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An update on regional variation in cardiovascular mortality within Europe

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Aims For risk assessment in primary prevention of cardiovascular disease, different risk charts are used for high-risk and low-risk countries. The objective of the present study was to analyse the current regional variation in cardiovascular mortality within Europe.

Methods and results Age-standardized mortality rates were calculated for ischaemic heart disease (IHD) and cerebrovascular disease (CVD) from data provided by Eurostat and the National Statistical Offices of the respective countries (2000). For age-standardization, the European standard population (1976) was taken. Rates were calculated both on a national and on a regional level. There is still a clear north–east to south–west gradient in mortality from IHD. With regard to CVD, there appears to be a 'green' circle of reduced mortality in the centre of Western Europe including countries such as France or the northern regions of Italy and Spain. Countries with higher mortality rates, such as the Central and East European countries as well as some Mediterranean countries including Greece, Portugal, and certain regions in Southern Spain and Italy, surround this circle.

Conclusion There is a changing pattern of cardiovascular mortality within Europe, which needs to be taken into account in the definition of high- and low-risk countries in the primary prevention of cardiovascular disease.

Keywords Regional variation • Cardiovascular mortality • Europe • Prevention

Introduction

Regional variations in cardiovascular mortality have been observed both between and within countries in Europe.[1–3] Sans *et al.*[1] reported a clear north–east to south–west gradient in cardiovascular disease mortality (1990–1992; 45–74 years age-adjusted) with the lowest rates for both men and women in France, Spain, Switzerland, and Italy. The highest rates were observed in Central and East European countries such as Ukraine, Bulgaria, or the Russian Federation. When dividing cardiovascular mortality into mortality due to ischaemic heart disease (IHD) and cerebrovascular disease (CVD), some differences in the regional distribution became apparent. For IHD, the north–east to south–west gradient was similar to that observed for cardiovascular diseases as a whole. For CVD, however, there appeared to be a predominantly east to west gradient in mortality. Regional variation within countries, similarly, can be huge.[2,4,5] In Germany, for example, there was an east–west gradient in mortality with a two-fold increased risk of dying from IHD in the state with the highest compared with the state with the lowest mortality.[2] A north–south gradient has been observed for Britain with higher cardiovascular mortality rates in the north compared with the south.[4] In France, similarly, mortality due to IHD showed a north–south gradient.[5]

There are many reasons for the observed regional variations in cardiovascular diseases. They include differences between populations in 'classic' coronary risk factors such as smoking, hypertension, hyperlipidaemia, diabetes, or overweight as well as socio-economic factors, lifestyle variables such as diet, alcohol use, physical activity, medical care, genetic factors, and environmental conditions. The current European Guidelines on Cardiovascular Disease Prevention in Clinical Practice take national variation in cardiovascular mortality into account.[6] In the primary prevention setting, the overall 10-year cardiovascular risk is estimated for different risk factor combinations. The assessment of cardiovascular risk takes into account the following risk factors:

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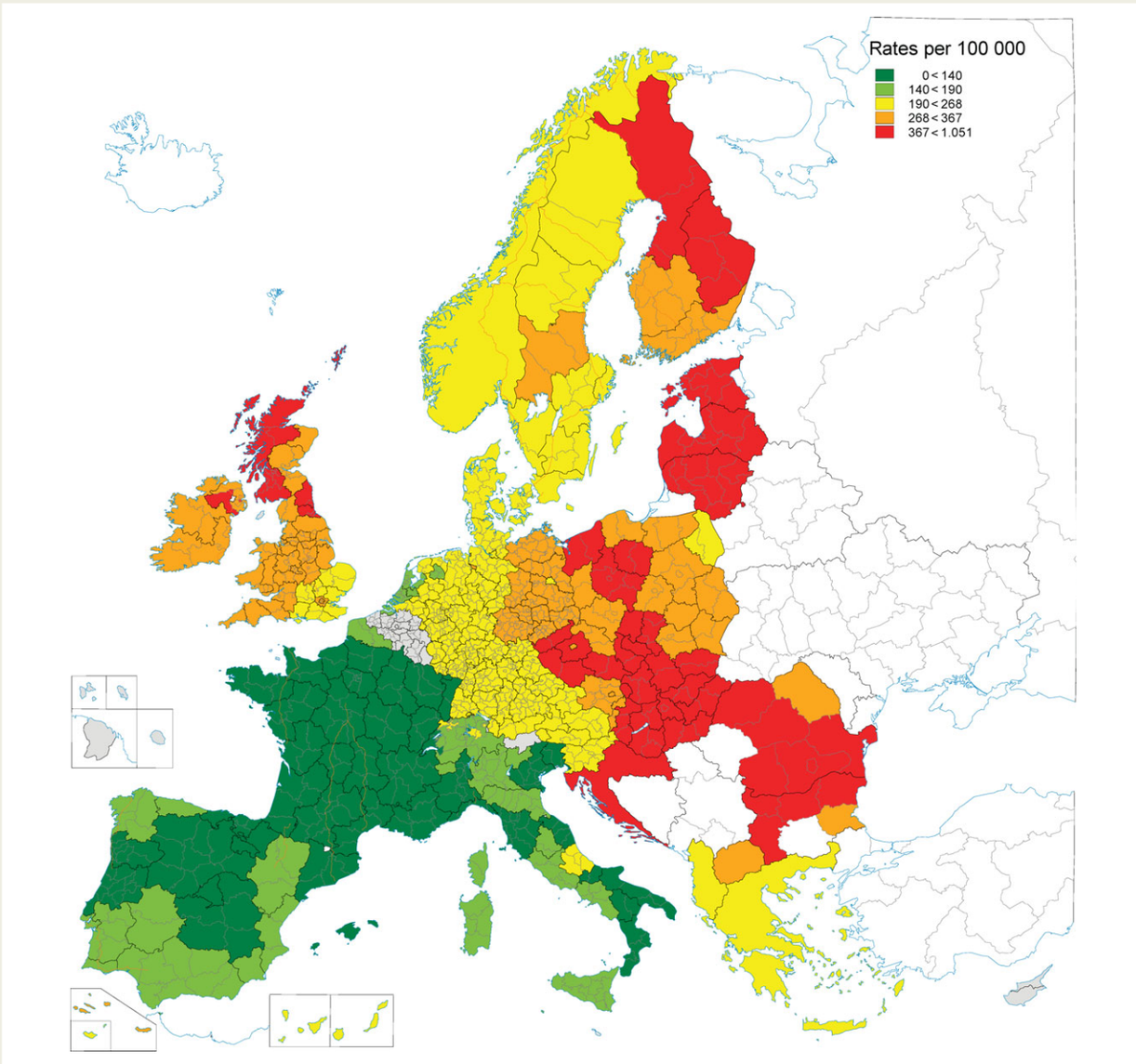

Figure 1 Age-standardized mortality from ischaemic heart disease in European regions (men; age group 45–74 years; year 2000)

age, sex, smoking, systolic blood pressure, and cholesterol. An increased risk ≥5% of a fatal cardiovascular event in the next 10 years should lead to increased preventive efforts, both with regard to lifestyle changes and medication. In the guidelines, the use of two different risk assessment charts is recommended: one for countries with high risk and one for countries with low risk. On the basis of a number of cohort studies assessing cardiovascular risk, countries with a low risk include Belgium, France, Greece, Italy, Luxembourg, Spain, Switzerland, and Portugal and countries with a high risk include all other European regions.

The objective of the present study was to analyse the current variation in cardiovascular mortality within Europe, both on a national and on a regional level.

Methods

Data sources

For cardiovascular mortality rates on a regional level, we contacted the National Statistical Offices of the respective European countries for the year 2000. For IHD and CVD, we used the International Classification of Diseases (ICD)-10 codes I20–I25 and I60–I69. For the assessment of cardiovascular mortality, i.e. IHD and CVD, we combined the respective ICD codes. We excluded countries such as Liechtenstein, Luxembourg, Iceland, and Malta from the analysis, because the year-to-year variation in small countries is too large. For Belgium, no data were available for the year 2000, neither on the regional nor the national level. For Italy, no data were available for the region of Bolzano.

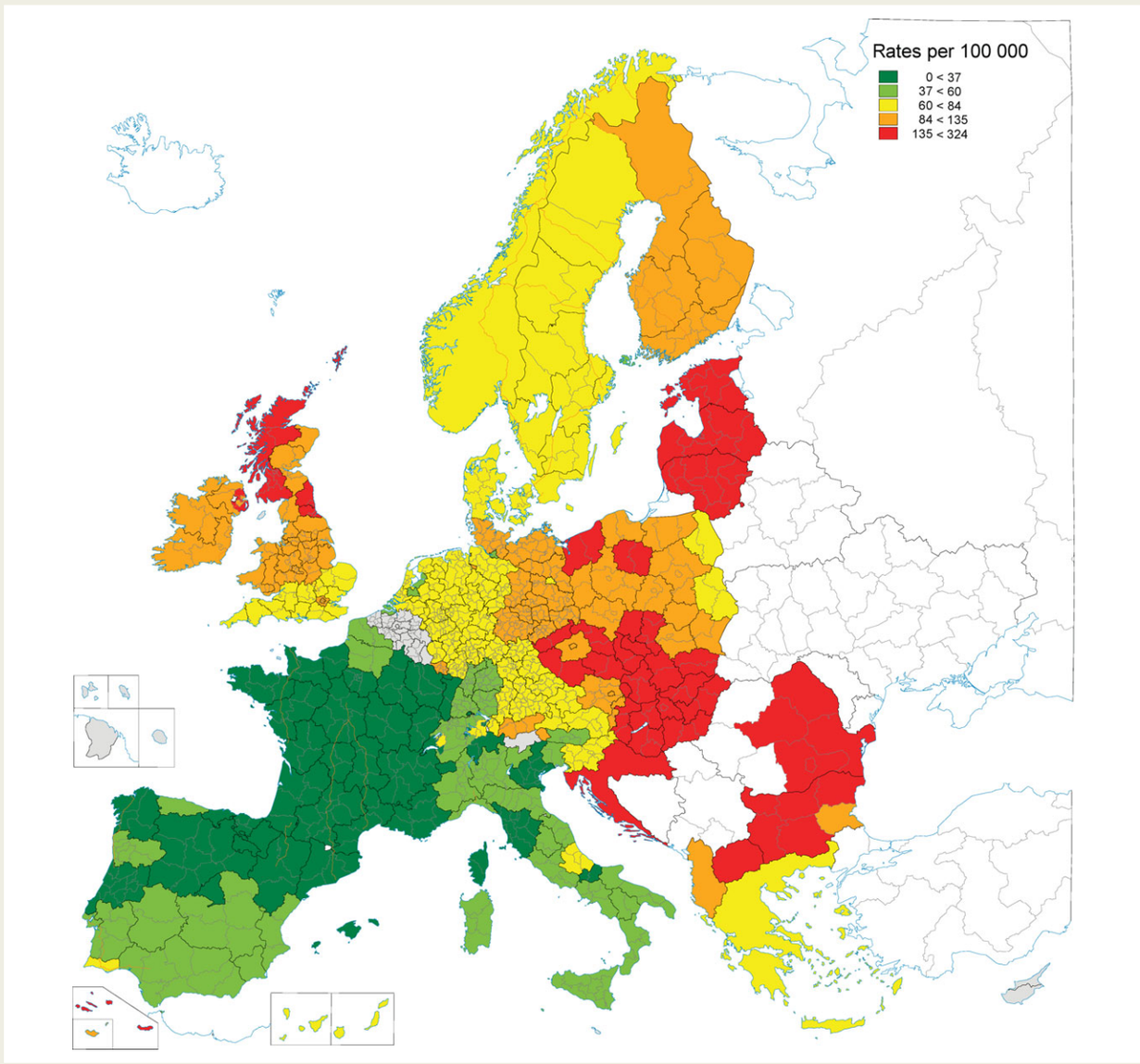

Figure 2 Age-standardized mortality from ischaemic heart disease in European regions (women; age group 45–74 years; year 2000)

Age-standardization

The statistical offices provided either number of deaths from IHD and CVD as well as population data per 5-year age group, or crude standardized mortality rates per 100 000 per 5-year age group. In case of absolute numbers of death, we calculated the standardized rates by dividing the number of deaths in the respective age group by the population number in this age group. Crude standardized rates were assessed for all, and separately for men and women; age-standardization was performed subsequently. As mortality in younger age groups is very low and may, therefore, dilute differences in mortality, we restricted the age-standardization to the age groups 45–74 years. For age-standardization using the direct method, the European standard population (1976) was taken. The weights used for standardization by 5-year age groups were 7 (45–54 years), 6 (55–59 years), 5 (60–64 years), 4 (65–69 years), and 3 (70–74 years).[7] The same weights were used for all, men, and women. All-cause mortality rates were calculated for comparison.

Cartographic and statistical analyses

We analysed the data from the corresponding regional level of each country. Age-standardized mortality rates were divided into five regular quintiles and displayed accordingly by different shades of colours.[8] In addition, rate ratios with the respective 95% confidence intervals (95% CIs) were calculated for men and women between the state with the highest mortality rate and the state with the lowest mortality rate. For the cartographic analyses and the calculation of age-standardized mortality rates as described above, EasyMap, Version 8.0, and SAS for Windows, Version 9.1, were used.

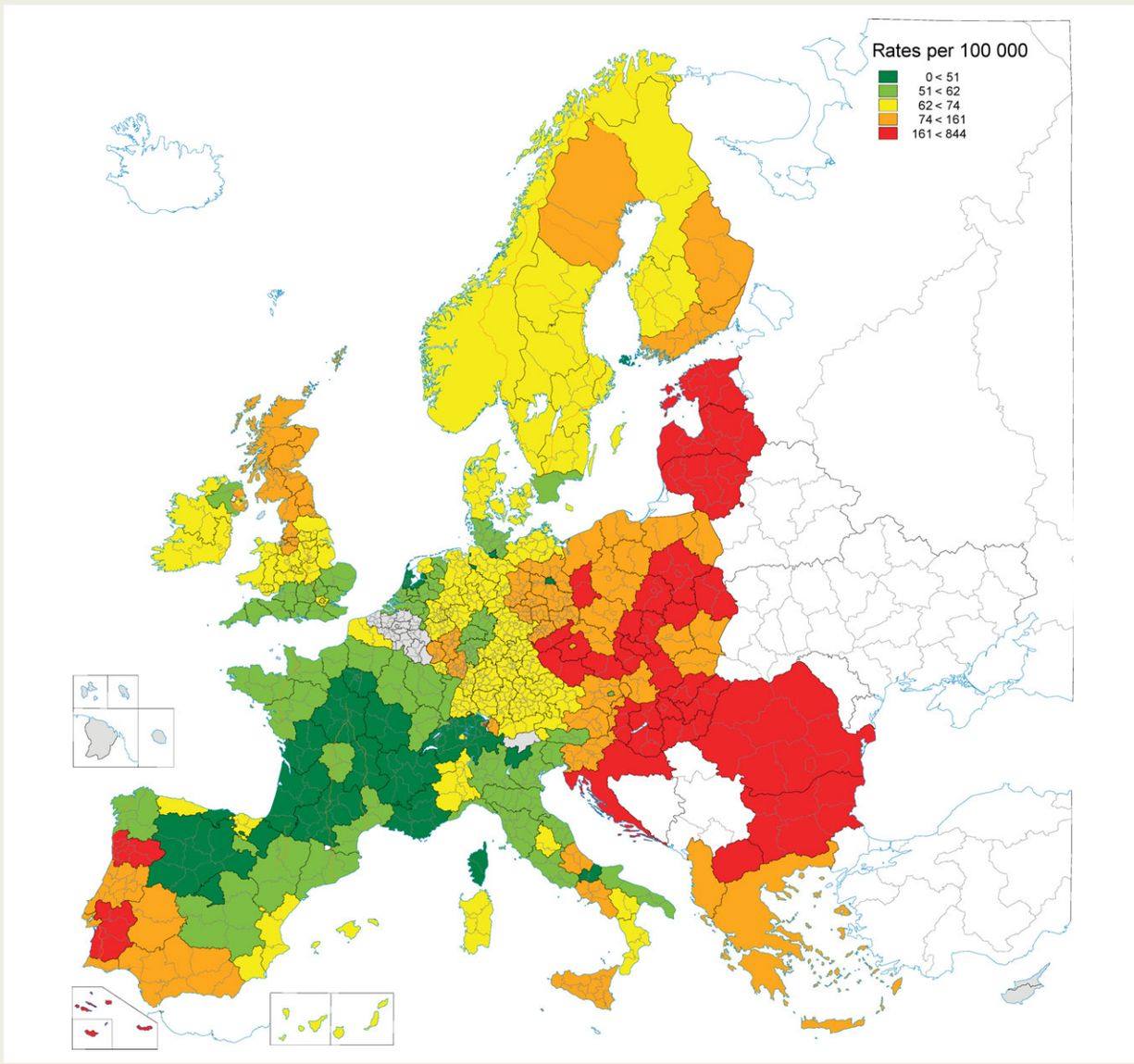

Figure 3 Age-standardized mortality from cerebrovascular disease in European regions (men; age group 45–74 years; year 2000)

Results

Within Europe, there is a considerable variation in cardiovascular and all-cause mortality both on a national and on a regional level (*Figures 1–6*, *Tables 1–3*). *Tables 1–3* summarize national mortality rates for IHD, CVD, and all-cause mortality for all, men, and women. *Figures 1–6* show mortality rates from IHD, CVD and cardiovascular disease, i.e. IHD and CVD combined, for both men and women in European regions in 2000. The rate ratio of dying from IHD between the countries with the highest mortality compared with the lowest mortality is 7.1 (95% CI, 6.6–7.6) for men (Latvia vs. France) and 9.9 (95% CI, 8.5–11.5) for women (Estonia vs. France). For CVD, the rate ratio is 14.5 (95% CI, 12.7–16.4) for men (Estonia vs. Switzerland) and 12.0 (95% CI, 10.2–14.1) for women (Estonia vs. Switzerland).

With regard to IHD, there is a clear north–east to south–west gradient in age-standardized mortality within Europe (*Figures 1* and *2*). Particularly, countries from Central and Eastern Europe have high mortality rates compared with other European countries. For IHD, the lowest mortality rates are found in France, Portugal, Italy, Spain, Switzerland, and the Netherlands. There is a considerable within-country variation in IHD in Germany, the UK, and Poland. With regard to cerebrovascular mortality rates (*Figures 3* and *4*), there is a different pattern of regional variation compared with IHD. Cerebrovascular mortality is reduced in the centre of Western Europe with the lowest national mortality rates in Switzerland, France, Norway, Spain, the Netherlands, and Italy. Countries and regions with higher mortality rates surround this circle of reduced mortality, such as the Central and East European countries as well as some Mediterranean countries including

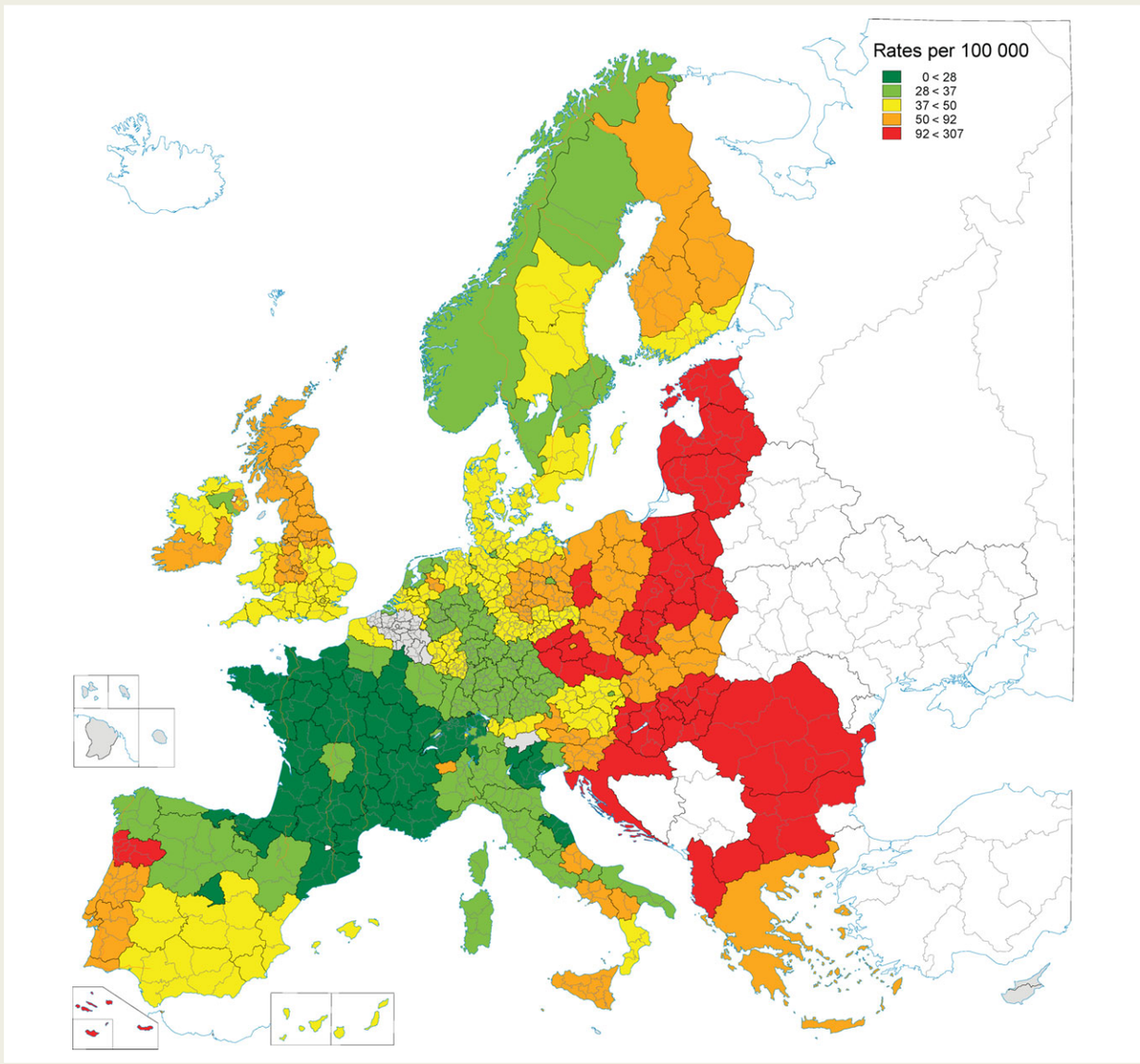

Figure 4 Age-standardized mortality from cerebrovascular disease in European regions (women; age group 45–74 years; year 2000)

Greece, Portugal, and certain regions in Southern Spain and Italy. There is a considerable within-country variation in cerebrovascular mortality in Italy, Spain, Portugal, and the UK. Cardiovascular disease (*Figures 5* and *6*) shows a similar north–east to south–west gradient compared with IHD.

Discussion

Within Europe, there is still a clear north–east to south–west gradient in mortality from cardiovascular disease and IHD. With regard to CVD, the pattern, however, is less clear. There appears to be a 'green' circle of reduced mortality in the centre of Western Europe with regard to countries such as France or the northern regions of Italy and Spain. Countries with higher mortality rates surround this circle, such as the Central and East European countries as well as some Mediterranean countries including Greece, Portugal, and certain regions in Southern Spain and Italy.

When analysing the regional variation in Europe, it has to be kept in mind that mortality from both IHD and CVD has continuously been decreasing in most West European countries over the last decades.[9,10] Kesteloot *et al.*[9] showed an age-adjusted annual percentage change in cardiovascular mortality rates in Western Europe of −1.8 in men and −2.1 in women, aged 45–75 years. In some West European countries such as Finland, efforts in reducing the risk factors with public health interventions on a population level have been enormous.[11] In most Central and East European countries, on the other hand, cardiovascular mortality increased during the 1970s and 1980s and started to decline in the early to mid-1990s.[9,10] Despite the recent decrease, mortality

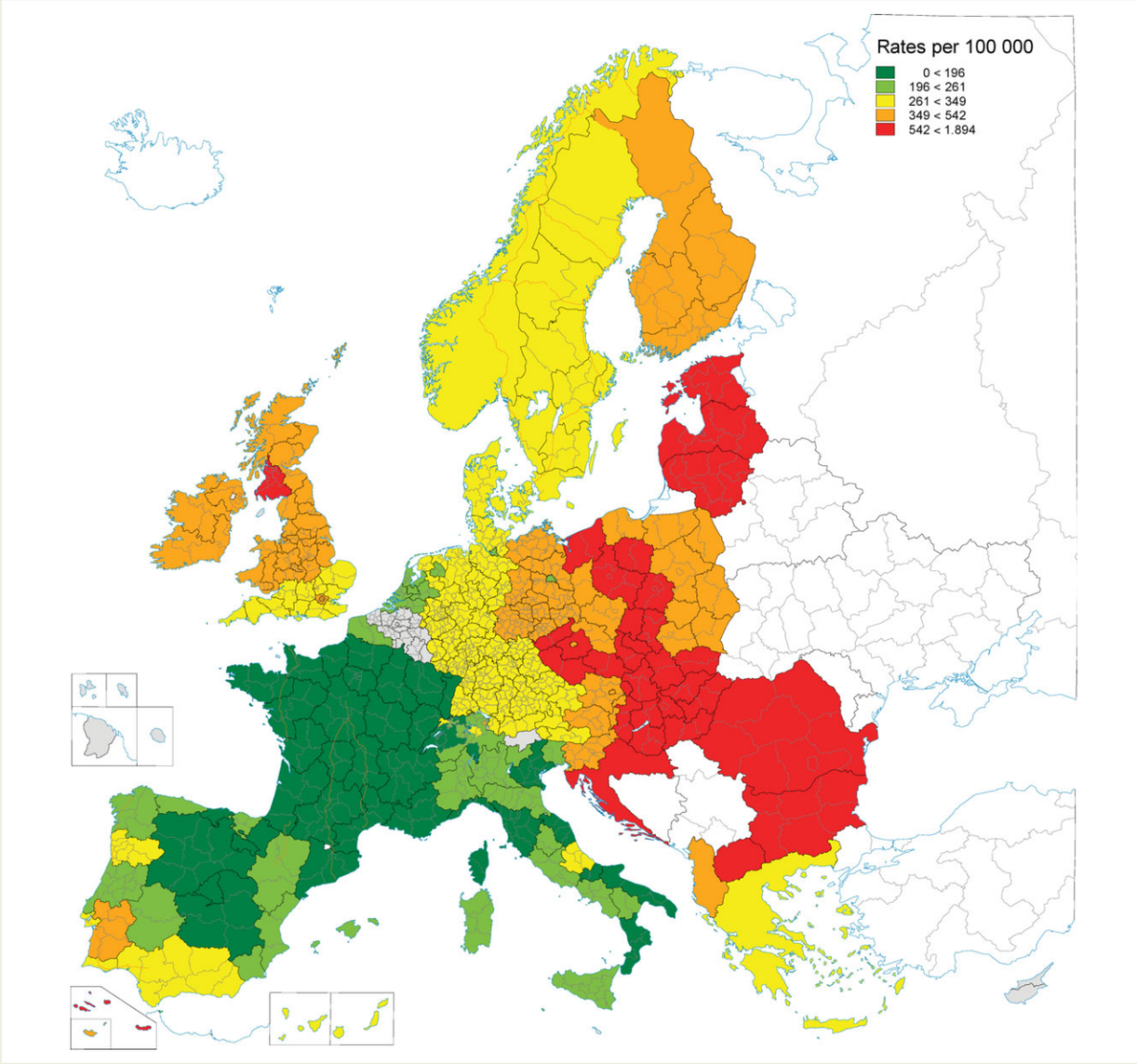

Figure 5 Age-standardized mortality from cardiovascular disease, i.e. ischaemic heart disease and cerebrovascular disease combined, in European regions (men; age group 45–74 years; year 2000)

rates are still considerable higher in most Central and East European countries compared with West European countries. Some countries such as the Ukraine reach almost top levels in a worldwide comparison.[10] Although most Central and East European countries appear to have reached their peak in cardiovascular mortality, the majority of them can clearly still be classified as high-risk countries.

A number of risk factors can be responsible for the variation on both the national and the regional level. Risk factors include socioeconomic variables such as income or employment status, psychosocial factors such as stress or the prevalence of depression, the 'classic' cardiovascular risk factors such as hypertension, hyperlipidaemia, and overweight, lifestyle variables such as physical activity, nutritional pattern, and smoking, environmental factors, or medical care. Studies such as the WHO Monica (monitoring of trends and determinants in cardiovascular diseases) Project or the Seven Countries Study allow the comparison of certain risk factors in European countries.[12,13] With regard to the east–west gradient in Europe, dietary fat intake appears to play a major role.[9,14,15] In Eastern Europe, a higher consumption of saturated fat has been reported compared with West European countries during the 1980s and early 1990s. In Poland, changes in dietary fat intake during the 1990s, leading to a more favourable ratio of polyunsaturated to saturated fat, were associated with a drop in mortality from IHD by approximately one quarter.[15] Other factors such as the consumption of fruit and vegetables, smoking, or alcohol consumption have been linked to the east–west gradient in mortality.[2]

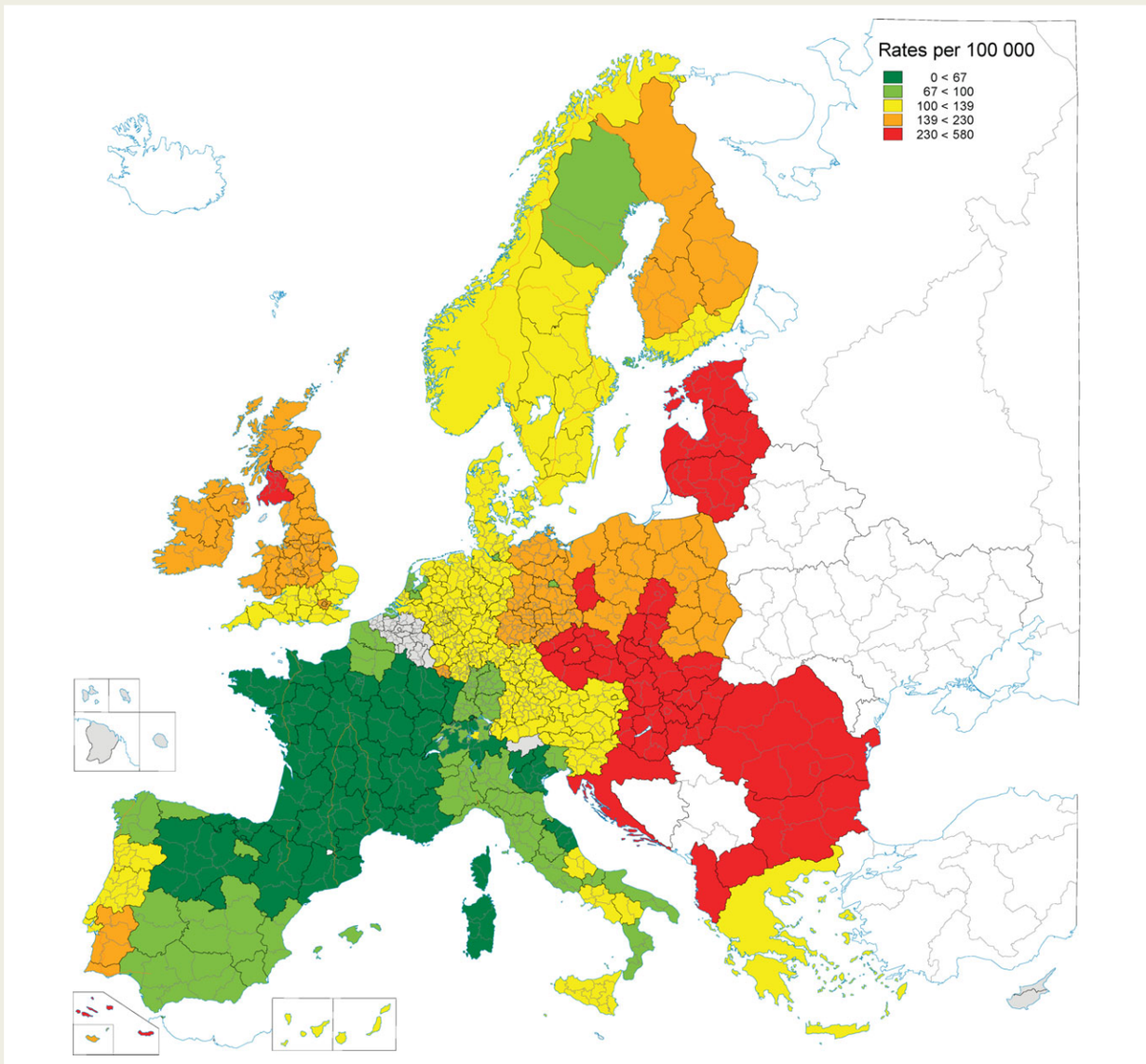

Figure 6 Age-standardized mortality from cardiovascular disease, i.e. ischaemic heart disease and cerebrovascular disease combined, in European regions (women; age group 45–74 years; year 2000)

The attribution of single risk factors to regional variation may also vary depending on the geographical location of the area of interest. For example, regional differences between Israel, Bavaria (Germany), and the Czech Republic were found to be associated particularly with differences in blood pressure levels.[16] Within England, on the other hand, the regional variation was associated to a large extent with differences in smoking prevalence.[4] In addition, secondary prevention in IHD may vary considerable between European countries as shown by the EUROASPIRE I and II surveys.[17] The EUROCISS Project (European Cardiovascular Indicators Surveillance Set) listed the existing population-based registers of acute myocardial infarction and stroke in Europe.[18] Whereas a number of countries such as Belgium, Denmark, Finland, France, Germany, Italy, Norway, Spain, and Sweden have registers for cardiovascular morbidity, there is a lack in other countries.

The analysis of regional variation in cardiovascular mortality is important for the classification of countries into high- and low-risk countries and the recommendations provided by current guidelines. Misclassification may have a huge impact at the population level with regard to the number of people over-(or under-)treated. Regular updates on the complex pattern of regional variation within Europe are needed to make efficient prevention possible. Although the SCORE model allows the insertion of national mortality data and data on prevalence of risk factor to produce national risk charts,[19,20] there is, of course, no substitute for risk assessment based on actual population data. The baseline survival curves in the SCORE project

Table 1 Age-standardized mortality rates (45–74 years) from ischaemic heart disease in Europe (2000)

All			Male			Female		
Country[a]	SMR	95% CI	Country	SMR	95% CI	Country	SMR	95% CI
France	65	59–71	France	110	103–118	France	24	21–28
Portugal	87	80–94	Portugal	132	123–141	Spain	39	34–43
Italy	91	84–98	Italy	147	138–156	Italy	43	38–47
Spain	92	85–99	Spain	151	142–161	Switzerland	43	39–48
Switzerland	97	90–104	Switzerland	158	149–167	Portugal	50	45–55
Netherlands	125	117–134	Netherlands	190	180–201	Netherlands	65	59–70
Denmark	134	126–143	Denmark	202	191–212	Greece	65	59–71
Slovenia	140	131–149	Norway	218	208–229	Slovenia	68	62–74
Greece	144	135–153	Slovenia	227	216–239	Denmark	72	66–78
Norway	144	136–153	Albania	228	216–239	Sweden	75	68–81
Sweden	153	144–162	Greece	231	219–242	Norway	76	70–82
Germany	157	148–167	Sweden	239	227–250	Germany	80	74–87
Albania	164	148–167	Germany	244	233–256	Austria	81	75–87
Austria	170	160–179	Austria	272	260–285	Finland	92	85–98
Scotland	175	166–185	England and Wales	307	294–320	Albania	100	93–107
England and Wales	202	191–212	Macedonia	328	314–342	England and Wales	104	97–112
Finland	222	211–233	Northern Ireland	346	332–360	Ireland	106	99–113
Ireland	223	212–234	Ireland	346	332–360	Poland	118	110–126
Northern Ireland	227	216–238	Finland	372	357–386	Northern Ireland	124	116–131
Macedonia	232	220–243	Poland	375	360–389	Croatia	136	128–145
Poland	232	221–244	Croatia	381	366–395	Macedonia	145	136–153
Croatia	242	231–254	Scotland	398	384–413	Czech Republic	147	138–153
Czech Republic	267	254–278	Bulgaria	404	389–419	Scotland	153	144–162
Bulgaria	271	259–284	Czech Republic	411	396–426	Bulgaria	157	148–166
Romania	322	308–335	Romania	449	433–465	Lithuania	189	179–198
Hungary	343	329–357	Hungary	529	512–547	Hungary	202	192–212
Lithuania	357	343–371	Slovakia	558	540–575	Romania	209	199–220
Slovakia	369	355–383	Lithuania	598	580–617	Slovakia	224	214–235
Estonia	446	430–461	Estonia	713	693–733	Latvia	242	231–253
Latvia	461	445–477	Latvia	781	760–802	Estonia	260	248–271

CI, confidence interval, SMR, standardized mortality rate.
[a]No data were available for Belgium for the year 2000.

Table 2 Age-standardized mortality rates (45–74 years) from cerebrovascular disease in Europe (2000)

All			Male			Female		
Country[a]	SMR	95% CI	Country	SMR	95% CI	Country	SMR	95% CI
Switzerland	27	23–31	Switzerland	34	30–38	Switzerland	21	17–24
France	37	32–41	France	50	44–55	France	26	22–29
Norway	47	41–52	Netherlands	56	51–62	Norway	33	29–37
Spain	48	43–53	Norway	62	56–68	Spain	35	31–39
Netherlands	49	44–54	Denmark	63	57–69	Italy	37	32–41
Italy	49	44–54	Spain	63	57–69	Sweden	38	34–43
Sweden	51	46–56	Italy	64	58–69	Germany	39	34–43
Germany	52	47–58	England and Wales	64	58–70	Netherlands	42	37–47
Denmark	54	48–59	Northern Ireland	64	58–70	Austria	44	40–49

Continued

Table 2 *Continued*

All			Male			Female		
Country[a]	SMR	95% CI	Country	SMR	95% CI	Country	SMR	95% CI
England and Wales	56	51–62	Sweden	65	59–70	Denmark	45	40–50
Austria	57	52–63	Ireland	66	61–72	England and Wales	49	44–54
Northern Ireland	58	52–63	Germany	68	63–74	Northern Ireland	53	47–58
Ireland	60	54–65	Austria	73	66–79	Finland	53	48–59
Finland	67	61–73	Finland	85	78–92	Ireland	54	48–59
Scotland	82	76–89	Scotland	96	89–103	Slovenia	63	58–69
Greece	87	80–94	Greece	108	101–116	Greece	68	62–74
Slovenia	99	92–107	Albania	137	129–145	Slovakia	71	65–77
Slovakia	107	100–114	Slovenia	146	137–154	Scotland	71	65–77
Portugal	121	113–129	Slovakia	154	145–163	Portugal	89	82–96
Czech Republic	127	119–135	Portugal	159	150–168	Czech Republic	95	88–101
Poland	128	120–137	Poland	166	157–176	Poland	98	91–105
Lithuania	140	131–148	Czech Republic	168	159–177	Lithuania	115	108–123
Albania	168	159–178	Lithuania	175	165–184	Hungary	125	117–133
Hungary	180	170–189	Hungary	254	242–265	Croatia	160	151–169
Croatia	209	198–219	Croatia	274	262–286	Lithuania	201	191–211
Romania	255	242–267	Macedonia	282	270–294	Albania	203	193–213
Latvia	259	248–271	Romania	302	289–314	Romania	207	196–217
Macedonia	263	252–275	Latvia	347	333–361	Bulgaria	220	209–230
Bulgaria	285	272–297	Bulgaria	361	347–375	Macedonia	246	235–258
Estonia	346	332–360	Estonia	487	471–504	Estonia	248	237–260

CI, confidence interval; SMR, standardized mortality rate.
[a]No data were available for Belgium for the year 2000.

Table 3 Age-standardized mortality rates (45–74 years) from all-cause mortality in Europe (2000)

All			Male			Female		
Country[a]	SMR	95% CI	Country	SMR	95% CI	Country	SMR	95% CI
Switzerland	731	711–752	Sweden	963	941–987	France	414	398–430
Sweden	765	745–786	Switzerland	985	962–1009	Spain	466	450–483
Italy	767	746–788	Italy	1058	1034–1082	Italy	515	498–532
Spain	786	765–807	Norway	1059	1035–1084	Switzerland	510	493–527
Greece	816	795–838	Greece	1133	1107–1158	Greece	533	516–550
Norway	826	804–848	Spain	1147	1121–1173	Sweden	584	566–602
France	845	823–868	England and Wales	1162	1137–1188	Finland	588	570–606
Austria	880	857–902	Netherlands	1181	1156–1207	Austria	593	575–612
Netherlands	913	891–936	Northern Ireland	1194	1169–1220	Norway	612	594–631
England and Wales	928	906–951	Austria	1209	1183–1236	Portugal	629	610–648
Finland	930	907–953	France	1221	1195–1248	Germany	629	610–648
Germany	935	912–958	Germany	1278	1251–1305	Albania	663	645–683
Northern Ireland	941	919–965	Ireland	1309	1283–1336	Netherlands	672	652–692
Portugal	948	925–971	Denmark	1314	1287–1341	England and Wales	715	695–735
Albania	996	973–1019	Finland	1321	1294–1349	Northern Ireland	723	703–743
Ireland	1032	1008–1056	Portugal	1325	1297–1353	Slovenia	741	721–762
Denmark	1096	1071–1121	Albania	1337	1310–1363	Ireland	772	752–793
Scotland	1180	1155–1206	Scotland	1500	1471–1529	Czech Republic	858	836–880

Continued

Table 3 *Continued*

All			Male			Female		
Country[a]	SMR	95% CI	Country	SMR	95% CI	Country	SMR	95% CI
Slovenia	1181	1156–1208	Slovenia	1724	1692–1755	Denmark	895	873–918
Czech Republic	1301	1274–1329	Macedonia	1820	1788–1853	Poland	899	876–921
Poland	1435	1406–1464	Czech Republic	1839	1806–1871	Scotland	904	881–926
Macedonia	1458	1430–1487	Poland	2107	2072–2142	Lithuania	906	883–929
Croatia	1456	1428–1484	Croatia	2130	2096–2165	Croatia	937	915–960
Lithuania	1514	1484–1545	Romania	2206	2170–2242	Slovakia	944	922–967
Slovakia	1532	1502–1562	Bulgaria	2222	2186–2258	Latvia	1046	1022–1071
Romania	1616	1586–1647	Slovakia	2287	2250–2323	Estonia	1073	1049–1099
Bulgaria	1617	1587–1648	Lithuania	2365	2328–2403	Bulgaria	1096	1072–1121
Hungary	1755	1723–1788	Hungary	2576	2537–2616	Romania	1113	1088–1138
Latvia	1759	1727–1792	Estonia	2735	2694–2775	Hungary	1124	1099–1150
Estonia	1763	1731–1796	Latvia	2782	2742–2824	Macedonia	1134	1110–1159

CI, confidence interval; SMR, standardized mortality rate.
[a]No data were available for Belgium for the year 2000.

are based on the selected cohort studies from the respective countries.[21] For the high-risk model, cohorts from Denmark, Finland, and Norway are used, whereas for the low-risk model, cohorts from Belgium, Italy, and Spain are used. Most of these cohort studies were conducted during the 1980s and 1990s. When analysing time trends in cardiovascular mortality, it seems that former high-risk West European countries now have similar mortality rates compared with those of the low-risk countries at the time of the cohort studies.[22–24] It is, therefore, indicated to reconsider the classification of countries into high-risk and low-risk countries for risk assessment in primary prevention of cardiovascular disease. For example, it may be more appropriate and practical to generally classify West European countries as low-risk countries and Central and East European countries as high-risk countries. Otherwise, there may be an overestimation of current cardiovascular risk in certain populations leading to unnecessary therapies and costs.

Further research into the underlying reasons of the observed differences in cardiovascular mortality in Europe both between and within countries is indicated. Multilevel analyses combining individual patient data if available with aggregate data may be a feasible approach to identify those risk factors attributing the most to the regional variation. Preventive strategies may then focus on specific risk factors. In addition, the monitoring of cardiovascular disease and risk in Europe may become more manageable when focusing on those risk factors with the highest attributable risk.

Acknowledgements

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Conflict of interest: none declared.

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