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Trends in Mortality from Ischaemic Heart Disease and Cerebrovascular Disease in Europe: 1980–2009

Running title: *Hartley et al.; Cardiovascular Mortality in Europe 1980-2009*

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Abstract

Background—Trends in cardiovascular mortality across Europe demonstrate significant geographical variation and an understanding of these has a central role in global public health.

Methods and Results—Ischaemic heart disease (IHD) and cerebrovascular disease (CVD) age standardised death rates (as per International Classification of Diseases ninth/ tenth editions) were collated from the World Health Organisation mortality database, for member states of the European Union. Trends were characterised by using Joinpoint regression analysis. An overall trend for reduction in IHD mortality is observed, most pronounced in Western Europe (greater than 60% for Netherlands, United Kingdom, Ireland) for both sexes 1980-2009. Eastern-European states – Romania, Croatia and Slovakia had very modest mortality reductions. Most recently (2009), Lithuania had the highest mortality for males and females (318.1/100,000 and 166.1/100,000 respectively), followed by Latvia and Slovakia. France had the lowest mortality - 39.8/100,000 for males and 14.7/100,000 for females. Analysis of CVD mortality revealed that Austria had the largest reduction for both sexes (76.8% males, 76.5% females) 1980-2009. The smallest improvement over this period is seen in Lithuania, Poland and Cyprus (-5% to +20% approximately). France has the lowest present-day CVD mortality for both males and females (23.9/100,000 and 17.3/100,000 respectively).

Conclusions—There is growing disparity in cardiovascular mortality between Western and Eastern Europe, for which diverse explanations are discussed. The need for population-wide health promotion and primary prevention policies are emphasized.

Key words: epidemiology; cardiovascular disease; cerebrovascular disorders

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Introduction

Cardiovascular disease is the leading cause of mortality worldwide[1] and trends in cardiovascular mortality have a crucial role in public health and epidemiology globally. This is an area of academic interest, and of great geographical variation.[2,3,4]

Analysis of cardiovascular mortality data relating to the Americas has demonstrated an inequality between the US and Canada, and Latin American nations, in age-standardised decline in cardiovascular mortality.[5] Previous studies on trends in Europe have highlighted a similar health gap between Western countries and Eastern, previously Communist-run, states.[2-4,6-8] Moreover, a North-East to South-West Europe gradient was identified in the 1980s.[6] Various hypotheses have been generated for this disparity, including lifestyle factors, diet and socioeconomic influences.[7]

No recent analysis comparing trends in cardiovascular mortality throughout Europe has been performed. The objective of this study was to describe current mortality rates for ischaemic heart disease (IHD) and cerebrovascular disease (CVD) across Europe. We also aimed to describe changes in IHD and CVD mortality between 1980-2009 and identify trends using Joinpoint analysis.

Methods

Data Sources

Mortality data for CVD and IHD for European countries were derived from the World Health Organisation (WHO) mortality database for the years 1980-2009.[9] The WHO evaluates the quality of the data to ensure comparability and reliability, without adjustment for under-reporting.[10] Member states of the European Union (EU) (28 countries as of 2015) were selected

to produce a defined group for analysis.[11] For simplicity and clarity mortality was restricted to that of CVD and IHD, excluding mortality from other cardiovascular causes. The mortality database is updated annually from deaths registered by national civil registration systems, International Classification of Diseases (ICD) coded, per 100,000 population. Data is collected according to ICD 9 and 10 publications, and is collated as per the 10th revision; a process which has been utilised previously with adequate validity and data robustness.[5] ICD codes were utilised for CVD mortality (430-438, I60-I69) and IHD mortality (410-414, I20-I25) for the 9th and 10th editions respectively.

The age-standardised death rate (ASDR) was calculated, defined as mortality weighted to the distribution of mortality per 5-year age group, according to the WHO standard population and world average age structure for 1998. This removes effects of historical events on age structure and controls for differences in age structure in populations, producing age-specific mortality rates, and more representative data.[12]

Estimated level of coverage for deaths with a recorded cause for death is calculated by actual reporting divided by estimated mortality rate. Population and birth recording in all countries exceeds 90%, as per the WHO standard for inclusion in the database.[13] Mortality data were missing in a small subset of countries for one or more calendar years. When values were not available, data from previous or subsequent years were replicated in a last observation carried forward method. A total of 4.7% of data were replicated from last and subsequent observations. Gender-specific trends in cardiovascular mortality are established and analysed for three-year periods every decade; in 1.1% averages were from two-year rather than three-year periods.

Statistical Analyses

Joinpoint regression analysis with annualised data (between 1979-2009, where available) was used to assess changes in linear slope for mortality trends over time,[14] as described previously by Rodriguez et al.[5] Briefly, Joinpoint analysis assesses the overall trends in mortality initially with no Joinpoints and tests for significant changes in the model with sequential addition of points where there is significant change in the slope of the line. Statistical trends were assessed using Joinpoint software (Version 4.1.1.1) provided by the United States National Cancer Institute Surveillance Research Program (http://surveillance.cancer.gov/joinpoint/). The model also computes an estimated annual percentage change (EAPC) for each trend by fitting a regression line to the natural logarithm of the rates.

Trends in IHD and CVD mortality are calculated as crude absolute differences between averaged 3-year data points for the earliest and most recent years available.

Differences in change in mortality between new EU-states and their older counterparts 1980-2009 were assessed with Wilcoxon rank-sum test. EU joining nations from 2004 or later were deemed 'new' – such countries include Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia and Slovenia.[11] Of note, Cyprus was excluded from this analysis owing to significantly outlying results based on few data points.

Post-Hoc Investigation

From the above *a priori* Joinpoint analyses, we observed a common trend in the decrease in mortality from IHD in the years following end of Communism. We performed a single *post-hoc* analysis to explore the overall effect that the end of Communism has on age-standardised death rates from IHD. For this investigation, all Communist countries were normalized to the year of the end of Communism, which is taken to be the reference year for trend analysis. We fitted a locally weighted scatterplot smoothing (LOWESS) line to age-standardised death rates in the

interval from 10 years prior to reference year until 20 years after the reference year. LOWESS regression is a standard non-parametric smoothing procedure which makes minimal assumptions about the data and corrects for the influence of outliers from the trend to obtain a more robust trend estimate. Plots with 95% confidence bands from this analysis were inspected visually to ascertain trends in the data. LOWESS regression analysis was performed using SAS software v9.4 (SAS Institute, Cary, NC, USA).

Results

Over the 30-year period studied, significant changes in cardiovascular mortality were observed across the EU. All countries have an estimated level of coverage of deaths that are registered with cause of death data of >95%, with the exception of Cyprus (>78.2%) and Croatia (>94.9%) (WHO, Census and civil registration coverage data by country, 2014). The quality and robustness of the data collected has been reviewed previously.[15] Of the 28 countries included in the analysis 24 had quality of reporting graded as 'High' or 'Medium'. A total of four of the countries (Cyprus, Greece, Poland, Portugal), assessed in this analysis were graded to have 'Low' reporting. Values were replicated from last and subsequent observations in 4.7% of data points, owing to incomplete reporting.

There was a statistically significant greater mortality reduction for both IHD ($p<0.01$) and CVD ($p<0.01$) when comparing older, and newer (2004 or later) EU countries. This is displayed in **Figure 1 A and B**, for IHD and CVD respectively.

Trends in IHD Mortality

Figure 2 and **Supplement Table 1** show IHD mortality from 1980-2009 for each country per gender. No data were available for EU member states Malta and Luxembourg on the WHO

mortality database, so have been omitted from further analysis.

The overall trend in IHD mortality across Europe was observed to be decreasing steadily over time. Western European countries and founder EU member states show the greatest reduction in mortality (**Figure 2**). The largest decrease was seen in the Netherlands (73.8% males, 72.0% females) and United Kingdom (67.3% males, 65.9% females) from 1980-2009. Very modest reductions in mortality were observed in previous member states of the Soviet Union and Eastern Europe 1980-2009, such as Lithuania (-13.1%, -30.4%), Poland (-14.4%, +16.1%), Hungary (-13.1%, -1.9%) and Slovakia (-7.0%, +4.8%) for males and females respectively. Furthermore, unfavourable trends in IHD mortality were observed from 1980-2009 in Croatia (+43.3%, +124.5%), Cyprus (+418.3%, +320.1%) and Romania (+30.2%, +14.8%) for males and females respectively. It should be noted that the IHD mortality figures for Cyprus (+418.3% for males and +320.1% for females) are based on only two time points with low mortality rates, adding ambiguity to the interpretation of these data.

Current IHD Mortality

Figure 3 A and B depict age-standardised death from IHD per 100,000 males and females respectively in 2009, to provide the most recent overview of mortality rate in EU member states. However, for Denmark and Belgium 2006 data was utilised, and 2008 data for France and Italy; these being the most recent figures available. Lithuania had the highest IHD mortality for both males and females (318.1/100,000 and 166.1/100,000 respectively). France had the lowest mortality for both males (39.8/100,000) and females (14.7/100,000). There is significant disparity between EU member states with the highest and lowest IHD mortalities (France and Lithuania, for 2008 and 2009 respectively) – approximately eight-fold for males and 11-fold for females.

Trends in CVD Mortality

Figure 4 and **Supplement Table 2** display CVD mortality from 1980-2009 for both males and females. Overall, there was a significant reduction in mortality across Europe; with Austria having the largest reduction for both sexes (76.8% males, 76.5% females). Western countries exhibit faster declining trends in mortality from CVD than IHD, with the exception of Denmark, Sweden and Netherlands. Over the 30-year period for males the least improvement is seen in Slovakia (-4.3%), whilst Romania (+7.4%), Lithuania (+13.7%), Cyprus (+14.4%) and Poland (+16.6%) all report an increase in male CVD mortality. Similarly, for females, Lithuania (-5.4%) and Poland (-4.5%) report the smallest improvements, with Cyprus (+23.6%) having increasing CVD mortality over the study period.

Using the 17 countries (Austria, Belgium, Bulgaria, Estonia, France, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Spain and United Kingdom) with available mortality data for 1980-82, all, with the exception of Portugal, demonstrated a smaller gender gap with CVD than IHD mortality (average difference 19.4/100,000 versus 103.7/100,000 respectively). This gender disparity reduced over the course of the study period, with a reduction of 18.1% for CVD and 36.1% for IHD mortality from 1980-82 to 2007-09.

Current CVD Mortality

Figure 3 C and D display the most recent calendar year data (2009) for CVD mortality, again substituting 2006 for Belgium and Denmark, and 2008 for France and Italy. For both genders, Bulgaria (154.2/100,000 for males, 112.7/100,000 for females), Romania (146.4/100,000 for males, 111.3/100,00 for females) and Latvia (121.3/100,000 for males, 84.8/100,000 for females) had the greatest ASDR. As with IHD mortality, France had the lowest CVD ASDR for both

males and females (23.9/100,000 and 17.3/100,000, respectively).

Joinpoint Analysis for IHD Mortality

Tables 1 and 2 present the results of IHD mortality Joinpoint analysis for 1980-2009 for males and females. We report significant trend changes in the data, and the EAPC in mortality for periods covered by each trend. For both genders, there is a general favourable trend in IHD mortality across Europe, with Netherlands, Portugal, Bulgaria and the United Kingdom having rapidly accelerating declines at the present day. Male mortality declined at a consistent rate across the study period, with only 1 Joinpoint in Denmark, Finland, Sweden and Slovakia. Mortality rates in Denmark, Latvia and Sweden also declined at a steady rate in females. Slovakia demonstrated increasing mortality rates in females with a single Joinpoint. Initial increased mortality trends followed by a subsequent reduction were seen for Bulgaria and Greece for both genders. Very variable trends with 3 or 4 Joinpoints, fluctuating between increasing and decreasing mortality rates, were seen in the Eastern-European countries of Croatia, Lithuania and Poland for males and females. Similar inconsistent trends were also reported for Slovenia, Poland, Latvia and Austria for males, and Romania for females.

Joinpoint Analysis for CVD Mortality

Tables 3 and 4 display similar data for CVD mortality. There is an overall downward CVD mortality trend, with the notable exceptions of Slovakia and Slovenia which have rapid increasing mortality for both genders. The most recent data for Ireland revealed a modest increase in male mortality, and slowing decline in female mortality. Initial increasing mortality followed by favourable trends were seen with Lithuania, Poland and Romania for both sexes, whilst Belgium and Estonia demonstrated this trend in males only. Mortality reductions at consistent rates, with a single Joinpoint, are seen with Bulgaria and Spain for males, and

Bulgaria and Finland for females. Precipitous declining mortality for both sexes is observed in Portugal and Estonia, after an initial small increase for male mortality in Estonia 1981-1994. Croatia had significantly fluctuating mortality, with multiple Joinpoints for males and females. In the United Kingdom there was a plateau, and even moderate increase in male mortality, around 2000. Denmark also experienced an increase male mortality, and levelling-out of female mortality, over the same time period. Both countries then resume mortality decline for males and females at a faster rate.

Smoothed Regression Fit for Former-Communist Countries

Figure 5 displays the LOWESS line of best fit with 95% confidence limits, using data for all of the previously Communist countries now in the EU. 'Time 0' represents the point of Communism ending in each of the constituent countries, with transition to Capitalist rule. The final 10 years of Communism, that is years -10 to 0 in **Figure 5**, has little change in IHD mortality. Mortality decline ensues 5-years after the end of Communist-rule.

Discussion

This study of 30-year cardiovascular mortality trends across Europe identifies significant mortality decline throughout the majority of EU member states. There is however an observed East-West disparity for both IHD and CVD. For IHD the United Kingdom and Netherlands have made the greatest improvements, with France having the current lowest mortality for both males and females. The smallest improvements were found in Lithuania, Hungary and Slovakia, relatively new EU states. Austria has the largest reduction in CVD mortality, and France again has the lowest present day mortality. Bulgaria, Romania and Latvia have small reductions, and current greatest, CVD mortality.

An East-West cardiovascular disease inequality across Europe has been previously recognised.[2-4,6-8] Although mortality overall is decreasing across the continent, this East-West gap appears to be widening. Furthermore, the impact of the transition from Communism can be appreciated. This suggests that there is no reduction in IHD mortality leading up to, and for approximately 5-years following the decline of Communism. One potential explanation for this is the turmoil associated with the changing of political landscapes. Once Capitalist regimes are in place, a decreasing IHD mortality trend ensues.

An unexpected finding is the impressive CVD mortality reduction in Austria over the time period studied; no such dramatic reduction is seen with IHD, indicating the presence of CVD-specific factors. Hypertension is a plausible underlying factor, given its key involvement in stroke pathophysiology.[16] The Austrian Heart Fund ran a campaign of hypertension awareness in 1978, the fruits of which could be being reaped long term. A high level of awareness of the risks of hypertension amongst the Austrian population has been demonstrated, although this appears to have waned recently.[17,18] Another factor could be the unregulated access to all levels of healthcare and free-provider choice delivered by the Austrian health service.[19] The Austrian acute stroke service is also efficient with fast admissions, good availability of investigation modalities and few delays.[20] Conversely, Bulgaria has the highest CVD mortality for both genders, but relatively low IHD mortality, possibly related to the prevalence of heavy alcohol use in the country.[21]

Lithuania has the present day highest rate of IHD mortality for both sexes, although there is a decreasing trend for mortality in this study. A cross-sectional study of middle-aged males in Lithuania and Sweden recognised that traditional risk factors may not be entirely responsible. Dietary antioxidants and the resistance of low-density lipoproteins to oxidation was found to

differ between the two groups.[22] A prospective study found that a low-risk cardiovascular profile was present in only 1% of middle-aged urban adults in Kaunas, Lithuania (1994 to 2010), with a worsening trend in body mass index, fasting glucose and healthy diet.[23]

Cyprus has very few mortality figures recorded on the WHO database. The little data available, however, shows substantial increases in both CVD and IHD, with the exception of female CVD mortality, which demonstrates declining death rates. Conceivable reasons for this comprise the effects of war, erroneous and episodic health data recording, as well as the effect of a small population size.

Various hypotheses have been postulated for the disparity in European cardiovascular disease mortality, ranging from the prevalence of socioeconomic inequality, differing diets, proportional health budget expenditure and access to healthcare. Rising levels of smoking, alcoholism, as well as poor diet and exercise participation were recorded in Russia after the Communist decline.[24] Using Russia as a post-socialist model, several legislative factors have been faced in health improvement, including lack of formal health policy, scanty health promotion and the absence of epidemiological surveillance systems.[25] The trend of IHD mortality has been examined in Germany 10-years after reunification, and demonstrated a clear East-West gradient with mortality approximately 50% greater in former-Communist East Germany.[26] This study found differences in classical cardiovascular risk factors (high cholesterol, hypertension, obesity, diabetes) as well as lifestyle factors (smoking, levels of exercise and diet) between East and West Germany.

The Eastern EU members have lower gross domestic product (GDP) per-capita than their Western counterparts; with resultant lower socioeconomic class, shorter life expectancy and lower healthcare expenditure.[27-29] Nonetheless, Eastern European countries have greater

mortality than levels of wealth would predict.[30] All-cause mortality has been found to be inversely proportional to educational attainment.[31] Furthermore, education is inversely related to blood pressure, smoking and obesity, and correlated to health knowledge and physical activity.[32] Smoking is more prevalent in Eastern European countries, and is thought to be a considerable causal factor in cardiovascular health inequalities.[33,34] Moreover, EU smoke-free legislation in public places has further reduced mortality and hospital admissions, a regulation not imposed stringently in many ex-socialist countries.[35-37]

Although not the focus of this study, there is observed narrowing of gender inequalities in cardiovascular mortality, in keeping with a previous WHO report.[38] This WHO paper notes that not only is the gap closing, but also is smaller still when healthy life expectancy is considered. There are many potential contributory factors for this trend, and the role of behavioural factors – smoking prevalence in particular – may be crucial. Male smoking rates have peaked and are declining in many countries across Europe, whereas female smoking rates are increasing, both for daily smokers and current smokers.[39] Additionally, females may be more sensitive to the harmful effects of cigarette smoking, perhaps related to hormonal factors.[40]

This study follows a heterogeneous group of countries temporally, allowing the observation of significant mortality developments over a 30-year period. With any epidemiological dataset as vast and diverse as the WHO database, issues of data reliability and accuracy of recording arise. There is reliance on retrospective data collection and death certification, and the robustness of this data needs to be considered. A potential contributing factor to the results of this study include the variation in assignment of causes of death, between and within countries, which may fluctuate with changing coding practices over time. Nevertheless, the WHO scrutinises death certification data for accurate levels of reporting, and

all the countries included in this analysis had satisfactory coverage. Conversely, Mathers et al. find that four countries in this study had 'Low' levels of reporting.[15] Further potential loss of data reliability in this study arises due to changes in international death certification coding over the studied period (ICD-9 to ICD-10). For several time points no data were available, allowing for the potential of un-documented variation. As a descriptive analysis little statistical evaluation is carried out, and moreover, all explanations for mortality trends are speculative at present.

Conclusions

There is a growing disparity in cardiovascular mortality between Western Europe and former-Soviet states of Eastern Europe. Diverse fundamental explanations exist for this disparity and the need for population-wide health promotion and primary prevention policies are emphasized to ensure these differences do not expand further.

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Clinical Perspective

Cardiovascular disease is the leading cause of mortality worldwide and trends in cardiovascular mortality have a central role in public health and epidemiology globally. Previous studies on trends in Europe have highlighted a health inequality between Western countries and Eastern, previously Communist-run, states. This study provides an up-to-date analysis of age standardised death rates from ischaemic heart disease (IHD) and cerebrovascular disease (CVD) across member states of the European Union between 1980 and 2010. The effect of changing political ideologies is explored in previously Communist-run countries. Data is collated from the World Health Organisation mortality database, using International Classification of Diseases ninth and tenth editions, and is analysed using Joinpoint regression analysis. An overall trend for reduction in mortality from IHD and CVD is seen across Europe, although very modest mortality reductions are observed in Eastern-European states, Romania, Poland and Slovakia for example. Lithuania and Bulgaria have the present day highest mortality for both genders for IHD and CVD respectively. Conversely, significant reductions are seen in cardiovascular mortality in Western countries, with the lowest mortality from IHD and CVD for both males and females observed in France. In pooled data for former Communist-run countries, a trend for no reduction in IHD mortality leading up to, and for a number of years following, the decline of Communism is noted. Reasons for the growing East-West disparity are explored, and topics highlighted that may address this inequality. The need for population-wide health promotion and primary prevention policies are emphasized.

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Table 1. Joinpoint analysis for male ischaemic heart disease mortality in 26 countries of the European Union, for years 1979-2009, where data available.

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1980-1982	+3.03	1982-1998	-1.31*	1998-2009	-4.25*		
Belgium	1979-1984	-1.83*	1984-1990	-5.82*	1990-1999	-0.38		
Bulgaria	1980-1985	+5.02*	1985-1997	+0.28	1997-2005	-3.68*	2005-2009	-7.39*
Croatia	1985-1990	-1.14	1990-1993	+25.79*	1993-2009	-1.74*		
Cyprus	1999-2009	+24.95*						
Czech Republic	1986-1992	-0.76	1992-2001	-5.78*	2001-2009	-1.16*		
Denmark	1994-2006	-6.89*						
Estonia	1981-1995	-0.72*	1995-2009	-4.27*				
Finland	1987-2009	-3.63*						
France	1979-1986	-0.12	1986-1990	-5.14*	1990-2001	-2.01*	2001-2008	-4.53*
Germany	1990-1995	+1.06	1995-2003	-4.03*	2003-2009	-5.48*		
Greece	1979-1989	+1.32*	1989-2004	-0.72*	2004-2009	-4.73*		
Hungary	1979-1981	+6.33	1981-1994	+0.17	1994-2009	-1.07*		
Ireland	1979-1985	+0.12	1985-1998	-2.96*	1998-2005	-7.28*	2005-2009	-2.26*
Italy	1979-2005	-2.39*	2005-2008	-5.93*				
Latvia	1980-1991	-1.48*	1991-1994	+8.81	1994-1997	-10.58	1997-2009	-1.84*
Lithuania	1981-1994	+0.82*	1994-1999	-5.43*	1999-2005	+1.94	2005-2009	-2.99
Netherlands	1979-1985	-1.52*	1985-1999	-3.99*	1999-2009	-7.52*		
Poland	1980-1991	+1.98*	1991-1997	-3.57*	1997-2000	+8.12	2000-2009	-4.34*
Portugal	1980-2004	-1.74*	2005-2009	-8.44*				
Romania	1980-1996	+3.60*	1996-2009	-2.11*				
Slovakia	1992-2009	-0.66*						
Slovenia	1985-1988	-11.08*	1988-1992	+11.95*	1992-2009	-4.34*		
Spain	1980-1999	-0.73*	1999-2009	-4.00*				
Sweden	1987-2009	-4.32*						
United Kingdom	1979-1985	-1.28*	1985-1993	-2.97*	1993-2002	-4.80*	2002-2009	-6.36*

EAPC, Estimated Annual Percentage Change
*Significantly different from 0 ($p<0.05$)

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Table 2. Joinpoint analysis for female ischaemic heart disease mortality in 26 countries of the European Union, for years 1979-2009, where data available.

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1980-1998	-0.07	1998-2010	-3.75*				
Belgium	1979-1984	-0.65	1984-1990	-5.61*	1990-1999	-0.32		
Bulgaria	1980-1985	+5.94*	1985-1998	-0.67*	1998-2003	-4.16*	2003-2009	-8.54*
Croatia	1985-1990	-0.27	1990-1993	+43.85*	1993-2009	-1.93*		
Cyprus	1999-2009	+22.70*						
Czech Republic	1986-1994	-1.49*	1994-2000	-6.60*	2000-2009	+0.06		
Denmark	1994-2006	-6.58*						
Estonia	1981-1985	+1.57	1985-2001	-2.67*	2001-2009	-6.35*		
Finland	1987-2002	-3.00*	2002-2009	-4.70*				
France	1979-1986	-0.27	1986-1994	-4.18*	1994-2002	-2.19*	2002-2008	-6.01*
Germany	1990-1995	-0.12	1995-2003	-3.18*	2003-2009	-6.25*		
Greece	1979-1989	+2.70	1989-2004	-0.48	2004-2009	-6.25*		
Hungary	1979-1999	+0.71*	1999-2002	-3.50	2002-2005	+4.81	2005-2009	-4.80*
Ireland	1979-1986	-0.29	1986-1998	-2.70*	1998-2005	-6.98*	2005-2009	-3.00*
Italy	1979-1986	-5.33*	1986-2005	-1.57*	2005-2008	-7.01*		
Latvia	1980-2009	-2.39*						
Lithuania	1981-1988	+0.90	1988-2000	-2.82*	2000-2006	+0.30	2006-2009	-4.50
Netherlands	1979-1996	-2.96*	1996-2002	-5.37*	2002-2009	-8.13*		
Poland	1980-1997	+0.80*	1997-2000	+13.47	2000-2009	-4.21*		
Portugal	1980-2004	-1.47*	2004-2009	-8.20*				
Romania	1980-1987	+4.66*	1987-1990	-1.36	1990-1996	+4.11*	1996-2009	-2.62*
Slovakia	1992-2009	+0.19						
Slovenia	1985-1987	-20.23*	1987-1992	+15.79*	1992-2009	-5.84*		
Spain	1980-1998	-0.76*	1998-2005	-3.59*	2005-2009	-5.90*		
Sweden	1987-2009	-3.81*						
United Kingdom	1979-1985	-0.35	1985-1993	-2.41*	1993-2003	-4.95*	2003-2009	-7.19*

EAPC, Estimated Annual Percentage Change
*Significantly different from 0 ($p<0.05$)

DOI: 10.1161/CIRCULATIONAHA.115.018931

Table 3. Joinpoint analysis for male cerebrovascular disease mortality in 26 countries of the European Union, for years 1979-2009, where data available.

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1980-2002	-4.38*	2002-2005	-14.03*	2005-2009	-3.56		
Belgium	1979-1983	+0.17	1983-1987	-7.04*	1987-2003	-2.60*	2003-2006	-8.27*
Bulgaria	1980-2009	-0.92*						
Croatia	1985-1994	-1.27*	1994-1999	+3.41	1999-2002	-9.08	2002-2009	-3.14*
Cyprus	1999-2009	+2.71						
Czech Republic	1986-1990	-2.10	1990-1997	-6.00*	1997-2003	-1.04	2003-2009	-9.00*
Denmark	1994-2000	-2.67*	2000-2003	+2.67	2003-2006	-7.10*		
Estonia	1981-1994	+0.17	1994-2006	-4.42*	2006-2009	-17.25*		
Finland	1987-1993	-1.82*	1993-2009	-4.33*				
France	1979-1986	-3.36*	1986-1989	-9.63*	1989-2002	-3.40*	2002-2008	-5.21*
Germany	1990-1995	-2.16*	1995-2009	-6.00*				
Greece	1979-2002	-1.19*	2002-2009	-5.99*				
Hungary	1979-2003	-1.58*	2003-2006	-10.07*	2006-2009	-2.37		
Ireland	1979-2001	-3.46*	2001-2006	-7.86*	2006-2009	+0.38		
Italy	1979-1985	-1.13	1985-2008	-3.86*				
Latvia	1980-1991	-0.20	1991-1994	+3.63	1994-2005	-2.66*	2005-2009	-7.52*
Lithuania	1981-1993	+1.13*	1993-2009	-0.07				
Netherlands	1979-1987	-2.79*	1987-1991	-0.28	1991-2002	-2.32*	2002-2009	-7.16*
Poland	1980-1997	+1.28*	1997-2000	+9.21	2000-2009	-3.74*		
Portugal	1980-1996	-2.66*	1996-2009	-6.38*				
Romania	1980-1991	+0.71*	1991-1994	+11.05	1994-2005	-1.47*	2005-2009	-5.22*
Slovakia	1992-2006	-1.97*	2006-2009	+9.15*				
Slovenia	1985-1992	-1.01	1992-2003	-4.54*	2003-2007	-8.54*	2007-2009	+10.57
Spain	1980-2009	-4.31*						
Sweden	1987-1998	-0.87*	1999-2010	-4.16*				
United Kingdom	1979-2000	-3.12*	2000-2003	+0.43	2002-2009	-6.96*		

EAPC, Estimated Annual Percentage Change
*Significantly different from 0 ($p<0.05$)

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Table 4. Joinpoint analysis for female cerebrovascular disease mortality in 26 countries of the European Union, for years 1979-2009, where data available.

	Trend 1		Trend 2		Trend 3		Trend 4	
	Years	EAPC	Years	EAPC	Years	EAPC	Years	EAPC
Austria	1980-2002	-4.21*	2002-2005	-14.00*	2005-2009	-4.16		
Belgium	1979-1983	-0.44	1983-1987	-6.87*	1987-2004	-2.86*	2004-2006	-7.23
Bulgaria	1980-2009	-1.46*				-		
Croatia	1985-1993	-1.91*	1993-1999	+2.63*	1999-2002	-9.11*	2002-2009	-2.86*
Cyprus	1999-2006	-7.13*	2006-2009	-9.19				
Czech Republic	1986-1997	-4.96*	1997-2002	+0.26	2002-2009	-8.27*		
Denmark	1994-1998	-3.22*	1998-2003	-0.32	2003-2006	-4.55*		
Estonia	1981-1993	-0.63*	1993-2003	-4.36*	2003-2006	-9.31	2006-2009	-17.14*
Finland	1987-2009	-4.25*						
France	1979-1986	-3.38*	1986-1989	-9.41*	1989-2003	-3.40*	2003-2008	-5.52*
Germany	1990-1993	-1.29	1993-2009	-5.22*				
Greece	1979-1985	-0.43	1985-2003	-1.58*	2003-2009	-6.33*		
Hungary	1979-2003	-2.23*	2003-2006	-10.09*	2006-2009	-3.75*		
Ireland	1979-1990	-4.58*	1990-2000	-2.83*	2000-2005	-8.64*	2005-2009	-0.05
Italy	1979-1985	-1.16	1985-2008	-3.73*				
Latvia	1980-1983	+4.34	1983-2003	-1.24*	2003-2009	-7.85*		
Lithuania	1981-1995	+0.37	1995-2009	-0.73*				
Netherlands	1979-1987	-2.90*	1987-1992	-0.18	1992-2002	-2.21*	2002-2009	-6.12*
Poland	1980-1997	+0.54*	1997-2000	+10.60	2000-2009	-4.91*		
Portugal	1980-1999	-3.06*	1999-2009	-7.14*				
Romania	1980-1991	+0.22	1991-1994	+7.32	1994-2005	-1.53*	2005-2009	-6.28*
Slovakia	1992-2006	-2.63*	2006-2009	+9.16				
Slovenia	1985-1993	-2.50*	1993-2003	-4.52*	2003-2006	-10.95	2006-2009	+6.99
Spain	1980-1991	-4.23*	1991-2009	-4.95*				
Sweden	1987-2002	-1.64*	2002-2005	-7.26*	2005-2009	-2.72*		
United Kingdom	1979-2000	-3.05*	2000-2003	-0.23	2003-2009	-6.39*		

EAPC, Estimated Annual Percentage Change
*Significantly different from 0 ($p<0.05$)

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Figure Legends:

Figure 1. Changes in age standardised death certification rates per 100 000 for countries joining the European Union prior to 2004 and 2004 or later, 1980-2009, for ischaemic heart disease (A) and cerebrovascular disease (B). Pre-2004 countries – Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Netherlands, Portugal, Spain, Sweden and United Kingdom. Post-2004 countries – Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia and Slovenia. * represents statistical significance at $p<0.01$.

Figure 2. Trends in age standardised death certification rates per 100 000 for ischaemic heart disease in countries joining the European Union prior to 2004 (A) and 2004 or later (B),1980–2009. Triangles, males; circles; females.

Figure 3. Age standardised death certification rates per 100 000 for ischaemic heart disease (males (A) and females (B)) and cerebrovascular disease (males (C) and females (D)) in 26 countries of the European Union in 2009 (2006 for Belgium and Denmark, 2008 for France and Italy).

Figure 4. Trends in age standardised death certification rates per 100 000 for cerebrovascular disease in countries joining the European Union prior to 2004 (A) and 2004 or later (B), 1980–2009. Triangles, males; circles; females.

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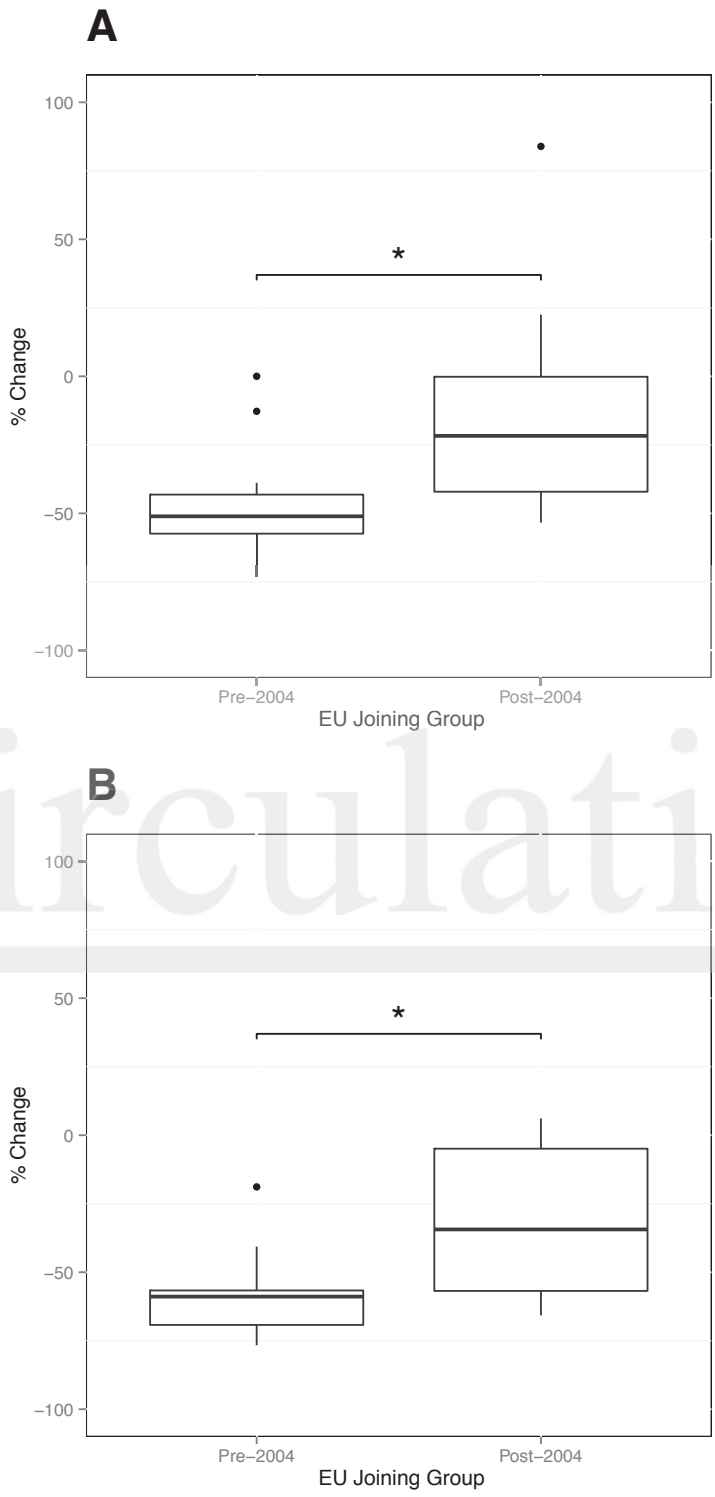
Figure 5. Locally weighted scatterplot smoothing (LOWESS) fit of age-standardised death certification rates per 100 000 for ischaemic heart disease, for individual former Communist countries now in the European Union. Year 0 represents the end of Communist rule. 95% confidence limits for the line of best fit are shown.

Figure 1



A

Figure 2

B

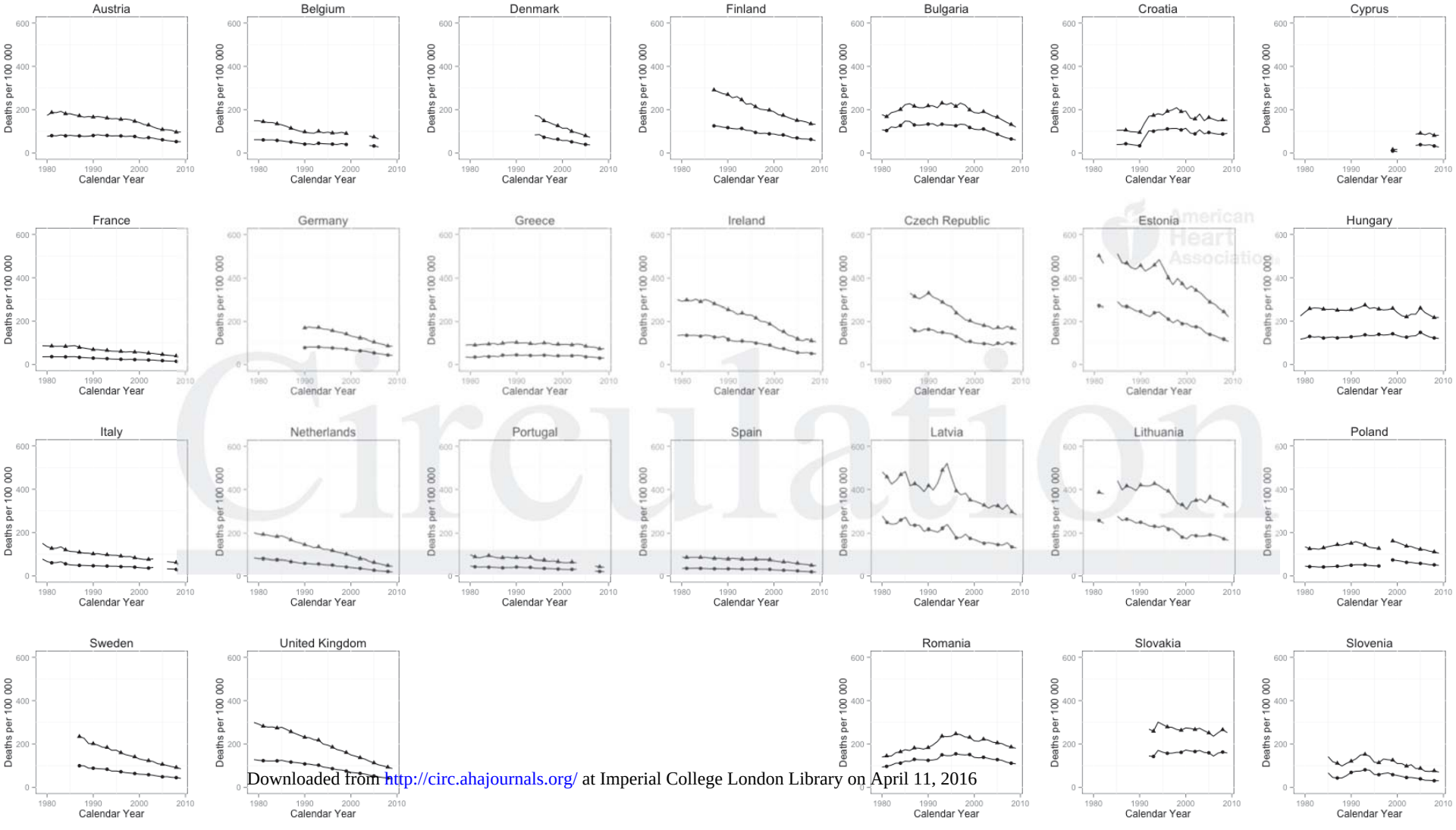
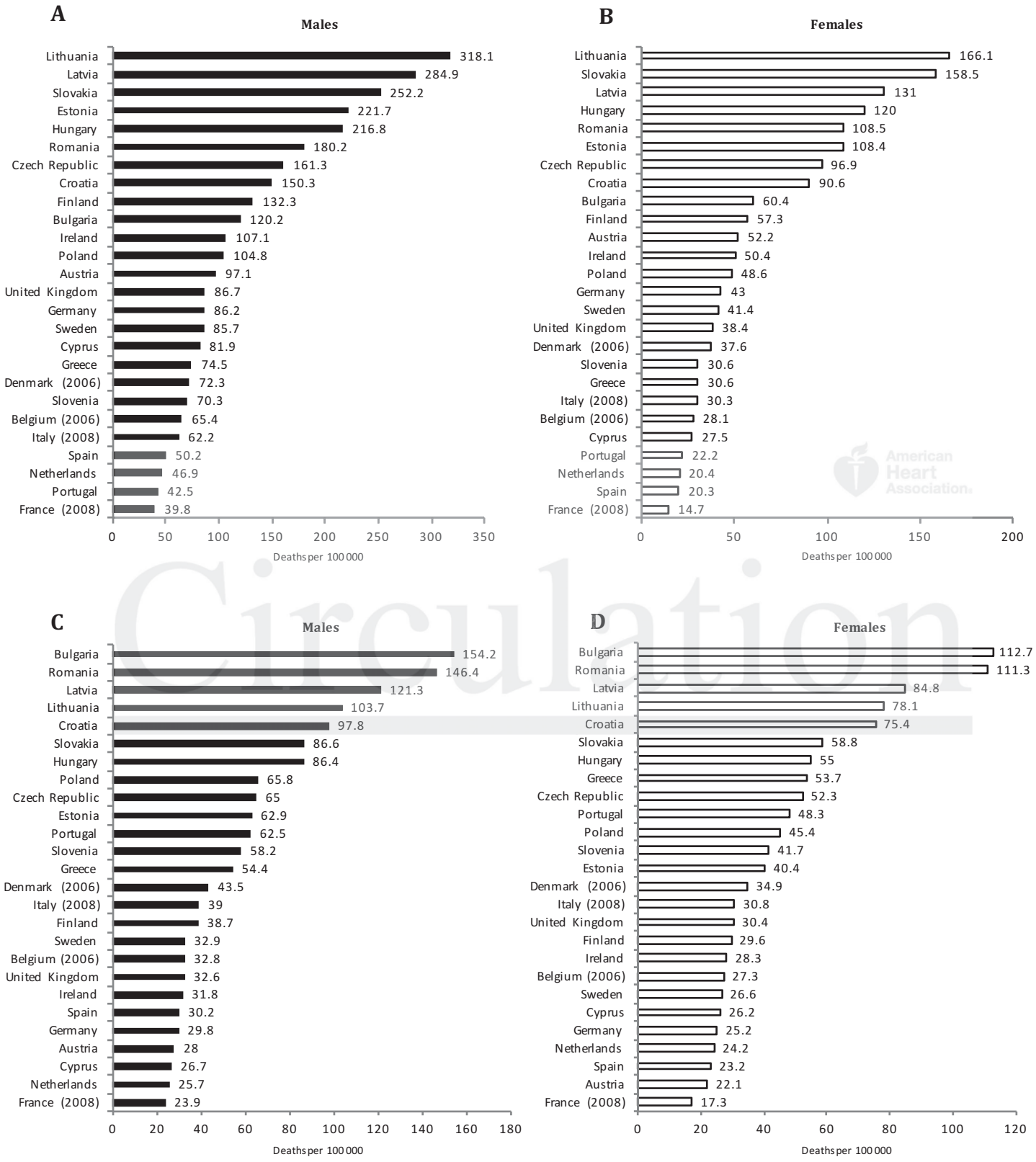


Figure 3



A

Figure 4

B

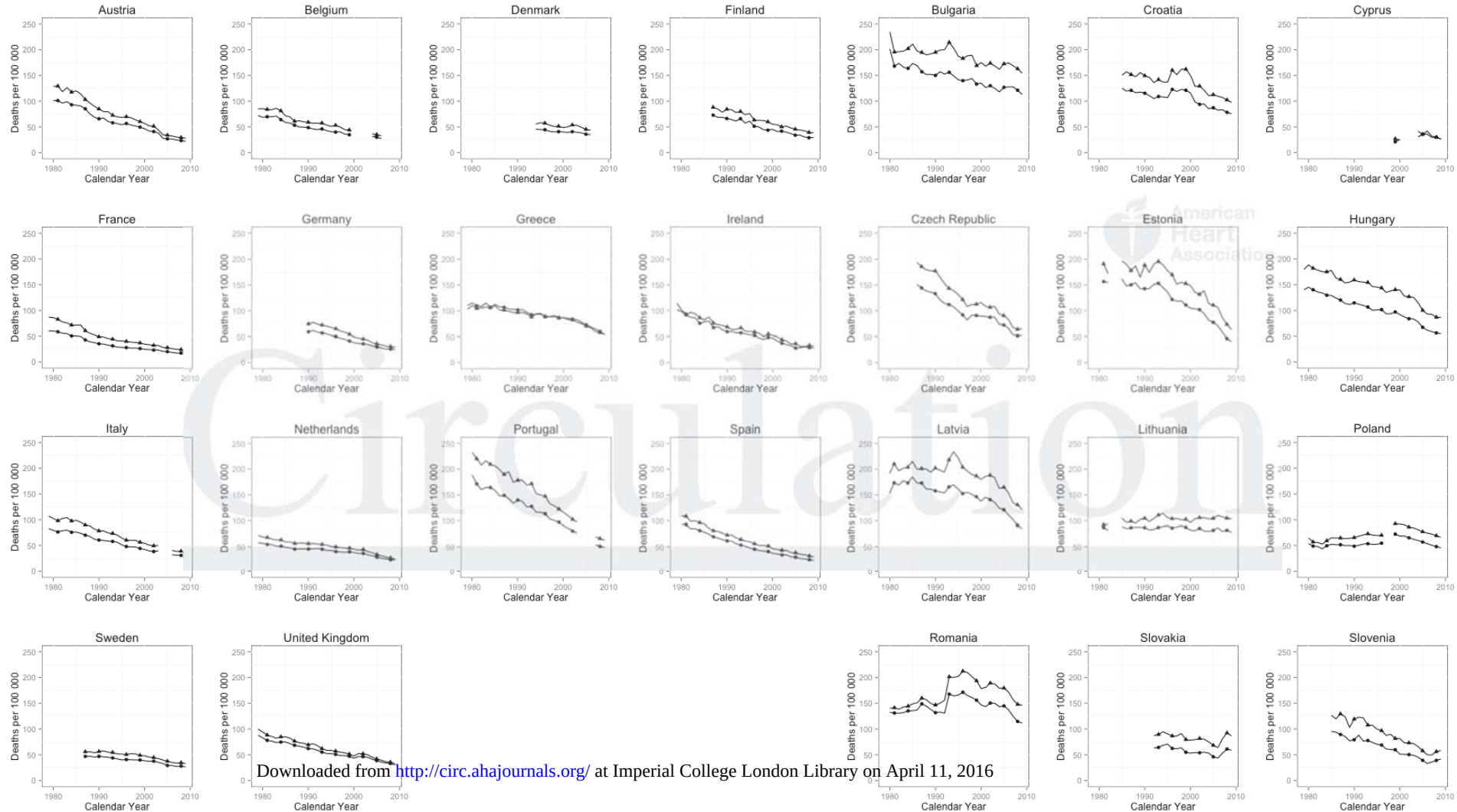
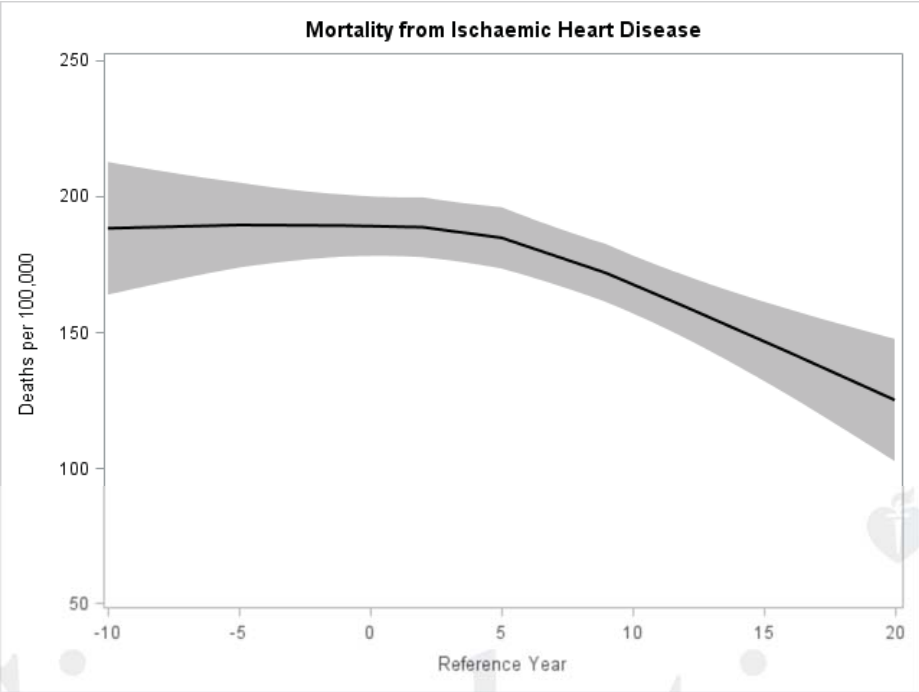


Figure 5



Trends in Mortality from Ischaemic Heart Disease and Cerebrovascular Disease in Europe: 1980-2009

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Supplemental Material

	Males					Females				
	1980-82	1989-91	1999-01	2007-09	% change 1980-82 v 2007-09	1980-82	1989-91	1999-01	2007-09	% change 1980-82 v 2007-09
Austria	182.3	167.7	139.6	99.5	-45.4	78.8	81.0	71.5	53.3	-32.3
Belgium*	145.0	96.9	92.5	72.4	-50.1*	60.8	42.6	40.7	31.7	-47.8*
Bulgaria	177.0	215.0	189.8	131.2	-25.9	110.4	132.9	111.8	65.0	-41.1
Croatia	x	110.0	181.6	150.6	43.3*	x	46.4	104.2	88.2	124.5*
Cyprus*	x	x	16.4	85.0	418.3*	x	x	7.8	32.8	320.1*
Czech Republic	x	319.0	194.0	168.8	-48.7*	x	161.8	102.9	100.8	-41.6*
Denmark*	x	x	118.3	80.1	-53.8*	x	x	59.7	39.9	-52.2*
Estonia*	484.7	443.0	362.2	242.3	-50.0*	269.0	242.3	184.7	116.4	-56.7*
Finland	x	266.1	188.2	136.8	-53.0*	x	116.3	86.4	61.7	-50.8*
France*	84.7	69.9	56.1	41.2	-51.4*	35.8	29.4	21.9	15.3	-57.3*
Germany*	x	171.1	133.2	89.2	-47.9*	x	81.3	68.2	45.3	-44.3*
Greece	92.4	103.0	94.7	76.5	-17.2	34.8	44.2	41.3	31.9	-8.3
Hungary	253.5	253.3	241.1	220.2	-13.1	125.4	127.3	134.4	123.0	-1.9
Ireland	294.6	255.4	174.0	112.2	-61.9	135.1	118.8	82.5	53.0	-60.7
Italy*	129.9	103.1	79.7	63.9	-50.8*	62.7	46.8	38.2	31.5	-49.8*
Latvia	455.5	401.9	346.6	304.3	-33.2	255.3	212.4	168.3	140.6	-44.9
Lithuania*	383.1	410.7	328.8	333.0	-13.1*	250.6	245.3	182.7	174.4	-30.4*
Luxembourg	x	x	x	x	x	x	x	x	x	X
Malta	x	x	x	x	x	x	x	x	x	X
Netherlands	193.6	146.9	94.6	50.7	-73.8	80.8	60.9	41.5	22.6	-72.0
Poland	128.4	152.3	154.2	109.9	-14.4	43.4	49.6	70.6	50.4	16.1
Portugal	91.1	85.4	65.6	45.3	-50.3	45.9	42.5	33.2	23.5	-48.9
Romania	142.9	184.8	219.2	186.0	30.2	97.6	125.8	141.9	112.0	14.8
Slovakia*	x	276.1	269.7	256.7	-7.0*	x	152.6	167.1	159.8	4.8*
Slovenia	x	120.7	114.9	73.3	-48.2*	x	65.7	54.5	31.2	-53.3*
Spain	87.0	80.9	72.7	52.6	-39.5	37.8	35.4	30.7	21.6	-42.9
Sweden	x	199.4	132.6	91.1	-61.1*	x	87.6	61.4	44.0	-55.8*
United Kingdom	283.9	233.0	151.3	93.0	-67.3	123.1	109.2	70.3	42.0	-65.9

Supplement Table 1. Three-year average trends in age standardised death certification rates per 100 000 for ischaemic heart disease, 1980–2009

*For Belgium 1997-99 and 2004-06 were used for 1999-2001 and 2007-09, with % change 1980-82 v 2004-06; for Croatia % change is 1985 v 2007-09; for Cyprus there was no value for 2001, with % change 1999-2000 v 2007-09; for Czech Republic % change was 1986 v 2007-09; for Denmark 2004-06 was used for 2007-09, with % change 1994 v 2004-06; for Estonia there was no value for 1980, with % change 1981-82 v 2007-09; for Finland % change was 1987 v 2007-09; for France 2006-08 was used for 2007-09, with % change 1980-82 v 2006-08; for Germany 1990-92 was used for 1989-91, with % change 1990-92 v 2007-09; for Italy 2006-08 was used for 2007-09, with % change 1980-82 v 2006-08; for Lithuania there was no value for 1980, with % change 1981-82 v 2007-09; for Slovakia 1992-94 was used for 1989-91, with % change 1992-94 v 2007-09; for Slovenia % change was 1985 v 2007-09; for Sweden % change was 1987 v 2007-09

x data not available

	Males					Females				
	1980-82	1989-91	1999-01	2007-09	% change 1980-82 v 2007-09	1980-82	1989-91	1999-01	2007-09	% change 1980-82 v 2007-09
Austria	125.5	84.9	56.4	29.2	-76.8	99.4	67.3	46.0	23.3	-76.5
Belgium*	84.3	58.7	46.1	34.9	-58.6*	69.4	48.1	37.0	29.7	-57.2*
Bulgaria	208.7	195.4	170.6	161.9	-22.4	180.8	153.0	131.6	120.6	-33.3
Croatia	x	150.4	147.0	102.4	-32.0*	x	114.5	111.9	79.0	-36.8*
Cyprus*	x	x	25.8	29.5	14.4*	x	x	23.3	28.7	23.6*
Czech Republic	x	173.6	112.3	65.4	-66.2*	x	130.2	89.6	52.5	-65.3*
Denmark*	x	x	50.0	45.9	-17.4*	x	x	40.1	36.4	-20.4*
Estonia*	181.5	176.1	145.9	74.2	-59.1*	155.7	142.8	106.5	48.4	-68.9*
Finland	x	82.2	56.5	40.2	-54.4*	x	66.4	43.4	29.7	-59.3*
France*	82.2	49.9	34.9	24.8	-69.9*	58.2	35.8	24.8	17.6	-69.7*
Germany*	x	75.2	50.2	30.8	-58.5*	x	59.5	39.1	25.8	-56.3*
Greece	106.6	96.6	85.1	57.1	-46.4	110.9	102.0	85.9	59.1	-46.7
Hungary	183.0	156.8	135.9	88.5	-51.6	140.4	112.8	92.2	56.8	-59.6
Ireland	97.0	67.5	52.1	32.2	-66.8	92.4	60.5	45.8	29.2	-68.4
Italy*	101.0	79.5	53.7	39.3	-61.1*	78.0	60.8	42.0	31.3	-59.9*
Latvia	199.5	198.0	184.2	128.8	-35.4	165.1	158.1	143.2	92.8	-43.8
Lithuania*	92.5	101.5	100.8	105.2	13.7*	84.4	85.6	83.4	79.8	-5.4*
Luxembourg	x	x	x	x	x	x	x	x	x	x
Malta	x	x	x	x	x	x	x	x	x	x
Netherlands	67.1	56.4	45.2	27.8	-58.6	54.9	45.5	38.4	25.0	-54.6
Poland	59.1	65.6	91.5	68.9	16.6	50.1	49.6	69.5	47.9	-4.5
Portugal	220.3	177.2	115.9	65.8	-70.1	173.3	136.9	91.0	50.7	-70.8
Romania	140.0	148.7	184.3	150.4	7.4	131.3	134.1	148.7	116.8	-11.0
Slovakia*	x	90.5	79.0	86.6	-4.3*	x	65.3	54.1	57.6	-11.7*
Slovenia	x	115.1	78.7	54.6	-56.9*	x	81.4	54.0	38.8	-59.3*
Spain	105.3	73.7	47.3	32.2	-69.4	89.9	61.8	37.8	24.7	-72.6
Sweden	x	55.9	47.4	33.7	-39.7*	x	46.1	38.4	27.3	-41.7*
United Kingdom	89.3	71.0	50.4	34.9	-60.9	79.1	62.7	45.7	32.5	-58.9

Supplement Table 2. Three-year average trends in age standardised death certification rates per 100 000 for cerebrovascular disease, 1980–2009

*For Belgium 1997-99 and 2004-06 were used for 1999-2001 and 2007-09, with % change 1980-82 v 2004-06; for Croatia % change is 1985 v 2007-09; for Cyprus there was no value for 2001, with % change 1999-2000 v 2007-09; for Czech Republic % change was 1986 v 2007-09; for Denmark 2004-06 was used for 2007-09, with % change 1994 v 2004-06; for Estonia there was no value for 1980, with % change 1981-82 v 2007-09; for Finland % change was 1987 v 2007-09; for France 2006-08 was used for 2007-09, with % change 1980-82 v 2006-08; for Germany 1990-92 was used for 1989-91, with % change 1990-92 v 2007-09; for Italy 2006-08 was used for 2007-09, with % change 1980-82 v 2006-08; for Lithuania there was no value for 1980, with % change 1981-82 v 2007-09; for Slovakia 1992-94 was used for 1989-91, with % change 1992-94 v 2007-09; for Slovenia % change was 1985 v 2007-09; for Sweden % change was 1987 v 2007-09

x data not available