

Global and Regional Patterns in Cardiovascular Mortality From 1990 to 2013

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Abstract—There is a global commitment to reduce premature cardiovascular diseases (CVDs) 25% by 2025. CVD mortality rates have declined dramatically over the past 2 decades, yet the number of life years lost to premature CVD deaths is increasing in low- and middle-income regions. Ischemic heart disease and stroke remain the leading causes of premature death in the world; however, there is wide regional variation in these patterns. Some regions, led by Central Asia, face particularly high rates of premature death from ischemic heart disease. Sub-Saharan Africa and Asia suffer disproportionately from death from stroke. The purpose of the present report is to (1) describe global trends and regional variation in premature mortality attributable to CVD, (2) review past and current approaches to the measurement of these trends, and (3) describe the limitations of existing models of epidemiological transitions for explaining the observed distribution and trends of CVD mortality. We describe extensive variation both between and within regions even while CVD remains a dominant cause of death. Policies and health interventions will need to be tailored and scaled for a broad range of local conditions to achieve global goals for the improvement of cardiovascular health. (*Circulation*. 2015;132:1667-1678. DOI: 10.1161/CIRCULATIONAHA.114.008720.)

Key Words: cardiovascular diseases ■ epidemiology ■ global health ■ mortality

Cardiovascular (CVD) and circulatory diseases are now recognized as the leading causes of death in the world. In 2013 there were >54 million deaths (95% uncertainty interval [UI], 53.6–56.3 million) globally and 32% of these deaths, or 17 million (95% UI, 16.5–18.1 million), were attributable to CVD.¹ The majority of these CVD deaths were attributable to either ischemic heart disease (IHD) or cerebrovascular disease. A detailed understanding of the global distribution of CVD has become essential as countries develop national strategies to reduce the burden of noncommunicable disease (NCD). The global focus on NCD prevention and control was highlighted by the United Nations High Level Meeting on NCDs in 2011 in which member states voluntarily agreed to work to reduce the risk of premature (defined by the World Health Organization as occurring from ages 30 to 70 years) death from NCDs, including CVD, cancer, chronic lung disease, and diabetes mellitus, by 25% by 2025.² The purpose of the present report is to (1) describe global trends and regional variation in premature mortality attributable to CVD, (2) review past and current approaches to the measurement of these trends, and (3) describe the limitations of existing models of epidemiological transitions for explaining the observed distribution and trends of CVD mortality.

Measuring the Global Cardiovascular Disease Burden

We provide an overview of death from CVD with particular attention paid to geographic patterns and trends over time. Our estimates are from the Global Burden of Disease (GBD) 2013 study. In the GBD study, CVD mortality is estimated separately for the 10 most common causes of CVD-related death, and, therefore, we have restricted our discussion to these conditions (Table 1).³ We have organized our discussion around 7 areas of the world, which are expanded to 21 globally exhaustive regions (Table I in the online-only Data Supplement). All rates are age-standardized to a global population. Detailed results and visualization tools are available at <http://www.healthdata.org/gbd>.

The ability to measure global disease epidemiology in a consistent and comparable way is relatively new. GBD methods combine all available data sources with statistical computing to create granular national and subnational estimates of deaths and disability attributable to CVD and other diseases including measures of uncertainty. Estimating global CVD burden complements other epidemiological methods, such as cohort studies and controlled trials, and can be useful to decision makers who seek to create, implement, and evaluate policies to improve population health.⁴

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A global description of the burden of CVD has a different goal than other types of CVD epidemiology, which often evaluate associations between exposures and disease within longitudinal, community-based cohort or cross-sectional studies. For example, the Framingham Heart Study was essential for identifying modifiable factors of risk, which led to the development of risk prediction tools that are widely used in clinical practice today.⁵ Subsequent community-based studies have provided invaluable information on the fundamental underpinning of CVD across different ages, communities, birth cohorts, and race/ethnic groups. More recent cohort studies have used strategies such as pooling across cohorts or linkage with administrative data to investigate novel causes of CVD.⁶

Multinational efforts in descriptive epidemiology have developed in parallel with smaller population-based cohorts. This began with the Seven Countries Study in 1958 that found CVD as the cause of 34% to 62% of all deaths.⁷ The World Health Organization–led Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) studies established consistent case definitions and data collection methods for coronary heart disease and stroke across 21 countries.⁸ More recently, multinational surveys of chronic disease have increased our understanding of CVD patterns in low- and middle-income countries (LMICs).^{9,10}

The GBD study now incorporates a wide range of data sources to estimate the global burden of CVD across all countries. The most recent mortality estimates, GBD 2013, used all available vital registration and verbal autopsy data, and statistical models, as well, to estimate mortality attributable to 240 diseases in 188 countries from 1990 to 2013. A large number of steps go into producing these estimates, including the correction of death certificate data and geospatial modeling using country-level data.¹¹

Limitations for the Measurement of Global Disease Mortality

The GBD 2013 study remained limited by the lack of mortality data from some of the world's poorest countries. Data to allow for the estimation of variation within countries is also not always available. For some conditions that are increasingly reported as a cause of CVD death, such as atrial

fibrillation and peripheral vascular disease, factors other than disease epidemiology may contribute to the observed trends. These include increased awareness, increased availability of screening, and better treatments for associated diseases such as IHD, stroke, diabetes mellitus, and tobacco-related diseases.^{12,13} These trends may also reflect increased willingness to formally attribute and report deaths attributable to these conditions.

Global Trends in Premature Cardiovascular Mortality

Premature Cardiovascular Mortality

The United Nations member states have targeted a 25% reduction in the probability of premature death attributable to CVD by the year 2025. Regional and even global benchmarking now plays an important role in the international community's efforts to track progress toward this goal. In 2013, the probability of premature death between the ages of 30 and 70 attributable to CVD was 0.108 for men and 0.067 for women globally. It was highest for men in Eastern Europe and for women in Oceania and lowest for both sexes in the high-income Asia-Pacific region (Table 2).

Premature mortality is massive not just for CVD but for all 4 major categories of NCDs (CVD, cancer, chronic obstructive lung disease, and diabetes mellitus). In 2013, these 4 NCDs accounted for most deaths among people ≥ 45 years of age (Figure 1). CVD increased steadily as a proportion of these deaths across older age groups, beginning at ages as young as 30 to 34 years, where it accounted for 11% (95% UI, 10.3–12.4) of all deaths. For every 5-year age group >40 , CVD was the most common cause of death.

Persistent Differences Between Men and Women

Globally, the average age-standardized CVD death rate has fallen over the past 2 decades, with the largest decline occurring between 2000 and 2005. Declines in rates of death attributable to both IHD and cerebrovascular disease accounted for most of this improvement (Figure I in the online-only Data Supplement). The improvement has been gradual and continuous, with similar declines of 11% among men and 14% among women between 1990 and 2013 (Figure 2). No change

Table 1. Causes of CVD Estimated for the Global Burden of Disease 2013 Study

Cause	Deaths in 2013	95% Uncertainty Interval
Ischemic heart disease	8 139 852	(7 322 942–8 758 490)
Ischemic stroke	3 272 924	(2 812 654–3 592 562)
Hemorrhagic and other nonischemic stroke	3 173 951	(2 885 717–3 719 684)
Hypertensive heart disease	1 068 585	(849 758–1 242 160)
Other cardiovascular and circulatory diseases	554 588	(499 143–654 152)
Cardiomyopathy and myocarditis	443 297	(370 111–511 997)
Rheumatic heart disease	275 054	(222 622–353 938)
Aortic aneurysm	151 493	(124 201–179 954)
Atrial fibrillation and flutter	112 209	(97 716–126 677)
Endocarditis	65 036	(48 593–79 435)
Peripheral vascular disease	40 492	(35 487–44 883)

Table 2. Unconditional Probability of Death Between 30 and 70 Years of Age Caused by CVD in 2013, Global and by Region

Region	Men	Women
Central Asia	0.223	0.129
Eastern Europe	0.217	0.100
Oceania	0.165	0.134
South Asia	0.152	0.104
North Africa and Middle East	0.125	0.090
Central Europe	0.118	0.054
Western Sub-Saharan Africa	0.110	0.110
Global	0.108	0.067
Caribbean	0.104	0.081
East Asia	0.099	0.056
Southern Sub-Saharan Africa	0.065	0.048
Southern Latin America	0.083	0.040
Central Latin America	0.070	0.044
High-income North America	0.067	0.033
Andean Latin America	0.053	0.040
Western Europe	0.047	0.020
Australasia	0.042	0.018
High-income Asia Pacific	0.037	0.016

has been seen in the well-established difference in CVD mortality between men and women. Because of this difference, in 2013, age-standardized CVD mortality rates among men had fallen only to the level observed among women in 1995 (333 deaths per 100 000 persons). However, the proportion of

deaths attributable to CVD rises rapidly for women after the age of 70, surpassing the proportion among men. This trend is driven predominantly by stroke deaths and explains the slightly higher proportion of deaths attributable to CVD for women overall.

Understanding Trends in CVD Death Rates Versus CVD Deaths

Demographic changes are major drivers of NCDs and of CVD in particular. Even as death rates have fallen, the ageing and growth of the world's population have led to rising numbers of CVD deaths. For example, in 1990, the global age-standardized death rate attributable to CVD was 376 per 100 000 (95% UI, 361–389) which had fallen to 293 per 100 000 (95% UI, 280–306) by 2013, a 22% decline (Figure 3). However, over the same time period, the number of CVD deaths increased from 12.3 million (95% UI, 11.8–12.8) to 17.3 million (95% UI, 16.5–18.1), a 41% increase. This increasing global burden of CVD is largely driven by increased numbers of deaths in LMICs.

Differences Between High-Income and Low- and Middle-Income Regions

The largest increase in premature mortality attributable to CVD over the past 20 years was in East, South, and Southeast Asia, and parts of Latin America, as well (Figure 4). Although age-standardized rates of death attributable to CVD fell in LMICs from 381 per 100 000 in 1990 (95% UI, 363–400) to 332 per 100 000 (95% UI, 312–347), a 13% decline, the number of deaths increased from 7.21 million (95% UI, 66.87–7.59) to

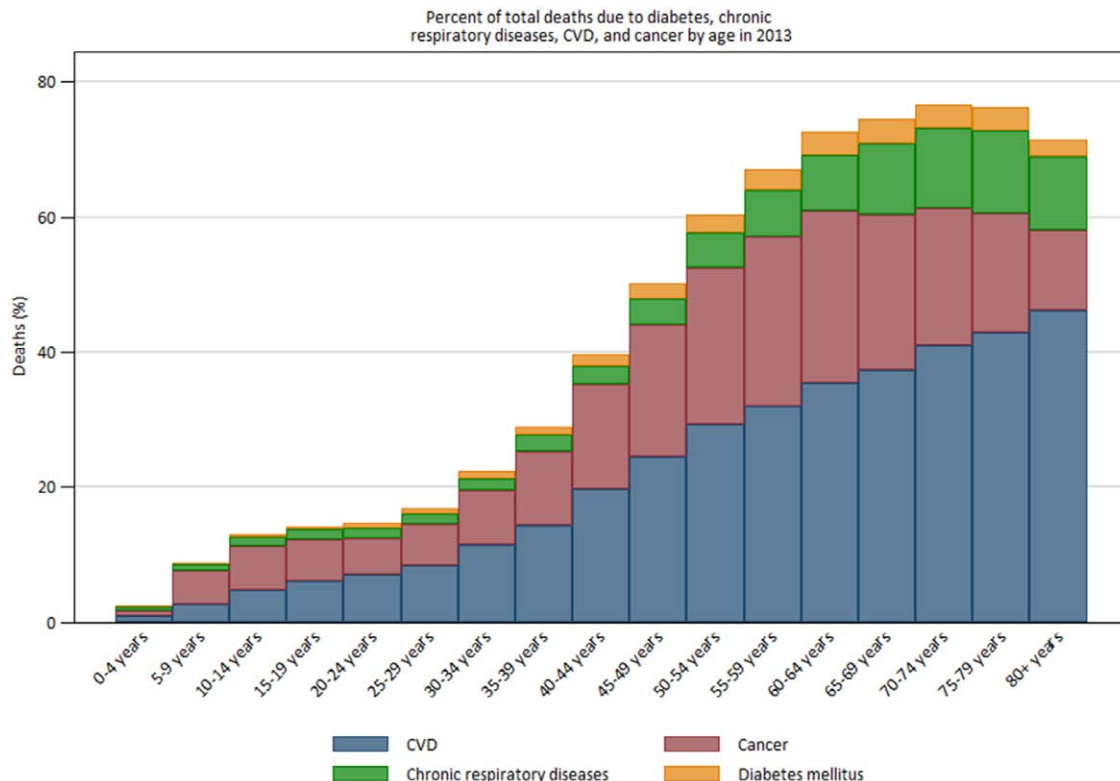


Figure 1. Proportion of total deaths attributable to diabetes mellitus, chronic respiratory diseases, CVD, and cancer by age in 2013. CVD indicates cardiovascular disease.

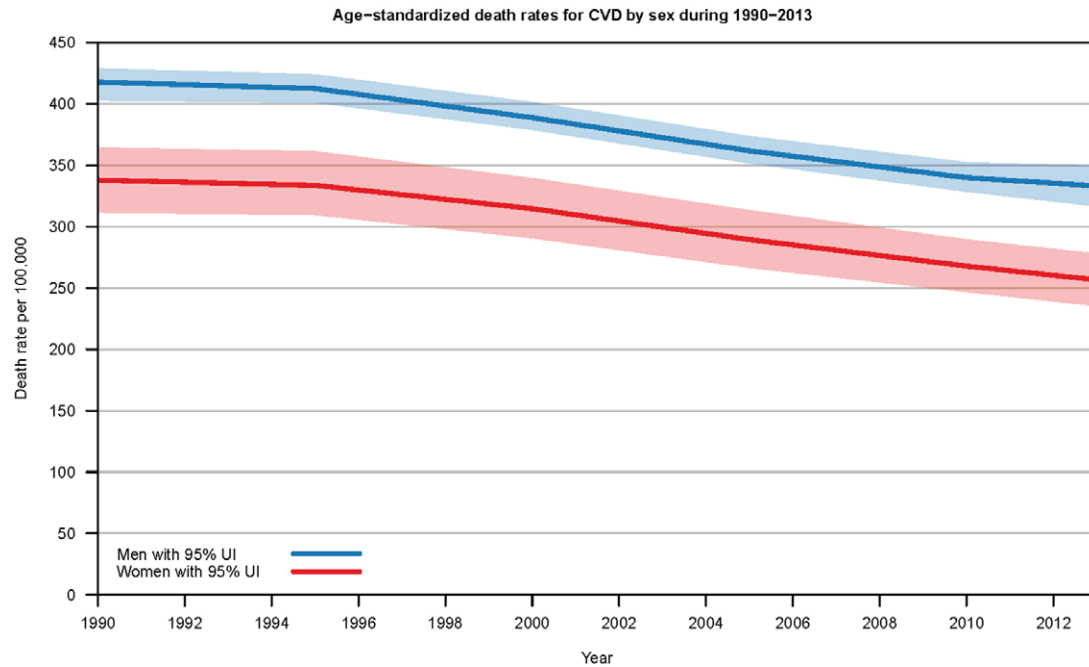


Figure 2. Age-standardized death rates for CVD stratified by sex, 1990 to 2013. CVD indicates cardiovascular disease; and UI, uncertainty interval.

12 million (95% UI, 11.25–12.6) in 2013, a 66% increase. In high-income countries (HICs), age-standardized death rates for CVD fell from 283 per 100 000 persons (95% UI, 268–291) in 1990 to 160 per 100 000 (95% UI, 154, 176) in 2013, a 43% decline. During the same period, the number of CVD-related deaths in HIC did not change significantly (3.14 million; 95% UI, 2.97–3.23 in 1990 to 3.12 million; 95% UI, 3.00–3.44 in 2013). The remarkable decline in death rates among HIC has been attributed to population-level changes in risk factors and, more recently, improvements in health care.¹⁴ Meanwhile, the growth and ageing of populations have increased the proportion of deaths attributable to CVD in many poorer regions of the world and, as a result, the

mortality gap between LMIC and HIC over the past 20 years has narrowed (Figure 5).

Regional Patterns in Deaths Attributable to Cardiovascular Diseases

Remarkable variation is seen when CVD mortality is examined at the level of individual countries (Figure 6). Global maps help us to understand the patterns and trends but should not obscure the potential variation that occurs within each of these areas. This fractal-like heterogeneity, reproduced across and within countries, cities, and even neighborhoods, is perhaps the most important observation that can be made about global patterns of CVD.

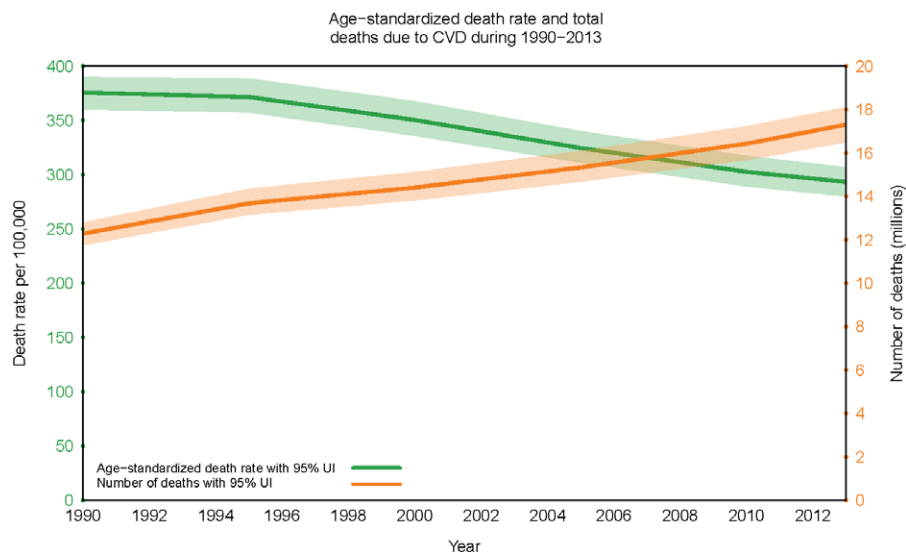


Figure 3. Change in age-adjusted CVD death rate and total number of CVD deaths, 1990 to 2013. CVD indicates cardiovascular disease; and UI, uncertainty interval.

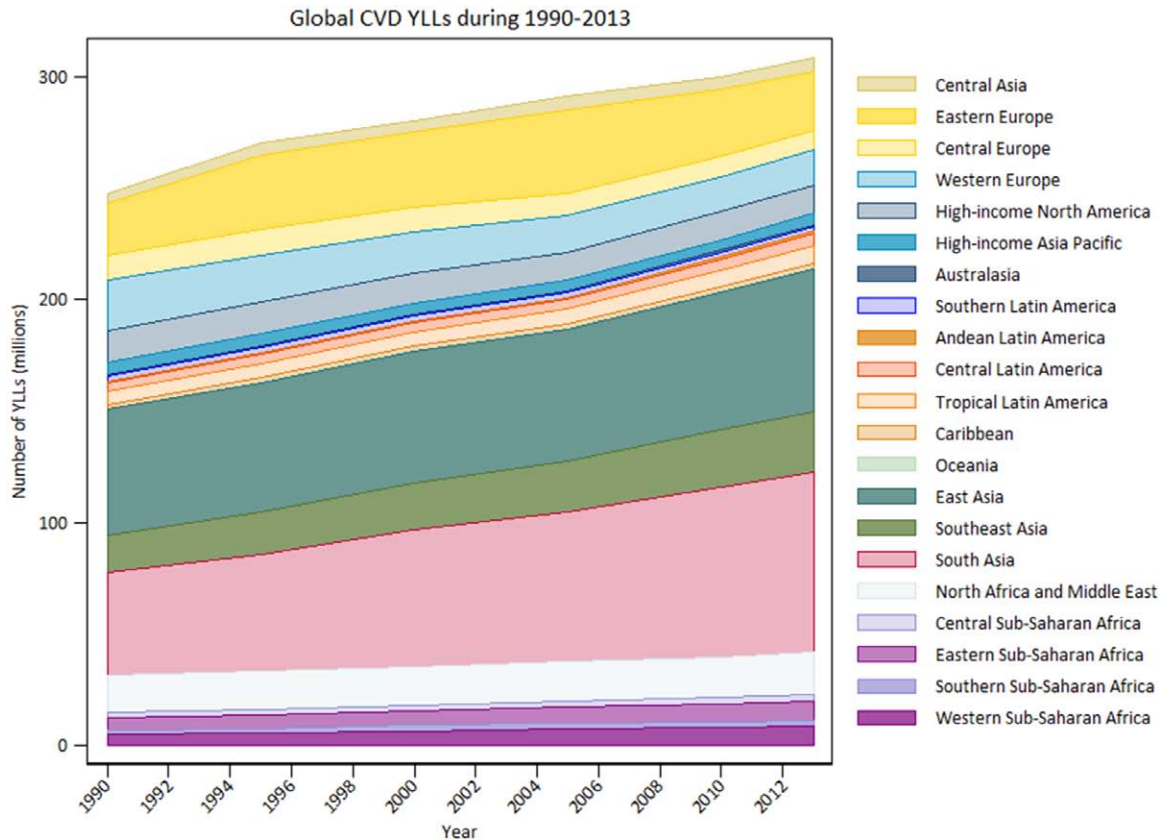


Figure 4. Number of years of life lost because of CVD by geographic region, 1990 to 2013. Years of life lost (YLL) is a measure of premature mortality calculated by using a normative goal for survival computed from the lowest observed death rate across countries. CVD indicates cardiovascular disease.

High Income Countries

HICs continue to have large differences in their CVD mortality in 2013. Japan has among the lowest rates of CVD mortality in the world (110 per 100 000; 95% UI, 101–125) along with Taiwan (125 per 100 000; 95% UI, 118–137), France (126 per 100 000; 95% UI, 113–138), Israel (132 per 100 000; 95% UI, 122–152), and Canada (140 per 100 000; 95% UI, 129–157). In Western Europe, after France, Spain has the next lowest rate of CVD mortality (142 per 100 000; 95% UI, 133–158). Australia, Switzerland, Italy, Iceland, the Netherlands, Norway, and the United Kingdom have similarly low rates. On the other hand, Germany has among the highest death rate in Western Europe (192 per 100 000; 95% UI, 183–210), likely because of the higher prevalence of CVD risk factors in comparison with many other HICs.^{15,16} CVD mortality rates in Austria, Finland, and Sweden are even higher than in Germany. Efforts to summarize the cause of this wide variation date back to the very beginning of their measurement and include observations on differences in dietary patterns and other risk factors.^{7,17–20} Less well understood is the regional variation in CVD case fatality rates, which likely reflects both case ascertainment and quality of healthcare services. Some have suggested that fundamental differences in political governance, and the resulting policy decisions, may explain observed differences in health between the United States and other similarly wealthy countries.²¹

East and Southeast Asia

Countries in East Asia represent some of the fastest growing economies. In 2013, 40% of their deaths were attributable to CVD, a proportion similar to the average proportion in HICs. However, the relative contribution of stroke and IHD is reversed in this region in compared with HICs. The ischemic ratio between ischemic stroke and IHD mortality rates is <0.4 for Latin American and HICs, whereas the Pacific Rim, Sub-Saharan, and Central European countries have a much higher ratio, ranging from 0.54 to 1.06 (Table 3). In China, Indonesia, Vietnam, and South Korea, there are twice as many deaths from stroke as from IHD, because, in addition to ischemic stroke, these countries have higher rates of death attributable to hemorrhagic stroke. This stroke-dominant pattern is also seen in Sub-Saharan Africa but is attenuated in higher-income Japan. It remains unclear how much of this variation is determined by the incidence or case fatality of stroke. Population-based studies in China have suggested higher case fatality rates in comparison with HICs, likely because of the predominance of hemorrhagic strokes over ischemic strokes and lower access to health care.^{22,23}

Central and Eastern Europe and Central Asia

The risk of dying prematurely owing to CVD remains highest in Central Asia, followed by Eastern Europe. In 2013, the geographic regions comprising most of the former Soviet Union (Central Europe, Eastern Europe, and Central Asia), taken

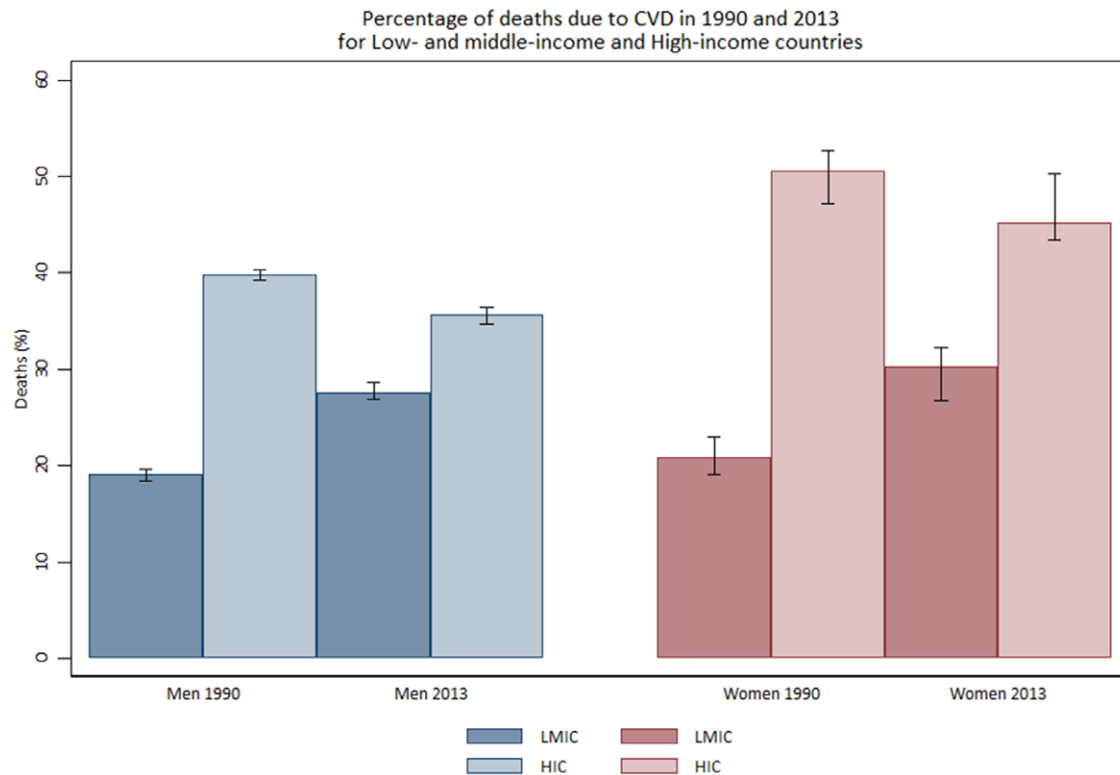


Figure 5. Proportion of total deaths attributable to CVD in HIC vs LMIC stratified by sex, 1990 to 2013. CVD indicates cardiovascular disease; HIC, high-income countries; and LMIC, low- and middle-income countries.

together, had the highest death rate attributable to CVD in the world (age-standardized CVD death rate 476 per 100 000; 95% UI, 466–486). Like most other regions outside East Asia

and Sub-Saharan Africa, IHD accounts for the majority of years lost prematurely to CVD (Figure II in the online-only Data Supplement). In this region in 2013, Kazakhstan had the

Age-standardized death rates due to CVD in 2013

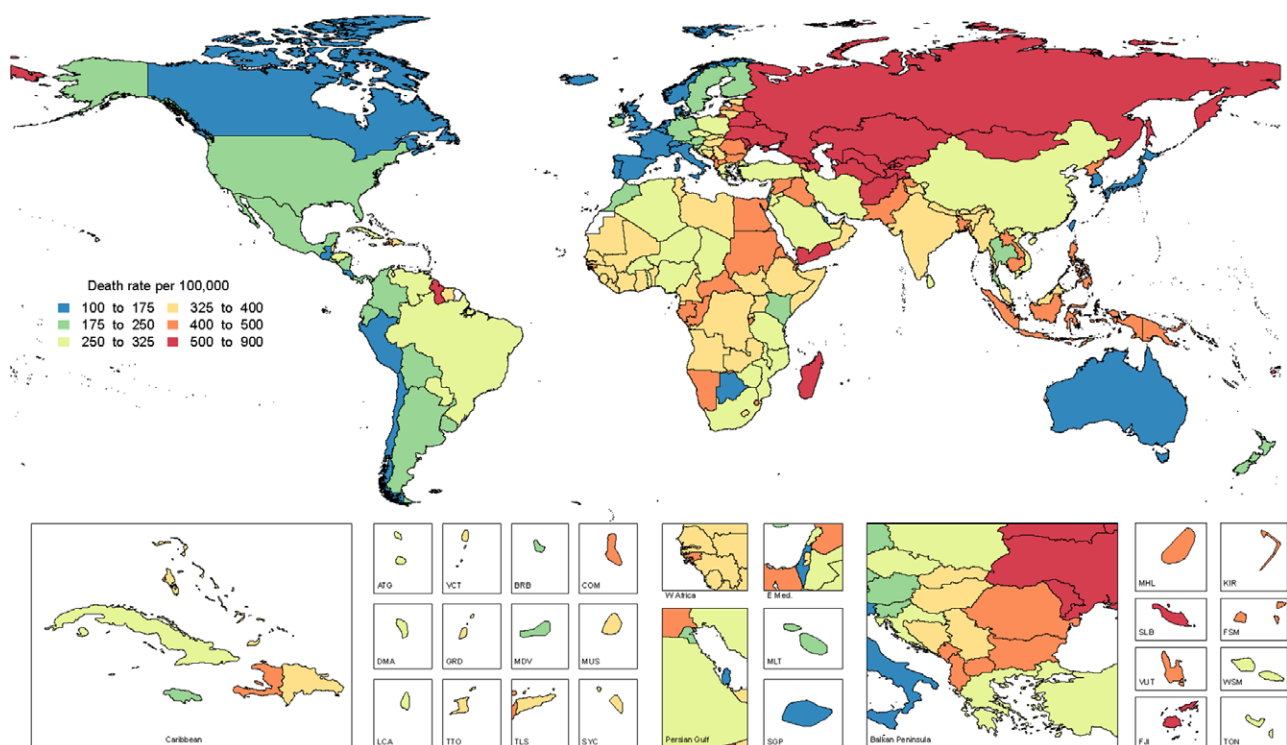


Figure 6. Map of age-adjusted death rates attributable to CVD, 2013. CVD indicates cardiovascular disease.

Table 3. Ratio of Age-Standardized Ischemic Stroke to Ischemic Heart Disease Death Rates, Globally and for 21 Globally Exhaustive Regions, 2013

World Region	Ischemic Stroke Deaths per 100 000 in 2013	Ischemic Heart Disease Deaths per 100 000 in 2013	Ratio of Ischemic Stroke to Ischemic Heart Disease Death Rates
Western Sub-Saharan Africa	99.1	93.1	1.06
Central Sub-Saharan Africa	98.4	108.7	0.91
High-income Asia Pacific	33.3	38.6	0.86
Eastern Sub-Saharan Africa	71.8	86.2	0.83
Southeast Asia	98.2	125.7	0.78
Southern Sub-Saharan Africa	58.4	94.4	0.62
Central Europe	93.8	153.2	0.61
East Asia	61.9	115.1	0.54
Caribbean	67.7	150.1	0.45
Tropical Latin America	49.5	114.9	0.43
Global	57.3	137.8	0.42
Eastern Europe	131.1	319.5	0.41
North Africa and Middle East	63.8	172.1	0.37
Southern Latin America	34.6	94.2	0.37
Andean Latin America	30.2	91.6	0.33
Western Europe	25.9	83.2	0.31
South Asia	63.8	211.8	0.30
Central Asia	98.6	367.5	0.27
High-income North America	17.3	112.1	0.15
Central Latin America	17.9	118.6	0.15
Oceania	33.9	264.6	0.13

highest death rate attributable to CVD (678 deaths per 100 000 both sexes age-standardized; 95% UI, 622–733). These high rates appear to reflect a complex combination of social and political forces surrounding the fall of the Soviet Union, and risk associated with heavy alcohol and tobacco use, as well.²⁴

Many countries within Central Asia and Eastern Europe experienced a substantial rise followed by dramatic declines in all-cause mortality after the collapse of the former Soviet Union, a phenomenon that has been referred to as a mortality crisis.²⁵ This rise-and-fall pattern is quite clear for CVD. In Russia in 2005, age-adjusted death rates for IHD among men were as high as 423 per 100 000 people, whereas in the Ukraine age-adjusted IHD death rates peaked at 515 per 100 000. More recently, improvements in diet, tobacco control, and healthcare delivery appear to have contributed to better health outcomes.²⁶ For example, the age-standardized death rates attributable to CVD have fallen substantially in the entire former Soviet region (644 per 100 000; 95% UI, 632–656 in 2005 to 476 per 100 000, 95% UI; 466–486 in 2013). Unfortunately, they still remain higher than anywhere else in the world.

Latin America and the Caribbean

CVD mortality in Latin American in 2013 varied widely from a rate of 143 per 100 000 (95% UI, 126–173) in Peru to 595 per 100 000 (95% UI, 497–697) in Guyana. The 4-fold difference in CVD-related mortality seen in this region suggests a complex distribution of risk factors and is only partially explained by varying levels of economic development. Higher rates

are seen in wealthier countries such as Uruguay, Argentina, and Brazil but are also seen in a less wealthy country such as Cuba. One explanation is that the prevalence of atherogenic risk factors is widely divergent across countries in this region, a hypothesis supported by recent studies of tobacco use and abdominal obesity prevalence.^{27–29} For example, in 2011, tobacco users in Suriname had the highest tobacco consumption per smoker in the world.³⁰

Estimating the burden of CVD attributable to Chagas disease, which is endemic to Latin America because of the typical range of *Trypanosoma cruzi* transmission, also poses a significant challenge. Death attributable to heart failure, by convention, is coded to its underlying cause, leading to misclassification of some death certificates, although redistribution methods using statistical models have been used to address this limitation.³¹ *T cruzi* seroprevalence ranges from 1% to 6% in Latin American countries but only 20% to 30% will experience clinically manifest disease.³² A systematic review of literature and hospital data suggests that even in Latin America only a small fraction of clinical heart failure is reported to be caused by Chagas disease, whereas the actual proportion is unknown.³³

South Asia

CVD accounted for 27% (95% UI, 24.7%–28.9%) of all deaths in South Asia in 2013. This has been a substantial rise since 1990 when CVD accounted for only 15% (95% UI, 13.8–15.8) of deaths. At the same time, estimates of age-standardized rates of death attributable to CVD have increased

from 376 per 100 000 (95% UI, 345–407) in 1990 to 398 per 100 000 in 2013 (95% UI, 352–443). The increasing total number of deaths, and age-standardized death rates, as well, suggests changes in risk exposures, not simply the ageing of the population. Patterns of CVD within this region vary, with higher death rates in Afghanistan and, for Bangladesh, significantly higher rates of death attributable to stroke and lower rates of death attributable to IHD than in India, Bhutan, Nepal, and Pakistan. Substantial uncertainty remains in this region owing to limited data and conflicting estimates from published and unpublished data sources.

Similar to other regions of the world, country-level estimates in South Asia mask variation between rural and urban areas. These differences have been demonstrated by verbal autopsy and household survey studies performed in India. Vascular deaths accounted for 37% to 41% of deaths in urban Chennai, India during 1995 to 1997 in comparison with 25% to 28% of deaths in rural Tamil Nadu in 2003.³⁴ The burden of CVD in South Asia is likely to rise even higher as populations move to urban areas and adopt dietary and physical activity behaviors that increase their risk for atherosclerotic vascular diseases.³⁵ At the same time, access to health care is likely to improve in urban settings, which may offer opportunities to decrease CVD risk. Data from the Prospective Urban Rural Epidemiological (PURE) cohort study suggest that CVD case fatality was higher in rural areas in comparison with urban areas in several middle-income countries including India (4.83 events [urban] versus 6.25 events [rural] per 1000 person-years, $P < 0.001$).³⁶ New sources of data are needed to better understand the distribution of CVD among rural and urban parts of South Asia.

Middle East and North Africa

Ischemic heart and cerebrovascular diseases were the leading causes of death in the Middle East and North Africa in 2013. Death rates attributable to CVD ranged from 145 per 100 000 (95% UI, 128–163) in Qatar to 548 per 100 000 (95% UI, 375–781) in Yemen. This region presents a rapidly changing pattern of CVD with significant variation between urban and rural areas. There is increasing obesity, and a change in dietary patterns, as well, from traditional to ones higher in calories and processed foods.³⁷ The prevalence of tobacco smoking, including water pipe smoking, is high among men in many Middle Eastern and North African countries.³⁸ Large disparities in physical activity have also been observed.³⁹

Sub-Saharan Africa

Over the past 2 decades, Sub-Saharan Africa has experienced relatively low levels of CVD burden, although the burden of CVD deaths has risen steadily.⁴⁰ Significant barriers to estimation of CVD exist in this region, including the lack of vital registration systems in most countries. Modeled estimates based on available verbal autopsy data from Tanzania, Ghana, Burkina Faso, Ethiopia, Mozambique, and South Africa, and vital registration data from South Africa, Mauritius, and Seychelles (with limited vital records in Mali, Mozambique, and Zimbabwe), as well, suggest higher rates of CVD in eastern and central Sub-Saharan Africa in comparison with

western and southern Sub-Saharan Africa, although the uncertainty intervals are wide. In general, verbal autopsy data suggest that $\approx 9\%$ to 13% of deaths are attributable to CVD, especially stroke, with higher proportions reported by the available vital registration systems. Injuries and communicable diseases account for much higher proportions of adult deaths than in other LMICs.⁴¹ Among CVDs, hypertensive heart disease and cardiomyopathy represent a much larger proportion of total death than in other regions of the world (Figure 7). Reflecting higher all-cause mortality and shorter lifespans overall, the mean age of death attributable to CVD in Sub-Saharan Africa in 2010 was the youngest in the world at 64.9 years (95% UI, 64.4–65.4) compared with 67.6 to 81.2 years for the rest of the world.⁴²

Regional Patterns of Rheumatic Heart Disease

Although rheumatic heart disease has an epidemic history, it is now best understood as an endemic disease concentrated among poorer individuals living in LMICs, mostly in Oceania, South Asia, Central Asia, Africa, and the Middle East. Some endemic countries have age-standardized death rates attributable to rheumatic heart disease ranging from 5 to 15 per 100 000. However, vital registration systems likely underreport death attributable to rheumatic heart disease and alternate data sources are uncommon. Population-based screening studies of children 5 to 14 years of age suggest a prevalence of 0.3 to 5.7 cases per 1000 individuals with the highest values coming from echocardiographic surveys in South Asia, Sub-Saharan Africa, and Oceania.⁴³ Assuming even low rates of case fatality, it is possible that vital records miss a significant proportion of rheumatic heart disease deaths.

The Epidemiological Transition: An Important Concept in Need of Expansion

In 1971, Abdel Omran introduced the concept of an epidemiological transition, updating the work of the demographer Frank Notestein on fertility and population growth by considering cause-specific mortality.^{44,45} Omran theorized that chronic diseases would expand as infectious epidemics declined. Additional stages have been proposed, including an “age of delayed degenerative diseases” and an “age of regression due to social upheaval,” and additional models of transition, as well.^{46–48} But this stepwise model of societal change and subsequent disease has remained a dominant paradigm for understanding global patterns of CVD epidemiology.

The idea of a stepwise transition does not account for the complexities of the currently observed pattern of CVD in several important ways. First, Mirzaei and colleagues⁴⁹ have described a range of patterns in IHD mortality, including the classic rise and fall to less conventional rising and flat patterns. Second, the standard model does not account for the effect of health systems. Not only can improvements in health system performance be expected to significantly influence morbidity and case fatality attributable to CVD, but good health at low cost may also be achievable in some countries without large-scale economic development.⁵⁰ Third, some regions of the world have experienced an increase in CVD burden without a concurrent decline in maternal, neonatal, and communicable

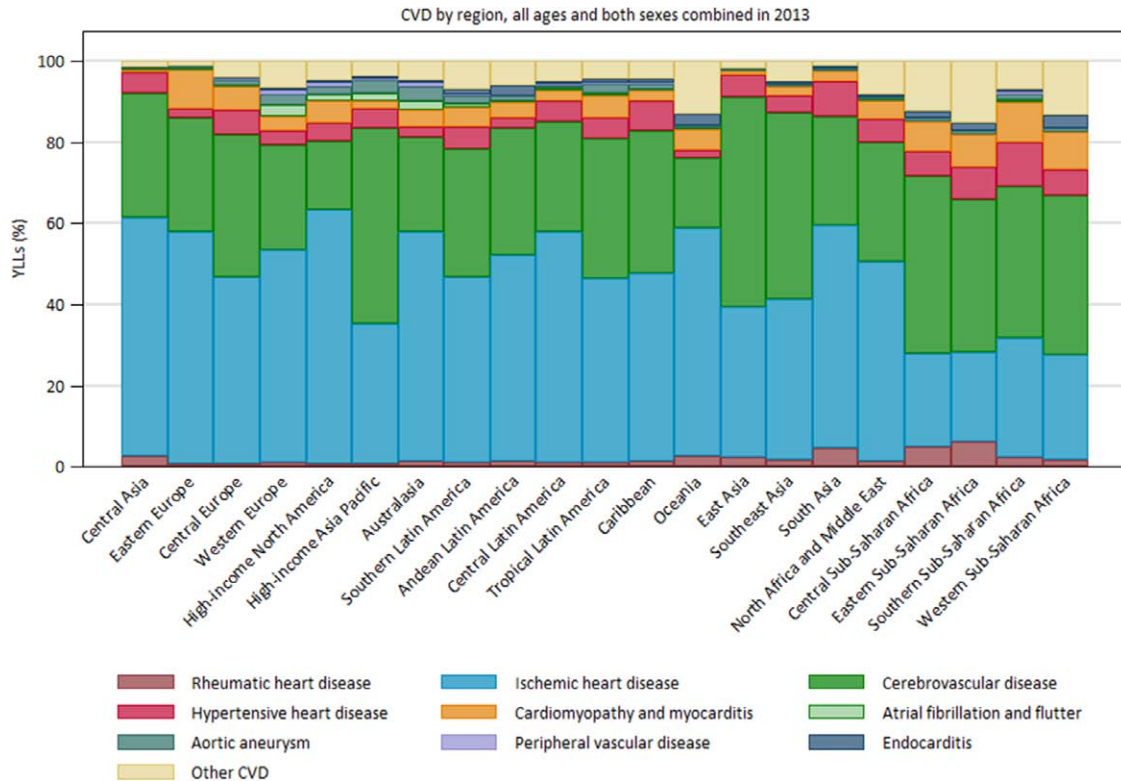


Figure 7. Proportion of years of life lost (YLL) because of CVD stratified by global region, 2013. YLL is a measure of premature mortality calculated by using a normative goal for survival computed from the lowest observed death rate across countries. CVD indicates cardiovascular disease.

conditions. This pattern, in which a population acquires the conditions of late stages in the epidemiological transition without resolving those from an earlier stage, has been referred to as a double burden.^{51,52} For example, countries in Eastern Europe and Central Asia have seen a rise in both CVD and maternal and communicable diseases since 1990, including Ukraine, Russia, Belarus, Uzbekistan, and Kyrgyzstan. Fourth, there is enormous variation in the prevalence of CVD among LMICs. These patterns are not always well explained by summary measures of development or economic growth. The death rate attributable to CVD in Guyana was almost twice that of its larger and wealthier neighbor Venezuela in 2013. Mongolia experienced age-standardized death rates attributable to CVD almost 50% greater than in neighboring China, despite significantly less economic development. These regional differences highlight the tension between the concept of societies progressing through epidemiological stages of development and the complexities that reflect local patterns of disease. Finally, there is reason to believe that CVD and other chronic diseases can interact with other important causes of death such as human immunodeficiency virus, alcohol use, and road traffic injuries, leading to a triple or even quadruple burden in certain low-income countries.⁵³

We suggest that the original, and even the updated, theories of an epidemiological transition may be inadequate to account for the range of observed patterns in CVD mortality. An expanded model of transition should account for the immense regional variation in disease burden, disparities in health systems, and the stacking of multiple kinds of epidemics within

small areas and over short periods of time. Trends in CVD mortality can be attributed to changes in its underlying causes, including the prevalence of CVD risk factors and access to health care. The effects of population growth and ageing, the leading contributors to CVD burden, should be included as well.³ An expanded theory will allow for robust forecasts of future trends used by countries to better balance the necessary investments in primary prevention with the costs of running a healthcare system. A more flexible and updateable model will be data-driven, reflect local CVD risk factor patterns, and form a foundation for evidence-based public health policy relevant to specific populations within countries. Such an approach will help to quickly identify new epidemics, novel risk factors, or health system disparities rather than fitting all cases to an expected paradigm.

Future Directions in Measuring the Global Cardiovascular Disease Burden

Efforts like the GBD study mirror earlier work in clinical medicine to adopt an empirical and evidence-based approach.⁵⁴ Measurements of disease burden are driven by an urgent need to inform governments and health systems facing daily choices across a range of policy options. Health policy makers cannot wait for perfect epidemiological studies to guide their decisions any more than a practicing physician can wait for new clinical trial results during a busy day in his or her clinic. As with evidence-based medicine, GBD can inform policy making by supplying an objective evaluation of what is already known. Gaps in knowledge, especially for subgroups, are expected

Table 4. Knowledge Gaps and Suggested Next Steps

Gaps in Knowledge	Suggested Next Steps
<ul style="list-style-type: none"> • Mortality data remain absent or of limited quality in some countries, particularly in the poorest regions • Little is known about variation in cardiovascular risk factors and disease burden within some countries • Changes in cardiovascular mortality are more complex than suggested by a stepwise model of epidemiological transition 	<ul style="list-style-type: none"> • Further national investment in sample and comprehensive vital registration systems • Sharing of best practices for data collection and verbal autopsy • Efforts to improve ascertainment of death • Expansion of household health examination surveys, with wider sharing of results • Broader collection of anthropometric and biomarker data including blood pressure, glycosylated hemoglobin and cholesterol levels • Renewed efforts for population-based surveillance of CVD events, including myocardial infarction and stroke • National health planning will need to consider a broad range of contextual factors, including local patterns of risk, policies that influence health, and current health system arrangements • Formal CVD costing studies in LMIC to address financial risk and health system efficiencies • Improved cross-cultural measures of disability related to CVD

CVD indicates cardiovascular disease; and LMIC, low- and middle-income countries.

because of the current data limitations. Methods that account for uncertainty and heterogeneity are therefore a vital aspect of measurement efforts. At the same time, future estimates of global CVD burden will be increasingly informed by new vital registration systems. Surveillance systems have been outlined as a key health information system priority for the forthcoming Sustainable Development Goals and will require human resources, infrastructure, technical capacity, and funding, particularly in LMICs.⁵⁵ High-quality and ongoing measurement of CVD incidence, such as at the remaining MONICA sites and other population-based registries, are an essential component that also deserves increased support. Household surveillance studies should include the collection of blood biomarkers and can increasingly take advantage of lower-cost portable technologies such as heart rhythm monitoring or ultrasound imaging. The measurement of CVD burden should also expand beyond death and disability to include estimates of healthcare quality, adherence to medications, microeconomic costs, including catastrophic health spending, distress financing, and other measures of financial risk associated with disease (Table 4).⁵⁶

Conclusions

The past 2 decades have seen dramatic declines in CVD mortality rates, whereas, simultaneously, LMICs are confronted by an increasing number of people experiencing these diseases at younger ages. The global distribution of CVD is complex and defined by national and regional characteristics as much as by global disease trends. There is extensive variation both between and within regions, yet CVD remains a dominant cause of death, even among individuals as young as 40 years of age. Policies and health interventions will need to be tailored and scaled for a broad range of local conditions to achieve the health goals set by the United Nations for 2025. These goals are a landmark for global health and will serve as important benchmarks for the measurement of future achievements.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Supplemental Table 1.....page 2

Global Burden of Disease Analytic Regions

Supplemental Figure 1.....page 3

Age-standardized death rate due to cardiovascular and circulatory diseases during 1990-2013

Supplemental Figure 2.....page 4

Cardiovascular and circulatory diseases by region, all ages and both sexes
combined in 2013

Footnote: Years of life lost (YLL) is a measure of premature mortality calculated using a normative goal for survival computed from the lowest observed death rate across countries.

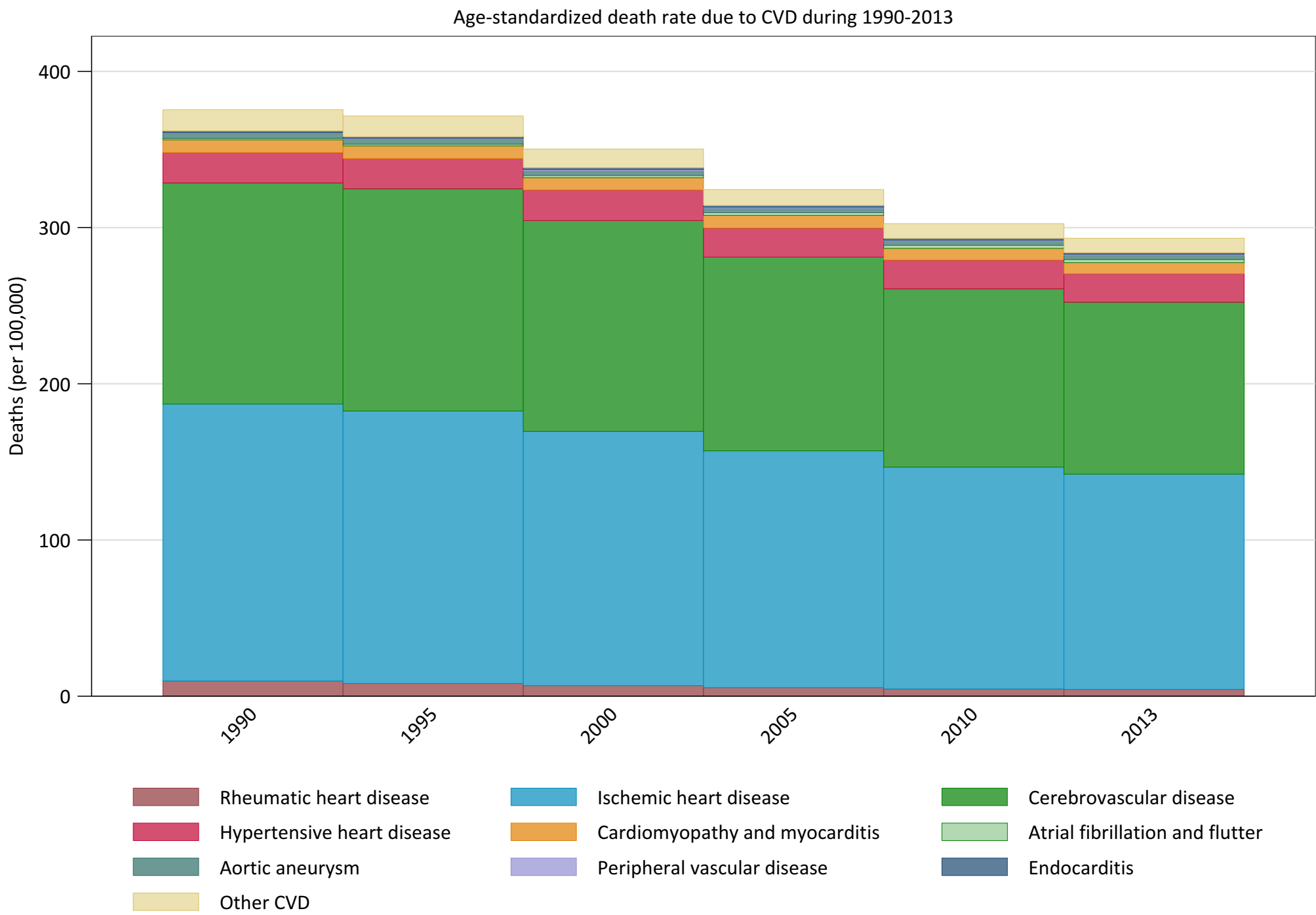
Supplemental Table 1

21 GBD regions organized by 7 GBD super-regions	
Super-region name	Region name
Central Europe, Eastern Europe, and Central Asia	Central Asia, Central Europe, Eastern Europe
High-income	High-income Asia Pacific, Australasia, Western Europe, Southern Latin America, High-income North America
Latin America and Caribbean	Caribbean, Andean Latin America, Central Latin America, Tropical Latin America
North Africa and Middle East	North Africa and Middle East
South Asia	South Asia
Southeast Asia, East Asia, and Oceania	East Asia, Southeast Asia, Oceania
Sub-Saharan Africa	Central Sub-Saharan Africa, Eastern Sub-Saharan Africa, Southern Sub-Saharan Africa, Western Sub-Saharan Africa

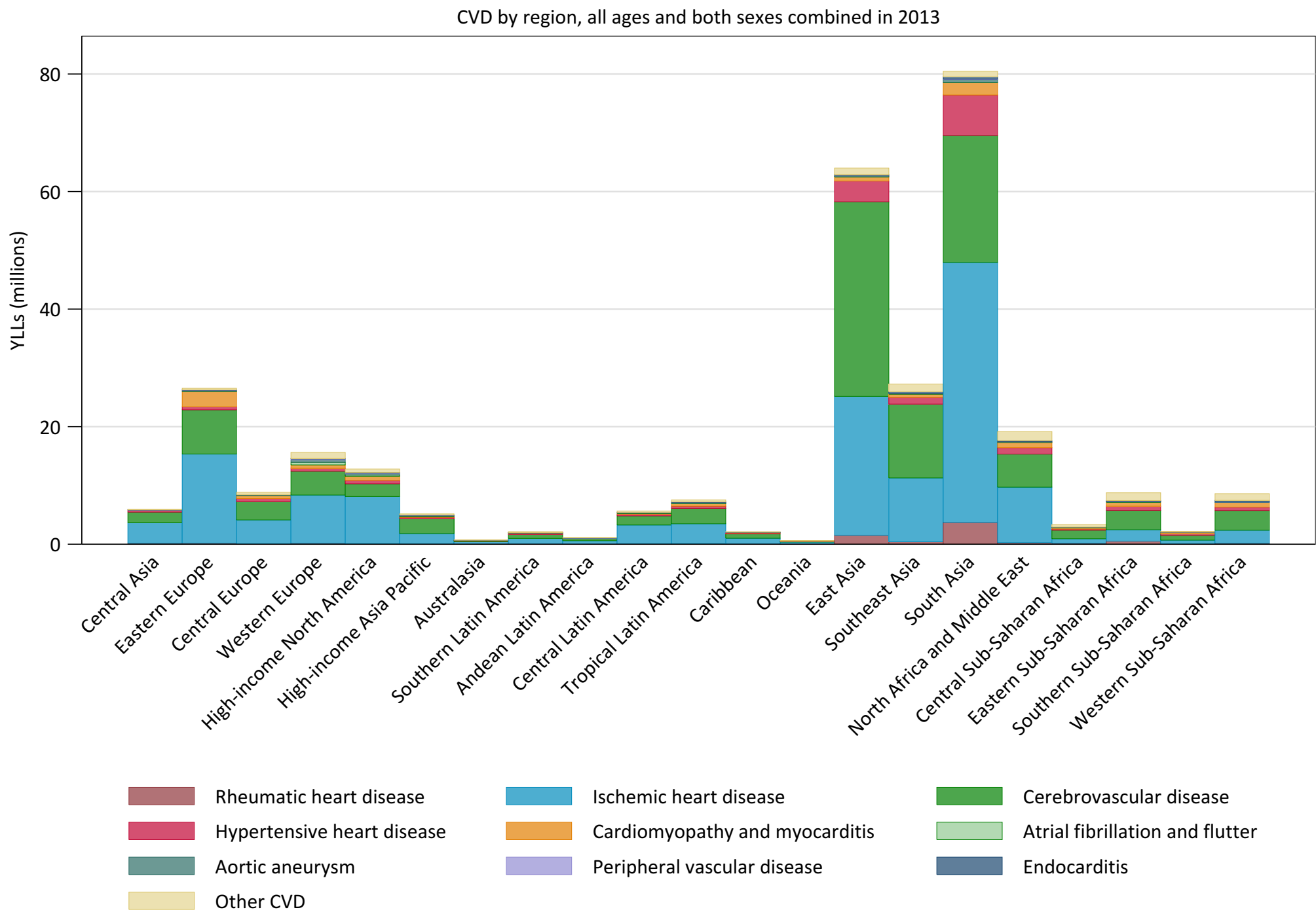
A complete list of countries is available at:

http://www.healthdata.org/sites/default/files/files/Projects/GBD/GBDRegions_countries.pdf

Supplemental Figure 1



Supplemental Figure 2



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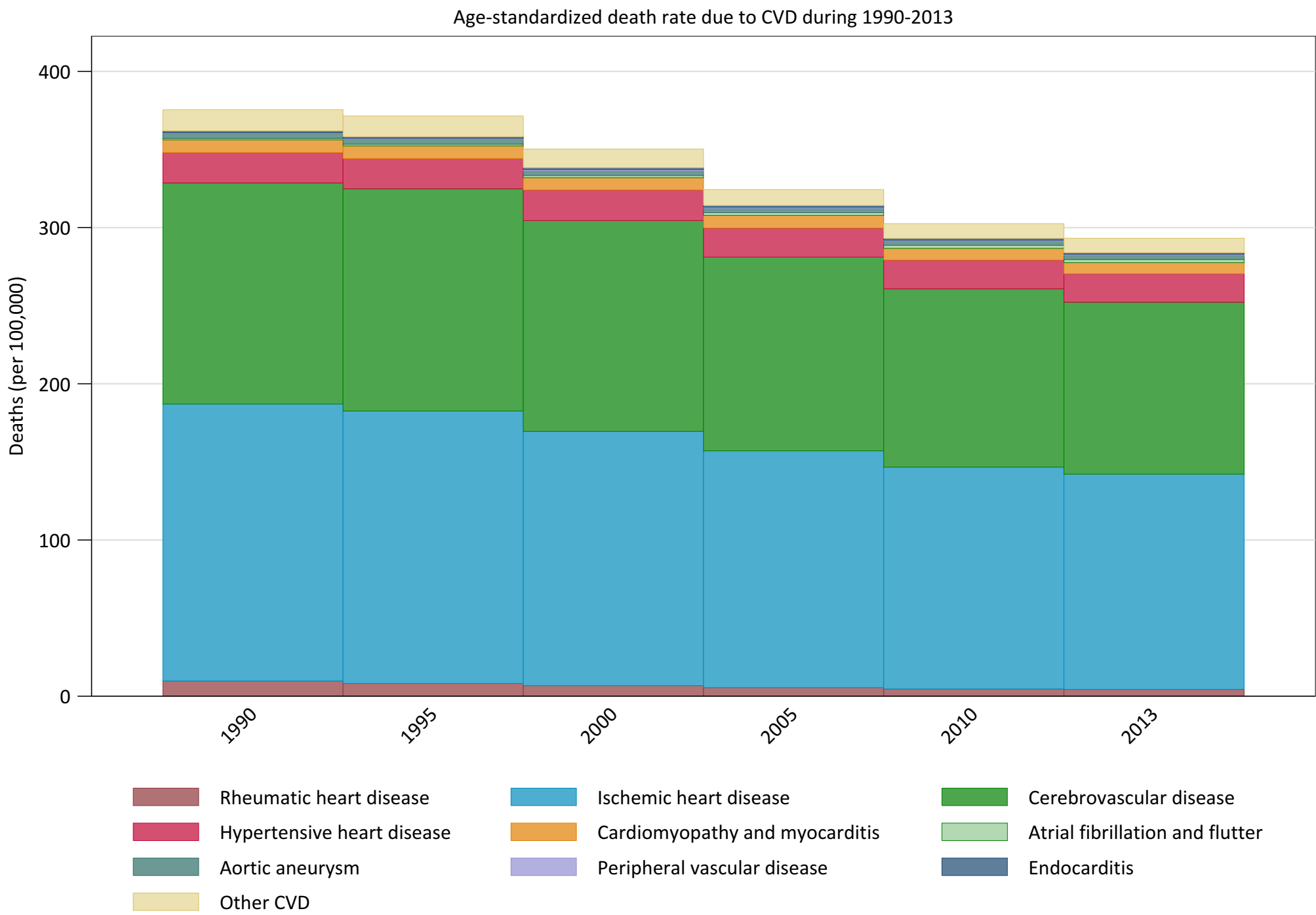
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Latin America and Caribbean	Caribbean, Andean Latin America, Central Latin America, Tropical Latin America
North Africa and Middle East	North Africa and Middle East
South Asia	South Asia
Southeast Asia, East Asia, and Oceania	East Asia, Southeast Asia, Oceania
Sub-Saharan Africa	Central Sub-Saharan Africa, Eastern Sub-Saharan Africa, Southern Sub-Saharan Africa, Western Sub-Saharan Africa

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Supplemental Figure 1



Supplemental Figure 2

