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Sex-specific trends in the global burden and risk factors of atrial fibrillation and flutter from 1990 to 2021

Xiaodong Peng[1,2,5], Jue Wang[1,2,5], Chen Tang[3,4,5], Liu He[1,2], Jiangtao Li[1], Shijun Xia[1,2], Xiangyi Kong[1,2]✉, Ning Zhou[1,2], Deyong Long[1,2], Caihua Sang[1,2], Xin Du[1,2], Jianzeng Dong[1,2] & Changsheng Ma[1,2]✉

Significant sex disparities exist in the burden of atrial fibrillation and flutter. However, comprehensive and systematic analysis of its global trend by sex is scarce. The Global Burden of Disease Study 2021 was used as data source for analysis. Sex-specific prevalence, incidence, disability-adjusted life years (DALY), and mortality rates per 100,000 population from atrial fibrillation and flutter were estimated using the Bayesian meta-regression method. Temporal trends of average annual percent change (AAPC) of age-standardized and age-specific burdens across age bands were evaluated using the joinpoint model stratified by socio-demographic index (SDI). Sex differences in trends were tested using pairwise comparison. From 1990 to 2021, the global age-standardized DALY rate [from 109.93 (95% uncertainty interval, 88.5 to 134.72) to 112.05 (93.3 to 135.28), *P* < 0.001], age-standardized mortality rate [from 4.20 (3.65 to 4.59) to 4.44 (3.94 to 4.81), *P* < 0.001] for atrial fibrillation and flutter significantly increased in males, while the age-standardized incidence rate decreased from 58.0 (44.98 to 75.8) to 57.11 (46.19 to 72.14) in males (*P* < 0.001). Countries with low and low-middle SDI exhibited significant increases in age-standardized prevalence and incidence rates in both females and males (all *P* < 0.001), with a faster increase in females. Across all age bands, a faster increase in mortality was observed among males, while females under age bands of 50 years showed a higher increase in prevalence and incidence on a global scale compared to males. High systolic blood pressure was the predominant risk factor contributing to atrial fibrillation and flutter-related DALY. Notably, the impact of high body-mass index on DALY of atrial fibrillation and flutter was increasing fast over last three decades, especially in males. Although the global burden of atrial fibrillation and flutter has substantially increased, disparities exist across different sexes, age bands, and countries with different socio-demographic status.

Keywords Atrial fibrillation, Atrial flutter, Global burden of disease, Epidemiology, Risk factors

Abbreviations

AAPC	Average annual percent change
DALY	Disability-adjusted life years
SDI	Socio-demographic index
YLD	Years lived with disability
YLL	Years of life lost

Atrial fibrillation is a major global health concern with well-documented sex disparities in its epidemiology[1]. The Framingham Heart Study reported an age-adjusted prevalence of atrial fibrillation nearly twice as high in men (96.2 per 1,000 person-years) compared to women (49.4 per 1,000 person-years) over a 50-year observation

[1]Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, No. 2, Anzhen Road, Chaoyang District, Beijing 100029, China. [2]National Clinical Research Center for Cardiovascular Diseases, Beijing, China. [3]Renal Division, Peking University First Hospital, Peking University Institute of Nephrology, Beijing, China. [4]Key Laboratory of Renal Disease, Key Laboratory of Chronic Kidney Disease Prevention and Treatment (Peking University), Ministry of Health of China, Ministry of Education, Beijing, China. [5]Xiaodong Peng, Jue Wang and Chen Tang contributed equally to this work. ✉email: xiangyikong@163.com; chshma@vip.sina.com

period[2]. Similar disparities have been observed in European and Asian populations[3,4]. While men generally show a higher incidence of atrial fibrillation, women with the condition often face higher rates of complications, such as stroke, heart failure, and mortality[5,6].

The mechanisms underlying these sex disparities are complex, involving a web of risk factors at individual, familial, community, and societal levels. Behavioral and metabolic risk factors play crucial roles[7,8], alongside differences in healthcare access and quality[9,10]. Despite the critical importance of understanding sex disparities in atrial fibrillation epidemiology and associated risk factors, there is a notable lack of studies offering a global perspective on this issue, with most published studies conducted in specific countries or regions[2–4]. While the Global Burden of Disease Study 2021 provides an updated and comprehensive dataset on AF[11], existing analyses have primarily focused on overall trends without exploring sex-specific differences in detail.

Our research aims to fill this gap by leveraging the Global Burden of Disease Study 2021 database, which provides standardized methods for quantifying the burden of diseases and risk factors across populations. By evaluating the global burden and attributable risk factors for atrial fibrillation and flutter with a focus on sex differences, we aim to provide comprehensive insights that can inform public health policies and clinical practices worldwide.

Methods

Data source

The Global Burden of Disease Study 2021 project produced estimates of prevalence, incidence, mortality, years of life lost (YLL), years lived with disability (YLD) and disability-adjusted life years (DALY) for 371 diseases and injuries across 204 countries and territories from 1990 to 2021[12,13]. Additionally, 88 risk factors and their risk-outcome pairs were included to estimate the risk attributable burdens[14]. This project adheres to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations, and its analytic procedures have been detailed in previous reports[12–14]. Briefly, Global Burden of Disease Study 2021 gathered extensive data from various sources, including surveys, censuses, vital statistics, and other health-related data, which were standardized for disease burden estimation.

Estimation of global burden of atrial fibrillation and flutter

The data were processed under the Bayesian meta-regression model framework, using DisMod-MR 2.1 modelling tool, to estimate the non-fatal burden of atrial fibrillation and flutter. A detailed description of the Bayesian meta-regression model and its prior assumptions can be found in the supplementary materials. Hospital and outpatient administrative data from certain geographies were excluded if they were implausibly low.

- *YLD estimation*: The unadjusted YLD were equal to the prevalence estimated from the DisMod-MR model multiplied by the disability weights for each atrial fibrillation and flutter-related sequela. Additionally, a micro-simulation adjusting for comorbidities was performed to generate the final estimate of comorbidity-adjusted YLD.
- *Mortality estimation*: Vital registration data were analyzed using the Cause of Death Ensemble modelling (CODEm) model to estimate the atrial fibrillation and flutter-related mortality identified by the corresponding *International Classification of Disease* codes (details in supplementary materials). An estimation model that integrated longitudinal prevalence and excess mortality data, combining DisMod-MR model and CODEm, was employed to mitigate the impact of changing death certification patterns[13]. This approach aimed to produce more accurate mortality estimates by adjusting for covariates (details in supplementary materials).
- *YLL calculation*: Calculated by multiplying the number of estimated atrial fibrillation and flutter-related deaths by the predicted life expectancy by age, sex, location and year.
- *DALY estimation*: Computed by adding YLL and YLD for each age, sex and location.

Estimation of risk factor attributable DALY rate of atrial fibrillation and flutter

A causal web of hierarchically organized risk factors based comparative risk assessment framework was reported in a previous study[14], and the definitions of risk exposures are listed in supplementary materials. Six risk factors from three categories of risk exposures, as discussed and determined by the Global Burden of Disease Study Scientific Council, were analyzed for their attributable DALY rate on atrial fibrillation and flutter:[14].

- *Environmental/occupational risks*: Lead exposure.
- *Behavioral risks*: Smoking, high alcohol use and diet high in sodium.
- *Metabolic risks*: High systolic blood pressure and high body-mass index.

The attributable DALY rate of a given risk factor refers to the potential reduction in outcome-related DALY if past population exposure had shifted to an ideal level of that risk factor. The estimation of risk attributable DALY—for risk-outcome pairs was calculated by multiplying the total DALY by the population attributable fraction. Population attributable fraction represents the proportion of risk that would be reduced in a given year if past exposure to a certain risk factor was reduced to the theoretical minimum risk exposure level.

Statistical analysis

Given that the data sources are derived from scientific studies reported with uncertainty, all estimates were generated by predicting 1,000 draws based on the variance-covariance matrix[13]. Results were presented as the mean of these draws, with 95% uncertainty intervals (UI, the 2.5th and 97.5th percentiles).

- *Age-standardization*: Prevalence, incidence, DALY, and mortality rates were calculated using the Global Burden of Disease Study reference population[13]. All rates were reported per 100,000 population.
- *The sex-specific burden analysis*: Evaluated by analyzing the male to female ratio of age standardized rates in terms of prevalence, incidence, DALY and mortality associated with atrial fibrillation and flutter.

The temporal trend in age-standardized burdens for atrial fibrillation and flutter and its attributable risk factors were analyzed using the Joinpoint regression models. The Joinpoint Regression Program software (version 4.9.1.0, National Cancer Institute, USA) was employed for this purpose, evaluating time trends by assessing the average annual percent change (AAPC) of the age-standardized rates. Initially, the joinpoint model established the minimum number of joinpoints, typically at zero, representing a straight line. The model then tests whether additional joinpoints should be added, up to a predetermined maximum, based on statistical significance. The 95% confidence intervals (CI) of AAPC were estimated using the Parametric method. This helped ascertain if perceived shifts in trends were statistically meaningful. Each trend between joinpoints was tested using Monte Carlo methods, with the significance level adjusted through a Bonferroni correction[15]. Trends were classified as increasing or decreasing based on whether the AAPC was positive or negative. The sex differences in the trends of disease burdens were compared by analyzing the differences in the AAPC between females and males using pairwise comparison[16].

The comparison of atrial fibrillation and flutter burden and its risk factors attributable burden between females and males was conducted across:

- Various age bands (in five-year intervals).
- Five socio-demographic index (SDI) regions.
- Seven world regions, and at the global level.

Additionally, Spearman's rank correlation (Spearman's ρ) was performed to evaluate the association of SDI with age-standardized burdens of atrial fibrillation and flutter, as well as the risk factors attributable DALY rates. The introduction and methods for calculating SDI are detailed in supplementary materials. The proportional burden of each risk factor was calculated by dividing the attributable burden of that factor by the total burden for atrial fibrillation and flutter.

R software (version 4.3.2) was used for the statistical analyses. A two-sided P value of less than 0.05 was considered statistically significant.

Results

In 2021, the age-standardized prevalence rate, age-standardized incidence rate, age-standardized DALY rate, and age-standardized mortality rate per 100,000 population of atrial fibrillation and flutter in females were 529.12 (95% UI, 430.79 to 663.14), 47.26 (95% UI, 37.38 to 60.87), 92.24 (95% UI, 76.84 to 111.24), and 4.29 (95% UI, 3.53 to 4.80), respectively. For males, these rates were 728.88 (95% UI, 601.91 to 895.81), 57.11 (95% UI, 46.19 to 72.14), 112.05 (95% UI, 93.30 to 135.28), and 4.44 (95% UI, 3.94 to 4.81), respectively (supplementary Table 1).

Sex disparities in the burden of atrial fibrillation and flutter across regions in 2021

There is a regional disparity in the sex distribution of the atrial fibrillation and flutter burden. The largest difference between two sexes in age-standardized DALY rate for atrial fibrillation and flutter was in the United States, where the male-to-female ratio was 4.65. Conversely, the smallest ratio of 0.41 was observed in South Africa (Fig. 1). Male-to-female ratios across 204 countries and territories in age-standardized prevalence rate (supplementary Fig. 1), age-standardized incidence rate (supplementary Fig. 2), and age-standardized mortality rate (supplementary Fig. 3) are provided in the supplementary materials.

Sex disparities in the burden of atrial fibrillation and flutter across socio-demographic index in 2021

The age-standardized prevalence rate and DALY rate of atrial fibrillation and flutter varied across areas with different SDI. The highest prevalence and DALY rates were observed in countries with a high SDI for both females and males (supplementary Table 1). For instance, at the country level, the highest prevalence rates were found in Sweden, with 1211.57 (95% UI, 898.26 to 1562.27) in females and 1852 (95% UI, 1421.38 to 2340.23) in males (supplementary Fig. 5).

A significant positive correlation was observed between the SDI and the male-to-female ratio of age-standardized prevalence rate (Spearman's $\rho = 0.513$, $P < 0.001$), age-standardized incidence rate (Spearman's $\rho = 0.373$, $P < 0.001$), and age-standardized DALY rate (Spearman's $\rho = 0.273$, $P < 0.001$), but not for age-standardized mortality rate (supplementary Fig. 6). Furthermore, the prevalence rate and DALY rate of atrial fibrillation and flutter were higher in older age bands for both females and males (supplementary Table 2).

Sex disparities in temporal trend of atrial fibrillation and flutter burdens by regions and socio-demographic index (1990–2021)

The global age-standardized prevalence rate of atrial fibrillation and flutter did not show an increasing trend. However, there were regional disparities. In countries with low and middle SDI, the age-standardized prevalence rate of atrial fibrillation and flutter increased significantly from 1990 to 2021. In contrast, countries with high and high-middle SDI presented a change in the age-standardized prevalence rate that aligned with the global trend (supplementary Table 1). Notably, despite both females and males experiencing a significant increase in the age-standardized incidence rate in low and low-middle SDI countries, the increment was larger in females

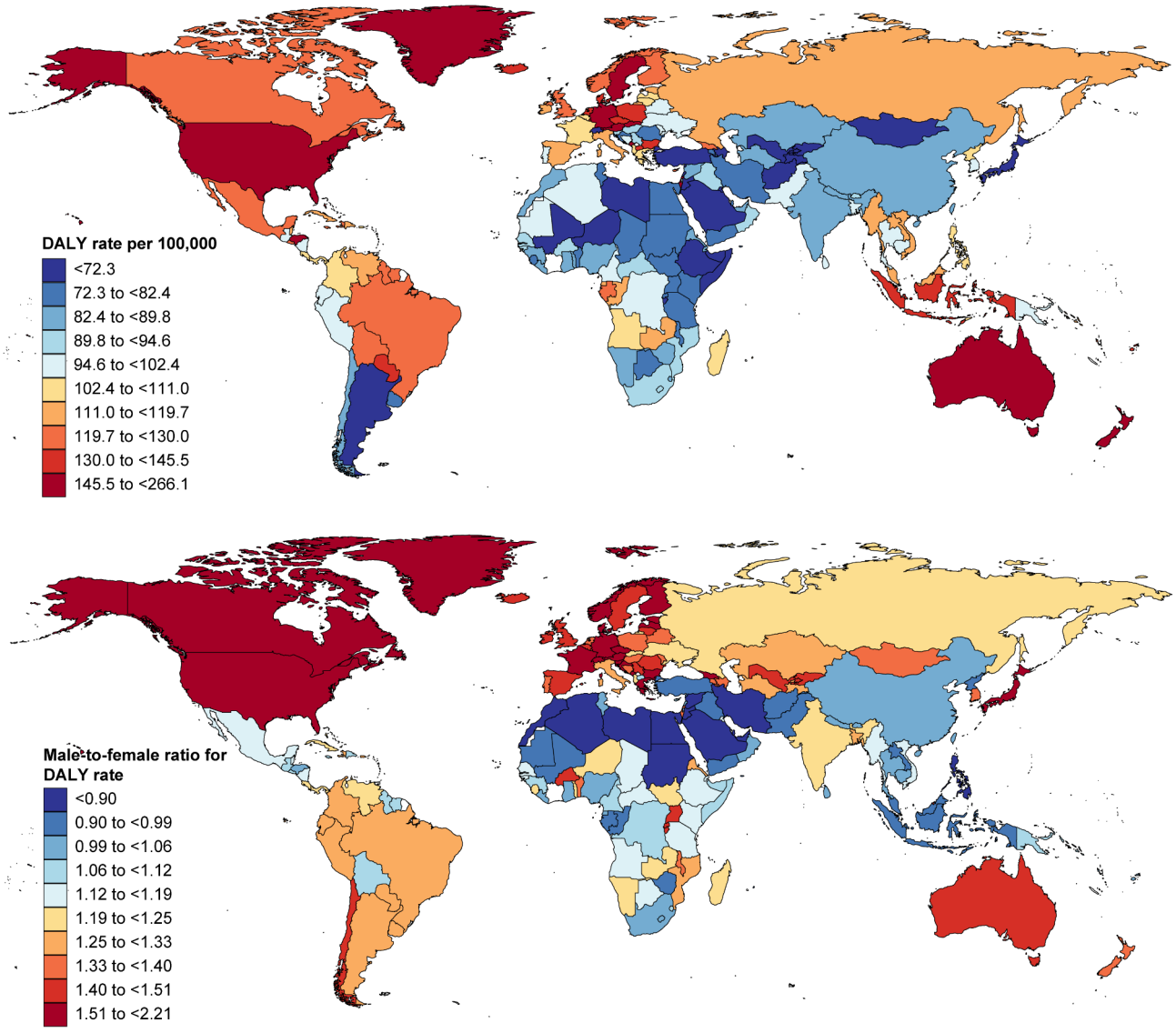

Fig. 1. Age-standardized disability adjusted life years (DALY) rate and male-to-female ratio for DALY rate of atrial fibrillation and flutter in 204 countries and territories in 2021.

compared to males (Fig. 2), with AAPC difference between females and males of 0.09 (95% CI, 0.06 to 0.12, $P < 0.001$) in low SDI countries and 0.05 (95% CI, 0.04 to 0.06, $P < 0.001$) in low-middle SDI countries.

At the super-region level, an increasing trend in the age-standardized prevalence rate was observed in both females and males in Central Europe, Eastern Europe, and Central Asia, South Asia, Southeast Asia, East Asia, Oceania, and Sub-Saharan Africa. The increasing speed seemed faster in female population in South Asia and Sub-Saharan Africa, and in male population in the other super-regions (supplementary Table 1).

The global trend in the age-standardized DALY rate increased more significant in males rather than females (Fig. 3). However, similar increasing trends were observed in countries with low and low-middle SDI for both population (supplementary Table 1). At the super-regions level, both females and males in North Africa and the Middle East experienced an increasing trend in the age-standardized DALY rate of atrial fibrillation and flutter, with a higher rate observed in females (AAPC difference between females and males, 0.20; 95% CI, 0.03 to 0.37, $P = 0.022$). A similar trend was observed in age-standardized mortality rates in countries with low and low-middle SDI (supplementary Fig. 4).

Sex disparities in age-specific trends of atrial fibrillation and flutter burden (1990–2021)

Regarding the age specific epidemic trend of prevalence and incidence rate of atrial fibrillation and flutter globally, higher increasing trend was observed in female population among age intervals under 50 years (supplementary Table 2). Conversely, a consistent decreasing trend of prevalence rate was found in both females and males among age bands over 75 years. Meanwhile, a faster increase in mortality was observed among male population across all age bands.

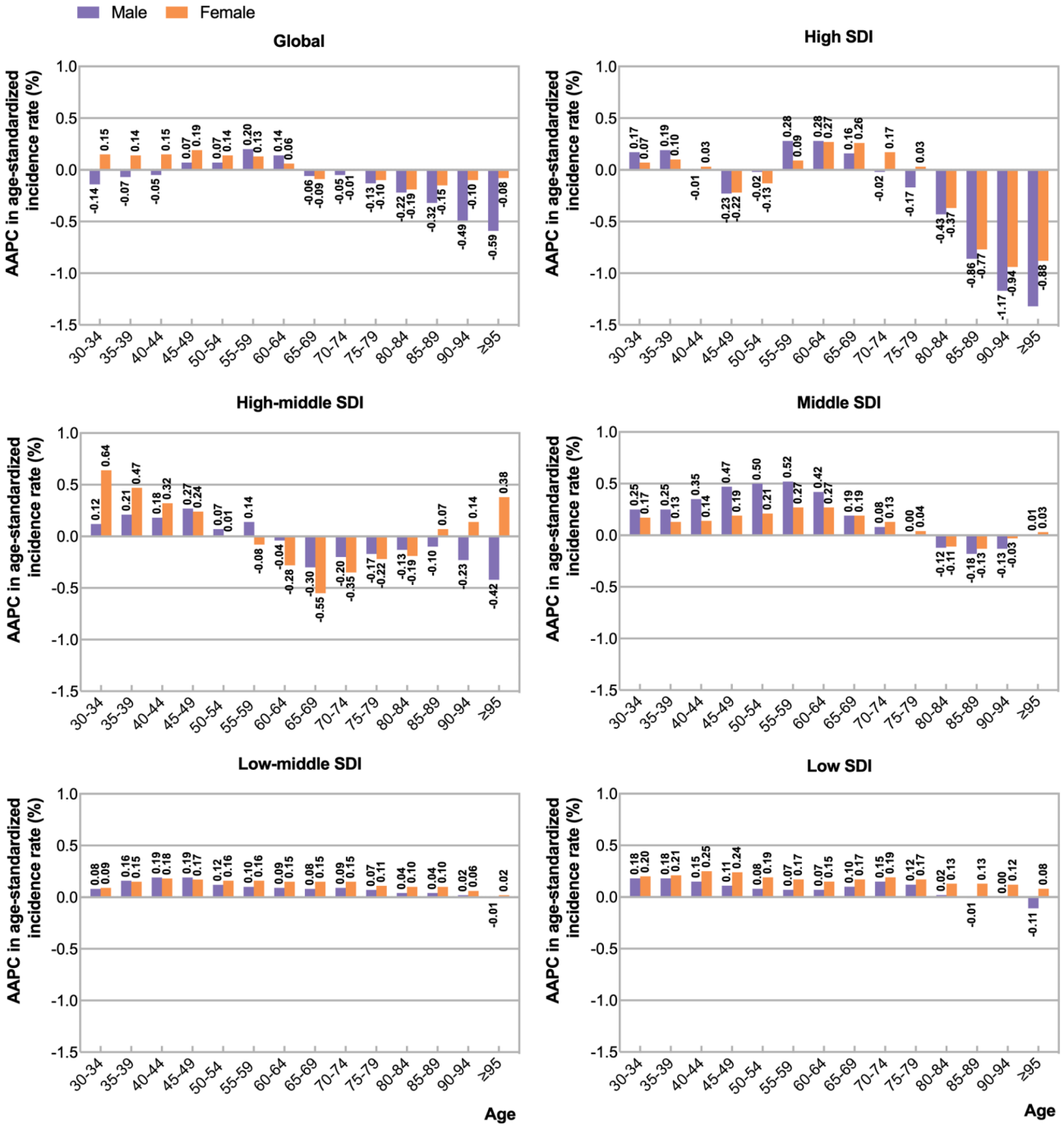

Fig. 2. Gender-specific average annual percent change (AAPC) in incidence rate of atrial fibrillation and flutter by age and socio-demographic index (SDI), from 1990 to 2021.

Sex disparities in attributable risk factors for atrial fibrillation and flutter in 2021

Globally, metabolic risk factors contributed most to the DALY rate of atrial fibrillation and flutter, followed by behavioral risk factors (Fig. 4). High systolic blood pressure consistently ranked as the top risk factor for the DALY of atrial fibrillation and flutter, accounting for 29.1% (95% UI, 10.3 to 46.5) and 30.9% (95% UI, 11.1 to 48.6) of total atrial fibrillation and flutter DALYs in 2021 for all-age males and females, respectively.

The second and third ranking risk factors are also observed globally by sex. In females, high body-mass index and high-sodium diet were the second and third ranking risks, whereas in males, smoking and high body-mass index occupied these positions. The influence of these risk factors on age-standardized DALY varies across countries with different SDI (supplementary Table 3). In high SDI countries, the top three risk factors in 2021 for both females and males were high systolic blood pressure, high body-mass index, and high alcohol use. Conversely, in low SDI countries, high systolic blood pressure remained the top risk factor for both females and

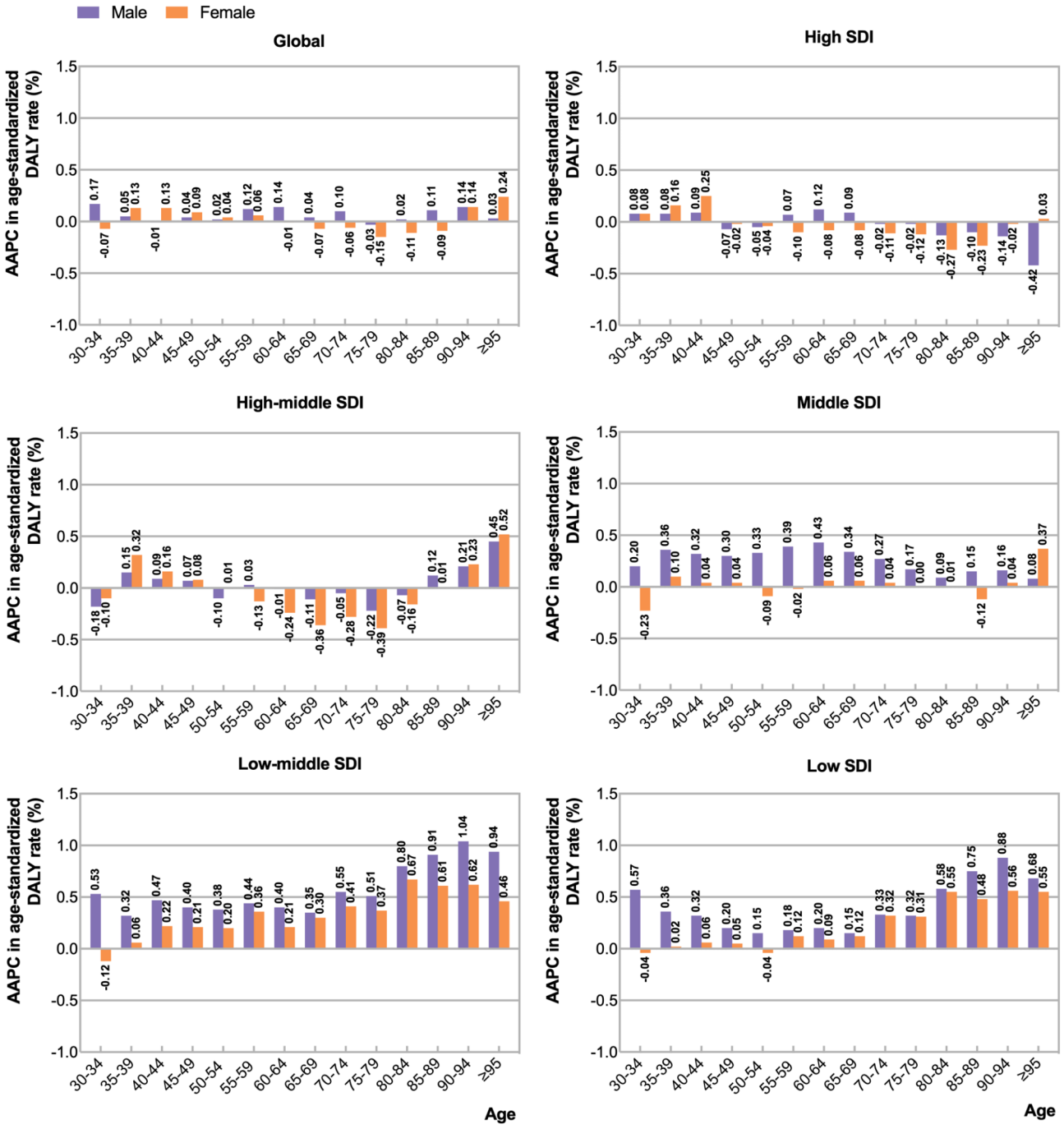

Fig. 3. Gender-specific average annual percent change (AAPC) in disability adjusted life years (DALY) rate of atrial fibrillation and flutter by age and socio-demographic index (SDI), from 1990 to 2021.

males, followed by lead exposure, with the third risk factor changing into smoking in males and high body-mass index in females (supplementary Table 3).

Sex disparities in regional variations of risk factors for atrial fibrillation and flutter in 2021

Correlations between SDI and risk attributable age-standardized DALY rates of atrial fibrillation and flutter were moderate to strong with respect to smoking (Spearman's $\rho = 0.428$, $P < 0.001$), high alcohol use (Spearman's $\rho = 0.619$, $P < 0.001$), lead exposure (Spearman's ρ=-0.531, $P < 0.001$), high systolic blood pressure (Spearman's $\rho = 0.500$, $P < 0.001$), and high body-mass index (Spearman's $\rho = 0.647$, $P < 0.001$) in males, while only a weak correlation between SDI and lead exposure (Spearman's $\rho = 0.143$, $P < 0.001$) was found in females (supplementary Fig. 7).

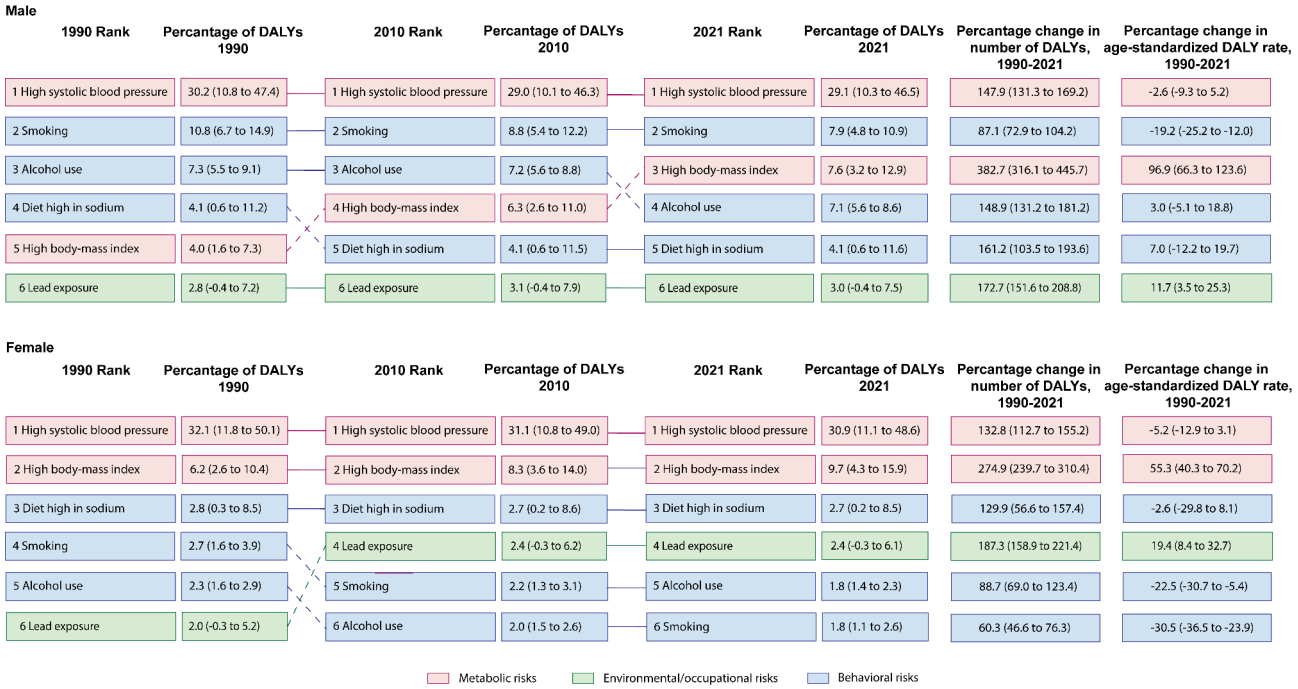

Fig. 4. Gender-specific proportion of all-age disability adjusted life years (DALY) rate of atrial fibrillation and flutter attributable to risk factors globally, from 1990 to 2021.

Sex disparities in temporal trends of risk factors for atrial fibrillation and flutter (1990–2021)

From 1990 to 2021, the global age-standardized DALY rates of atrial fibrillation and flutter attributable to high systolic blood pressure and smoking decreased in both females and males. However, there were rising trends of high body-mass index and lead exposure attributable DALY rates in both females and males, and rising trends of high alcohol use and a high-sodium diet attributable DALY rates in males (Fig. 4 and supplementary Table 3).

Over the past three decades, temporal trends for risk factor attributable DALY rates varied between females and males across different SDI status and age groups. In countries with low and low-middle SDI, the age-standardized DALY rates of atrial fibrillation and flutter attributable to high systolic blood pressure, high body-mass index, and high alcohol use have significantly increased, especially in males (Fig. 5 and supplementary Table 3). For young females in the age intervals of 35 to 44 years, high systolic blood pressure and high body-mass index attributable DALY rate rose much faster compared to males (Fig. 6 and supplementary Table 4).

Discussion

Based on data from the Global Burden of Disease Study 2021, several key findings were identified (Table 1). The global burden of atrial fibrillation and flutter significantly increased from 1990 to 2021, particularly in countries with low and low-middle SDI. Over 30-year period, prevalence and incidence of atrial fibrillation and flutter decreased in older age intervals but increased in younger intervals, particularly females below 50 years old. The rising trends were faster among females in terms of prevalence and incidence rates, whereas males experienced higher increase in DALY and mortality rates. Among risk factors, metabolic risks contributed mostly to DALY rates for both sexes. The impact of metabolic and behavioral risks was notably correlated with socio-demographic status in males but not females. While burdens attributable to environmental and behavioral risks decreased, DALY rates attributed to metabolic risks increased. These findings highlight the growing burden of atrial fibrillation and flutter and underscore sex-specific disparities.

Increasing burdens of atrial fibrillation and flutter

Regional disparities in the age-standardized prevalence and incidence rates of atrial fibrillation and flutter from 1990 to 2021 were evident. Low-SDI countries experienced notable increases, consistent with previous findings that poor financial resources, such as unemployment[17] and low household income[18], are associated with higher incidence of atrial fibrillation. Conversely, high-SDI countries exhibited stable trends, exemplified by data from the US Centers for Medicare & Medicaid Services, which reported a consistent 9% prevalence among the US American Indian and Alaska Native population from 2015 to 2019[19].

Compared to previous studies, our analysis found that females in low to low-middle SDI regions experienced a higher increase in prevalence and incidence than males. The results from Atherosclerosis Risk in Communities study identified an education-sex interaction, where females with the lower education level had a higher risk of atrial fibrillation, an association not seen in males[18]. Similarly, females in higher-deprivation areas had a higher risk of atrial fibrillation hospitalization, a trend not observed in males[20]. These disparities warrant more active

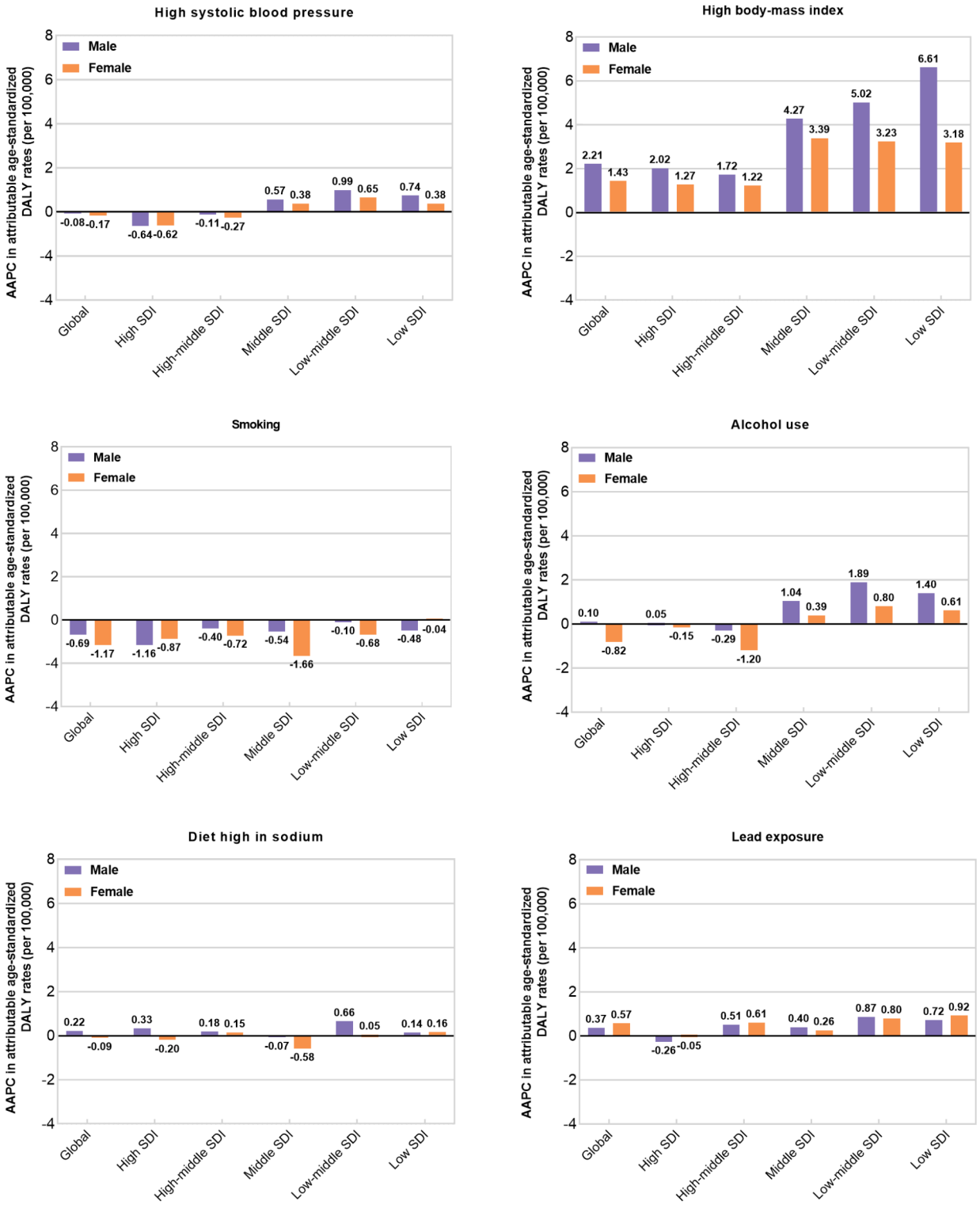

Fig. 5. Gender-specific average annual percent change (AAPC) in proportion of age-standardized disability adjusted life years (DALY) rate of atrial fibrillation and flutter attributable to risk factors by socio-demographic index (SDI), from 1990 to 2021.

interventions. Improving socio-economic status, such as through education, may be effective in reducing atrial fibrillation risk among females[21].

Atrial fibrillation, an age related disease, imposes a growing burden with population aging[22]. The Framingham Heart Study reported an almost three-fold increase in the prevalence of atrial fibrillation over the past five decades[2]. In Denmark, the lifetime risk of atrial fibrillation increased by 6.7% from 2000-2010 to 2011-2022[23].

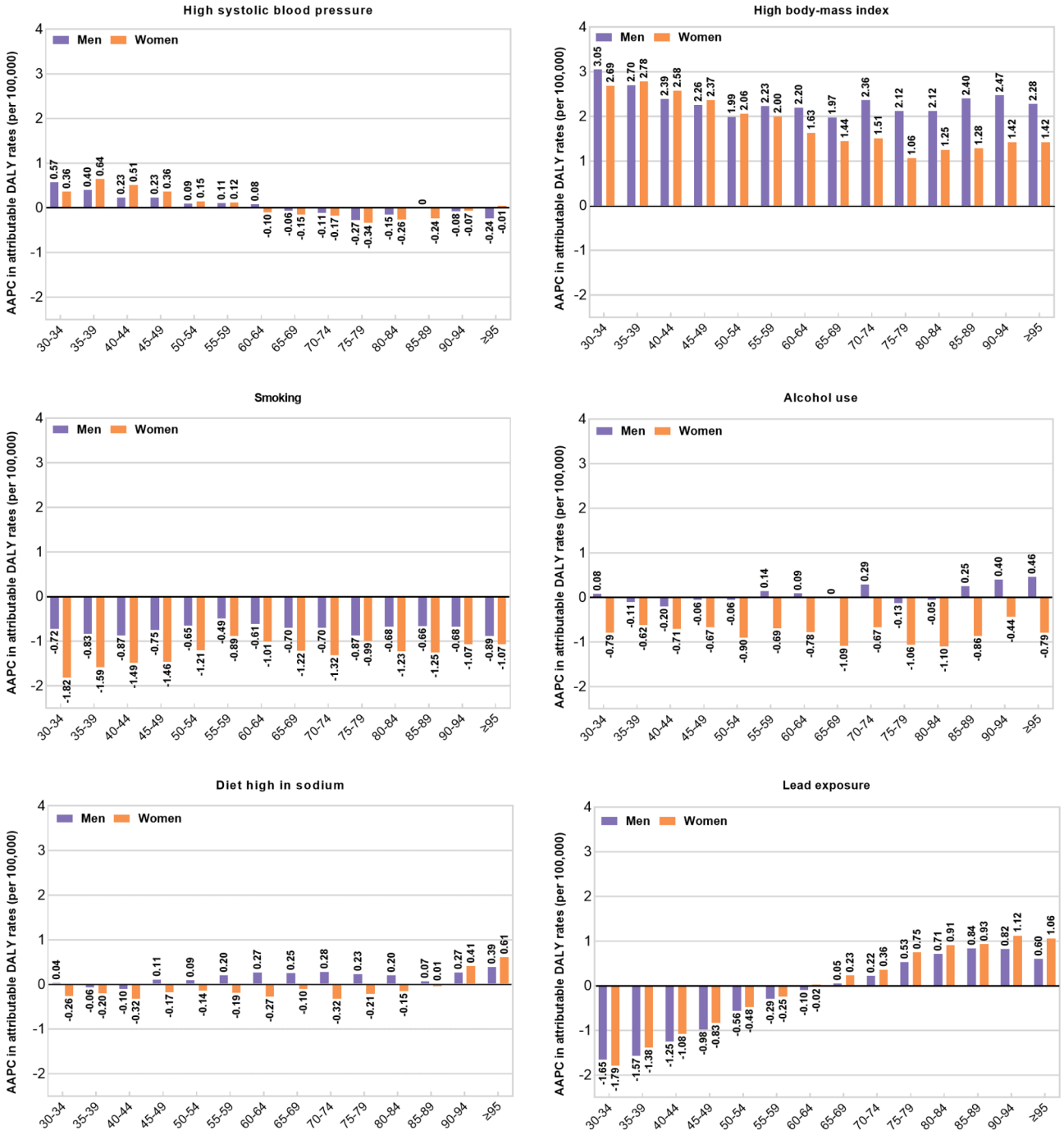

Fig. 6. Gender-specific average annual percent change (AAPC) in proportion of age-standardized disability adjusted life years (DALY) rate of atrial fibrillation and flutter attributable to risk factors by age, from 1990 to 2021.

Our analysis revealed that while prevalence and incidence decreased among older-age population, it increased among younger-age population. Similar trends were observed in Norway, where cases rose significantly among those under 45 but remained stable in older adults[24]. These findings suggest a shift in atrial fibrillation onset towards younger individuals, with a notably higher growth rate in young females.

Atrial fibrillation is closely associated with stroke and heart failure, increasing severe disability risk[25] and healthcare burden[26]. Our results showed an increasing DALY and mortality rate of atrial fibrillation and flutter in low and low-middle SDI countries, particularly among males. The discrepancy in prevalence and DALY rates between sexes highlight healthcare imbalance in developing countries. In these regions, females with established cardiovascular diseases may have better control over risk factors[10], including high systolic blood pressure and smoking, which are important promotors of the progression of atrial fibrillation[27]. This shift also reflects

	Age trends globally	Regional differences*
Prevalence	Females: higher increase in age group < 55 years	Females: higher increase in low and low-middle SDI regions Males: higher increase in middle-SDI regions
Incidence	Females: higher increase in age group < 50 years and lower decrease in age group > 85 years	Females: higher increase in low and low-middle SDI regions
DALYs	Males: higher increase in age group > 60 years	Females: lower decrease in high-SDI regions Males: higher increase in middle-SDI regions
Mortality	Males: higher increase in all age group	No significant sex differences observed
Risk factor	For both sexes, high systolic blood pressure is the leading risk factor, while high-body mass index is the fastest-growing risk factor	

Table 1. Major sex differences in atrial fibrillation and flutter burden from 1990 to 2021. *Average annual percent change in age-standardized burden stratified by socio-demographic index (SDI). DALYs = disability-adjusted life years.

changes in the disease spectrum with regional development[28] and underscores the need for greater efforts to raise awareness of atrial fibrillation and implement effective interventions.

Metabolic risk factors contributed most to the disability adjusted life years (DALY) of atrial fibrillation and flutter

The attributable risk factors for atrial fibrillation and flutter have significantly changed over the past 30 years, with metabolic risks becoming dominant. High systolic blood pressure remains the top risk factor, while the DALY attributable to high body-mass index has increased globally. The Rotterdam Study found that cardiometabolic risks are strongly associated with the lifetime risk of atrial fibrillation, particularly in females and younger individuals[29]. Our analysis shows that, although behavioral and environmental risks attributable DALY have decreased in age bands under 60 years, the DALY attributable to metabolic risks has significantly increased. There is a notable sex difference in the 35 to 45 age band, where females have a higher rate of increase. This rise in metabolic risks among younger population partly explains the shift in atrial fibrillation onset from older to younger individuals, especially in females.

Metabolic risk factors are prevalent worldwide and exhibit sex-specific patterns. The global trend of obesity continues to rise, with projections indicating almost 18% of males and over 21% of females will be obese by 2025[30]. According to data from the US National Health and Nutrition Examination Survey, the body-mass index increased more in females than males from 2001 to 2016[31]. Notably, females experience a more rapid increase in blood pressure in their early life, despite a higher overall prevalence in males[32], likely influenced by sex hormones[33]. In younger population, the association between hypertension and atrial fibrillation was stronger in females[34]. These sex differences in the prevalence of metabolic risk factors provide perspective on understanding sex-specific trends in the global burden of atrial fibrillation.

Regional differences are another important issue concerning the metabolic risks epidemic. Our analysis found that atrial fibrillation burden attributable to high systolic blood pressure decreased in high and high-middle SDI regions, but increased in low to middle SDI regions, particularly in males. On the other hand, although globally females had higher DALY rates attributable to high body-mass index in 2021, the increase was faster in males over the past 30 years, especially in those over 60 years old. Male population in high-SDI regions had greater high body-mass index attributable DALY rates, in line with previous study, which reported that the association between body-mass index and atrial fibrillation was more significant in males than in females[7]. This sex-specific trend aligns with findings from a global epidemiological survey on central obesity, which revealed a more rapid increase in males[35]. These findings underscore the need for region- and sex-specific public health strategies to address metabolic risks.

Effective strategies are essential to addressing the rising global burden of atrial fibrillation and its sex-specific disparities. Hypertension management remains a key priority, as elevated systolic blood pressure is the leading risk factor for atrial fibrillation and its associated DALYs. Individualized antihypertensive therapy and lifestyle modifications can improve blood pressure control, but sex-specific considerations are crucial. Males with high cardiovascular risk are less likely to receive or adhere to treatment, highlighting the need for targeted efforts to improve prescription and compliance[10]. In contrast, young females face a growing atrial fibrillation burden due to high body-mass index and lower rates of weight control, underscoring the importance of structured weight loss programs and lifestyle interventions[36].

Early detection through opportunistic screening in high-risk populations can enable timely intervention. Early rhythm control could reduce cardiovascular death and heart failure hospitalization[37], while anticoagulation lowers stroke risk[38]. Notably, the widespread use of wearable electrocardiogram monitoring significantly increase atrial fibrillation detection, but it also raises challenges in determining who requires intervention[39]. Current evidence suggests that treatment decisions should be based on atrial fibrillation burden, symptoms, and stroke risk[40,41]. Integrating these strategies into public health policies is especially critical in low-SDI regions, where the atrial fibrillation burden is rapidly increasing.

Limitations

Several limitations of this study should be noted. Firstly, the estimation of atrial fibrillation burdens was constrained by the exclusion of non-literature-based data, apart from hospital and claims data. Additionally, reliance on modelling where data were unavailable and variations in measurement methods across data sources, and inherent biases could not be completely eradicated despite mitigation efforts. Secondly, the exclusion

of hospital data in certain regions where data were implausibly low and outpatient administrative data with consistently zero prevalence may have restricted the accuracy of the estimations due to data adjustment constraints. Thirdly, the need for ECG confirmation of atrial fibrillation also required adjustments for alternative data sources, potentially introducing inaccuracies. Fourthly, differences in healthcare access and screening quality across countries may have led to underestimations in low-SDI regions, highlighting the importance of considering socioeconomic factors in the analysis. Moreover, the sensitivity of the trend changes assessed by AAPC may be limited by the study period length. Although we analyzed the sex differences in the trends of atrial fibrillation and flutter burdens over 1990–2021 to mitigate misinterpretations, subtle fluctuations may not achieve statistical significance and could be disregarded. Therefore, these findings should therefore be interpreted with caution.

Conclusion

The increasing burden of atrial fibrillation and flutter warrants urgent action, including improved healthcare access and quality in countries with low and low-middle SDI, with a specific emphasis on mitigating the impact of metabolic risks. Sex-specific tailored public health interventions, alongside efforts to curb the growing prevalence and incidence among young population, are crucial measures in alleviating the global burden of atrial fibrillation and flutter.

Data availability

The results from Global Burden of Disease Study 2021 are publicly available through the interactive platform of the Institute for Health Metrics and Evaluation (IHME). Global Burden of Disease Results. Seattle, WA: IHME, University of Washington, 2024. Available from https://vizhub.healthdata.org/gbd-results/ (Accessed May 17, 2024).

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Author contributions

X.P., J.W. and C.T. contributed equally to this work. X.P., J.W. and L.H. conceived the study. X.P. and C.T. collected and analyzed the data. L.H., J.L. and X.K. double checked the data and results. X.P., J.W. and C.T. drafted the manuscript. L.H., X.K. and C.M. supervised and coordinated the study. S.X., N.Z., X.D., D.L. and J.D. provided important comments on the manuscript. L.H., X.K. and C.M. revised the final version of the manuscript. L.H., X.K. and C.M. are guarantors for this study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Declarations

Competing interests

Dr Ma has received honoraria for presentations from AstraZeneca, Bayer Healthcare, Boehringer Ingelheim, Bristol-Myers Squibb, Johnson & Johnson, and Pfizer. Dr Dong has received honoraria for presentations from Johnson & Johnson. All other authors declare no competing interests.

Ethics approval and consent to participate

No human participants, human data, human tissue and animals were involved in this study.

Additional information

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Correspondence and requests for materials should be addressed to X.K. or C.M.