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ORIGINAL ARTICLE

Sex differences in the etiology and burden of heart failure across country income level: analysis of 204 countries and territories 1990–2019

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Background Heart failure (HF) is a global epidemic.

Objective To assess global sex differences in HF epidemiology across country income levels.

Methods and results Using Global Burden of Disease (GBD) data from 204 countries and territories 1990–2019, we assessed sex differences in HF prevalence, etiology, morbidity, and temporal trends across country sociodemographic index or gross national income. We derived age-standardized rates. Of 56.2 million (95% uncertainty interval [UI] 46.4–67.8 million) people with HF in 2019, 50.3% were females and 69.2% lived in low- and middle-income countries; age-standardized prevalence was greater in males and in high-income countries. Ischaemic and hypertensive heart disease were top causes of HF in males and females, respectively. There were 5.1 million (95% UI 3.3–7.3 million) years lived with disability, distributed equally between sexes. Between 1990 and 2019, there was an increase in HF cases, but a decrease in age-standardized rates per 100 000 in males (9.1%, from 864.2 to 785.7) and females (5.8%, from 686.0 to 646.1). High-income regions experienced a 16.0% decrease in age-standardized rates (from 877.5 to 736.8), while low-income regions experienced a 3.9% increase (from 612.1 to 636.0), largely consistent across sexes. There was a temporal increase in age-standardized HF from hypertensive, rheumatic, and calcific aortic valvular heart disease, and a decrease from ischaemic heart disease, with regional and sex differences.

Conclusion Age-standardized HF rates have decreased over time, with larger decreases in males than females; and with large decreases in high-income and small increases in low-income regions. Sex and regional differences offer targets for intervention.

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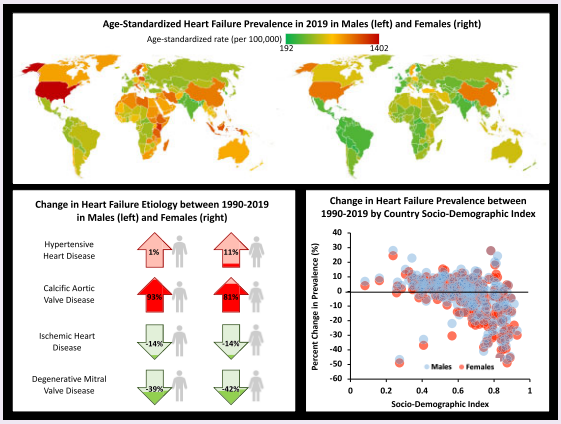
Graphical Abstract



Keywords Epidemiology • Male • Female • Global Burden of Disease • Morbidity

Introduction

Recent estimates from the 2019 Global Burden of Disease (GBD) study indicate that ∼56 million individuals worldwide live with heart failure (HF), a diagnosis that is a leading cause of disability and death.[1] The capacity for healthcare systems to improve outcomes in HF is contingent on evidence-based interventions that address the underlying causes and burden of HF in both males and females.

Socio-biological differences in risk factor profiles contribute to sex differences in the etiology and clinical outcomes of HF.[2] While traditional cardiovascular risk factors are present in both sexes, smoking, with its strong associations with ischaemic heart disease in younger people, is more prevalent in males worldwide.[3] Sex plays a role in the regulation of blood pressure and in the risk for end-organ damage associated with hypertension as well as diabetes.[2,4] There are also several non-traditional risk factors unique to females including gestational diabetes and pre-eclampsia or eclampsia.[2,5]

Access to primary and secondary HF treatments, quality of life, and mortality vary between the sexes, and country socioeconomic deprivation may have a differential impact in females more than males.[2,6,7] Knowledge to date is based primarily on studies in high-income countries with little reported about sex differences across the world. A global survey-based study, which examined the incidence and mortality of cardiovascular disease in young adults (mean age 51 years) across 27 countries, found that females in the cohort had a lower burden of traditional risk factors measured by established cardiovascular risk scores. While the incidence of a composite of cardiovascular events was reported, the relative contribution of risk factors to HF in both sexes was not reported.[8] Previous analyses of the GBD dataset have examined the prevalence of HF across regions,[9,10] but have not assessed the burden of HF disaggregated by sex, age, geographic region, and country income or development.

In this study, we aimed to examine sex differences in the etiology and burden of HF across country income and development categories using GBD data from 204 countries and territories between 1990 and 2019. We assessed the sex-specific prevalence and etiology of HF across age categories and geographic regions in 2019, and assessed temporal trends between 1990 and 2019 accounting for country income or socio-demographic index (SDI). Using morbidity and mortality measures of years lived with disability (YLD), years of life lost (YLL), and disability-adjusted life years (DALY), we examined sex differences in the relative contribution of HF to the overall morbidity and mortality associated with the underlying cardiovascular etiologies.

Methods

Data source

Data were extracted from the publicly available Global Health Data Exchange maintained by the Institute of Health Metrics and Evaluation.[11] Collaborators worldwide contribute to the collection of sex and age-stratified data in a standardized approach at regional and national levels. These data are used to produce estimates of epidemiological metrics. The collection and handling of GBD data have been reported by GBD investigators to adhere to GATHER guidelines.[1] Twenty-two diseases were etiologically linked to the development of HF. Our search parameters included International Classification of Diseases 10 term 'heart failure' and 'impairment' pertaining to causes of HF in adults worldwide between 1990 and 2019 (the most recent data available).[11] Data were included from 204 countries and territories, grouped into 21 geographical regions (Supplementary material online, *Table S1*). Estimates for prevalence, YLD, YLL, and DALY were extracted in absolute number, rate, and percentage by country or territory, age, and sex. Age-standardized rates were used to compare rates across populations with varying age distributions; these represented the weighted average of age-specific rates, where weights were proportions derived from a standard population.[1]

The 22 HF etiologies were grouped into eight general categories (Supplementary material online, *Table S2*): (i) Ischaemic heart disease, (ii) hypertensive heart disease, (iii) chronic respiratory disease (including chronic obstructive pulmonary disease, interstitial lung disease and pulmonary sarcoidosis, asbestosis, coal workers pneumoconiosis, and other pneumoconiosis), (iv) non-ischaemic cardiomyopathy and endomyocarditis (including alcoholic and other cardiomyopathy, endocarditis, and myocarditis), (v) rheumatic heart disease, (vi) non-rheumatic valvular disease (including non-rheumatic degenerative mitral valve disease, non-rheumatic calcific aortic valve disease, and other non-rheumatic valve disease), (vii) congenital heart disease, and (viii) other (including all remaining etiologies). The category of chronic respiratory diseases was excluded from analysis, given that it is largely applicable to right-sided HF; the remaining 16 causes were carried forward for analysis.

Years lived with disability were calculated as the product of prevalence and disability weight of HF at four severity levels[12]: treated, mild, moderate, and severe; disability weights ranged from 0 (full health) to 1 (death). Mild HF was described as HF with breathlessness and fatigue upon moderate physical activity, with no rest symptoms (disability weight

0.041). Moderate HF was HF with breathlessness and fatigue upon minimal physical activity, with no rest symptoms (disability weight 0.072). Severe HF was HF with rest symptoms and avoidance of any physical activity for fear of worsening breathlessness (disability weight 0.179). Treated HF was described as a chronic disease that required medication daily and caused worry but was associated with minimal interference with daily activities (disability weight 0.049).

The burden of HF was further assessed by examining the relative contribution of HF to the overall morbidity of its parent condition. As HF was defined in the GBD as a state of impairment, it was not linked to mortality, which was instead attributed to 1 of the 16 underlying causes. This precluded traditional analyses with YLL and DALYs. To better understand the morbidity of HF, we assessed the fractional contribution of HF to the total YLD of the etiological condition, including ischaemic heart disease, hypertensive heart disease, non-ischaemic cardiomyopathy, valvular, rheumatic, and congenital heart disease. A higher fractional contribution of HF to the total YLD of the parent condition was consistent with a greater contribution of HF to the total morbidity associated with the parent condition.

Developed by the GBD team, SDI[13] is a composite indicator of development calculated as the geometric mean of 0–1, and is estimated using indices of fertility in those <25 years, mean education in individuals ≥15 years, and lag distributed income per capita. An SDI of 0 corresponds to the minimum level of development relevant to health, and 1 represents the maximum. Countries were divided into five SDI quintiles bound by limits of <0.455 (low SDI), 0.455–0.608 (low-middle SDI), 0.608–0.690 (middle SDI), 0.690–0.805 (high-middle SDI), and >0.805 (high SDI).[12] World Bank income regions were used to stratify countries into four regions (low, lower-middle, upper-middle, and high) based on the gross national income per capita in 2019.[14]

All estimates extracted are publicly accessible on the Institute of Health Metrics and Evaluation website.[11] The methods used to generate these publicly accessible estimates, including data collection and analysis, including statistical modelling have been described previously.[1,11] Uncertainty intervals (UIs) for estimates represent the broader range of uncertainty associated with the generation of population level estimates from multiple data sources, modelling choices and extrapolation or imputation of incomplete data.[1]

Data analysis

We performed descriptive analyses examining the prevalence and etiology of HF by sex, age, SDI, and geography. Heart failure etiology was ranked according to the 16 underlying causes and stratified by geographic region, with separate analyses for males and females. The proportion of HF attributable to each etiology across age in males and females was also examined. We assessed the change in the prevalence of HF between 1990 and 2019. All estimates are reported with corresponding 95% UI. Data were analysed using R studio (version 1.1.456).

Results

Prevalence of heart failure in 2019

Of an estimated 56.2 million (95% UI 46.4–67.8 million) cases of HF worldwide in 2019, 50.3% were in females (28.2 million [95% UI 23.5–34.2 million]) and sex distribution varied with age. There was female predominance among older adults, who accounted for the greatest proportion of those living with HF, and male predominance in younger ages. Youth < 15 years represented 0.9% of the global HF cases (0.52 million cases [95% UI 0.38–0.70 million]), of which 52.6% were males. Young adults 15–49 years accounted for 6.6% of HF cases, or 3.7 million (95% UI 2.9–4.9 million) cases, with 57.3% males. Adults 50–69 years represented 31.3% of HF cases (17.6 million [95% UI 13.2–23.1 million]), with 56.3% males. Adults > 70 years accounted for 62.2% of the world's HF cases (34.4 million [95% UI 27.1–43.8 million]), with female predominance (54.1%).

While 69.2% of HF cases in 2019 (38.9 million) were in low- and middle-income countries, age-standardized rates per 100 000 were greater in higher-income countries across both sexes (Central Illustration, Supplementary material online, *Figure S1*). The highest reported rates of HF per 100 000 people across age groups were in North America and the lowest rates were in South Asia (Supplementary material online, *Figure S1*).

Etiology of heart failure in 2019

Globally, the top causes of HF in order of decreasing prevalence were ischaemic, hypertensive, and rheumatic heart disease (*Figure 1*). Chagas disease was a leading cause of HF in Latin America, but not prevalent elsewhere. Non-rheumatic valve disease was ranked between the third and fifth most common cause of HF in most regions of Europe and Asia, but fell to ninth to twelfth position in Africa and Latin America. Heart anomalies were a leading cause of HF in South Asia.

Ischaemic heart disease and hypertensive heart disease were the leading causes of HF in males and females, respectively (*Figure 1*). Rheumatic heart disease and non-rheumatic degenerative valve disease were ranked highly in both females and males. Alcoholic cardiomyopathy and Chagas disease were ranked higher in males, whereas endocarditis was ranked higher in females.

The proportional distribution of HF etiologies varied across age group (*Figure 2*). In 2019, congenital heart disease was the predominant etiology in youth < 20 years in both sexes. The proportion of HF due to an ischaemic etiology increased in both sexes with increasing age, but was greater in males than females until >80 years of age. Hypertensive heart disease was the predominant cause of HF in females overall, with the proportion of HF due to hypertension in females peaking at 40–49 years and prominent until 80 years, after which it was surpassed by ischaemic heart disease. Rheumatic heart disease had the greatest contribution to HF in females 20–49 years. Alcoholic cardiomyopathy, while not among the top three causes of HF, was more common in males than females 20–49 years.

Morbidity of heart failure: contribution of heart failure to years lived with disability in 2019

The morbidity of HF in 2019, estimated at 5.1 million YLDs, was distributed equally between males and females (2.5 million YLDs [95% UI 1.6–3.6 million] in each sex). This accounted for 0.2 million YLDs [95% UI 0.1–0.3 million] in low SDI regions and 1.3 million YLDs [95% UI 0.9–1.8 million] in high SDI regions. Individuals < 70 years of age had 2.0 million YLDs [95% UI 1.3–2.9 million], while individuals ≥ 70 years of age had 3.1 million YLDs [95% UI 2.0–4.6 million]. Of the 5.1 million YLDs, 19.7% (997 thousand YLD; 95% UI 581 thousand-1.5 million YLD) were related to treated HF, 8.4% (425 thousand YLD; 95% UI 232–712 thousand YLD) to mild HF, 9.4% (474 thousand YLD; 273–754 thousand YLD) to moderate HF, and 62.5% (3.2 million YLD; 2.0–4.6 million YLD) to severe HF.

The relative contributions of HF to the overall burden of its underlying conditions in 2019 are listed in *Table 1*. Heart failure accounted for 34.8% of the YLDs of ischaemic heart disease, 67.9% of YLD of non-rheumatic valvular heart disease, 9.9% of YLDs of rheumatic heart disease, and 8.2% of YLDs of congenital heart disease. Heart failure accounted for all estimated YLDs of non-ischaemic cardiomyopathy, myocarditis, and hypertensive heart disease. Of note, hypertension causing stroke is classified separately than hypertensive heart disease causing HF.

The proportional contribution of HF to the morbidity of its underlying condition varied with country SDI in both males and females (*Figure 3*). As SDI increased, HF accounted for a larger proportion of

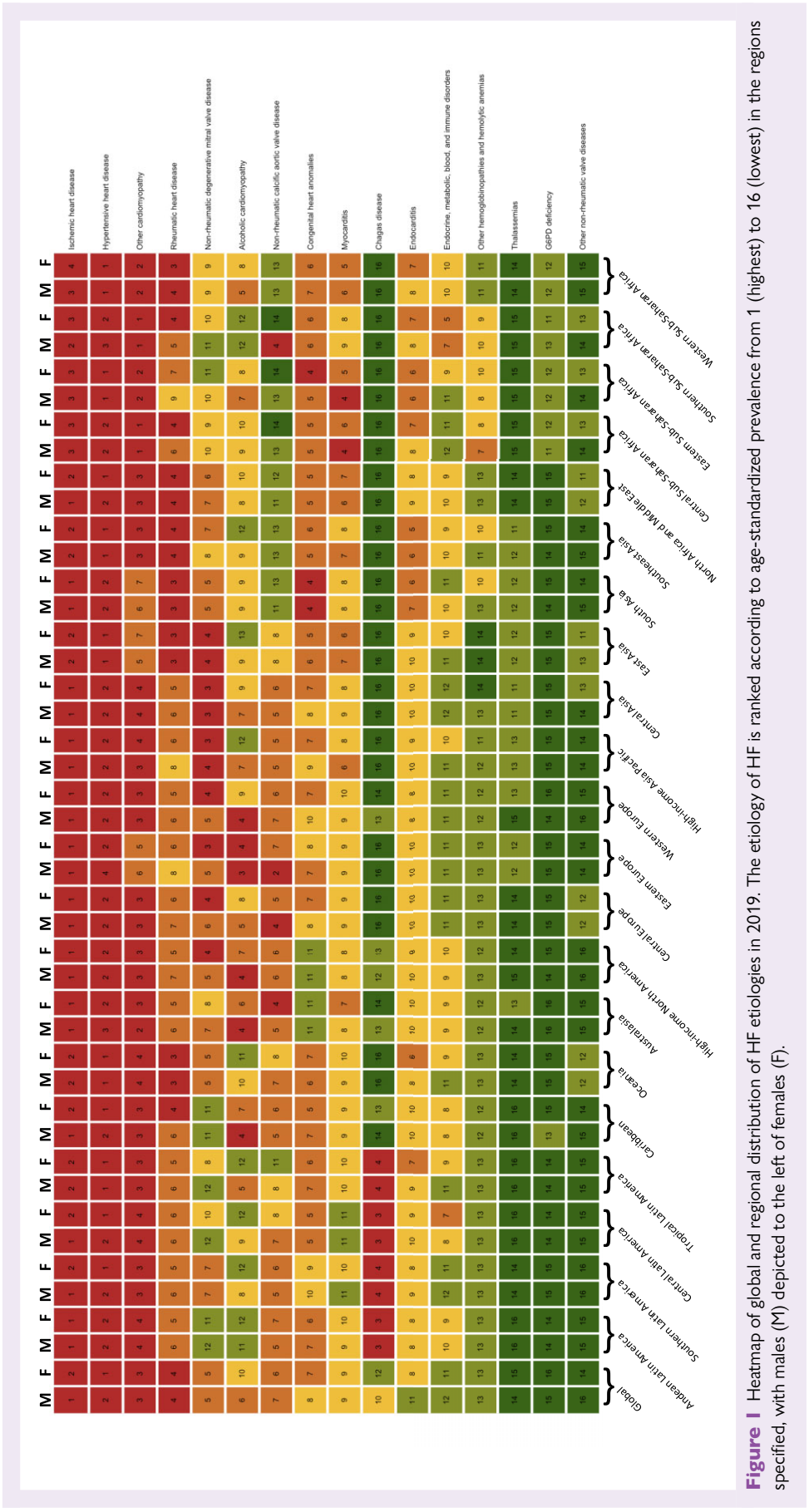


Figure 1 Heatmap of global and regional distribution of HF etiologies in 2019. The etiology of HF is ranked according to age-standardized prevalence from 1 (highest) to 16 (lowest) in the regions specified, with males (M) depicted to the left of females (F).

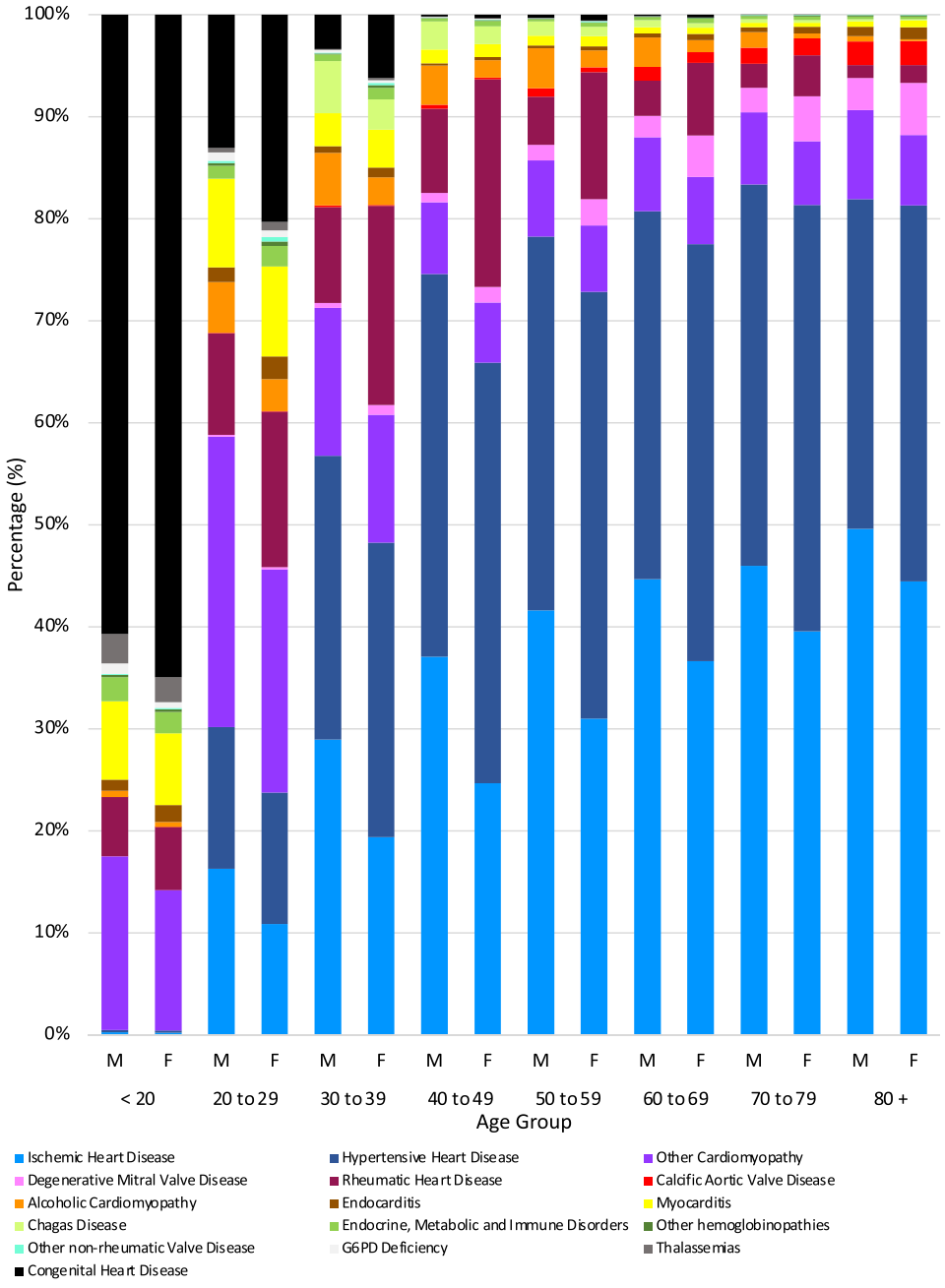


Figure 2 Percentage distribution of HF etiologies across age groups in 2019, stratified by sex. M, males; F, females.

the morbidity of ischaemic and rheumatic heart disease, and a lower proportion of the morbidity of non-rheumatic valvular heart disease. The contribution of HF to the overall morbidity of congenital heart disease did not appear to change with SDI. Similar patterns were seen in both sexes, with few exceptions (*Figure 3*).

Trends in heart failure prevalence and age-standardized rates 1990–2019

From 1990 to 2019, there was a 106.3% increase in the global number of HF cases from 27.2 million (95% UI 22.2–33.4 million) to 56.2 million (95% UI 46.4–67.8 million). There was a 106.0% increase in females, from 13.7 million (95% UI 11.2–16.8 million) to 28.2 million (95% UI 23.5–34.2 million) and a 106.6% increase in males, from 13.5 million (95% UI 10.9–16.6 million) to 28.0 million (95% UI 23.0–33.9 million). Accounting for population growth however, the age-standardized rate of HF per 100 000 people decreased by 7.1% worldwide, from 766.0 (95% UI 626.3–936.0) in 1990 to 711.9 (95% UI 591.1–858.3) in 2019. This represented a 5.8% decrease in females, from 686.0 (95% UI 561.6–834.7) to 646.1 (95% UI 537.4–783.0) and a 9.1% decrease in males, from 864.2 (95% UI 703.7–1048.4) to 785.7 (95% UI 649.5–944.9) per 100 000.

Table 1 Morbidity of underlying conditions attributed to HF in all ages and sexes globally in 2019

Etiology	DALYs (95% UI)	YLLs (95% UI)	YLDs (95% UI)	YLDs due to HF (95% UI)	Percentage of YLD due to HF*
Ischaemic heart disease	182 030 144 (170 206 778–193 504 630)	176 634 916 (165 028 829–188 453 377)	5 395 228 (3 632 733–7 581 058)	1 877 022 (1 141 806–2 792 022)	34.8%
Hypertensive heart disease[ϕ]	21 508 002 (16 400 051–23 899 879)	19 991 580 (14 951 099–22 179 674)	1 516 422 (933 299–2 326 612)	1 673 118 (1 001 353–2 596 522)	100% by estimates
Non-ischaemic cardiomyopathy and myocarditis	9 135 764 (7 864 970–10 039 922)	8 718 969 (7 407 225–9 630 072)	416 795 (276 188–593 227)	438 042 (283 271–642 536)	100% by estimates
Non-rheumatic valvular heart disease	2 793 750 (2 518 737–3 129 035)	2 472 425 (2 236 236–2 706 346)	321 325 (183 003–532 069)	218 139 (121 591–365 688)	67.9%
Rheumatic heart disease	10 673 882 (9 207 379–12 121 608)	8 683 950 (7 431 179–9 774 672)	1 989 931 (1 200 919–3 044 823)	196 420 (122 540–293 936)	9.9%
Congenital heart anomalies	18 693 016 (15 173 046–22 646 133)	18 102 135 (14 682 679–22 106 512)	590 881 (285 913–980 683)	48 672 (28 964–77 827)	8.2%

*Due to the estimated nature of these values, the percentage of YLD due to HF does exceed 100% in cases, for these cases we presume that the entirety of YLDs of hypertensive heart disease, non-ischaemic cardiomyopathy, and myocarditis are due to HF.
[ϕ]Hypertensive heart disease as an etiological factor of HF is coded as a separate entity from hypertension causing stroke.
DALY, disability-adjusted life years; YLL, years of life lost; YLD, years lived with disability.

The greatest decreases in age-standardized HF rates between 1990 and 2019 occurred in Australasia and high-income Asia Pacific, with decreases of 35.4%, from 1161.1 (95% UI 929.1–1404.3) to 750.2 (95% UI 603.6–904.9) per 100 000 and 22.1%, from 571.6 (95% UI 471.9–699.0) to 445.3 (95% UI 384.7–514.5) per 100 000 respectively. The greatest increases in age-standardized rates were in Eastern and Western sub-Saharan Africa with increases of 6.7%, from 761.6 (95% UI 601.1–958.1) to 812.6 (95% UI 640.9–1019.9) and 7.0%, from 593.1 (95% UI 467.7–746.6) to 634.5 (95% UI 497.2–807.2) per 100 000 respectively.

Stratified by sex, regions including Australasia, high-income Asia Pacific, East Asia, Western Europe, Southern Latin America, and Southern sub-Saharan Africa experienced consistent temporal decreases in age-standardized HF rates in both sexes (*Figure 4*). Australasia experienced the largest decreases in age-standardized HF rates in both sexes, at 39.0 and 32.2%, respectively. In North Africa and the Middle East, there was an overall 3.7% decrease in age-standardized HF in males and a 1.7% increase in females (*Figure 4*). This includes decreases in age-standardized rates in males and females in Bahrain (10.5 and 13.0%), Qatar (9.9 and 10.5%) and Turkey (35.9 and 7.2%). In contrast, South and Southeast Asia, Eastern and Western sub-Saharan Africa, and certain countries in the Middle East (including Saudi Arabia, Oman, and Sudan) experienced increases in age-standardized HF prevalence in both sexes (*Figure 4*). South and Southeast Asia had a 5.5 and 2.8% increase in HF prevalence in females and a 3.7 and 5.0% increase in males. Eastern and Western sub-Saharan Africa had increases of 4.9 and 5.6% in females and 10.1 and 7.9% in males. Notably, despite modest changes in the region of North Africa and the Middle East, countries including Oman, Saudi Arabia, and Sudan experienced increases of 15–30% in age-standardized HF cases.

Countries with an SDI > 0.8 experienced decreases in age-standardized HF prevalence in both sexes (*Figure 5*). Countries in Asia, Europe and North America with an SDI > 0.8 experienced a decrease in age-standardized HF prevalence over time. The largest decreases in age-standardized HF prevalence were in Canada in both females and males at 48.9 and 46.5%, respectively. High-SDI countries with increases in age-standardized HF prevalence in both sexes included Saudi Arabia (18.2 and 20.3% in females and males, respectively); Latvia (9.7 and 24.2%, respectively); and the United Arab Emirates (4.0 and 4.4%, respectively); Kuwait, with a 0.1% decrease in females but a 1.9% increase in males; and Slovakia, with a 16.7% decrease in females but a 5.8% increase in males. Countries in Northern Europe experienced substantially larger (10–15%) absolute decreases in the age-standardized HF rates in females relative to males.

Similar trends were seen when stratifying by gross national income. Between 1990 and 2019, on average, high-income regions experienced a decrease of 16.0% in age standardized rates of HF cases, from 877.5 (95% UI 725.3–1052.2) to 736.8 (95% UI 634.4–855.0) per 100 000 population, while low income regions experienced an increase of 3.9%, from 612.1 (95% UI 478.4–785.5) to 636.0 (95% UI 501.6–812.6) per 100 000 population between 1990 and 2019.

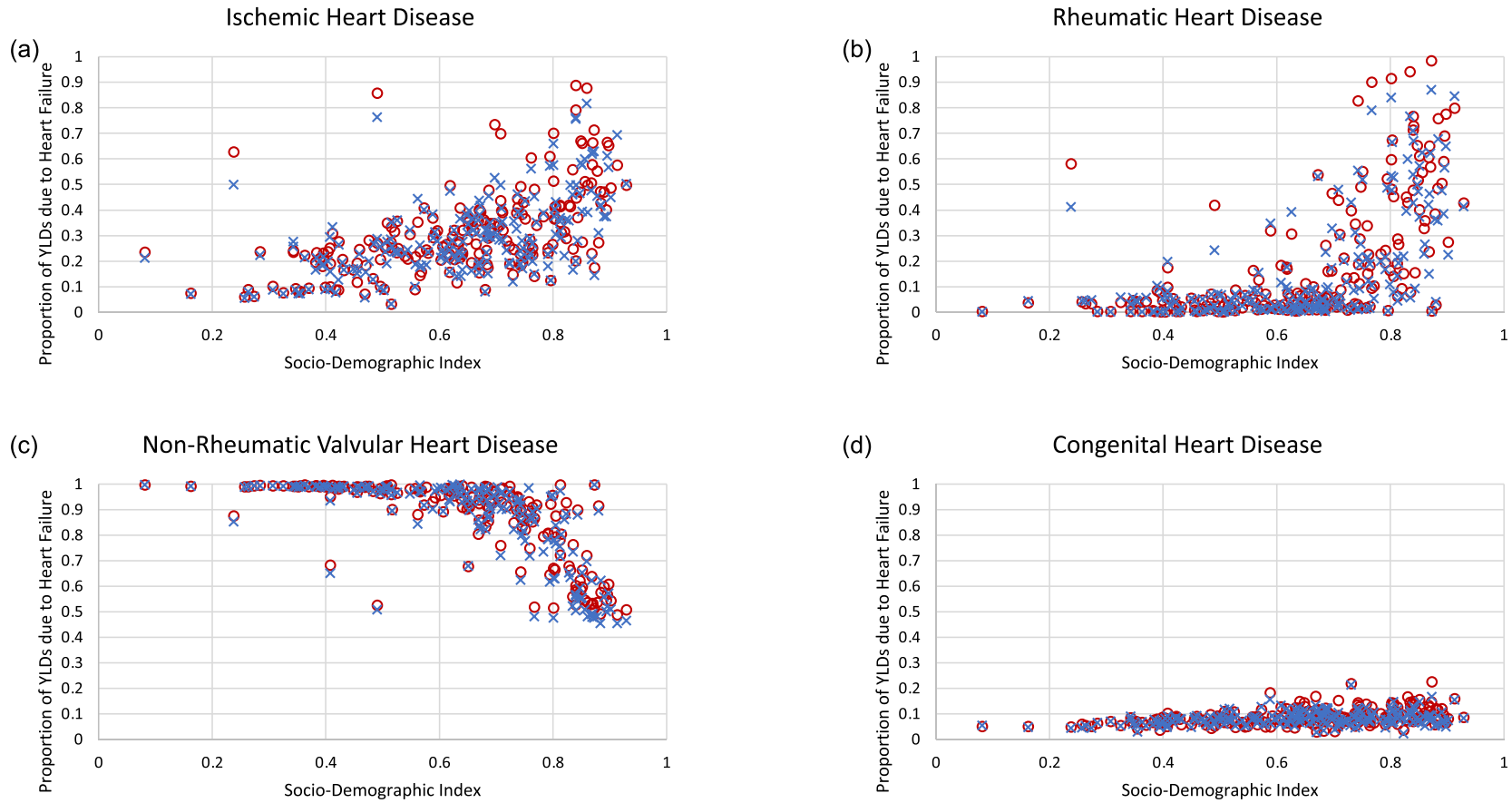


Figure 3 Relative contribution of HF to overall morbidity of the underlying etiology classified according to SDI. Etiologies include (*A*) ischaemic heart disease, (*B*) rheumatic heart disease, (*C*) non-rheumatic valvular heart disease, and (*D*) congenital heart disease. Females are represented by circles; males by X's. YLD, years lived with disability. Hypertensive heart disease, non-ischaemic cardiomyopathy and myocarditis are not shown as the morbidity from these conditions is entirely linked to heart failure according to GDB classification schemes.

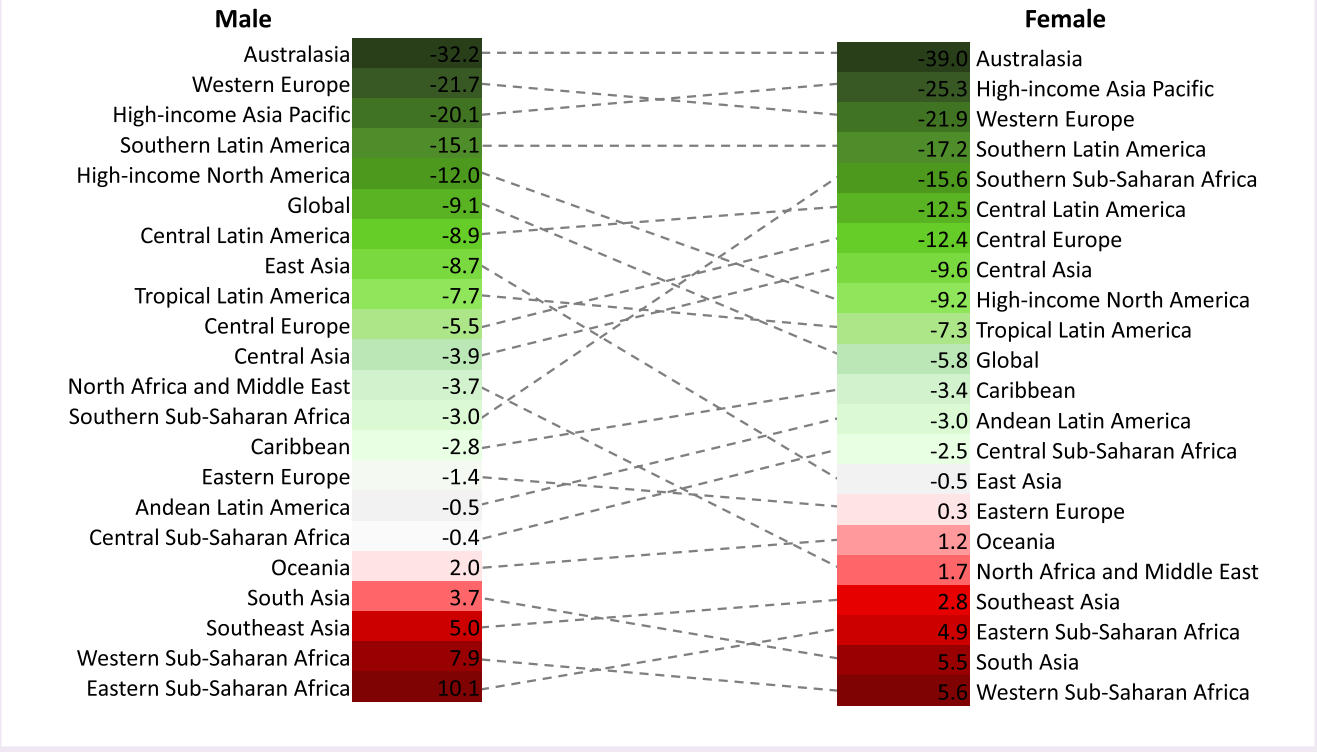


Figure 4 Change in age-standardized HF rate per 100 000 by region and sex 1990–2019. Regions are ordered by % change in HF prevalence in males (left) and females (right). Green represents temporal decreases and red represents increases.

Trends in heart failure etiology 1990–2019

Despite an overall decrease in the age-standardized prevalence of HF due to ischaemic heart disease between 1990 and 2019, low- and low-middle SDI regions (including South and Southeast Asia and Eastern and Western sub-Saharan Africa) experienced increases ranging from 5 to 25% over time; these findings were consistent in males and females (Supplementary material online, *Figure S2*). Age-standardized HF rates from hypertensive heart disease were largely unchanged over time in both sexes, except for females in high-middle SDI regions who experienced a 22.3% increase. Age-standardized prevalence of HF from rheumatic heart disease increased over time; this was driven by increasing rates in males in low (5% increase) and low-middle SDI regions (9.2% increase), and most notably in Andean Latin America (16.7% increase). Heart failure from rheumatic heart disease decreased in both males and females in middle, high-middle and high-SDI regions. However, there was a large increase in the age-standardized prevalence of HF due to calcific aortic valve disease across all SDI regions in both sexes. High-SDI regions experienced a decrease in age-adjusted HF resulting from all etiologies other than calcific aortic valve disease. In contrast, low-SDI regions experienced an increase in HF from several etiologies.

Discussion

In this analysis of the GBD dataset of 204 countries and territories, we found that of 56.2 million living with HF in 2019, just over half were females and >2/3 lived in low- and middle-income countries. Ischaemic and hypertensive heart disease were top causes of HF in males and females, respectively. Alcoholic cardiomyopathy and Chagas disease were etiologically ranked higher in males than females, and endocarditis was ranked higher in females than males. Years lived with disability were distributed equally between sexes. The prevalence of HF more than doubled between 1990 and 2019, but age-standardized HF rates decreased overall, with larger decreases in males than females; relatively large decreases in high-income regions (other than the Middle East), and small increases in low-income regions. High-SDI countries in Asia, Europe, and North America, experienced decreases up to 50% in age-standardized rates while countries in the African subcontinent, the Middle East, and South-East Asia experienced increases up to 30%. There has been an increase in age-standardized HF rates due to hypertensive, rheumatic, and calcific aortic valve disease, and a decrease due to ischaemic heart disease, although regional and sex differences are noted.

Except for the Middle East, regional trends in the age-standardized HF prevalence reflect a socioeconomic gradient, with greatest temporal increases in regions of socioeconomic deprivation and greatest decreases in regions of wealth, across both sexes. These gradients are multifactorial, driven by differences in environment and lifestyle, underlying risk factors, and access to primary and specialized care to prevent and manage both, the underlying etiology and ensuing HF.[15] We found that rates of HF due to ischaemic heart disease increased in the Middle East and Eastern and Western sub-Saharan Africa. An international database found significantly higher rates of hypertension and diabetes in the Middle East than in other regions.[16] There has been a significant change in the epidemiology of HF in Africa, from non-ischaemic etiologies such as rheumatic heart disease and infection

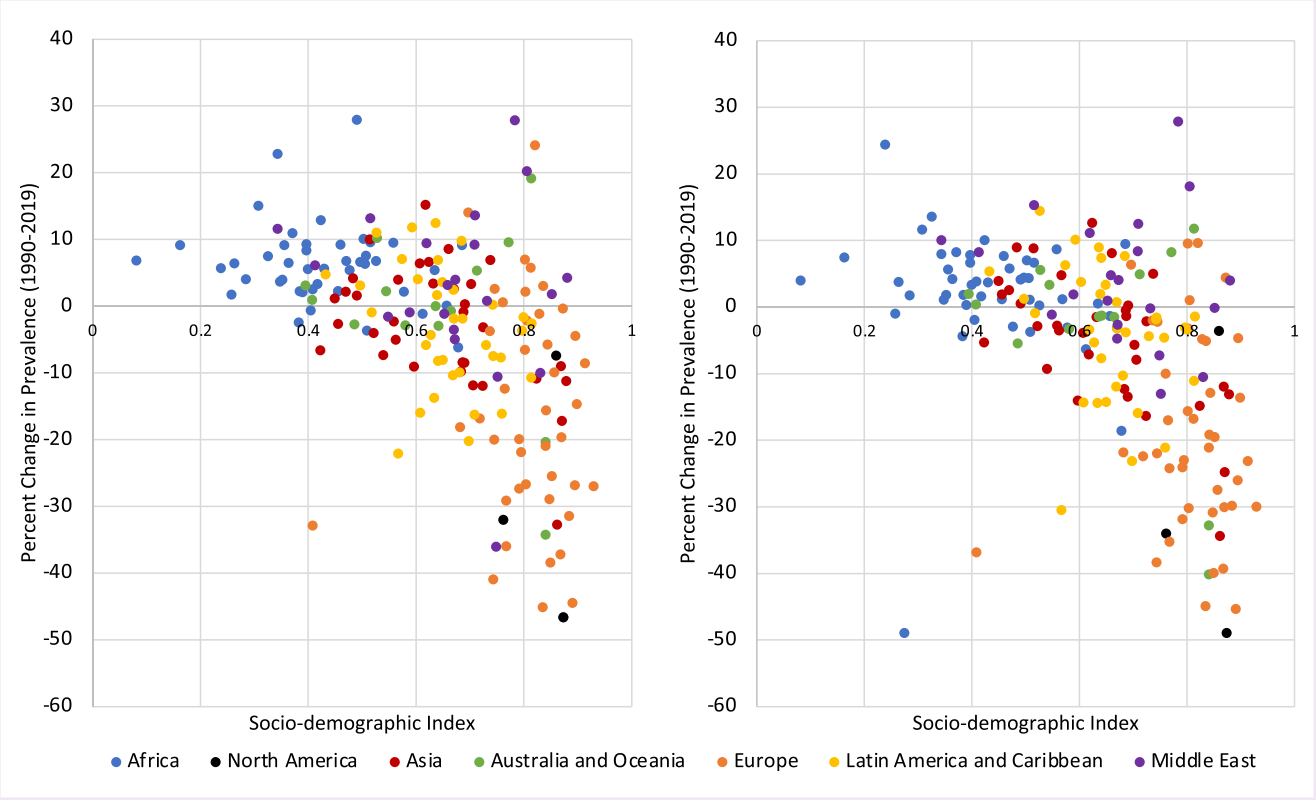


Figure 5 Change in age-standardized HF rate per 100 000 as a function of SDI in 204 countries and territories in males (left) and females (right).

to hypertensive or ischaemic etiologies.[17] Paradoxically, the regions with the greatest number of people living with HF and an increase in age-standardized HF rates remain deprived of the benefits of both clinical services and trial participation.[18]

The contribution of HF symptoms to the overall morbidity of the underlying etiology varies with country income. HF has a greater contribution to the morbidity of ischaemic heart disease as country SDI increases. In ischaemic heart disease, there appears to be a trade-off between morbidity from HF vs. ischaemic/anginal symptoms affecting daily life; the burden of HF and angina may have an inverse association. The greater access to anti-anginal therapies and greater effective treatment for acute myocardial infarction in high SDI regions may translate to lower burden from angina and greater survival to develop HF.[19] Indeed even in high SDI countries, people with socioeconomic deprivation are undertreated in the setting of myocardial infarction.[20] Among those with non-rheumatic valvular heart disease, the morbidity from HF decreases with increasing country SDI likely due to better access to valve interventions. The disability associated with post-intervention valve disease is lower than that of HF and is reflected in a lower overall disability burden.[21] In individuals with rheumatic valve disease, the morbidity of HF increases with increasing SDI likely due to improved survival from better care of the underlying disease but late complications of valve interventions. The highest age-standardized mortality of rheumatic heart disease is in lower SDI countries, where HF accounts for <10% of the overall burden of rheumatic valve disease (as measured by YLD)[22]; when mortality from a condition is high, years lived with disability is low.

Across most regions and in both sexes, ischaemic, hypertensive, alcohol, and rheumatic heart disease remain prevalent causes of HF, and efforts should be shifted upstream to policy and practice aimed at primordial prevention, and early detection and treatment of risk factors. Ischaemic heart disease has increased in prevalence in low- and low-middle SDI regions in both sexes, and hypertensive heart disease, the leading cause of HF in females up to 80 years of age, has increased in high- and high-middle SDI regions. Recent consensus statements suggest that cardiovascular risk from hypertension is accentuated in females, when compared with males.[4] Middle-income countries outperform high-income and low-income nations in treatment and control of hypertension,[23] but treatment in females remains variable. Regional sodium-replacement strategies, community screening programs, and policies aimed at nutrition, physical activity, and tobacco and alcohol misuse are targets for the primary and secondary prevention of HF. Education campaigns and antibiotic treatment for streptococcal pharyngitis could prevent rheumatic heart disease, particularly in low- and middle-income regions where it is a growing cause of HF. Clinical trial inclusion of females and individuals from low-income countries could improve knowledge, infrastructure, awareness, and access to treatments in these regions.[18,24]

The global doubling in the rate of HF due to calcific aortic valve disease, including 10–15-fold increases in some regions where surgical access and valve interventions are limited, poses a concern. With no evidence-based medications to slow disease progression, calcific aortic valve disease remains a public health concern with significant health and economic consequences.[25] Chagas disease remains a leading cause of HF in Latin America and is more prevalent in males than females. While its prevalence has decreased in Latin America, it has grown in Western Europe and high-income Asia Pacific, likely secondary to climate change and human migration patterns.[26]

Access, affordability, and use of HF guideline-directed medical therapy (GDMT) and device therapies are important factors in regional differences in outcomes. A meta-analysis of HF studies from sub-Saharan Africa found that there was a relative under-utilization of

beta blockers and mineralocorticoid receptor antagonists, pillars of GDMT, at 31 and 52% respectively. Instead, the emphasis was on the use of loop diuretics as symptomatic management in 82% of the study population.[27] In a sampling survey of nine countries across World Bank income levels, the cost of GDMTs relative to monthly income was the highest in low-income countries.[28,29] Data also demonstrated an association between population literacy and the use of GDMT; gaps in literacy corresponded to more advanced symptoms.[16] The use of implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy-defibrillators (CRT-Ds) that prolong life and improve symptoms remains low outside of North America, Australia, and Western Europe, explaining the lower age-standardized prevalence due to premature death in the these regions.[30]

Limitations

The GBD data estimates are based on diverse data sources, ranging from robust registration systems and censuses to less reproducible methods including verbal autopsy data. Estimates likely underrepresent disease burden in resource-poor regions, including African countries that lack adequate clinical and research infrastructure for diagnosis and data collection. This may be more pronounced in diagnoses requiring medical imaging such as degenerative aortic and mitral valve disease. Though rigorous statistical methods are used, estimates are often imputed from limited data sources. The uncertainty intervals reflect the range of values in which the correct estimate is likely found and reflects measurement error and assumptions used in modelling and imputing for incomplete data.[31] Furthermore, the role of improved diagnosis and case ascertainment in regions reporting temporal increases in prevalence of conditions cannot be determined. The data do not differentiate between HF with preserved and reduced ejection fraction, which differ in etiologies and outcomes. Also, estimates in the GBD database are made on the premise that HF is a downstream disability of various etiologies; estimates of prevalence, and not incidence are provided, making it difficult to assess whether increasing prevalence is due to increasing incidence or decreasing mortality rates. Not factored into the burden of disease is the loss of economic productivity and associated caregiving costs of relatives, which may compound the psychological burden of illness.

Conclusions

HF represents a growing public health burden with socioeconomic gradients in trends. High-income regions represent a minority of HF cases, although diagnosis is likely more complete in these regions. Globally, the age-standardized prevalence of HF has decreased, more so in males than females. Except for the Middle East, where HF is increasing, high-income countries have experienced decreases in age-standardized HF rates while low- and middle-income regions have experienced increases. There has been an increase in age-standardized HF rates due to hypertensive, rheumatic, and calcific aortic valve disease, and a decrease due to ischaemic heart disease, although regional and sex differences are noted. Ischaemic and hypertensive heart disease remain the commonest causes of HF and represent ongoing targets for intervention. The identification of sex specific differences and trends in HF etiology allows for targeted research and public health endeavours.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

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Data availability

The data underlying this article are available in the Global Health Data Exchange, at https://ghdx.healthdata.org/gbd-results-tool. The datasets were derived from sources in the public domain.

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