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Global Burden of Atrial Fibrillation and Its Attributable Risk Factors (1990-2021)

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Abstract

Objectives: To report the global burden of atrial fibrillation (AF) and its risk factors among adults from 1990 to 2021, with a focus on age-specific trends, sex disparities, and the role of modifiable risk factors, particularly in older adults.

 $\textbf{Design:} \ A \ \text{systematic analysis based on data from the Global Burden of Disease (GBD) 2021 } \\ \text{study.}$

Outcome Measures: The point prevalence of AF, mortality, and disability-adjusted life years (DALYs) were reported from the GBD 2021 study, presented as counts and age-standardized rates per 100,000 population, along with 95% uncertainty intervals (UIs).

Results: In 2021, the global age-standardized prevalence of AF was 620.5 per 100,000, with corresponding mortality and DALY rates of 4.4 and 101.4 per 100,000, respectively. The highest prevalence rates were observed in Sweden (1,529.8 per 100,000), Austria (1,217.2 per 100,000), and Israel (1,155.5 per 100,000), while the lowest were recorded in Turkey (282.9 per 100,000), Yemen (337.2 per 100,000), and Afghanistan (338.8 per 100,000). Between 1990 and 2021, the most significant increases in prevalence were noted in Austria (89.3%), whereas the largest decreases occurred in Romania (-27.4%). The prevalence of AF rose markedly with age, peaking among individuals aged 95 years and older, with males generally exhibiting higher rates than females. Globally, high systolic blood pressure (30%), high body mass index (8.7%), and smoking (4.7%) were the leading risk factors for AF.

Conclusions: AF represents a growing global public health challenge, particularly in low- and middle-income countries, primarily driven by hypertension and obesity. Targeted interventions focusing on modifiable risk factors are essential to reduce the global burden of AF.

Keywords: Atrial fibrillation, Prevalence, Disability, Risk factors, Epidemiology

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Introduction

Cardiovascular diseases remain the leading cause of death and disability worldwide, encompassing a wide range of disorders affecting the heart and blood vessels. Among these, atrial fibrillation (AF) significantly contributes to the global morbidity burden. The incidence of AF rises exponentially with age.

AF is a prevalent and clinically significant cardiac

arrhythmia characterized by irregular and often rapid heart rhythms.⁴ It poses a substantial public health challenge due to its association with various adverse cardiovascular outcomes, including elevated risks of heart failure, stroke, and overall mortality.⁵⁻⁷ AF impairs the heart's ability to pump blood effectively, resulting in systemic circulatory complications and impaired organ perfusion. Moreover, it is frequently associated with comorbidities such as



hypertension, diabetes, and coronary artery disease, which complicate its management and heighten the risk of adverse outcomes.^{8,9} Older adults with AF often face compounded challenges due to comorbidities such as hypertension, diabetes, and frailty, which complicate management and worsen outcomes.¹⁰

Given AF's high prevalence and its profound impact on patients' quality of life and healthcare systems, early diagnosis and effective management are essential to reduce complications and enhance long-term outcomes. A growing body of evidence has identified several key risk factors contributing to the rising global burden of AF. High systolic blood pressure (SBP) remains the most important modifiable risk factor, accounting for a substantial proportion of AF-related mortality worldwide. High body mass index (BMI) is also a critical contributor to AF mortality and morbidity. 12,13 These findings underscore the urgent need for targeted management strategies that target modifiable risk factors to reduce the future global burden of AF.

This study aimed to report the global burden of AF and its attributable risk factors from 1990 to 2021. By analyzing data spanning three decades, the study highlights trends in prevalence, disability-adjusted life years (DALYs), and mortality due to AF across diverse populations worldwide. Additionally, it sought to identify and quantify the relative contributions of modifiable risk factors driving the burden of AF.

Methods Overview

The 2021 iteration of the Global Burden of Disease (GBD) study evaluated AF across 204 countries and territories, encompassing 21 regions grouped into seven larger superregions, from 1990 to 2021. This extensive assessment employed methodologies consistent with previous GBD cycles to quantify disease burden and its temporal trends. Detailed descriptions of the overall GBD framework and methodological updates specific to the 2021 cycle can be found in previously published reports.^{14,15}

Case Definition and Data Inputs

AF is a supraventricular arrhythmia characterized by chaotic atrial depolarization. Diagnosis is typically based on an electrocardiogram (ECG) findings showing: (1) irregularly irregular RR intervals, provided there is no complete atrioventricular (AV) block; (2) absence of distinct P waves on the surface ECG; and (3) variable atrial cycle length, generally shorter than 200 milliseconds when visible.

A systematic literature review was undertaken for GBD 2021, marking the first update since GBD 2015. Searches were performed in Embase, PubMed, and the Virtual Health Library databases, covering sources from January 1, 2015, to December 31, 2019. The search strategies are fully described in a previous publication.¹⁴

Hospital and claims data were used for estimating

prevalence, while non-literature-based data were excluded. To ensure comparability, hospital data were adjusted for readmissions, primary-to-secondary diagnosis shifts, and inpatient-to-outpatient utilization ratios using correction factors derived from USA claims data. Data from specific regions (e.g., Brazil, Japan, Tibet, Kenya, Chile, China, Ecuador, Mexico, Botswana, Nepal, India, and the Philippines) were excluded due to implausibly low prevalence rates. Similarly, all outpatient administrative data were omitted, as many datasets reported zero prevalence across all age and sex groups.

The reference case definition for AF required an ECG-based diagnosis. Data based on alternative sources (e.g., insurance claims and inpatient records) were adjusted using MR-BRT crosswalking, consistent with standard GBD procedures. Prevalence data with age ranges exceeding 25 years were split using the global sex-specific age patterns derived from a DisMod model, with data restricted to populations under 25 years. This approach enabled the inclusion of broader datasets with wider age ranges, which previously hindered accurate modeling of age-related increases in AF and flutter prevalence.

Modelling Strategy

To address inconsistencies in coding practices for AF, which resulted in unrealistic increases in mortality rates derived from death certificates, a prevalence-based modeling approach was employed. This method, which combines DisMod-MR and CODEm models, was initially used in GBD 2015 and allows for more accurate estimations by integrating observed prevalence and incidence rates alongside modeled excess mortality rates derived from prevalence and cause-specific mortality estimates.

In the first step, deaths from AF were estimated using the standard CODEm approach, supported primarily by vital registration (VR) data. Outliers were removed from International Classification of Diseases-8 (ICD-8) and ICD-9 VR datasets when they showed discontinuity within the time series or exhibited implausible temporal trends. Additional data points with unrealistically low values across multiple age groups were also excluded. Detailed descriptions of this modeling approach, along with the list of outlier locations, are available in previous publications.¹⁴

In the second step, prevalence rates were estimated using DisMod-MR, based on data from published cohort surveys, cross-sectional surveys, primary care facility databases, and claims data covering both inpatient and outpatient visits in the United States, as well as inpatient hospital data from 24 countries.

For GBD 2021, inpatient hospital data were adjusted using age- and sex-specific information, including data on readmissions within 12 months, transitions from primary diagnoses to secondary diagnoses, and inpatient-to-outpatient visit ratios. Clinical informatics data were further adjusted using Meta-Regression—

Bayesian, Regularized, Trimmed (MR-BRT) to correct for misclassification bias relative to ECG -confirmed reference data.

Key model assumptions included no remission and a cap on excess mortality set at 0.4 across all age groups. The Healthcare Access and Quality (HAQ) Index was included as a country-level fixed-effect covariate for excess mortality, while the log-transformed, age-standardized summary exposure value (SEV) scalar served as a countrylevel fixed-effect covariate for prevalence.

In the third step, the excess mortality rate (EMR) for 2021, defined as the ratio of the cause-specific mortality rate (CSMR) estimated from CODEm to the prevalence rate obtained from DisMod-MR. A subset of 21 countries was selected based on the following criteria, including VR quality rating of four or five stars and availability of prevalence data from the published literature.

Six additional locations (New Zealand, Ireland, Israel, Norway, Portugal, and Brazil) were added to improve the regression's robustness. The MR-BRT model was then applied to estimate log-transformed EMR as a function of sex, a cubic spline of age, and the HAQ Index. This model produced age-, sex-, and year-specific EMR predictions for countries not included in the regression. For the countries included in the regression, direct empirical values were retained. These EMR data points were subsequently entered into the non-fatal database for FURTHER modelling.

Step 4 involved re-running DisMod-MR with the input data from Step 2 and the EMR estimates from Step 3. The HAQ Index was again included as a fixed-effect, country-level covariate on excess mortality, while the log-transformed, age-standardized SEV scalar for AF and flutter was used as a fixed-effect covariate on prevalence. A prior value of 0 was set for remission across all ages, with similar prior values for excess mortality and incidence for individuals aged 0 to 30.

The final prevalence estimates generated by the DisMod-MR model in Step 4 were used as outputs for comorbidity adjustments and for calculating years lived with disability (YLDs) and disability-adjusted life years (DALYs). Model evaluation was conducted based on expert feedback, consistency with previous GBD results, and model fit. No major modifications were made to the modeling approach in GBD 2021.

Severity and Years Lived With Disability

The ICD codes for AF are I48-I48.9 in ICD-10 and 427.3 in ICD-9. AF was classified into symptomatic and asymptomatic groups using standard GBD proportion data. In GBD 2021, heart failure resulting from AF was incorporated into the severity distribution. Table S1 presents lay descriptions and disability weights for each severity level of AF. The prevalence of each severity category was multiplied by its respective disability weight to calculate the YLDs.

Compilation of Results

The years of life lost (YLLs) were calculated by multiplying the number of deaths in each age group by the remaining life expectancy for that age group, as specified in the GBD standard life table. DALYs were then calculated as the sum of YLLs and YLDs. To account for uncertainty, 1,000 random samples were drawn at each step of the calculation, integrating uncertainties from various sources, including input data, corrections for measurement error, and residual non-sampling error estimates. Uncertainty intervals (UIs) were defined by the 25th and 975th ranked values of these ordered samples. The percentage of DALYs from AF attributed to high SBP, high BMI, smoking, alcohol use, lead exposure, and a high sodium diet was also estimated. These risk factors and their relative risks for AF are defined in a previous publication.15

Results Global-level

In 2021, the global prevalence of AF was estimated at 52,552,045 cases (95% UI: 43,137,876 to 64,963,854), corresponding to an age-standardized rate of 620.5 per 100,000 population (95% UI: 511.4 to 768.9). Between 1990 and 2021, the global age-standardized prevalence rate demonstrated a marginal increase of 0.6% (95% UI: -3.3 to 5.7). The estimated number of global deaths due to AF in 2021 was 338,947 (95% UI: 288,954 to 368,613), with an age-standardized mortality rate of 4.4 (95% UI: 3.7 to 4.8), reflecting a 2.9% change (95% UI: -6 to 12.3) since 1990. In terms of DALYs, AF accounted for 8,358,894 DALYs (95% UI: 6,970,688 to 10,133,489) globally in 2021, corresponding to an age-standardized rate of 101.4 (95% UI: 84.9 to 122.4). This rate remained relatively stable, showing only a 0.6% change (95% UI: -5 to 6.8) over the three-decade period (Table 1).

Regional-level

In 2021, AF prevalence rates varied significantly across GBD regions. High-income North America recorded the highest age-standardized prevalence rate at 1031.2 per 100,000 (95% UI: 952.3 to 1117.9), followed by Australasia at 913.6 per 100,000 (95% UI: 725.7 to 1163.5), and Western Europe at 844.9 per 100,000 (95% UI: 717.1 to 992.5). In contrast, the lowest prevalence rates were found in the North Africa and Middle East region at 366.9 per 100,000 (95% UI: 291.6 to 468.4), Southern Latin America at 391.1 (95% UI: 328.2 to 476.3), and Central Sub-Saharan Africa at 424.6 per 100,000 (95% UI: 332.0 to 559.7). These findings demonstrate substantial regional disparities, with the largest rates occurring in high-income regions and the lowest in certain parts of Latin America and Sub-Saharan Africa (Table S2).

Between 1990 and 2021, notable regional increases in the prevalence of AF were observed across several regions. The largest increase occurred in East Asia, where the agestandardized rate rose by 13.8% (95% UI: 10.2 to 17.8),

Table 1. Prevalent Cases, Deaths, and DALYs Due to Atrial Fibrillation and Flutter in 2021 and the Percentage Change in ASRs per 100,000 by GBD Region (1990-2021)

	Pre	UI)	Deaths (95% UI)			DALYs (95% UI)			
	No (95% UI)	ASRs per 100,000 (95% UI)	Percentage Change in ASRs Between 1990 And 2021	No (95% UI)	ASRs per 100,000 (95% UI)	Percentage Change in ASRs Between 1990 And 2021	No (95% UI)	ASRs per 100,000 (95% UI)	Percentage Change in ASRs Between 1990 And 2021
Global	52552045 (43137876, 64963854)	620.5 (511.4 , 768.9)	0.6 (-3.3 , 5.7)	338947 (288954 , 368613)	4.4 (3.7 , 4.8)	2.9 (-6 , 12.3)	8358894 (6970688 , 10133489)	101.4 (84.9 , 122.4)	0.6 (-5 , 6.8)
High-income North America	7106415 (6544296 , 7755026)	1031.2 (952.3 , 1117.9)	14.5 (-5.5 , 37)	39066 (32116 , 42759)	5.1 (4.3 , 5.6)	30 (24.6 , 34.4)	1015978 (854240 , 1202900)	144.4 (121 , 171.4)	18.9 (5.6 , 31.3)
Australasia	508534 (400838 , 650591)	913.6 (725.7 , 1163.5)	3.2 (-14.3 , 24)	4337 (3529 , 4789)	6.6 (5.4 , 7.3)	-5.9 (-12.7 , 0)	87583 (72120 , 105463)	147.8 (121.5 , 179.6)	-3.9 (-12.6 , 5.8)
High- income Asia Pacific	2165450 (1737905 , 2727227)	465.2 (383.8 , 577)	-12.8 (-17.3 , -7.5)	17112 (13415 , 19331)	2.5 (2 , 2.7)	-19.6 (-28.3 , -13.8)	364512 (301067 , 443767)	69 (56.4 , 84.7)	-16.9 (-22 , -12.8)
Western Europe	8410140 (7063579 , 10013004)	844.9 (717.1 , 992.5)	3.3 (-4.7 , 12.9)	72184 (58846 , 79292)	5.5 (4.6	1.8 (-4.6 , 6.1)	1440284 (1208224 , 1709735)	131.1 (108.9 , 156.7)	0.3 (-4.6 , 4.9)
Southern Latin America	348813 (291741 , 425439)	391.1 (328.2 , 476.3)	-17.7 (-25.2 , -8.5)	3299 (2853 , 3562)	3.5 (3.1 , 3.8)	-2.2 (-9.6 , 2.8)	67844 (58167 , 78537)	74.7 (63.8 , 86.8)	-9.4 (-15.8 , -3.5)
Eastern Europe	2327313 (1805306, 3029889)	648.9 (507 , 836.3)	11 (9.5 , 12.8)	15697 (14042 , 17056)	4.3 (3.9 , 4.7)	11.8 (-1.4 , 26.4)	388580 (318353 , 470379)	107.7 (88.2 , 130.3)	13 (5.1 , 21.5)
Central Europe	1585129 (1281858 , 1949452)	679 (554.3 , 827.2)	10.1 (3.5 , 18.5)	11104 (9859 , 11914)	4.5 (4 , 4.9)	-10.9 (-16.9 , -3.7)	265917 (225064 , 316547)	112.3 (94.6 , 134.3)	-2.7 (-7.9 , 2.3)
Central Asia	392829 (305783 , 509896)	536.7 (410.8 , 698.7)	4.5 (2.3 , 7.4)	1386 (1241 , 1519)	2.4 (2.1 , 2.6)	26.9 (7.3 , 47.5)	52600 (41314 , 67337)	75 (59.9 , 95.5)	13.2 (6.3 , 21.8)
Central Latin America	1711299 (1340757 , 2226156)	707 (552.6 , 921.1)	0.6 (-0.7 , 1.8)	10354 (8980 , 11386)	4.6 (4 , 5)	-8.6 (-16.2 , -0.7)	269931 (218012 , 327388)	113.6 (91.9 , 137.8)	-2.1 (-7.1 , 2.5)
Andean Latin America	371258 (290314 , 478820)	647.4 (505.2 , 835.5)	7.9 (5.2 , 10.7)	2079 (1699 , 2494)	3.8 (3.1 , 4.6)	-17.4 (-32.4 , 1.8)	56583 (44608 , 69532)	99.9 (78.7 , 122.3)	-6.6 (-16.3 , 5.5)
Caribbean	367640 (289060 , 476682)	678.6 (533.4 , 881.1)	0.2 (-2.2 , 2.4)	2731 (2349 , 3048)	4.9 (4.2 , 5.4)	-13 (-21.3 , -3.5)	63053 (51870 , 76838)	115.2 (94.6 , 140.7)	-6.2 (-11.5 , 0)
Tropical Latin America	2004719 (1580577 , 2599905)	794.8 (625.6 , 1025.2)	-1 (-2.4 , 0.8)	11540 (9640 , 12679)	4.9 (4.1 , 5.3)	-2.6 (-7.7 , 1.5)	304099 (245416, 375972)	122.8 (99.6 , 151.7)	-0.1 (-2.5 , 2.5)
East Asia	11215165 (8885909 , 14572495)	526.4 (420.6 , 683.6)	13.8 (10.2 , 17.8)	67666 (54232 , 80814)	4.3 (3.4 , 5.2)	-12.9 (-34.3 , 12.6)	1723468 (1364785 , 2143575)	89.8 (72.4 , 109.6)	-4.3 (-19.3 , 13)
Southeast Asia	3898608 (3091004 , 5118881)	662.3 (519.6 , 854.4)	3.9 (2.7 , 5.3)	22401 (18974 , 25759)	5.3 (4.4 , 6.1)	24.5 (-1.8 , 53.7)	612969 (501403 , 745497)	115.4 (95.9 , 139.1)	12.8 (-1.4 , 26.8)
Oceania	34994 (27519 , 45179)	578.4 (455.2 , 750.2)	3.6 (0.9 , 7)	185 (132 , 238)	4.3 (3.2 , 5.5)	-4.1 (-20.2 , 11.8)	6606 (5044 , 8584)	110.2 (86.2 , 141.7)	-0.1 (-11.8 , 11.8)
North Africa and Middle East	1417367 (1140557 , 1788911)	366.9 (291.6 , 468.4)	6.1 (2.2 , 10.4)	11182 (9280 , 12594)	3.9 (3.2 , 4.4)	12 (-13.5 , 45)	265649 (218559, 309833)	76.1 (63.3 , 88.6)	6.3 (-11 , 25.1)
South Asia	6882583 (5295961 , 9026139)	530.9 (410.2 , 696.7)	2.2 (1.2 , 3.1)	36165 (27041 , 46073)	3.7 (2.7 , 4.7)	55.1 (14.8 , 111.4)	1071260 (820127 , 1366680)	88.3 (68 , 111.4)	23 (5.9 , 43)
Southern Sub-Saharan Africa	258590 (201941 , 342437)	512.8 (398.2 , 671)	0.5 (-1.3 , 2.3)	1413 (1228 , 1551)	4 (3.4 , 4.4)	41.6 (10.9 , 72.1)	41787 (34114 , 50581)	90.4 (74.6 , 109)	20.1 (7.3 , 34.8)
Western Sub-Saharan Africa	716915 (561805 , 945355)	434.8 (339.5 , 567.1)	10.6 (9.5 , 11.6)	4568 (3662 , 5235)	4.5 (3.7 , 5.1)	-1 (-21.6 , 29.8)	118819 (92666 , 146393)	86.1 (68.4 , 104.1)	2.3 (-12.1 , 20.7)
Eastern Sub-Saharan Africa	645690 (507531 , 839253)	448.8 (354.1 , 589.5)	10.1 (8.4 , 11.9)	3166 (1927 , 4731)	3.3 (2 , 4.9)	3.4 (-15.7 , 30)	103373 (74839 , 140257)	79.2 (57.1 , 108.3)	4.5 (-8.3 , 18.1)
Central Sub-Saharan Africa	182594 (142529 , 241993)	424.6 (332 , 559.7)	-0.6 (-3.3 , 2.5)	1311 (886 , 1982)	4.7 (3.2 , 7.1)	13.7 (-13.9 , 47.3)	37999 (27202 , 52014)	98.4 (70.8 , 138.2)	7.5 (-11.2 , 29.4)

Note. DALY: Disability-adjusted life year; ASR: Age- Standardized rates; GBD: Global burden of disease; UI: Uncertainty interval. Data sourced from http://ghdx.healthdata.org/gbd-results-tool

followed by Eastern Europe with an increase of 11.0% (95% UI: 9.5 to 12.8) and Western Sub-Saharan Africa with a 10.6% increase (95% UI: 9.5 to 11.6). In contrast, Southern Latin America experienced the greatest decline, with a 17.7% decrease (95% UI: -25.2 to -8.5), while Highincome Asia Pacific exhibited a reduction of 12.8% (95% UI: -17.3 to -7.5). These results reflect a growing AF burden in certain Asian and African regions, whereas Southern Latin America and High-income Asia Pacific experienced declines (Table S2). The sex-specific prevalence estimates and their percentage changes are presented in Figures S1 and S2.

In 2021, mortality rates due to AF varied widely by region. Australasia recorded the largest age-standardized death rate at 6.6 per 100,000 (95% UI: 5.4 to 7.3), followed by Western Europe at 5.5 per 100,000 (95% UI: 4.6 to 6.0), and Southeast Asia at 5.3 per 100,000 (95% UI: 4.4 to 6.1). Conversely, the lowest death rates were observed in Central Asia, with an age-standardized death rate of 2.4 per 100,000 (95% UI: 2.1 to 2.6); High-income Asia Pacific at 2.5 per 100,000 (95% UI: 2.0 to 2.7), and Eastern Sub-Saharan Africa at 3.3 per 100,000 (95% UI: 2.0 to 4.9). These data illustrate a varied distribution of mortality impacts, with high-income and Australasian regions exhibiting greater mortality rates compared to many Asia and Sub-Saharan African regions (Table S3).

From 1990 to 2021, the age-standardized death rates due to AF showed significant regional variation. The largest increase occurred in South Asia, where death rates rose by 55.1% (95% UI: 14.8 to 111.4), followed by Southern Sub-Saharan Africa with a 41.6% increase (95%) UI: 10.9 to 72.1), and High-income North America with a 30% rise (95% UI: 24.6 to 34.4). Conversely, High-income Asia Pacific experienced the largest decrease in mortality, with a 19.6% reduction (95% UI: -28.3 to -13.8). The Caribbean also exhibited a decrease of 13% (95% UI: -21.3 to -3.5), while Central Europe observed a decline of 10.9% (95% UI: -16.9 to -3.7). These trends indicate a growing mortality burden in South Asia and Sub-Saharan Africa, while declines were observed in high-income regions such as the Asia Pacific and parts of Central America (Table S3). The sex-specific death rates and their percentage changes are illustrated in Figures S3 and S4.

DALYs, reflecting the overall burden of AF, also demonstrated strong regional disparities. Australasia had the highest age-standardized DALY rate at 147.8 per 100,000 (95% UI: 121.5 to 179.6), followed by Highincome North America at 144.4 per 100,000 (95% UI: 121.0 to 171.4), and Western Europe at 131.1 per 100,000 (95% UI: 108.9 to 156.7). In contrast, the lowest DALY rates were observed in High-income Asia Pacific at 69.0 per 100,000 (95% UI: 56.4 to 84.7), Southern Latin America at 74.7 per 100,000 (95% UI: 63.8 to 86.8), and Central Asia at 75.0 per 100,000 (95% UI: 59.9 to 95.5), as depicted in Table S4. This variation highlights a significant AF burden in high-income and Australasian regions, with comparatively lower impact in certain Latin

American and Asian regions. South Asia experienced the greatest increase in DALYs, rising by 23.0% (95% UI: 5.9 to 43.0), followed by Southern Sub-Saharan Africa with a 20.1% increase (95% UI: 7.3 to 34.8), and High-Income North America with an 18.9% increase (95% UI: 5.6 to 31.3). Conversely, High-Income Asia Pacific experienced the most substantial decline in DALYs, with a 16.9% decrease (95% UI: -22.0 to -12.8), whereas Southern Latin America recorded a 9.4% reduction (95% UI: -15.8 to -3.5). These results highlight an increasing disease burden in South Asia and Sub-Saharan Africa, in contrast to declining trends primarily observed in high-income regions and parts of Latin America (Table S4). The sexspecific DALY rates and their percentage changes are displayed in Figures S5 and S6.

National-level

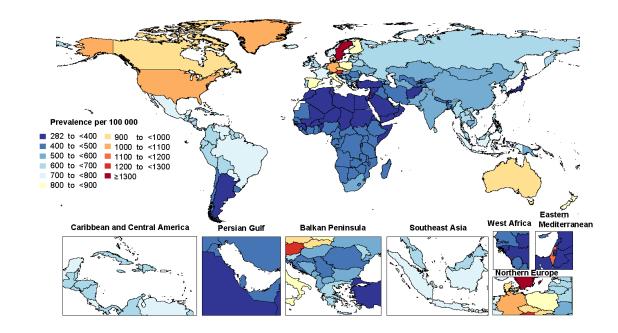
In 2021, the age-standardized prevalence of AF varied considerably across countries. Sweden reported the highest prevalence rate, with 1,529.8 cases per 100,000 population (95% UI: 1,166.6 to 1,943.3), followed by Austria at 1,217.2 per 100,000 (95% UI: 1,164.8 to 1,272.2) and Israel at 1,155.5 per 100,000 (95% UI: 958.3 to 1,312.4). Conversely, the lowest prevalence rates were found in Turkey, with an age-standardized rate of 282.9 per 100,000 (95% UI: 252.2 to 314.7), followed by Yemen at 337.2 per 100,000 (95% UI: 255.8 to 443.6) and Afghanistan at 338.8 per 100,000 (95% UI: 257.5 to 442.8), as observed in Table S2 and Figure 1A.

Between 1990 and 2021, the largest rises in the age-standardized prevalence rate of AF were observed in Austria, which recorded an 89.3% rise (95% UI: 71.1 to 107.3), followed by Sweden with a 51.3% increase (95% UI: 37.5 to 66.8) and Czechia with a 47.4% rise (95% UI: 19.4 to 88.4). These upward trends reflect a growing prevalence of AF across European countries, likely due to factors such as aging populations and improved detection rates. Conversely, Romania experienced the greatest decline in prevalence, with a 27.4% reduction (95% UI: -41.9 to -11.2), followed by Argentina with a 26.3% decline (95% UI: -38.0 to -11.7) and Finland with a similar 26.2% decrease (95% UI: -37.4 to -11.9), as illustrated in Table S2 and Figure 1B.

In terms of mortality, the highest age-standardized death rates due to AF were found in Montenegro, with 17.3 deaths per 100,000 population (95% UI: 13.4 to 21.4), followed by Nauru at 10.3 per 100,000 (95% UI: 6.4 to 18.4) and Sweden at 9.5 per 100,000 (95% UI: 7.7 to 10.6). In contrast, the lowest death rates were recorded in Tajikistan at 1.2 per 100,000 (95% UI: 0.9 to 1.4), Singapore at 1.2 per 100,000 (95% UI: 1.0 to 1.3), and Uzbekistan at 1.4 per 100,000 (95% UI: 1.2 to 1.6). This indicates that AF imposes a particularly high mortality burden in Montenegro and several island nations, whereas lower death rates were found in parts of Central Asia and Southeast Asia (Table S3 and Figure 2A).

Sweden experienced a substantial 93.3% increase (95%

A





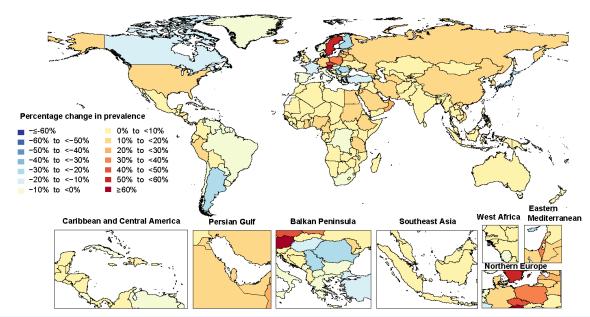
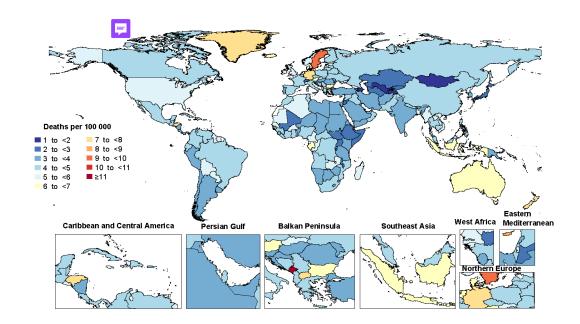


Figure 1. (A) Age-standardized Prevalence of Atrial Fibrillation Per 100,000 Population in 2021, by country; (B) Percentage Change in Age-Standardized Prevalence of Atrial Fibrillation From 1990 to 2021, by Country Data sourced from http://ghdx.healthdata.org/gbd-results-tool)

UI: 77.5 to 108) in the age-standardized death rate due to AF, followed by Indonesia with a 76.6% increase (95% UI: 26.0 to 134.8) and Nepal with a 75.5% rise (95% UI: 26.1 to 159.8). These trends indicate a rising mortality burden in both developed and developing countries, potentially due to aging populations and shifts in cardiovascular risk profiles. In contrast, the largest decrease in death rates were seen in Guam, with a 71.6% reduction (95% UI: -76.5 to -66.5), followed by San Marino with a 48.9% decrease (95% UI: -64.2 to -24.3), and Qatar with a 44.9% decline (95% UI: -61.9 to -27.3, as depicted in Table S3 and Figure 2B.

DALYs attributed to AF showed notable variation across countries. Montenegro recorded the highest agestandardized DALY rate at 266.1 per 100,000 (95% UI: 221.2 to 320.0), followed by Sweden at 222.0 per 100,000 (95% UI: 175.7 to 277.2) and Nauru at 204.4 per 100,000 (95% UI: 146.7 to 299.1). In contrast, Singapore exhibited the lowest DALY rate at 50.5 per 100,000 (95% UI: 38.4 to 65.6), followed by Tajikistan at 54.3 per 100,000 (95% UI: 39.7 to 72.3) and Uzbekistan at 59.0 per 100,000 (95% UI: 44.7 to 77.9). These findings highlight a significant disability burden from AF in countries such as Montenegro and Sweden, whereas Singapore and several

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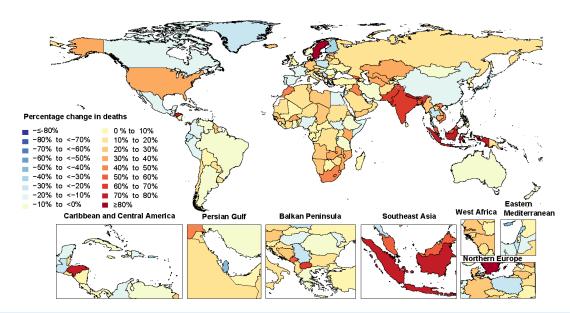


Figure 2. (A) Age-Standardized Death Rate Due to Atrial Fibrillation Per 100,000 Population in 2021, by Country; (B) Percentage Change in Age-Standardized Death Rate Due to Atrial Fibrillation From 1990 to 2021, by Country Data sourced from http://ghdx.healthdata.org/gbd-results-tool

Central Asian nations experienced a comparatively lower impact (Table S4 and Figure S7).

In terms of temporal changes, Sweden exhibited the greatest increase in DALYs, with a 61.1% rise (95% UI: 49.9 to 73.5), followed by Austria with a 47.4% increase (95% UI: 37.7 to 56.7), and Honduras with a 38.6% rise (95% UI: 7.9 to 71.9). These increases reflect a rising burden of AF in both developed and developing regions, likely influenced by demographic changes and healthcare access. Conversely, the largest decreases in DALYs were seen in Cyprus, with a 40.4% reduction (95% UI: -53.5 to -20.1), followed by Guam with a 36.1% decrease (95% UI: -45.2 to -27.3) and Finland with a 33.1% decline (95% UI:

-39.2 to -25.9), as illustrated in Table S4 and Figure S8.

Age- and Sex-Pattern

The analysis of AF prevalence revealed distinct trends in both prevalence rates and counts across different age groups, with notable sex differences. The highest prevalence counts were observed in the 70-74 age group, with males having significantly more cases than females. Conversely, the peak prevalence rate occurred in the 95+age range, again showing a higher rate among males compared to females. Overall, prevalence counts generally increased with age, and prevalence rates rose more sharply in the oldest age brackets. Specifically, both

males and females experienced increasing prevalence rates as they aged, peaking in the 95 + age group. However, prevalence counts tended to plateau after reaching the 70-74 age range. This pattern suggests that while aging correlates with higher AF prevalence counts, prevalence rates exhibit a steeper rise in the oldest segments of the population (Figure 3A).

In 2021, global trends in deaths due to AF varied by age and sex. Overall, both death counts and rates were higher in males compared to females, particularly in younger and middle-aged groups. However, in older age groups, females exhibited higher counts and rates. Specifically, in the 70-74 age range onward, female death counts either matched or exceeded those of males, peaking in the 90-94 age range. In this age group, females accounted for

49,854 deaths compared to 23,904 deaths in males, with corresponding death rates of 413.36 per 100,000 for females and 410.13 per 100,000 for males. The highest death rates were found in the 95+age group for both sexes, where females exhibited marginally higher rates (597.57 per 100,000) than males (592.94 per 100,000). These findings underscore that while males generally experience greater AF-related mortality in earlier life stages, females face a greater burden in later life, particularly after 70 years of age, culminating in the 90-94 age range (Figure 3B).

In 2021, the global trends of DALYs due to AF varied significantly across age groups and between sexes. Among younger and middle-aged populations, males generally had higher DALY counts and rates compared to females. However, in older age groups, females displayed higher

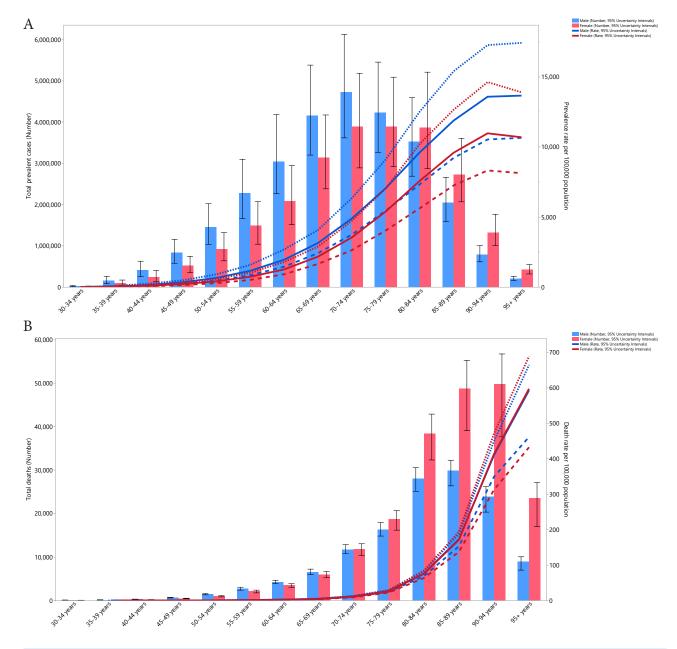


Figure 3. (A) Global Prevalent Cases and Age-Standardized Point Prevalence of Atrial Fibrillation Per 100,000 Population, by Age and Sex, in 2021; (B) Global Deaths and Age-Standardized Death Rate of Atrial Fibrillation Per 100,000 Population, by Age and Sex, in 2021 *Note.* Dotted and dashed lines represent the 95% upper and lower uncertainty intervals, respectively.

DALY values, particularly at ages 75-79. In the 80-84 age group, the highest DALY counts were reported for both males and females. Before this point, DALY counts for both sexes increased steadily, with males consistently recording higher values until the 75-79 years age group, where females surpassed them. For DALY rates, the peak for both males and females occurred in the 95 + years age group. Before reaching this peak, DALY rates showed a gradual rise across age groups, reflecting the increasing burden of AF with advancing age. After peaking in the 80-84 years group, DALY counts began to decline, but rates continued to climb, reaching their maximum in the 95+age group. These findings indicate that while males generally experienced a greater burden of AF during earlier years, females faced a larger impact in advanced age, particularly from the 75-79 years group onward, with counts peaking in the 80-84 years range and rates peaking in the 95 + years range (Figure S9).

Association Between Burden and Socio-Demographic Index

The Socio-Demographic Index (SDI) showed a positive correlation with the burden of AF, showing an increase in burden up to an SDI level of approximately 0.8. Beyond this point, a negative association emerged, indicating a decline in AF burden at higher SDI levels. Regions such as Australasia, Western Europe, Oceania, Southeast Asia, the Caribbean, Central Latin America, and Andean Latin America exhibited a higher-than-expected AF burden throughout the period. In contrast, regions such as High-Income Asia Pacific, Southern Latin America, East Asia, Southern Sub-Saharan Africa, Central Asia, North Africa and the Middle East, and South Asia reported a lowerthan-expected AF burden from 1990 to 2021. This pattern underscores the complex relationship between SDI level and AF burden, suggesting that socio-economic factors may influence AF outcomes differently across world regions (Figure 4).

At the country level in 2021, a generally positive correlation was observed between SDI and AF burden, with the burden typically increasing alongside higher SDI values. However, some countries deviated notably from this trend. For instance, Montenegro, Sweden, and Nauru experienced a much higher-than-expected AF burden, suggesting disproportionately significant impacts relative to their SDI levels. In contrast, Singapore, Uzbekistan, and Mali displayed much lower-than-expected burdens, implying that country-specific factors may mitigate AF outcomes. Overall, this analysis highlights that although a general trend exists between SDI and AF burden, national-level variations play a significant role in shaping the observed outcomes (Figure S10).

Risk Factors

The global burden of AF is significantly influenced by several key modifiable risk factors, with high SBP, high BMI, and smoking emerging as the most prominent contributors. Globally, high SBP accounts for 30% of the AF burden, followed by high BMI (8.7%0 and smoking (4.7%). Regionally, the effect of these risk factors varied substantially. In terms of AF-related DALYs, the burden attributable to high SBP was highest in Southern Sub-Saharan Africa (34.1%), followed by Eastern Europe (33.9%) and Western Sub-Saharan Africa (33.6%). For high BMI, the highest attributable burdens were observed in High-income North America (16.3%), North Africa and the Middle East (16.1%), and Southern Sub-Saharan Africa (15.8%). Smoking exerted the most substantial impact in Oceania (7.4%), East Asia (6.8%), and Southeast Asia (6.0%).

Additional risk factors, including alcohol use, a high-sodium diet, and lead exposure, also significantly contributed to the AF burden in various regions. Alcohol use had the greatest impact in Australasia (7.8%), Western Europe (7.6%), and Central Europe (6.6%). For sodium intake, East Asia reported the highest population attributable fractions (PAF) at 6.5%, followed by Central Europe at 6.0%, and both Southeast Asia and Highincome Asia Pacific regions at 4.5%. Lead exposure contributed considerably to the AF burden in South Asia (4.7%), North Africa and the Middle East (3.8%), and the Caribbean (3.8%). These findings highlight the need for targeted interventions that account for regional variations in risk factors to effectively mitigate the global burden of AF (Figure 5). The burden of AF attributable to these risk factors, stratified by sex, is presented in Figures S11 and S12.

Discussion

AF remains the most common cardiac arrhythmia encountered in clinical settings and poses a significant public health challenge. Its annual economic impact is substantial, with costs estimated at approximately \$6.65 billion. Global trends indicate a progressive rise in AF burden, as evidenced by rising prevalence, DALYs, and mortality rates worldwide. However, this pattern is not consistent across all regions. For instance, Southern and Tropical Latin America and the High-Income Asia-Pacific region demonstrate divergent trends. Studies also reveal a noticeable shift in AF burden toward middle-income countries, where prevalence rates continue to climb, contrasting with plateauing rates in high-income countries. Despite these regional variations, the overall burden of AF tends to increase with higher SDI levels.

A higher AF burden is closely associated with an elevated risk of stroke and heart failure. Individuals with sporadic episodes of AF have a lower annual stroke risk without anticoagulation (1% per year) compared with those suffering from persistent or permanent AF (3% per year), while those with paroxysmal AF face an intermediate risk of 2% per year. Research further indicates that AF episodes lasting more than five minutes are significantly associated with higher risks of developing clinical AF (risk ratio: 4.18) and stroke (risk ratio: 2.49). Moreover,

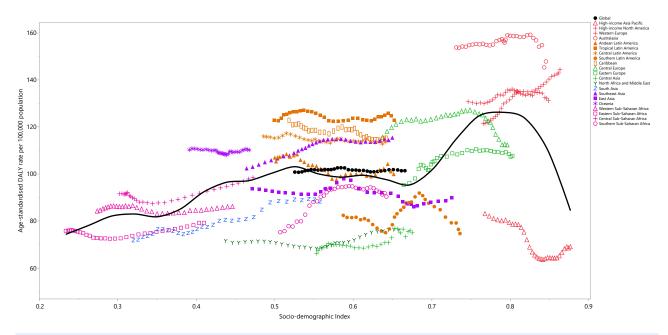


Figure 4. Age-Standardized DALY Rates for Atrial Fibrillation Per 100,000 Population Across the 21 Global Burden of Disease Regions by SDI From 1990 to 2021. Note. DALY: Disability-adjusted life year; SDI: Sociodemographic index. Expected values, based on SDI and disease rates in all locations, are shown as the black line.

Data sourced from http://ghdx.healthdata.org/gbd-results-tool.

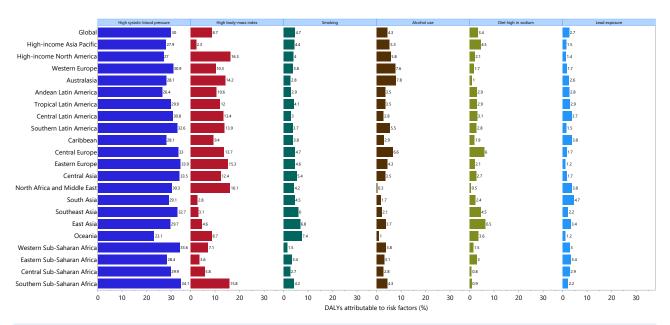


Figure 5. Percentage of Atrial Fibrillation-Related Age-standardized DALYs Attributable to Smoking for Both Sexes Across the 21 Global Burden of Disease Regions in 2021

Note. DALY: disability-adjusted life year.

Data sourced from http://ghdx.healthdata.org/gbd-results-tool

each additional hour spent in AF increases stroke risk by approximately 2%, highlighting AF duration as a key predictor of clinical outcomes and future stroke risk, with an approximately linear relationship between AF burden and stroke risk. ¹⁹ The clinical importance of AF burden is further underscored by evidence that early rhythm control in patients recently diagnosed with AF and cardiovascular conditions can reduce adverse outcomes, such as stroke and heart failure. ¹⁸ These findings underscore the vital role of AF prevention in mitigating both primary arrhythmia and secondary cardiovascular complications. ²⁰

Preventing AF necessitates addressing its underlying risk factors through targeted interventions, including region-specific strategies. Globally, high blood pressure exerts the greatest impact on AF, particularly in Eastern Europe, Central Asia, and Sub-Saharan Africa. High BMI is most influential in Southern Sub-Saharan Africa, North Africa, the Middle East, and High-Income North America. At the same time, smoking has the greatest effect in Oceania and East Asia. Alcohol consumption is particularly impactful in Australia and Western Europe, whereas high sodium intake poses the greatest risk in

East Asia and Central Europe. Lead exposure remains a particular concern in South Asia. Consistent with previous findings, high systolic blood pressure continues to be the leading risk factor for AF incidence, prevalence, mortality, and DALYs globally, with high BMI ranking second.21

Public health interventions should primarily focus on addressing these two key issues. Recent studies on cardiovascular disease highlight the substantial, yet often overlooked, burden of AF. Despite its relatively low incidence compared to other cardiovascular conditions, AF results in severe complications that impact public health across countries, irrespective of socio-demographic status. Furthermore, the YLLs and YLDs demonstrate the urgent need to prioritize mortality reduction in future healthcare strategies, particularly in South and Central Asia and Africa.21

Globally, hypertension remains the leading cause of cardiovascular disease and premature death, serving as the primary risk factor for developing AF.²² The World Health Organization (WHO) Global Report on Hypertension reveals a dramatic increase in adult hypertension cases between 1990 and 2019, with a 41% rise in Europe and the Americas and an alarming 144% surge in Southeast Asia and the Western Pacific.²³ The increase in AF can be largely attributed to hypertension. Regional variations in hypertension risk factors, such as obesity, low potassium intake, physical inactivity, high sodium intake, alcohol use, and unhealthy diets, contribute significantly to this disparity.22 A recent study examining trends in high blood pressure trends (1975-2015) reported the highest increases in SBP across sub-Saharan Africa and Central and South Asia, which aligns with the rising AF rates observed in these regions.²² Currently, more than 30% of adults worldwide are estimated to have hypertension, with higher prevalence in low- and middle-income countries (LMICs) compared to high-income nations. Despite this high prevalence, awareness, treatment, and blood pressure control remain inadequate, especially in LMICs.²⁴ These challenges necessitate targeted public health interventions and socioeconomic strategies.

Obesity represents the second most important factor contributing to the global rise in AF prevalence, affecting both its incidence and progression.²⁵ Between 1990 and 2021, global deaths and DALYs associated with high BMI more than doubled for both genders. Agestandardized DALY rates rose by 21.7% for females and 31.2% for males, with the highest increases found in low-middle SDI countries, while the smallest changes occurred in high SDI countries. This trend aligns with the rising AF pattern in low- to middle-SDI countries.²⁶ Effective obesity prevention requires lowering overall BMI levels and reducing the progression of individuals into higher BMI categories by promoting healthy weight maintenance. Prevention strategies should be populationbased and multilevel, involving environmental, policy, and behavioral interventions across diverse settings and

sectors to engage both the general population and highrisk groups. Previous studies highlight the importance of public health interventions, behavioral approaches, health education, and personal accountability, while also addressing social factors.^{27,28} Comprehensive public health policies and environmental changes are essential for effective obesity prevention. Key initiatives include the Food and Drug Administration (FDA) regulations for calorie labeling on food products and banning trans fats. Local governments can support healthier environments by limiting fast-food outlets near schools and encouraging access to healthy food vendors, while schools should enhance physical education programs and promote active commuting. Economic measures, such as taxing unhealthy foods and subsidizing nutritious options, also play a role, despite ethical considerations. Family-based interventions are essential for longterm weight management, with structured dietary programs like the "traffic light" diet aiding maintenance. Moreover, reducing weight bias in healthcare is critical, as both explicit and implicit biases can impair care quality. Training healthcare providers to recognize the multifactorial causes of obesity, use non-stigmatizing language, and adopt a holistic health perspective can improve patient support and outcomes.²⁹⁻³¹

The American Heart Association's Life's Simple 7 (LS7) framework, which outlines and tracks ideal cardiovascular health, may play a crucial role in AF prevention. While significant progress has been made in the secondary prevention of AF, primary prevention among at-risk individuals remains limited. Most LS7 components, such as hypertension management, smoking cessation, weight control, regular exercise, and diabetes management, are modifiable and overlap with key AF risk factors. Although the effects of lipid management and dietary changes on AF risk are less clearly defined, enhancing overall cardiovascular health through LS7 could significantly reduce AF incidence by addressing shared cardiovascular risk factors.16,32

Preventing AF requires addressing lifestyle factors such as diet, alcohol consumption, and smoking, all of which significantly impact cardiovascular health. Smoking elevates AF risk by promoting inflammation and oxidative stress.33 Excessive alcohol consumption is associated with AF due to its detrimental effects on atrial structure, highlighting the need for moderation or abstinence.34 Furthermore, a heart-healthy diet can help mitigate AF risk by improving blood pressure, lowering cholesterol, and reducing inflammation.³⁵ Public health interventions are essential to raise awareness of these factors and provide resources for smoking cessation, responsible alcohol use, and dietary modifications. Community-based programs, public education campaigns, and accessible support systems can empower individuals to adopt these changes, thus reducing AF incidence and its public health burden.

AF prevalence increases with age, showing no significant gender differences. However, AF-related mortality also

rises with age, highlighting increased age-related risks. Mortality data further reveal distinct age distributions, with AF cases appearing at younger ages in middle- and low-income countries compared to older populations in high-income countries. These trends underscore the critical need for sustained, lifelong AF management to reduce complications across diverse income levels.¹⁷

This study has several limitations that should be considered when interpreting its findings. First, the estimates rely on data from the GBD 2021 study, which, despite its comprehensiveness, uses modeled data where empirical information is limited. In particular, the exclusion of outpatient administrative data, due to zero prevalence values in some regions, may underestimate AF burden, especially in LMICs where access to hospital-based care and diagnostic tools such as ECG is limited. This exclusion limits the generalizability of findings in regions with underdeveloped health information systems.

Second, the analysis does not account for potential synergistic effects among risk factors. PAFs were estimated for individual risk factors without evaluating potential interactions (e.g., obesity combined with hypertension), which may underestimate the joint burden of clustered risk exposures.

Third, several known or emerging AF risk factors, such as air pollution, sedentary lifestyle, and psychosocial stress, were excluded from the GBD 2021 framework and thus not assessed in this study. This omission may result in an incomplete understanding of modifiable contributors to AF burden.

In addition, although ECG is the gold standard for diagnosing AF, its limited availability in many LMICs may contribute to diagnostic gaps and underreporting. Alternative methods, such as pulse palpation or portable ECG devices, are often used for preliminary screening in these settings. These methods, though useful, vary in sensitivity and specificity, potentially introducing bias into prevalence estimates and affecting the reported AF burden.

Conclusions

AF represents a growing global public health challenge, driven primarily by rising rates of hypertension and obesity, particularly in LMICs, where recognition and management are often inadequate. The increasing burden underscores the urgent need for targeted interventions, with a particular focus on managing these key modifiable risk factors. Effective strategies should encompass population-based approaches, lifestyle modifications, and environmental policies. Public health policies, community-based initiatives, and healthcare provider training are essential for comprehensive AF prevention and management. These efforts aim to reduce AF prevalence and mortality while enhancing overall cardiovascular health, particularly among vulnerable populations across diverse socio-economic settings.

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Authors' Note

This study is based on publicly available data and solely reflects the authors' opinions, not those of the Institute for Health Metrics and Evaluation.

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Data availability statement

The data used in this study are publicly available at http://ghdx. healthdata.org/gbd-results-tool.

Ethical approval

This study was approved by the Tabriz University of Medical Sciences, Tabriz, Iran (IR.TBZMED.REC.1403.560).

Consent for publication

Consent for publication was not required.

Competing interests

None declared.

Supplementary files

Supplementary file 1 contains Tables S1-S4 and Figures S1-S12.

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