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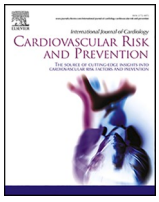

The Global Burden of premature cardiovascular disease, 1990–2019

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ABSTRACT

Aims: Premature cardiovascular disease (pCVD) definition varies in literature, with age cut-offs ranging from 50-65 years. While there is some literature available on pCVD in North America, comprehensive data on its global burden is still lacking which hinders the development of efficient strategies for early detection and prevention. In this study we aimed to investigate the global trends in pCVD related morbidity and mortality from 1990 to 2019.
Methods: The 1990-2019 Global Burden of Disease (GBD) database was utilized to examine global trends in cardiovascular disease-related total mortality, mortality rates, and Disability-Adjusted Life Years (DALYs) within individuals aged 15-49 years. The findings were further analyzed based on factors such as age, sex, and Socio-Demographic Index (SDI).
Results: From 1990 to 2019, the number of global annual pCVD deaths increased by 25%, from 992,067 (95% UI 1,042,261 – 946,383) to 1,241,484 (95% UI 1,339,193 –1,146,252). The rate of associated mortality decreased by 13%. Metabolic conditions were the most significant risk factors for pCVD mortality. Ischemic heart disease and stroke are the leading causes of death across all age groups. pCVD mortality presented progressive widening between high and low SDI regions. Additionally, sex-specific disparities in CVD mortality were significantly greater in the premature age group as compared to all-age groups.
Conclusion: pCVD is an increasingly significant global cause of morbidity and mortality that disproportionately affects males and individuals living in less privileged regions. Furthermore, ischemic heart disease and stroke were identified as the main drivers of pCVD global burden.

Disclosures

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1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, responsible for an estimated 18.56 million deaths in 2019 [1]. CVD is also associated with significant disability and loss of productivity, with 40.8 million disability-adjusted life years (DALYs) and 4.5 million years lived with disability (YLD) linked to CVD diseases annually [2].

Despite substantial advancements in our understanding of disease progression and prevention strategies, CVD is increasingly diagnosed in younger ages. In fact, the average age for a first cerebrovascular accident (CVA) dropped to 69.3 years in 2012 from 71.7 years in 2000 [3], and the overall incidence of stroke in those under 60 years of age has been steadily rising from 2003 to 2017 [4]. In addition, the incidence of myocardial ischemic events for those under 40 years has been increasing by 2% annually for the past decade in the US [5]. These trends are concerning, as younger disease onset projects increased healthcare costs and burden, as well as decreased productivity within the global

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workforce.

Investigating the burden of premature CVD (pCVD) becomes even more crucial given the rising trend of central obesity and its associated diseases, such as diabetes, as well as metabolic syndrome, which are major risk factors for CVD. The incidence of type 2 diabetes in individuals aged 30–34 years increased by 70% between 2001 and 2016 [6], and childhood and adolescent obesity rates have tripled in the United States over the past three decades [7], with 80% of obese adolescents going on to become obese adults [8]. Risk factors for CVD are becoming more prevalent at earlier ages.

The current literature on pCVD is scarce and focused on specific regions, particularly North America[9 10 11 12 13]. Thus, in this study we sought to investigate the global trends in pCVD burden from 1990 to 2019.

2. Methods

2.1. Definition of premature cardiovascular disease

For this study, pCVD was defined as the occurrence of the disease between the ages of 15 and 49 years. In the literature, premature CVD is loosely defined with maximum ages ranging from 50 to 65 years, with thresholds usually differing for men and women [9–11,12]. We used an age cutoff at the low end of the scale as we were interested in analyzing the cardiovascular disease burden for patients that would be considered young by almost all standards. We also used the same cutoff for men and women, though we included a sex stratification in our analysis. Finally, we picked a minimum age of 15 years as we wanted to focus our investigation on the burden of acquired cardiovascular disease as opposed to congenital heart disease which might affect younger age groups at a much higher relative rate. While it was not possible to individually filter out congenital heart disease as it is not independently modelled in the GBD methodology, “other cardiovascular and circulatory diseases” are small to negligible contributors to CVD mortality in our selected age range, while they are major contributors in the 5–14 years age group (Supplemental Fig. 1).

2.2. Data source

We obtained our data from the Global Burden of Disease (GBD) study. GBD compiles global health data from various literature sources and official data to provide a comprehensive understanding of morbidity and mortality in 195 countries, ranging from 1990 to 2019. This publicly available data can be accessed through the Global Health Data Exchange (GHDx) tool at the following website: https://vizhub.healthdata.org/gbd-results. The methodology of GBD complies with the Guidelines for Accurate and Transparent Health Estimate Reporting (GATHER) [13] set by the World Health Organization (WHO) [14]. A detailed explanation of the GBD methodology can be found in the publication “GBD 2019 Diseases and Injuries Collaborators” [15].

The GHDx interface offers several options for filtering data, including specific causes of death or injury, risk factors linked to death or injury, and demographic factors such as age, sex, location, and sociodemographic index (SDI). The output of the data query provides information on the burden of disease in various forms such as deaths and Disability-Adjusted Life Years, which is the sum of Years of Life Lost (YLL) and Years Lived with Disability (YLD). The output can be displayed in the form of tables, graphs, raw numbers, rates per 100,000 people, or percentages, depending on the nature of the query.

2.3. GBD database analyses

We used the GHDx tool to investigate global trends in pCVD burden. As such, we filtered by age (15–49 years) and ran queries on cardiovascular disease burden with various additional demographic filters. The main two measures of cardiovascular disease burden that were used were deaths and DALYs. First, we examined the overall trend of premature cardiovascular mortality throughout the past three decades (1990–2019) and extracted data on deaths and DALYs in the form of crude numbers and rates. We then filtered by risk factors (metabolic, behavioral, and environmental) as we were interested in the proportion of premature cardiovascular disease that is attributable to each of those. We also ran additional queries stratified by sex, sociodemographic index, and age groups within the premature category (eg. 15–19, 20–24, etc). In the age group stratification, we also ran a query in which we stratified the cause by type of cardiovascular disease. Standard agreed-upon case definitions are used by the GBD study to identify specific cardiovascular causes of death [16].

2.4. Determining sub-type of pCVD in case of comorbidity

In the GBD methodology, each subtype of CVD has a structured definition based on International Classification of Disease (ICD) codes which helps guide the development of incidence and prevalence statistics (see supplemental data). In addition, specific causes of mortality are estimated using vital registration data which uses this system. As for the calculation of DALYs, individual conditions have weights from 0 to 1, and the effects of multiple comorbid conditions is cumulative [17].

3. Results

3.1. Change in pCVD deaths and DALYs over the past 3 decades

In 2019 the total number of pCVD deaths was 1,241,484 (95% UI 1,146,252 - 1,339,193), representing a 25% increase from 1990’s 992,067 (95% UI 946,383 - 1,042,261) (Fig. 1A). Over the same timeframe DALYs increased from 53,538,845 (95% UI 50,928,501 - 56,295,221) in 1990 to 67,233,492 (95% UI 62,399460 - 72,235,639) (Fig. 1C). Despite, this increase in the absolute number of pCVD deaths, when accounting for populational growth, the pCVD death and DALYs rate (per 100,000) experienced a 14% and 13% reduction, respectively, in the same period (Fig. 1B and D).

3.2. Rate of pCVD deaths, stratified by sex

In 2019, there were 41.68 (95% UI 38.15–45.33) pCVD deaths and 2175 (95% UI 1999–2359) DALYs per 100,000 males worldwide. There were 21.18 (95% UI 18.92–23.23) pCVD deaths and 1231 (95% UI 1114–1356) DALYs per 100,000 females worldwide. As such, the rate of pCVD mortality was 97% higher for males compared to females, and the rate of DALYs was 77% higher (Supplemental Fig. 2).

The 2019 data on CVD mortality rate in all ages and stratified by gender was used as a comparison. There were 248.03 (95% UI 229.43–264.99) CVD deaths and 5727.09 (95% UI 5318.89–6111.43) DALYs per 100,000 males worldwide. There were 231.73 (95% UI 205.47–251.66) CVD deaths and 4429.95 (95% UI 4052.35–4769.18) DALYs per 100,000 females worldwide. Thus, there was no significant difference in mortality between males and females in all age groups, though there was a significant difference in DALYs (Supplemental Fig. 2). The percentage difference in death rate between males and females increased incrementally early on in the premature age group, plateauing between ages 35–49. Meanwhile the difference begins to decrease after 60 years of age, with the trend flipping and the female CVD death rate becoming higher in individuals over the age of 95 (Supplemental Fig. 3).

In 2019, the number of pCVD deaths among males accounted for 8.6% of total CVD deaths among males. DALYs in the premature male age group accounted for 19.5% of total CVD disease related DALYs for males. The number of pCVD deaths among females accounted for 4.6% of total CVD deaths. DALYs in the premature female age group accounted for 14% of total CVD disease related DALYs in females (Supplemental Table 2).

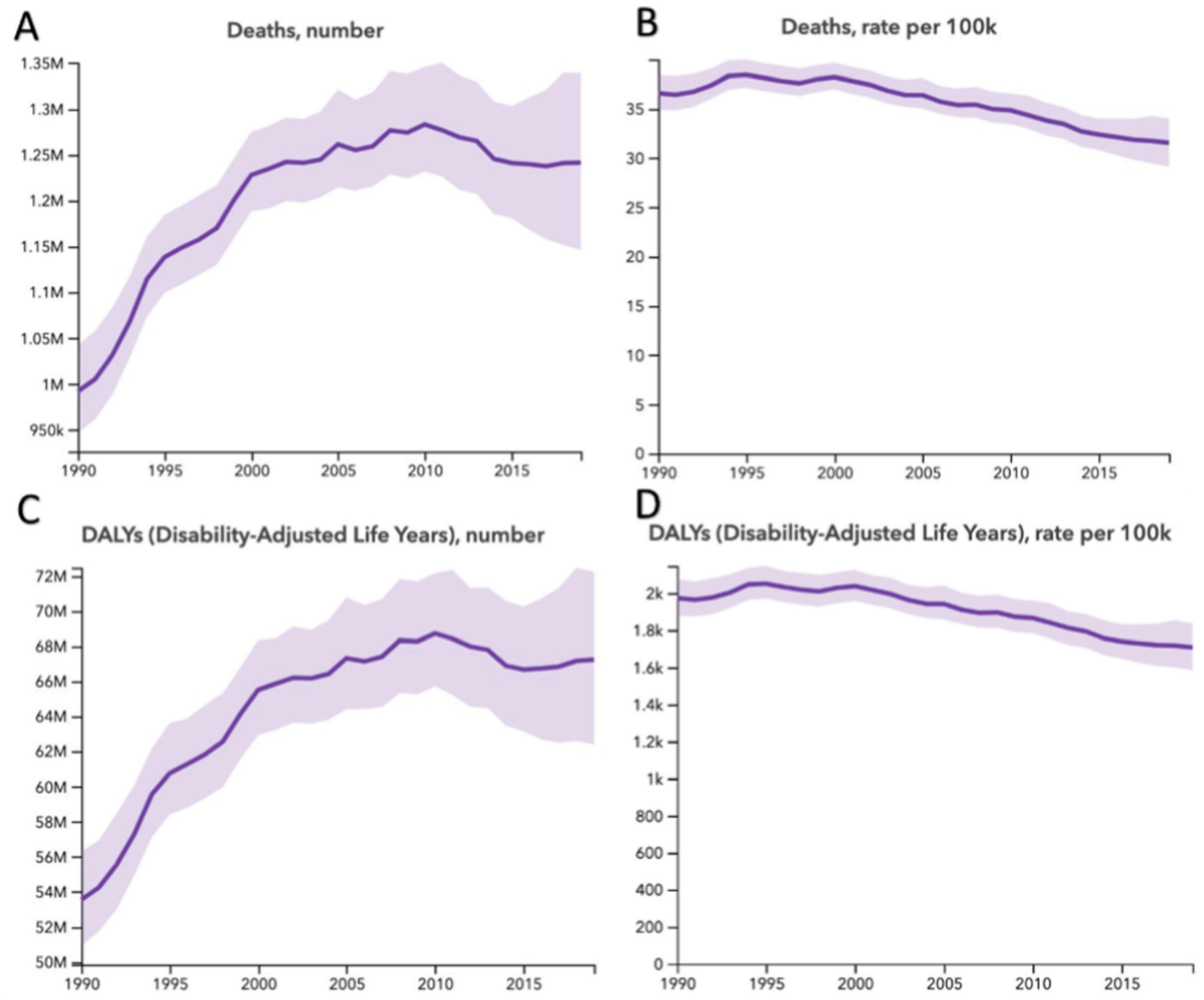

Fig. 1. Absolute number and rate (per 100,000 individuals) of global pCVD deaths (A,B) and disability adjusted life years (DALYs) (C,D) from 1990 to 2019.

3.3. Risk factors associated with pCVD mortality and DALYs, stratified by sex

Metabolic risk factors led as causes of pCVD morbidity and mortality in females, accounting for 14.88 (95% UI 12.88–16.96) deaths and 809.73 (95% UI 706.83–920.71) DALYs per 100,000. In males, there was no significant difference between the contribution of metabolic risk factors and behavioral risk factors[1]*. Environmental risk factors[2]* contributed the least to deaths and DALYs in both sexes, accounting for 20.5% and 22.5% of pCVD deaths and DALYs in males and females, respectively. The burden of each class of risk factors has not changed substantially since 1990 (Fig. 2).

3.4. Type of pCVD affecting each sub-age group

Fig. 3 describes the leading causes of pCVD mortality rates across 5-year age groups: 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, and 45–49 years. Over the course of 1990–2019, ischemic heart disease was the leading cause of pCVD mortality across all age groups. In the youngest age group (15–19 years), it shared this position with stroke, which was the second greatest contributor to pCVD mortality. The difference between the top two contributors and the remaining causes increased with age. For ages 15–35 years, rheumatic heart disease was the third leading cause of pCVD mortality, with cardiomyopathies and myocarditis following closely behind. After age 35 years, cardiomyopathies and myocarditis began to surpass rheumatic heart disease as the third leading cause. Hypertensive heart disease, which was the fifth most common cause of pCVD mortality for ages 20–40, started to surpass rheumatic heart disease and cardiomyopathy at age 40. By age 45, it had become the third leading contributor to pCVD mortality, behind ischemic heart disease and stroke (Fig. 3).

3.5. Type of pCVD affecting each sex

Ischemic heart disease (IHD) and stroke are also the top causes of morbidity and mortality in males and females independently. In 2019, the premature male death rate per 100,000 for ischemic heart disease was 22.7 (95% UI 20.63–25.08), while it was 11.65 (95% UI 10.48–12.87) for stroke. In the same year, the premature female death rate per 100,000 for ischemic heart disease was 8.9 (95% UI 7.89–9.86), while it was 7.11 (95% UI 6.35–7.89) for stroke. The IHD death rate was 95% higher than stroke in males, while the difference was only 25% in

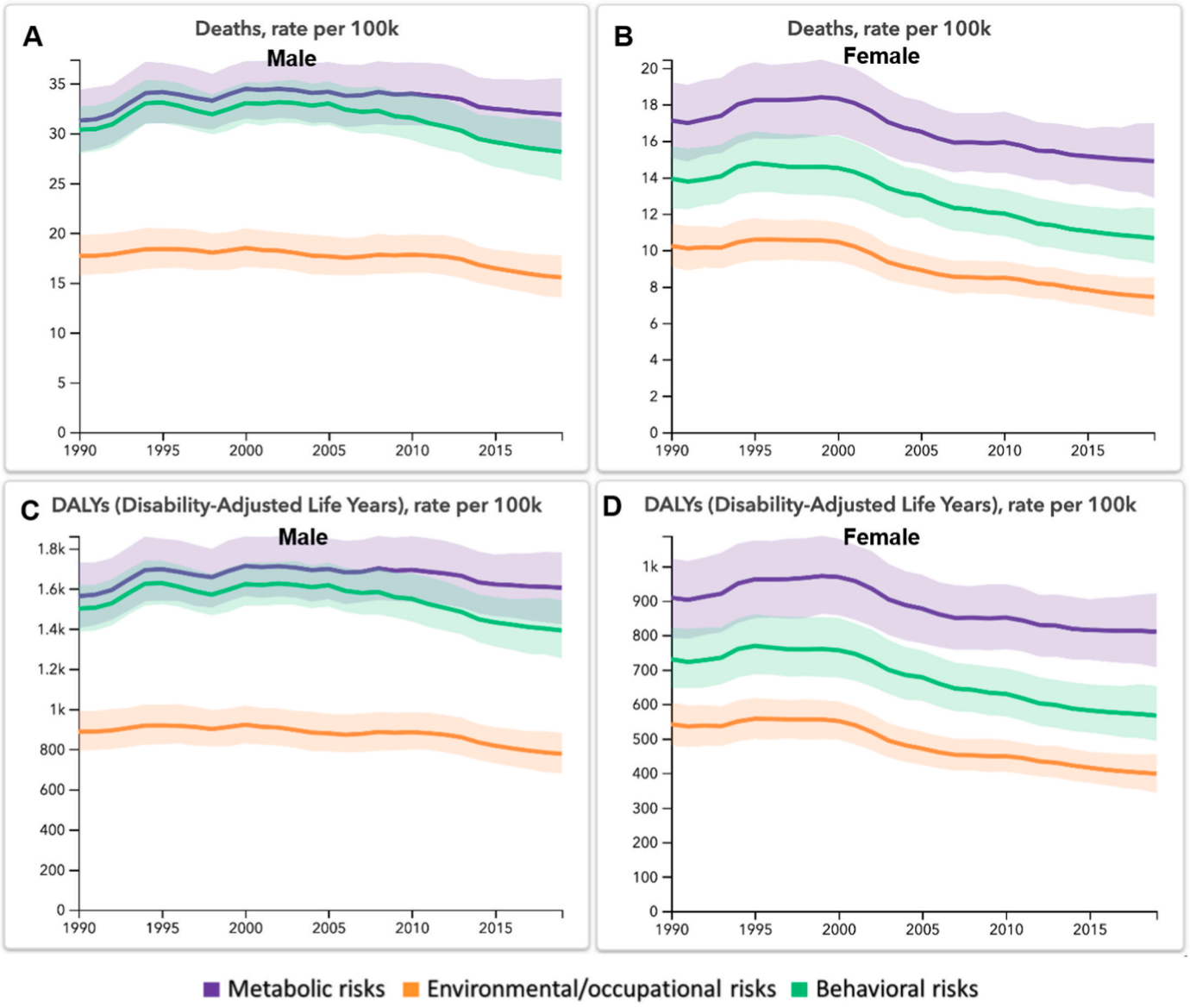

Fig. 2. Sex-stratified rate (per 100, 000 individuals) of pCVD deaths (A&B) and disability adjusted life years (DALYs) (C&D) from 1990 to 2019 attributable to metabolic, environmental/occupational, and behavioral risks.

females. In previous years, stroke has topped IHD as a cause of premature mortality in females. Stroke and IHD are equal contributors to DALYs in females 15–49 years of age, while the rate of DALYs attributable to IHD was 72% higher than that of stroke in males of the same age range (Supplemental Fig. 4). Ultimately, the substantially higher IHD burden in males compared to females, was one of the main drivers of the overall higher male pCVD mortality and DALYs rates.

3.6. Difference in death rate affecting each sub-age group

The pCVD mortality and DALY rates rise as the age of the patients increase. From 1990 to 2019, there was a consistent decrease in the death rate across all age groups, with the largest decrease occurring in the 15–19 and 45–49 age groups, at 32.5% and 30.5% respectively, with DALYs exhibiting a similar trend (Supplemental Fig. 5). The decrease in pCVD mortality rate in the remaining age groups ranged from 21.9% to 24.2% (Supplemental Table 1). When examining the data from 2019, the difference in mortality rate between the age groups appears to increase exponentially (Supplemental Fig. 6A); when plotted on a logarithmic scale, the increase is linear, with a correlation coefficient of 0.997 (Supplemental Fig. 6B).

3.7. Rate of pCVD death and DALYs, stratified by sociodemographic index (SDI)

Over the past three decades (1990–2019), there were no marked differences in pCVD mortality between high-middle, middle, low-middle, and low SDI countries. However, the pCVD mortality rate was substantially lower in high SDI countries compared to the others (Supplemental Fig. 7A). The pattern was similar for DALYs (Supplemental Fig. 7B). In the year 2019, high SDI countries recorded 16.81 (95% UI 15.84 to 16.81) pCVD deaths and 943.7 (95% UI 880.9 to 1018.0) DALYs per 100,000 people. On the other hand, the pCVD mortality rate in high-middle, middle, and low SDI countries had a mortality rate ranging from 31.4 to 38.1 and DALYs ranging from 1647.5 to 2045.0 per 100,000 people, respectively, with no apparent pattern (Supplemental Fig. 8).

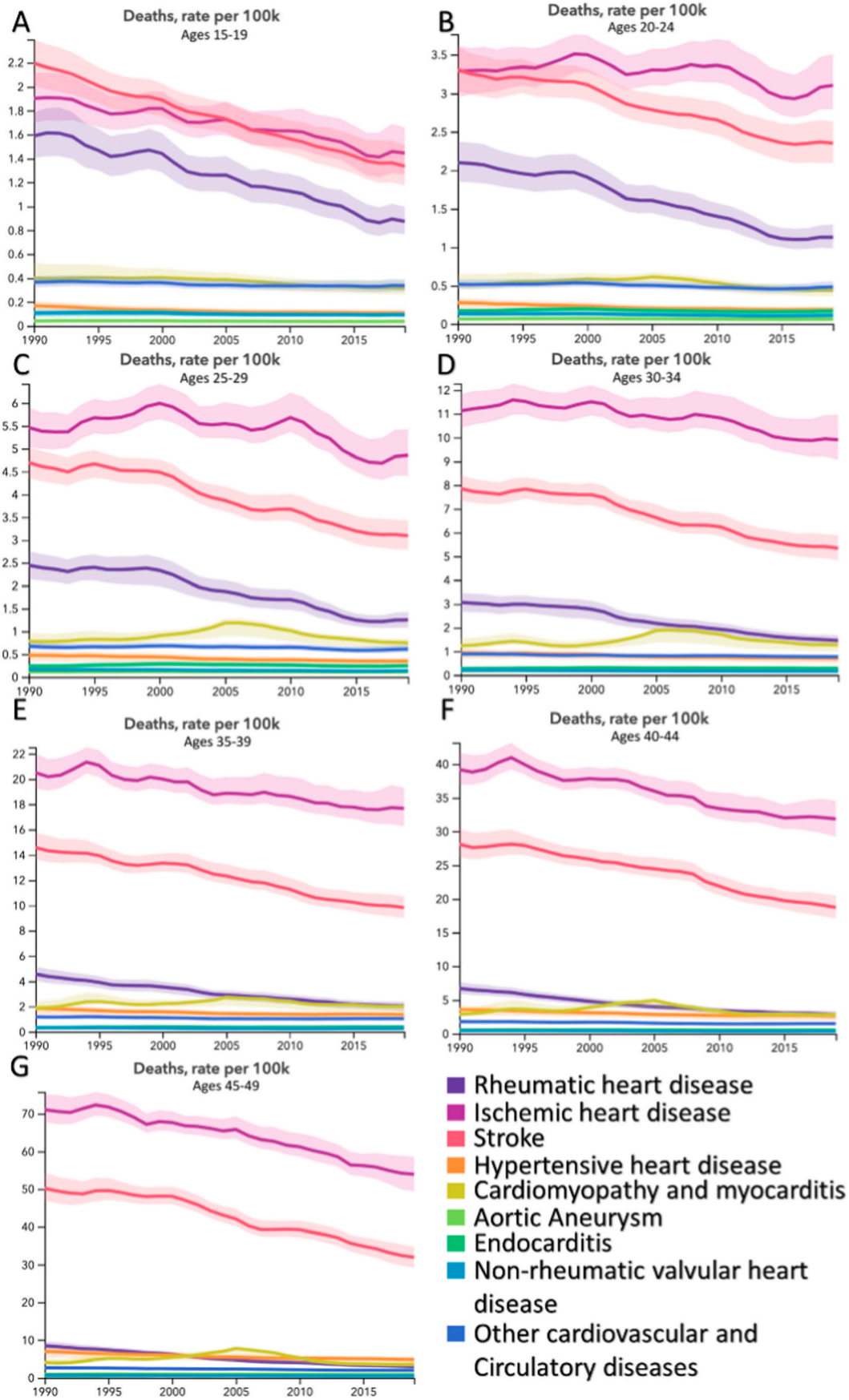

Fig. 3. Leading causes of pCVD deaths rates (per 100, 000 individuals) from 1990 to 2019 according to 5-year age groups: 15-19 (A), 20-24 (B), 25-29 (C), 30-34 (D), 35-39 (E), 40-45 (F) and 45-49 (G) years.

3.8. Specific risk factors and their burden

Out of all metabolic risk factors, high systolic blood pressure has been the leading cause of pCVD morbidity and mortality in the past 3 decades, accounting for 16.32 (95% UI 13.70–19.03) deaths and 838.46 (95% UI 711.06–978.89) DALYs in 2019, which is 37% of the total burden attributable to metabolic factors. High body-mass index and high LDL cholesterol shared the position as second most significant metabolic risk factors to contribute to pCVD, with a burden of around 25% each. High fasting plasma glucose and kidney dysfunction were less important contributors to CVD in this young age group (Supplemental Figs. 9A–B).

Dietary risks were the most significant behavioral factor to contribute to pCVD, accounting for 15.33 (95% UI 13.08–15.33) deaths and 775.88 (95% UI 665.19–899.72) DALYs in 2019. They accounted for 60% of the pCVD deaths and DALYs attributable to behavioral risk factors (Supplemental Figs. 9C–D). Though there is not enough data to fully discern which of the dietary factors contributed the most, a diet low in whole grains seemed to take this place, followed closely by a diet high in sodium. Other important dietary risks were a diet low in fruits and low in legumes (Supplemental Fig. 10). Tobacco smoke accounted for 8.5 (95% UI 7.67–9.38) deaths and 416.72 (95% UI 377.07–458.31) DALYs in 2019, amounting to 33% of the behavioral factor burden. The remaining 7% is attributed to alcohol use and low physical activity (Supplemental Figs. 9C–D).

Air pollution was the environmental factor that contributed the most to pCVD, accounting for 9.94 (95% UI 8.73–11.24) deaths and 511.85 (450.87–589.07) DALYs in 2019, which was roughly 80% of the total environmental factor burden of deaths and DALYs. The remaining 20% was contributed by non-optimal temperature and other environmental risks, like lead exposure and residential radon (Supplemental Figs. 9E–F).

3.9. Premature CV mortality rate across the globe

Fig. 4 is a world map displaying the 2019 pCVD mortality rate (per 100,000 people) in every country. The highest rates seem to be concentrated in Asia, Oceania, and eastern Europe. The 3 countries with the highest rates are Solomon Islands (190.81), Kiribati (155.89), and Nauru (147.52), which are all parts of Oceania. The 3 countries with the lowest rates are Norway (6.57), Switzerland (6.13) and Israel (5.59). The United States has the 67th highest rate of premature CV mortality, at 34.4.

4. Discussion

Premature CVD presents a major public health challenge. With the increasing incidence of obesity among young adults and other contributing factors, there is growing concern that this issue could become even more pressing. Despite this, there is limited literature available on its global impact. To the best of our knowledge, this paper is the first to use the Global Burden of Disease (GBD) to examine worldwide trends of pCVD.

Between 1990 and 2019, the annual rate of pCVD death decreased by 13% (Fig. 1). However, the number of deaths and DALYs increased by 25% and 25.6%, respectively, over the same period (Fig. 1). Males in the premature age group had significantly higher rates of death and DALYs compared to females. In 2019, pCVD deaths accounted for 8.6% of total male cardiovascular deaths and 4.6% of total female cardiovascular

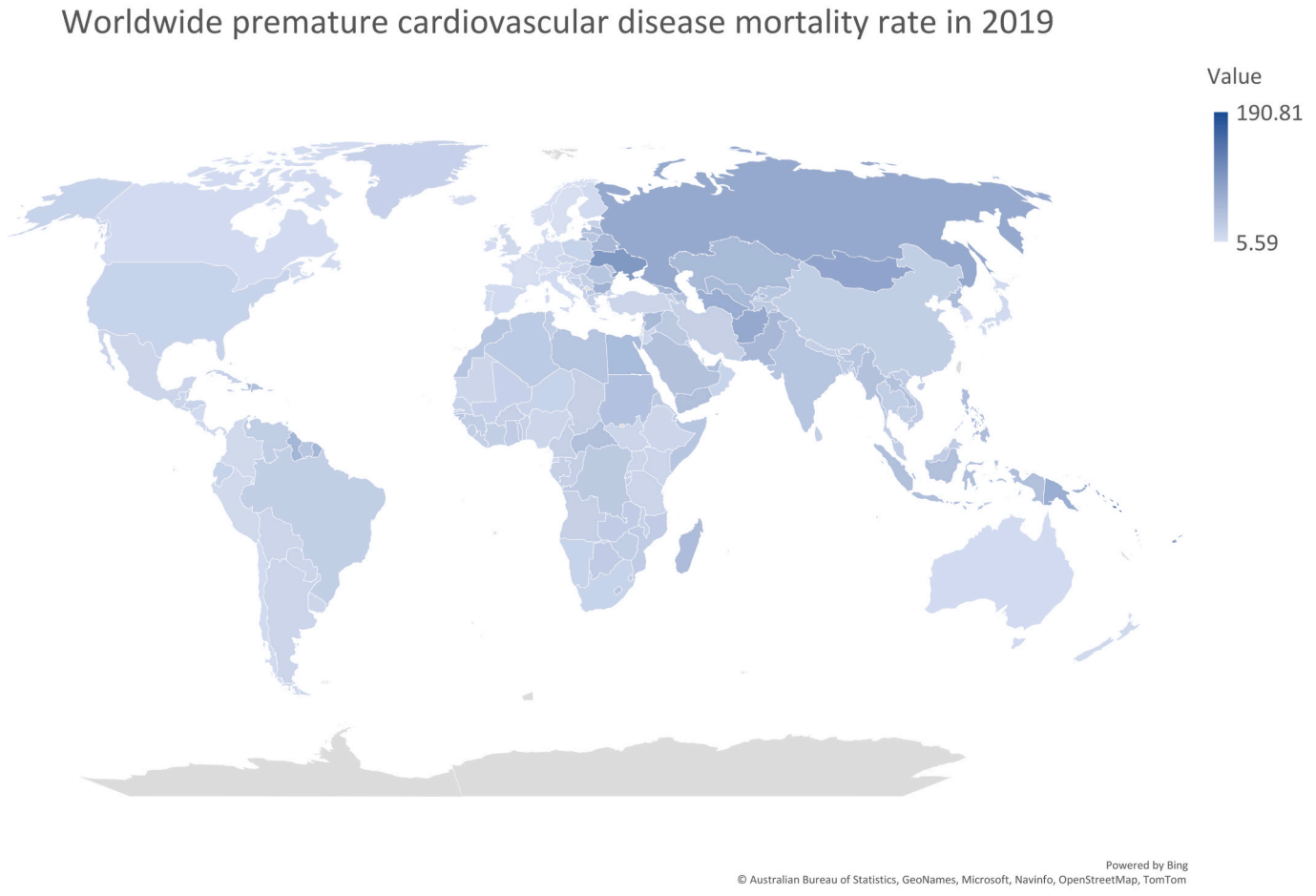

Fig. 4. Global distribution of pCVD mortality rates (per 100,000 individuals) in 2019.

deaths. Of these cases, ischemic heart disease (IHD) was the leading cause of death, followed by stroke, even among individuals as young as 15–19 years old (Fig. 3). In females, the risk of IHD and stroke were similar, while there was a 95% difference between the two in males (Supplemental Fig. 4). Metabolic factors, especially high systolic blood pressure were the most significant contributor to pCVD, followed by behavioral risk factors like smoking. Environmental risk factors, led by air pollution, had the least significant contribution (Fig. 2 & Supplemental Fig. 9). The relationship between age and pCVD mortality was found to be exponential, with increasing mortality as age increases (Supplemental Figs. 5 and 6). Regions with high SDI had significantly lower rates of pCVD mortality (16.81%) compared to regions with high-normal, normal, normal-low, and low SDI (31.4–38.1%). No relationship was found between SDI and pCVD in the latter four regions (Supplemental Figs. 7 and 8).

Several previous studies have explored pCVD at smaller scales, with somewhat inconsistent results. Two studies conducted in the United States produced differing outcomes, with one observing a decrease in fatal pCVD among 14,464 patients [9], while the other observed no change in the pCVD mortality rate over two decades [10]. A Canadian study revealed a plateau in pCVD mortality over the past decade, following a 31% decrease from the previous decade [11]. A study in the United Kingdom found an overall decrease in pCVD mortality from 1979 to 2013, though hospital admissions increased [18]. Based on the current literature, the rate of pCVD has declined since the late 20th century, but the rate of decline has slowed in recent years. The findings of this study also suggest that the rate of pCVD has been decreasing. However, in absolute terms, the worldwide impact of pCVD remains significant, with a 25% increase in premature deaths attributed to CVD between 1990 and 2019.

Significant advances pertaining to changes in frequency of prescription and surgery utilization have contributed to the overall decrease in pCVD since 1990 [19,20]. Additionally, improvements in hypertension control and awareness about its dangers have further reduced mortality [19]. A study by Yan et al. found that in high and middle-income countries, the cardiovascular medication utilization has increased by an annual 3% from 2008 to 2018 [21]. Since statins were introduced in 1987, they became a staple in CVD prevention, partially explaining the decline in pCVD mortality over the past three decades [22]. Specifically, the prescription rate of statins has trended upwards, seeing a 24.7% global increase in utilization [23–25]. However, the challenge of statin adherence remains an issue worldwide [26]. In the United States, bariatric surgery, which has been associated with lowering incidence of obesity and CVD, has seen a substantial increase in number since 1990, though this trend has since plateaued since 2010 [27,28]. However, low and middle-income countries continue to have substantially less access to life-saving cardiac surgeries compared to high-income countries [29–31]. This may contribute to the large disparity between pCVD morbidity and mortality in high-SDI regions and all other regions (Supplemental Fig. 7), in addition to lack of medication availability and adherance [32]. Even domestically, Khan et al. found that the mortality rate was higher in US counties with higher social vulnerability indices (SVI) [12], the inverse of SDI.

The data currently available suggests that there are higher age-specific rates of CVD in men than women [33,34], as seen in the premature age group investigated in this study. Our findings show that as age increases up to 35 years, there is an increase in the difference in pCVD mortality between the sexes. However, after 60 years of age, the difference in pCVD burden between the sexes appears to diminish (Supplemental Fig. 3). This can be attributed to the fact that other risk factors have had enough time to develop, while the influence of baseline demographic risk factors like sex remains dominant in the premature age group. Thus, it is important to target specific at-risk populations for more intensive pCVD screening at younger ages, particularly males in low-SDI countries.

Ischemic heart disease and stroke remain the leading cause of pCVD mortality among all age groups. Risk factors for atherosclerosis, such as obesity, smoking, and depression, continue to increase in young adult populations and in low-and-middle-income countries (LMIC), contributing to early ischemic heart disease [35,36]. In our study, a great part of the male vs. female differences in pCVD mortality and DALYs was led by the substantial differences in IHD burden. In part, this can be explained by the significant sex-specific biological differences in IHD [37]. Markedly, menopause represents an important cardiovascular biological transition that strongly increases CVD risk in women aged >55 years, while men tend to present with IHD at earlier ages [37]. Among stroke subtypes, ischemic stroke is the most prevalent compared to hemorrhagic stroke, and is more closely associated with increased rates of smoking and obesity [38,39]. The burden of stroke relative to other CVDs is greater in women (Supplemental Fig. 4) and this may be attributed to hormonal factors such as contraceptive use, pregnancy, and hormone replacement therapy [40]. The findings indicate that the third leading cause changes across age groups. Rheumatic heart disease (RHD) primarily affects children and young adults, remaining as the most acquired cardiovascular disease in individuals of <25 years of age worldwide, and is widely attributable to overcrowding and poor healthcare access in low-SDI countries [41,42]. Cardiomyopathy and myocarditis also present a public health issue in young adults, contributing as a predominant cause of sudden death [43]. In their sample, Fu et al. found that 1-year mortality hazard ratios due to dilated cardiomyopathy were greatest in individuals 30 to <50 and 50 to <70 years of age [44]. Alcohol abuse plays a factor in the later age incidence for cardiomyopathy, as alcoholic cardiomyopathy accounts for 40% of dilated cardiomyopathy cases and risk is greatest after five years of heavy drinking [45].

Several studies have investigated risk factors for pCVD mortality, with some emphasizing the importance of metabolic factors. For example, Viscasillas et al. found that almost half (44.7%) of the premature patients in their sample had diabetes, hypercholesterolemia, or were otherwise classified as “high risk” [46]. Other studies have highlighted the contribution of familial hypercholesterolemia to pCVD [47–49]. Both childhood and adult obesity have also been implicated as risk factors for pCVD mortality [50,51]. The issue is compounded by the high likelihood of comorbidity, with several metabolic risk factors occurring as a constellation in metabolic syndrome.

Insight into the specific metabolic factors that are most important in pCVD can inform preventive strategies. We found that elevated systolic blood pressure (SBP) is by far the metabolic factor that is most implicated in pCVD. Hypertension is a known risk factor for CVD, with risk of adverse cardiovascular outcomes doubling for every 10 mmhg increase in SBP above 115 mmhg [52]. Primary hypertension, and namely elevated SBP is on the rise in young adults, affecting 7–13% of individuals under the age of 30 [53]. These individuals often go undiagnosed, with a retrospective analysis by Johnson et al. finding that only 56% and 62% of hypertensive individuals aged 18–24 and 25–31 years, respectively, were diagnosed, even with regular primary care usage. As such, it is important that high or borderline blood pressure readings be followed up on, even if patients lack classic risk factors like obesity and dyslipidemia. Immigrants in the US, as well as residents of low-SDI countries have a higher rate of undiagnosed hypertension, often due to lack of awareness of the seriousness of the disease [54,55]. Therefore, a high yield avenue to decrease the burden of pCVD is more widespread and accessible education on the diagnosis of hypertension.

Dietary risk factors such as low fiber, whole grain, and high sodium diets have been shown to be the top behavioral factors contributing to pCVD (Supplemental Figs. 9–10). These factors contribute to the development of hypertension and other metabolic risk factors, but are also independent risk factors for pCVD via mechanisms such as increasing inflammatory markers [56–58]. A 2016 study revealed that 89% of American Adults and 90% of children exceed their daily recommended sodium intake [59]. It is necessary to decrease sodium and increase fiber intake, especially in children, and possible avenues could

include providing better options in school lunch programs through which some kids consume more than 50% of their calories [60].

Another major behavioral risk factor implicated in pCVD is tobacco use (Supplemental Fig. 9). Lee et al. conducted a literature review and found that smoking (OR 2.28) was strongly implicated in pCVD mortality [61]. We found that behavioral factors were equally as critical as metabolic factors in males, and this likely due to the increased prevalence and greater quantity of smoking among males compared to females [62,63]. Educating the public about smoking cessation could reduce the burden of pCVD. In fact, A Norwegian study found that educational differences regarding smoking were the driving force behind pCVD mortality [64]. Vasan et al. suggest that the global decrease in smoking has contributed to the falling rates of pCVD mortality [9].

Dietary risks and alcohol consumption may also contribute to the increased importance of behavioral factors to pCVD in males. Generally, males are more likely to succumb to unhealthy lifestyle habits such as smoking, poor diet and excessive drinking due to a variety of factors including lack of social support, work stress, higher rates of depression and less agreeable personality types [65]. Considering the social risks in males, measures such as more frequent and thorough depression and anxiety screening during health checkup visits could be implemented. The availability of social support networks should also be discussed during these visits, with physicians referring vulnerable patients to ancillary services where necessary.

The decline in pCVD mortality is not progressing as quickly as it should, and studies suggest that the decline in overall CVD mortality is showing signs of reversal in recent years [19,20]. Metabolic factors play a significant role in this observation. Ischemic heart disease and stroke, which are both atherosclerotic diseases, were the primary culprits behind CVD mortality in all premature age subgroups. Their strong relationship with obesity and metabolic syndrome highlights the importance of controlling these metabolic risk factors from a young age. This study reveals that the rate of pCVD mortality increases exponentially with age, as metabolic factors accumulate and exert their effect. With the increasing rates of childhood obesity, there should be more concerted efforts to educate the public about these risk factors. Screening and early medical management for young patients with familial hypercholesterolemia are also imperative.

This study has some limitations. Firstly, there is no consensus on the definition of “premature cardiovascular disease”, so the relatively narrow age range (15–49 years) used in this study may have excluded relevant data. The GBD database was used as a data source, which utilizes various statistical methods to ensure adequate validity and reliability. However, the level of uncertainty that comes with such wide-scale data, particularly when collected from multiple sources, can be high. Furthermore, in many cases, the cause of death may be unclear, especially since patients with CVD have multiple preexisting morbidities. The recent COVID-19 pandemic may further obscure the true cause of death in some cases. Stroke, one of the top two causes of pCVD mortality, is acute in nature and easier to link to a death. On the other hand, more chronic conditions like hypertensive and rheumatic heart disease may be underrepresented as a cause of death. Additionally, multi-morbidity cannot be ascertained from the GBD which poses a limitation for the comprehensive understanding of global epidemiology of pCVD. Despite these limitations, this study provides valuable insight into the worldwide burden of pCVD. To date, it is the most wide-scale study to address this topic, but further research should be conducted, particularly in developing countries where data is sparse.

5. Conclusion

Cardiovascular disease continues to affect young individuals in higher numbers every year. Over the past three decades, there has been an absolute increase in cardiovascular morbidity, measured as DALYs, and mortality in the 15–49-year-old age group. Metabolic factors, namely high systolic blood pressure, appear to be the driving factor behind the increase in premature CV deaths, though behavioral factors such as poor diets and smoking were also found to be significant. Ischemic heart disease and stroke are the leading cause of CV mortality in the premature age group, even in patients as young as 15–19 years old. Though the sex-related difference in CV morbidity and mortality is negligible in the general population, males in the premature age group are disproportionately affected compared to females. Lastly, living in a high sociodemographic index (SDI) region appears to be a protective factor against premature CV disease. There is an increasing need to develop strategies to prevent cardiovascular disease in younger patients.

Credit author statement

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Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcrp.2023.200212.

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