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Hearts apart: exploring sex disparity in the global and regional burden of ischemic heart disease; a systematic analysis from the global burden of disease study 1990–2021

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Abstract

Background Worldwide, ischemic heart disease is less prevalent in women than in men, but this gap has narrowed in recent decades. This study aims to evaluate trends and gender differences in the global burden of ischemic heart disease (IHD) across demographics and regions from 1990 to 2021.

Methods We utilized the data of the Global Burden of Disease Study from 1990 to 2021. The standard epidemiological measurements, including incidence, prevalence, mortality rates, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs), were obtained to estimate the burden of IHD concerning age, sex, and the sociodemographic index, allowing for comparisons over time.

Results The sex parity ratio (SPR), defined as the ratio of females to males, has increased globally. The SPR of age-standardized prevalence (ASPR) and age-standardized incidence (ASIR) rose from 0.610 to 0.631 in 1990 to 0.653 and 0.670 in 2021, respectively. From 1990 to 2021, the SPRs for ASPR and ASIR of IHD increased across all age groups. However, the SPRs for the age-standardized mortality rate (ASMR) and the age-standardized DALY rates (ASDR) of IHD declined. This decrease in the SPR for both ASMR and ASDR of IHD was observed in most regions of this study.

Conclusions While progress has been made in reducing the burden of IHD, the increasing sex disparities in specific regions and age groups emphasize the need for continuous monitoring, adaptive health policies, and sex-specific healthcare practices to ensure equitable health outcomes for all populations.

Clinical trial number not applicable.

Keywords Ischemic heart disease, Coronary artery disease, Global burden of disease, Sex disparity

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Introduction

Cardiovascular diseases (CVD) are responsible for approximately one-third of global mortality [1]. Ischemic heart disease (IHD) is the most common CVD [2] and is recognized as a significant public health threat in the 21st century [3]. IHD can impose fatal consequences and lead to high years of lost life (YLL) and non-fatal consequences with impaired quality of life and years lived with disability (YLD) [4]. The rising incidence of IHD is projected to persist, mostly because of the growing prevalence of diabetes, obesity, and metabolic syndrome, as well as the aging population [5, 6]. The World Heart Federation reports that the financial impact of CVD worldwide was around 863 billion US$ in 2010 and is projected to exceed 1 trillion US$ by 2030 [7]. However, despite the known high burden of IHD and related morbidity and mortality, there are some inconsistencies in the literature regarding risk factors that contribute to developing efficient approaches for prevention and control [8].

Risk factors for IHD can be categorized into modifiable, including abnormal cholesterol levels, hypertension, and obesity, and non-modifiable, including age, family history, and male sex [9]. IHD typically develops in women about ten years later than in men. However, women experience worse outcomes, marked by higher mortality rates and increased health-related complications [10, 11]. This disparity can be attributed to a combination of factors, including a higher prevalence of comorbid conditions in women, delays in both presentation and treatment, and lower utilization of guideline-based therapies [12]. Women also have higher incidences of traditional risk factors, including dyslipidemia, diabetes, and obesity. Additionally, alongside these common cardiovascular disease risk factors, there are sex-specific factors that are either more prevalent or unique to women. These additional factors heighten the risk of cardiovascular disease through mechanisms such as inflammation, autonomic dysregulation, and the disruption of the hypothalamic-pituitary-adrenal hormonal axis [13].

Studies indicate that there are sex-based differences in the pathophysiology of heart disease. Women typically have fewer calcified lesions and more nonobstructive plaques than men, potentially leading to variations in the presentation and risk of ischemic heart disease [14]. In addition to these anatomical differences, there are functional variations, including differing blood pressure trajectories and the aging of the myocardium and vasculature, which further impact the risk of ischemic heart disease [15]. Furthermore, women are more likely to suffer from microvascular disease, which often goes undetected by traditional risk assessment models that primarily focus on obstructive coronary artery disease [14].

On the other hand, sex hormones, particularly estrogen, significantly influence cardiovascular risk. It is believed that estrogen provides protective benefits against ischemic heart disease in premenopausal women; however, this protection diminishes after menopause, leading to an increased risk [16, 17]. Thus, Worldwide, CVDs are significantly less common in women aged 35–64 than in men, but this difference disappears in those over 65 [18].

Accurate assessments of the worldwide burden of disease play a vital role in enhancing the understanding of the effects of illnesses and injuries on population health, as well as evaluating progress toward global health objectives. Since the early 1990s, the Global Burden of Diseases (GBD) has been providing comprehensive estimates of global health and health loss. These estimates cover various age groups, regions, and sexes systematically and comprehensively [19, 20]. The GBD 2021 report highlights the identification of both new and existing health risks that require priority on global public health agendas. The GBD 2021 estimates will provide current information on health disparities within and between populations. This will enable the assessment of changes in these disparities over time, the measurement of health improvements, and the identification of policies or interventions that offer the most promising opportunities for impact in the post-COVID-19 era [21]. Therefore, our goal was to present up-to-date information on the differences in IHD incidence and prevalence between sexes using the GBD 2021 data. We further analyzed the YLD, YLL, and subsequent disability-adjusted life year (DALY) of IHD between sexes in various countries, along with examining the worldwide distribution and changes in the disease burden of IHD from 1990 to 2021, utilizing publicly accessible databases.

Methods and materials

Study data

This study utilized data from the Global Burden of Disease Study 2021 (GBD 2021). The GBD 2021 is a multinational study led by the Institute for Health Metrics and Evaluation (IHME) and conducted in collaboration with more than 10,000 researchers worldwide. It provides an extensive database that covers 371 diseases and injuries, impairments based on the International Classification of Diseases (ICD), and 88 risk factors across 204 countries and territories worldwide from 1990 to 2021. The GBD study was initiated in 1990 and has been updated with new databases to facilitate the comparison of findings across time. The detailed protocols of the GBD study have been published elsewhere [22–26]. The GBD study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) to report health estimations and ensures the precision and comparability of data by implementing several essential mechanisms. It employs a structured cause list that

standardizes the causes of death and disability across different regions and countries. Researchers utilize a variety of data sources, including registration systems, randomized controlled trials, cohort studies, household surveys, and health surveys, to compile information.

The GBD study utilizes statistical models, such as CODEm (Cause of Death Ensemble modeling), to fill data gaps and mitigate biases, thereby ensuring the accurate assignment of causes of death. Moreover, it employs a technique known as CoDCorrect to ensure that cause-specific deaths do not exceed overall deaths in any given year. By incorporating uncertainty intervals in the findings, the study effectively communicates the robustness of the evidence and enhances transparency. In regions with limited data access, the GBD initiative also uses verbal autopsies and demographic surveillance systems to collect cause-of-death data [27].

While data quality varies across regions and countries-especially in low- and middle-income areas where health data may be incomplete or less reliable- GBD addresses these differences with sophisticated statistical methods, such as Bayesian models, to mitigate issues of underreporting and data deficiencies. When faced with sparse or missing data, GBD employs statistical techniques to estimate and rectify biases. Furthermore, researchers utilize mapping techniques to ensure consistency in the data across various editions of the ICD [28].

The original database for the current study is available from the Global Health Data Exchange (https://ghdx.healthdata.org/record/ihme-data/cvd-1990-2021). Ethical Approval and informed consent were not applicable to the study, as the GBD benefits from anonymized collective data.

Definitions

IHD is defined as ICD-10 codes I20 to I25, which include angina pectoris (I20), acute myocardial infarction (AMI) (I21), subsequent myocardial infarction (I22), complications following acute myocardial infarction (I23), other acute ischemic heart diseases (I24), and chronic ischemic heart disease (I25). The GBD study utilizes a hierarchical four-level classification for risk factors. Level 1 comprises a broad cluster of behavioral, metabolic, and environmental/occupational risks. Level 2 encompasses 20 risk factors, including Unsafe water, sanitation and handwashing, non-optimal temperature, tobacco/alcohol/drug use, dietary risks, child and maternal malnutrition, air pollution, low physical activity, and high BMI. Level 3 is composed of more specific risk factors, including particulate matter pollution and child growth failure, and Level 4 is the most detailed class, which includes solid fuels household air pollution and child wasting [29, 30].

The included data was categorized into four levels as follows: global, sociodemographic, super regions and regions, and individual countries or territories. For the sociodemographic category, the Sociodemographic Index (SDI) was utilized, a complex indicator of development status that has a strong correlation with health outcomes. Total fertility rate, average educational levels, and income per capita were used to measure SDI. It divides countries and regions into 5 groups as follows: low, low-middle, middle, high-middle, and high SDI [31].

Additionally, the world was divided into seven super-regions and further sub-grouped into 21 GBD Regions based on epidemiological similarities and geographic proximity. The seven super-region categories are as follows: (1) Central Europe, Eastern Europe, and Central Asia, (2) High-Income Asia Pacific and North America, (3) Latin America and the Caribbean, (4) North Africa and the Middle East, (5) South Asia, (6) South-East Asia, East Asia, and Oceania, and (7) Sub-Saharan Africa. The last category included and analyzed 204 separate countries and territories.

Measurement framework

In the GBD study, standard epidemiological measurements, including incidence, prevalence, mortality rates, YLLs, YLDs, and DALYs, were used to estimate the burden of IHD in terms of age, sex, and SDI, allowing for comparisons over time. Incidence and prevalence rates were estimated based on updated and standardized analytical procedures. YLLs resulting from IHD were calculated by measuring the difference between the country-specific life expectancy of a person of that age and the age at the time of death. YLDs were calculated by multiplying the disability weight by the prevalence of IHD. DALYs were measured as the aggregate of YLDs and YLLs.

In this study, we introduced the Sex Parity Ratio (SPR), which is calculated to assess the sex disparity of IHD between women and men. The SPR is simply calculated by measuring the ratio of female to male in terms of incidence, prevalence, Mortality, DALY, YLL, or YLD. An SPR lower than one indicates a higher burden in men, while an SPR higher than one indicates a greater burden in women. An SPR of one also means an equal burden on men and women. We estimated the SPR of incidence, prevalence, Mortality and DALY in different spatial levels including; global, SDI quantiles, super regions, regions, countries, and five age groups including 50–55 years, 55–59 years, 60–64 years, 65–69 years, and >70 years. The SPR estimations were compared between 1990 and 2021.

Statistical analysis

In this study, we have reported the sex disparities between males and females for incidence, prevalence, mortalities, YLLs, YLDs, and DALYs of IHD between

1990 and 2021. The age-standardized prevalence rate (ASPR), age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and age-standardized disability-adjusted life years (ASDR) rates were used to remove the effects of age distributions in different populations and periods, enabling their comparability. The trends in age-standardized rates are indicators of human disease patterns and changes in risk factor exposure; therefore, the estimated annual percentage change (EAPC) was used to explain the shifts in ASR over specific period intervals. The ASDRs take into account the population-level age distribution discrepancies, thus enabling comparisons across geography. The summary exposure value (SEV) was used to calculate the SPR of exposure to different risk factors. The SEV is a standardized metric that considers both the prevalence of exposure in the population and the severity of exposure relative to the theoretically optimal risk exposure level. It is expressed as a percentage ranging between 0% (no excess exposure, with the entire population at an optimal risk level) and 100% (the entire population at the highest-risk exposure level). In other words, the SEV combines the frequency and severity of a risk exposure in a population, comparing it to an ideal scenario and representing the overall magnitude of exposure at the population level [30]. The SPR of SEV to different risk factors was then calculated as the ratio of SEV in women to men for each risk factor. The significance level for p-values was set at 0.05. All statistical analyses and data illustrations were done using R version 4.2.

Results

Sex disparity in prevalence & incidence of IHD

In 2021, an estimated 254 million people were living with ischemic heart disease globally, of which approximately 57% were males (145 million people), and the remaining 43% were females (109 million people). The global ASPR of IHD was 3610.2 cases (95% CI: 3153.1–4165) per 100,000 people for males in 2021, with a change of -2.1% (95% CI: -5.9-2.2) since 1990. In contrast, the 2021 global ASPR of IHD was 2357.6 (95% CI: 2063.3-2751.9) per 100,000 people for females, which increased by 4.8% (95% CI: 0.6–9.8) compared to 1990. Altogether, these figures led to an increase in the global SPR for ASPR from 0.610 in 1990 to 0.653 in 2021. All related data are available in Supplementary Tables 1 and 2.

Regarding incidence, globally, 32 million cases of ischemic heart disease were reported in 2021. As shown in Figs. 1 and Supplementary Fig. 1, the ASIR were 450.4 cases (95% CI: 373.7-534.6) per 100,000 people for males and 301.6 (95% CI: 248.6-360.7) per 100,000 people for females in 2021, indicating a decreasing trend in both males and females by 13.7% (95% CI: 12.1–15.4) and 8.5% (95% CI: 6.6–10.6), respectively, since 1990. According to these ASIRs of IHD, the SPR for the ASIR rose from 0.631 in 1990 to 0.670 in 2021.

Sex disparity in the global burden of IHD

At the global level, ischemic heart disease accounted for total DALYs of 188 million in 2021, divided into 115 million years for males and 73 million years for females. The ASDR of IHD for males was 2890.7 (95% CI: 2714.8-3091.3) per 100,000, while it was significantly lower for women, with an ASDR of 1596.1 (1464-1706.9) per 100,000. Compared to 1990, these statistics indicated an obvious decrease in DALY rates in both sexes, by 25.4% (95% CI: 19.9–30.3) in men and 33.7% (95% CI: 29.2–38.1) in women (Supplementary Table 2).

In both males and females, the age-standardized YLL rates accounted for almost all ASDR in 2021, with the age-standardized YLL rate of 2831.8 (95% CI: 2661.0-3023.5) per 100,000 in men and 1559 (95% CI: 1431.2-1668.5) per 100,000 in women. These rates indicate a significant decrease in YLL rates in both sexes, by 34.2% (95% CI: 29.6–38.6) in females and 25.8% (95% CI: 20.2–30.7) in males. As a result, the SPR fell greatly from 0.621 in 1990 to 0.551 in 2021. In addition, the 2021 age-standardized YLD rates remained almost constant for both sexes compared to 1990, with 58.8 (95% CI: 38.3–81.4) per 100,000 in females and 58.8 (95% CI: 38.3–81.4) per 100,000 in males. Correspondingly, the SPR for age-standardized YLD rate didn't change significantly during these years, from 0.645 in 1990 to 0.631 in 2021.

Altogether, it can be seen that the SPR for the ASDR rate decreased considerably from 0.621 in 1990 to 0.552 in 2021, reflecting a reduction in the global burden of IHD for women, mostly attributable to a pronounced decrease in YLL. More details can be seen in Supplementary Table 2.

Sex disparity in burden of IHD by age groups

As shown in Fig. 2, from 1990 to 2021, SPRs for the ASPR and ASIR of IHD increased across all age groups, but the SPRs for ASMR and ASDR of IHD declined. During this period, the age groups of adults 70 + years continuously had the highest SPRs, remaining at the top from 1990 to 2021. Also, it can be seen that the SPR for ASDR and ASMR in this age group had the highest decrease between 1990 and 2021. This suggests that while improvements have occurred across all age groups, the disparity among older people has diminished more over time.

Sex disparity in burden of IHD by regions

According to Fig. 3, among the regions of this study, a decrease of the SPR for the ASMR of IHD was observed in most of the regions, except for five of them, including

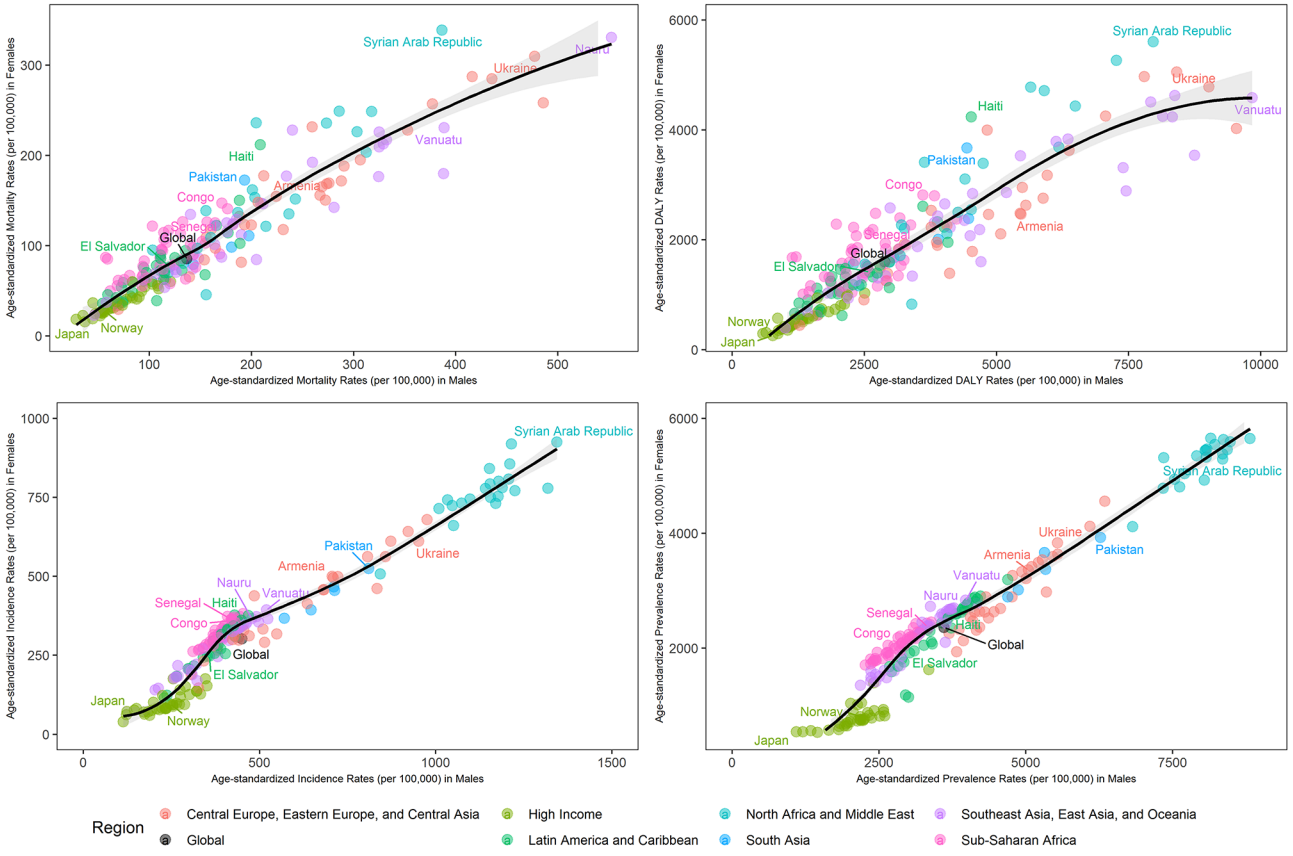

Fig. 1 Comparative analysis of age-standardized mortality, DALY, incidence, and prevalence rates of ischemic heart disease in males and females by region (2021)

Southern sub-Saharan Africa, Central Europe, and Central Asia, with an increase of 0.054, 0.029 and 0.015, respectively. In contrast to these regions, the SPR in Western sub-Saharan Africa declined significantly, from 1.032 in 1990 to 0.855 in 2021. However, the SPR peaked in this region in 2021 compared to the others. Furthermore, this downward trend in the SPR of ASMR was highest in East Asia (from 0.774 to 0.587) and Central Latin America (from 0.812 to 0.634) from 1990 to 2021 (Supplementary Table 2).

Additionally, the SPR for the ASDR of IHD exhibited a downward trend in almost all GBD regions since 1990, with the exception of three regions: Southern sub-Saharan Africa (from 0.539 to 0.581), Central Asia (from 0.541 to 0.577), and Central Europe (from 0.472 to 0.488). On the other hand, the parity ratio for the ASDR diminished greatly in East Asia (from 0.758 to 0.547), Western sub-Saharan Africa (from 0.952 to 0.790), and Southeast Asia (from 0.728 to 0.567). These results indicate that the burden of IHD for women has declined in most regions of the world compared to 1990. Detailed statistics are provided in Supplementary Table 2.

Sex disparity in burden of IHD by SDI super-regions

In 2021, according to Fig. 4, the SPRs for the ASDR of IHD have decreased in all SDI groups compared to 1990. However, this trend was more pronounced in the low-middle SDI super-region, where the SPR decreased from 0.752 to 0.593. Similarly, low- and middle-income SDI countries also exhibited a significant decrease in the SPR for the ASDR since 1990, by 0.141 and 0.126, respectively. Conversely, the SPRs for the ASDR were relatively constant between 1990 and 2021 in high and high-middle SDI countries and decreased slightly by 0.038 and 0.036, respectively (Supplementary Table 2).

On the other hand, the SPR for ASMR of IHD has also decreased across all SDI super-regions. The low-middle and low SDI countries marked the most substantial declines of 0.184 and 0.159, respectively, while the SPR for the ASMR persisted roughly the same in high SDI and high-middle SDI groups, with the SPR dropping from 0.559 to 0.508 in high SDI countries and from 0.731 to 0.679 in high-middle SDI countries (Supplementary Table 2).

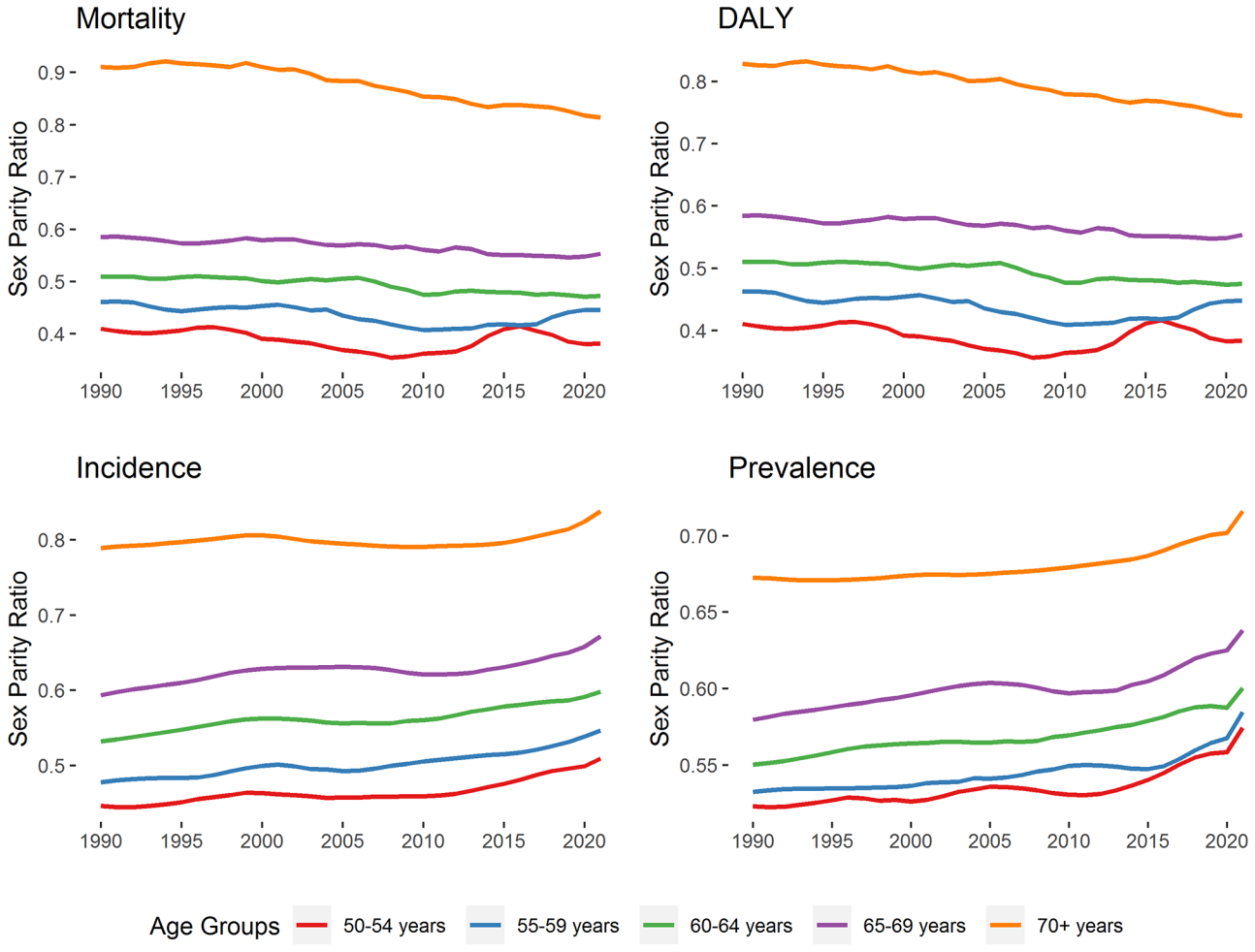

Fig. 2 Sex parity ratios (SPRs) for the global burden of ischemic heart disease (IHD) from 1990 to 2021. The figure illustrates SPRs for mortality, disability-adjusted life years (DALYs), incidence, and prevalence across various age groups. SPRs for IHD prevalence and incidence increased across all age groups, while SPRs for IHD-related mortality and DALYs decreased, indicating diminishing sex disparity. The most pronounced changes in mortality and DALY SPRs occurred in adults over 70 years old

Sex disparity in the burden of IHD by countries

As demonstrated in Figs. 1 and Supplementary Fig. 1, the SPR of age-standardized rates ranged widely across different countries in both 1990 and 2021. At the national level, Afghanistan saw the highest, and Yemen saw the lowest SPR for the ASDR of ischemic heart disease in 2021, with an SPR of 3.056 and 0.243, respectively (Fig. 5). Since 1990, the largest increase in the SPR for the ASDR of IHD has also occurred in Afghanistan, with an increase of 2.284, while the largest decrease is observed in Zimbabwe, with a decrease of 0.436, from 1.297 in 1990 to 0.861 in 2021 (Fig. 6).

The SPR for the ASMR of IHD varied greatly in different countries. Nationally, Afghanistan had the highest SPR for the ASMR of IHD in 2021, with an SPR of 3.630. Conversely, Yemen exhibited the lowest SPR of 0.291. Interestingly, Afghanistan also witnessed the greatest increase in SPR since 1990, with a difference of 2.813, while the United Kingdom experienced the largest decline, from 1.034 in 1990 to 0.510 in 2021. The sex parity in the burden of IHD worldwide is illustrated in more detail in Figs. 5 and 6.

Sex disparity in exposure to risk factors

Generally, the SPR for exposure to different risk factors ranged substantially. As shown in Figs. 7 and Supplementary Fig. 2, among all of the exposures evaluated in this study worldwide, women faced much higher exposure to low physical activity than men in both 1990 and 2021. The SPR for low physical activity was 1.514 in 1990, and alarmingly, it increased further to 1.568 by 2021. This upward trend in the SPR suggests that, compared to 1990, women in 2021 faced an even greater relative risk of exposure to low physical activity. On the opposite end, smoking exhibited the lowest SPR among the estimated exposures, both in 1990 and 2021. Furthermore, the SPR for smoking declined from 0.267 in 1990 to 0.214 in 2021.

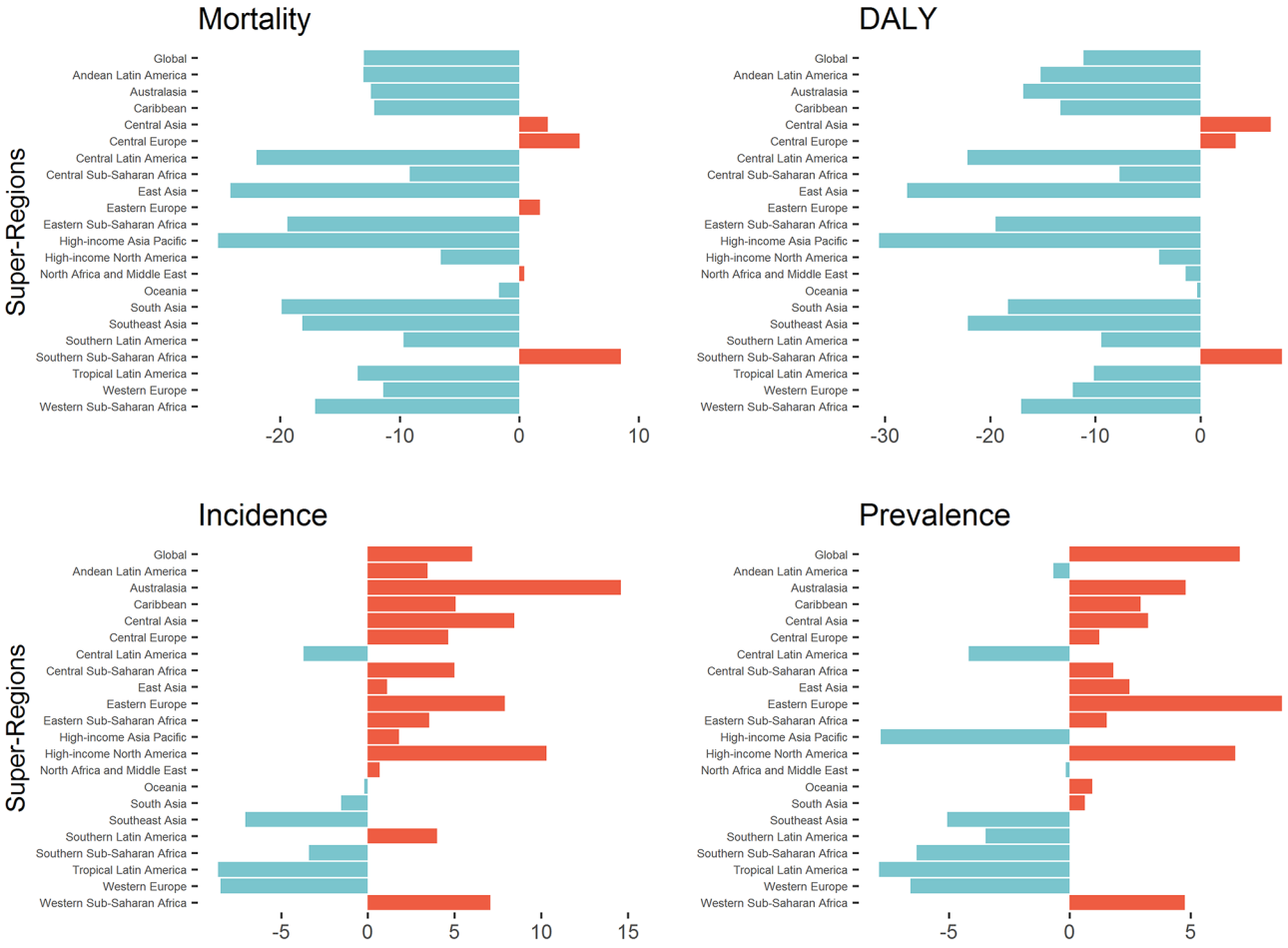

Fig. 3 The percentage of change in Sex parity ratios (SPR) for mortality, disability-adjusted life years (DALY), incidence, and prevalence of IHD by super-region from 1990 to 2021. Red bars indicate the increased percentage of SPRs from 1990 to 2021, while blue bars indicate the diminished SPRs. The overall mortality and DALY SPRs decreased, with the most significant decrease observed in the High-income Asia Pacific region. In contrast, the overall SPRs for incidence and prevalence increased, with the most substantial increases noted in Australia and Eastern Europe, respectively. In addition, the prevalence and incidence of IHD show more varied SPRs across different regions

This decrease indicates that women in 2021 faced a relatively lower risk of being exposed to smoking compared to 1990. Additionally, from 1990 to 2021, diets low in seafood omega-3 fatty acids and secondhand smoking were the exposures that experienced the largest increases and decreases in the sex parity ratio, with changes of + 0.122 and − 0.177, respectively. The SPR for high systolic blood pressure and high body-mass index decreased from 0.907 to 1.154 to 0.845 and 1.118, respectively. On the other hand, the SPR of high LDL cholesterol and high fasting plasma glucose has increased from 1.064 to 1.068 and from 0.864 to 0.906, respectively. The global and regional sex disparities in exposure to IHD risk factors in 2021 are presented in Supplementary Table 3.

Discussion

Based on the GBD 1990 and 2021 data, this study provides an in-depth analysis of the sex differences in the global and regional burden of IHD. Given the significant impact of IHD on human health, policymakers can gain valuable insights by analyzing the sex disparities in the IHD burden. These analyses will help formulate effective health policies and distribute resources efficiently. Furthermore, by analyzing data for various age groups and from several SDI regions, we can observe the varied patterns and features of the global IHD burden (Figs. 3 and 4). The findings from this study highlight significant trends and sex disparities in the burden of IHD globally and across various demographics and regions from 1990 to 2021. These results underscore the evolving nature of IHD as a public health challenge and the necessity of targeted interventions to address sex disparities and regional variations.

There are significant differences in the global and regional burden of IHD between men and women. Consistent with previous studies, our study indicated that the IHD burden in men was significantly greater than in women [32, 33]. Men may bear a higher disease burden

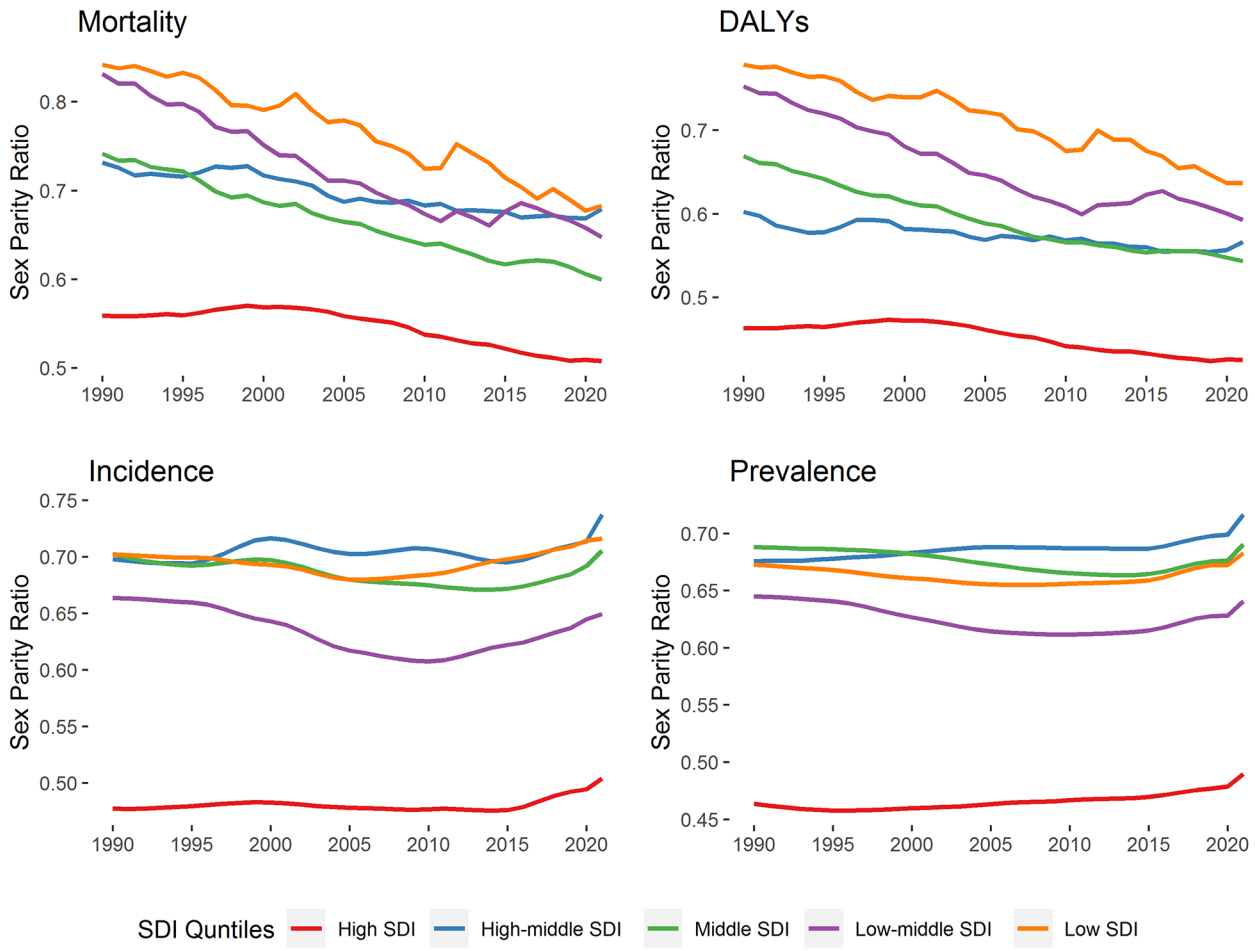

Fig. 4 Trends in sex parity ratios for ischemic heart disease by socio-demographic index (SDI) from 1990 to 2021. This figure illustrates the changes in sex parity ratios (SPRs) for mortality, disability-adjusted life years (DALYs), incidence, and prevalence of IHD across five SDI quintiles. The data shows a significant decrease in SPRs in mortality and DALYs, particularly in lower SDI regions, while disparities in incidence and prevalence have remained more stable across all regions. Notably, the most substantial declines in sex disparity for mortality and DALYs occurred in low-middle and low-SDI countries, while high and high-middle SDI countries showed minimal changes

from IHD due to greater exposure to most major risk factors, including elevated rates of high systolic blood pressure and high fasting plasma glucose, along with unhealthy habits such as cigarette smoking, excessive alcohol consumption, staying up late, and a diet high in fat. Additionally, men are more likely than women to delay seeking medical help for health issues [34].

One of the primary risk factors for CVDs with the lowest SPR of SEV is smoking, indicating that males usually make up the majority of tobacco users [35]. In 2019, there were 1.14 billion smokers worldwide. The ASPR of tobacco smoking among individuals aged 15 and older was 32.7% for males and 6.62% for females. Despite a notable decrease in smoking rates since 1990 (27.5% among males and 37.7% among females aged 15 and older), population growth has contributed to an increase in the total number of smokers, rising from 0.99 billion in 1990 to 1.14 billion in 2019. Data from the GBD indicate that from 1990 to 2019, the prevalence of male tobacco use declined significantly in 135 countries (66%), while among females, it decreased substantially in only 68 countries (33%) [36]. Men are substantially more likely to smoke in low- and middle-income nations where regions lack the resources necessary to control tobacco use effectively [37, 38].

Furthermore, global CVD mortality linked to smoking has increased from 1,781,364 in 1990 to 2,247,325 in 2021, representing a 26.16% rise. However, the ASMR decreased from 46.47 per 100,000 in 1990 to 26.29 per 100,000 in 2021. During this period, the incidence of smoking-related CVD remained consistently higher among men. Moreover, the decline in disease burden has advanced more slowly for men than for women, with an estimated annual percentage change in ASMR of -1.78 for men compared to -3.25 for women [39]. Our result demonstrated that while men have much more exposure

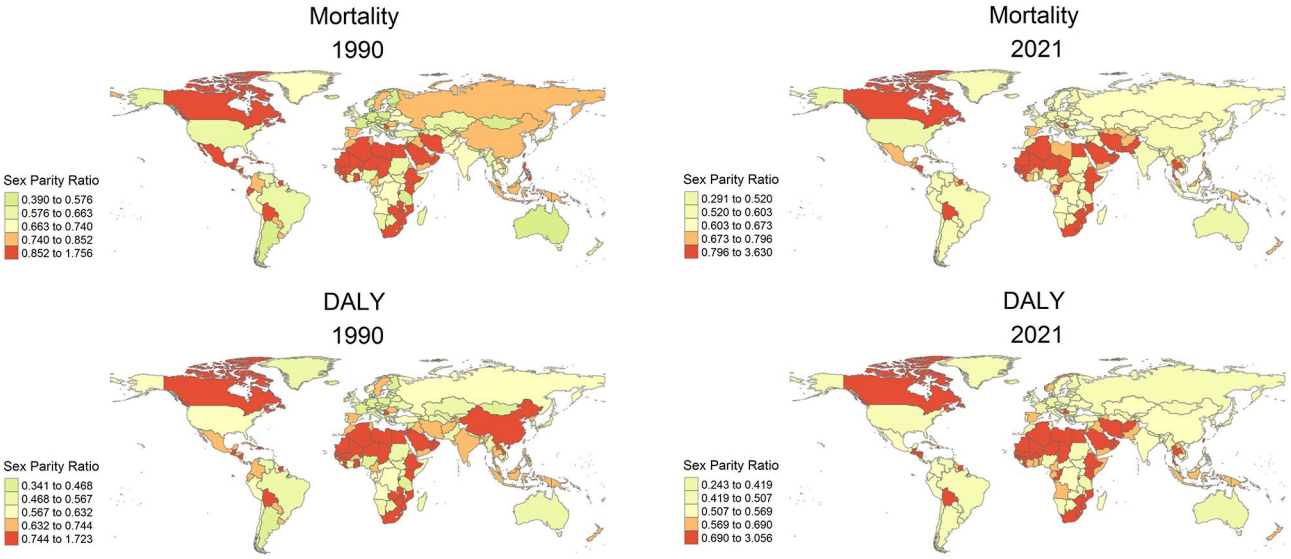

Fig. 5 Geographical distribution of sex parity ratios (SPR) for IHD in 1990 and 2021 for Age-standardized mortality rate and Age-standardized DALY rate

to smoking, the exposure of women to secondhand smoke is higher compared to men. However, the SPR of exposure to smoking and being a secondhand smoker has decreased from 1990 to 2021. These trends can also explain a portion of the observed results regarding the decrease in the SPR of IHD's burden, as well as the higher burden among males in low-SDI and low-middle SDI regions.

According to the GBD 2019 report, global trends in CVD deaths and DALYs related to poor physical activity showed a steady rise in these patterns for both sexes, with females outnumbering males. In contrast, a steady decline in ASMR and ASDR was observed in both sexes. The number of deaths and DALYs attributed to low physical activity was higher in males compared to females before the age group of 70–74. However, this trend changed, with females subsequently experiencing higher rates than males [40]. The estimated annual percentage change of -1.44 indicates that the associated ASMR has shown a downward trend, decreasing from 12.55 in 1990 to 8.6 in 2019. Similarly, the ASDR has an estimated annual percentage change of -1.3 and declined from 181.64 to 127. Before reaching the 75–79 age group, females had slightly higher rates than males, with minimal differences between the two up to the 85–89 age group. However, beyond this range, females exhibited significantly higher rates than males. Furthermore, both male and female ASDRs consistently increased with age, particularly showing a notable rise after the 75–79 age group [40].

Although our findings aligns with the previous reports regarding the decrease in ASMR and ASPR due to IHD, previous studies have only addressed the DALY and Mortality attributed to risk factors such as low physical activity in IHD, but have failed to address the change in sex differences of risk factors, regardless of their attributed burden. While previous studies have demonstrated that the ASDR and ASMR attributed to low physical activity have decreased with similar trends in both sexes, we found that women are experiencing more sex differences regarding exposure to low physical activity compared to 1990, indicating the increasing gap between women and men in terms of physical activity.

On the other hand, women face sex-specific risk factors. Traditional risk factors for CVD include hypertension, obesity, diabetes mellitus, and metabolic syndrome, all of which are recognized as inflammatory conditions [41]. Women are disproportionately affected by these conditions, with noticeable sex differences emerging from adolescence. Hormonal fluctuations associated with reproductive events such as menarche, pregnancy, and menopause are believed to contribute to a pro-inflammatory state in females. Furthermore, women experiencing inflammatory conditions like polycystic ovarian syndrome (PCOS), gestational diabetes, or pre-eclampsia demonstrate a cardiometabolic phenotype that heightens their risk of myocardial infarction, stroke, and coronary heart disease [42]. Generally, women who do not have significant CVD risk factors experience a certain degree of cardiovascular protection before menopause. However, after the decline of estrogen's protective effects, women face a greater risk of major cardiovascular events compared to men [43].

Across all age groups, the SPR for IHD prevalence increased from 1990 to 2021, with adults aged 70 + years consistently showing the highest disparities. Sex differences in CVD tend to diminish with advancing age due to hormonal fluctuations and the progression of

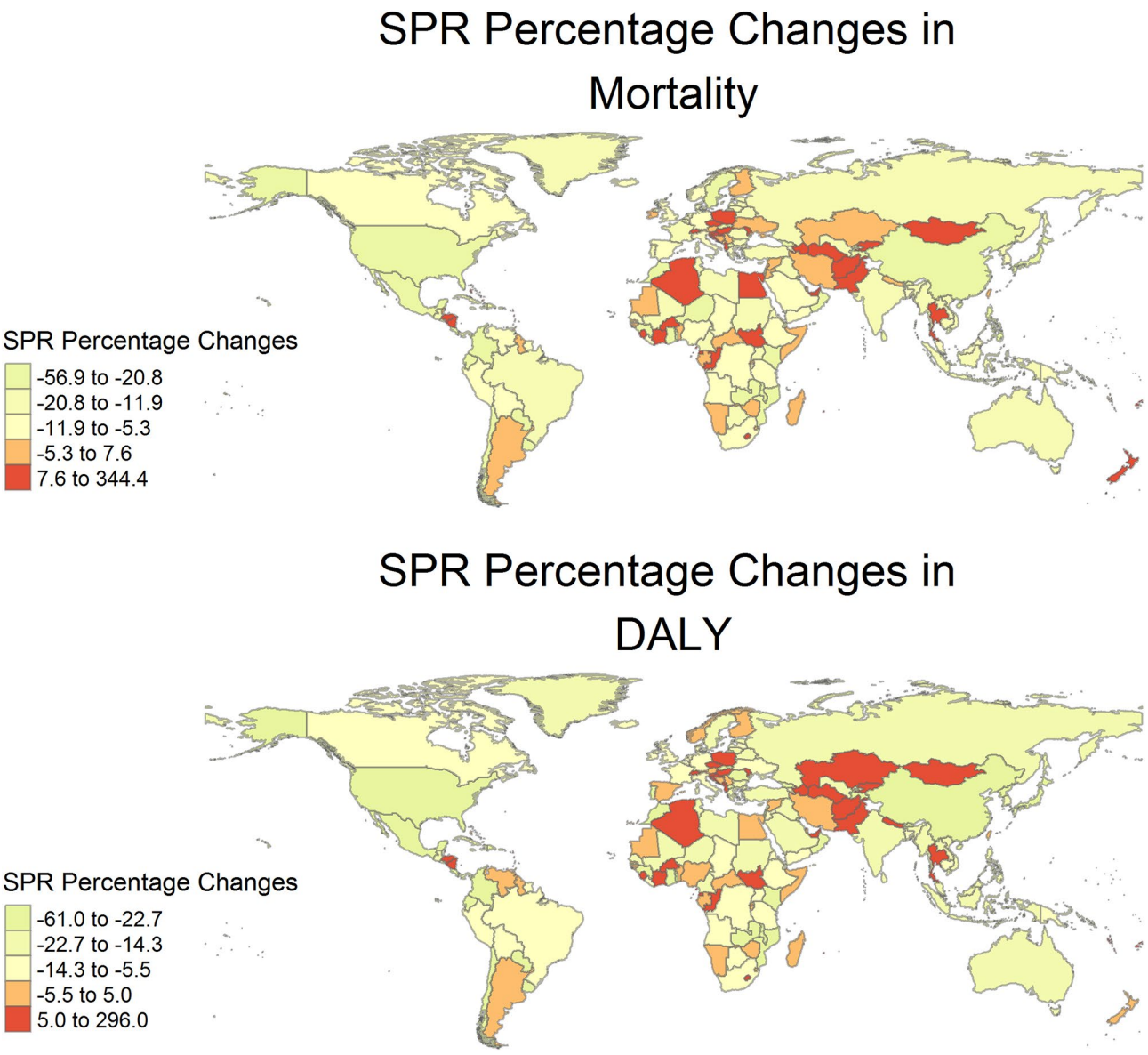

Fig. 6 Geographical distribution of percentage changes in sex parity ratios (SPRs) for Age-standardized mortality rate and Age-standardized DALY rate due to IHD from 1990 to 2021

cardiovascular aging mechanisms. Premenopausal women benefit from estrogen, which exhibits vasodilatory properties and influences the excretion of nitric oxide, thereby promoting cardiovascular health. Following menopause, the reduction in estrogen levels is linked to increased arterial stiffness and a heightened risk of CVD in women, subsequently narrowing the risk disparity between genders [44–46]. Aging induces significant changes in cardiac structure and function, as evidenced by increased myocardial stiffness and left ventricular remodeling. These changes are observed in both genders; however, they tend to be more pronounced in women after menopause. This discrepancy may be due to differences in β-adrenergic receptor signaling and mineralocorticoid receptor expression, suggesting that these biological pathways provide greater protective benefits in premenopausal women [15, 47]. The lowest SPR was observed in the 50–54 age group, remaining relatively stable over the period. These findings highlight the importance of age-specific strategies in addressing IHD, particularly in older populations.

Globally, the estimated prevalence of IHD has shown subtle changes over the decades. In 2021, the ASPR of IHD was higher for males than for females. However, while the ASPR for males has decreased slightly since 1990, the ASPR for females increased by 4.8%. This divergence resulted in an increased SPR from 0.610 in 1990 to 0.653 in 2021, indicating a relative rise in IHD prevalence

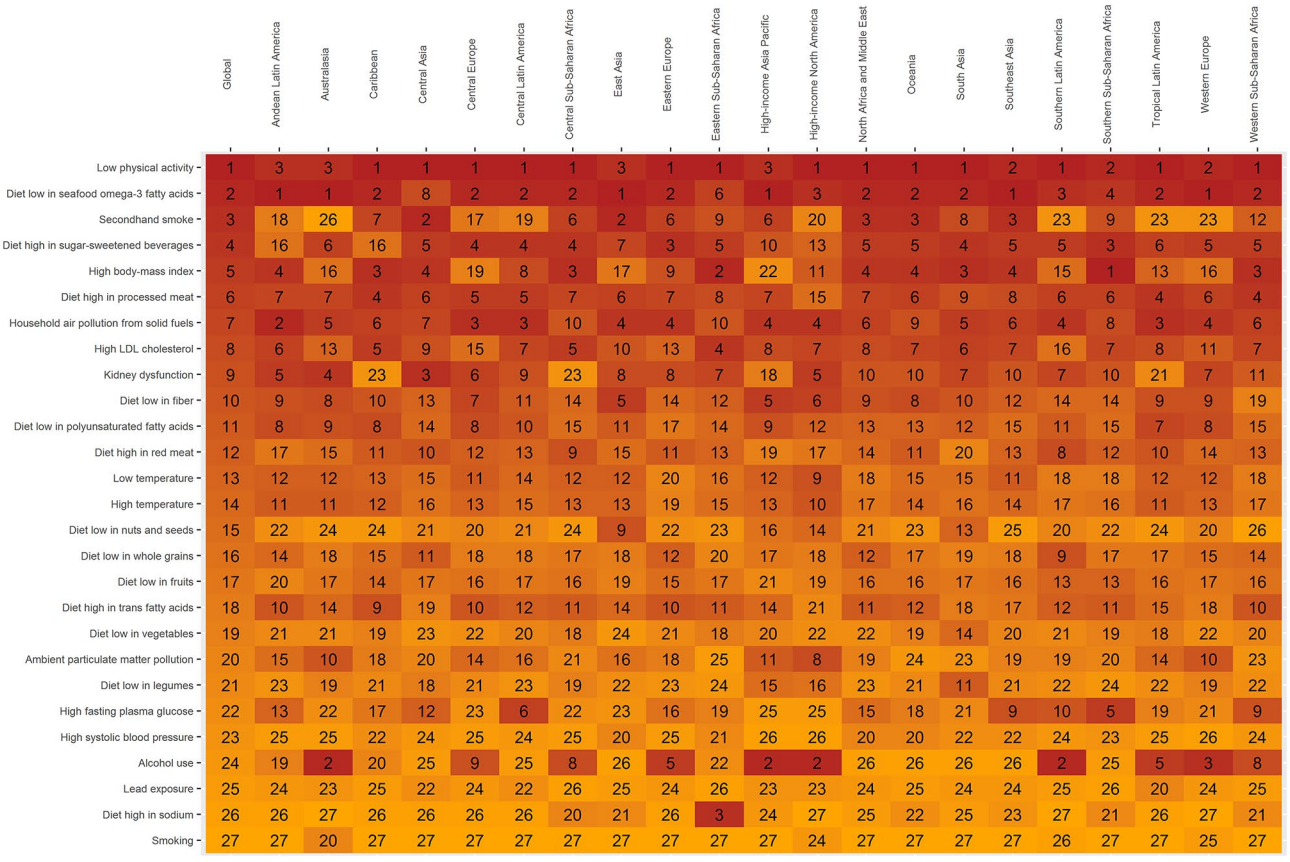

Fig. 7 The global and regional sex disparity in exposure to IHD risk factors in 2021. The lowest numbers indicate risk factors with the highest SPR, while higher numbers indicate risk factors with the lowest SPR

among women compared to men. Additionally, the SPR for the ASPR of IHD showed substantial regional differences. East Asia and Southern sub-Saharan Africa had the highest SPRs in 1990 and retained this position in 2021, indicating persistent sex disparities. Conversely, regions such as Southern Latin America and Western Europe had the lowest SPRs, which continued to decrease over time. The most significant increases in SPR were observed in Eastern Europe and Western sub-Saharan Africa, indicating a rise in sex-specific vulnerabilities in these regions. In contrast, regions such as Southern sub-Saharan Africa and High-income Asia Pacific experienced notable declines in SPR, pointing towards more equitable healthcare improvements or effective public health interventions targeting women.

The SPR for the ASPR of IHD increased in all SDI super-regions, except in low-middle SDI countries, which may be attributed to the underdiagnosis of women due to disparities in access to healthcare and undeveloped screening programs for IHD. The middle SDI super-region, which had the highest SPR in 1990, was surpassed by the high-middle SDI super-region in 2021. This shift highlights the importance of focusing on middle-income countries, where economic transitions may be affecting health outcomes differently across sexes. The high SDI group maintained the lowest SPR, reflecting better healthcare access and preventive measures for women in high-income countries.

The incidence of IHD showed a decreasing trend globally, with ASIR falling for both males and females. The ASIR for males and females decreased by 13.7% and 8.5%, respectively, since 1990. Despite these reductions, the SPR for ASIR increased from 0.631 to 0.670, indicating a slower decline in new IHD cases among women. The mortality rate for IHD also decreased significantly for both sexes, but while the incidence of IHD decreased more significantly in men than in women, the SPR for mortality decreased from 0.717 in 1990 to 0.624 in 2021. The total DALYs due to IHD decreased for both sexes from 1990 to 2021, with a more pronounced reduction in women (33.7%) compared to men (25.4%), leading to a decrease in the SPR for DALYs.

The increase in the SPR of ASIR, coupled with a decrease in the SPR of ASMR and ASDR, can be attributed to several factors. The smaller decrease in ASIR for women may be partly due to improved diagnosis of IHD in this group. Recent advancements in diagnostic technologies, such as coronary imaging and the use of

biomarkers, have facilitated the earlier and more precise identification of IHD in women [10]. Consequently, there has been a notable increase in the number of women diagnosed with IHD, which accounts for the observed rise in incidence rates—despite concurrent improvements in actual health outcomes. Moreover, the higher mortality rate among men, despite a larger reduction in incidence, suggests potential differences in disease severity and treatment adherence.

On the other hand, women with a history of diabetes, smoking, or hypertension exhibit a significantly elevated relative risk for CVD when compared to their male counterparts with identical risk factors. Notably, in the context of diabetes, although the prevalence of the condition is higher among men, studies indicate that diabetes increases cardiovascular risk by approximately three to seven times in women, compared to a two to three times increase observed in men [48, 49]. It is also evident that with the exception of women aged 30 to 44 years, female smokers face a 25% heightened risk of CVD in comparison to their male counterparts [50]. Additionally, the use of oral contraceptives further exacerbates the risk of CVD in women who engage in smoking behaviors [51]. Therefore, it can be assumed that modifying risk factors in women may have a more pronounced effect than in men. Additionally, medications like angiotensin-converting enzyme inhibitors and statins show slightly more significant improvements in cardiovascular outcomes for women than for men [52, 53]. The high proportion of YLL in the DALY rates highlights the fatal nature of IHD, while the relatively constant SPR for years lived with disability (YLD) indicates ongoing challenges in reducing the non-fatal impact of IHD on women.

Significant national variations in the SPR of ASMR for IHD were observed. Afghanistan had the highest SPR in 2021 (3.630), suggesting severe sex disparities in the IHD burden. Conversely, Yemen had the lowest SPR (0.291), indicating more equitable health outcomes. Countries like Afghanistan and the United Kingdom saw the most substantial changes in SPR, with Afghanistan experiencing the greatest increase (+2.813) and the United Kingdom the largest decrease (-0.525). These differences reflect the varied success of national health policies and interventions in addressing sex disparities in IHD.

Despite recent advances in managing IHD, significant sex-related challenges remain to be addressed. Multiple studies indicate that women are less frequently prescribed medications that provide cardiovascular protection compared to men. This trend is evident in both primary and secondary prevention contexts [54, 55]. Various factors may clarify this gap: women, typically smaller, tend to exhibit higher blood concentrations of medications, which can result in more pronounced side effects. Furthermore, numerous studies on drug effectiveness have historically focused on males, and factors like lower socioeconomic status among women could affect prescription practice patterns. The infrequent prescription of cardiovascular preventive medications for women leads to reduced success in controlling risk factors, ultimately hindering optimal cardiovascular outcomes for this population [56–58].

These results highlight the evolving nature of IHD as a public health challenge and the need for targeted interventions to address sex disparities and regional variations. Therefore, it is important to develop distinct IHD prevention programs tailored to specific SDI regions for each sex. Consequently, based on our findings, we recommend initiatives such as implementing smoking cessation programs targeted at male populations in low-SDI regions, enhancing cardiovascular screening and diagnostic accuracy for women in high-SDI areas, and addressing the changing risk factor profiles that emerge from economic transitions in middle-SDI countries. Furthermore, Public health initiatives should promote active lifestyles among women.

Limitations

This study holds significance as it can help countries design customized policies and initiatives that prioritize primary preventive efforts for IHD. Nonetheless, it is important to recognize that our study has several limitations. We were unable to pinpoint the precise contributions of some key IHD subtypes, such as heart failure, chronic stable angina, acute MI, and chronic IHD, to the total death burden. The GBD data itself may have biases and limitations regarding countries and data accessibility. On the other hand, although the SPR offers a clear numerical value that represents the disparity between sexes across various health metrics, allowing for standardized comparisons between different populations or regions, it also has limitations. The SPR alone does not reflect the absolute magnitude of the disease burden, which can lead to misrepresentation in cases where sex-specific absolute numbers may still be significantly high or low, despite similar ratios. Factors affecting both genders equally, such as improvements in healthcare infrastructure, may not be captured by the SPR, potentially resulting in misinterpretation or underestimation of the progress made. Additionally, SPR may not be the ideal variable to assess sex differences, as it can be influenced by both worsening numbers for women and improving numbers for men. Thus, applying this variable in practice might be challenging. Notwithstanding this drawback, our study remains useful for guiding the development of a more targeted health policy and the allocation of resources.

Conclusion

The study findings emphasize significant trends and gender disparities in the global burden of IHD across demographics and regions from 1990 to 2021. They highlight the critical need for targeted public health interventions to address sex and regional disparities in IHD. Strategies should include improving awareness and diagnostic practices for women, addressing lifestyle and risk factors, and ensuring equitable access to preventive and therapeutic healthcare services. The rising prevalence and incidence rates among women in certain regions necessitate enhanced public health efforts tailored to female populations. Additionally, localized strategies are crucial for effectively addressing IHD, given the significant regional differences in SPRs. Overall, while progress has been made in reducing the burden of IHD, the increasing sex disparities in certain regions and age groups emphasize the need for continuous monitoring, adaptive health policies, and sex-specific healthcare practices to ensure equitable health outcomes for all populations.

Abbreviations

CVD	Cardiovascular diseases
IHD	Ischemic heart disease
YLL	Years of lost life
YLD	Years lived with disability
MI	Myocardial infarction
GBD	Global Burden of Diseases
DALY	Disability-adjusted life year
SDI	Sociodemographic index
SPR	Sex Parity Ratio
ASRs	Age-standardized rates
ASMRs	Age-standardized mortality rates
ASDRs	Age-standardized DALY rates
ASPR	Age-standardized prevalence rate
EAPC	Estimated annual percentage change
APC	Annual percent change
SEV	Summary exposure value
ASIR	Age-standardized incidence rates

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions

M.M., R.N-J., K.H., K.B., K.I., and H.S. have contributed to designing the study, data analysis, and drafting the manuscript. R.E., A.A., A.H., R.T., H.M., A.W., and W.A. have contributed to the conception and critical revising of the manuscript. All authors read and approved the final manuscript.

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Data availability

The data underlying this article is available from the Global Health Data Exchange (https://ghdx.healthdata.org/record/ihme-data/cvd-1990-2021).

Declarations

Ethics approval and consent to participate

The study was carried out in the public domain secondary database without any nominal identity. Hence, the ethical approval was exempted.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

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