

Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980–2009

Melanie Nichols^{1,2*}, Nick Townsend¹, Peter Scarborough¹, and Mike Rayner¹

¹British Heart Foundation Health Promotion Research Group, Department of Public Health, University of Oxford, Oxford OX3 7LF, UK; and ²WHO Collaborating Centre for Obesity Prevention, Faculty of Health, Deakin University, Geelong, Australia

Received 6 January 2013; revised 14 March 2013; accepted 16 April 2013; online publish-ahead-of-print 25 June 2013

See page 3014 for the editorial comment on this article (doi:10.1093/eurheartj/ehs362)

Aims

Recent decades have seen very large declines in coronary heart disease (CHD) mortality across most of Europe, partly due to declines in risk factors such as smoking. Cardiovascular diseases (predominantly CHD and stroke), remain, however, the main cause of death in most European countries, and many risk factors for CHD, particularly obesity, have been increasing substantially over the same period. It is hypothesized that observed reductions in CHD mortality have occurred largely within older age groups, and that rates in younger groups may be plateauing or increasing as the gains from reduced smoking rates are increasingly cancelled out by increasing rates of obesity and diabetes. The aim of this study was to examine sex-specific trends in CHD mortality between 1980 and 2009 in the European Union (EU) and compare trends between adult age groups.

Methods

Sex-specific data from the WHO global mortality database were analysed using the joinpoint software to examine trends and significant changes in trends in age-standardized mortality rates. Specific age groups analysed were: under 45, 45–54, 55–64, and 65 years and over. The number and location of significant joinpoints for each country by sex and age group was determined (maximum of 3) using a log-linear model, and the annual percentage change within each segment calculated. Average annual percentage change overall (1980–2009) and separately for each decade were calculated with respect to the underlying joinpoint model.

Results

Recent CHD rates are now less than half what they were in the early 1980s in many countries, in younger adult age groups as well as in the population overall. Trends in mortality rates vary markedly between EU countries, but less so between age groups and sexes within countries. Fifteen countries showed evidence of a recent plateauing of trends in at least one age group for men, as did 12 countries for women. This did not, however, appear to be any more common in younger age groups compared with older adults. There was little evidence to support the hypothesis that mortality rates have recently begun to plateau in younger age groups in the EU as a whole, although such plateaus and even a small number of increases in CHD mortality in younger subpopulations were observed in a minority of countries.

Conclusion

There is limited evidence to support the hypothesis that CHD mortality rates in younger age groups in the member states of the EU have been more likely to plateau than in older age groups. There are, however, substantial and persistent inequalities between countries. It remains vitally important for the whole EU to monitor and work towards reducing preventable risk factors for CHD and other chronic conditions to promote wellbeing and equity across the region.

Keywords

Coronary heart disease • Mortality • Trends • Young adults

Introduction

Recent decades have seen very large declines in cardiovascular disease (CVD), and coronary heart disease (CHD) mortality

specifically, across the European Union (EU), with rates of CVD mortality falling by >30% in both sexes and CHD mortality falling by a third in men and over a quarter in women between 1985–89 and

* Corresponding author. Tel: +61 3 5227 8446, Fax: +61 3 5227 8376, Email: melanie.nichols@deakin.edu.au

2000–04.¹ These trends have been attributed to improved treatment and care, which has helped to reduce case–fatality ratios, as well as improved primary prevention and risk factor management which has reduced incidence rates of disease.²

Cardiovascular disease remains, however, the main cause of death in most European countries, with CHD and stroke accounting for the majority of these deaths.³ Furthermore, many risk factors for CHD, particularly obesity⁴ and diabetes,⁵ have been increasing substantially over the same period,⁶ while rates of hypertension have plateaued after substantial declines. Trends in the prevalence of these risk factors vary widely between countries and age groups, and it is not yet clear what impact these changes will have on mortality rates in the context of improved treatment and care for CHD. Smoking rates are still quite high on a world scale in some EU countries, despite a general trend to reductions in smoking prevalence, and it is probable that this contributes to inequalities in the region.³

It is hypothesized that recent upwards trends in obesity and diabetes may be beginning to cancel out the beneficial effect of reduced smoking rates and improved care and treatment on CHD mortality, and that this effect may be demonstrated by examining CHD mortality trends in younger age groups. Although mortality rates in younger age groups make a relatively small contribution to total CHD mortality, developments in younger age groups are important indicators for public health, which may represent a cohort effect that—if maintained—would result in significant future impacts on the burden of CHD.⁷ Evidence of CHD mortality rates beginning to plateau in younger age groups has been demonstrated to varying extents and at differing time points in England and Wales,^{7,8} Scotland,⁹ USA,¹⁰ and Australia.¹¹

The aim of this study is to investigate whether plateauing of mortality rates in younger age groups is demonstrated in an examination of age- and sex-specific trends in CHD mortality rates between 1980 and 2009 in the member states of the EU.

Methods

Data on cause-specific numbers of deaths and population numbers, by sex and in 5-year age groups (up to 85 and over) for each country of the EU, were extracted from the WHO global mortality database. Age- and sex-specific mortality rates were calculated and aggregated rates were standardized to the European Standard Population¹² using the direct method. Coronary heart disease as a cause of death was defined according to the following International Classification of Disease codes: ICD-10 (International Classification of Diseases, tenth revision) codes I20–I25; ICD-9 and ICD-8 codes 4100–4149.

Data were extracted and analysed for the years 1980 (or the establishment of the present-day country if later) to 2009 where available. In some countries, death registration or population data were missing for some years. Cyprus was excluded from analyses due to a high level of unreliable and missing data. Data for Germany for years prior to 1990 were obtained by combining death registration and population data for the former Democratic Republic of Germany and the former Federal Republic of Germany and calculating overall rates. England, Wales, Scotland, and Northern Ireland were analysed together as the UK. The age groups analysed were (i) <45 years, (ii) 45–54 years, (iii) 55–64 years, and (iv) 65 years and over. All age groups up to 45 years were combined due to the low numbers of deaths before this age, and because subgroups that contain any year with 0 deaths must be excluded from joinpoint analyses.

Age-standardized mortality rates by country, sex, and age group were calculated. In the descriptive tables, 5-year average mortality rates are presented, to show more representative and stable rates and minimize the effect of year-to-year fluctuations in death rates, (particularly among younger age groups where rates are relatively low and therefore percentage changes over time are more affected by small absolute changes in rates). The average rate in the five most recent years of data (2005–09) was compared with earlier 5-year periods to describe crude proportional changes in death rates over time. Data for mortality rates in all individual years were, however, used in the joinpoint analysis.

Joinpoint regression was performed to identify periods with statistically distinct log-linear trends in death rates from CHD over time within each age group, by sex and country. This analysis identifies inflexion points ('joinpoints') at which there is a significant change in the trends, using a series of permutation tests, with Bonferroni adjustment for multiple comparisons. The two-sided significance level was set at $p < 0.05$ for all tests. The number and location of significant joinpoints for each country by sex and age group (maximum of 3) was determined using a log-linear model, and the annual percentage change within each segment calculated. Use of a log-linear model enables the analysis of constant percentage (rather than absolute) change in prevalence over time. The log-linear model is also more robust in rare conditions, as CHD generally is in younger subpopulations.¹³ Evidence to suggest a recent plateau in a population group was defined as the situation where the final joinpoint segment (in the best fitted model) was less steeply negative compared with the preceding segment (or indeed, was flat or positive), that is, that the final segment showed less of a decrease than the segment before it. Average annual percentage changes (AAPCs) were also calculated overall (1980–2009) and separately for each decade with respect to the underlying joinpoint model.

All analyses were conducted using Stata version 11.2 (StataCorp, TX, USA) and Joinpoint Regression Program version 3.5.4 (Statistical Research and Applications Branch, National Cancer Institute, USA).

Results

Table 1 provides an overview of the available years of data and the population size, total numbers of deaths, and CHD deaths by country and sex for 2009 (or the most recent year available). Complete data for all 30 study years were available in just over half (14) of the 26 countries included. A further three countries had 29 years of data available, two had 28 years, and three had 27 years. The lowest data availability was for Slovakia, where data were only available from 1992 onwards (18 years), followed by Belgium (23 years). There were more CHD deaths among men than women in 19 of 26 countries in 2009, and a higher percentage of deaths among men were caused by CHD in 18 countries.

Average annual percentage changes: overall trends in mortality

Figures 1 and 2 summarize the AAPCs for CHD mortality by country, age group, and sex overall and for each decade. Almost all countries in the EU have demonstrated very large and significant decreases in death rates from CHD in the last three decades among both men and women when all ages were considered together (Table 2). In many countries, age-standardized mortality rates in 2005–09 were less than half what they were in 1980–84.

The median AAPC for all age groups combined between 1980 and 2009 was -2.7% for men and -2.4% for women. The largest decreases

Table 1 Overview of data availability, and numbers of deaths and population in 2009 by country and sex

	Data years	Males 2009 ^a			Females 2009 ^a		
		Total population	Total deaths	CHD deaths (% of total)	Total population	Total deaths	CHD deaths (% of total)
Austria	1980–2009	4 072 866	36 630	6899 (19)	4 290 174	40 751	7954 (20)
Belgium	1980–99, 2004–06	5 162 615	49 575	5784 (12)	5 385 347	50 527	4548 (9)
Bulgaria	1980–2009	3 670 296	56 849	7349 (13)	3 914 835	51 219	5980 (12)
Czech Republic	1986–2009	5 150 509	54 080	12 101 (22)	5 340 983	53 341	13 664 (26)
Denmark	1980–2006	2 690 179	27 013	3257 (12)	2 744 388	28 205	2979 (11)
Estonia	1981–82, 1985–2009	617 311	8010	1881 (23)	722 960	8089	2451 (30)
Finland	1980–2009	2 618 360	25 152	6024 (24)	2 720 511	24 752	5510 (22)
France	1980–2008	30 082 922	271 671	21 525 (8)	32 047 596	260 803	16 219 (6)
Germany	1980–2009	40 133 272	404 969	67 938 (17)	41 741 500	449 575	67 475 (15)
Greece	1980–2009	5 587 096	57 015	7461 (13)	5 695 655	51 301	4461 (9)
Hungary	1980–2009	4 759 975	66 324	15 588 (24)	5 262 675	64 090	17 598 (27)
Ireland	1980–2009	2 217 664	15 044	2919 (19)	2 241 641	13 854	2209 (16)
Italy	1980–2003, 2006–09	29 219 912	286 619	37 544 (13)	30 972 784	301 819	36 483 (12)
Latvia	1980–2009	1 040 285	14 564	4027 (28)	1 214 549	15 368	4566 (30)
Lithuania	1981–82, 1985–2009	1 553 499	21 828	6416 (29)	1 785 956	20 204	8001 (40)
Luxembourg	1980–2009	247 126	1798	189 (11)	250 667	1823	116 (6)
Malta	1980–2009	206 094	1673	366 (22)	207 897	1549	309 (20)
Netherlands	1980–2009	8 179 936	65 365	6184 (9)	8 350 452	68 870	4481 (7)
Poland	1980–96, 1999–2009	18 423 344	203 826	25 407 (12)	19 730 046	181 114	22 368 (12)
Portugal	1980–2003, 2007–09	5 145 385	53 691	3950 (7)	5 487 097	51 273	3608 (7)
Romania	1980–2009	10 457 219	137 550	26 687 (19)	11 012 740	119 663	25 588 (21)
Slovakia	1992–2009	2 633 428	27 446	7717 (28)	2 784 946	25 467	9295 (36)
Slovenia	1985–2009	1 011 767	9293	1059 (11)	1 030 568	9457	929 (10)
Spain	1980–2009	22 670 866	199 095	20 320 (10)	23 258 612	185 838	15 294 (8)
Sweden	1980–2009	4 626 362	43 753	8414 (19)	4 672 153	46 424	7138 (15)
UK	1980–99, 2001–09	30 374 010	270 804	47 306 (17)	31 417 946	288 813	35 425 (12)

^aData are for 2009, or most recent available year.

in mortality rates were in Denmark, Malta, the Netherlands, Sweden, and the UK (AAPCs $\leq -4.0\%$ among men and $\leq -3.9\%$ among women from 1980 and 2009) (Table 2). The exceptions to these significant decreases in mortality rates among men were in Hungary, Latvia, Lithuania, and Poland (negative but non-significant AAPCs 1980–2009) and Romania (significantly positive AAPC of 1.0%). Among women, non-significant changes were found in Greece, Hungary, Lithuania, Poland, Romania, and Slovakia. No country showed significantly positive AAPCs for women of all ages combined between 1980 and 2009. In the most recent decade, the general pattern was for larger annual decreases in mortality than overall or in previous decades in nearly all countries. Among both men and women, the median AAPC between 2000 and 2009 was -4.1% .

Mortality rates from CHD before age 45 ranged between 2.1 and 14.6 per 100 000 among men, while the rate was <2 per 100 000 among women in 23 of 26 countries. Although absolute mortality rates among young adults are low compared with older age groups, in percentage terms, CHD mortality rates (up to 45 years) decreased between 1980 and 2009 at an equal or greater rate than for all ages combined in 22 of 26 countries for men and around half of countries for women (Table 3). A very notable exception to this was Greece,

where for both men and women, it was the only country to record a net increase in age-standardized CHD mortality rates for those aged <45 years. In most countries, the annual decrease in mortality among those aged under 45 years in the 2000 s was as great or greater than the overall and earlier decreases. The AAPCs for the full range of years in the 65 and over age group were generally somewhat smaller than in the younger age groups, with a median AAPC of -2.3% among men and -2.2% among women between 1980 and 2009. Full details of the trends in other age groups are included in Supplementary material online, Tables S1–S4.

Joinpoint analysis: identifying inflexion points and evidence for plateaus in mortality trends

Joinpoint analyses revealed wide variation in trends of CHD mortality over the last three decades and little in the way of clear patterns within or between age groups and sexes. In each of the age and sex groups examined, there was a mixture of countries demonstrating continuous linear trends (no joinpoints identified) and models which contained one to three joinpoints over the 30 years of analysis.

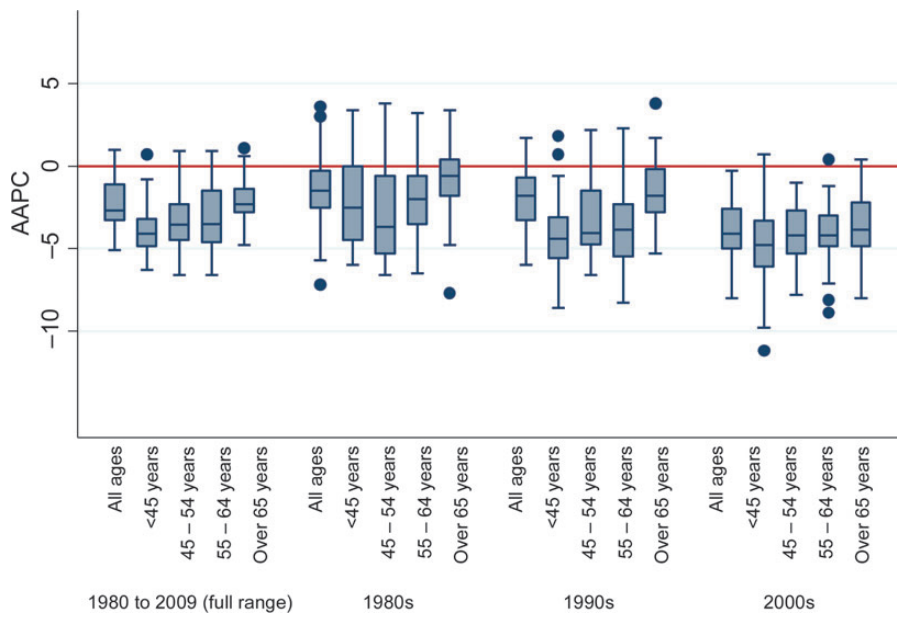


Figure 1 Boxplot of distribution of average annual percentage changes in coronary heart disease among men overall and for each decade across age groups.

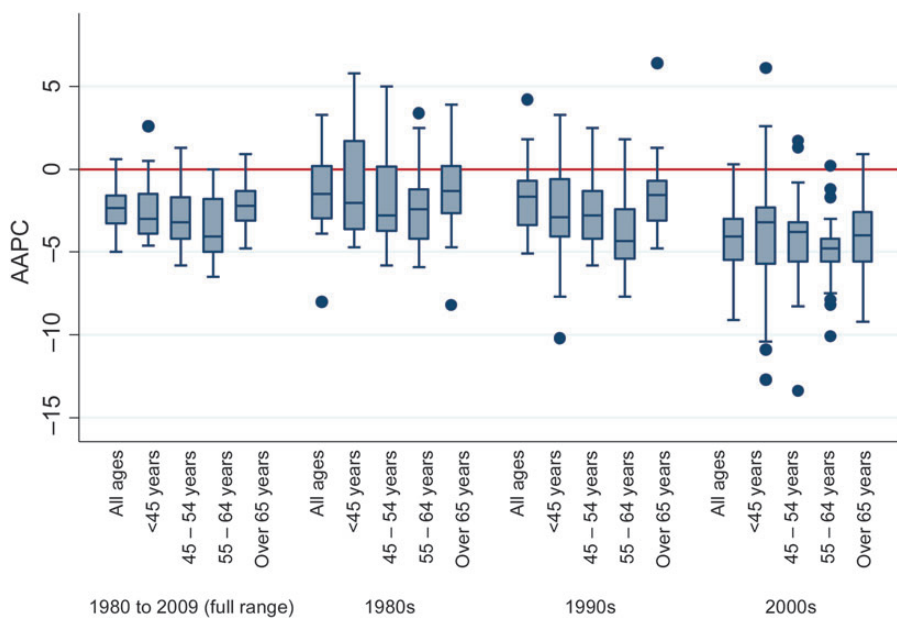


Figure 2 Boxplot of distribution of average annual percentage changes in coronary heart disease among women overall and for each decade across age groups.

In all age groups and both sexes, there were a number of countries that had segments of significantly positive trend in mortality, although these were clearly the exceptions.

Table 4 summarizes the available evidence of a recent plateauing of trends in CHD mortality. Overall, across the 26 countries in this study, evidence of a recent plateau in CHD mortality trends

Table 2 Age-standardized mortality rates, total percentage change, average annual percentage changes, and Joinpoint analysis by country and sex, all ages combined

	Age-standardized mortality per 100 000: 5-year average rates					Average annual percentage change (AAPC) for mortality rates				Joinpoints—annual percentage change (APC) and end year for each segment in the best fitting model			
	1980–84	1990–94	2000–04	2005–09	25-year crude total % change ^a	1980–2009	1980–89	1990–99	2000–09	Segment 1	Segment 2	Segment 3	Segment 4
Males													
Austria	243	218	171	139	–43	–2.0*	–0.3	–1.6*	–4.1*	3.1 1982	–1.2* 1998	–4.1* 2009	
Belgium	187	126	104	93	–50	–2.9*	–4.2*	–0.3	–3.8*	–2.6* 1985	–6.2* 1990	0.1 1998	–3.8* 2006
Bulgaria	244	291	242	188	–23	–1.1*	3.0*	–0.6	–5.4*	5.1* 1985	0.3 1997	–3.7* 2005	–7.5* 2009
Czech Republic	381 ^b	400	241	228	^b	–2.8*	–0.6	–4.9*	–1.4*	–0.6 1992	–6.1* 2000	–1.4* 2009	
Denmark	365	267	141	103	–72	–5.1*	–2.5*	–6.0*	–8.0*	–2.5* 1990	–6.0* 2001	–8.4* 2006	
Estonia	646	606	462	348	–46	–2.9*	–1.6*	–1.6*	–5.6*	–1.6* 2002	–6.7* 2009		
Finland	421	334	232	192	–54	–3.1*	–1.8*	–3.6*	–3.6*	–1.8* 1989	–3.6* 2009		
France	111	87	70	57	–49	–2.6*	–1.7*	–2.0*	–4.1*	0.0 1986	–5.1* 1990	–2.0* 2002	–4.8* 2008
Germany	249 ^b	226	165	127	–49	–2.8*	–1.0*	–2.3*	–5.0*	–1.0* 1995	–3.9* 2003	–5.5* 2009	
Greece	123	136	124	104	–16	–0.8*	1.3*	–0.7*	–3.2*	1.3* 1992	–1.2* 2004	–4.8* 2009	
Hungary	334	343	306	309	–7	–0.6	0.1	0.1	–1.5	0.1 1999	–5.4 2002	5.2 2005	–4.3* 2009
Ireland	391	320	201	152	–61	–3.3*	–1.2*	–3.3*	–5.1*	0.1 1985	–2.7* 1998	–7.6* 2005	–2 2009
Italy	171	136	111	85	–50	–2.8*	–2.8*	–1.3*	–4.2*	–3.0* 1988	–1.0* 1998	–4.2* 2009	
Latvia	604	595	472	426	–30	–1.4	–1.5*	–1.1	–1.6*	–1.5* 1991	8.4 1994	–9.3 1997	–1.6* 2009
Lithuania	511	597	458	462	–10	–0.7	1.1*	–3.1*	–0.3	1.1* 1995	–8.2* 1999	2.0 2005	–3.0 2009
Luxembourg	217	157	118	95	–56	–3.3*	–3.3*	–3.3*	–3.3*	–3.3* 2009			
Malta	409	270	197	174	–57	–4.1*	–7.2*	–2.6*	–2.6*	–15.8* 1983	–2.6* 2009		
Netherlands	252	180	110	74	–71	–4.7*	–2.5*	–4.0*	–7.5*	–1.3* 1985	–4.0* 1999	–7.5* 2009	
Poland	165	190	186	152	–7	–0.5	1.9*	0.2	–4.3*	1.9* 1992	–6.4 1995	4.7* 2000	–4.3* 2009
Portugal	121	110	87	65	–46	–2.4*	–0.9*	–2.2*	–4.2*	–0.9* 1991	–2.3* 2003	–5.1 2009	
Romania	199	279	286	257	29	1.0*	3.6*	1.7*	–2.0*	3.6* 1996	–2.0* 2009		
Slovakia	381 ^b	366	371	337	^b	–0.6*		–0.6*	–0.6*	–0.6* 2009			
Slovenia		184	136	102		–2.6*	–5.7	–0.9	–4.3*	–11.1* 1988	12.2* 1992	–4.3* 2009	
Spain	114	106	90	74	–36	–1.8*	–0.7*	–0.7*	–3.9*	–0.7* 1999	–3.9* 2009		
Sweden	378	251	164	130	–66	–4.1*	–4.1*	–3.8*	–4.5*	–2.9* 1986	–6.4* 1989	–3.3* 1995	–4.5* 2009
UK	371	291	177	132	–64	–4.0*	–1.9*	–4.2*	–6.2*	–1.0* 1985	–3.0* 1993	–4.7* 2002	–6.4* 2009
Females													
Austria	107	110	95	78	–27	–1.4*	0.2	–0.7*	–3.7*	0.2 1995	–1.9* 2003	–4.6* 2009	
Belgium	80	56	47	41	–48	–2.8*	–3.8*	–1.0	–3.7*	–3.8* 1992	2.5 1996	–3.7* 2006	
Bulgaria	155	177	142	97	–37	–1.8*	3.1*	–1.0*	–7.2*	6.2* 1985	–0.6 1998	–4.2* 2003	–8.6* 2009
Czech Republic	206 ^b	206	132	137	^b	–2.2*	–1.5*	–4.3*	0.3	–1.5* 1994	–6.5* 2000	0.3 2009	
Denmark	176	133	74	53	–70	–5.0*	–2.7*	–5.1*	–9.1*	–2.7* 1993	–8.7* 1997	–1.2 2000	–9.1* 2006

Continued

Table 2 Continued

	Age-standardized mortality per 100 000: 5-year average rates					Average annual percentage change (AAPC) for mortality rates				Joinpoints—annual percentage change (APC) and end year for each segment in the best fitting model							
	1980–84	1990–94	2000–04	2005–09	25-year crude total % change ^a	1980–2009	1980–89	1990–99	2000–09	Segment 1	Segment 2	Segment 3	Segment 4				
Estonia	366	322	245	172	–53	–3.5*	–2.1*	–2.1*	–6.4*	–2.1*	2002	–7.6*	2009				
Finland	169	151	111	89	–47	–2.5*	–0.5	–2.9*	–4.1*	–0.2	1988	–2.9*	2002	–4.4*	2009		
France	48	37	28	22	–54	–3.1*	–1.6*	–3.0*	–5.0*	–0.3	1986	–4.0*	1994	–2.2*	2003	–6.6*	2008
Germany	109 ^b	110	88	67	–39	–2.1*	0.0	–1.3*	–5.2*	0.0	1995	–2.9*	2003	–6.3*	2009		
Greece	48	63	56	45	–6	–0.4	2.9*	–0.2	–4.0*	2.9*	1993	–1.7*	2004	–5.9*	2009		
Hungary	168	176	177	178	6	–0.1	0.7*	0.7*	–1.3	0.7*	1999	–3.0	2002	4.7	2005	–4.8*	2009
Ireland	180	149	98	74	–59	–3.3*	–1.7*	–2.4*	–5.5*	–1.7*	1998	–8.0*	2005	–2.3	2009		
Italy	84	67	59	43	–49	–2.8*	–3.6*	0.0	–4.7*	–4.8*	1987	0.6	1998	–4.7*	2009		
Latvia	344	295	246	207	–40	–2.0*	–2.0*	–2.0*	–2.0*	–2.0*	2009						
Lithuania	343	375	257	251	–27	–1.6	0.4	–4.2*	–1.0	0.4	1996	–12.9*	1999	1.0	2006	–5.0	2009
Luxembourg	88	65	52	44	–50	–3.0*	–3.0*	–3.0*	–3.0*	–3.0*	2009						
Malta	252	166	118	95	–62	–4.8*	–8.0	–3.4*	–3.4*	–22.0*	1984	10.9	1987	–3.4*	2009		
Netherlands	105	78	50	33	–69	–4.7*	–3.0*	–3.7*	–7.5*	–3.0*	1996	–5.3*	2002	–8.1*	2009		
Poland	56	66	87	72	28	0.6	1.0*	4.2*	–4.2*	1.0*	1995	8.4*	2000	–4.2*	2009		
Portugal	60	56	46	37	–39	–1.9*	–1.3*	–1.3*	–3.3	–1.3*	2003	–4.3	2009				
Romania	140	182	183	160	15	0.6	3.3*	1.8*	–2.5*	4.7*	1987	–1.5	1990	4.1*	1996	–2.5*	2009
Slovakia	206 ^b	205	239	214	^b	0.3		0.3	0.3	0.3	2009						
Slovenia		103	65	45		–2.9*	–3.7	–1.3	–5.8*	–20.2	1987	16.2*	1992	–5.8*	2009		
Spain	51	47	39	31	–39	–2.1*	–0.7*	–1.0*	–4.6*	–0.7*	1998	–3.5*	2005	–5.9*	2009		
Sweden	175	114	79	64	–64	–3.9*	–3.9*	–3.9*	–3.9*	–3.9*	2009						
UK	164	138	84	61	–63	–3.9*	–1.1*	–4.0*	–6.6*	0.1	1985	–2.5*	1993	–4.8*	2003	–7.2*	2009

Values are unadjusted averages of rates for each 5-year period, or for as many years as data were available within the period. Exceptions, where data were not available for all years, are: Belgium (to 2006); Denmark (to 2006); France (to 2008); Italy (no data 2005); Lithuania (no data 1980, 1983, 1984); Portugal (no data 2004 to 2006); and Slovenia (no data before 1985).

^a25-year total crude change calculated from difference between 1980–84 average rate and 2005–09 average rate.

^bData for Germany prior to 1990 calculated from raw data for the Former East and West Germany. 1980–84 data for Czech Republic and Slovakia are combined data from Czechoslovakia, therefore, not directly comparable.

*Rate of change significantly different from 0 at $P < 0.05$

(where the rate of CHD mortality decrease in the most recent period was less pronounced than the previous period in the model) was seen in at least one age group of men from 15 countries, and women from 12 different countries. Countries from all geographical parts of Europe were represented in this group, as were older and newer members of the EU. While there was variability between age groups, there was little to suggest a consistent pattern of plateauing among younger adults (aged under 45 or aged 45–54 years) when compared either to the older age groups, or to all ages combined.

In each of the age groups, the countries in which the most recent segment of trend showed evidence of a possible plateau were outnumbered by the countries in which the most recent trend in CHD mortality was a steeper decrease than previously. Owing to the relatively small numbers of deaths in younger age groups, resulting in less stable rates from year-to-year and reduced statistical power, there were noticeably more countries for which there were no joinpoints identified in the two younger age groups.

In the majority of subgroups for which there was evidence of a recent plateau in trends, the trend in the most recent segment still represented a statistically significant annual decrease in CHD mortality. There was only one subgroup for which the final segment was significantly positive after a previous decline; women aged under 45 in Lithuania (APC +6.1%, 2000–2009). In addition, there were three subgroups (all in Greece) for which no joinpoints were identified, but the trend over the entire 30 years of analysis was significantly positive; both sexes aged under 45 (women APC +2.6%, men APC +0.7%), and women 45–54 years (APC +1.3%).

Evidence of a recent plateau was shown for all age groups combined in two countries for both sexes (Czech Republic and Ireland) and three further countries among men only (Latvia, Malta, and Poland).

On examining the two younger age groups, there was evidence of recent plateauing of trends in six countries each for men and women in the under 45 year age group, although these were not all the same countries (Latvia, Lithuania, and the UK for both sexes; plus Italy, Poland and Slovakia among men; and Czech Republic, France, and Italy among women). In the 45–54 year age group, Latvia and the UK again showed evidence of a possible plateau in mortality among both sexes, as did Lithuania for women and Sweden, Austria, Czech Republic, and Slovakia for men. Greek women in this age group showed a constant, significantly increasing trend over the entire period of analysis (APC +1.3%, no joinpoints identified).

Discussion

Across the EU as a whole, there is little evidence to support the hypothesis that there has been a consistent pattern of recent plateaus in CHD mortality rates, or that any recent plateaus have occurred largely or exclusively in younger age groups. Overall, the rate of decrease in CHD mortality appears to be either stable or accelerating in the majority of countries and age groups, across both sexes. Specifically in younger age groups, the proportional rates of decline in premature CHD mortality appear to be broadly similar to the rates of decline observed in older populations in the EU as a whole. In the majority of countries, the most recent reductions in AAPC in CHD mortality were as great as or greater than they have been previously.

There is, of course, substantial heterogeneity across the EU, and when individual countries are examined, it is clear that there are some countries with cause for concern, where rates of decrease in CHD mortality do appear to have slowed, including in the UK, consistent with previously published work.^{7–9} In addition there are two countries (Greece and Lithuania) in which CHD mortality rates have begun to significantly increase in recent years or decades in younger subpopulations.

Given the relative scarcity of high quality age-specific data on most CHD risk factors, it is difficult to draw conclusions about the reasons for the plateauing or increasing trends observed among younger age groups in some countries. In those countries that have experienced increases in CHD mortality rates (Greece and Lithuania), the evidence appears to suggest that overall rates of major CHD risk factors are relatively high by European standards. In Greece, where CHD mortality has increased steadily from a very low base in the 1980s, rates of diabetes and hypertension are low by European standards. Conversely, in 2009, Greece had the highest smoking rates in the EU (42% of adults overall), and smoking rates among those aged 25–54 year old (54–57%) were more than double the rate among those aged 55 years and over (23%).¹⁴ The most recent available data show that Greece also had one of the highest adult obesity prevalence rates in Europe; however, these data are drawn from a subnational sample and are now 10 years old.^{15,16} Among children, data from 2010 showed that >40% of Greek children aged 10–12 years were overweight or obese, the highest rate in the EU.^{17,18} For Lithuania as well, there is a paucity of age-specific data on risk factors for CHD mortality. There is, however, evidence of an increase in smoking among young people, at least until 2002,¹⁹ and of a trend to increasing diabetes prevalence among adults.³ There is also evidence of high rates of risk factors for NCDs overall.²⁰ Conversely, some recent studies have indicated that obesity prevalence may be decreasing among Lithuanian adults, although these estimates are based on self-reported data, which may introduce a degree of bias.²¹

In many cases, the AAPCs found in this study for the full range of years showed greater reductions in CHD mortality among younger age groups when compared with the 65 years and older group. This apparently smaller reduction in mortality among older adults may be a result of delayed rather than averted CHD mortality, where reductions in mortality among (for example) those aged 65–74 are partially offset by lower rates of reduction among the very old.

The existing body of published evidence on this topic has provided very important evidence, in a number of individual countries in Europe and beyond,^{7–11,22} that despite overall very impressive reductions in CHD mortality in recent decades, it is possible that the increasing prevalence of risk factors, such as diabetes and obesity, and plateaus in the prevalence of hypertension, are attenuating these reductions for younger populations. While this is clearly true in some countries, our study has demonstrated that there is in fact substantial variation between EU countries in how these trends are playing out. It remains very plausible that observed increases in preventable risk factors for CHD will have an impact on mortality rates in all age groups including young adults in the future. This effect is, however, not yet clearly apparent across the EU, and there may still be time for public health policy and action to have an impact on these risk factors to prevent such impacts. It

Table 3 Age-standardized mortality rates, total percentage change, average annual percentage changes and Joinpoint analysis by country and sex, ages <45 years

	Age-standardized mortality per 100 000: 5-year average rates					Average annual percentage change (AAPC) for mortality rates				Joinpoints—annual percentage change (APC) and end year for each segment in the best fitting model			
	1980–84	1990–94	2000–04	2005–09	25-year crude total % change ^a	1980–2009	1980–89	1990–99	2000–09	Segment 1	Segment 2	Segment 3	Segment 4
Males													
Austria	8.6	6.3	4.2	2.9	–66	–4.4*	–2.6*	–3.1*	–7.3*	–2.6* 1998	–7.3* 2009		
Belgium	7.9	4.6	2.5	2.7	–66	–4.5*	–4.5*	–4.5*	–4.5*	–4.5* 2006			
Bulgaria	12.7	16.4	12.5	9.8	–23	–0.9*	2.6*	–1.2*	–4.2*	2.6* 1994	–4.2* 2009		
Czech Republic	15.1 ^b	12.4	5.5	3.6	^b	–6.3*	1.3	–7.9*	–7.9*	1.3 1990	–7.9* 2009		
Denmark	7.6	4.5	2.6	2.4	–69	–5.0*	–5.0*	–5.0*	–5.0*	–5.0* 2006			
Estonia	25.7	25.3	12.7	6.4	–75	–5.4*	0.0	–5.6*	–9.8*	0.0 1994	–9.8* 2009		
Finland	14.6	7.9	4.3	3.1	–79	–6.0*	–6.0*	–6.0*	–6.0*	–6.0* 2009			
France	4.6	4.0	2.9	2.3	–50	–2.9*	–0.9	–3.2*	–4.6*	–5.2 1982	3.0 1986	–3.2* 2000	–4.6* 2008
Germany	7.4 ^b	5.8	4.0	3.1	–58	–3.8*	–3.1*	–3.1*	–5.5*	–3.5* 1988	0.4 1992	–4.1* 2006	–8.3* 2009
Greece	7.8	8.8	9.2	9.6	24	0.7*	0.7*	0.7*	0.7*	0.7* 2009			
Hungary	26.5	24.9	13.8	9.7	–64	–3.9*	–0.5	–4.1*	–6.9*	–0.5 1994	–6.9* 2009		
Ireland	12.9	7.8	4.6	3.5	–73	–4.9*	–4.9*	–4.9*	–4.9*	–4.9* 2009			
Italy	7.0	4.8	3.0	2.3	–67	–4.1*	–3.7*	–5.3*	–3.3*	–3.7* 1996	–8.4 1999	–3.3* 2009	
Latvia	34.5	37.9	16.2	14.6	–58	–3.4	–2.5	–6.4	–2.6*	–2.5 1989	9.3 1994	–26 1997	–2.6* 2009
Lithuania	23.2	31.7	13.7	14.2	–39	–1.7	3.4*	–7.1	–1.1	3.4* 1994	–22.7 1997	–1.1 2009	
Luxembourg	9.6	6.2	3.4	3.6	–63	–5.0*	–5.0*	–5.0*	–5.0*	–5.0* 2009			
Malta	7.6	5.3	4.5	3.1	–59	–2.4	–2.4	–2.4	–2.4	–2.4 2009			
Netherlands	8.2	5.2	3.3	2.4	–70	–4.7*	–4.7*	–4.7*	–4.7*	–4.7* 2009			
Poland	18.0	18.5	7.5	5.2	–71	–5.0*	0.7	–8.6*	–7.5*	–6.9 1982	2.9* 1991	–13.8* 1994	–7.5* 2009
Portugal	6.2	6.3	5.4	2.2	–64	–4.0*	–0.6	–0.6	–11.2*	–0.6 2003	–16.1 2009		
Romania	12.8	19.4	15.2	11.3	–12	–0.8	1.8*	1.8*	–6.1*	1.8* 1989	8.6* 1995	–6.1* 2009	
Slovakia	15.1 ^b	13.8	7.4	6.3	^b	–4.4*		–6.6*	–2.3	–6.6* 2005	3.4 2009		
Slovenia		7.2	4.3	3.2		–4.2*	–4.2*	–4.2*	–4.2*	–4.2* 2009			
Spain	6.8	5.3	4.0	3.1	–55	–3.2*	–2.1*	–2.1*	–5.2*	–2.1* 1999	–5.2* 2009		
Sweden	5.9	3.8	2.6	2.1	–64	–4.1*	–4.1*	–4.1*	–4.1*	–4.1* 2009			
UK	12.4	7.8	5.2	4.5	–64	–4.0*	–4.7*	–4.3*	–2.9*	–4.7* 1997	–2.9* 2009		
Females													
Austria	1.7	1.5	1.0	0.5	–69	–4.6*	–1.1	–1.1	–10.9*	–1.1 1999	–10.9* 2009		
Belgium	1.9	1.0	0.6	0.7	–64	–4.0*	–4.0*	–4.0*	–4.0*	–4.0* 2006			
Bulgaria	1.9	3.0	3.1	1.7	–9	–1.5	2.8*	2.8*	–10.4*	2.8* 2003	–16.3* 2009		
Czech Republic	1.8 ^b	1.9	1.0	0.8	^b	–4.3*	–2.0*	–7.2*	–2.6*	–2.0* 1996	–16.7 1999	–2.6* 2009	
Denmark	1.6	1.0	0.8	0.7	–56	–3.2*	–3.2*	–3.2*	–3.2*	–3.2* 2006			

Estonia	2.4	2.8	2.4	0.9	-61	-3.9*	0.6	0.6	-12.7*	0.6	2001	-14.3*	2009				
Finland	1.4	0.9	0.8	0.4	-69	-4.4*	-4.4*	-4.4*	-4.4*	-4.4*	2009						
France	0.6	0.5	0.5	0.5	-19	-1.5	-3.6	-0.6*	-0.6*	-13.4	1982	-0.6*	2008				
Germany	1.2 ^b	1.1	0.9	0.8	-30	-1.5*	-0.2	-0.9*	-3.3*	-0.2	1997	-3.3*	2009				
Greece	1.1	1.2	1.6	2.0	88	2.6*	2.6*	2.6*	2.6*	2.6*	2009						
Hungary	5.1	5.8	3.8	2.7	-47	-2.3*	1.7	-3.2*	-5.5*	1.7	1993	-5.5*	2009				
Ireland	1.8	1.1	1.0	0.9	-53	-2.8*	-2.8*	-2.8*	-2.8*	-2.8*	2009						
Italy	1.1	0.9	0.5	0.4	-60	-3.7*	-3.6*	-4.1	-2.4*	-7.0*	1984	-0.7	1997	-14.9	2000	-2.4*	2009
Latvia	5.0	5.8	2.0	1.9	-62	-3.0	1.8	-10.2	-0.8	1.8	1995	-29.4	1998	-0.8	2009		
Lithuania	2.8	4.5	1.7	2.5	-11	0.5	5.8*	-7.7*	6.1*	5.8*	1994	-17.2*	2000	6.1*	2009		
Luxembourg	2.2	1.2	0.7	0.7	-69												
Malta	1.8	1.2	1.4	0.3	-81												
Netherlands	1.7	1.3	1.3	0.9	-48	-3.1*	-4.7*	2.6	-7.2*	-4.7*	1989	2.6	1999	-7.2*	2009		
Poland	2.2	2.8	1.2	0.9	-60	-3.6*	3.8*	-6.6*	-7.9*	3.8*	1991	-7.9*	2009				
Portugal	1.6	1.2	1.0	0.6	-62	-2.9*	-2.9*	-2.9*	-2.9*	-2.9*	2009						
Romania	2.9	3.7	3.5	2.6	-8	-0.7	1.0	3.3*	-5.7*	1.0	1990	8.0*	1996	-5.7*	2009		
Slovakia	1.8 ^b	2.2	1.3	1.3	^b	-3.9*		-3.9*	-3.9*	-3.9*	2009						
Slovenia		0.9	0.6	0.3													
Spain	1.0	0.8	0.7	0.6	-44	-2.1*	-2.1*	-2.1*	-2.1*	-2.1*	2009						
Sweden	1.0	1.0	0.6	0.6	-46	-2.9*	-2.9*	-2.9*	-2.9*	-2.9*	2009						
UK	2.1	1.5	1.2	1.0	-52	-3.0*	-4.4*	-2.3*	-2.3*	-5.5*	1986	-2.3*	2009				

Values are unadjusted averages of rates for each 5-year period, or for as many years as data were available within the period. Exceptions, where data were not available for all years, are: Belgium (to 2006); Denmark (to 2006); France (to 2008); Italy (no data 2005); Lithuania (no data 1980, 1983, 1984); Portugal (no data 2004 to 2006); and Slovenia (no data before 1985). AAPCs and APCs cannot be calculated when there are 0 deaths in any group.

^a25-year total crude change calculated from difference between 1980–84 average rate and 2005–09 average rate.

^bData for Germany prior to 1990 calculated from raw data for the Former East and West Germany. 1980–84 data for Czech Republic and Slovakia are combined data from Czechoslovakia, therefore, not directly comparable.

*Rate of change significantly different from 0 at $P < 0.05$.

Table 4 Summary of number of countries exhibiting evidence for recent plateauing in trends in coronary heart disease mortality

	All ages	<45 years	45–54 years	55–64 years	65 years and over	Total countries ^a
Men						
Evidence for recent plateau—final segment less steeply decreasing than previous segment	5	6	6	8	4	15
No evidence of recent plateau—final segment more steeply decreasing than previous segment	19	10	14	15	19	—
No evidence of recent plateau—no joinpoints identified (consistent trend)	2	10	6	3	3	—
Women						
Evidence for recent plateau—final segment less steeply decreasing than previous segment	2	6	3	7	4	12
No evidence of recent plateau—final segment more steeply decreasing than previous segment	20	8	11	13	18	—
No evidence of recent plateau—no joinpoints identified (consistent trend)	4	12	12	6	3	—

^aTotal number of unique countries showing evidence of a recent plateau in at least one age group.

is crucial that future research continues to monitor trends in CHD risk factors and mortality across the EU and to examine the relationships between preventable risk factors and CHD among younger adults. Any indications of potential plateauing of CHD mortality trends among younger age groups—which were evident in this study for some countries but not yet for the EU as a whole—would be an important advance warning of potentially very high future burden of CHD as the cohort ages.

An important consideration in interpreting the trends observed in this study is the limitation inherent in using mortality as the sole outcome. Given the very low rates of CHD mortality among younger age groups, it could be the case that mortality rates in this age group have been stable or decreasing despite an increase in incidence in CHD. Indeed, there is some evidence from France that younger female patients comprised an increasing proportion of hospital presentations for myocardial infarction between 1995 and 2010.²³ If this is the case across Europe, these less favourable trends in incidence among younger populations may yet translate into increased CHD mortality rates in the future. Further research is needed to determine the underlying trends in incidence and case–fatality rates among varying age groups. In addition, further exploration of trends in sudden death rates would provide important insights into the changing epidemiology of CHD in Europe.

The method used to define ‘recent plateau’ in trends brings together joinpoint analyses across a very large number of subgroups (260) and enables assessment at the EU level of whether there is an emerging overall pattern of plateauing trends in CHD mortality rates. This synthesis is, however, necessarily a simplification which provides an overview of the patterns across 26 countries, but may not give a holistic indication of a ‘recent plateau’ for a small number of subgroups or countries. This is especially the case where some segments of trend are very brief in the joinpoint model that was fit to the data. As an example, women aged under 45 years in France were

classified as having ‘evidence of a recent plateau’ as the most recent joinpoint segment has an APC of -0.6% , while the preceding segment had an APC of -13.4% . The first segment, however, only spans the years 1980–1982, and after that period there has been a consistent annual percentage reduction in mortality rates. In addition, while these segments are significantly different in trend to each other, only the most recent segment is statistically significantly different from 0. An additional potential limitation of the joinpoint analysis approach used in this study was the setting of a maximum limit of three joinpoints in the model. While a greater number of joinpoints may have created models with a closer fit to the observed data, the maximum three joinpoints were identified only in relatively few of the subgroups analysed, particularly for women and younger age groups.

The mortality and population data compiled by the WHO offer an extremely valuable resource to enable large-scale analysis and inter-country comparisons such as those in this study. While the data are generally of high quality, and in the EU, generally have very high coverage, there are limitations to using internationally aggregated vital statistics, and direct comparisons between countries require some caution. There is variability between countries in both the coverage and the quality of the vital statistics databases collected and reported to the WHO. In addition, there is variability between countries in ICD coding practices. For instance in France, it has been documented that CHD deaths are under-reported compared with other countries, and a high proportion of deaths are coded as ‘other causes’, meaning the true rates of CVD and CHD deaths are likely to be higher than recorded.²⁴ Further limitations of the data include missing years for some countries, and the necessity for historical studies to take in periods of time spanning the use of several versions of the ICD. The effect of this last limitation, is however, minimized by the use of relatively broad disease categories, for which the implications of coding changes are small.

Conclusion

The last three decades have seen significant reductions in CHD mortality in all age groups and both sexes in most EU countries and to date, there is little evidence to suggest that these reductions are plateauing in younger age groups across the EU as a whole. However, in a small number of countries there was evidence of recent plateauing in some age groups. It remains vitally important for the whole EU to monitor and work towards reducing preventable risk factors for CHD and other chronic conditions to promote wellbeing and equity across the region.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Acknowledgements

This study arises from the European Heart Health Strategy II project (EuroHeart II) which has received co-funding from the European Union, in the framework of the Health Programme. The sole responsibility for the text lies with the authors and the Executive Agency for Health and Consumers is not responsible for any use that may be made of the information contained herein. The authors would like to thank the EuroHeart II Steering committee and work package leaders for their support of the project and comments on this manuscript.

Funding

This work was supported by the European Heart Health Strategy II project (EuroHeart II) which has received co-funding from the European Union, in the framework of the Health Programme (MN). N.T., M.R., and P.S. positions at the University of Oxford are fully supported by the British Heart Foundation.

Conflict of interest: none declared.

References

- Levi F, Chatenoud L, Bertuccio P, Lucchini F, Negri E, La Vecchia C. Mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world: an update. *Eur J Cardiovasc Prev Rehabil* 2009;**16**:333–350.
- Smolina K, Wright FL, Rayner M, Goldacre MJ. Determinants of the decline in mortality from acute myocardial infarction in England between 2002 and 2010: linked national database study. *Br Med J* 2012;**344**:d8059.
- Nichols M, Townsend N, Scarborough P, Luengo-Fernandez R, Leal J, Gray A, Rayner M. *European Cardiovascular Disease Statistics 2012*. Brussels: European Heart Network, Sophia Antipolis: European Society of Cardiology, 2012.
- Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, Singh GM, Gutierrez HR, Lu Y, Bahalim AN, Farzadfar F, Riley LM, Ezzati M. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet* 2011;**377**:557–567.
- Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, Lin JK, Farzadfar F, Khang YH, Stevens GA, Rao M, Ali MK, Riley LM, Robinson CA, Ezzati M. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet* 2011;**378**:31–40.
- Rayner M, Allender S, Scarborough P. Cardiovascular disease in Europe. *Eur J Cardiovasc Prev Rehabil* 2009;**16**(Suppl. 2):S43–S47.
- O'Flaherty M, Ford E, Allender S, Scarborough P, Capewell S. Coronary heart disease trends in England and Wales from 1984 to 2004: concealed levelling of mortality rates among young adults. *Heart* 2008;**94**:178–181.
- Allender S, Scarborough P, O'Flaherty M, Capewell S. Patterns of coronary heart disease mortality over the 20th century in England and Wales: Possible plateaus in the rate of decline. *BMC Public Health* 2008;**8**:148.
- O'Flaherty M, Bishop J, Redpath A, McLaughlin T, Murphy D, Chalmers J, Capewell S. Coronary heart disease mortality among young adults in Scotland in relation to social inequalities: time trend study. *BMJ* 2009;**339**:b2613.
- Ford ES, Capewell S. Coronary heart disease mortality among young adults in the U.S. from 1980 through 2002: concealed leveling of mortality rates. *J Am Coll Cardiol* 2007;**50**:2128–2132.
- O'Flaherty M, Allender S, Taylor R, Stevenson C, Peeters A, Capewell S. The decline in coronary heart disease mortality is slowing in young adults (Australia 1976–2006): a time trend analysis. *Int J Cardiol* 2012;**158**:193–198.
- Waterhouse J, Correa P, Muir C, Powell J eds. *Cancer Incidence in Five Continents*. Vol. 3. 6: 456. Lyon: International Agency for Research on Cancer; 1976.
- Bertuccio P, Levi F, Lucchini F, Chatenoud L, Bosetti C, Negri E, La Vecchia C. Coronary heart disease and cerebrovascular disease mortality in young adults: recent trends in Europe. *Eur J Cardiovasc Prev Rehabil* 2011;**18**:627–634.
- European Commission. *Special Eurobarometer 332 'Tobacco' / Wave 72.3 – TNS Opinion & Social*. http://ec.europa.eu/public_opinion/index_en.htm. Brussels, Belgium; 2010.
- Koukoulis GN, Sakka C, Katsaros F, Goutou M, Tsiros S, Tsiapali E, Piterou A, Stefanidis I, Stathakis N. High rates of obesity prevalence in adults living in central Greece: data from the ARGOS study. *Hormones (Athens)* 2010;**9**:253–262.
- International Association for the Study of Obesity. *IASO Obesity Data Portal: World Map of Obesity*. <http://www.iaso.org/resources/world-map-obesity/>.
- Farajian P, Risvas G, Karasouli K, Pounis GD, Kastorini CM, Panagiotakos DB, Zampelas A. Very high childhood obesity prevalence and low adherence rates to the Mediterranean diet in Greek children: The GRECO study. *Atherosclerosis* 2011;**217**:525–530.
- International Association for the Study of Obesity. *IASO Obesity Data Portal: Overweight in children in EU 27*. <http://www.iaso.org/resources/obesity-data-portal/resources/tables/>.
- Zaborskis A, Sumska L, Zemaitiene N, Grabauskas V, Vergy A, Petkevicius R. Trends of smoking prevalence among Lithuanian school-aged children in 1994–2006. *Medicina (Kaunas)* 2009;**45**:798–806.
- Grabauskas V, Klumbiene J, Petkeviciene J, Petrauskiene A, Tamosiunas A, Kriaucioniene V, Ramazauskiene V. Risk factors for noncommunicable diseases in Lithuanian rural population: CINDI survey 2007. *Medicina (Kaunas)* 2008;**44**:633–639.
- Webber L, Kilpi F, Marsh T, Rtveladze K, McPherson K, Brown M. Modelling obesity trends and related diseases in Eastern Europe. *Obesity Rev* 2012;**13**:744–751.
- Vaartjes I, O'Flaherty M, Grobbee DE, Bots ML, Capewell S. Coronary heart disease mortality trends in the Netherlands 1972–2007. *Heart* 2011;**97**:569–573.
- Puymirat E, Simon T, Steg PG, Schiele F, Gueret P, Blanchard D, Khalife K, Goldstein P, Cattani S, Vaur L, Cambou JP, Ferrieres J, Danchin N, Investigators UU, Investigators FM. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. *JAMA* 2012;**308**:998–1006.
- WHO Monica Project. *MONICA Monograph and Multimedia Sourcebook: World's Largest Study of Heart Disease Stroke, Risk Factors and Population trends 1979–2002*. Edited by Hugh Tunstall-Pedoe for the WHO MONICA Project. Geneva: WHO; 2003.