



Review

Global Trends in Atherosclerotic Cardiovascular Disease

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ABSTRACT

Purpose: Cardiovascular disease (CVD) is the leading cause of morbidity and mortality, affecting over 523 million people globally. Atherosclerotic diseases, particularly ischemic heart disease (IHD) and stroke, are the primary mediators of CVD burden and trends, with half of CVD deaths attributed to IHD, and another quarter to ischemic stroke. The aim of this review was to provide an overview of world-wide trends in the burden of atherosclerotic CVD.

Methods: A literature review of published studies reporting regional or global trends or burden of CVD was undertaken, with a specific focus on atherosclerotic-mediated CVDs.

Findings: While long-term trends in age-standardized rates of CVD mortality and incidence indicate substantial declines in disease burden, the impact of population growth and ageing has contributed to a continued increase in the absolute number of people living with CVD. Additionally, when data are restricted to the most recent decade, there are indications that even declines in age-standardized CVD rates may have attenuated. Trends are also heterogeneous across countries and regions, with a relative increase in CVD burden in developing countries and differing trends within countries. The impact of the COVID-19 pandemic resulted in substantial short-term reductions in hospitalization rates for major atherosclerotic CVDs including acute coronary syndromes and heart failure in some countries.

Implications: Recent attenuation of declines in atherosclerotic CVDs with increasing absolute burden has significant implications for health systems and resource availability, with the impact of the COVID-19 pandemic on longer-term trends in CVD yet to be clearly established.

Introduction

Despite a sustained decline in cardiovascular disease (CVD) morbidity and mortality over the past four decades, CVD remains a leading cause of disease burden globally.¹ Population growth and ageing means that ischemic heart disease (IHD) and stroke are leading contributors to increases in the burden of disability adjusted life years (DALYs), while age-standardized measures of CVD burden are generally declining.¹ Reversal of downward trends in different settings mean that some trends are heterogeneous by region and sociodemographic profile. CVD remains a growing problem in developing regions,² with almost 80% of global CVD cases now occurring in low- and middle-income countries, where ageing and urbanization trends have accelerated the increase in CVD burden.

The decades-long decline in CVD mortality is underpinned by a combination of reductions in the prevalence of major cardiovascular risk factors, particularly smoking, hypertension and dyslipidemia, as well as improvements in acute treatment and better secondary prevention.³

However, increasing rates of obesity and diabetes may have a detrimental effect on these trends, and the more recent impact of the COVID-19 pandemic has the potential to have immediate and downstream effects on CVD trends.

Given the significant contribution of underlying atherosclerotic pathophysiology to CVD burden, this review will focus on trends in atherosclerotic-mediated CVDs. Examples are provided for specific atherosclerotic CVDs where available, including for IHD, stroke, and peripheral arterial disease (PAD), and summaries of trends and burden of total CVD are also provided for context. For some conditions, such as heart failure, which can be mediated by ischemic and non-ischemic etiology, data are reported for ischemic-related measures where available.

CVD Mortality

In developed countries, the sustained reductions in CVD mortality in the second half of the 20th century mirror those seen for infec-

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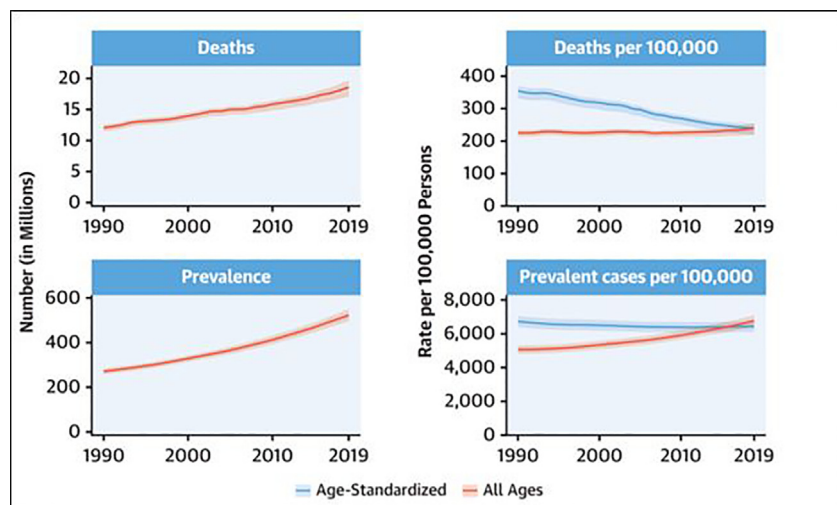


Figure 1. Total numbers and age-standardized rates of deaths and prevalence due to cardiovascular disease from 1990 to 2019. Adapted with permission.⁵

tious diseases in the first half of the 20th century, and are primarily attributed to reductions in major risk factor prevalence, and improving treatments and secondary prevention.^{3,4} Age-standardized CVD mortality rates have reduced by nearly 30% globally since 1990, contrasting with a limited decline in crude (“all ages”) CVD mortality rates (Figure 1), and with the number of deaths attributed to CVD more than doubling during this period (Figure 1).² The difference between trends in age-standardized and crude mortality rates occurs because age-standardization accounts for the increasing age of the general population during the period. The apparent disparity between declining age-standardized rates and the increase in the number of CVD deaths is because the size of the global population has increased significantly, which combined with an ageing population, increases the number of people at risk of a CVD-related death.

The declines in age-standardized mortality have been experienced in almost all regions globally. However, since 2010, the reduction in CVD mortality rates may have slowed (–11% from 2010 to 2019), with some regions, including in northern Africa, south Asia, and some US states, experiencing increases in age-standardized CVD mortality.⁵ In South America, while long-term trends have been downward, some countries including Chile, Colombia, Peru, and parts of Brazil have experienced greater declines since 2010 than other South American countries.⁵ In the United States, the annual rate of decline in CVD mortality between 2000 and 2011 was 3.8%, with a slowing of downward trends in subsequent years.⁶

CVD mortality rates are predominated by atherosclerotic diseases, particularly IHD and stroke. IHD contributes around half of CVD deaths (49.2%), while stroke contributes another quarter, of which around half are of ischemic aetiology.⁵ While IHD has been the leading cause of death in most developed countries for decades,^{7–10} deaths due to dementia and Alzheimer's disease are now either the leading, or among the leading, causes of death in some of these countries. The leading cause of death in England in 2021 was dementia/Alzheimer's disease,¹¹ while in Australia, it has been reported as the leading cause of death in women for the past four years.¹² In other countries, IHD remains the leading cause of death, including in Canada,¹³ New Zealand,¹⁴ and the United States.⁸ Variation between countries in the classification of dementia/Alzheimer's disease as an underlying cause of death is a likely contributor to this shift,¹⁵ although ageing populations with greater life expectancy in these countries has also contributed to this trend. Epidemiological transitions in many developing countries mean that where the leading causes of death were previously infectious diseases (respiratory or diarrheal related) or peri- or neonatal deaths, atherosclerotic-mediated diseases such as IHD and stroke are now some of the highest-ranked causes of death in those countries.¹⁶

CVD Incidence

The number of incident cases of CVD increased by 77% globally, from 31.3 million cases in 1990 to 55.5 million in 2019.² After age-standardization, a global reduction in CVD incidence of around 11% between 1990 and 2019 is reported,² generally underpinned by larger declines in North America, Western Europe, and some parts of Latin America, and as seen for mortality trends, suggesting the impact of population growth and ageing on crude estimates. However, when these data are restricted to the most recent decade (2010–2019), the reduction in age-standardized CVD incidence is 1.6%, indicating an attenuation of the previous moderate declines,¹ and heterogeneous trends by region, with increases in some regions (Figure 2).^{2,17}

Longer-term global declines in CVD incidence are driven by reductions in atherosclerotic CVDs particularly IHD and PAD, while the incidence of other CVDs such as nonrheumatic valvular diseases are increasing. The incidence of IHD declined by 3.6% from 2010 to 2019, with greater reductions in males than females, and concomitant declines in PAD incidence of 3.2% during the same period.¹ While there are reports of declines of 15% to 20% in stroke incidence since 1990,¹⁵ declining trends since 2010 have attenuated, while the number of incident stroke cases increased by nearly 25% during the same period.

Heart failure incidence has followed a downward trajectory, albeit at a lower rate of decline than seen for other major CVDs. Most studies report data from developed countries, with declines ranging from around 7% from 2002 to 2014 in the United Kingdom¹⁸; 29% in men and 43% in women from 2000 to 2010 from the Olmsted County study¹⁹; and 17% in men while incidence remained unchanged in women from the Framingham Heart Study.²⁰ However, whole-country studies with more recent data indicate that downward trends may be slowing or reversing,^{21,22} and trends may be mediated by increasing incidence in younger populations, particularly those aged under 55 years.^{21–24} Data are limited on trends by etiology, although one study from New Zealand suggests that the contribution of IHD etiology to heart failure incidence has declined.²² These data are concomitant with an increasing proportion of heart failure patients having heart failure with preserved ejection fraction (HFpEF),²⁵ potentially indicating that increases in heart failure incidence are driven by non-IHD etiological factors.

CVD Prevalence

The number of prevalent cases of CVD globally is increasing. Over 271 million people were estimated to be living with CVD in 1990; this estimate increased to 523 million by 2019.⁵ Age-standardized CVD prevalence declined marginally during the same period, while crude prevalence

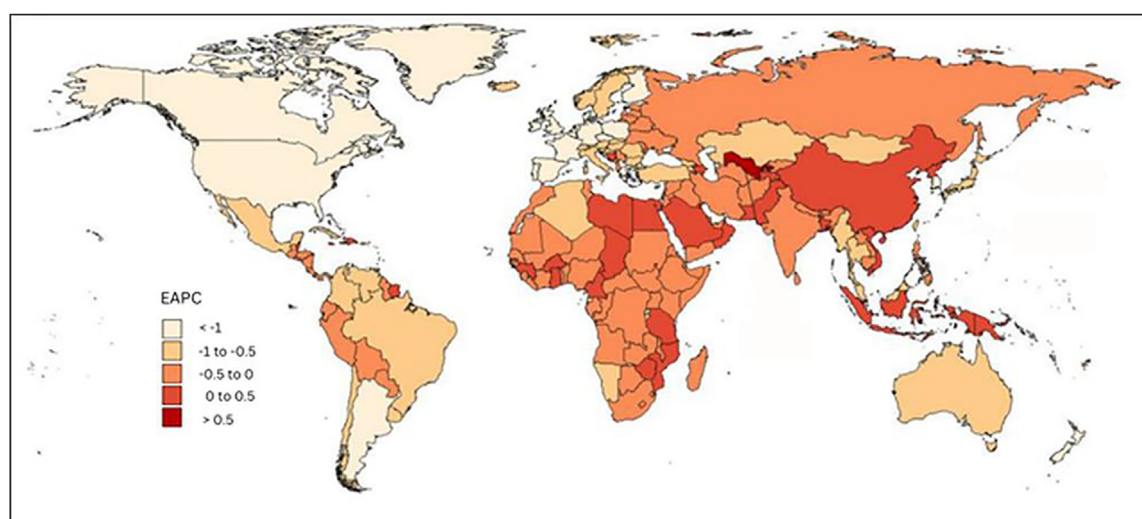


Figure 2. Estimated annual percentage change in cardiovascular disease incidence in 204 countries and territories. EAPC, estimated annual percentage change. Adapted with permission.²

lence rates increased, again indicating that the ageing population is contributing to increased number of prevalent cases globally (Figure 1). However, the limited improvement in trends of CVD incidence combined with improved survival in people with CVD is also a significant driver of the global increase in prevalent CVD cases.

While longer-term trends in IHD and stroke prevalence are marginally downward,⁷ there are contrasting trends by disease in the most recent decade. Since 2010, there has been no significant change in the age-standardized prevalence of IHD (0.1%, 95% uncertainty interval [UI] −0.3, 0.5), while age-standardized prevalence of stroke has marginally increased (1.9%, 95% UI 0.6, 3.2),⁵ driven by increasing prevalence of ischemic stroke.¹ The latter trend is particularly underpinned by increasing stroke prevalence in China, Indonesia, and parts of the United States. In contrast, the age-standardized global population prevalence of PAD declined by 22% between 1990 and 2019, although also in the setting of marked increases in crude prevalence.²⁶ Similarly, the most recent decade of data suggest a slowing of this trend, with only a 3.5% reduction in age-standardized prevalence of PAD since 2010.⁵ The overall reductions in age-standardized CVD prevalence, albeit marginal, may be masking differing age-specific trends, with reports from some countries of increasing prevalence of IHD in women, and stroke in men and women, in people aged under 55 years, concurrent with declining prevalence in older age groups.²⁷

Trends in Subtypes of IHD and Stroke

Over the past 2 decades, the composition of acute coronary syndromes (ACS), comprising ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina, has changed, influencing trends in myocardial infarction (MI) and ACS incidence.²⁸ Downward trends in MI incidence and event rates were reported from most western countries through the 1980s and 1990s.^{29–31} The introduction of the Universal Definition of MI in 2000, including the shift to troponin assays as the preferred diagnostic biomarker for MI and increasing reliance on biomarker changes, contributed to a plateauing of previous downward trends in MI.^{32–34} This was primarily underpinned by increasing diagnosis of non-ST-elevation MI (NSTEMI) cases with increasing troponin assay sensitivity and shifting diagnostic thresholds.^{32,34} Rates of NSTEMI hospitalizations have increased by up to 10% in some countries, while hospitalizations for unstable angina have shown a converse marked decline.^{35,36} The downward trends in unstable angina are due to a shift in the diagnosis to NSTEMI, although studies showing reductions in overall angina rates suggest real reduc-

tions in disease burden.^{37,38} Concurrently, the incidence of STEMI is declining, although this trend predates the introduction of troponin,³⁴ indicating the effectiveness of improvements in risk factor management and prevention.

Global reductions in the age-standardized incidence of stroke since 1990 reflect declines in the incidence of ischemic stroke,⁵ although trends differ across regions. There are marked declines in ischemic stroke rates reported from regions such as southern Latin America (−38%)¹⁵; yet the age-standardized incidence of ischemic stroke incidence increased by 35% in China from 1990 to 2019,³⁹ with smaller increases seen in other east Asian countries.¹⁵ These heterogeneous trends are accompanied by consistent reductions in age-standardized rates of hemorrhagic stroke across all regions, suggesting that trends in atherosclerotic-mediated stroke are driving overall stroke trends in most regions. This is supported by data showing that decreasing small vessel occlusion strokes are reported in Western populations where there has been improved control of conventional vascular risk factors over time.⁴⁰

Impact of COVID-19 on CVD Trends

The impact of the COVID-19 pandemic on global trends in atherosclerotic CVD is still emerging. In people with COVID-19, higher rates of adverse outcomes are associated with the presence of atherosclerotic CVD risk factors and established CVD.⁵ The effects of COVID-19 on the provision of health care for people with CVD in countries where there was a significant COVID-19 burden on the health care system appear substantial. During the early months of the pandemic, reductions in CVD-related hospitalization rates reduced substantially in the United Kingdom (up to 53% decline between March and May 2019)⁴¹ and in the United States (43.4% comparing March 2020 with March 2019).⁴² A 40% reduction in ACS admissions after the initial UK lockdown in 2020 was observed (compared to 1.7% reduction in the year prior) and a 49% drop in heart failure admissions, despite previously increasing rates of admission.⁴¹ With subsequent data as the pandemic unfolded, the pattern persisted although with less dramatic reductions. The annual number of emergency admissions for ACS was 8% fewer than expected in England (although not in Scotland and Wales), while heart failure admissions were constant, although fewer than expected in Wales (13%).⁴³ By 2021, ACS and heart failure admissions were as expected across the United Kingdom, while the impact on CVDs requiring nonurgent hospital care was still observed, with lower than expected rates of elective admissions for PAD in 2020 (−40%) and 2021 (−31%).⁴³ These studies also demonstrated that, at least in England, those CVD patients who did present

to hospital had significantly higher levels of comorbidity suggesting decreased prevention and later presentation.⁴³ Concomitantly, drug therapy for CVD declined significantly, with reports of decreases in new dispensing of antihypertensives, lipid-lowering medications, and anticoagulation medications. In the United Kingdom, this pattern was seen in relation to the timing of lockdowns, with declining medication prescriptions between lockdowns without subsequent increases following lockdown cessation.⁴⁴

While the indirect effects of COVID-19 on trends in CVD have been relatively contemporaneous with the pandemic onset, impacts on longer-term CVD trends may be delayed and more difficult to ascertain. Data on CVD mortality are the most readily available. A number of countries have reported significant increases in CVD deaths or increases in excess CVD deaths from 2019 to 2020, including 7.6% in Germany, 8% in England, and 30% in Wuhan, China.⁴⁵ In some countries where COVID-19 was highly prevalent in the early stages of the pandemic, increases in CVD deaths varied greatly between regions, with studies from Brazil reporting increases ranging from 10.1% to 46.1%, depending on the region; in Italy, a similar pattern was seen with regional increases in CVD deaths ranging from 7.5% to 17%. Changes in in-hospital mortality attributed to CVD also varied greatly between countries, with increases seen in England for patients suffering out of hospital cardiac arrest; a 7% increase in heart failure patients admitted to hospital in Germany; and a more than doubling of inpatient CVD mortality in the United States from a study including 13 hospitals in New York.⁴⁵ In Australia, where the disease burden of COVID-19 was low in the early phases of the pandemic due to strict government regulations, all-cause mortality rates decreased, underpinned in part by reductions in IHD deaths.⁴⁶

Implications of Current Trends

Trends in atherosclerotic CVDs continue to drive trends in CVD globally. Downward trends across most CVD subtypes were attenuated in the recent decade, particularly for incidence and prevalence, highlighting the need to focus on contemporary trends and ongoing surveillance. The limited decline in age-standardized CVD prevalence is likely an impact of small reductions in incidence, concurrent with continued marked declines in CVD mortality (and thus improving survival). Given declines in age-standardized measures of CVD, marked increases in the absolute number of people with atherosclerotic CVDs across mortality, incidence, and prevalence indicates that population growth and ageing are contributing to upward trends in case numbers. There are some contrasting between-country trends, which may be due to differences in disease classification and recording between jurisdictions; inequitable access to diagnostic services and health resources can also cause apparent differences in disease burden. The implications of the large absolute burden of CVD cases globally, and increasingly in low- to middle-income settings, are important for health systems and resource availability, and indicate the need for better primary prevention. Furthermore, if adverse trends in risk factors continue, this is likely to result in continuing attenuation or reversal in declining age-standardized trends, particularly for atherosclerotic CVDs.

Monitoring of age-specific trends is essential, with a potential increasing burden in premature CVD in some settings. A recent study including 1.95 million MI events from England, Australia, Canada, and New Zealand reported that downward trends in MI mortality rates in adults aged under 55 years are almost completely due to improvements in 30-day case fatality, with concurrent plateauing or increases in MI event rates.⁴⁷ This implies that prevention of MI occurrence is suboptimal in this age group, although survival post-MI is high. A similar pattern for younger adults has also been reported for stroke.⁴⁸ Global Burden of Disease data show that in middle and high sociodemographic index regions, the increasing number of incident cases includes increases from the age of 25 years and above.² The fact that similar patterns are increasingly seen for heart failure and stroke, mainly reported from high-income countries, suggests a complex interplay of changing prevalence

of CVD risk factors as well as potentially more sensitive diagnostic tests and screening.

The impact of the COVID-19 pandemic on longer-term CVD trends is yet to transpire, with possible short-term adverse effects from reduced health care access during pandemic-related lockdowns, and ongoing impacts of long COVID and postviral effects on CVD status. The fact that current trends across the globe are at different stages and that rates are increasing in many countries will impact actions to control the future disease burden. Data on atherosclerotic CVD incidence postpandemic are essential for determining ongoing impacts of COVID-19 on CVD burden.

Conclusions

Despite long-term declines in age-standardized CVD mortality and incidence, the number of people with CVD is increasing globally, and alarmingly, trends over the recent decade indicate that this burden is worsening. CVD remains the largest contributor to the global burden of disease, primarily driven by trends and burden in atherosclerotic CVDs. The impact of population growth and ageing is a major contributor to the increasing absolute number of CVD deaths and incidence globally. However, the impact of increases in the prevalence of some cardiovascular risk factors, emerging cardiovascular risk factors such as ambient air pollution, and the as yet undocumented impacts of COVID-19 on longer-term CVD trends, indicates the importance of improved disease surveillance. There is an imperative for strengthening public health and health system measures to reduce the growing burden of CVD.

Author contributions

LN conceived and wrote the paper; all authors provided intellectual input, reviewed the manuscript, and approved the final version of the paper.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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