Global, regional, and national burdens of heart failure in adolescents and young adults aged 10–24 years from 1990 to 2021: an analysis of data from the Global Burden of Disease Study 2021

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Summary

Background Prior studies suggest prevalence of heart failure (HF) has remained steady or progressively decreased over past 30 years in the general population. Whether this favourable trend occurred in adolescents and young adults aged 10–24 years has yet to be elucidated. We aim to identify the trends in the burden of HF in this young population from 1990 to 2021 to inform areas for targeted intervention and prevention efforts.

Methods We analyzed data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. The case number and rates per 100,000 population of prevalence and years lived with disability (YLDs) of HF at the global, regional, and national level in the population aged 10–24 years from 1990 to 2021 were reported. In addition, the HF trends by age, sex, and socio-demographic index (SDI) were analyzed. Furthermore, we calculated the average annual percentage changes (AAPC) and identified the year with the most pronounced changes in the trends with the joinpoint regression analysis. In detail, we divided the study population into three age groups: 10–14 years old, 15–19 years old, and 20–24 years old. We also employed the Bayesian age-period-cohort models (BAPC) to predict the future burden of HF up to 2030.

Findings Globally, the prevalence and YLDs rates of HF among adolescents and young adults in 2021 were 148.1 (95% uncertainty interval [UI]: 118.8–185.7) and 14.4 (9.2–21.2) per 100 000 population, increased from 125.5 (100.0–157.7) and 12.2 (7.8–17.8) in 1990 respectively. Noticeable changes in HF prevalence were found in 1994, 2001, 2004, 2010, and 2018. Regionally, East Asia had the most pronounced increase in HF prevalence rate (AAPC = 1.35 [1.28–1.43]) and YLDs rate (AAPC = 1.32 [1.27–1.38]), while the highest HF prevalence rates per 100,000 population were observed in High-income North America (232 [185.4–292]). The prevalence and YLDs of HF increased in most countries except Australia, Canada, and Spain. The largest increase in HF prevalence rate was observed in China (AAPC = 1.39 [1.31–1.48]). By SDI quintile, the middle-SDI quintile countries had the largest increase in prevalence and YLDs rates. By sex, males had a higher prevalence rate per 100,000 population than females (158.0 [95% UI: 126.7–198.9] vs 137.6 [95% UI: 110.0–172.2]) in 2021. Among three age groups, the largest increase in HF prevalence from 1990 to 2021 was found in individuals aged 20–24 years (AAPC = 0.61 [0.6–0.61]). Among all causes of HF, cardiomyopathy and myocarditis accounted for the highest proportion (32.7%) of prevalence cases of HF in 2021, followed by congenital birth defects (27.3%), and rheumatic heart disease (23.8%). The BAPC analysis predicted that the cases of HF prevalence and YLDs would show a rising trend from 2022 to 2030.

Interpretation The burden of HF in adolescents and young adults aged 10–24 years was still increasing globally, which may be obscured by the burden trend of general population. According to different underlying causes of HF, both high-income countries and low- and middle-income countries need to better prevent HF in adolescents and young adults.

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Keywords: Heart failure; Adolescents; Young adults; Prevalence; Years lived with disability

Research in context

Evidence before this study

Heart failure (HF) is a complex clinical syndrome consisting of cardiac symptoms, such as breathlessness and fatigue, and physical signs, including ankle swelling, pulmonary crackles, and elevated jugular venous pressure. Any structural and/or functional abnormality of heart can result in HF. A few studies suggest that prevalence of HF has remained steady or progressively decreased over past 30 years in the general population. Adolescents and young adults of 10–24 year old have distinct underlying causes, symptoms and signs of HF. However, the burden trends of HF in adolescents and young adults aged 10–24 years has yet to be elucidated. We searched PubMed up to November 12, 2024, for papers published with no language restrictions, using the terms ("adolescents and young adults") AND ("heart failure"). Our search yielded 45 results. Previous studies have solely focused on specific populations within only one scenario.

Added value of this study

For the first time, we analyzed the cases and rates of prevalence and years lived with disability (YLDs) among adolescents and young adults aged 10–24 years at the global, regional, and national locations, stratified by socio-demographic index (SDI) from 1990 to 2021. Our results indicate that global burden of HF among adolescents and young adults was still increasing during the past 32 years. Particularly, the middle SDI quintile countries experienced the most significant upsurge in HF prevalence and YLDs rates, which are currently the highest in high SDI quintile countries. The predominant causes of HF are cardiomyopathy and myocarditis, congenital birth defects, and rheumatic heart disease (RHD), with a notable decline in the proportion of RHD from 1990 to 2021.

Implications of all the available evidence

The burden of HF in adolescents and young adults aged 10–24 years was still increasing across the globe, which may be obscured by the burden trend of general population. According to different underlying causes of HF, both high-income countries and low- and middle-income countries need to better prevent HF in the adolescents and young adults.

Introduction

Heart failure (HF) is a complex clinical syndrome with symptoms and signs that result from any structural or functional impairment of ventricular filling or ejection of blood.[1] HF is a major global health and economic burden, affecting more than 60 million population worldwide.[2] From a clinical viewpoint, HF is mainly characterized by symptoms such as breathlessness and fatigue, and physical signs, including ankle swelling, pulmonary crackles, and elevated jugular venous pressure. These clinical presentations are typically seen in HF patients aged 70 years and older, among whom ischemic heart disease (ICH) and chronic obstructive pulmonary disease (COPD) are common causes.[3] By contrast, previous studies have indicated that congenital heart disease (CHD), cardiomyopathy, and myocarditis are common causes of HF in adolescents and young adults of 10–24 years old.[4–6] The clinical presentation of HF in the population of 10–24 years old can vary markedly by age, underlying etiology, and disease severity. In addition to respiratory symptoms and peripheral edema signs, growth retardation, failure to thrive, peripheral cyanosis and pallor, chest pain, and syncope due to decreased cardiac output, intracardiac shunt, and arrhythmias may be observed.[7] Therefore, the symptoms and signs of HF in young patients of 10–24 years old may be different from those in the elderly.

Prior investigations into HF mainly focus on the elderly population. A few studies suggest that the prevalence of HF has remained steady or progressively decreased over the past 30 years in the elderly.[3,8] Several studies concerning the US population have reported that HF-related mortality stayed stable or decreased between the 1990s and 2011 or 2012, followed by an increase till 2018 or 2019.[9–11] This trend is also observed in young patients of 15–44 years old.[12] The advancements in medicine and shifts in cardiovascular risk factors could lead to these changes in the burden of HF. However, the burden trends of HF in adolescents and young adults of 10–24 years old have yet to be elucidated, given their distinct underlying causes of HF.

The adolescents and young adults aged 10–24 years have long been overlooked in global health and social policy.[13] Besides, most studies concerning the adolescents and young adults aged 10–24 years focus on transmitted infections and mental disorders.[14,15] It is estimated that people diagnosed with HF at the age of

20 years would live 36 years less than their peers without HF.[16] However, few studies have assessed the health burden of HF in this age group. A prior study investigated the burden of non-communicable diseases (NCD) among adolescents and young adults aged 10–24 years in the Southeast Asia and Western Pacific regions.[17] The authors revealed that cardiovascular diseases were the second leading cause of NCD burden in all 42 countries and the leading cause of NCD deaths in 21 countries. In the same period, cardiovascular diseases were the fourth leading cause of NCD burden in the European Union.[18] These studies suggest that more attention should be paid to cardiovascular diseases in adolescents and young adults of 10–24 years old. Furthermore, the true burden of HF in adolescents and young adults in some countries with poor resources might be unknown due to a lack of high-quality national-level epidemiological data.

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 provides a comprehensive assessment of the prevalence and years lived with disability (YLDs) of HF across different age groups and regions, allowing for a detailed analysis of trends over the past three decades.[19] In this study, we present a trend analysis of the global, regional, and national burdens of HF in adolescents and young adults of 10–24 years old from 1990 to 2021 utilizing data from GBD 2021. Our objective is to identify trends, risk factors, and potential differences in the prevalence and YLDs rates associated with HF in this population, thereby informing targeted intervention and prevention efforts.

Methods

Data sources and case definitions

We used data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 (https://vizhub.healthdata.org/gbd-results/). The detailed methods used for the GBD 2021 have been described elsewhere.[19] In brief, the GBD 2021 estimated health loss due to 371 diseases and injuries using 100,983 data sources in 204 countries and territories. Original data were collected from disease-specific registries, health service contact data, vital registration systems, censuses, household surveys, and other sources. The data were then synthesized with the Cause of Death Ensemble model (CODEm), spatiotemporal Gaussian process regression, and a Bayesian meta-regression modeling tool (DisMod-MR 2.1). The GBD study uses deidentified data, and a waiver of informed consent was approved by the University of Washington Institutional Review Board.

The definition of HF in the GBD database is in line with that in the data sources. The underlying causes of HF in the adolescents and young adults were selected according to the GBD 2021 database, a review of the literature and expert opinion (Supplementary Table S1).

Years lived with disability (YLDs) were calculated by multiplying cause-age-sex-location-year-specific prevalence of sequelae by their respective disability weights, for each disease and injury. Adolescence is defined as teen-ages aged 10–19 years by WHO.[20] In order to investigate in more detail, we divided adolescents into younger adolescents (aged 10–14 years) and older adolescents (aged 15–19 years), in addition to young adults aged 20–24 years.

The socio-demographic index (SDI) was calculated to explore the relationship between the burden of HF of adolescents and young adults and the development status of a region or country. It is calculated from national-level income per capita, educational attainment in the population ≥15 years old, and women' fertility rate <25 years old.[21] The SDI is a composite indicator of social development levels that correlate with health outcomes. It ranges from 0 (minimum development) to 1 (maximum development). The 204 countries and territories are categorized into five groups based on SDI quintiles in 2021: low SDI (<0.466), low-middle SDI (≥0.466 and <0.619), middle SDI (≥0.619 and <0.720), high-middle SDI (≥0.720 and <0.810), and high SDI (≥0.810).

All estimates produced by the GBD come with uncertainty intervals (UI), which provide a measure of the precision of the estimates. 95% UIs were generated as the 2.5th and 97.5th percentiles values of 500 draws. Uncertainty was propagated at each step of the estimation process.

Statistical analysis

The prevalence, YLDs, and underlying causes of HF were analyzed by sex (male or female) and age group (10–14 years, 15–19 years, and 20–24 years) at regional, national, and SDI levels. To identify the direction and magnitude of changes in the prevalence and YLDs of HF over time, we calculated the annual percentage change (APC) and average APC (AAPC) and the corresponding 95% confidence interval (CI) with joinpoint regression analysis. A positive APC or AAPC indicates an increase, while a negative value indicates a decrease. The AAPC between 1990 and 1999, between 2000 and 2009, between 2010 and 2021, and between 1990 and 2021 were calculated.

In order to identify the year with the most marked changes, we detected trends in the data over time and fitted the optimal model curve to the data by segmenting the data into multiple linear pieces on a logarithmic graph using joinpoint regression analysis. These segmented points are referred to as "joinpoints". The "joinpoints" were data-driven (based on statistical significance). In detail, when we perform the joinpoint regression analysis, a logarithmic linear model ($\ln y = \beta *x$) is used for segmented regression, and the grid search method (GSM) is used to establish all possible connection points. The mean squared errors (MSE) corresponding to each possible scenario are calculated, and the grid point with the smallest MSE is selected as

the connection point. Then, the establishment of the optimal model for the regression of connection points (i.e. the number of connection points) is determined using the Monte Carlo permutation test. We set the maximum number of potential connection points to 5 and the minimum number of potential connection points to 0. The permutation test starts with the number of connection points k = 0 and k_max = 5. If k≠k_max, set k = k+1 to continue the test until the model corresponding to k = k_max is selected as the optimal model. For instance, the most basic model, which has no joinpoints, is represented by a single straight line. When additional joinpoints are incorporated, each is evaluated using the Monte Carlo permutation approach.

The Bayesian age-period-cohort models (BAPC) with integrated nested Laplace approximation (INLA) was employed to predict the prevalence and YLDs of future HF in the adolescents and young adults of 10–24 years old till 2030.

All the data analyses were conducted with the R program (Version 4.3.2, R core team). A two-tailed p-value <0.05 was considered as statistically significant.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Global trends

In 2021, there were 2.79 million (95% UI: 2.24–3.51) HF cases in adolescents and young adults of 10–24 years old across the globe. Among these cases, 1.53 million (95% UI: 1.23–1.92) were males and 1.27 million (95% UI: 1.01–1.58) were females. The global prevalence of HF among adolescents and young adults increased gradually from 1990 to 2021 (AAPC = 0.53 [95% CI: 0.52–0.55], p < 0.001). The HF prevalence rate per 100 000 population was 148.1 (95% UI: 118.8–185.7) in 2021, higher than the prevalence in 1990 (125.5 [95% UI: 100.0–157.7]). The increase rate was lower between 2010 and 2021 (AAPC = 0.42 [95% CI: 0.40–0.44]) than those between 1990 and 1999 (AAPC = 0.58 [95% CI: 0.56–0.60]) and between 2000 and 2009 (AAPC = 0.65 [95% CI: 0.61–0.70]; Table 1). The joinpoint regression analysis revealed noticeable changes in HF prevalence in 1994, 2001, 2004, 2010, and 2018 (Fig. 1A). The global YLDs of HF also significantly increased from 1990 to 2021 (AAPC = 0.55 [95% CI: 0.54–0.56, p < 0.001]; Table 2 & Fig. 1B).

Global trends by sex

By sex, the prevalence of HF increased significantly in both males and females from 1990 to 2019 (Table 2). The AAPC in females was 0.53 (95% UI: 0.52–0.55), which was comparable to that of males (0.54 [95% UI: 0.53–0.55]). In 2021, the prevalence rate per 100 000 population in the males (158.0 [95% UI: 126.7–198.9]) was higher than the prevalence in the females (137.6 [95% UI: 110.0–172.2]). At the same time, the prevalence cases in the males were 1.53 million (95% UI: 1.23–1.92), more than those in the females (1.27 million [95% UI: 1.01–1.58]). The YLDs of HF followed a similar pattern of prevalence.

Year	Prevalence		YLDs	
	AAPC (95% CI)	p value	AAPC (95% CI)	p value
1990–99	0.58 (0.56–0.60)	<0.001	0.58 (0.57–0.59)	<0.001
2000–09	0.65 (0.61–0.70)	<0.001	0.65 (0.63–0.67)	<0.001
2010–21	0.42 (0.40–0.44)	<0.001	0.46 (0.45–0.47)	<0.001
1990–2021	0.53 (0.52–0.55)	<0.001	0.55 (0.54–0.56)	<0.001

AAPC, average annual percentage change; YLDs, years lost due to disability; CI, confifidence interval.

Table 1: **Global AAPC in prevalence and YLDs of heart failure in adolescents and young adults of 10–24 year old.**

Global trends by age group

In global, the largest increase of HF prevalence from 1990 to 2021 was found in individuals aged 20–24 years (AAPC = 0.61 [0.6–0.61]), higher than the increase of prevalence in those aged 15–19 years (AAPC = 0.57 [0.54–0.60]) and 10–14 years (AAPC = 0.45 [0.43–0.46]). These data indicated that the increase rate of HF prevalence rates increased with age. However, the prevalence rates and prevalence cases decreased with age and peaked in individuals of 10–14 years, with a prevalence of 156.7 (95% UI: 122.6–198.6) per 100 000 population and 1.05 million cases (95% UI: 0.82–1.32 million) in 2021. Over the same period, the trends of increase in HF YLDs among three age groups were similar to those of HF prevalence (Table 2).

Global trends by SDI

Overall, the HF prevalence increased in countries in all five SDI quintiles from 1990 to 2021 (Table 2). The largest increase in HF prevalence rate per 100 000 population was observed in the middle-SDI quintile countries (from 107.4 [85.7–134.3] to 137 [110.5–169.1]; AAPC = 0.79 [0.74–0.84]). During this period, the middle-SDI quintile countries also had the largest increase of HF YLDs rate per 100 000 population (from 10.6 [6.8–15.6] to 13.4 [8.7–19.6]; AAPC = 0.78 [0.74–0.82]). Notably, in 2021, the countries in the high-SDI quintile had the most prevalence rate per 100 000 population (187.6 [150–236.1]) and YLDs rate per 100 000 population (17.8 [11.4–26.5]), compared with other SDI regions.

Regional and national trends

Stratified by regional levels, the most pronounced increase in HF prevalence rate per 100 000 population from 1990 to 2021 was found in East Asia (from 69.3 [54.5–85.6] to 104.5 [81.2–130.8]; AAPC = 1.35

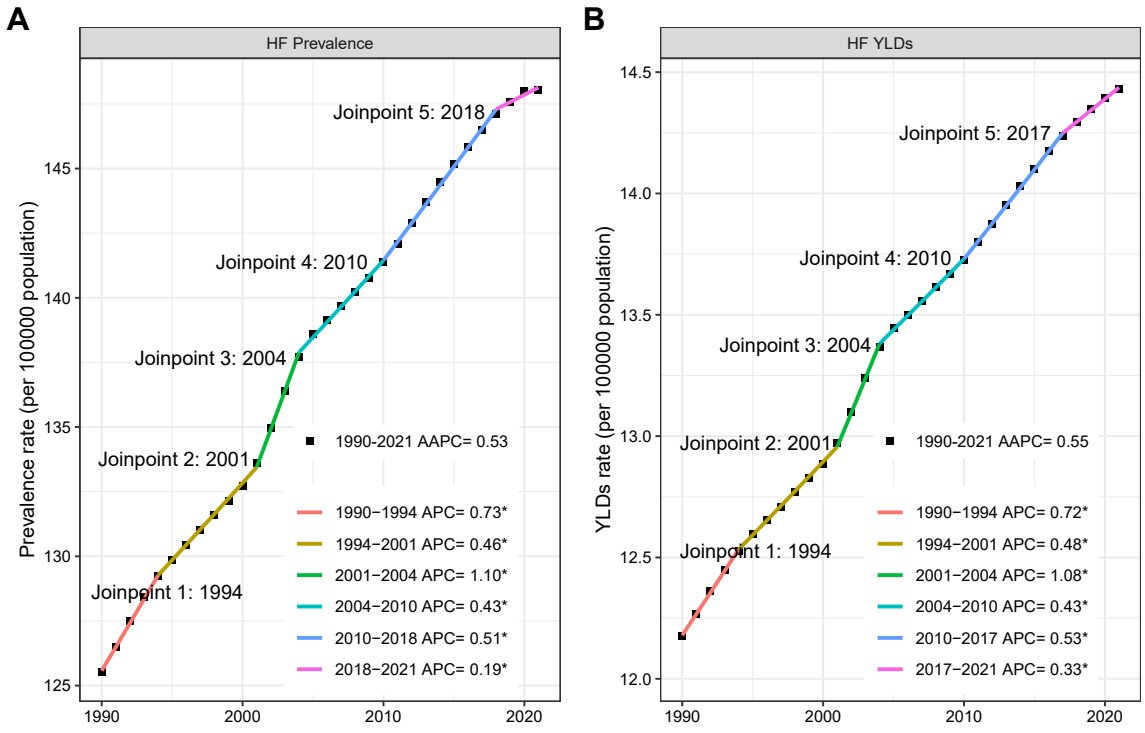

Fig. 1: Joinpoint regression analysis of global HF prevalence (A) and YLDs (B) in adolescents and young adults aged 10–24 years from 1990 to 2021. The y-axes presented are truncated. APC, annual percentage change; AAPC, average APC; HF, heart failure; YLDs, years lost due to disability.

[1.28–1.43]), more than three times of other regions. In 2021, the highest HF prevalence rates per 100 000 population were observed in High-income North America (232 [185.4–292]), Central Europe (200 [160–248.2]), and Eastern Europe (185.5 [149.3–229.3]). During the same period, the largest increase in HF YLDs rate was also observed in East Asia (from 6.7 [4.5–10.0] to 10.1 [6.6–15.1]; AAPC = 1.32 [1.27–1.38]). The highest HF YLDs rates were found in the same regions as the highest HF prevalence rates (Table 2).

At the national level, the prevalence and YLDs of HF increased in most countries except Australia, Canada, and Spain (Fig. 2; Supplementary Table S2). The largest increase in HF prevalence rate per 100 000 population from 1990 to 2021 was observed in China (from 68.9 [54.3–84.8] to 105.1 [81.6–131.5]; AAPC = 1.39 [1.31–1.48]; Supplementary Fig. S1), followed by Netherlands (AAPC = 1.10 [0.82–1.37]) and Oman (AAPC = 0.70 [0.64–0.77]). The most pronounced increase in the YLDs was also found in the above-mentioned three countries. In 2021, the highest HF prevalence and YLDs rates per 100 000 population were observed in Sweden, Poland, and the United States of America.

Underlying causes of HF

Globally, among all causes of HF, cardiomyopathy and myocarditis (CM) accounted for the highest proportion (32.7%) of prevalence cases of HF in 2021, followed by congenital birth defects (CBD, 27.3%), RHD (23.8%), IHD (6.1%), hypertensive heart disease (HHD, 3.3%), endocarditis (3.2%), other cardiovascular and circulatory diseases (2.4%), pulmonary arterial hypertension (0.7%), endocrine, metabolic, blood, and immune disorders (0.4%), non-rheumatic valvular heart disease (0.1%), and atrial fibrillation and flutter (0%). From 1990 to 2021, the proportion of RHD slightly decreased (from 28.3% to 23.8%; Fig. 3, Supplementary Table S3), while the proportion of CM slightly increased (from 30.1% to 32.7%). The causes leading to HF YLDs followed similar trends of prevalence (Supplementary Fig. S2).

In adolescents aged 10–14 years, the CBD (42.7%) was the leading cause of HF in 2021 (Supplementary Figs. S3 and S4). At the same time, the CM was the leading cause of HF in adolescents aged 15–19 years (34.9%) and young adults aged 20–24 years (33.5%). Surprisingly, IHD was the third leading cause of HF in young adults aged 20–24 years (15.4%), exceeding RHD. The underlying causes of HF were generally similar by sex.

The CM was the leading cause of HF in most regions in terms of prevalence rate per 100 000 population (Fig. 4). Of note, the CBD was the major cause of HF in East Asia (49.3 [34.8–68.2]), Central Latin America (52.6

	Prevalence						YLDs					
	Cases (n), 1990	Prevalence (per 100,000 population), 1990	Cases (n), 2021	Prevalence (per 100,000 population), 2021	AAPC, 1990–2021	p value	Cases (n), 1990	YLDs (per 100,000 population), 1990	Cases (n), 2021	YLDs (per 100,000 population), 2021	AAPC, 1990–2021	p value
Global	1,942,065 (1,547,578–2439,855)	125.5 (100.0–157.7)	2,794,879 (2,241,993–3505,217)	148.1 (118.8–185.7)	0.53 (0.52–0.55)	<0.001	188,376 (121,264–275,777)	12.2 (7.8–17.8)	272,434 (174,058–400690)	14.4 (21.2–9.2)	0.55 (0.54–0.56)	<0.001
Sex												
Women	889,157 (709,070–1113,213)	116.8 (93.2–146.3)	1,266,455 (1,012,319–1584,485)	137.6 (110.0–172.2)	0.53 (0.52–0.55)	<0.001	86,116 (55,676–125,898)	11.3 (7.3–16.5)	123,104 (78,957–179,919)	13.4 (8.6–19.5)	0.54 (0.53–0.55)	<0.001
Men	1,052,908 (838,171–1324,786)	133.9 (106.6–168.5)	1,528,424 (1,225,278–1924,204)	158.0 (126.7–198.9)	0.54 (0.53–0.55)	<0.001	102,259 (65,687–149,879)	13.0 (8.4–19.1)	149,331 (95,276–220,161)	15.4 (9.8–22.8)	0.55 (0.55–0.56)	<0.001
Age group, years												
10–14	732,831 (569,090–935,891)	136.8 (106.2–174.7)	1,046,369 (817,486–1324,156)	156.7 (122.6–198.6)	0.45 (0.43–0.46)	<0.001	71,078 (45,566–103685)	13.3 (8.5–19.4)	101,701 (65,853–149,408)	15.3 (9.9–22.4)	0.45 (0.44–0.47)	<0.001
15–19	632,230 (487,963–814,736)	121.7 (93.9–156.8)	904,722 (699,247–1168,494)	145.0 (112.1–187.3)	0.57 (0.54–0.6)	<0.001	61,592 (39,005–92386)	11.9 (7.5–17.8)	88,737 (56,261–134,002)	14.2 (9.0–21.5)	0.59 (0.56–0.62)	<0.001
20–24	577,004 (453,965–723,473)	117.3 (92.3–147.0)	843,787 (663,675–1049,507)	141.3 (111.1–175.8)	0.61 (0.6–0.61)	<0.001	55,705 (35,804–80719)	11.3 (7.3–16.4)	81,996 (52,689–118,716)	13.7 (8.8–19.9)	0.63 (0.61–0.64)	<0.001
Sociodemographic index												
High	331,375 (265,407–415,435)	169.2 (135.5–212.1)	348,226 (278,361–438,213)	187.6 (150–236.1)	0.34 (0.32–0.35)	<0.001	31,300 (20,321–45662)	16.0 (10.4–23.3)	32,973 (21,241–49098)	17.8 (11.4–26.5)	0.34 (0.33–0.36)	<0.001
High-middle	321,106 (257,461–402170)	113.2 (90.7–141.7)	314,061 (250,449–390,998)	139 (110.9–173.1)	0.66 (0.63–0.69)	<0.001	30,970 (20,318–45277)	10.9 (7.2–16.0)	30,237 (19,871–44444)	13.4 (8.8–19.7)	0.65 (0.62–0.68)	<0.001
Middle	589,241 (470,239–736,964)	107.4 (85.7–134.3)	757,090 (610,845–934,752)	137 (110.5–169.1)	0.79 (0.74–0.84)	<0.001	58,012 (37,419–85397)	10.6 (6.8–15.6)	74,343 (47,962–108471)	13.4 (8.7–19.6)	0.78 (0.74–0.82)	<0.001
Low-middle	485,920 (375,637–620,861)	134.3 (103.8–171.6)	822,200 (651,032–1038,913)	148.7 (117.8–188)	0.33 (0.32–0.34)	<0.001	47,088 (30,079–69923)	13.0 (8.3–19.3)	80,359 (50,736–118,788)	14.5 (9.2–21.5)	0.36 (0.34–0.37)	<0.001
Low	212,479 (160,625–277,327)	136.5 (103.2–178.2)	551,259 (425,498–719,283)	149.2 (115.2–194.7)	0.29 (0.28–0.3)	<0.001	20,817 (12,995–31814)	13.4 (8.3–20.4)	54,322 (81,170–34977)	14.7 (9.5–22.0)	0.31 (0.29–0.32)	<0.001
Region												
Andean Latin America	16,531 (12,302–21509)	134.3 (99.9–174.7)	26,154 (19,829–33983)	151.5 (114.9–196.8)	0.39 (0.38–0.4)	<0.001	1673 (1051–2539)	13.6 (8.5–20.6)	2644 (1615–3937)	15.3 (9.4–22.8)	0.39 (0.36–0.41)	<0.001
Southern Latin America	19,160 (13,921–25464)	144.8 (105.2–192.4)	23,298 (17,436–30739)	151.9 (113.7–200.4)	0.15 (0.13–0.17)	<0.001	1854 (1137–2782)	14.0 (8.6–21.0)	2238 (1405–3390)	14.6 (9.2–22.1)	0.12 (0.06–0.19)	<0.001
Central Latin America	76,464 (60,576–95849)	140.9 (111.6–176.7)	101,315 (80,229–126,709)	155.8 (123.4–194.8)	0.32 (0.31–0.34)	<0.001	7678 (4895–11312)	14.2 (9–20.8)	10,083 (6582–14862)	15.5 (10.1–22.9)	0.29 (0.27–0.32)	<0.001
Tropical Latin America	72,059 (56,891–91879)	150.6 (118.9–192)	82,296 (65,352–102543)	162.7 (129.2–202.7)	0.25 (0.23–0.27)	<0.001	6927 (4367–10243)	14.5 (9.1–21.4)	7856 (5009–11655)	15.5 (9.9–23.0)	0.22 (0.2–0.25)	<0.001
Caribbean	15,225 (11,380–19995)	142.6 (106.6–187.2)	16,437 (12,188–21699)	145.1 (107.6–191.6)	0.06 (0.04–0.08)	<0.001	1465 (920–2197)	13.7 (8.6–20.6)	1601 (972–2404)	14.1 (8.6–21.2)	0.1 (0.06–0.13)	<0.001
High-income North America	137,740 (110,029–171,327)	225.2 (179.9–280.1)	165,400 (132,154–208133)	232 (185.4–292)	0.1 (0.06–0.13)	<0.001	12,935 (8299–18856)	21.1 (13.6–30.8)	15,580 (9961–23087)	21.9 (14.0–32.4)	0.11 (0.08–0.13)	<0.001
Oceania	1910 (1351–2609)	91.3 (64.6–124.7)	3787 (2648–5142)	93.9 (65.7–127.5)	0.09 (0.09–0.1)	<0.001	181 (108–281)	8.7 (5.2–13.5)	358 (206–556)	8.9 (5.1–13.8)	0.08 (0.03–0.14)	0.003
Australasia	8505 (6571–11123)	176.8 (136.6–231.2)	10,545 (8045–13649)	183.8 (140.2–237.9)	0.13 (0.11–0.15)	<0.001	793 (500–1206)	16.5 (10.4–25.1)	986 (593–1478)	17.2 (10.3–25.8)	0.14 (0.08–0.21)	<0.001
High-income Asia Pacific	55,085 (43,280–69734)	130.8 (102.7–165.5)	37,958 (30,407–47464)	145.4 (116.5–181.8)	0.35 (0.32–0.38)	<0.001	5211 (3328–7708)	12.4 (7.9–18.3)	3599 (2275–5283)	13.8 (8.7–20.2)	0.35 (0.31–0.38)	<0.001

(Table 2 continues on next page)

	Prevalence						YLDs					
	Cases (n), 1990	Prevalence (per 100,000 population), 1990	Cases (n), 2021	Prevalence (per 100,000 population), 2021	AAPC, 1990–2021	p value	Cases (n), 1990	YLDs (per 100,000 population), 1990	Cases (n), 2021	YLDs (per 100,000 population), 2021	AAPC, 1990–2021	p value
(Continued from previous page)												
East Asia	257,822 (202,887–318,556)	69.3 (54.5–85.6)	253,843 (197,336–317,815)	104.5 (81.2–130.8)	1.35 (1.28–1.43)	<0.001	25,094 (16,568–37161)	6.7 (4.5–10.0)	24,502 (15,974–36657)	10.1 (6.6–15.1)	1.32 (1.27–1.38)	<0.001
Southeast Asia	136,257 (105,329–171,015)	91.8 (71–115.3)	170,383 (131,216–214,627)	99.6 (76.7–125.5)	0.27 (0.25–0.29)	<0.001	13,912 (8916–20554)	9.4 (6.0–13.9)	17,391 (11,222–25930)	10.2 (6.6–15.2)	0.26 (0.25–0.28)	<0.001
South Asia	472,791 (374,309–599,942)	141.4 (111.9–179.4)	814,847 (648,327–1024,456)	155 (123.3–194.8)	0.3 (0.29–0.31)	<0.001	45,237 (28,675–66413)	13.5 (8.6–19.9)	78,483 (49,747–115,620)	14.9 (9.5–22.0)	0.33 (0.3–0.36)	<0.001
Central Asia	28,758 (21,549–37402)	145 (108.7–188.6)	35,045 (26,354–46216)	158.4 (119.1–208.9)	0.29 (0.26–0.33)	<0.001	2849 (1800–4298)	14.4 (9.1–21.7)	3465 (2219–5208)	15.7 (10–23.5)	0.28 (0.25–0.31)	<0.001
North Africa and Middle East	168,922 (130,309–217,555)	155.1 (119.7–199.8)	271,413 (204,999–350,766)	167.2 (126.3–216.1)	0.23 (0.21–0.26)	<0.001	16,413 (10,552–24203)	15.1 (9.7–22.2)	26,587 (16,704–40017)	16.4 (10.3–24.7)	0.26 (0.23–0.29)	<0.001
Eastern Europe	79,398 (64,669–97299)	168.1 (136.9–206)	61,194 (49,246–75672)	185.5 (149.3–229.3)	0.32 (0.29–0.34)	<0.001	7554 (4913–11278)	16.0 (10.4–23.9)	5777 (3744–8507)	17.5 (11.3–25.8)	0.3 (0.27–0.33)	<0.001
Central Europe	53,029 (42,763–66062)	181.6 (146.5–226.3)	36,229 (29,009–45007)	200 (160–248.2)	0.31 (0.26–0.35)	<0.001	5129 (3326–7456)	17.6 (11.4–25.5)	3492 (2277–5133)	19.3 (12.6–28.3)	0.29 (0.25–0.33)	<0.001
Western Europe	121,066 (95,746–153,493)	147.3 (116.5–186.7)	111,536 (88,225–141,424)	154.7 (122.4–196.2)	0.16 (0.1–0.22)	<0.001	11,423 (7399–16627)	13.9 (9.0–20.2)	10,548 (6768–15568)	14.6 (9.4–21.6)	0.16 (0.1–0.23)	<0.001
Eastern Sub-Saharan Africa	86,671 (65,014–113,556)	139.7 (104.8–183.1)	221,021 (168,376–290,029)	152 (115.8–199.4)	0.29 (0.25–0.32)	<0.001	8509 (5280–13185)	13.7 (8.5–21.3)	21,768 (13,931–32748)	15.0 (9.6–22.5)	0.3 (0.26–0.34)	<0.001
Central Sub-Saharan Africa	23,152 (16,308–314,523)	133.8 (94.2–181.7)	66,069 (47,500–88568)	147 (105.7–197.1)	0.3 (0.29–0.31)	<0.001	2317 (1377–3596)	13.4 (8–20.8)	6616 (4040–10126)	14.7 (9–22.5)	0.3 (0.24–0.35)	<0.001
Western Sub-Saharan Africa	85,579 (65,679–110,931)	143 (109.8–185.4)	251,057 (193,715–322,926)	155.6 (120–200.1)	0.27 (0.25–0.29)	<0.001	8655 (5495–13122)	14.5 (9.2–21.9)	25,417 (16,449–37867)	15.8 (10.2–23.5)	0.27 (0.25–0.28)	<0.001
Southern Sub-Saharan Africa	25,941 (19,887–33595)	151.8 (116.4–196.6)	35,050 (26,691–45262)	160.7 (122.4–207.5)	0.18 (0.15–0.22)	<0.001	2567 (1620–3872)	15.0 (9.5–22.7)	3444 (2206–5144)	15.8 (10.1–23.4)	0.15 (0.13–0.18)	<0.001

Abbreviations as in Table 1.

Table 2: **The prevalence and YLDs of heart failure, and their temporal trends from 1990 to 2021 at the global and regional levels.**

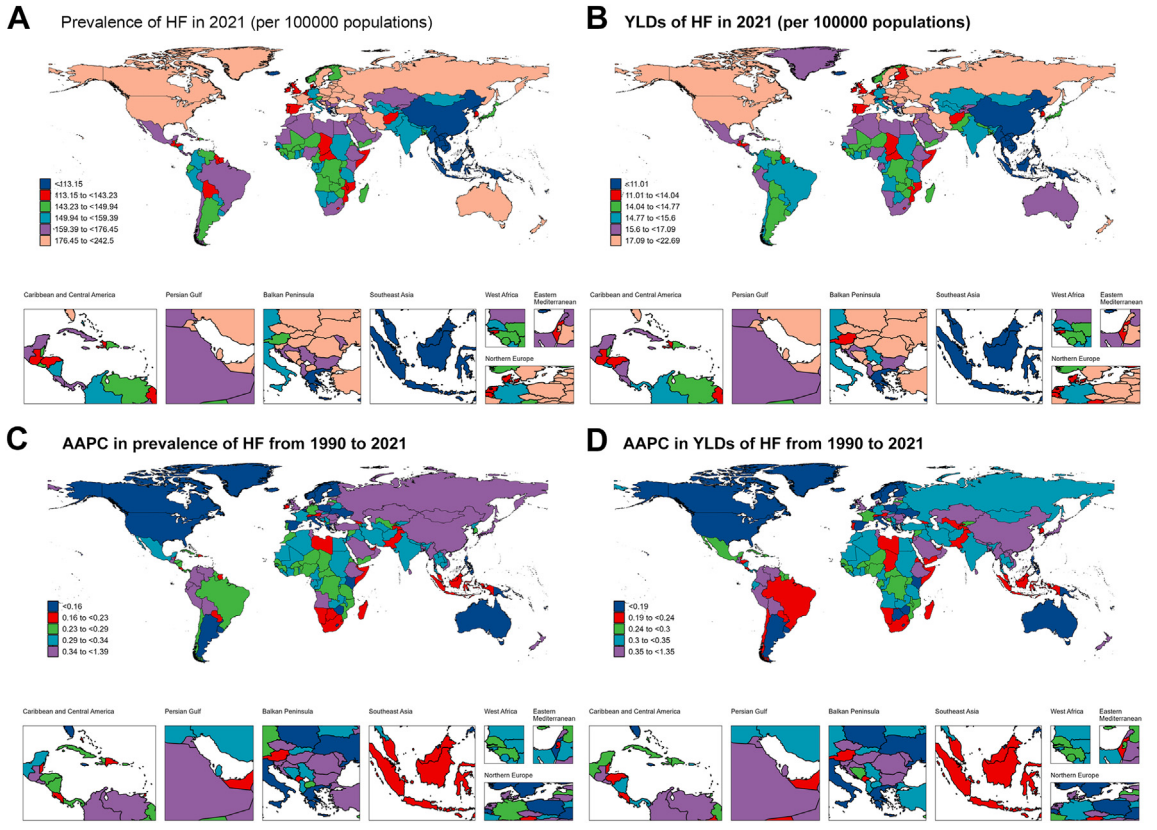

Fig. 2: Global map of 2021 HF prevalence (A) and YLDs (B), and AAPC in prevalence (C) and YLDs (D) from 1990 to 2021. Abbreviations as in Fig. 1.

[37.0–73.0]), North Africa and Middle East, and middle SDI region. The RHD was the leading cause of HF in South Asia (71.4 [51.3–95.5]) and low-middle SDI region (49.9 [35.9–67.4]).

Predictions of HF burden

With the BAPC analysis, we found that the cases of HF prevalence and YLDs showed a rising trend from 2022 to 2030 (Fig. 5; Supplementary Table S4). Globally, there will be 2.98 million (95% CI: 2.48–3.49) HF cases and 292,572 (95% CI: 241,477–343,667) YLDs cases in adolescents and young adults aged 10–24 years in 2030, which increase by 6.8% and 7.4% compared with those in 2021 respectively. During the same period, the prevalence and YLDs rates will increase by 1.6 and 2.2% respectively.

Discussion

For the first time, we scrutinized the cases and rates of prevalence and YLDs among adolescents and young adults aged 10–24 years at the global, regional, and national locations, stratified by SDI from 1990 to 2021. Our results indicate that the global burden of HF among adolescents and young adults was still increasing during the past 32 years. Particularly, the middle SDI quintile countries experienced the most significant upsurge in HF prevalence and YLDs rates, which are currently the highest in high SDI quintile countries. The predominant causes of HF in this age group are cardiomyopathy and myocarditis (CM), congenital birth defects (CBD), and RHD, with a notable decline in the proportion of RHD from 1990 to 2021.

Several studies have demonstrated that the prevalence rate of HF decreased since the early 1990s in the general population, particularly in high-income countries.[3,8] By contrast, our results demonstrated that the prevalence rate of HF increased in the adolescents and young adults aged 10–24 years at both the global and regional levels. This divergent trend may be attributed to the larger population size and distinct etiological factors in older HF patients. People aged 25 years and above constitute over 90% of HF patients, with IHD, hypertensive heart disease (HHD), and COPD being the predominant causes, accounting for over 80% of HF prevalence.[3,22] Partially due to the development and promotion of percutaneous coronary intervention, the prognosis of IHD is greatly improved.[23] Besides, the

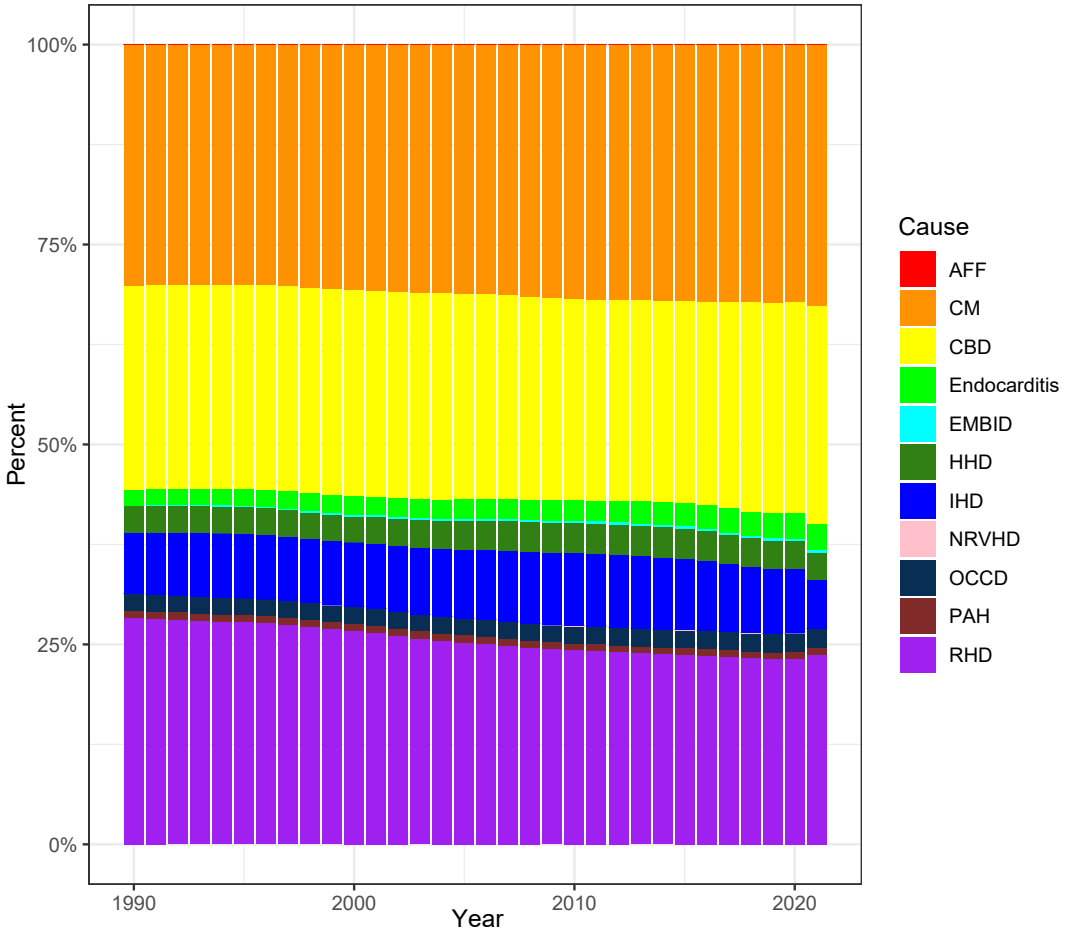

Fig. 3: The proportion of prevalence cases of heart failure due to each cause from 1990 to 2021. AFF, atrial fibrillation and flutter; CM, cardiomyopathy and myocarditis; CBD, congenital birth defects; EMBID, endocrine, metabolic, blood, and immune disorders; HHD, hypertensive heart disease; IHD, ischemic heart disease; NRVHD, non-rheumatic valvular heart disease; OCCD, other cardiovascular and circulatory diseases; PAH, pulmonary arterial hypertension; RHD, rheumatic heart disease.

awareness and treatment rates of primary hypertension have significantly increased during the past three decades.[24,25] Hence, the prevalence rate of HF in the general population decreased during this period, which obscured the increasing trend of prevalence rate of HF in adolescents and young adults, likely due to their smaller population size compared to older patients. It is possible that the medical advancements in treating HF in the elderly have not been paralleled in adolescents and young adults, highlighting an urgent need to enhance the management of HF causes in this population.

Understanding the burden trends of underlying causes is crucial for mitigating the increasing prevalence of HF among adolescents and young adults. We identified CM, CBD, and RHD as the predominant causes of HF. The proportion of RHD decreased from 1990 to 2021, which is consistent with previous reports.[3,26,27] This reduction is likely due to enhancements in hygiene standards and improved access to healthcare, which have led to a decrease in the incidence of rheumatic fever and, consequently, the prevalence of RHD.[28,29] It is imperative to draw attention to regions such as South Asia and Oceania, where RHD remains the leading cause of HF. The urgent need for improvements in basic sanitation and the implementation of secondary prophylaxis for rheumatic fever in these areas cannot be overstated. Such measures are vital to further reduce the burden of RHD and, by extension, HF in this population.

The proportion of CM demonstrated a modest increase from 1990 to 2021. Specifically, over the past three decades, there has been a decline in the incidence rate of myocarditis among individuals aged 10–24 years, likely due to significant improvement in the treatment of myocarditis.[30,31] Concurrently, the rise in the

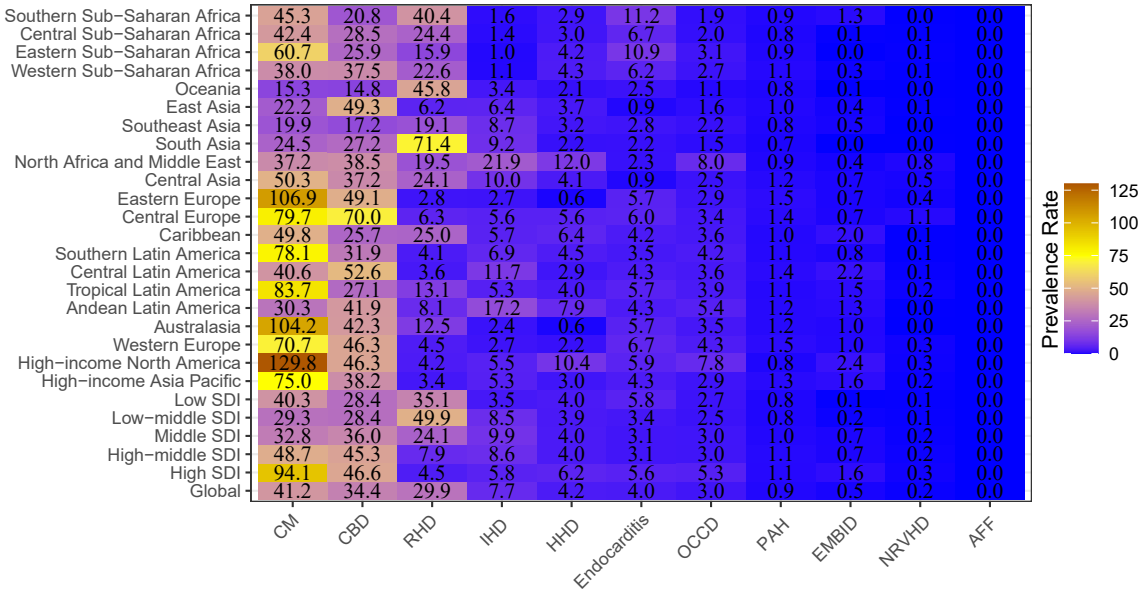

Fig. 4: Ranking of all underlying causes of heart failure according to the prevalence rate due to each cause in 2021, stratified by GBD region. GBD, Global Burden of Disease, Injuries, and Risk Factors Study; SDI, socio-demographic index. Disease abbreviations as in Fig. 3.

prevalence of CM can likely be ascribed to an increased incidence of cardiomyopathies.[32,33] The introduction and refinement of diagnostic technologies, such as the polymerase chain reaction (PCR) and widespread adoption of echocardiography in the 1990s,[34] along with the advent of cardiac magnetic resonance imaging in the 2000s, have enhanced the diagnostic capabilities for cardiomyopathies.[35] In fact, the WHO introduced the contemporary classification of cardiomyopathies based on new diagnostic techniques in 1996.[36,37] These technological advancements likely account for some of the observed increase in the prevalence of cardiomyopathies. It is noteworthy that while progress has been made in pharmacological and invasive therapies for cardiomyopathies in adults, similar advancements in the treatment of adolescents with cardiomyopathies have been limited.[38] This underscores an area of clinical practice that requires further attention and research.

Globally, the proportion of CBD as a cause of HF has remained relatively stable from 1990 to 2021. CHD stands as the predominant form of CBD leading to HF in adolescents and young adults aged 10–24 years. HF represents the terminal stage of CHD, which underscores the importance of CHD prevention. A recent study derived from GBD 2019 data showed CHD was the leading cause of death from non-communicable diseases (NCD) and the leading birth defect with the highest burden of mortality in the population under 20 years old.[39] Therefore, concerted efforts should be directed toward reducing the incidence of CHD, with prenatal examinations being the most efficacious preventative measure. Noteworthily, our results indicate CBD as the leading cause of HF in several regions, including East Asia, Central Latin America, and North Africa and Middle East. This highlights an urgent need for enhanced prenatal education, healthcare, and examination services in these areas.

Social development status could have a substantial impact on the burden of HF. Prior research indicated a decline in HF prevalence rates among all age groups in high SDI countries from 1990 to 2019.[3] However, our study demonstrated that the prevalence of HF in adolescents and young adults of 10–24 years old increased in all the five SDI quintiles from 1990 to 2021, with the largest increase in the middle-SDI quintile countries. Furthermore, with the joinpoint regression analysis, we found the global prevalence rate of HF increased most substantially between 2001 and 2004. These trends may be partially attributable to the changes in the burden of HF in China, where a marked increase in HF prevalence occurred concurrently. This period coincided with China's economic reform and opening-up policies, which catalyzed advancements in economic and medical sciences, thereby improving patient access to hospitals and diagnostic accuracy. In addition, China's accession to the World Trade Organization in 2001 and subsequent rapid economic growth facilitated the detection of a large number of HF cases. Besides, under the one-couple-one-child family planning policy, some pregnant women may avoid prenatal examinations when having a second or third child, which might lead to an increase in the incidence of CHD.

Noteworthily, the relatively low prevalence of HF in the low SDI countries contrasts with the highest

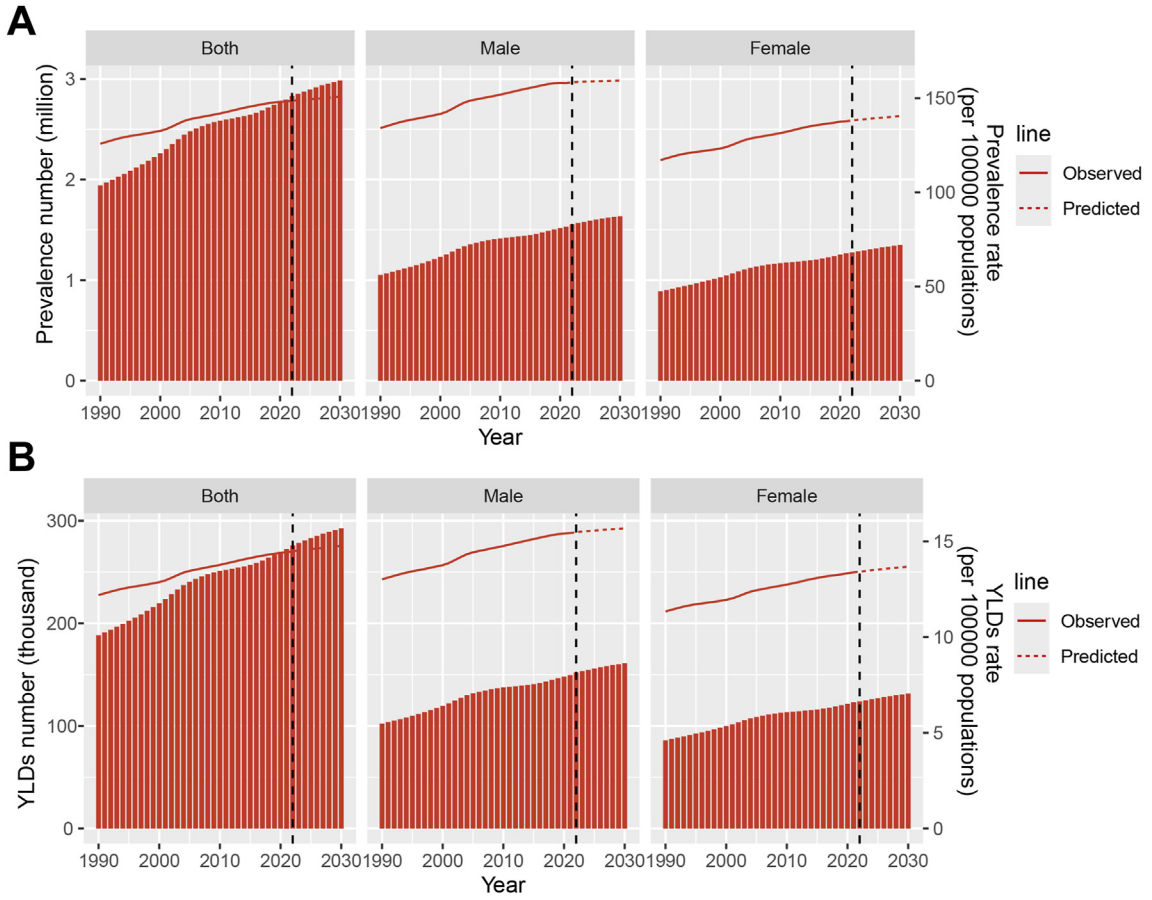

Fig. 5: Prevalence (A) and YLDs (B) of heart failure from 1990 to 2021, and their predictions to 2030, stratified by gender. The columns show the case numbers. The dark red lines show the rates. The known data from 1990 to 2021 and predicted data from 2022 to 2030 were divided by a black dashed line. YLDs, years lost due to disability.

prevalence of HF in the high SDI countries. With advances in medical and surgical management over the past three decades, most children born with CHD are expected to survive to adulthood, particularly in high-income countries.[39] The expertise of healthcare providers and the availability of advanced medical technology in high SDI countries facilitate early diagnosis and superior treatment of HF, contributing to the observed increase in prevalence among adolescents and young adults with CHD. Raissadati et al. conducted a comprehensive study of 10 635 patients who underwent congenital heart surgery in Finland, revealing that 20% of these patients required HF medications during long-term follow-up.[40] In contrast, under-reporting may occur in low SDI countries, where healthcare systems may be inadequate. With the advancement of socio-economic and healthcare conditions, more efficient detection and management of HF may lead to an increase in the prevalence of HF in adolescents and young adults in the future.

Of note, obesity, type 2 diabetes, and hypertension have emerged as significant global health concerns in adolescents and young adults over the past three decades, irrespective of a country's wealth.[41] The global prevalence of metabolic syndrome was 4.8% for adolescents in 2020,[42] and such metabolic conditions in adolescence are predictive of HF in later life. Furthermore, a study by Robertson et al. enrolled 1,668,893 adolescent men and revealed that obesity in adolescent men may be a potential cardiomyopathy risk in midlife.[43] However, the role of metabolic syndrome in HF in adolescents and young adults of 10–24 years old has been less extensively evaluated, given it may take several years for the metabolic syndrome to result in HF. Our study observed that IHD was the third leading cause of HF in young adults aged 20–24 years, which may highlight the promoting effect of metabolic syndrome in HF in young adults.

Regarding gender differences, the increased rate of prevalence and proportion of underlying causes of HF were comparable between males and females aged 10–24 years. Nonetheless, the prevalence of HF was higher among men compared to females. Previous

studies suggest that the overall prevalence of HF in males is higher than that in females before the age of 80 years.[44] Estrogen is known to confer broad cardiovascular protection, and fertile women tend to exhibit a less severe inflammatory and immune response to myocardial injury, which correlates with a lower incidence of HF.[45] Besides, females were less likely to undergo diagnostic testing or receive health care in accordance with established guidelines compared to males.[46] This disparity may suggest the presence of gender inequalities in the management of HF among adolescents and young adults.

The overall burden trend of YLDs was similar to that of prevalence. Both the number and rate of HF-related YLDs in adolescents and young adults aged 10–24 years increased markedly from 1990 to 2021, diverging from the trend observed in the elderly population.[3] The largest increase in the YLDs occurred in countries in the middle-SDI and high-SDI quintile countries. This suggests that the burden of HF in these regions may have been previously underestimated, as indicated by the relatively low rates of YLDs. Consequently, it is imperative for these countries to enhance the accessibility and quality of diagnosis and treatment for HF in the adolescent and young adult population.

Our study has implications for further management of HF. The current clinical trials of medications for HF are mainly carried out in relatively older patients. It is necessary to verify their efficacy in adolescents and young adults aged 10–24 years, given the rates of prevalence and YLDs were still increasing while they were decreasing in the older patients in high-SDI quintile countries during the same period. Furthermore, the underlying causes of HF in adolescents and young adults varied greatly from those in the general population. To reduce the burden of HF, it could be effective for low-income and middle-income countries to popularize prenatal examinations and improve basic sanitation conditions. Prenatal diagnosis, including gene-based diagnosis, may help to further reduce the burden of hereditary heart disease and CHD in the high-income countries.

Our study has several limitations. First, the accuracy of our analysis is hindered by varied collection methods and reporting standards of data. Particularly, it is not possible to use a universal definition of HF when the data were collected for GBD given the definition of HF has been evolving over the past three decades, in part due to the introduction of diagnostic techniques, such as BNP. Therefore, the trends of HF may be limited by changes in HF definition. Second, like all GBD assessments, the accessibility and quality of original data vary markedly among nations, particularly when it comes to health information for adolescents and young adults. Third, the prevalence rates of HF among adolescents and young adults were possibly under-reported in low-income countries and middle-income, potentially skewing our findings. Fourth, while we presented correlations between the HF burden and the SDI, these correlations should not be interpreted as causal relationships. Fourth, because there are differences in HF causes between adolescents and young adults according to our analysis, there may have been differences in burden between older and younger people in this age range if they were analyzed separately. Last but not least, because the GBD database does not provide data on HF-related mortality rates, it is not possible for us to analyze HF-related mortality in adolescents and young adults.

The burden of HF in adolescents and young adults aged 10–24 years was still increasing across the globe, which may be obscured by the burden trend of general population. According to different underlying causes of HF, both high-income and low- and middle-income countries need to better prevent HF in adolescents and young adults.

Contributors

AT and CZ designed the study. CY, YJ, ZJ, YM, and XB analyzed the data and performed the statistical analyses. CY and YJ drafted the initial manuscript. All authors reviewed the drafted manuscript and approved the final version. All authors have directly accessed and verified the underlying data reported in the manuscript.

Data sharing statement

All data and statistical code will be made available on request to the corresponding author.

Editor note

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Declaration of interests

There are no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102998.

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