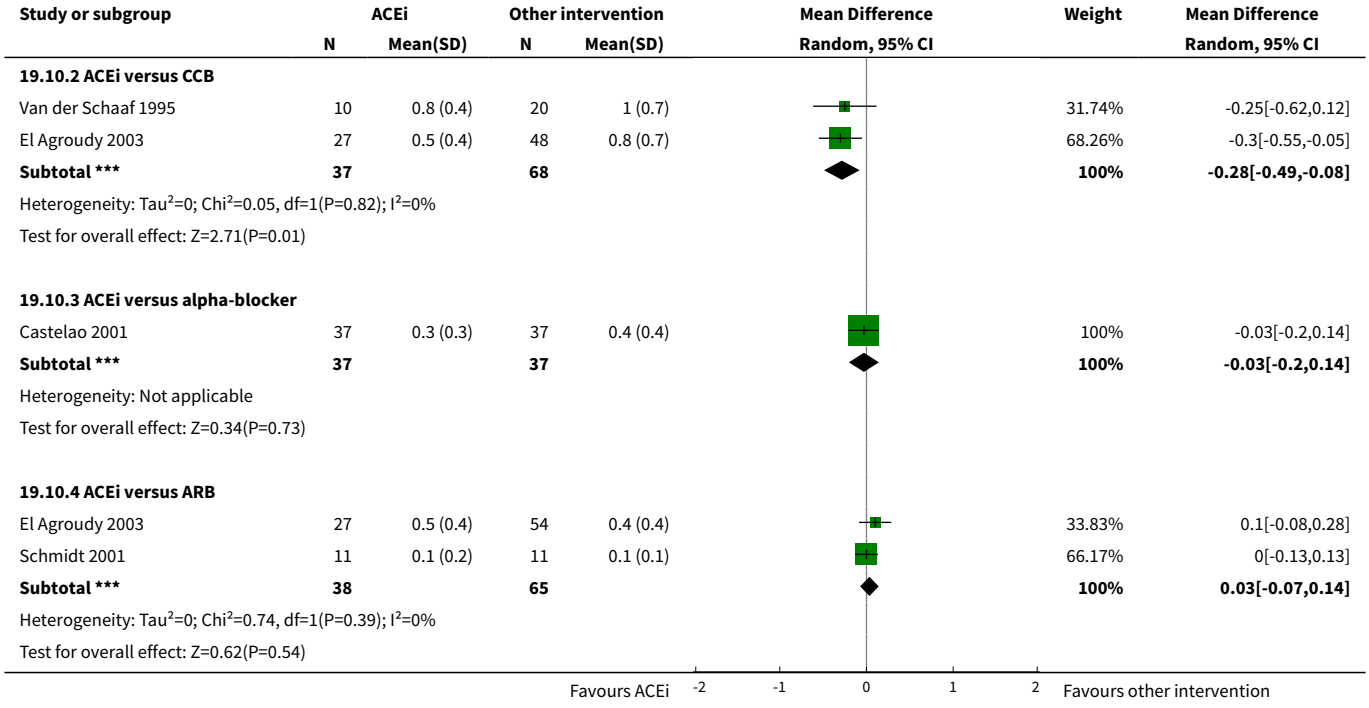


Study or subgroup	ACEi N	ACEi Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Beckingham 1995	15	131 (15)	10	145 (19)		17.25%	-14[-28.01,0.01]
Hernandez 2000	24	140.6 (19.1)	28	150.7 (18.1)		22.2%	-10.1[-20.27,0.07]
Van der Schaaf 1995	10	153 (11)	20	165 (13)		24.02%	-12[-20.88,-3.12]
Paoletti 2007	36	-5 (14)	34	-7 (13)		27.61%	2[-4.33,8.33]
Subtotal ***	**94**		**103**			**100%**	**-5.65[-14.12,2.82]**
Heterogeneity: Tau²=57.27; Chi²=12.22, df=4(P=0.02); I²=67.27%							
Test for overall effect: Z=1.31(P=0.19)							
19.9.2 ACEi versus CCB							
Sennesael 1995	10	159.7 (13.3)	10	156.4 (12)		22.09%	3.3[-7.8,14.4]
Halimi 2007	33	140 (19)	34	139 (17)		36.46%	1[-7.64,9.64]
Van der Schaaf 1995	10	153 (11)	20	148 (10)		41.45%	5[-3.1,13.1]
Subtotal ***	**53**		**64**			**100%**	**3.17[-2.05,8.38]**
Heterogeneity: Tau²=0; Chi²=0.44, df=2(P=0.8); I²=0%							
Test for overall effect: Z=1.19(P=0.23)							
19.9.3 ACEi versus alpha-blocker							
Castelao 2001	37	140 (14)	37	142 (15)		100%	-2[-8.61,4.61]
Subtotal ***	**37**		**37**			**100%**	**-2[-8.61,4.61]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.59(P=0.55)							
19.9.4 ACEi versus beta-blocker							
Hausberg 1999	48	-8 (27.7)	48	-9 (20.8)		100%	1[-8.8,10.8]
Subtotal ***	**48**		**48**			**100%**	**1[-8.8,10.8]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.2(P=0.84)							
19.9.5 ACEi versus ARB							
Yildiz 2001	15	121 (11)	12	130 (25)		30.47%	-9[-24.2,6.2]
Schmidt 2001	11	127 (13)	11	127 (11)		69.53%	0[-10.06,10.06]
Subtotal ***	**26**		**23**			**100%**	**-2.74[-11.13,5.65]**
Heterogeneity: Tau²=0; Chi²=0.94, df=1(P=0.33); I²=0%							
Test for overall effect: Z=0.64(P=0.52)							

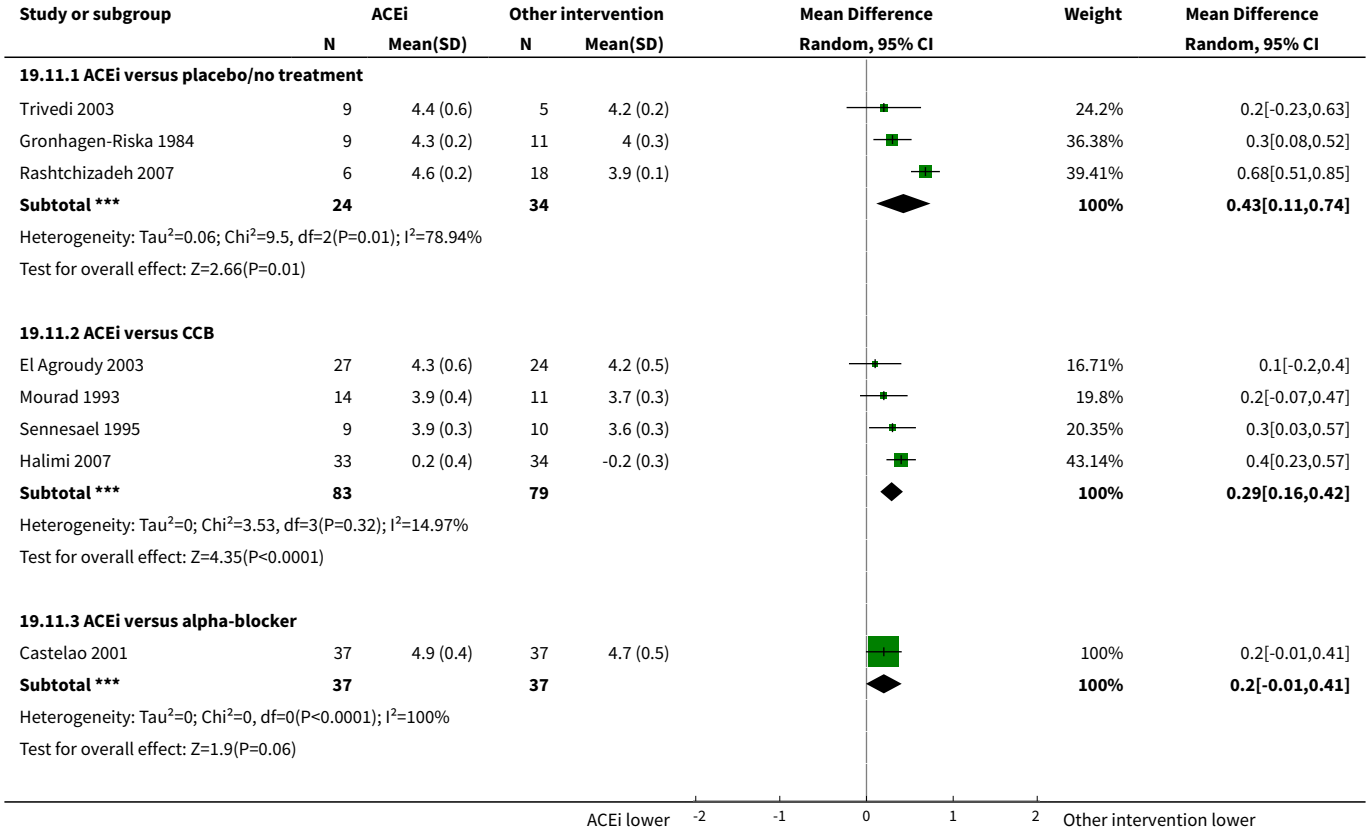
Analysis 19.10. Comparison 19 ACEi versus any other intervention, Outcome 10 Proteinuria (g/24 h) at last follow-up.

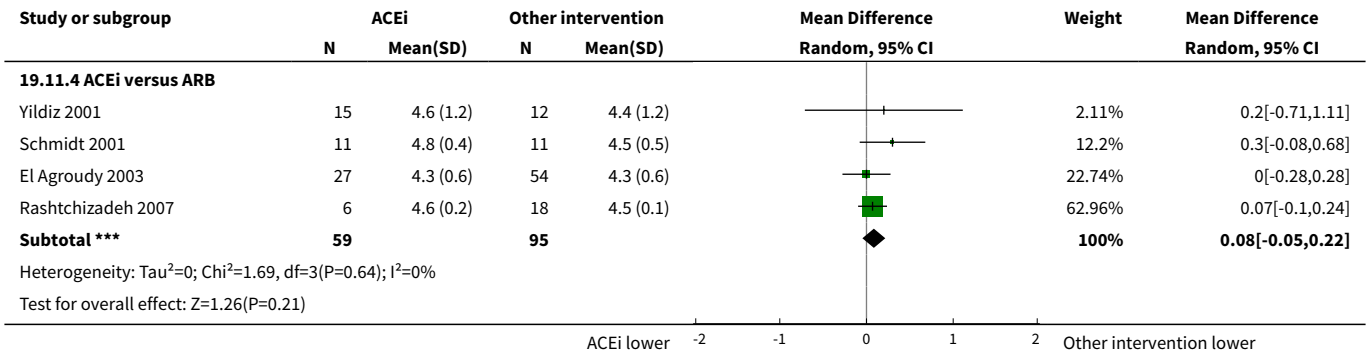


Study or subgroup	ACEi N	ACEi Mean(SD)	Other intervention N	Other intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
19.10.1 ACEi versus placebo/no treatment							
Kim 2002a	33	1.2 (2)	32	1.3 (2)		2.38%	-0.15[-1.12,0.82]
Van der Schaaf 1995	10	0.8 (0.4)	20	1 (0.5)		23.2%	-0.2[-0.51,0.11]
Paoletti 2007	36	-0.1 (0.3)	34	-0.1 (0.4)		74.42%	-0.03[-0.2,0.14]
Subtotal ***	**79**		**86**			**100%**	**-0.07[-0.22,0.08]**
Heterogeneity: Tau²=0; Chi²=0.9, df=2(P=0.64); I²=0%							
Test for overall effect: Z=0.94(P=0.34)							

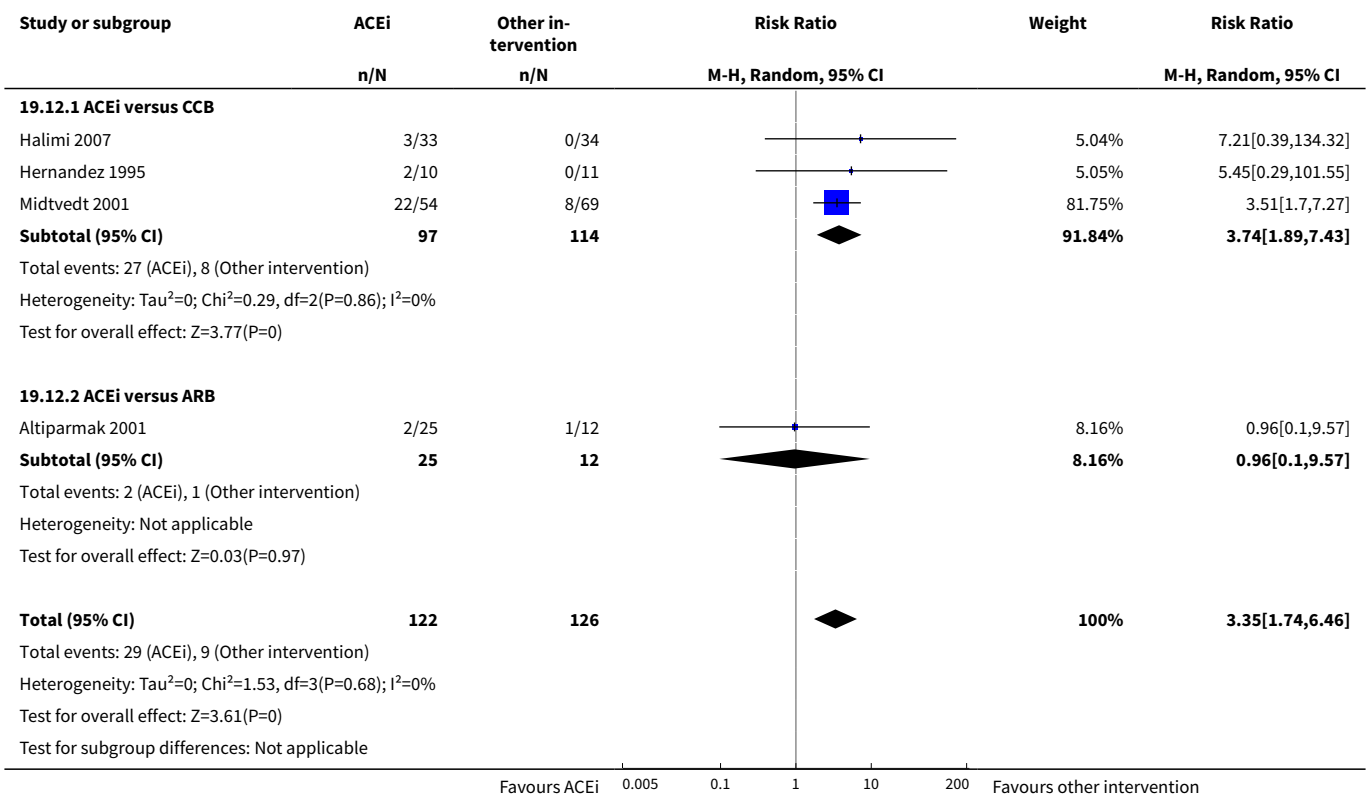


Analysis 19.11. Comparison 19 ACEi versus any other intervention, Outcome 11 Serum potassium (mmol/L) at last follow-up.

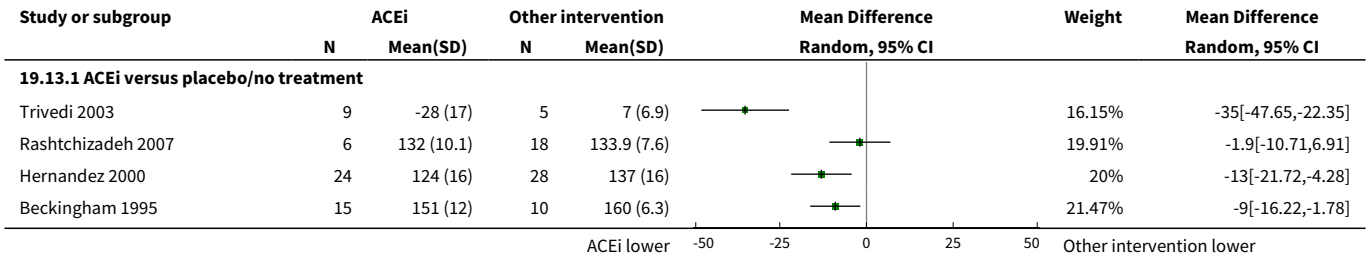


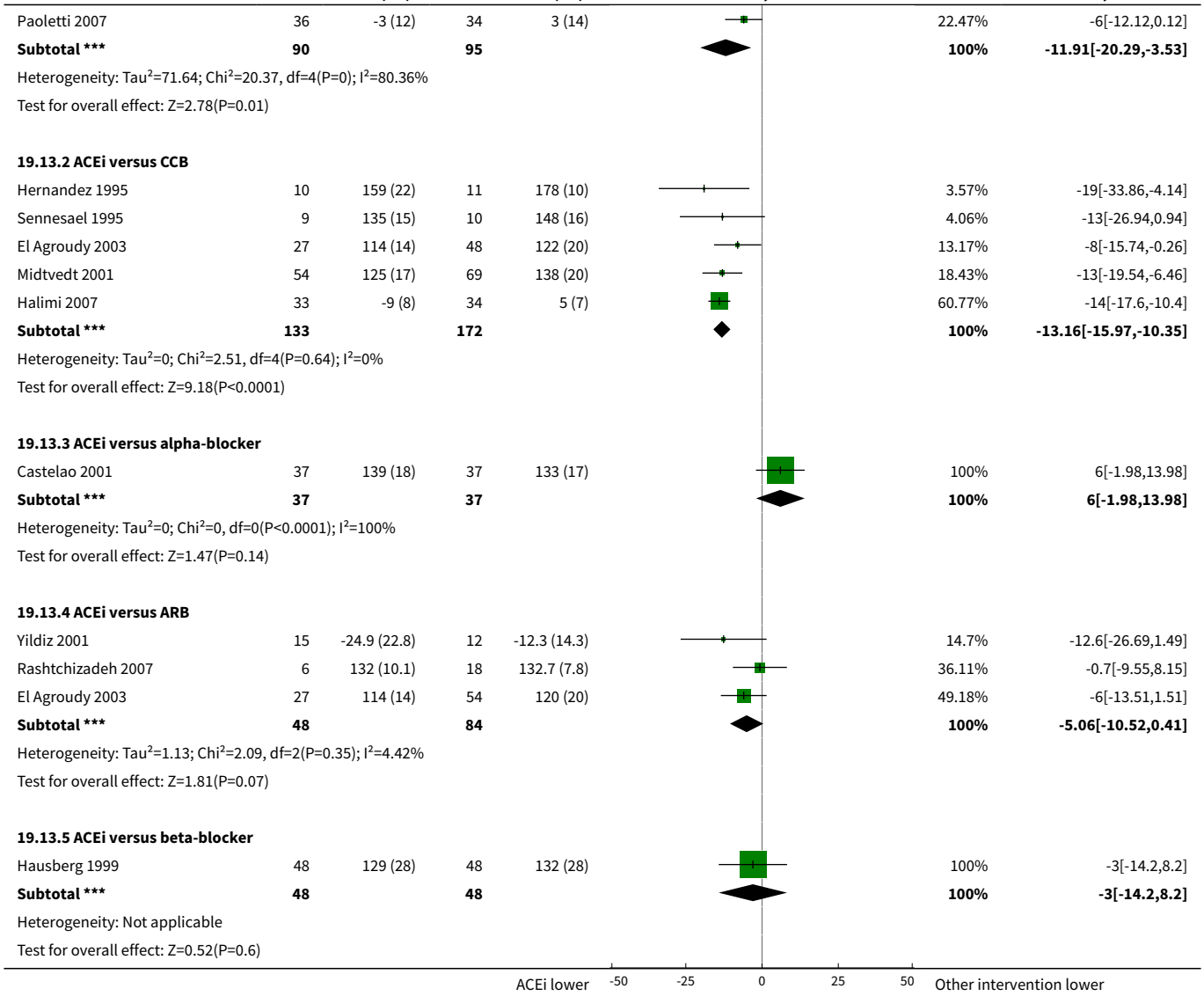


Analysis 19.12. Comparison 19 ACEi versus any other intervention, Outcome 12 Hyperkalaemia at last follow-up.

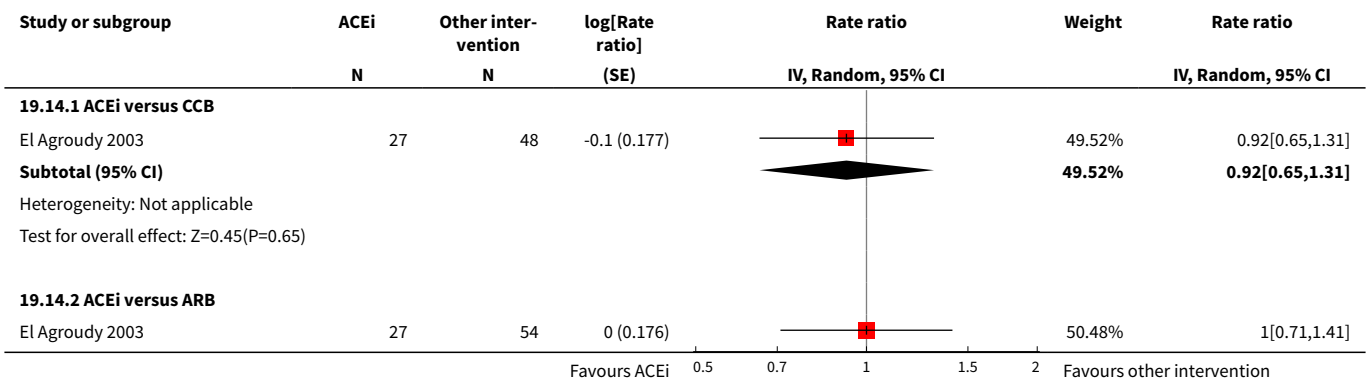


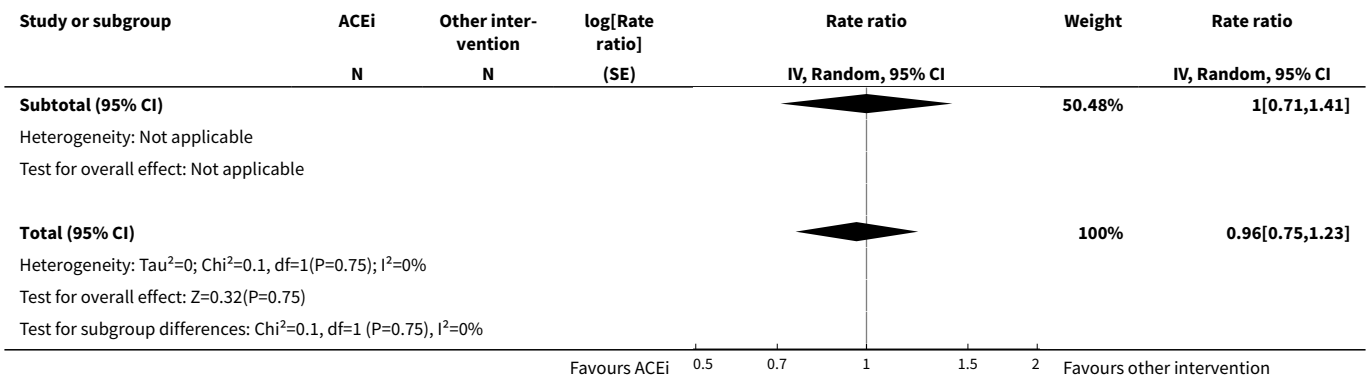
Analysis 19.13. Comparison 19 ACEi versus any other intervention, Outcome 13 Haemoglobin (g/L) at last follow-up.





Analysis 19.14. Comparison 19 ACEi versus any other intervention, Outcome 14 Rejection rate.

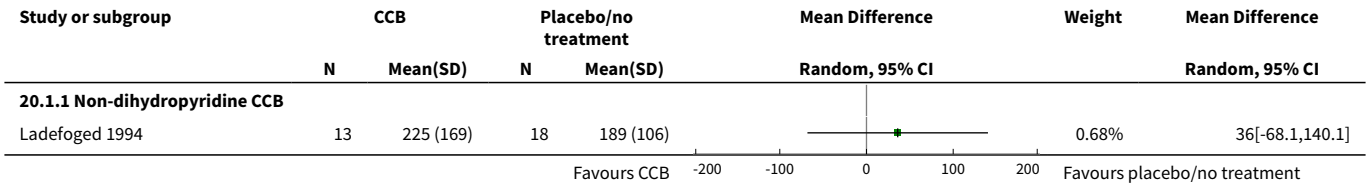


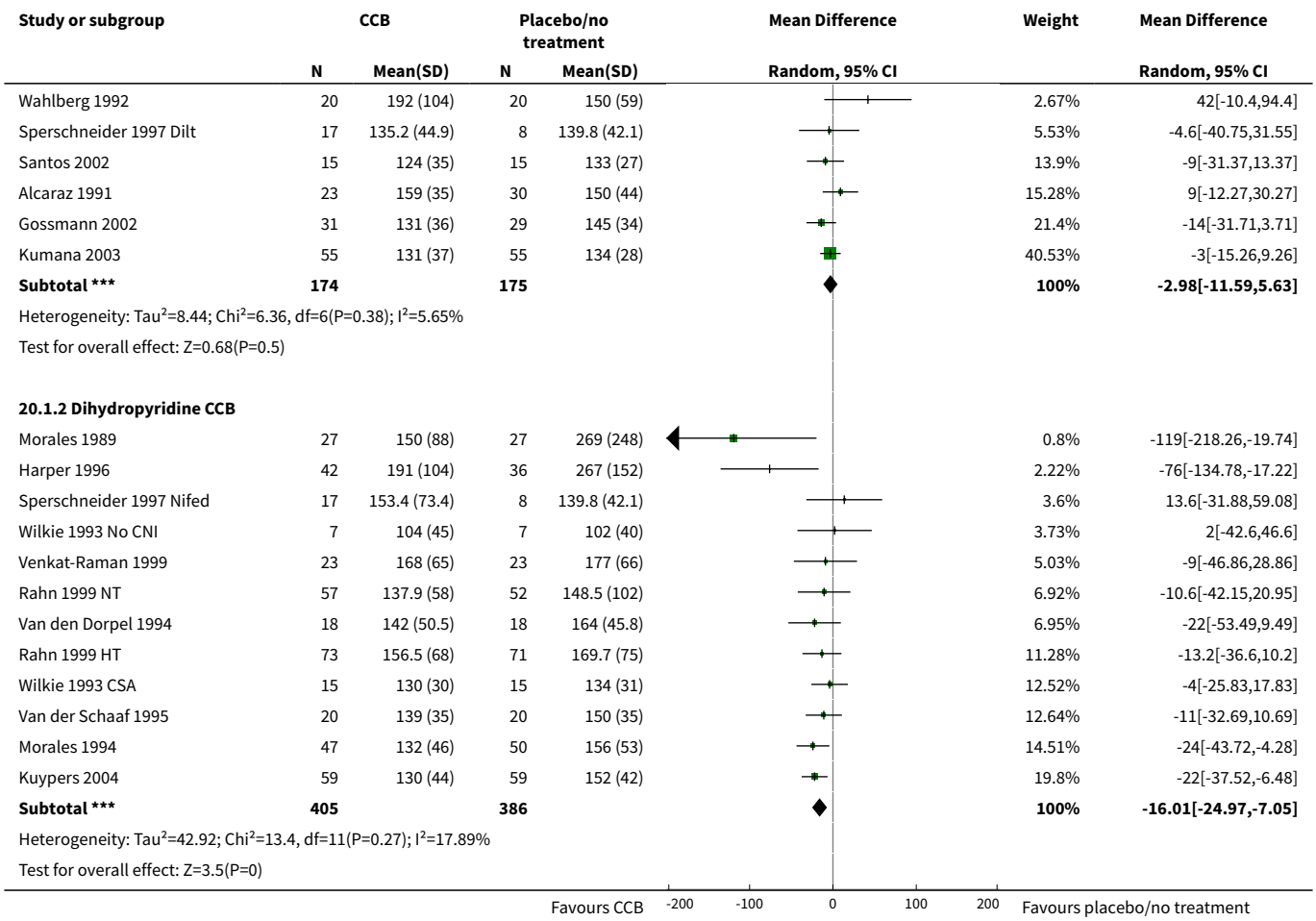


Comparison 20. CCB versus placebo/no treatment (stratified analyses)

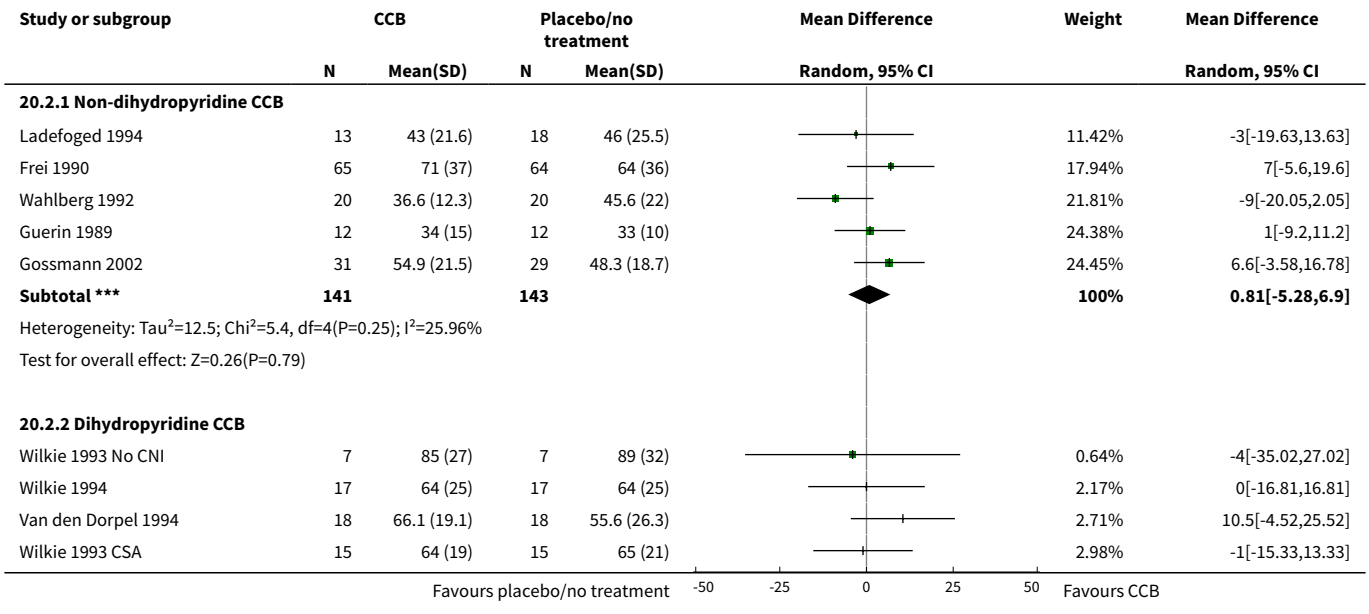
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum creatinine by CCB subtype	19		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Non-dihydropyridine CCB	7	349	Mean Difference (IV, Random, 95% CI)	-2.98 [-11.59, 5.63]
1.2 Dihydropyridine CCB	12	791	Mean Difference (IV, Random, 95% CI)	-16.01 [-24.97, -7.05]
2 GFR by CCB subtype	18		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Non-dihydropyridine CCB	5	284	Mean Difference (IV, Random, 95% CI)	0.81 [-5.28, 6.90]
2.2 Dihydropyridine CCB	13	835	Mean Difference (IV, Random, 95% CI)	5.27 [2.79, 7.74]
3 Graft loss at last follow-up	17		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 Less than 12 months	4	143	Risk Ratio (M-H, Random, 95% CI)	1.28 [0.33, 4.92]
3.2 12 months or more	13	1112	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.53, 0.95]

Analysis 20.1. Comparison 20 CCB versus placebo/no treatment (stratified analyses), Outcome 1 Serum creatinine by CCB subtype.

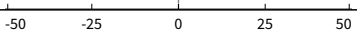




Analysis 20.2. Comparison 20 CCB versus placebo/no treatment (stratified analyses), Outcome 2 GFR by CCB subtype.



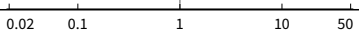
Study or subgroup	CCB N	CCB Mean(SD)	Placebo/no treatment N	Placebo/no treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Rump 2000	24	47 (19.6)	26	49 (30.6)		3.06%	-2[-16.14,12.14]
Van der Schaaf 1995	20	54 (20)	20	49 (16)		4.86%	5[-6.22,16.22]
Venkat-Raman 1999	23	49 (20)	23	47 (15)		5.86%	2[-8.22,12.22]
Morales 1994	47	79.2 (27)	50	67.9 (22.8)		6.15%	11.3[1.32,21.28]
Madsen 1998	27	49 (18)	24	40 (16)		7.03%	9[-0.33,18.33]
Rahn 1999 NT	57	-1.4 (20.4)	52	-1.4 (18.7)		11.36%	0[-7.34,7.34]
Rahn 1999 HT	73	1 (19.7)	71	-6 (17.7)		16.38%	7[0.89,13.11]
Kuypers 2004	53	50.1 (16.2)	53	42 (15.4)		16.9%	8.1[2.08,14.12]
Harper 1996	42	43.9 (12.3)	36	39.4 (12.6)		19.89%	4.5[-1.05,10.05]
Subtotal * **	**423**		**412**			**100%**	**5.27[2.79,7.74]**
Heterogeneity: Tau²=0; Chi²=8.56, df=12(P=0.74); I²=0%							
Test for overall effect: Z=4.17(P<0.0001)							



Favours placebo/no treatment — Favours CCB

Analysis 20.3. Comparison 20 CCB versus placebo/no treatment (stratified analyses), Outcome 3 Graft loss at last follow-up.

Study or subgroup	CCB n/N	Placebo/no treatment n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
20.3.1 Less than 12 months					
Morales 1989	1/15	1/15		17.62%	1[0.07,14.55]
Wahlberg 1992	3/20	1/20		23.09%	3[0.34,26.45]
Wilkie 1994	1/17	5/17		24.93%	0.2[0.03,1.54]
Ladefoged 1994	6/19	2/20		34.36%	3.16[0.72,13.76]
Subtotal (95% CI)	**71**	**72**		**100%**	**1.28[0.33,4.92]**
Total events: 11 (CCB), 9 (Placebo/no treatment)					
Heterogeneity: Tau²=0.81; Chi²=5.28, df=3(P=0.15); I²=43.15%					
Test for overall effect: Z=0.36(P=0.72)					
20.3.2 12 months or more					
Campistol 1991	0/12	0/25			Not estimable
Pirsch 1993	2/32	1/28		1.53%	1.75[0.17,18.28]
Alcaraz 1991	1/23	2/30		1.54%	0.65[0.06,6.76]
Guerin 1989	1/14	3/15		1.83%	0.36[0.04,3.04]
Chrysostomou 1993	2/32	3/39		2.82%	0.81[0.14,4.57]
Van den Dorpel 1994	2/25	6/25		3.73%	0.33[0.07,1.5]
Rahn 1999 (both)	4/130	7/123		5.81%	0.54[0.16,1.8]
Dawidson 1991	4/30	7/26		6.82%	0.5[0.16,1.5]
Santos 2002	5/15	5/15		8.21%	1[0.36,2.75]
Wagner 1986	7/30	10/33		12.22%	0.77[0.34,1.77]
Frei 1990	9/65	11/64		12.81%	0.81[0.36,1.81]
Morales 1994	13/47	14/50		20.46%	0.99[0.52,1.88]
Lehtonen 2000	13/94	23/90		22.21%	0.54[0.29,1]
Subtotal (95% CI)	**549**	**563**		**100%**	**0.71[0.53,0.95]**
Total events: 63 (CCB), 92 (Placebo/no treatment)					
Heterogeneity: Tau²=0; Chi²=4.94, df=11(P=0.93); I²=0%					
Test for overall effect: Z=2.34(P=0.02)					



Favours CCB — Favours placebo/no treatment

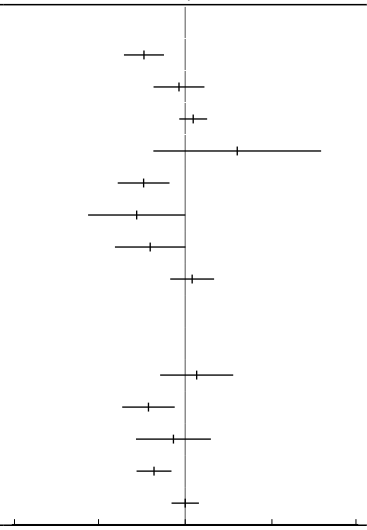
Comparison 21. ACEi or ARB versus placebo/no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any blood pressure (BP) measure at last follow-up	12		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 Systolic BP (mm Hg)	8		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Mean Arterial BP (mm Hg)	4		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Death	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1 At 3 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 At 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Graft loss at last follow-up	3		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Any GFR measure at last follow-up	5	126	Mean Difference (IV, Random, 95% CI)	-2.15 [-7.89, 3.60]
4.1 Creatinine clearance (mL/min)	2	40	Mean Difference (IV, Random, 95% CI)	-9.41 [-33.13, 14.31]
4.2 Measured GFR (mL/min/1.73 m^2 or mL/min)	2	65	Mean Difference (IV, Random, 95% CI)	-5.51 [-15.31, 4.30]
4.3 Nankivell eGFR	1	21	Mean Difference (IV, Random, 95% CI)	2.60 [-6.49, 11.69]
5 Serum creatinine (µmol/L) at last follow-up	8	378	Mean Difference (IV, Random, 95% CI)	8.01 [1.72, 14.29]
6 Haematocrit (%) at last follow-up (by selection criteria)	5	128	Mean Difference (IV, Random, 95% CI)	-4.84 [-8.02, -1.65]
6.1 Erythrocytosis	3	58	Mean Difference (IV, Random, 95% CI)	-7.29 [-10.34, -4.24]
6.2 Unselected or hypertensive	2	70	Mean Difference (IV, Random, 95% CI)	-1.29 [-2.93, 0.35]
7 Haemoglobin (g/L) at last follow-up (by selection criteria)	7	343	Mean Difference (IV, Random, 95% CI)	-9.80 [-15.47, -4.14]
7.1 Erythrocytosis	2	39	Mean Difference (IV, Random, 95% CI)	-21.46 [-46.92, 4.00]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Unselected or hypertensive	5	304	Mean Difference (IV, Random, 95% CI)	-6.98 [-11.75, -2.20]
8 Proteinuria (g/24 h) at last follow-up	3	175	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.23, 0.06]
9 Serum potassium (mmol/L) at last follow-up	5		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 21.1. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 1 Any blood pressure (BP) measure at last follow-up.

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	Placebo/No treatment N	Placebo/No treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
21.1.1 Systolic BP (mm Hg)						
Andres 2006	52	136.5 (15)	54	148.4 (15.3)		-11.9[-17.67,-6.13]
Tylicki 2006	14	118.6 (10.1)	14	120.4 (9.7)		-1.8[-9.14,5.54]
Weidanz 2005	11	138 (4.2)	10	135.7 (5.1)		2.3[-1.72,6.32]
Gronhagen-Riska 1984	9	160 (27)	11	145 (28)		15[-9.19,39.19]
Van der Schaaf 1995	20	153 (11)	20	165 (13)		-12[-19.46,-4.54]
Beckingham 1995	15	131 (15)	10	145 (19)		-14[-28.01,0.01]
Hernandez 2000	24	140.6 (19.1)	28	150.7 (18.1)		-10.1[-20.27,0.07]
Paoletti 2007	36	-5 (14)	34	-7 (13)		2[-4.33,8.33]
21.1.2 Mean Arterial BP (mm Hg)						
Rashtchizadeh 2007	18	100.3 (11.8)	9	97 (13.8)		3.3[-7.24,13.84]
Trivedi 2003	9	100.4 (8.2)	5	111 (6.1)		-10.6[-18.17,-3.03]
Rashtchizadeh 2007	12	93.6 (10.5)	9	97 (13.8)		-3.4[-14.2,7.4]
Kim 2002a	33	107 (10.7)	32	116 (10)		-9[-14.03,-3.97]
Takahara 2002	41	94 (7)	35	94 (10)		0[-3.95,3.95]

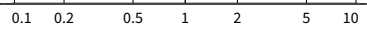


Analysis 21.2. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 2 Death.

Study or subgroup	ACEi/ARB n/N	Placebo/No treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
21.2.1 At 3 months				
Gronhagen-Riska 1984	1/15	1/15		1[0.07,14.55]
21.2.2 At 1 year				
Weidanz 2005	0/11	0/10		Not estimable

Analysis 21.3. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 3 Graft loss at last follow-up.

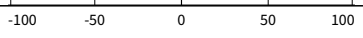
Study or subgroup	ACEi/ARB n/N	Placebo/No treatment n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Gronhagen-Riska 1984	2/14	2/14		1[0.16,6.14]
Kim 2002a	5/33	14/32		0.35[0.14,0.85]
Weidanz 2005	0/11	0/10		Not estimable



Favours ACEi/ARB | Favours placebo/no treatment

Analysis 21.4. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 4 Any GFR measure at last follow-up.

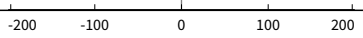
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	Placebo/No treatment N	Placebo/No treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
21.4.1 Creatinine clearance (mL/min)							
Gronhagen-Riska 1984	7	31 (14)	5	58 (34)		3.24%	-27[-58.55,4.55]
Tylicki 2006	14	60.8 (11.6)	14	61.8 (11.6)		34.71%	-1.08[-9.66,7.5]
Subtotal ***	**21**		**19**			**37.95%**	**-9.41[-33.13,14.31]**
Heterogeneity: Tau^2=196.74; Chi^2=2.41, df=1(P=0.12); I^2=58.57%							
Test for overall effect: Z=0.78(P=0.44)							
21.4.2 Measured GFR (mL/min/1.73 m^2 or mL/min)							
Beckingham 1995	15	54.9 (17.4)	10	66.8 (26.2)		9.1%	-11.9[-30.37,6.57]
Van der Schaaf 1995	20	46 (21)	20	49 (16)		21.24%	-3[-14.57,8.57]
Subtotal ***	**35**		**30**			**30.34%**	**-5.51[-15.31,4.3]**
Heterogeneity: Tau^2=0; Chi^2=0.64, df=1(P=0.42); I^2=0%							
Test for overall effect: Z=1.1(P=0.27)							
21.4.3 Nankivell eGFR							
Weidanz 2005	11	60.5 (11.8)	10	57.9 (9.4)		31.71%	2.6[-6.49,11.69]
Subtotal ***	**11**		**10**			**31.71%**	**2.6[-6.49,11.69]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.56(P=0.57)							
Total ***	**67**		**59**			**100%**	**-2.15[-7.89,3.6]**
Heterogeneity: Tau^2=5.59; Chi^2=4.57, df=4(P=0.33); I^2=12.42%							
Test for overall effect: Z=0.73(P=0.46)							
Test for subgroup differences: Chi^2=1.51, df=1 (P=0.47), I^2=0%							



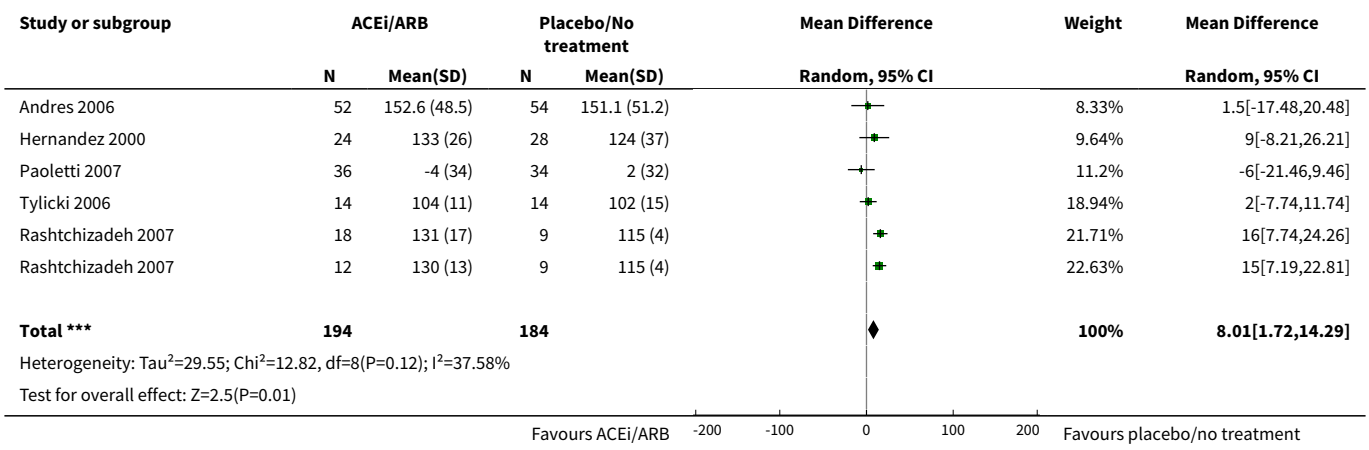
Favours placebo/no treatment | Favours ACEi/ARB

Analysis 21.5. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 5 Serum creatinine (µmol/L) at last follow-up.

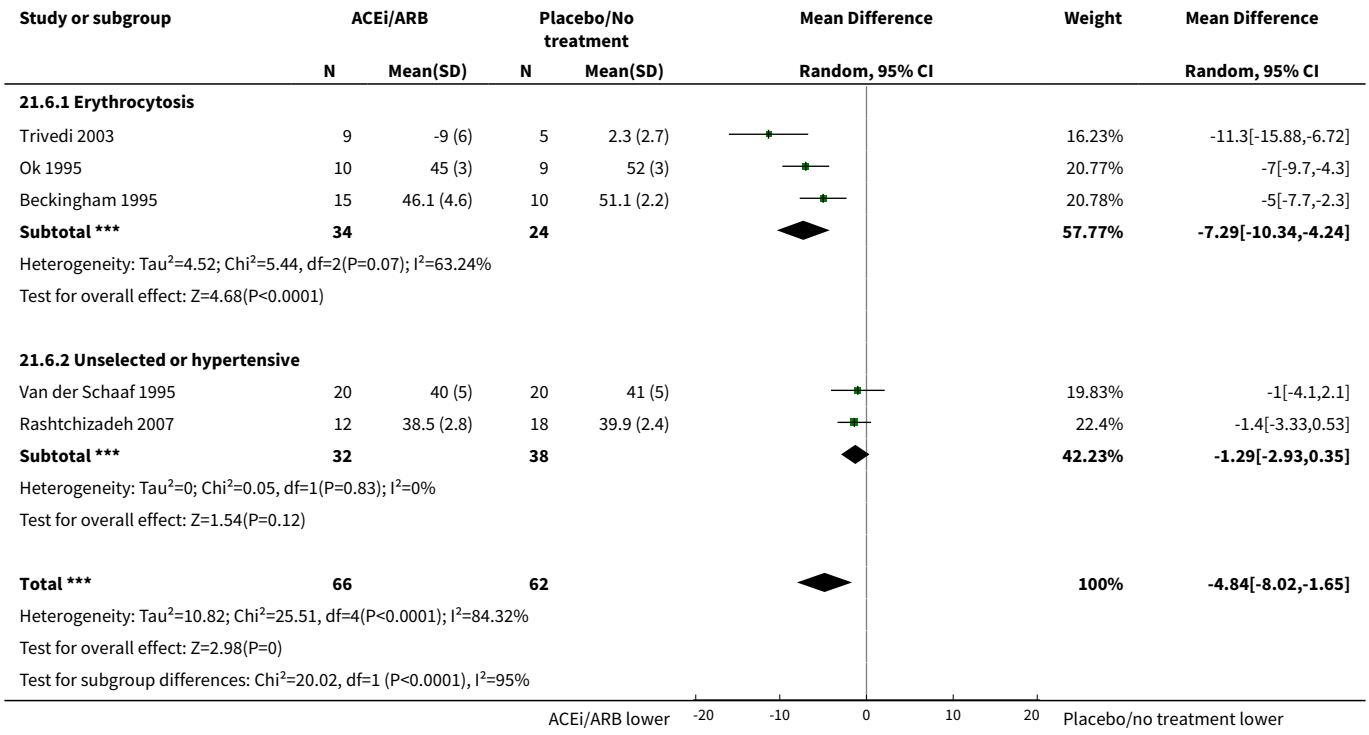
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	Placebo/No treatment N	Placebo/No treatment Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Gronhagen-Riska 1984	9	192 (101)	11	136 (83)		0.57%	56[-26.22,138.22]
Trivedi 2003	9	141 (35)	5	141 (62)		1.1%	0[-58.96,58.96]
Van der Schaaf 1995	20	152 (41)	20	150 (35)		5.88%	2[-21.63,25.63]



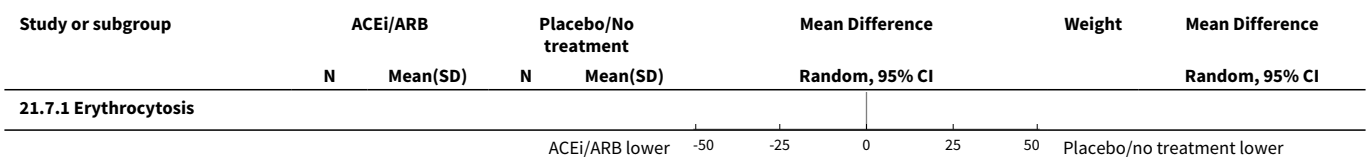
Favours ACEi/ARB | Favours placebo/no treatment

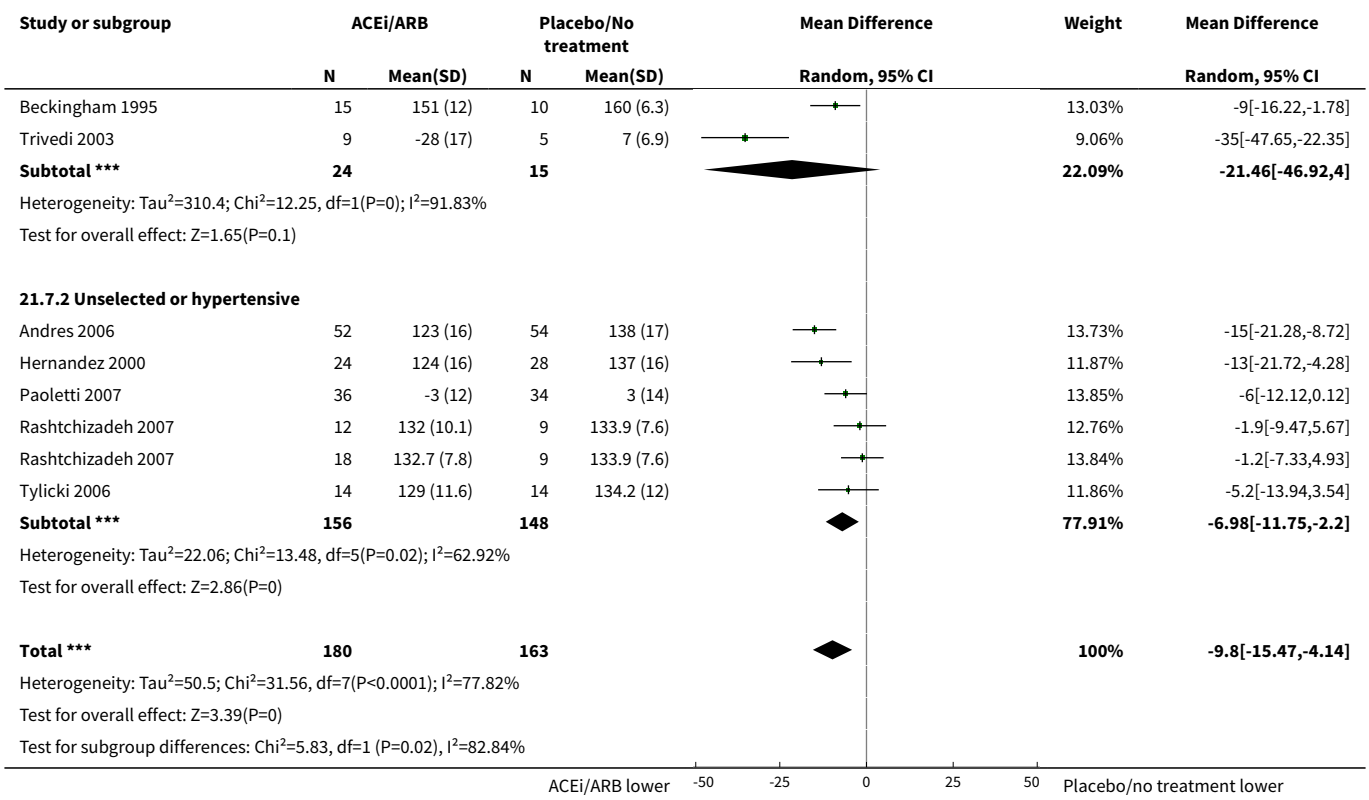


Analysis 21.6. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 6 Haematocrit (%) at last follow-up (by selection criteria).

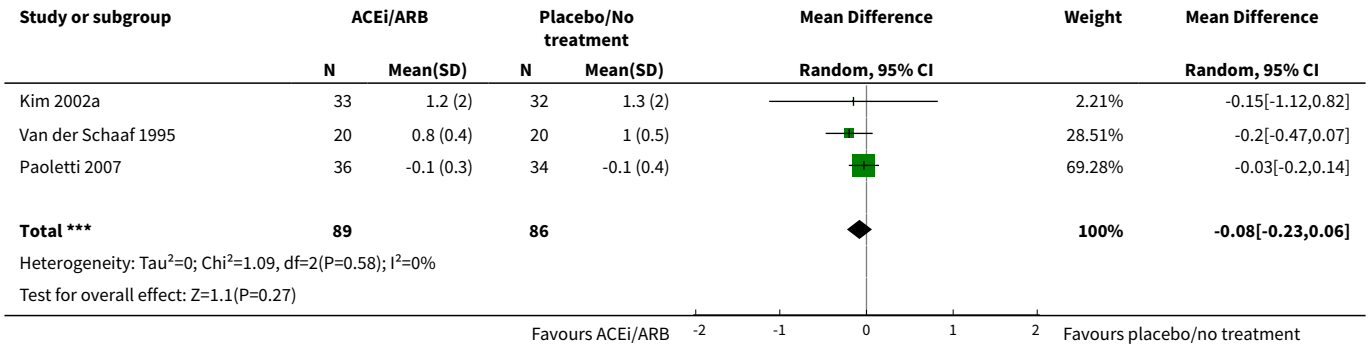


Analysis 21.7. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 7 Haemoglobin (g/L) at last follow-up (by selection criteria).

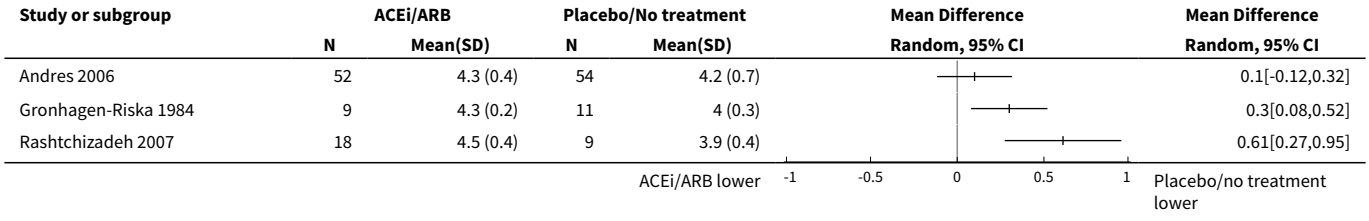




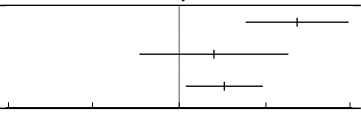
Analysis 21.8. Comparison 21 ACEi or ARB versus placebo/ no treatment, Outcome 8 Proteinuria (g/24 h) at last follow-up.



Analysis 21.9. Comparison 21 ACEi or ARB versus placebo/no treatment, Outcome 9 Serum potassium (mmol/L) at last follow-up.



Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	Placebo/No treatment N	Placebo/No treatment Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Rashtchizadeh 2007	12	4.6 (0.2)	9	3.9 (0.4)		0.68[0.38,0.98]
Trivedi 2003	9	4.4 (0.6)	5	4.2 (0.2)		0.2[-0.23,0.63]
Tylicki 2006	14	4.4 (0.3)	14	4.1 (0.3)		0.26[0.04,0.48]



Comparison 22. ACEi or ARB versus CCB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any blood pressure (BP) measure at last follow-up	9		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Systolic BP	3	127	Mean Difference (IV, Random, 95% CI)	3.51 [-1.21, 8.22]
1.2 Mean arterial pressure	6	249	Mean Difference (IV, Random, 95% CI)	-1.24 [-5.74, 3.27]
2 All-cause mortality	2	221	Risk Ratio (M-H, Random, 95% CI)	4.03 [0.45, 35.82]
2.1 At 6 months	1	67	Risk Ratio (M-H, Random, 95% CI)	3.09 [0.13, 73.20]
2.2 At 1 year	1	154	Risk Ratio (M-H, Random, 95% CI)	5.13 [0.25, 105.13]
3 Graft loss	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.1 At 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Any GFR measure at last follow-up	7	330	Mean Difference (IV, Random, 95% CI)	-11.42 [-15.61, -7.24]
4.1 Creatinine clearance (mL/min)	2	88	Mean Difference (IV, Random, 95% CI)	-15.66 [-33.79, 2.47]
4.2 Radioisotope GFR	5	242	Mean Difference (IV, Random, 95% CI)	-10.56 [-15.02, -6.09]
5 Serum creatinine (µmol/L) at last follow-up	11	542	Mean Difference (IV, Random, 95% CI)	9.87 [3.89, 15.85]
6 Any rejection	2	221	Risk Ratio (M-H, Random, 95% CI)	1.54 [1.14, 2.07]
6.1 At 6 months	1	67	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
6.2 At 2 years	1	154	Risk Ratio (M-H, Random, 95% CI)	1.54 [1.14, 2.07]
7 Rejection rate	1		Rate ratio (Random, 95% CI)	Totals not selected
8 Serum potassium (mmol/L)	7	328	Mean Difference (IV, Random, 95% CI)	0.29 [0.17, 0.40]
8.1 At last follow-up	6	261	Mean Difference (IV, Random, 95% CI)	0.25 [0.13, 0.38]
8.2 Change in serum potassium	1	67	Mean Difference (IV, Random, 95% CI)	0.4 [0.23, 0.57]
9 Hyperkalaemia at last follow-up	4	267	Risk Ratio (M-H, Random, 95% CI)	3.90 [2.03, 7.47]
9.1 'Transient' hyperkalaemia	1	123	Risk Ratio (M-H, Random, 95% CI)	3.51 [1.70, 7.27]
9.2 > 5.5 mmol/L	2	88	Risk Ratio (M-H, Random, 95% CI)	6.27 [0.79, 49.59]
9.3 > 6.0 mmol/L	1	56	Risk Ratio (M-H, Random, 95% CI)	5.59 [0.72, 43.44]
10 Proteinuria (g/24 h) at last follow-up	4	230	Mean Difference (IV, Random, 95% CI)	-0.21 [-0.41, -0.01]
11 Haemoglobin (g/L) at last follow-up	7	413	Mean Difference (IV, Random, 95% CI)	-12.14 [-15.56, -8.72]
12 Haematocrit (%) at last follow-up	4	153	Mean Difference (IV, Random, 95% CI)	-3.68 [-6.18, -1.19]
13 Myocardial Infarction	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
13.1 At 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
14 New onset angina	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
14.1 At 1 year	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
15 Ankle oedema	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
15.1 Leading to withdrawal	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16 Serum creatinine (µmol/L) at follow-up (subgrouped by treatment length)	10		Mean Difference (IV, Random, 95% CI)	Subtotals only
16.1 1-3 months treatment	7	412	Mean Difference (IV, Random, 95% CI)	5.28 [-2.16, 12.73]
16.2 6-12 months treatment	6	357	Mean Difference (IV, Random, 95% CI)	2.22 [-10.16, 14.61]
16.3 2 years treatment	1	25	Mean Difference (IV, Random, 95% CI)	15.0 [-5.98, 35.98]
17 Serum creatinine change (µmol/L) at follow-up (subgrouped by treatment length)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
17.1 6-12 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
18 Serum potassium (mmol/L) at follow-up (subgrouped by treatment length)	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
18.1 2 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
18.2 6-12 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
18.3 2 years treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
19 Serum potassium change (mmol/L) at follow-up (subgrouped by treatment length)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
19.1 6-12 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
20 Haemoglobin (g/L) at follow-up (subgrouped by treatment length)	6		Mean Difference (IV, Random, 95% CI)	Subtotals only
20.1 1-3 months treatment	4	215	Mean Difference (IV, Random, 95% CI)	-3.98 [-9.13, 1.16]
20.2 6-12 months treatment	3	246	Mean Difference (IV, Random, 95% CI)	-11.43 [-16.23, -6.63]
21 Haemoglobin change (g/L) at follow-up (subgrouped by treatment length)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
21.1 6-12 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
22 Haematocrit (%) at follow-up (subgrouped by treatment length)	3		Mean Difference (IV, Random, 95% CI)	Totals not selected

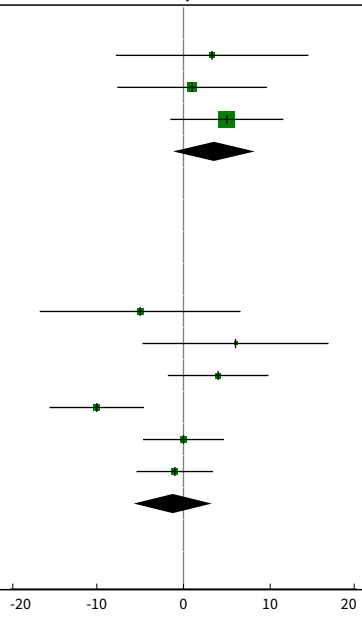
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
22.1 1 month treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
22.2 6-12 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
22.3 2 years treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
23 Haematocrit change (%) at follow-up (sub-grouped by treatment length)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
23.1 6-12 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
24 Diastolic blood pressure (mm Hg) at fol-low-up (subgrouped by treatment length)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
24.1 1-2 months	2	60	Mean Difference (IV, Random, 95% CI)	4.34 [0.42, 8.27]
24.2 6-12 months	1	67	Mean Difference (IV, Random, 95% CI)	0.0 [-4.14, 4.14]
25 Mean arterial blood pressure (mm Hg) at follow-up (subgrouped by treatment length)	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
25.1 1-2 months treatment	2	60	Mean Difference (IV, Random, 95% CI)	3.42 [-1.28, 8.13]
25.2 6-12 months treatment	3	190	Mean Difference (IV, Random, 95% CI)	-0.27 [-3.07, 2.52]
26 Mean arterial pressure change (mm Hg) at follow-up (subgrouped by treatment length)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
26.1 6-12 months treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
26.2 2 years treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
27 Systolic blood pressure (mm Hg) at fol-low-up (subgrouped by treatment length)	3	127	Mean Difference (IV, Random, 95% CI)	3.51 [-1.21, 8.22]
27.1 1-2 months treatment	2	60	Mean Difference (IV, Random, 95% CI)	4.56 [-1.05, 10.18]
27.2 6-12 months treatment	1	67	Mean Difference (IV, Random, 95% CI)	1.0 [-7.64, 9.64]
28 Creatinine clearance (mL/min)	2		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
28.1 Creatinine clearance at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
28.2 Change in creatinine clearance at 6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
29 Proteinuria (g/24 h)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
29.1 At 1 month	2	142	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.37, 0.12]
29.2 At 3 months	1	102	Mean Difference (IV, Random, 95% CI)	-0.40 [-0.68, -0.12]
29.3 At 6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
29.4 At 1 year	1	102	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.52, -0.08]
30 GFR (mL/min/1.73 m^2)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
30.1 At 6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
30.2 At 1 year	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
31 GFR at 1-2 months treatment (mL/min or mL/min/1.73 m^2)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
31.1 Measured GFR	2	60	Mean Difference (IV, Random, 95% CI)	-7.11 [-15.60, 1.37]
32 GFR at 6-12 months treatment (mL/min or mL/min/1.73 m^2)	4	236	Mean Difference (IV, Random, 95% CI)	-12.57 [-18.94, -6.20]
32.1 Creatinine clearance	1	21	Mean Difference (IV, Random, 95% CI)	-12.0 [-34.69, 10.69]
32.2 Creatinine clearance change	1	67	Mean Difference (IV, Random, 95% CI)	-23.0 [-37.14, -8.86]
32.3 Measured GFR	2	148	Mean Difference (IV, Random, 95% CI)	-10.46 [-17.10, -3.82]
33 GFR at 2 years treatment (mL/min or mL/min/1.73 m^2)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
33.1 Cockcroft-Gault	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

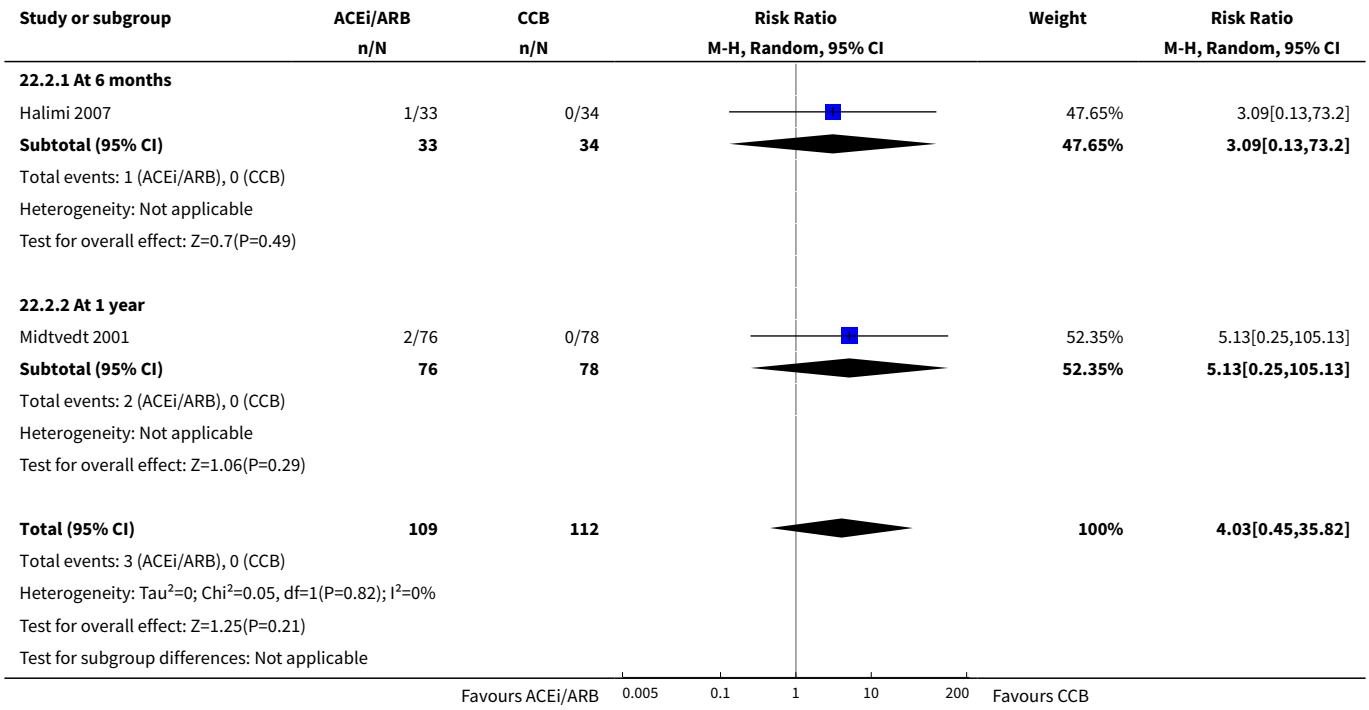
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
33.2 Creatinine clearance	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
33.3 Measured GFR	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
34 Measured GFR (by time)	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
34.1 1-2 months	2	60	Mean Difference (IV, Random, 95% CI)	-7.11 [-15.60, 1.37]
34.2 6-12 months	2	148	Mean Difference (IV, Random, 95% CI)	-10.46 [-17.10, -3.82]
34.3 2 years	1	25	Mean Difference (IV, Random, 95% CI)	-12.0 [-26.76, 2.76]

Analysis 22.1. Comparison 22 ACEi or ARB versus CCB, Outcome 1 Any blood pressure (BP) measure at last follow-up.

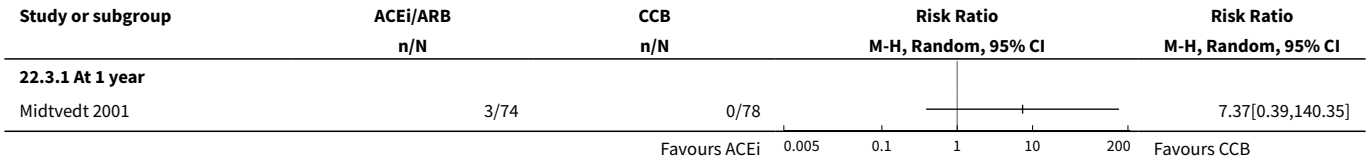
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.1.1 Systolic BP							
Sennesael 1995	10	159.7 (13.3)	10	156.4 (12)		18%	3.3[-7.8,14.4]
Halimi 2007	33	140 (19)	34	139 (17)		29.72%	1[-7.64,9.64]
Van der Schaaf 1995	20	153 (11)	20	148 (10)		52.28%	5[-1.52,11.52]
Subtotal ***	**63**		**64**			**100%**	**3.51[-1.21,8.22]**
Heterogeneity: Tau²=0; Chi²=0.53, df=2(P=0.77); I²=0%							
Test for overall effect: Z=1.46(P=0.14)							
22.1.2 Mean arterial pressure							
Mourad 1993	14	-18 (11)	11	-13 (17)		9.66%	-5[-16.58,6.58]
Hernandez 1995	10	105 (13)	11	99 (12)		10.61%	6[-4.73,16.73]
Inigo 2001	17	96 (10)	17	92 (7)		18.51%	4[-1.8,9.8]
Barenbrock 2001	6	89 (5)	7	99 (5)		19.2%	-10[-15.45,-4.55]
El Agroudy 2003 ARB	54	95 (9)	24	95 (10)		20.76%	0[-4.67,4.67]
El Agroudy 2003	54	94 (7)	24	95 (10)		21.26%	-1[-5.41,3.41]
Subtotal ***	**155**		**94**			**100%**	**-1.24[-5.74,3.27]**
Heterogeneity: Tau²=19.76; Chi²=15.46, df=5(P=0.01); I²=67.66%							
Test for overall effect: Z=0.54(P=0.59)							



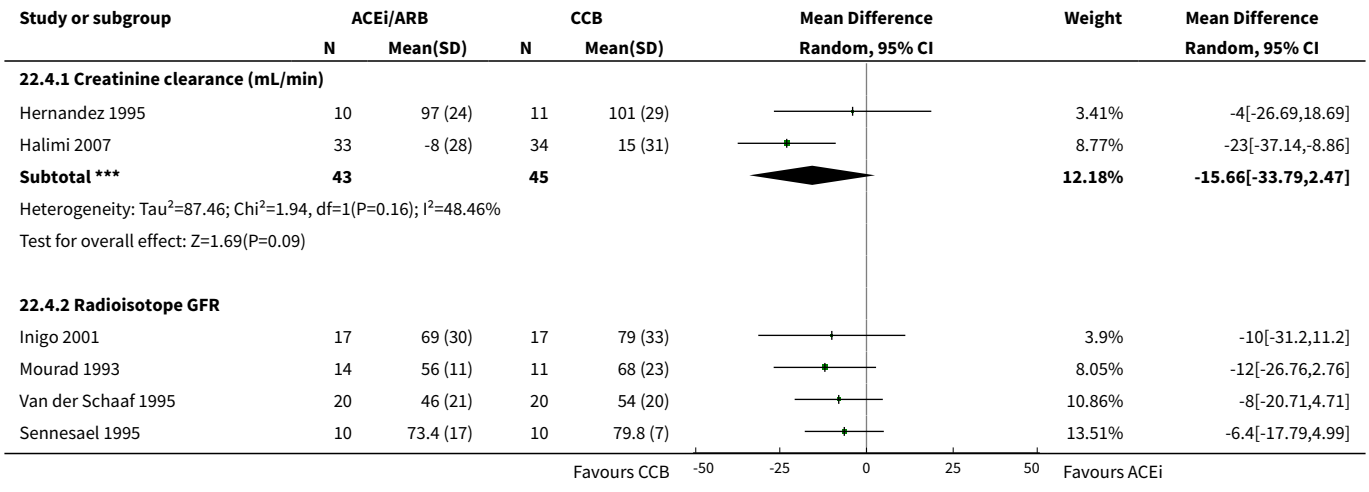
Analysis 22.2. Comparison 22 ACEi or ARB versus CCB, Outcome 2 All-cause mortality.

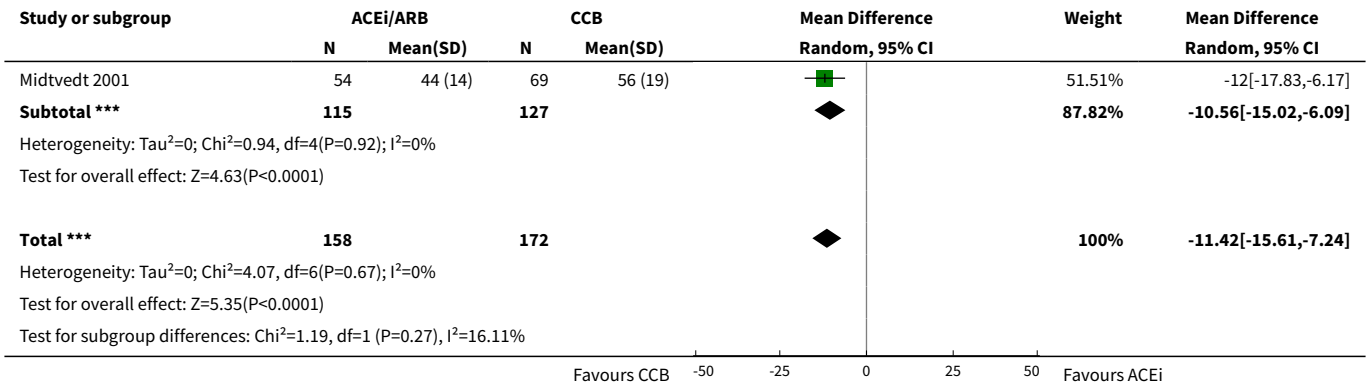


Analysis 22.3. Comparison 22 ACEi or ARB versus CCB, Outcome 3 Graft loss.

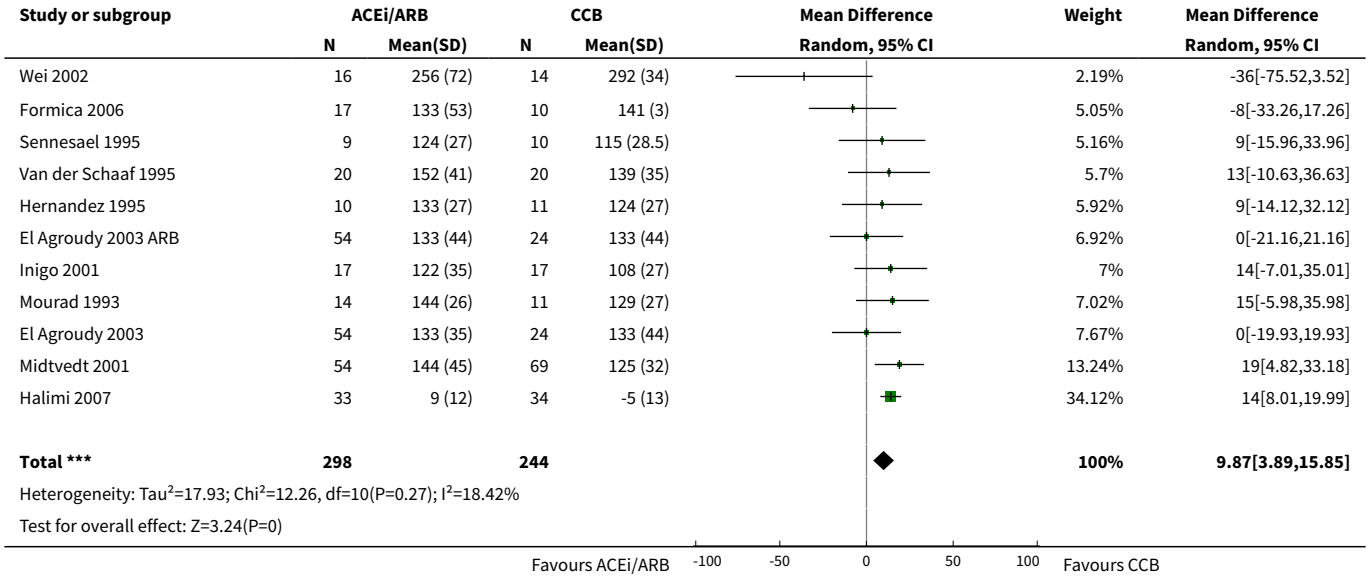


Analysis 22.4. Comparison 22 ACEi or ARB versus CCB, Outcome 4 Any GFR measure at last follow-up.

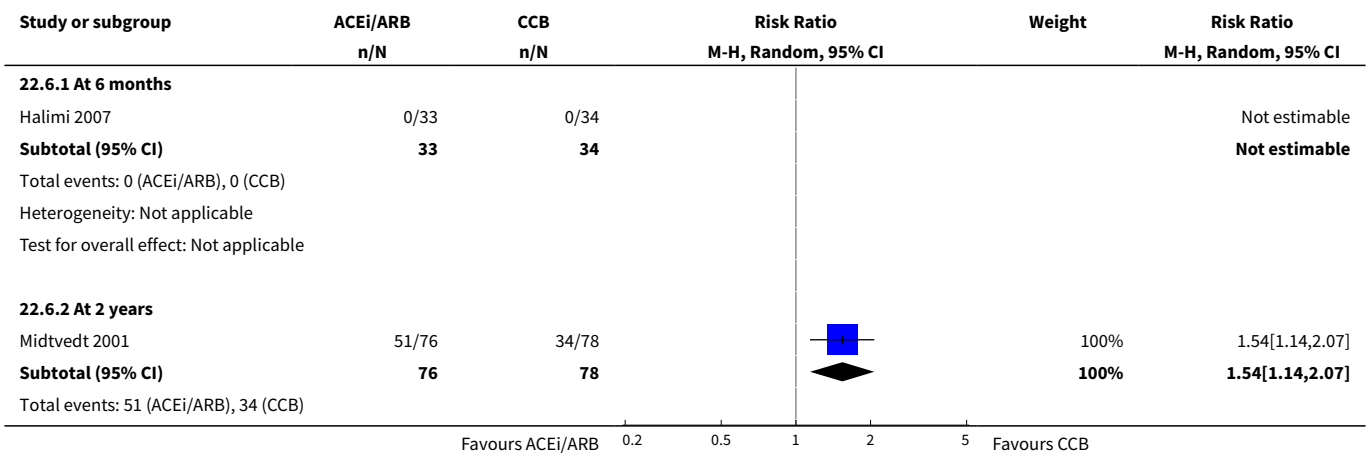


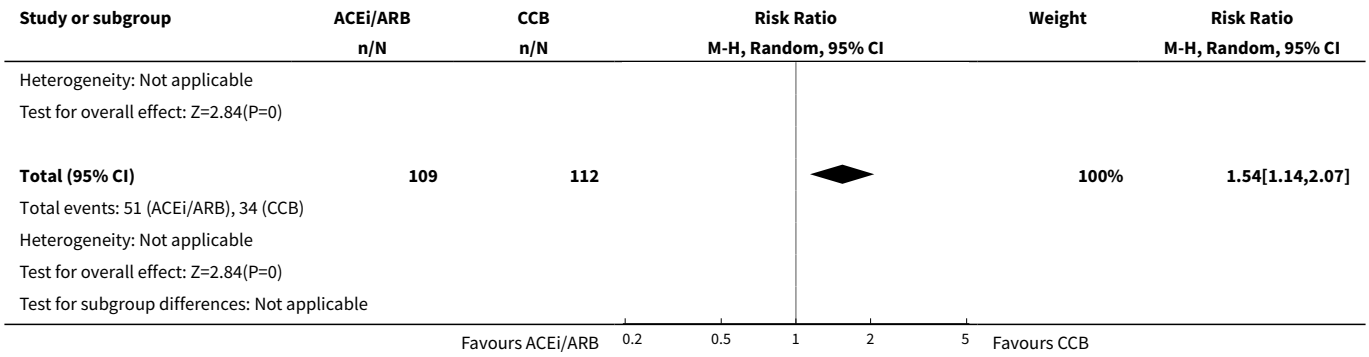


Analysis 22.5. Comparison 22 ACEi or ARB versus CCB, Outcome 5 Serum creatinine (µmol/L) at last follow-up.

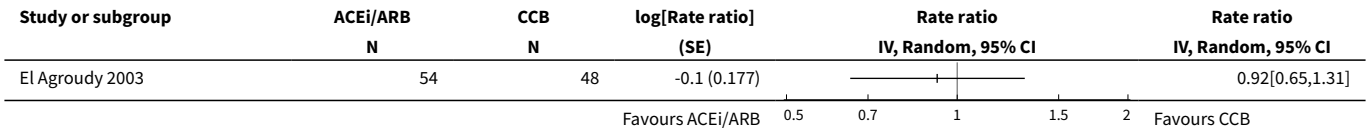


Analysis 22.6. Comparison 22 ACEi or ARB versus CCB, Outcome 6 Any rejection.

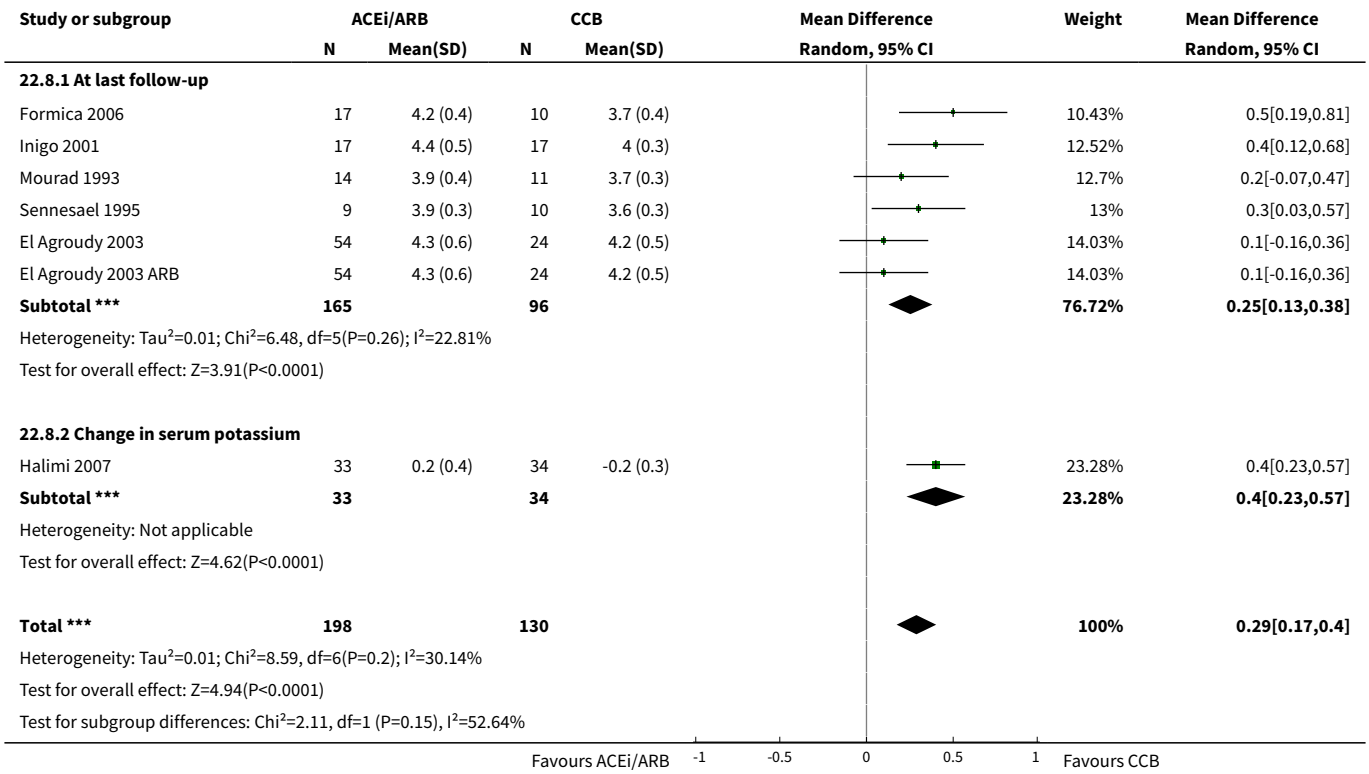




Analysis 22.7. Comparison 22 ACEi or ARB versus CCB, Outcome 7 Rejection rate.

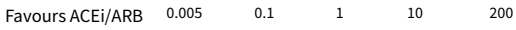


Analysis 22.8. Comparison 22 ACEi or ARB versus CCB, Outcome 8 Serum potassium (mmol/L).



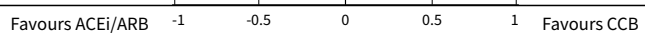
Analysis 22.9. Comparison 22 ACEi or ARB versus CCB, Outcome 9 Hyperkalaemia at last follow-up.

Study or subgroup	ACEi/ARB n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
22.9.1 'Transient' hyperkalaemia					
Midtvedt 2001	22/54	8/69		80.07%	3.51[1.7,7.27]
Subtotal (95% CI)	**54**	**69**		**80.07%**	**3.51[1.7,7.27]**
Total events: 22 (ACEi/ARB), 8 (CCB)					
Heterogeneity: Not applicable					
Test for overall effect: Z=3.39(P=0)					
22.9.2 > 5.5 mmol/L					
Halimi 2007	3/33	0/34		4.94%	7.21[0.39,134.32]
Hernandez 1995	2/10	0/11		4.94%	5.45[0.29,101.55]
Subtotal (95% CI)	**43**	**45**		**9.88%**	**6.27[0.79,49.59]**
Total events: 5 (ACEi/ARB), 0 (CCB)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.89); I^2=0%					
Test for overall effect: Z=1.74(P=0.08)					
22.9.3 > 6.0 mmol/L					
Formica 2006	6/29	1/27		10.05%	5.59[0.72,43.44]
Subtotal (95% CI)	**29**	**27**		**10.05%**	**5.59[0.72,43.44]**
Total events: 6 (ACEi/ARB), 1 (CCB)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.64(P=0.1)					
Total (95% CI)	**126**	**141**		**100%**	**3.9[2.03,7.47]**
Total events: 33 (ACEi/ARB), 9 (CCB)					
Heterogeneity: Tau^2=0; Chi^2=0.43, df=3(P=0.93); I^2=0%					
Test for overall effect: Z=4.1(P<0.0001)					
Test for subgroup differences: Not applicable					



Analysis 22.10. Comparison 22 ACEi or ARB versus CCB, Outcome 10 Proteinuria (g/24 h) at last follow-up.

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Van der Schaaf 1995	20	0.8 (0.4)	20	1 (0.7)		19.22%	-0.25[-0.58,0.08]
El Agroudy 2003	54	0.5 (0.4)	24	0.8 (0.7)		21.2%	-0.3[-0.6,-0]
El Agroudy 2003 ARB	54	0.4 (0.4)	24	0.8 (0.7)		21.2%	-0.4[-0.7,-0.1]
Inigo 2001	17	0.1 (0.1)	17	0.1 (0.1)		38.38%	-0.04[-0.1,0.02]
Total ***	**145**		**85**			**100%**	**-0.21[-0.41,-0.01]**
Heterogeneity: Tau^2=0.03; Chi^2=9.09, df=3(P=0.03); I^2=67%							
Test for overall effect: Z=2.05(P=0.04)							



Analysis 22.11. Comparison 22 ACEi or ARB versus CCB, Outcome 11 Haemoglobin (g/L) at last follow-up.

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Hernandez 1995	10	159 (22)	11	178 (10)		4.93%	-19[-33.86,-4.14]
Sennesael 1995	9	135 (15)	10	148 (16)		5.55%	-13[-26.94,0.94]
Formica 2006	17	122 (22)	10	139 (13)		6.14%	-17[-30.2,-3.8]
El Agroudy 2003 ARB	54	120 (20)	24	122 (20)		10.77%	-2[-11.62,7.62]
El Agroudy 2003	54	114 (14)	24	122 (20)		12.43%	-8[-16.83,0.83]
Midtvedt 2001	54	125 (17)	69	138 (20)		19.86%	-13[-19.54,-6.46]
Halimi 2007	33	-9 (8)	34	5 (7)		40.31%	-14[-17.6,-10.4]
Total * **	**231**		**182**			**100%**	**-12.14[-15.56,-8.72]**

Heterogeneity: Tau^2=4.17; Chi^2=7.45, df=6(P=0.28); I^2=19.42%

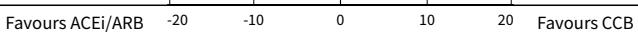
Test for overall effect: Z=6.96(P<0.0001)

Analysis 22.12. Comparison 22 ACEi or ARB versus CCB, Outcome 12 Haematocrit (%) at last follow-up.

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Mourad 1993	14	38 (5)	11	44 (8)		14.32%	-6[-11.4,-0.6]
Hernandez 1995	10	49 (6)	11	55 (3)		19.93%	-6[-10.12,-1.88]
Van der Schaaf 1995	20	40 (5)	20	40 (5)		26.09%	0[-3.1,3.1]
Halimi 2007	33	-3.6 (2.7)	34	0.5 (2.3)		39.66%	-4.1[-5.3,-2.9]
Total * **	**77**		**76**			**100%**	**-3.68[-6.18,-1.19]**

Heterogeneity: Tau^2=3.71; Chi^2=7.75, df=3(P=0.05); I^2=61.27%

Test for overall effect: Z=2.89(P=0)



Analysis 22.13. Comparison 22 ACEi or ARB versus CCB, Outcome 13 Myocardial Infarction.

Study or subgroup	ACEi/ARB n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
22.13.1 At 1 year				
Midtvedt 2001	0/54	0/69		Not estimable

Analysis 22.14. Comparison 22 ACEi or ARB versus CCB, Outcome 14 New onset angina.

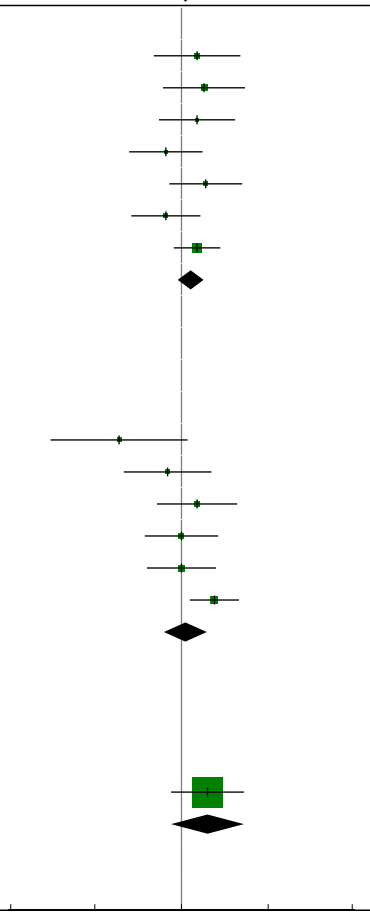
Study or subgroup	ACEi/ARB n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
22.14.1 At 1 year				
Midtvedt 2001	3/54	1/69		3.83[0.41,35.83]

Analysis 22.15. Comparison 22 ACEi or ARB versus CCB, Outcome 15 Ankle oedema.

Study or subgroup	ACEi/ARB n/N	CCB n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
22.15.1 Leading to withdrawal				
Midtvedt 2001	0/54	2/69		0.25[0.01,5.19]

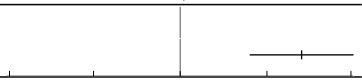
Analysis 22.16. Comparison 22 ACEi or ARB versus CCB, Outcome 16 Serum creatinine (µmol/L) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.16.1 1-3 months treatment							
Sennesael 1995	9	124 (27)	10	115 (28.5)		8.9%	9[-15.96,33.96]
Van der Schaaf 1995	20	152 (41)	20	139 (35)		9.93%	13[-10.63,36.63]
Formica 2006	17	124 (35)	23	115 (35)		11.52%	9[-12.94,30.94]
El Agroudy 2003 ARB	54	124 (44)	24	133 (44)		12.39%	-9[-30.16,12.16]
Inigo 2001	17	122 (35)	17	108 (27)		12.56%	14[-7.01,35.01]
El Agroudy 2003	54	124 (35)	24	133 (44)		13.97%	-9[-28.93,10.93]
Midtvedt 2001	54	146 (39)	69	137 (36)		30.74%	9[-4.43,22.43]
Subtotal ***	**225**		**187**			**100%**	**5.28[-2.16,12.73]**
Heterogeneity: Tau²=0; Chi²=5.29, df=6(P=0.51); I²=0%							
Test for overall effect: Z=1.39(P=0.16)							
22.16.2 6-12 months treatment							
Wei 2002	16	256 (72)	14	292 (34)		7.76%	-36[-75.52,3.52]
Formica 2006	17	133 (53)	10	141 (3)		14.56%	-8[-33.26,17.26]
Hernandez 1995	10	133 (27)	11	124 (27)		16.15%	9[-14.12,32.12]
El Agroudy 2003 ARB	54	133 (44)	24	133 (44)		17.77%	0[-21.16,21.16]
El Agroudy 2003	54	133 (35)	24	133 (44)		18.88%	0[-19.93,19.93]
Midtvedt 2001	54	144 (45)	69	125 (32)		24.88%	19[4.82,33.18]
Subtotal ***	**205**		**152**			**100%**	**2.22[-10.16,14.61]**
Heterogeneity: Tau²=108.09; Chi²=9.46, df=5(P=0.09); I²=47.12%							
Test for overall effect: Z=0.35(P=0.72)							
22.16.3 2 years treatment							
Mourad 1993	14	144 (26)	11	129 (27)		100%	15[-5.98,35.98]
Subtotal ***	**14**		**11**			**100%**	**15[-5.98,35.98]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.4(P=0.16)							



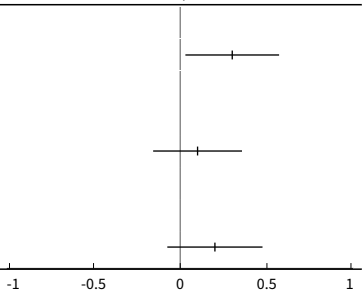
Analysis 22.17. Comparison 22 ACEi or ARB versus CCB, Outcome 17 Serum creatinine change (µmol/L) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.17.1 6-12 months treatment						
Halimi 2007	33	9 (12)	34	-5 (13)		14[8.01,19.99]



Analysis 22.18. Comparison 22 ACEi or ARB versus CCB, Outcome 18 Serum potassium (mmol/L) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.18.1 2 months treatment						
Sennesael 1995	9	3.9 (0.3)	10	3.6 (0.3)		0.3[0.03,0.57]
22.18.2 6-12 months treatment						
El Agroudy 2003	54	4.3 (0.6)	24	4.2 (0.5)		0.1[-0.16,0.36]
22.18.3 2 years treatment						
Mourad 1993	14	3.9 (0.4)	11	3.7 (0.3)		0.2[-0.07,0.47]

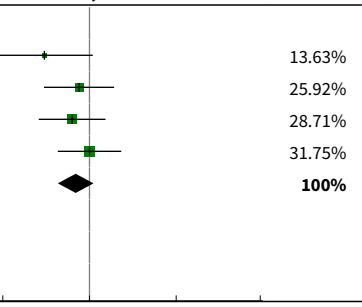


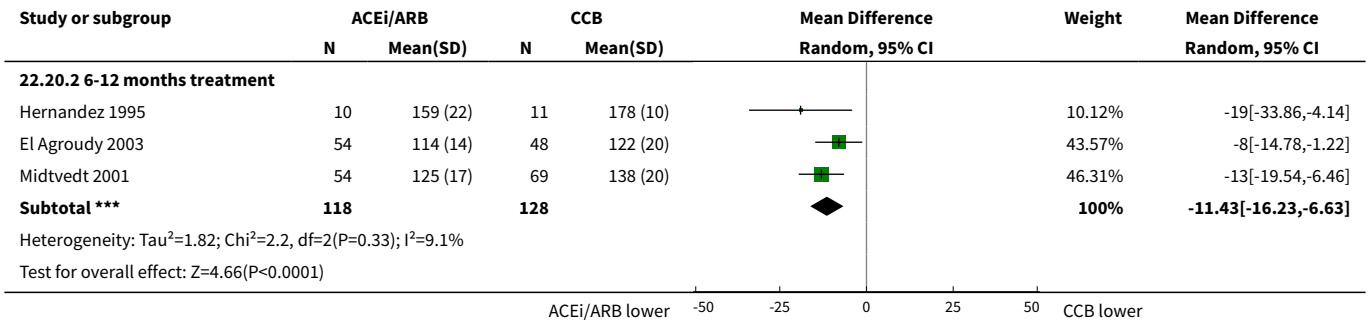
Analysis 22.19. Comparison 22 ACEi or ARB versus CCB, Outcome 19 Serum potassium change (mmol/L) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.19.1 6-12 months treatment						
Halimi 2007	33	0.2 (0.4)	34	-0.2 (0.3)		0.4[0.23,0.57]

Analysis 22.20. Comparison 22 ACEi or ARB versus CCB, Outcome 20 Haemoglobin (g/L) at follow-up (subgrouped by treatment length).

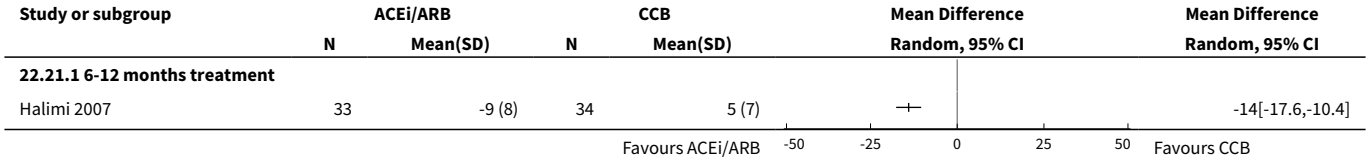
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.20.1 1-3 months treatment							
Sennesael 1995	9	135 (15)	10	148 (16)		13.63%	-13[-26.94,0.94]
El Agroudy 2003	54	119 (25)	24	122 (19)		25.92%	-3[-13.11,7.11]
Formica 2006	17	119 (13)	23	124 (18)		28.71%	-5[-14.61,4.61]
El Agroudy 2003 ARB	54	122 (19)	24	122 (19)		31.75%	0[-9.14,9.14]
Subtotal ***	**134**		**81**			**100%**	**-3.98[-9.13,1.16]**
Heterogeneity: Tau^2=0; Chi^2=2.42, df=3(P=0.49); I^2=0%							
Test for overall effect: Z=1.52(P=0.13)							





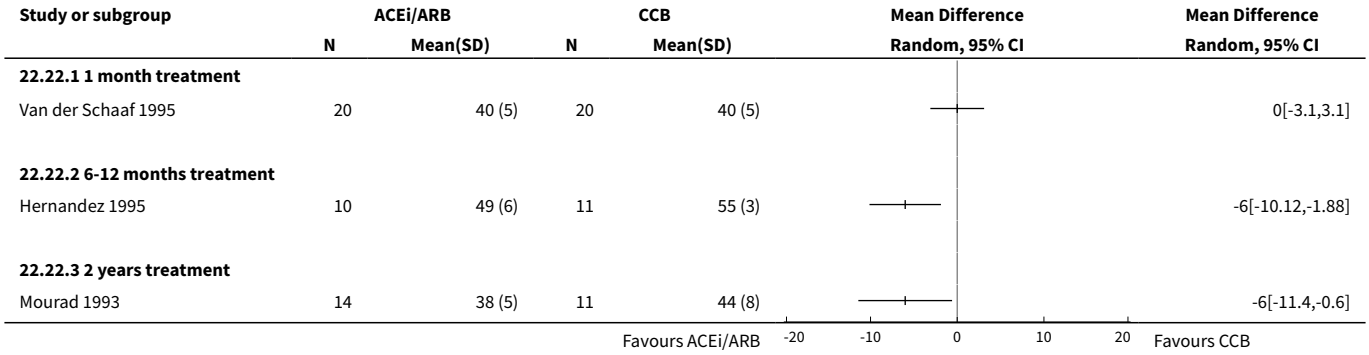
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.20.2 6-12 months treatment							
Hernandez 1995	10	159 (22)	11	178 (10)		10.12%	-19[-33.86,-4.14]
El Agroudy 2003	54	114 (14)	48	122 (20)		43.57%	-8[-14.78,-1.22]
Midtvedt 2001	54	125 (17)	69	138 (20)		46.31%	-13[-19.54,-6.46]
Subtotal ***	**118**		**128**			**100%**	**-11.43[-16.23,-6.63]**
Heterogeneity: Tau²=1.82; Chi²=2.2, df=2(P=0.33); I²=9.1%							
Test for overall effect: Z=4.66(P<0.0001)							

Analysis 22.21. Comparison 22 ACEi or ARB versus CCB, Outcome 21 Haemoglobin change (g/L) at follow-up (subgrouped by treatment length).



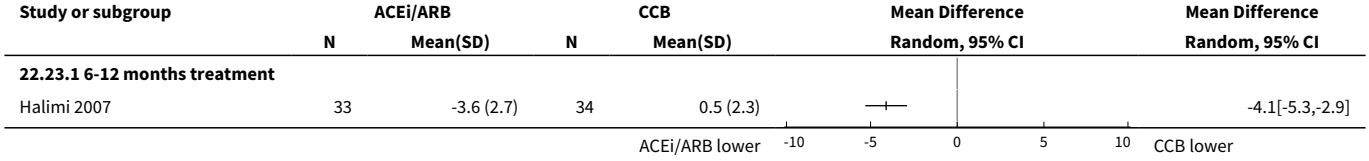
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.21.1 6-12 months treatment						
Halimi 2007	33	-9 (8)	34	5 (7)		-14[-17.6,-10.4]

Analysis 22.22. Comparison 22 ACEi or ARB versus CCB, Outcome 22 Haematocrit (%) at follow-up (subgrouped by treatment length).



Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.22.1 1 month treatment						
Van der Schaaf 1995	20	40 (5)	20	40 (5)		0[-3.1,3.1]
22.22.2 6-12 months treatment						
Hernandez 1995	10	49 (6)	11	55 (3)		-6[-10.12,-1.88]
22.22.3 2 years treatment						
Mourad 1993	14	38 (5)	11	44 (8)		-6[-11.4,-0.6]

Analysis 22.23. Comparison 22 ACEi or ARB versus CCB, Outcome 23 Haematocrit change (%) at follow-up (subgrouped by treatment length).



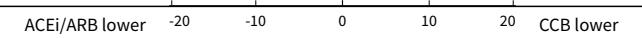
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.23.1 6-12 months treatment						
Halimi 2007	33	-3.6 (2.7)	34	0.5 (2.3)		-4.1[-5.3,-2.9]

Analysis 22.24. Comparison 22 ACEi or ARB versus CCB, Outcome 24 Diastolic blood pressure (mm Hg) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.24.1 1-2 months							
Sennesael 1995	10	95.4 (6)	10	91.7 (6.6)		50.45%	3.7[-1.83,9.23]
Van der Schaaf 1995	20	97 (9)	20	92 (9)		49.55%	5[-0.58,10.58]
Subtotal ***	**30**		**30**			**100%**	**4.34[0.42,8.27]**
Heterogeneity: Tau²=0; Chi²=0.11, df=1(P=0.75); I²=0%							
Test for overall effect: Z=2.17(P=0.03)							
22.24.2 6-12 months							
Halimi 2007	33	80 (10)	34	80 (7)		100%	0[-4.14,4.14]
Subtotal ***	**33**		**34**			**100%**	**0[-4.14,4.14]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

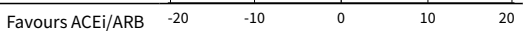
Analysis 22.25. Comparison 22 ACEi or ARB versus CCB, Outcome 25 Mean arterial blood pressure (mm Hg) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.25.1 1-2 months treatment							
Sennesael 1995	10	117.9 (12.3)	10	115.9 (7)		28.8%	2[-6.77,10.77]
Van der Schaaf 1995	20	115 (9)	20	111 (9)		71.2%	4[-1.58,9.58]
Subtotal ***	**30**		**30**			**100%**	**3.42[-1.28,8.13]**
Heterogeneity: Tau²=0; Chi²=0.14, df=1(P=0.71); I²=0%							
Test for overall effect: Z=1.43(P=0.15)							
22.25.2 6-12 months treatment							
El Agroudy 2003	54	94 (7)	48	95 (10)		68%	-1[-4.39,2.39]
Halimi 2007	33	100 (13)	34	100 (10)		25.22%	0[-5.57,5.57]
Hernandez 1995	10	105 (13)	11	99 (12)		6.78%	6[-4.73,16.73]
Subtotal ***	**97**		**93**			**100%**	**-0.27[-3.07,2.52]**
Heterogeneity: Tau²=0; Chi²=1.5, df=2(P=0.47); I²=0%							
Test for overall effect: Z=0.19(P=0.85)							



Analysis 22.26. Comparison 22 ACEi or ARB versus CCB, Outcome 26 Mean arterial pressure change (mm Hg) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.26.1 6-12 months treatment						
Mourad 1993	14	-12 (11)	11	-15 (10)		3[-5.25,11.25]
22.26.2 2 years treatment						



Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Mourad 1993	14	-18 (11)	11	-13 (17)		-5[-16.58,6.58]

Favours ACEi/ARB -20 -10 0 10 20 Favours CCB

Analysis 22.27. Comparison 22 ACEi or ARB versus CCB, Outcome 27 Systolic blood pressure (mm Hg) at follow-up (subgrouped by treatment length).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.27.1 1-2 months treatment							
Sennesael 1995	10	159.7 (13.3)	10	156.4 (12)		18%	3.3[-7.8,14.4]
Van der Schaaf 1995	20	153 (11)	20	148 (10)		52.28%	5[-1.52,11.52]
Subtotal ***	**30**		**30**			**70.28%**	**4.56[-1.05,10.18]**
Heterogeneity: Tau^2=0; Chi^2=0.07, df=1(P=0.8); I^2=0%							
Test for overall effect: Z=1.59(P=0.11)							
22.27.2 6-12 months treatment							
Halimi 2007	33	140 (19)	34	139 (17)		29.72%	1[-7.64,9.64]
Subtotal ***	**33**		**34**			**29.72%**	**1[-7.64,9.64]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.23(P=0.82)							
Total ***	**63**		**64**			**100%**	**3.51[-1.21,8.22]**
Heterogeneity: Tau^2=0; Chi^2=0.53, df=2(P=0.77); I^2=0%							
Test for overall effect: Z=1.46(P=0.14)							
Test for subgroup differences: Chi^2=0.46, df=1 (P=0.5), I^2=0%							

Favours ACEi/ARB -20 -10 0 10 20 Favours CCB

Analysis 22.28. Comparison 22 ACEi or ARB versus CCB, Outcome 28 Creatinine clearance (mL/min).

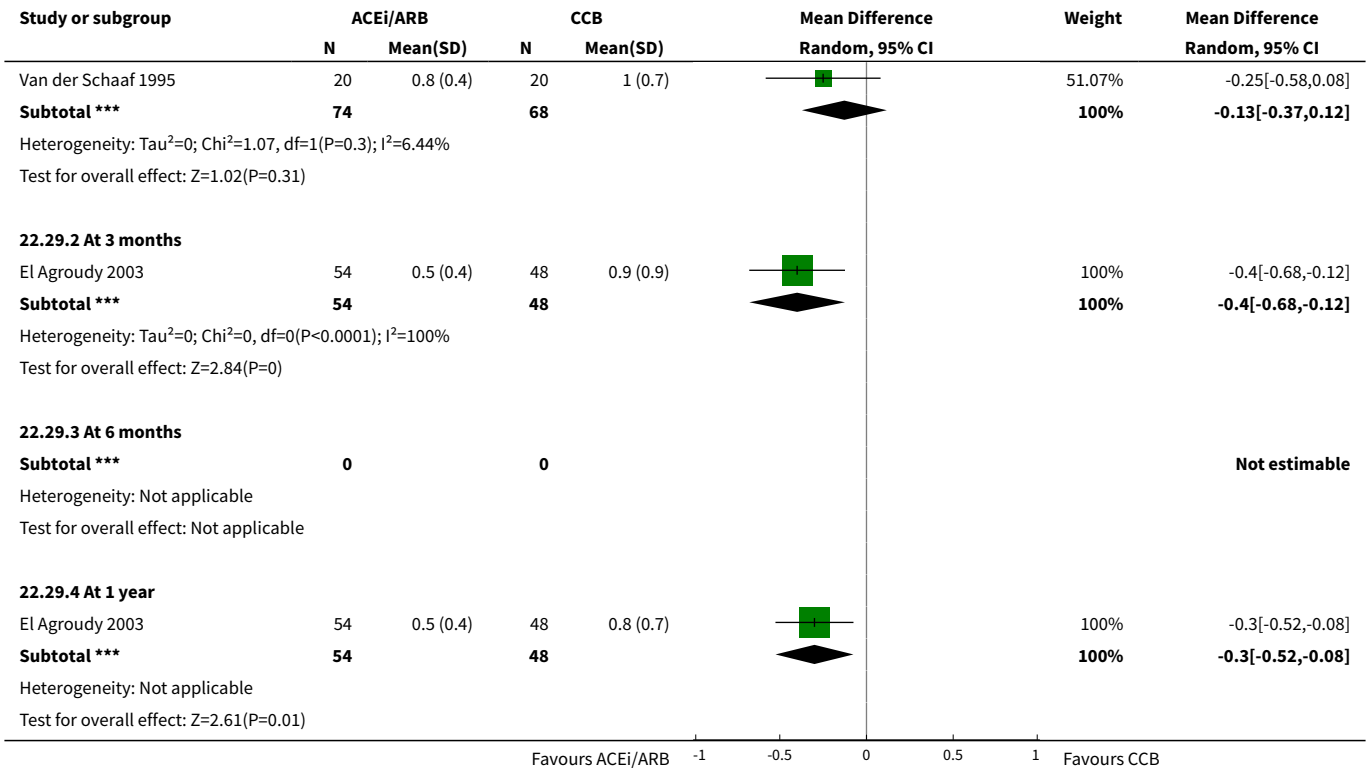
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.28.1 Creatinine clearance at 6 months						
Hernandez 1995	10	97 (24)	11	109 (29)		-12[-34.69,10.69]
22.28.2 Change in creatinine clearance at 6 months						
Halimi 2007	33	-8 (28)	34	15 (31)		-23[-37.14,-8.86]

Favours CCB -50 -25 0 25 50 Favours ACEi/ARB

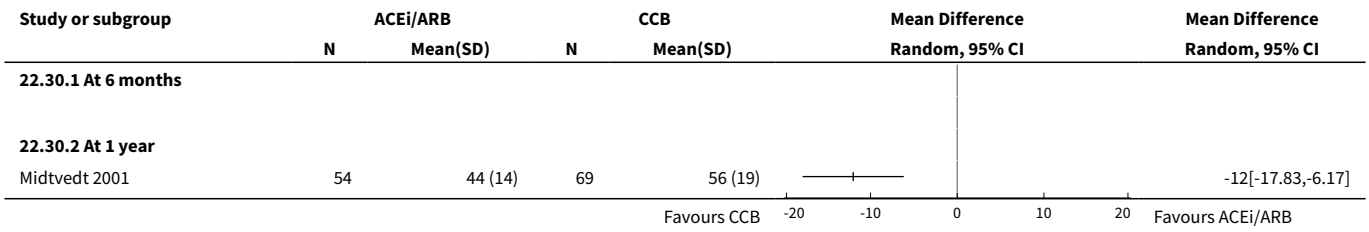
Analysis 22.29. Comparison 22 ACEi or ARB versus CCB, Outcome 29 Proteinuria (g/24 h).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.29.1 At 1 month							
El Agroudy 2003	54	0.9 (0.7)	48	0.9 (1)		48.93%	0[-0.34,0.34]

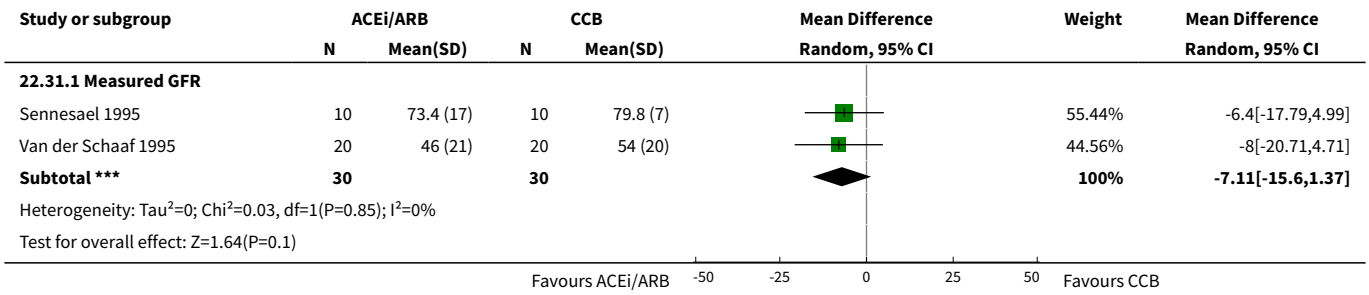
Favours ACEi/ARB -1 -0.5 0 0.5 1 Favours CCB



Analysis 22.30. Comparison 22 ACEi or ARB versus CCB, Outcome 30 GFR (mL/min/1.73 m²).

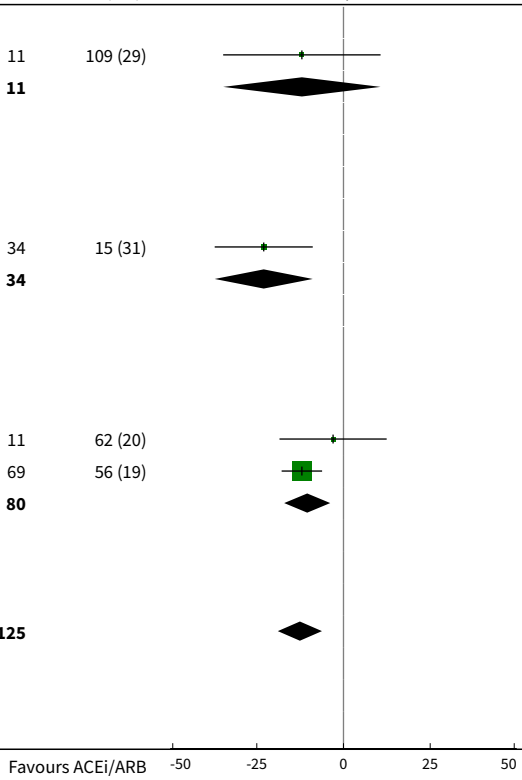


Analysis 22.31. Comparison 22 ACEi or ARB versus CCB, Outcome 31 GFR at 1-2 months treatment (mL/min or mL/min/1.73 m²).



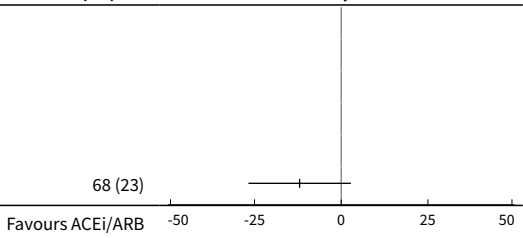
Analysis 22.32. Comparison 22 ACEi or ARB versus CCB, Outcome 32 GFR at 6-12 months treatment (mL/min or mL/min/1.73 m²).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.32.1 Creatinine clearance							
Hernandez 1995	10	97 (24)	11	109 (29)		7.4%	-12[-34.69,10.69]
Subtotal ***	**10**		**11**			**7.4%**	**-12[-34.69,10.69]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.04(P=0.3)							
22.32.2 Creatinine clearance change							
Halimi 2007	33	-8 (28)	34	15 (31)		17.4%	-23[-37.14,-8.86]
Subtotal ***	**33**		**34**			**17.4%**	**-23[-37.14,-8.86]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.19(P=0)							
22.32.3 Measured GFR							
Mourad 1993	14	59 (19)	11	62 (20)		14.91%	-3[-18.45,12.45]
Midtvedt 2001	54	44 (14)	69	56 (19)		60.28%	-12[-17.83,-6.17]
Subtotal ***	**68**		**80**			**75.2%**	**-10.46[-17.1,-3.82]**
Heterogeneity: Tau^2=4.99; Chi^2=1.14, df=1(P=0.29); I^2=12.33%							
Test for overall effect: Z=3.09(P=0)							
Total ***	**111**		**125**			**100%**	**-12.57[-18.94,-6.2]**
Heterogeneity: Tau^2=8.66; Chi^2=3.6, df=3(P=0.31); I^2=16.68%							
Test for overall effect: Z=3.87(P=0)							
Test for subgroup differences: Chi^2=2.46, df=1 (P=0.29), I^2=18.7%							



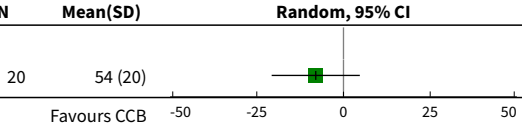
Analysis 22.33. Comparison 22 ACEi or ARB versus CCB, Outcome 33 GFR at 2 years treatment (mL/min or mL/min/1.73 m²).

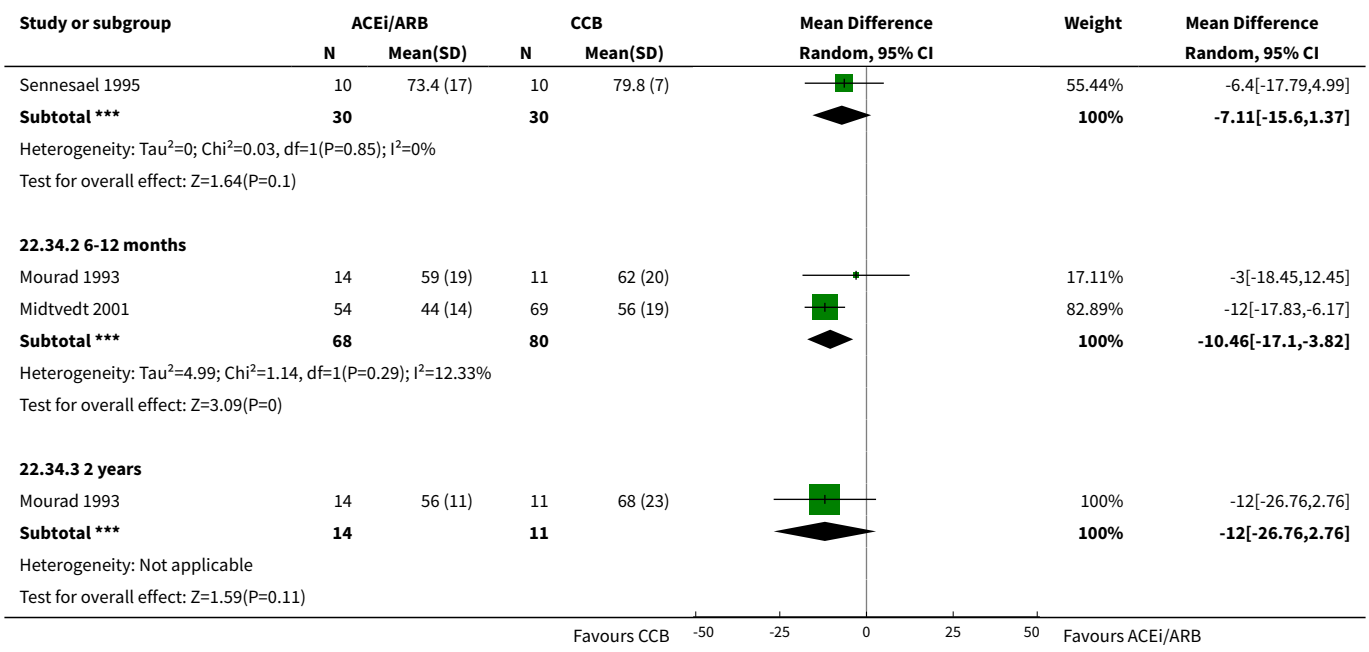
Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
22.33.1 Cockcroft-Gault						
22.33.2 Creatinine clearance						
22.33.3 Measured GFR						
Mourad 1993	14	56 (11)	11	68 (23)		-12[-26.76,2.76]



Analysis 22.34. Comparison 22 ACEi or ARB versus CCB, Outcome 34 Measured GFR (by time).

Study or subgroup	ACEi/ARB N	ACEi/ARB Mean(SD)	CCB N	CCB Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
22.34.1 1-2 months							
Van der Schaaf 1995	20	46 (21)	20	54 (20)		44.56%	-8[-20.71,4.71]





ADDITIONAL TABLES

Table 1. Summary of interventions

Study Id	Patients (n)	Intervention(s), daily oral dose	Comparator	Enrolment (months post-transplant)	Patient selection by comorbidity	Exposure duration (months)	Antihypertensive cointerventions
CCB versus no treatment/non-antihypertensive							
Alcaraz 1991	53	Diltiazem 120 mg (+ IV)	IV dopamine (at transplant)	0	No	12	Unclear
Campistol 1991	37	Diltiazem dose unknown	No treatment	< 3	No	12	Unclear
Chrysostomou 1993	113	Diltiazem 180 mg	No treatment	0	No	12	Unclear
Dawidson 1991	59	Verapamil 240 mg (+ IV)	No treatment	0	No	2 weeks[a]	Non-CCB
Frei 1990	129	Diltiazem 180 mg (+ IV)	No treatment	0	No	12	Unclear
Guerin 1989	29	Diltiazem 120-180 mg (+ IV)	No treatment	0	No	12	Unclear
Harper 1996	97	Nifedipine 30-120 mg	No treatment	0	No	24	Any
Morales 1994	97	Nifedipine (sustained release) 40-80 mg	No treatment	> 1	DBP ≥ 95 mm Hg	60	Non-CCB
Patton 1994	76	Diltiazem 120 mg	No treatment	< 1 week	No	12	Unclear
Rump 2000	50	Nitrendipine OR nifedipine 10-60 mg	No treatment	> 3	BP > 140/90	36	BB then diuretic then BB

Table 1. Summary of interventions *(Continued)*

Santos 2002	32	Diltiazem 90 mg	No treatment	Unclear	No	60	Unclear
Sperschneider 1997 Dilt; Sperschneider 1997 Nifed [b]	51	Diltiazem (dose unknown) VERSUS nifedipine (dose unknown)	No treatment	0	No	3	Unclear
Wagner 1986	63	Diltiazem 120 mg (+ IV in 42/63)	No treatment	0	No	48	Unclear
Wahlberg 1992	40	Diltiazem 240 mg (+ IV)	No treatment	0	No	3	Unclear
CCB versus placebo							
Gossmann 2002	60	Gallopamil 200 mg	Placebo	> 6	No	3	Unclear
Kumana 2003	110	Diltiazem 30-60 mg	Placebo	Unclear	No	6	Any except CCB
Kuypers 2004	131	Lacidipine 2-6 mg	Placebo	0	No	24	BB then ACEi then diuretic
Ladefoged 1994	39	Diltiazem 180-360 mg (+ IV)	Placebo	0	No	3	Unclear
Lehtonen 2000	184	Israpidine 10 mg (+ IV)	Placebo	0	No	3 weeks[a]	Unclear
Madsen 1998	99	Felodipine (extended release) 10 mg	Placebo	0	No	3	Diuretic/BB/pinacidil any order
Morales 1989	30	Nifedipine (sustained release) 40 mg	Placebo	0	No	2 weeks[a]	Unclear

Table 1. Summary of interventions *(Continued)*

Pirsch 1993	64	Verapamil 160 mg	Placebo	0	No	12	Sublingual nifedipine
Rahn 1999 HT; Rahn 1999 NT	253	Nitrendipine 20-40 mg	Placebo	1.5-3	DBP 90-115 or on antihypertensive therapy (n = 144) OR DBP < 90 (n = 109)	24	Diuretic then BB then ACEi then αB
Van den Dorpel 1994	50	Israpidine 5 mg (+ IV)	Placebo	0	No	12	Labetolol/guanfacine
Van Riemsdijk 2000	210	Israpidine 5 mg (+IV)	Placebo	0	No	12	Yes, unclear which
Venkat-Raman 1999*	30	Amlodipine 5 mg	Placebo	> 3	No	2	Unclear; baseline drugs continued
Wilkie 1993 CSA*; Wilkie 1993 No CNI*	22	Nifedipine (sustained release) 20 mg	Placebo	> 12	No	1	Not stated
Wilkie 1994	34	Nifedipine (sustained release) 40 mg	Placebo	0	No	3	Yes, not CCB
ACEi versus placebo/no treatment/non-antihypertensive							
Beckingham 1995	25	Enalapril 2.5 mg	Placebo	> 12	HCT > 0.5	4	Diuretic
Gronhagen-Riska 1984	30	Captopril 62.5 mg	No treatment	0	No	3	Yes
Hernandez 2000	57	Lisinopril 10mg	Placebo	Mean 69.5	HT > 150/90, on 2 antihypertensives and LVH	12	Yes, except ACEi/ARB
Kim 2002a	65	Enalapril 5-10 mg	Placebo		CAN on histology	Mean 23	Unclear
Ok 1995	19	Enalapril 10 mg	No treatment	Mean 6	HCT > 0.51	2	Yes

Table 1. Summary of interventions *(Continued)*

Paoletti 2007	74	Lisinopril 2.5-20 mg	No treatment	3-6	LVH	18	Yes, except ACEi/ARB
Rashtchizadeh 2007 [g]	37	Enalapril 10 mg	No treatment	> 6	No	2	Unclear
Takahara 2002	76	Benazepril (dose unknown)	No treatment	Mean 96	Unclear	12	CCB/BB/αB
Trivedi 2003*	9	Fosinopril 10-20 mg	Theophylline	Mean 36	HCT > 0.5	3	Unclear
CCB versus ACEi							
El Agroudy 2003 [c]	102	Amlodipine 5 mg	Captopril 50 mg	Mean 39	SBP 140-170 and/or DBP 85-100	12	Diuretic/BB/αB in any order
Halimi 2007 [d]	67	Amlodipine 5 mg	Enalapril 5 mg versus both	> 12	BP > 140/90 and dipstick proteinuria	6	Diuretic BB
Hernandez 1995	21	Nifedipine (dose unknown)	Captopril (dose unknown)	> 6	BP treated with nifedipine AND HCT > 0.5 over 6 months	6	Unclear
Midtvedt 2001	154	Nifedipine (controlled release) 30-60 mg	Lisinopril 10-20 mg	< 3 weeks	DBP > 95	24	Yes, not CCB/ACEi/ARB
Mourad 1993	31	Nifedipine (sustained release) 20-60 mg	Lisinopril 5-15 mg	Mean 5	DBP > 95	30	Yes, diuretic in ACEi arm, BB in CCB arm
Sennesael 1995*	10	Amlodipine 5-10 mg	Perindopril 2-8 mg	Mean 29.7	DBP 95-115	2	No
Van der Schaaf 1995*[e]	20	Amlodipine 5-10 mg	Lisinopril 5-10 mg	12-84	DBP 95-125	1	Unclear
ACEi versus ARB							

Table 1. Summary of interventions *(Continued)*

Altiparmak 2001	37	Enalapril 5-10 mg	Losartan 25-50 mg	3-61	No	12	Unclear
Celik 2000*	10	Enalapril 10 mg	Losartan 50 mg	> 6	HCT > 0.51	1	Unclear
El Agroudy 2003 [c]	102	Captopril 50 mg	Losartan 50 mg	Mean 39	SBP 140-170 and/or DBP 85-100	12	Diuretic/BB/αB in any order
Rashtchizadeh 2007 [g]	35	Enalapril 10 mg	Losartan 50 mg	> 6	No	2	Unclear
Schmidt 2001*	13	Enalapril 10 mg	Losartan 50 mg	> 12	BP 140-159/90-99	3 weeks	Diuretic/BB/αB /CCB in any order
Yildiz 2001	27	Enalapril 10 mg	Losartan 50 mg	Mean 12.5	HCT > 0.5	2	Unclear
CCB versus ARB							
Barenbrock 2001	13	Amlodipine (dose unknown)	Candesartan (dose unknown)	Unclear	'Hypertensive'	6	Unclear
El Agroudy 2003 ARB [c]	102	Amlodipine 5 mg	Losartan 50 mg	Mean 39	SBP 140-170 and/or DBP 85-100	12	Diuretic/BB/αB in any order
Formica 2006	56	Amlodipine up to 20 mg	Losartan up to 100 mg	< 1	'Needed treatment for hypertension'	12	BB/αB/diuretic
Inigo 2001*	17	Amlodipine 5 mg	Losartan 50 mg	Mean 90	BP 140-170/85-100	6 weeks	αB
Wei 2002	28	Amlodipine 5-10 mg	Candesartan 16-32 mg	Mean 34	CAN	Mean 13.6	Non-ACEi
CCB versus BB							
Barri 1995*	15	Israpidine 5-20 mg	Metoprolol 50-200 mg + hydrochlorthiazide 25-50 mg	3-18	'Mild to moderate hypertension'	3	Unclear

Table 1. Summary of interventions *(Continued)*

Chanard 2003	48	Amlodipine 5-10 mg	Tertatolol 5-10 mg	> 6	BP 140-180/90-100	2	Unclear
ACEi versus αB							
Castelao 2001*	42	Enalapril 2.5-20 mg	Doxazosin 1-8 mg	Mean 61	SBP > 140 or DBP > 90	11 weeks	Unclear
ACEi versus BB							
Hausberg 1999	96	Quinapril 5-40 mg	Atenolol 12.5-100 mg	1.5-3	BP > 140/90	24[a]	Yes, diuretic first, then others
ARB versus no treatment/placebo							
Weidanz 2005	21	Losartan 25-100 mg	No treatment	> 6	No	12	Yes, any except ARB
Rashtchizadeh 2007 [g]	42	Losartan 50 mg	No treatment	> 6	No	2	Unclear
Andres 2006	106	Valsartan 80 mg	Placebo	> 6	SBP 140-165 and/or DBP 90-105	2	Diuretic
Tylicki 2006*[f]	16	Losartan 50-100 mg	Placebo	> 6	Hypertensive on 1 or 2 agents	2	αB
ARB versus BB							
Tylicki 2006*[f]	16	Losartan 50-100 mg	Carvedilol 12.5-25 mg	> 6	Hypertensive on 1 or 2 agents	2	αB
αB versus placebo							
Vanrenterghem 1988	99	Hydergine 13.5 mg (+ IV)	Placebo	0	No	6	Unclear

+ IV = intervention also administered intravenously at or around time of transplantation; CCB = calcium channel blocker; BB = beta-blocker; αB = alpha-blocker; ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; SBP = systolic blood pressure (mm Hg); DBP = diastolic blood pressure (mm Hg); HCT = haematocrit; CAN = chronic allograft nephropathy; LVH = left ventricular hypertrophy on echocardiography

*crossover study

[a] Post exposure outcomes reported (Dawidson 1991 at 12 months, Lehtonen 2000 at 60 months, Morales 1989 at 1 month, Hausberg 1999 at 60 months)

[b] Three arm study nifedipine versus diltiazem versus no treatment.
[c] Three arm study: ACEi versus ARB versus CCB
[d] Three arm study: ACEi versus CCB versus both
[e] Three arm study: ACEi versus CCB versus placebo
[f] Three arm study: ARB versus αB versus placebo
[g] Four arm study: ACEi versus ARB versus both versus no treatment

Table 2. Calcium channel blocker (CCB) versus placebo/no treatment: meta-regression of potential confounding factors

	Outcomes RR or MD (95% CI), P					
Potential confounder	**Death (RR)**	**Graft loss (RR)**	**Acute rejection (RR)**	**GFR (mL/min) (MD)**	**Serum creatinine (µmol/L) (MD)**	**BP (mm Hg) (MD)**
CCB subtype (DHP versus non DHP)	1.0 (0.1 to 7.0), 1.0	0.7 (0.4 to 1.3), 0.3	1.2 (0.8 to 1.8), 0.3	4.4 (-1.3 to 10.1), 0.13	**-13.1 (-24.3 to -2.0), 0.02**	-3.4 (-19.5 to 12.8), 0.7
Enrolment ≤ 1 month post-transplant versus later	0.2 (0.03 to 1.7), 0.2	0.9 (0.5 to 1.8), 0.8	None reported in studies enrolling > 1 month post-transplant	0.2 (-4.3 to 4.7), 0.9	-0.4 (-15.8 to 15.0), 1.0	2.5 (-6.1 to 11.1), 0.6
Hypertensive patients only versus other	4.1 (0.6 to 29.6), 0.2	1.1 (0.6 to 2.0), 0.9	No hypertensive patients	2.9 (-2.3 to 8.1), 0.3	-8.4 (-22.6 to 5.9), 0.3	-5.1 (-14.6 to 4.4), 0.3
Follow-up ≥12 months versus less	1.9 (0.3 to 12.3), 0.5	**0.2 (0.09 to 0.7), 0.006**	1.0 (0.7 to 1.5), 1.0	3.2 (-1.7 to 8.1), 0.2	-9.9 (-21.1 to 1.3), 0.08	4.8 (-2.9 to 12.7), 0.2
Allocation concealment adequate versus unclear or inadequate	None were adequate	0.7 (0.2 to 2.5), 0.6	None were adequate	-0.4 (-5.8 to 5.0), 0.9	-2.4 (-23.1 to 18.4), 0.8	0.2 (-9.7 to 10.0), 1.0
ITT analysis versus none/unclear	0.5 (0.05 to 4.3), 0.5	0.6 (0.3 to 1.5), 0.3	1.1 (0.7 to 1.6), 0.7	1.5 (-3.0 to 6.1), 0.5	-8.9 (-21.3 to 3.4), 0.16	-4.7 (-12.8 to 3.4), 0.3
Journal publication versus abstract only	None were abstracts	1.3 (0.7 to 2.4), 0.4	None were abstracts	None were abstracts	-1.1(-25.9 to 23.5), 0.9	None were abstracts
Parallel versus crossover studies	None cross over	None were crossover	None were crossover	2.6 (-4.3 to 9.6), 0.5	-4.1 (-19.9 to 11.8), 0.6	2.9 (-6.0 to 11.8), 0.5

RR = risk ratio, DHP = dihydropyridine; ITT = intention-to-treat; MD = mean difference

APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	1. MeSH descriptor Antihypertensive Agents explode all trees 2. MeSH descriptor Angiotensin-Converting Enzyme Inhibitors explode all trees 3. MeSH descriptor Angiotensin II Type 1 Receptor Blockers explode all trees 4. MeSH descriptor Diuretics explode all trees 5. MeSH descriptor Adrenergic alpha-Antagonists explode all trees 6. MeSH descriptor Adrenergic beta-Antagonists explode all trees 7. MeSH descriptor Calcium Channel Blockers explode all trees 8. MeSH descriptor Vasodilator Agents explode all trees 9. MeSH descriptor Ganglionic Blockers explode all trees

(Continued)

	10.(calcium channel blocker*):ti,ab,kw in Clinical Trials 11.(antihypertensive adj (therapy or agent*)):ti,ab,kw in Clinical Trials 12.(antihypertensive* adj (therapy or agent*)):ti,ab,kw in Clinical Trials 13.(antihypertensive agent*):ti,ab,kw in Clinical Trials 14.(angiotensin converting enzyme inhibitor*):ti,ab,kw in Clinical Trials 15.(angiotensin II receptor antagonist*):ti,ab,kw in Clinical Trials 16.(ACE inhibitor*):ti,ab,kw or (ACE-I*):ti,ab,kw or (ACEI*):au in Clinical Trials 17.(ACE inhibitor*):ti,ab,kw or (ACE-I*):ti,ab,kw or (ACEI*):ti,ab,kw in Clinical Trials 18.(alpha blocker*):ti,ab,kw or (beta blocker*):ti,ab,kw in Clinical Trials 19.(candesartan):ti,ab,kw in Clinical Trials 20.(carvedilol):ti,ab,kw in Clinical Trials 21.(eprosartan):ti,ab,kw in Clinical Trials 22.(esmolol):ti,ab,kw in Clinical Trials 23.(irbesartan):ti,ab,kw in Clinical Trials 24.(quinapril):ti,ab,kw in Clinical Trials 25.(telmisartan):ti,ab,kw in Clinical Trials 26.(terazosin):ti,ab,kw in Clinical Trials 27.(trandolopril):ti,ab,kw in Clinical Trials 28.(#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 320 OR #21 OR #22 OR #23 OR 324 OR #25 OR #26 OR #27) 29.MeSH descriptor Kidney Transplantation explode all trees 30.(#28 AND #29)
MEDLINE	1. exp Antihypertensive Agents/ 2. exp Angiotensin-Converting Enzyme Inhibitors/ 3. exp Angiotensin II Type 1 Receptor Blockers/ 4. exp Diuretics/ 5. exp Adrenergic alpha-Antagonists/ 6. exp Adrenergic beta-Antagonists/ 7. exp Calcium Channel Blockers/ 8. exp Vasodilator Agents/ 9. exp Ganglionic Blockers/ 10.calcium channel blocker$.tw. 11.(antihypertensive adj (therapy or agent$)).tw. 12.angiotensin converting enzyme inhibitor$.tw. 13.angiotensin II receptor antagonist$.tw. 14.(ACE inhibitor$ or ACE-I).tw. 15.alpha blocker$.tw. 16.beta blocker$.tw. 17.candesartan.tw. 18.carvedilol.tw. 19.eprosartan.tw. 20.esmolol.tw. 21.irbesartan.tw. 22.quinapril.tw. 23.telmisartan.tw. 24.terazosin.tw. 25.trandolopril.tw. 26.or/1-25 27.Kidney Transplantation/ 28.and/26-27 29.randomised controlled trial.pt.

(Continued)

	30.controlled clinical trial.pt. 31.randomized.ab. 32.placebo.ab. 33.clinical trials as topic/ 34.randomly.ab. 35.(crossover or cross-over).tw. 36.Cross-over Studies/ 37.trial.ti. 38.or/29-37 39.animals/ not (humans/ and animals/) 40.38 not 39 41.and/28,40
EMBASE	1. exp Antihypertensive Agent/ 2. exp Angiotensin Receptor Antagonist/ 3. exp Diuretic Agent/ 4. exp Beta Adrenergic Receptor Blocking Agent/ 5. exp Alpha Adrenergic Receptor Blocking Agent/ 6. exp Calcium Channel Blocking Agent/ 7. exp Vasodilator Agent/ 8. exp Ganglion Blocking Agent/ 9. or/1-8 10.exp kidney transplantation/ 11.and/9-10 12.randomised controlled trial/ 13.crossover procedure/ 14.double-blind procedure/ 15.single-blind procedure/ 16.random$.tw. 17.factorial$.tw. 18.(crossover$ or cross-over$).tw. 19.placebo$.tw. 20.(double$ adj blind$).tw. 21.(singl$ adj blind$).tw. 22.assign$.tw. 23.allocat$.tw. 24.volunteer$.tw. 25.or/12-24 26.and/11,25

WHAT'S NEW

Date	Event	Description
30 November 2009	Amended	References updated

HISTORY

Protocol first published: Issue 2, 2002

Review first published: Issue 3, 2009

Date	Event	Description
6 August 2009	Amended	Contact details updated.
12 May 2007	Amended	New authors

CONTRIBUTIONS OF AUTHORS

- Nicholas Cross updated the protocol, reviewed titles and abstracts of all studies retrieved in searches, assessed study quality, extracted, entered, checked, analysed and interpreted data, wrote and corrected the manuscript.
- Angela Webster reviewed titles and abstracts, assessed study quality, extracted data, assisted with analysis, wrote and corrected the manuscript.
- Philip Masson assessed study quality, extracted data, and wrote and corrected the manuscript.
- Philip O'Connell interpreted data and wrote and corrected the manuscript.
- Jonathan Craig assisted with data analysis, interpreted data, and wrote and corrected the manuscript.

DECLARATIONS OF INTEREST

None known

SOURCES OF SUPPORT

Internal sources

- School of Public Health, University of Sydney, Australia.
- Children's Hospital at Westmead, Australia.

External sources

- National Health and Medical Research Council, Australia.

  Medical Postgraduate Scholarship No. 402981
- National Health and Medical Research Council, Australia.

  Screening and Diagnostic Test Evaluation Program (Program Grant No. 402764)
- National Health and Medical Research Council, Australia.

  Centre for Clinical Research Excellence in Renal Medicine (Centre for Kidney Research, Children's Hospital at Westmead)

INDEX TERMS

Medical Subject Headings (MeSH)

Angiotensin II Type 1 Receptor Blockers [therapeutic use]; Angiotensin-Converting Enzyme Inhibitors [therapeutic use]; Antihypertensive Agents [*therapeutic use]; Calcium Channel Blockers [therapeutic use]; Glomerular Filtration Rate [drug effects]; Graft Rejection [prevention & control]; Graft Survival [drug effects]; Hypertension [*drug therapy] [etiology]; Kidney Transplantation [*adverse effects]; Randomized Controlled Trials as Topic

MeSH check words

Humans