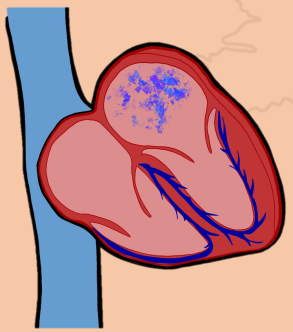
Trends in Incidence and Mortality from Atrial Fibrillation Across Europe

1990 - 2017

Background



Atrial Fibrillation

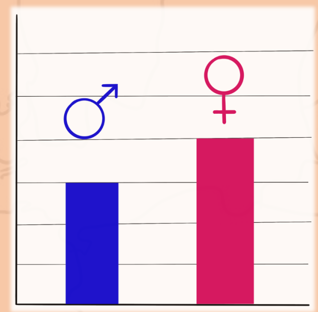
- Commonly diagnosed.
- Associated with significant morbidity.
- Study of its epidemiology in Europe is scarce.

Design

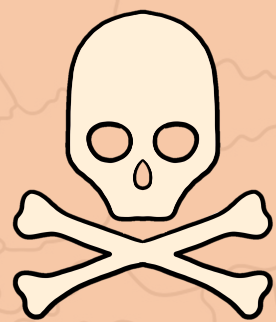
Observational Analysis

- Using the Global Burden of Disease Database.
- Data was extracted between 1990 to 2017.
- Analysed using Joinpoint Regression Analysis.
- 20 Countries included based on:
    - population > 4 million.
    - Data quality rated 4* and above.

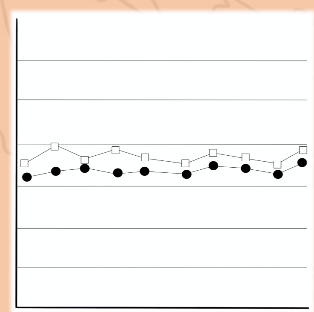
Observations



Higher per-case mortality rate in females versus males.



Higher rates of Atrial Fibrillation-associated mortality in higher GDP nations.



Heterogeneity in incidence and mortality trends throughout Europe.

Paradoxical Impact of Socioeconomic Factors on Outcome of Atrial Fibrillation in Europe: Trends in Incidence and Mortality from Atrial Fibrillation Across Europe

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Aims: To understand the changing trends in Atrial Fibrillation (AF) incidence and mortality across Europe from 1990 to 2017, and how socioeconomic factors and sex differences play a role.

Methods and Results: We performed a temporal analysis of data from the 2017 Global Burden of Disease Database for 20 countries across Europe using Joinpoint regression analysis. Age-adjusted incidence, mortality and mortality to incidence ratios (MIRs) to approximate case fatality rate are presented. Incidence and mortality trends were heterogenous throughout Europe, with Austria, Denmark and Sweden experiencing peaks in incidence in the middle of the study period. Mortality rates were higher in wealthier countries with the highest being Sweden for both men and women (8.83 and 8.88 per 100,000, respectively) in 2017. MIRs were higher in women in all countries studied, with the disparity increasing the most over time in Germany (43.6% higher in women versus men in 1990 to 74.5% higher in women in 2017).

Conclusion: AF incidence and mortality across Europe did not show a general trend, but unique patterns for some nations were observed. Higher mortality rates were observed in wealthier countries, potentially secondary to a survivor effect where patients survive long enough to suffer from AF and its complications. Outcomes for women with AF were worse than men, represented by higher MIRs. This suggests there is widespread healthcare inequality between the sexes across Europe, or that there are biological differences between them in terms of their risk of adverse outcomes from AF.

Keywords: Atrial Fibrillation, Europe, Epidemiology

Paradoxical Impact of Socioeconomic Factors on Outcome of Atrial Fibrillation in Europe: Trends in Incidence and Mortality from Atrial Fibrillation

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Introduction

Atrial fibrillation (AF) is one of the most commonly diagnosed arrhythmias, however data remains scarce regarding its epidemiology in Europe. Despite innovations in AF treatment, ranging from anticoagulation to ablation, previous studies have shown a global increase in AF-associated mortality in the last 20 years[1]. Newer therapies are likely to confer increasing economic strain in the context of a growing and ageing patient population, with estimates suggesting that AF accounts for 1% of the UK National Health Service's budget[2,3].

AF also has a mortality burden, particularly associated with cardiovascular complications such as progressive heart failure. However, it is unclear whether trends in AF mortality vary across different European countries. While it could be speculated that mortality rates would favour developed countries as with many other diseases[4], some data suggests that the burden of AF is higher in developed countries[1]. This may relate to improved survival into older age leading to a higher risk population, both for the development of AF, and for its adverse consequences. There is also evidence of sex disparity in mortality in AF in some nations, with women having a higher rate of AF-related mortality than men[5]. Whether this holds true throughout Europe is not known.

No recent study comparing trends in AF-related incidence and mortality across Europe has been undertaken. This study aims to elucidate the trends in incidence and mortality from AF across Europe from 1990 to 2017. We aim to ascertain the heterogeneity of AF impact throughout Europe. Where there is heterogeneity we aim to understand if this is associated with varying GDP across Europe. We also aim to determine whether the incidence and mortality of AF is different between men and women and, if so, how uniform this is across Europe.

Methods

Data Source

Annual AF incidence and mortality data between the years 1990 to 2017, inclusive, were collected from the Global Burden of Disease (GBD) Study database, a comprehensive global program that assesses mortality and morbidity from major disease. Incidence and mortality rates from the GBD database are collated by the Institute of Health Metrics and Evaluation. The GBD data is made publicly available online (via http://ghdx.healthdata.org/gbd-results-tool). 20 countries from within the European Union (EU) were chosen to give a representative sample across Europe. Countries were included if they had a population over 4 million, scored 4 stars and above by the GBD database in terms of data reliability, and were dichotomised based on whether their gross domestic product (GDP) per capita was above or below the 2017 EU mean. Whilst a single timepoint was used for GDP per capita, relative stability of countries' ranks above or below the EU mean were confirmed on review of annual data provided by the World Bank database[6]. All countries in this study recorded data according to the 9th and 10th ICD revisions, and was limited to the "AF/Flutter" code (I48) for clarity. Causes of death recorded in the GBD database are determined via vital registration (VR) and verbal autopsy (VA), with each death being attributed to a single underlying cause. To aid comparability, data is standardised by garbage code redistribution algorithms and correcting for under-registration. The GBD maintains quality of the data by assessing the completeness of VA and VR data by location-year and excluding sources with less than 50% completeness of reporting. Each country included in this analysis had 90% or greater VR and VA data completeness between 1990 to 2017. The GBD also rates the reliability of each country's data on a scale of 0-5 stars. 7 of the 20 countries studied scored 5 stars (Austria, Finland, Hungary, Ireland, Italy, Sweden, and the U.K.) equating to 85-100% of mortality data being well certified. The remaining countries scored 4 stars (Belgium, Bulgaria, Croatia, Czech Republic, Denmark, France, Germany, Greece, Netherlands, Poland, Portugal, Romania, Spain) equating to 65-84% of the data being well certified.

Age-standardised mortality and incidence rates from AF and atrial flutter were calculated by weighing the distribution of mortality per 5 year age group to the GBD standard population[7].

Statistical Analysis

Trends were assessed using Joinpoint regression analysis (Joinpoint Version 4.6.0.0, provided by the United States National Cancer Institute Surveillance Research Program) as we have done previously[8]. Joinpoint regression allows for identification of points of significant changes in trend data and is useful in characterising trends in incidence and mortality rates. The overall trend is initially calculated with no Joinpoints and then tested for significant improvement in model fit with sequential addition of Joinpoints in regions of significant slope change. Estimated annual percentage change with 95% confidence intervals are determined for each separate segment using logarithmic regression. Regarding missing data, this was imputed using the last observation carried forward.

Differences in median AF mortality rates from 2015 to 2017 between countries above and below the EU mean GDP per capita, as well as Eastern (Bulgaria, Croatia, Czech Republic, Greece, Hungary, Poland and Romania) versus Western (Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Netherlands, Portugal, Spain, Sweden and the United Kingdom) European countries were assessed using the Wilcoxon rank-sum test.

Mortality to incidence ratios (MIRs) were calculated by dividing the mortality rate by the incidence rate for each country for the 28-year period studied. MIR trends were then graphically inspected to identify changes in sex disparity over time. MIRs help to identify whether a country has a higher or lower mortality rate per case diagnosed. Where statistical comparisons were performed $p<0.05$ was deemed statistically significant.

Results

Trends in AF Incidence

Figure 1 shows age-standardised AF incidence rates from 1990 to 2017 with superimposed Joinpoint data, highlighting periods with different rates of change (as EAPC) over time, whilst supplementary Table 1 presents the full Joinpoint analysis for the 20 countries studied. AF incidence is shown to be consistently higher in males than in females in all countries throughout the period studied. No overarching trend descriptive of all nations was identified over the 28-year period, although there were some unique patterns in some nations. Austria, for example, showed an initial slow increase in incidence followed by a more rapid rise identified by Joinpoint regression in both men (4.3% estimated annual rise between 1995-2000) and women (+3.7% per year between 1995 and 2001). There was then a subsequent decline in incidence from around 2005-2017. Although somewhat less marked, a similar pattern to that of Austria was seen in Denmark and Sweden. In the lower GDP nations, there was less variability with a general, steady decline in incidence over the years, except in Portugal where there was a sharp drop in incidence (-6.1% per year for men and -7.7% for women, 2006-2009) and in Italy where there was a sharp rise in the late 1990s in incidence for men (+3.5% per year estimated annual rise between 1995-2001). Croatia also had an unusual pattern, with a decline in AF incidence to some of the lowest levels in Europe over the first 10-20 years of the study (down to 39.2 per 100,000 in 2000 in men and 24.3 per 100,000 in 2006 for women) with a subsequent sharp increase in incidence for men (+2.5% per year 2006-2010) and a slower and later increase for women (+1.2% per year 2010-2017).

Trends in AF-Associated Mortality

Figure 2 shows age-standardised AF-associated mortality rates from 1990 to 2017, with the accompanying Joinpoint data highlighting periods of inflection and their associated rates of change, whilst supplementary Table 2 presents the full Joinpoint analysis. No overarching pattern encompassing all 20 nations can be described, although unique patterns for individual nations are present. It is immediately evident that mortality is not as different between the sexes as is incidence, suggesting that females have a higher case mortality than men (explored further utilising mortality to incidence ratios below). Mortality in part mirrors incidence in Austria, Denmark and Sweden. The most marked rise was in Swedish men (+5.7% estimated annual rise per year 2001-2006). Unlike in the incidence data, particularly for Sweden and Denmark, a decline in mortality did not follow this initial rise such that their mortality rates were amongst the highest by the end of the study. Germany also had a rapid and sustained increase in mortality, particularly in women throughout the 2000s (+4% per year 2000-2009). In developing nations, there were less marked changes in mortality rates over time. Bulgaria is notable for having a sustained difference between male and female mortality throughout the studied period – this is reflected in the more equal mortality to incidence ratios between the sexes for this nation than anywhere else in Europe (see below).

Current AF Incidence and Mortality

Figure 3 shows age-standardised AF incidence and mortality rates for 2017. The highest incidence rates were seen in Sweden for men (80.04 per 100,000) and Austria for women (52.36 per 100,000). The highest mortality rates for men and women were seen in Sweden (8.83 and 8.88 per 100,000, respectively). Countries above the mean EU GDP were generally observed to have higher incidence and mortality rates. Figure 4 shows significantly higher mortality rates in higher GDP per capita countries in both men and women compared to lower GDP nations.

Mortality to Incidence Ratios

Figure 5 shows MIR trends from 1990 to 2017. Most nations showed fairly static MIRs through the study period, although again there are notable exceptions such as the general increases in MIR seen in Sweden, Germany and Denmark in both men and women.

Female MIRs were consistently higher than male MIRs in all countries studied, although this difference varied from relatively small (5.4% higher MIR in women versus men in Bulgaria in 2017) to great (74.5% higher MIR in women versus men in Germany in 2017). Over time, sex difference in MIR have stayed fairly static, although there are exceptions. Germany's MIR has increased rapidly in females over the last 15 years, but less-so in males leading to a greater disparity over time (from 43.6% higher in women compared to men in 1990, to 74.5% higher in women in 2017). Austria is following the opposite pattern with the disparity decreasing from 45.7% higher in women in 1990, to 19% higher in women in 2017. Greece had a period of larger sex disparity in MIR in the late 2000s and early 2010s (up to 63.4% higher MIR in women versus men in 2012), which is now closing gradually (32.2% higher in women in 2017).

Discussion

Our study identifies several key findings. Firstly, the rates of change of incidence and mortality are heterogeneous throughout Europe with some nations faring better than others over the 28 years studied, with a significantly higher mortality in countries above the mean European GDP per capita. Secondly, mortality attributable to AF per case, or at least its approximation in the form of MIR, has not improved over time, and in many nations is actually increasing, despite apparent advances in AF care. Thirdly, MIRs were higher in women than men in all countries studied, with some nations faring worse than others in terms of this sex disparity.

Heterogeneity of Incidence and Mortality

Although no single overarching trend can describe incidence and mortality changes across Europe over the 28-year period studied, the Joinpoint analysis points to some nations with unique trends in their incidence and mortality relating to AF. These are explored above in detail but are briefly summarised as follows: Austria, Denmark and Sweden have incidences peaking in the middle of the study period which then decline toward the end. Italy has a sharp rise in incidence in the late 1990s, and in Portugal there is a period of rapid decline in AF incidence between 2006 and 2009.

Whilst previous projections have suggested that the burden of AF will increase to endemic proportions throughout Europe, bringing with it higher rates of hospitalisation[9], this does not seem to be borne from any increases in incidence rates. The heterogeneity of AF incidence throughout Europe are reflected in similar trends in mortality, implying that increases in prevalence long-term are driven more by an increasingly elderly population or improvements in management of chronic disease. This is contrary to other studies that have presented AF incidence as increasing over time[1].

Regarding mortality, this in part follows incidence in the early part of the studied period although this, in the main, is flat through the studied period with notable exceptions described above. Sweden, Denmark and Germany in particular have had periods in which mortality increases significantly, leading to these nations having the highest mortality ascribed to AF by the end of the studied period.

Higher age-standardised mortality rates were noted in richer EU member states (Figures 2 and 4). This disparity, favouring less developed member states, is not usually seen in epidemiological studies of Europe, with the inverse relationship commonly being true for other conditions such as ischaemic heart disease[8]. Other studies have also shown that developed countries have a greater overall AF burden[1,10]. Individuals in low GDP countries in Europe suffer wealth inequality, with more individuals residing in a lower socioeconomic class and reduced healthcare expenditure per capita[11]. It seems somewhat counterintuitive therefore that there was a lower AF related mortality and incidence in these countries – mainly Eastern European and the Baltic nations in our study. Conversely, Germany and Sweden's health expenditure per capita far exceeds the EU mean and these nations had amongst the highest AF-related mortality rates in 2017 (Figure 2C and D).

Understanding the distribution of risk factors across Europe may help explain the disparity in AF outcomes favouring less developed member states. The prevalence of modifiable risk factors (such as obesity, high alcohol intake, smoking and physical activity) as well as commonly associated comorbidities (such as hypertension, diabetes mellitus and coronary artery disease) vary substantially across geographical regions[12]. For example, alcohol intake, sedentary behaviour and rates of dyslipidaemia tended to be higher in Western European countries, whilst lower levels were recorded in Eastern Europe[12,13]. Conversely, rates of diabetes mellitus and hypertension were higher in relatively lower income European countries[13], suggesting that there are other aspects to the observed disparity in AF mortality than just risk factor distribution. Behavioural and cultural differences towards prevention strategies across the region may contribute to these variations, as has been previously shown with coronary artery disease in Europe[14]. It is possible that in richer countries there is a survivor effect in which individuals in these countries live long enough to be diagnosed with and/or suffer from the serious sequelae of AF[4,8]. Another reason for the disparity could include that the diagnosis is less likely to be made in poorer health systems with less widespread access to ECGs, potentially resulting in misclassification of causes of death in individuals in these nations. Alternatively, AF may be more likely to occur relating to the taller stature of individuals in nations with a higher GDP[15], owing to a significant positive correlation between height and risk of AF[16].

The ecological fallacy ought to be mentioned here so that we do not fall into the trap of thinking that higher income individuals are more likely to suffer AF related mortality. A frequently cited early example of the ecological fallacy is the link between suicide rates and religious denominations in late 19th century Prussia[28]. Here, the regional correlation between suicide rate and proportion of Protestants could be taken to show that suicide rates are higher in Protestants – this would be an incorrect assumption as it could just have well have been the Catholics committing suicide in largely Protestant provinces[29]. Similarly, there is a positive correlation between average national income and obesity[30] – this makes sense since the average individual is better nourished and the body mass index distribution is generally shifted up. On an individual level, however, this correlation falls down – the highest income individuals are not the most obese[30].

Our relationship between AF related mortality and GDP may represent something similar – i.e. we certainly would not want to state that higher income individuals are more likely to die of AF-related complications – there is some evidence of the opposite correlation at the individual level[31]. Our proposed explanations must function at the national level – the survivor effect described above does this. An alternative explanation would be that the same excesses that lead to increased levels of obesity in higher income countries may also lead to higher levels of sleep apnea and insulin resistance and all these factors may result in higher population levels of atrial fibrillation. We would not expect this relationship necessarily to hold at the individual level – just as the richest 20% of individuals seem to be able to avoid obesity[30], so too perhaps the higher income individuals within a nation might be better able to avoid the excesses that result in AF-related complications.

Mortality to Incidence Ratios (MIRs) not Improving Despite Advances in AF Management

Age-standardised mortality to incidence ratios showed no overarching trend through the study period, although particular national trends are outlined in the Joinpoint analysis. In particular, the sustained elevation in mortality despite declining incidences of AF in Sweden, Germany and Denmark has led to these nations having the largest rises in MIRs over time. Most other nations have had fairly static MIRs over the studied period.

However, static MIRs despite advances in management since 1990 suggests either a failed opportunity to improve outcomes for AF patients throughout Europe, or perhaps that AF-related mortality is one of the inevitable consequences of improving survival from other diseases. Whilst our data was adjusted for age, this may not adjust for the comorbidity that comes with aging[17] and the survival of other diseases which may cause death more commonly in less developed nations. Envisage, for example, a 70-year-old lady who has effective treatment of breast cancer with cardiotoxic chemotherapy in a developed higher GDP nation, only to suffer chemotherapy induced cardiomyopathy with a subsequent heart failure death related to incident AF. On a national basis, the enhanced survival from breast cancer may translate into an increase in AF-related mortality.

Increased MIRs may also be linked to the increased prevalence of risk factors for the development of AF in older age groups, such as hypertension and obesity which have ascended into the top 5 factors causing early death and disability in the 2017 GBD study. The 2020 European Society of Cardiology guidelines highlight the importance of managing these risks factors as well as the advancements in intervention, but notes that rhythm and rate control mainly confer symptomatic benefit rather than long term morbidity and mortality benefits[3]. Whilst there is some evidence of a therapeutic advantage of direct oral anticoagulants over traditional anticoagulants, mortality secondary to stroke is relatively small compared to other causes. Cardiovascular mortality makes up 61% of deaths in anticoagulated patients with AF, but a relatively small percentage (7%) relates to stroke or peripheral thromboembolus[18]. The majority of cardiovascular deaths in AF relate to sudden death (22%) and progressive heart failure (15%). Other non-cardiovascular deaths make up a large number of deaths in AF patients (35%, including cancer and respiratory failure), although these non-cardiovascular deaths may be less relevant to our study given that AF would have to have been classified as the main cause of death by the physician completing the death certificate. WHO classifies underlying cause of death as "the disease or injury which initiated the train of morbid events leading directly to death" and it would be unlikely a physician would assign AF the prominence on the death certificate to be defined the underlying cause of death for these non-cardiovascular causes.

Sex Disparities in AF Mortality to Incidence Ratios across Europe

With regards to sex, our investigation highlighted higher MIRs and therefore higher mortality per case in women throughout all countries studied. Several theories have previously been proposed to explain this disparity, such as women being referred less than men for specialist arrhythmia care[19], and often presenting later and more comorbid[20]. Higher rates of AF-related strokes in women[3] likely also contribute to higher MIRs versus men. Female sex in the presence of other CHA2DS2-VASc factors has been shown to be a significant risk modifier for thromboembolism[21] and should be taken into account when deciding on anticoagulation. In light of the long established benefits of anticoagulation in significantly reducing rates of thromboembolism secondary to AF[22] (and the subsequent associated mortality), our study supports the careful consideration of anticoagulation in women given their higher MIRs.

Our data, therefore, are consistent with previous data showing a higher risk of AF-related mortality in women[5,23]. There are certainly disparities in care between men and women between nations[24]. However, our data also shows that the sex difference is present across Europe, suggesting that biological differences likely play a role, as well as the possible role of healthcare inequality. On the other hand, the degree of the sex disparity in MIRs varied greatly across Europe (from 5.4% higher MIR in women versus men in Bulgaria in 2017, to 74.5% higher MIR in women versus men in Germany in 2017). There is also variation in whether this sex disparity is increasing (e.g. in Germany) or decreasing (e.g. in Austria) over time. While it is beyond the scope of this study to understand why this is, our data suggests that healthcare services in different European nations could learn from each other regarding how to improve this sex disparity.

Limitations

The process of collecting data for the GBD database is reliant on a broad network of international collaborators, and access to administrative data related to healthcare encounters and death certification[25]. Access to such information may be limited depending on the country, which has implications for data robustness. Variations in mortality rates over time may be partly due to improvements in certification, as well as the altered perception of AF amongst the public and certifying doctors[26]. There is likely to be some underestimation of mortality in the GBD database as there will be cases in which death is attributed to secondary sequalae of atrial fibrillation. However, the GBD study attributes each death to a single underlying cause “that initiated the series of events leading to death”. This implies that deaths from, for example, heart failure or stroke that are the result of AF, should be listed as such. It is also the case that our study is mainly interested in trends within nations and comparisons between nations and as such as long as the methodology is not varying, our results are still valid.

Unfortunately, correcting for residual confounders such as social class, obesity, smoking and alcohol use was not possible due to such information not being available within the GBD database. Although AF and flutter were classified together based on the available granularity of the data in the GBD database, we recognise that the two arrhythmias do not carry the same risk, with higher rates of stroke, hospitalisation for heart failure and mortality in patients with AF versus flutter[27].

Whilst assumptions are made regarding the relationship between AF trends and economic output in European countries, it is worth noting that all countries in the analysis are relatively wealthy compared to the global mean GDP per capita and are considered 'developed'.

With regards to the use of Joinpoint regression analysis; imputing missing data using the last observation carried forward method would likely underestimate incidence and mortality rates; whilst data imputed using this method is of questionable veracity, it likely had minimal impact due to the low amount of missing data to begin with. As a descriptive analysis of the observational data, explanations for trends remain speculative and we are unable to make causal statements.

Conclusion

AF incidence and mortality does not show a general rise or fall across European countries between 1990 and 2017 but there are unique patterns for specific nations. Overall, AF-related mortality is increasing more rapidly than AF incidence in the highest GDP countries. As a result, AF-related mortality is significantly greater in higher GDP versus lower GDP countries. We outline potential reasons for this above; a survivor effect is one possibility with patients surviving long enough to suffer AF and its adverse consequences in higher GDP countries. MIRs are rising faster in the highest GDP nations which is consistent with this hypothesis. We also find elevated MIRs in women compared with men in all European countries, perhaps relating to biological difference and/or healthcare disparity. That this difference is as low as 5.4% in some nations and as high as 74.5% in other nations suggests that nations can learn from each other regarding how to improve these sex disparities in outcomes in AF.

References

1. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, Gillum RF, Kim YH, McAnulty JH, Zheng ZJ, Forouzanfar MH, Naghavi M, Mensah GA, Ezzati M, Murray CJL. Worldwide epidemiology of atrial fibrillation: A global burden of disease 2010 study. Circulation. 2014;129(8):837–47.
2. Stewart S. Cost of an emerging epidemic: an economic analysis of atrial fibrillation in the UK. Heart [Internet]. 2004;90(3):286–92. Available from: http://heart.bmj.com/cgi/doi/10.1136/hrt.2002.008748
3. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, Boriani G, Castella M, Dan G-A, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau J-P, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL, Kirchhof P, Kühne M, Aboyans V, Ahlsson A, Balsam P, Bauersachs J, Benussi S, Brandes A, Braunschweig F, Camm AJ, Capodanno D, Casadei B, Conen D, Crijns HJGM, Delgado V, Dobrev D, Drexel H, Eckardt L, Fitzsimons D, Folliguet T, Gale CP, Gorenek B, Haeusler KG, Heidbuchel H, Iung B, Katus HA, Kotecha D, Landmesser U, Leclercq C, Lewis BS, Mascherbauer J, Merino JL, Merkely B, Mont L, Mueller C, Nagy K V, Oldgren J, Pavlović N, Pedretti RFE, Petersen SE, Piccini JP, Popescu BA, Pürerfellner H, Richter DJ, Roffi M, Rubboli A, Scherr D, Schnabel RB, Simpson IA, Shlyakhto E, Sinner MF, Steffel J, Sousa-Uva M, Suwalski P, Svetlosak M, Touyz RM, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, Boriani G, Castella M, Dan G-A, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau J-P, Lettino M, Lip GYH, Pinto FJ, Neil Thomas G, Valgimigli M, Van Gelder IC, Watkins CL. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS).

Eur Heart J. 2020;

4. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1459–544.

5. Stewart S, Hart CL, Hole DJ, McMurray JJV. A population-based study of the long-term risks associated with atrial fibrillation: 20-Year follow-up of the Renfrew/Paisley study. Am J Med. 2002;113(5):359–64.

6. Wolrd Bank Database [Internet]. [cited 2020 May 14]. Available from: https://www.worldbank.org

7. Ahmad OB, Boschi-pinto C, Lopez AD. Age standardization of rates: a new WHO standard. GPE Discuss Pap Ser. 2001;(31):1–14.

8. Hartley A, Marshall DC, Salciccioli JD, Sikkel MB, Maruthappu M, Shalhoub J. Trends in mortality from ischemic heart disease and cerebrovascular disease in Europe: 1980 to 2009. Circulation. 2016;133(20):1916–26.

9. Krijthe BP, Kunst A, Benjamin EJ, Lip GYH, Franco OH, Hofman A, Witteman JCM, Stricker BH, Heeringa J. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. Eur Heart J. 2013;34(35):2746–51.

10. Colilla S, Crow A, Petkun W, Singer DE, Simon T, Liu X. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. Am J Cardiol [Internet]. 2013;112(8):1142–7. Available from: http://dx.doi.org/10.1016/j.amjcard.2013.05.063

11. Mackenbach JP, Stirbu I, Roskam A-JR, Schaap MM, Menvielle G, Leinsalu M, Kunst AE. Health Inequalities in Europe. N Engl J Med [Internet]. 2008;358(23):2468–81.

Available from: www.nejm.org

12. Sorbets E, Fox KM, Elbez Y, Danchin N, Dorian P, Ferrari R, Ford I, Greenlaw N, Kalra PR, Parma Z, Shalnova S, Tardif JC, Tendera M, Zamorano JL, Vidal-Petiot E, Steg PG. Long-term outcomes of chronic coronary syndrome worldwide: Insights from the international CLARIFY registry. Eur Heart J. 2020;41(3):347–55.

13. Wilkins E, Wilson L, Wickramasinghe K, Bhatnagar P. European Cardiovascular Disease Statistics 2017. Eur Hear Netw. 2012;10–123.

14. Kotseva K, Wood D, De Bacquer D, De Backer G, Rydén L, Jennings C, Gyberg V, Amouyel P, Bruthans J, Castro Conde A, Cífková R, Deckers JW, De Sutter J, Dilic M, Dolzhenko M, Erglis A, Fras Z, Gaita D, Gotcheva N, Goudevenos J, Heuschmann P, Laucevicius A, Lehto S, Lovic D, Mili D, Moore D, Nicolaides E, Oganov R, Pajak A, Pogosova N, Reiner Z, Stagmo M, Störk S, Tokgözolu L, Vulic D. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. Eur J Prev Cardiol. 2016;23(6):636–48.

15. Grasgruber P, Cacek J, Kalina T, Sebera M. The role of nutrition and genetics as key determinants of the positive height trend. Econ Hum Biol. 2014;(15):81–100.

16. Chugh SS, Roth GA, Gillum RF, Mensah GA. Global burden of atrial fibrillation in developed and developing nations. Global Heart. 2014.

17. IHME. Global Burden of Disease Study 2017. Lancet [Internet]. 2017;5:1–7. Available from: http://www.healthdata.org/sites/default/files/files/policy_report/2019/GBD_2017_Booklet.pdf

18. Marijon E, Le Heuzey J-Y, Connolly S, Yang S, Pogue J, Brueckmann M, Eikelboom J, Themeles E, Ezekowitz M, Wallentin L, Yusuf S. Causes of Death and Influencing

Factors in Patients With Atrial Fibrillation. Circulation. 2013;128(20):2192–201.

19. Roten L, Rimoldi S, Schwick N, Sakata T, Heimgartner C, Fuhrer J, Delacretaz E, Tanner H. Gender Differences in Patients Referred for Atrial Fibrillation Management to a Tertiary Center. Pacing Clin Electrophysiol. 2009;32:622–6.

20. Ball J, Carrington MJ, Wood KA, Stewart S. Women Versus Men with Chronic Atrial Fibrillation: Insights from the Standard Versus Atrial Fibrillation spEcific managemenT studY (SAFETY). PLoS One. 2013;8(5).

21. Nielsen PB, Skjøth F, Overvad TF, Larsen TB, Lip GYH. Female Sex Is a Risk Modifier Rather Than a Risk Factor for Stroke in Atrial Fibrillation. Circulation. 2018;137(8):832–40.

22. Poller L, Aronow WS, Karalis DG, Chandrasekaran K, Mintz GS, Petersen P, Boysen G, Godtfredsen J, Singer DE, Hughes RA, Gress DR, Sheehan MA, Oertel LB, Maraventano SW, Blewett DR, Rosner B, Kistler JP, Chesebro JH, Fuster V, Halperin JL. The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. N Engl J Med. 1991;325(2):129–32.

23. Andersson T, Magnuson A, Bryngelsson IL, Frøbert O, Henriksson KM, Edvardsson N, Poçi D. All-cause mortality in 272 186 patients hospitalized with incident atrial fibrillation 1995-2008: A Swedish nationwide long-term case-control study. Eur Heart J. 2013;34(14):1061–7.

24. Bowling A, Bond M, McKee D, McClay M, Blackman I, Banning AP, Dudley N, Elder A, Martin A. Equity in access to exercise tolerance testing, coronary angiography, and coronary artery bypass grafting by age, sex and clinical indications. Heart. 2001;85(6):680–6.

25. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328

diseases and injuries for 195 countries, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1211–59.

26. Duncan ME, Pitcher A, Goldacre MJ. Atrial fibrillation as a cause of death increased steeply in England between 1995 and 2010. Europace. 2014;16(6):797–802.

27. Lin YS, Chen TH, Chi CC, Lin MS, Tung TH, Liu CH, Chen YL, Chen MC. Different implications of heart failure, ischemic stroke, and mortality between nonvalvular atrial fibrillation and atrial flutter-A view from a national cohort study. J Am Heart Assoc. 2017;6(7).

28. Durkheim É. Suicide: A study in sociology. Suicide: A Study in Sociology. 2005. 1–374 p.

29. Piantadosi S, Byar DP, Green SB. The ecological fallacy. Am J Epidemiol. 1988;127(5):893–904.

30. Masood M, Reidpath DD. Effect of national wealth on BMI: An analysis of 206,266 individuals in 70 low-, middle-and high-income countries. PLoS One. 2017;12(6).

31. Misialek JR, Rose KM, Everson-Rose SA, Soliman EZ, Clark CJ, Lopez FL, Alonso A. Socioeconomic status and the incidence of atrial fibrillation in whites and blacks: The Atherosclerosis Risk in Communities (ARIC) Study. J Am Heart Assoc. 2014;3(4).

Figure Legends

Figure 1. Trends in age-standardised incidence rates per 100,000 for atrial fibrillation throughout Europe. Countries are categorised based on whether they are above (A) the mean EU GDP per capita, or below (B). Open squares indicate males, and solid circles indicate females. Estimated annual percentage change is overlaid with red indicating males, and blue indicating females; Significant periods of change are demarcated.

Figure 2. Trends in age-standardised mortality rates per 100,000 for atrial fibrillation throughout Europe. Countries are categorised based on whether they are above (A) the mean EU GDP per capita, or below (B). Open squares indicate males, and solid circles indicate females. Estimated annual percentage change is overlaid with red indicating males, and blue indicating females; Significant periods of change are demarcated.

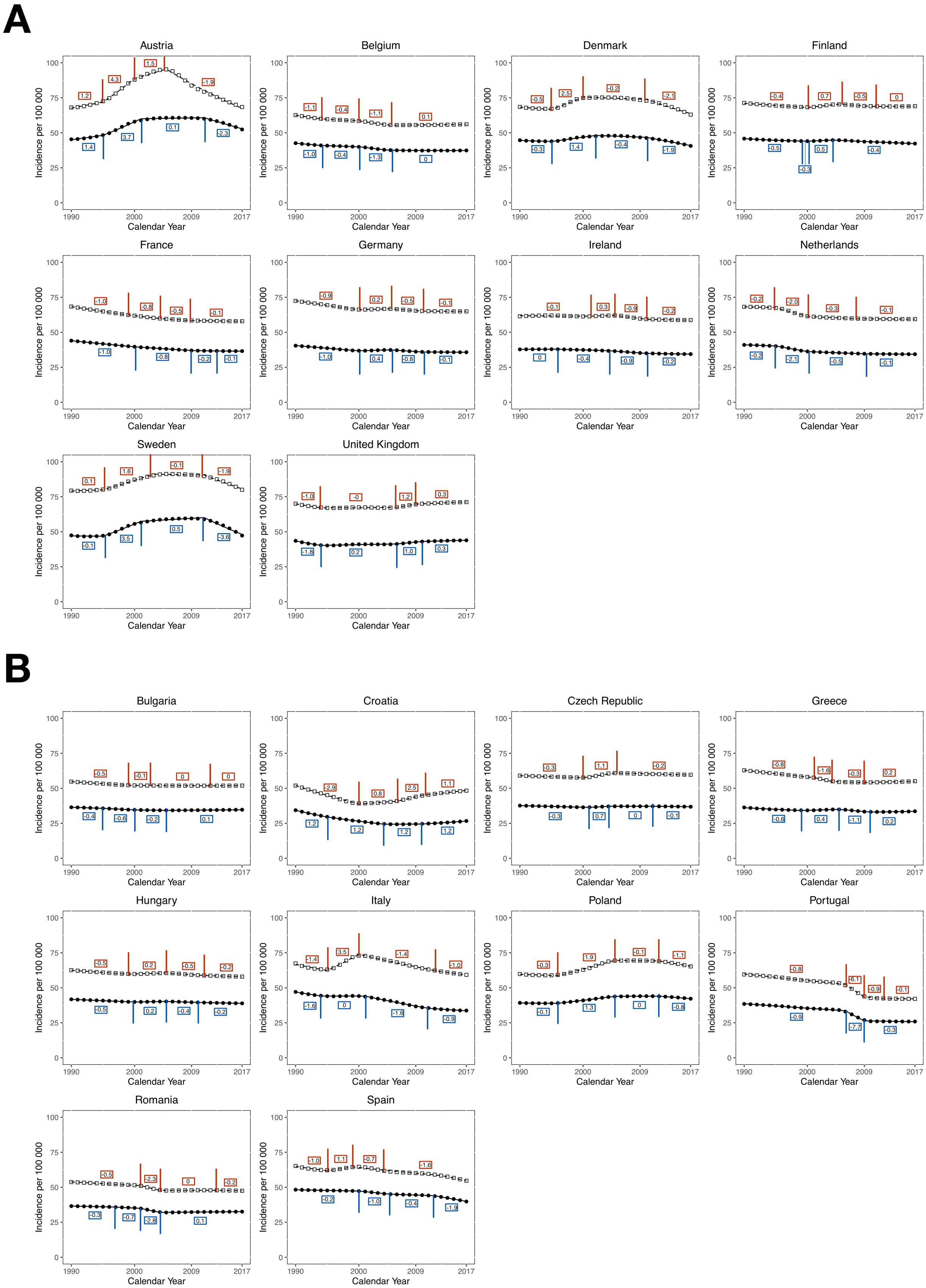
Figure 3. Age-standardised incidence rates per 100,000 in 2017 (males, **A** and females, **B**) and age-standardised death rates per 100,000 in 2017 (males, **C** and females, **D**) for atrial fibrillation.

Figure 4. Differences in age-standardised death rates per 100,000 from 2015-2017 between relative upper and lower GDP per capita countries, in males (A) and females (B). Significant differences were found between upper versus lower income countries in both men ($p = 0.0073$) and women ($p = 0.0010$).

Figure 5. Trends in mortality to incidence ratios (denoted as ASDR/ASIR) for atrial fibrillation throughout Europe. Countries are categorised based on whether they are above (A) the mean EU GDP per capita or below (B). Open squares indicate males, and solid circles indicate females. *ASDR, age standardized death rate; ASIR, age standardized incidence rate.*

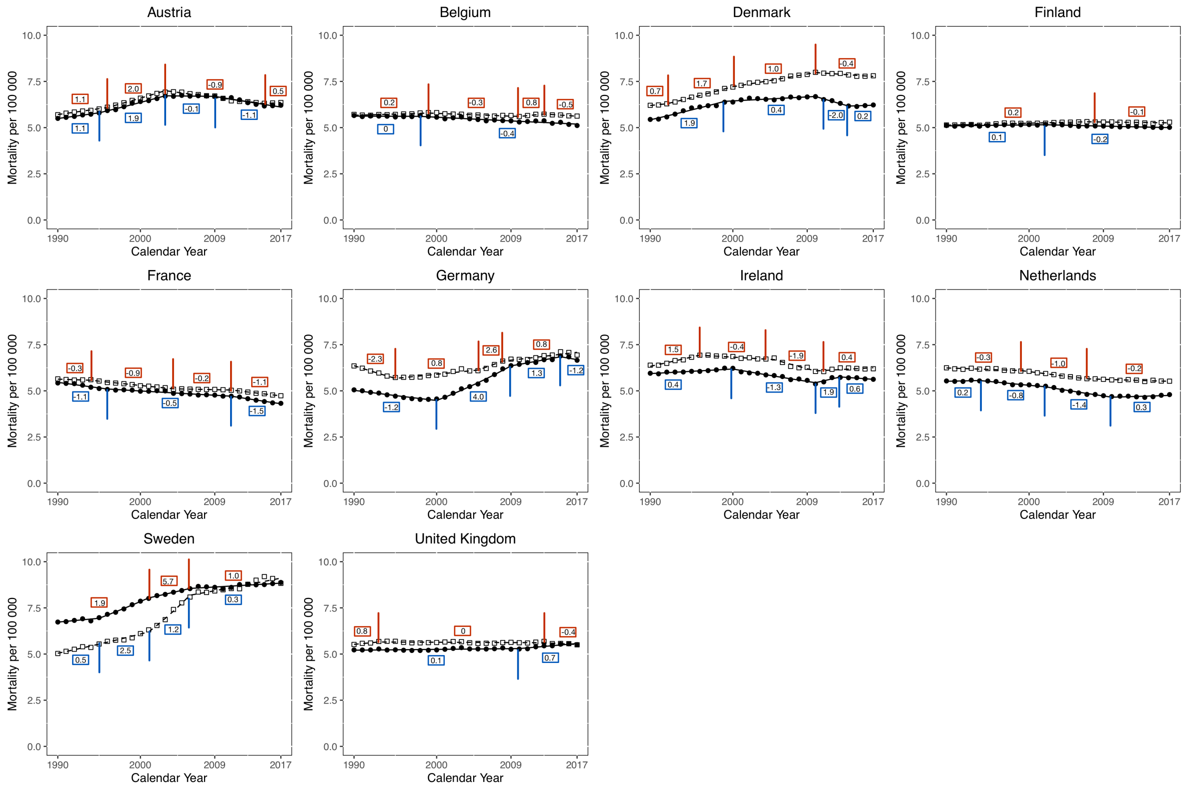
Supplementary Figure Legends

Supplementary Figure 1. Differences in age-standardised death rates per 100,000 in 2017 between Eastern and Western European countries, in males (A) and females (B). Significance was found between Eastern and Western European countries in females with $p = 0.0038$.

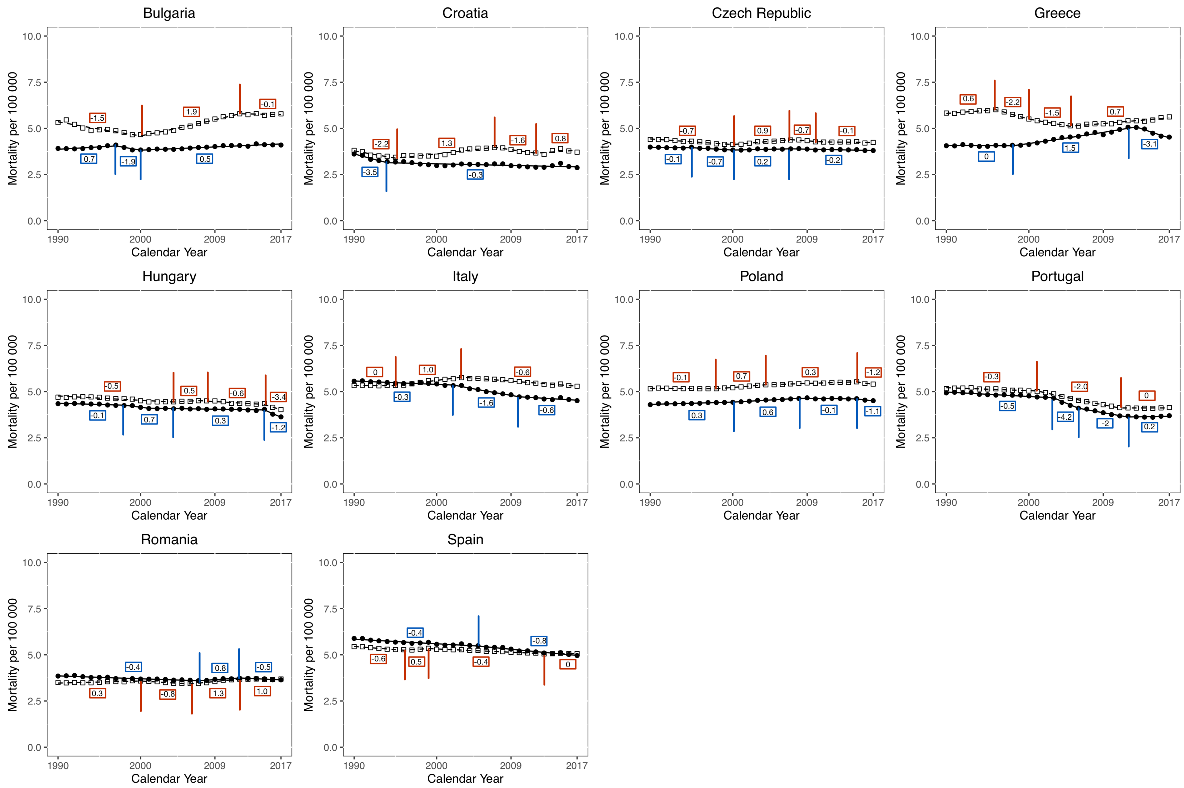


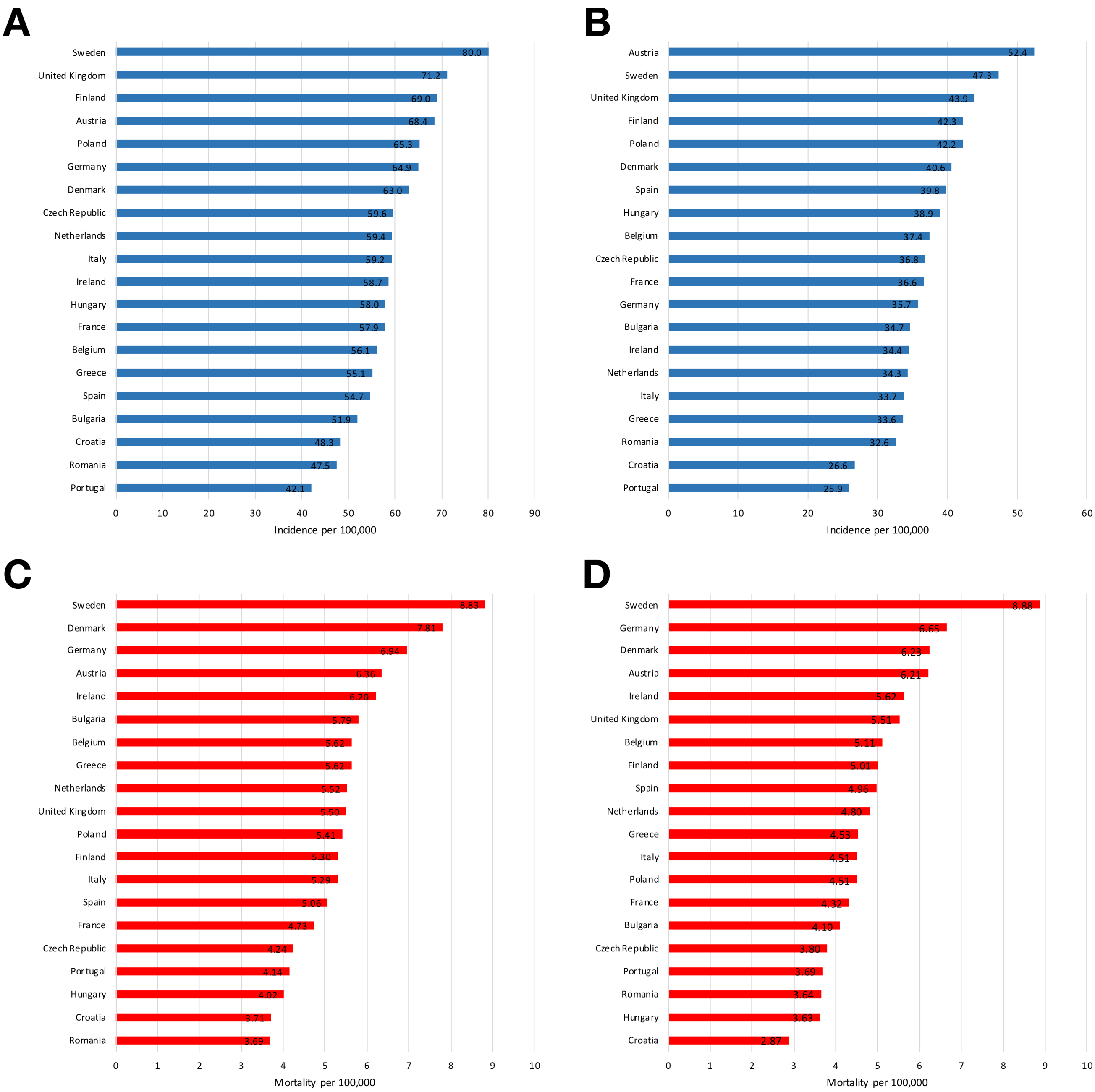
A
Austria
Belgium
Denmark
Finland
France
Germany
Ireland
Netherlands
Sweden
United Kingdom
B
Bulgaria
Croatia
Czech Republic
Greece
Hungary
Italy
Poland
Portugal
Romania
Spain
Incidence per 100 000
Calendar Year

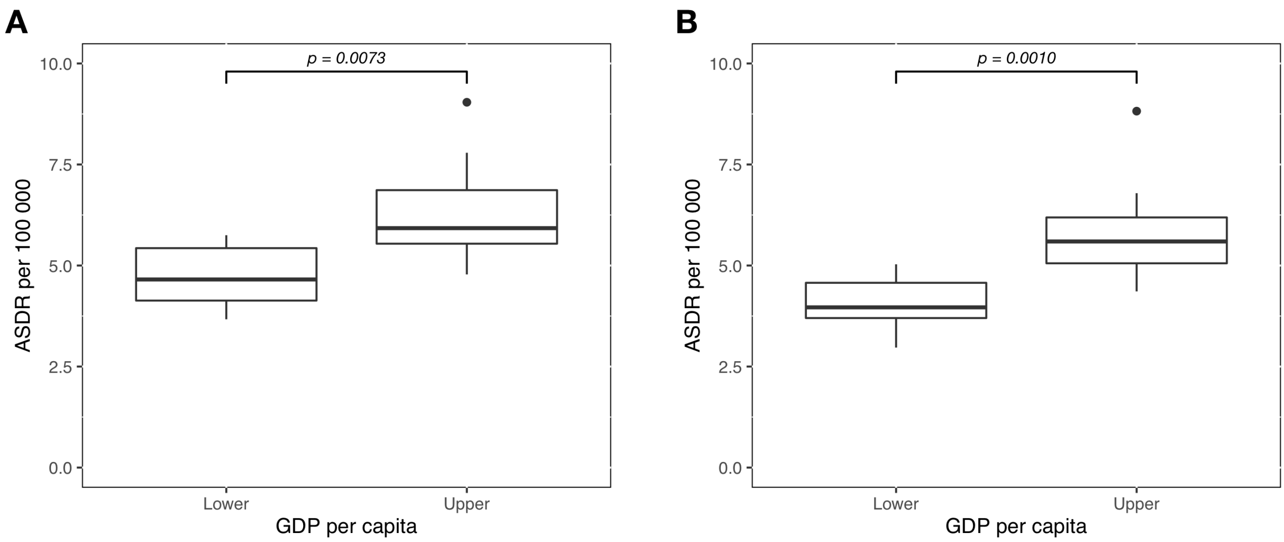
A

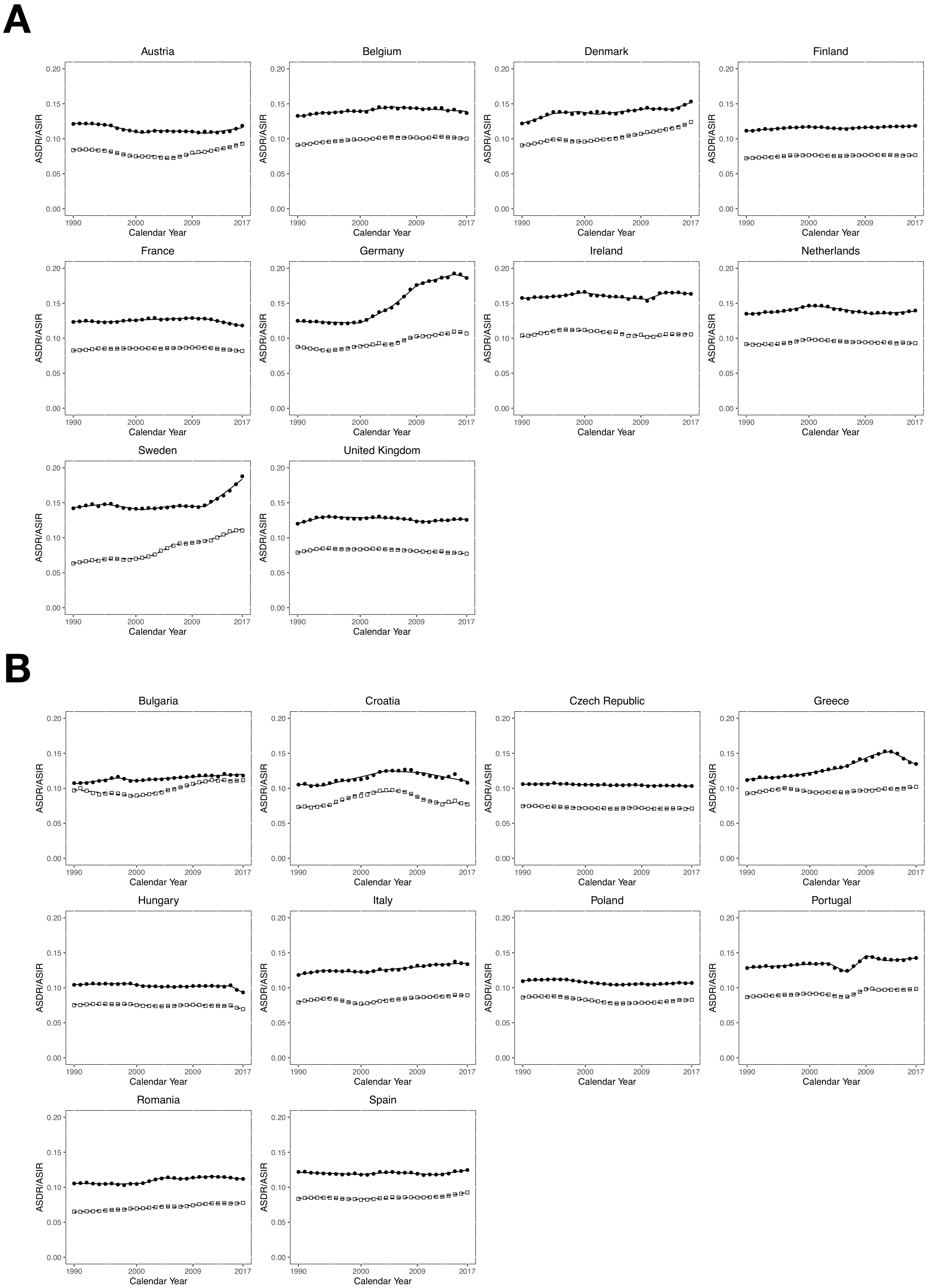

Austria
Belgium
Denmark
Finland
France
Germany
Ireland
Netherlands
Sweden
United Kingdom
Mortality per 100 000
Calendar Year

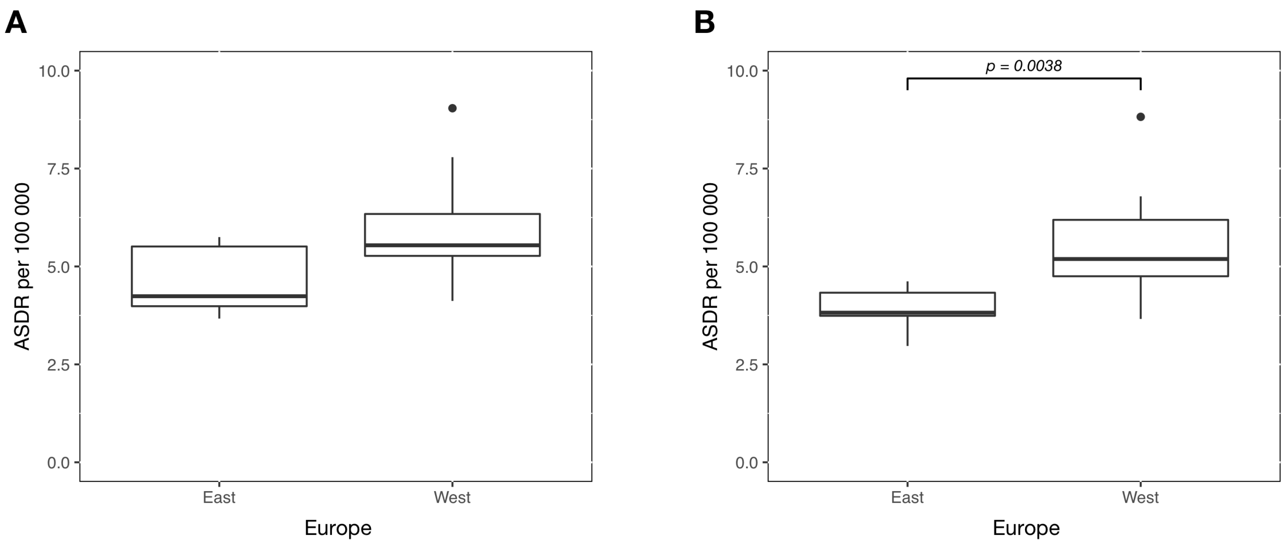
B


Bulgaria
Croatia
Czech Republic
Greece
Hungary
Italy
Poland
Portugal
Romania
Spain
Mortality per 100 000
Calendar Year


A
Sweden 80.0
United Kingdom 71.2
Finland 69.0
Austria 68.4
Poland 65.3
Germany 64.9
Denmark 63.0
Czech Republic 59.6
Netherlands 59.4
Italy 59.2
Ireland 58.7
Hungary 58.0
France 57.9
Belgium 56.1
Greece 55.1
Spain 54.7
Bulgaria 51.9
Croatia 48.3
Romania 47.5
Portugal 42.1
0 10 20 30 40 50 60 70 80 90
Incidence per 100,000
B
Austria 52.4
Sweden 47.3
United Kingdom 43.9
Finland 42.3
Poland 42.2
Denmark 40.6
Spain 39.8
Hungary 38.9
Belgium 37.4
Czech Republic 36.8
France 36.6
Germany 35.7
Bulgaria 34.7
Ireland 34.4
Netherlands 34.3
Italy 33.7
Greece 33.6
Romania 32.6
Croatia 26.6
Portugal 25.9
0 10 20 30 40 50 60
Incidence per 100,000
C
Sweden 8.83
Denmark 7.81
Germany 6.94
Austria 6.36
Ireland 6.20
Bulgaria 5.79
Belgium 5.62
Greece 5.62
Netherlands 5.52
United Kingdom 5.50
Poland 5.41
Finland 5.30
Italy 5.29
Spain 5.06
France 4.73
Czech Republic 4.24
Portugal 4.14
Hungary 4.02
Croatia 3.71
Romania 3.69
0 1 2 3 4 5 6 7 8 9 10
Mortality per 100,000
D
Sweden 8.88
Germany 6.65
Denmark 6.23
Austria 6.21
Ireland 5.62
United Kingdom 5.51
Belgium 5.11
Finland 5.01
Spain 4.96
Netherlands 4.80
Greece 4.53
Italy 4.51
Poland 4.51
France 4.32
Bulgaria 4.10
Czech Republic 3.80
Portugal 3.69
Romania 3.64
Hungary 3.63
Croatia 2.87
0 1 2 3 4 5 6 7 8 9 10
Mortality per 100,000


A
B
p = 0.0073
p = 0.0010
ASDR per 100 000
10.0
7.5
5.0
2.5
0.0
Lower
Upper
GDP per capita


A
Austria
Belgium
Denmark
Finland
France
Germany
Ireland
Netherlands
Sweden
United Kingdom
B
Bulgaria
Croatia
Czech Republic
Greece
Hungary
Italy
Poland
Portugal
Romania
Spain
ASDR/ASIR
0.00
0.05
0.10
0.15
0.20
Calendar Year
1990
2000
2009
2017


A
B
10.0
7.5
5.0
2.5
0.0
ASDR per 100 000
East
West
Europe
p = 0.0038

1A

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1990-1995	1.2 (0.6 – 1.9)	1995-2000	4.3 (3.4 – 5.2)	2000-2005	1.5 (0.6 – 2.3)	2005-2017	-2.9 (-3 – -2.7)
Belgium	1990-1994	-1.1 (-1.1 – -0.4)	1994-2000	-0.4 (-0.5 – -0.3)	2000-2005	-1.1 (-1.2 – -1)	2005-2017	0.1 (0.1 – 0.1)
Bulgaria	1990-1999	-0.5 (-0.6 – -0.5)	1999-2002	-0.1 (-0.2 – 0)	2002-2011	0	2011-2017	0
Croatia	1990-2000	-2.9 (-3 – -2.8)	2000-2006	0.8 (0.6 – 1.1)	2006-2010	2.5 (2 – 3)	2010-2017	1.1 (0.9 – 1.2)
Czech Republic	1990-2000	-0.3 (-0.3 – 1.2)	2000-2005	1.1 (1.1 – 1.2)	2005-2017	-0.2 (-0.3 – -0.2)		
Denmark	1990-1995	-0.5 (-0.8 – -0.2)	1995-2000	2.5 (2.1 – 3)	2000-2010	-0.2 (-0.3 – -0.1)	2010-2017	-2.1 (-2.3 – -1.9)
Finland	1990-2000	-0.4 (-0.5 – -0.4)	2000-2005	0.7 (0.6 – 0.8)	2005-2010	-0.5 (-0.6 – -0.4)	2010-2017	0 (0 – 0.1)
France	1990-1999	-1 (-1 – -0.8)	1999-2004	-0.8 (-0.9 – -0.8)	2004-2009	-0.5 (-0.5 – -0.5)	2009-2017	-0.1 (-0.1 – -0.1)
Germany	1990-2000	-0.9 (-1 – -0.9)	2000-2005	0.2 (0.1 – 0.3)	2005-2010	-0.5 (-0.6 – -0.4)	2010-2017	-0.1 (-0.1 – 0)
Greece	1990-2001	-0.8 (-0.8 – -0.8)	2001-2004	-1.6 (-2 – -1.3)	2004-2009	-0.3 (-0.3 – -0.2)	2009-2017	0.2 (0.2 – 0.2)
Hungary	1990-1999	-0.5 (-0.5 – -0.5)	1999-2005	0.2 (0.2 – 0.3)	2005-2011	-0.5 (-0.5 – -0.5)	2011-2017	-0.2 (-0.3 – -0.2)
Ireland	1990-2001	-0.1 (-0.1 – 0)	2001-2005	0.3 (-0.2 – 0.7)	2005-2010	-0.9 (-1.2 – -0.6)	2010-2017	-0.2 (-0.3 – 0)
Italy	1990-1995	-1.4 (-1.6 – -1.1)	1995-2000	3.5 (3.1 – 3.9)	2000-2012	-1.4 (-1.5 – -1.3)	2012-2017	-1 (-1.3 – -0.8)
Netherlands	1990-1995	-0.2 (-0.2 – -0.1)	1995-2000	-2 (-2 – -1.9)	2000-2008	-0.3 (-0.4 – -0.3)	2008-2017	-0.1 (-0.1 – 0)
Poland	1990-1996	-0.3 (-0.4 – -0.3)	1996-2005	1.9 (1.8 – 2)	2005-2012	-0.1 (-0.3 – 0.1)	2012-2017	-1.1 (-1.3 – -0.9)
Portugal	1990-2006	-0.8 (-0.8 – -0.8)	2006-2009	-6.1 (-6.9 – -5.4)	2009-2012	-0.9 (-1.7 – -0.2)	2012-2017	-0.1 (-0.1 – -0.1)
Romania	1990-2001	-0.5 (-0.5 – -0.4)	2001-2004	-2.3 (-2.4 – 2.1)	2004-2013	0	2013-2017	-0.2 (-0.2 – 0.1)
Spain	1990-1995	-1 (-1.4 – -0.6)	1995-1999	1.1 (0.2 – 2)	1999-2013	-0.7 (-0.8 – -0.6)	2013-2017	-1.6 (-2.1 – -1)
Sweden	1990-1995	0.1 (0 – 1.5)	1995-2003	1.6 (1.5 – 1.8)	2003-2011	-0.1 (-0.2 – 0.1)	2011-2017	-1.9 (-2.1 – -1.7)
United Kingdom	1990-1994	-1 (-1.2 – -0.9)	1994-2006	0 (0 – 0.1)	2006-2009	1.2 (0.7 – 1.7)	2009-2017	0.3 (0.3 – 0.4)

1B

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1990-1995	1.4 (1 – 1.8)	1995-2001	3.7 (3.3 – 4.1)	2001-2011	0.1 (0 – 0.3)	2011-2017	-2.3 (-2.6 – -2)
Belgium	1990-1994	-1 (-1.1 – -0.8)	1994-2000	-0.4 (-0.5 – -0.3)	2000-2005	-1.3 (-1.4 – -1.2)	2005-2017	0 (-0.1 – 0)
Bulgaria	1990-1995	-0.4 (-0.5 – -0.4)	1995-2000	-0.6 (-0.7 – -0.6)	2000-2005	-0.2 (-0.2 – -0.1)	2005-2017	0.1 (0.1 – 0.1)
Croatia	1990-1995	-3 (-3.1 – -2.8)	1995-2004	-2.1 (-2.2 – -2)	2004-2010	-0.1 (-0.1 – 0.2)	2010-2017	1.2 (1.1 – 1.3)
Czech Republic	1990-2001	-0.3 (-0.3 – -0.3)	2001-2004	0.7 (0.6 – 0.8)	2004-2011	0	2011-2017	-0.1 (-0.2 – -0.1)
Denmark	1990-1995	-0.3 (-0.6 – -0)	1995-2002	1.4 (1.1 – 1.6)	2002-2010	-0.4 (-0.5 – -0.2)	2010-201	-1.9 (-2.1 – -1.7)
Finland	1990-1999	-0.5 (-0.6 – -0.4)	1999-2000	-0.3 (-0.4 – -0.1)	2000-2004	0.5 (0.2 – 0.7)	2004-2017	-0.4 (-0.5 – -0.4)
France	1990-2000	-1 (-1 – -1)	2000-2009	-0.8 (-0.8 – -0.8)	2009-2013	-0.2 (-0.3 – -0.2)	2013-2017	-0.1 (-0.1 – 0)
Germany	1990-2000	-1 (-1 – -0.9)	2000-2005	0.4 (0.3 – 0.5)	2005-2010	-0.8 (-0.9 – -0.7)	2010-2017	-0.1 (-0.1 – 0)
Greece	1990-1999	-0.6 (-0.7 – -0.6)	1999-2005	0.4 (0.2 – 0.6)	2005-2010	-1.1 (-1.4 – -0.9)	2010-2017	0.2 (0.1 – 0.3)
Hungary	1990-2000	-0.5 (-0.5 – 0.5)	2000-2005	0.2 (0.1 – 0.3)	2005-2010	-0.4 (-0.4 – 0.3)	2010-2017	-0.2 (-0.3 – -0.2)
Ireland	1990-1996	0 (0 – 0.1)	1996-2004	-0.4 (-0.4 – 0.3)	2004-2010	-0.9 (-0.9 – -0.8)	2010-2017	-0.2 (-0.2 – -0.2)
Italy	1990-1994	-1.6 (-1.9 – -1.2)	1994-2001	0 (-0.2 – 0.2)	2001-2011	-1.6 (-2.3 – -2.1)	2011-2017	-0.9 (-1.1 – -0.7)
Netherlands	1990-1995	-0.2 (-0.2 – 0)	1995-2000	-2.1 (-2.1 – -2)	2000-2009	-0.5 (-0.5 – -0.5)	2009-2017	-0.1 (-0.1 – -0.1)
Poland	1990-1996	-0.1 (-0.2 – 0)	1996-2005	1.3 (1.3 – 1.4)	2005-2012	0	2012-2017	-0.8 (-0.9 – -0.7)
Portugal	1990-2006	-0.9 (-0.9 – -0.8)	2006-2009	-7.7 (-8.4 – -0.2)	2009-2017	-0.3 (-0.3 – -0.2)		
Romania	1990-1997	-0.3 (-0.3 – -0.2)	1997-2001	-0.7 (-0.8 – -0.5)	2001-2004	-2.8 (-3.1 – - 2.5)	2004-2017	0.1 (0.1 – 0.1)
Spain	1990-2000	-0.2 (-0.2 – -0.2)	2000-2005	-1 (-1.1 – -0.8)	2005-2012	-0.4 (-0.4 – -0.3)	2012-2017	-1.9 (-2 – -1.8)
Sweden	1990-1995	-0.1 (-0.6 – 0.4)	1995-2001	3.5 (3 – 4)	2001-2011	0.5 (0.2 – 0.7)	2011-2017	-3.6 (-4 – -3.3)
United Kingdom	1990-1994	-1.8 (-2.2 – -0.5)	1994-2006	0.2 (0.1 – 0.3)	2006-2010	1 (0.5 – 1.6)	2010-2017	0.3 (0.1 – 0.4)

Supplementary Table 1: Joinpoint analysis accompanying Figure 1 for atrial fibrillation age-standardised incidence rates in males (A) and females (B). Estimated Annual Percentage Change (EAPC) is shown with 95% confidence intervals in brackets.

2A

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1990-1996	1.1 (0.9 – 1.3)	1996-2003	2 (1.8) – 2.2)	2003-2015	-0.9 (-1 – -0.8)	2015-2017	0.5 (-0.8 – 1.8)
Belgium	1990-1999	0.2 (0.1 – 0.4)	1999-2010	-0.3 (-0.4 – -0.2)	2010-2013	0.8 (-0.6 – 2.1)	2013-2017	-0.5 (-1 – -0.1)
Bulgaria	1990-2000	-1.5 (-1.8 – -1.2)	2000-2012	1.9 (1.7 – 2.2)	2012-2017	-0.1 (-1 – 0.8)		
Croatia	1990-1995	-2.2 (-3.6 – -0.7)	1995-2007	1.3 (0.9 – 1.8)	2007-2012	-1.6 (-3.7 – 0.5)	2012-2017	0.8 (-0.7 – 2.3)
Czech Republic	1990-2000	-0.7 (-0.8 – -0.6)	2000-2007	0.9 (0.6 – 1.2)	2007-2011	-0.7 (-1.6 – 0.1)	2011-2017	-0.1 (-0.4 – 0.2)
Denmark	1990-1992	0.7 (-0.6 – 2.1)	1992-2000	1.7 (1.5 – 1.9)	2000-2010	1 (0.9 – 1.1)	2010-2017	-0.4 (-0.6 – -0.2)
Finland	1990-2007	0.2 (0.2 – 0.2)	2007-2017	-0.1 (-0.2 – 0.2)				
France	1990-1994	-0.3 (-0.5 – -0.1)	1994-2004	-0.9 (-0.9 – -0.8)	2004-2011	-0.2 (-0.3 – -1.2)	2011-2017	-1.1 (-1.2 – -1)
Germany	1990-1995	-2.3 (-2.9 – -1.6)	1995-2005	0.8 (0.5 – 1.1)	2005-2008	2.6 (-0.6 – 5.8)	2008-2017	0.8 (0.5 – 1.1)
Greece	1990-1996	0.6 (0.2 – 0.9)	1996-2000	-2.2 (-3.1 – -1.2)	2000-2005	-1.5 (-2 – -0.9)	2005-2017	0.7 (0.6 – 0.8)
Hungary	1990-2004	-0.5 (-0.6 – -0.4)	2004-2007	0.5 (-2.1 – 3.2)	2007-2015	-0.6 (-0.9 – -0.2)	2015-2017	-3.4 (-5.9 – -0.8)
Ireland	1990-1996	1.5 (1.1 – 2)	1996-2005	-0.4 (-0.7 – -0.1)	2005-2010	-1.9 (-2.6 – -1.2)	2010-2017	0.4 (0.1 – 0.7)
Italy	1990-1995	0 (-0.4 – 0.3)	1995-2003	1 (0.8 – 1.3)	2003-2017	-0.6 (-0.7 – -0.6)		
Netherlands	1990-1999	-0.3 (-0.4 – -0.1)	1999-2007	-1 (-1.1 – -0.8)	2007-2017	-0.2 (-0.3 – -0.1)		
Poland	1990-1998	-0.1 (-0.1 – 0)	1998-2004	0.7 (0.5 – 0.9)	2004-2015	0.3 (0.2 – 0.3)	2015-2017	-1.2 (-2 – -0.4)
Portugal	1990-2001	-0.3 (-0.4 – 0.2)	2001-2011	-2 (-2.1 – 1.9)	2011-2017	0 (-0.2 – 0.2)		
Romania	1990-2000	0.3 (0.2 – 0.4)	2000-2006	-0.8 (-1.1 – 0.4)	2006-2012	1.3 (0.9 – 1.6)	2012-2017	-0.1 (-0.4 – 0.2)
Spain	1990-1996	-0.6 (-0.7 – -0.5)	1996-1999	0.5 (-0.2 – 1.3)	1999-2013	-0.4 (-0.4 – -0.3)	2013-2017	0 (-0.2 – 0.2)
Sweden	1990-2001	1.9 (1.6 – 2.2)	2001-2006	5.7 (4.4 – 7)	2006-2017	1 (0.7 – 1.2)		
United Kingdom	1990-1993	0.8 (-0.1 – 1.6)	1993-2013	0 (-0.1 – 0)	2013-2017	-0.4 (-1 – 0.1)		

2B

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1990-1995	1.1 (0.5 – 1.6)	1995-2003	1.9 (1.5 – 2.2)	2003-2009	-0.1 (-0.6 – 0.5)	2009-2017	-1.1 (-1.4 – -0.9)
Belgium	1990-1998	0 (-0.3 – 0.2)	1998-2017	-0.4 (-0.5 – -0.3)				
Bulgaria	1990-1997	0.7 (0.3 – 0.6)	1997-2000	-1.9 (-4.4 – 0.6)	2000-2017	0.5 (0.4 – 0.6)		
Croatia	1990-1994	-3.5 (-5.4 – -0.2)	1994-2017	-0.3 (-0.5 – -0.2)				
Czech Republic	1990-1995	-0.1 (-0.4 – 0.2)	1995-2000	-0.7 (-1.1 – -0.2)	2000-2007	0.2 (0 – 0.5)	2007-2017	-0.2 (-0.3 – -0.1)
Denmark	1990-1999	1.9 (1.6 – 2.2)	1999-2010	0.4 (0.1 – 0.6)	2010-2014	-2 (-3.5 – 0.5)	2014-2017	0.2 (0.2 – 1.8)
Finland	1990-2002	0.1 (0 – 0.2)	2002-2017	-0.2 (-0.3 – -0.2)				
France	1990-1996	-1.1 (-1.5 – -0.8)	1996-2011	-0.5 (-0.6 – -0.4)	2011-2017	-1.5 (-1.8 – 5.8)		
Germany	1990-2000	-1.2 (-1.3 – -1)	2000-2009	4 (3.7 – 4.2)	2009-2015	1.3 (0.7 - 1.8)	2015-2017	-1.2 (-3.6 – 1.3)
Greece	1990-1998	0 (-0.4 – 0.3)	1998-2013	1.5 (1.3 – 1.7)	2013-2017	-3.1 (-4.1 – -2)		
Hungary	1990-1998	-0.1 (-0.1 – 0)	1998-2004	0.7 (0.5 – 0.9)	2004-2015	0.3 (0.2 – 0.3)	2015-2017	-1.2 (-2 – -0.4)
Ireland	1990-2000	0.4 (0.3 – 0.5)	2000-2010	-1.3 (-1.4 – 1.1)	2010-2013	1.9 (0.2 – 3.6)	2013-2017	-0.6 (-1.1 – 0)
Italy	1990-2002	-0.3 (-0.5 – -0.2)	2002-2010	-1.6 (-1.9 – -1.3)	2010-2017	-0.6 (-0.9 – -0.3)		
Netherlands	1990-1994	0.2 (-0.6 – 0.9)	1994-2002	-0.8 (-1.1 – -0.5)	2002-2010	-1.4 (-1.7 – -1.1)	2010-2017	0.3 (0 – 0.6)
Poland	1990-2000	0.3 (0.2 – 0.4)	2000-2008	0.6 (0.4 – 0.7)	2008-2015	-0.1 (-0.3 – 0.1)	2015-2017	-1.1 (-1.1 – 0.1)
Portugal	1990-2003	-0.5 (-0.6 – -0.4)	2003-2006	-4.2 (-5.8 – -2.6)	2006-2012	-2 (-2.4 – -1.7)	2012-2017	0.2 (-0.1 – 0.6)
Romania	1990-2007	-0.4 (-0.5 – -0.3)	2007-2012	0.8 (0.2 – 1.5)	2012-2017	-0.5 (-1 – -0.1)		
Spain	1990-2005	-0.4 (-0.5 – -0.7)	2005-2017	-0.8 (-0.9 – -0.7)				
Sweden	1990-1995	0.5 (0.2 – 1.1)	1995-2001	2.5 (2 – 1.9)	2001-2006	1.2 (0.6 – 1.9)	2006-2017	0.3 (0.2 – 0.4)
United Kingdom	1990-2010	0.1 (0 – 0.1)	2010-2017	0.7 (0.4 – 1)				

Supplementary Table 2: Joinpoint analysis accompanying Figure 2 for atrial fibrillation age-standardised death rates in males (A) and females (B). Estimated Annual Percentage Change (EAPC) is shown with 95% confidence intervals in brackets.