Original research

Trends of global burden of atrial fibrillation/flutter from Global Burden of Disease Study 2017

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ABSTRACT

Objective This study aimed to estimate the global burden of atrial fibrillation/atrial flutter (AF/AFL).

Methods We retrieved data from the Global Health Data Exchange query tool and estimated the age-standardised rates (ASRs) of prevalence, incidence and disability-adjusted life-years (DALYs) of AF/AFL, as well as the population attributable fraction (PAF) of risk factors contributing to DALYs. ASRs and sociodemographic index (SDI) were assessed using Pearson's correlation coefficients.

Results In 2017, there were 37.6 million (95% uncertainty interval (UI) 32.5 to 42.6 million) individuals with AF/AFL globally. The prevalence rates increased with increased SDI values in most regions for all years. Men had a higher prevalence than women across all regions except for China. From 1990 to 2017, global prevalence rate decreased by 5.08% (95% UI −6.24% to −3.82%), with the largest decrease noted in the region with high SDI values. The global DALYs rate declined by 2.53% (95% UI −4.16 to −0.29). PAF of elevated systolic blood pressure for attributable DALYs accounted for the highest percentage, followed by high body mass index, alcohol use, high-sodium diet, smoking and lead exposure.

Conclusions Although the ASRs of prevalence, incidence and DALYs decreased from 1990 to 2017, the absolute number of patients with AF/AFL, annual number of new AF/AFL cases and DALYs lost due to AF/AFL increased. This indicates that the burden of AF/AFL is likely to remain high. Systematic surveillance is needed to better identify and manage AF/AFL so as to prevent its various risk factors and complications.

INTRODUCTION

Atrial fibrillation/atrial flutter (AF/AFL) are the most common arrhythmias. They contribute to the high incidence of heart failure and cerebral stroke, resulting in high rates of cardiovascular and cerebrovascular morbidity and mortality.[1 2] Occurrence of these adverse events has substantial healthcare costs and constitutes a significant public health burden.

Past observational studies have shown that the incidence and prevalence rates of AF/AFL are increasing, with these increases differing among the USA and countries in Europe.[3–8] Data from these countries differed, depending on the setting, comorbidities of the patients, sex, age, body mass index (BMI), smoking and alcohol intake, and social circumstances. There is a paucity of studies looking at the occurrence and adverse outcome of AF/AFL across the globe.

Therefore, the present analysis estimated the global prevalence, disability-adjusted life-years (DALYs) and incidence of AF/AFL from 1990 to 2017 to gain the most updated data on the epidemiological trends of AF/AFL and to assist in formulating effective management strategies for AF/AFL.

METHODS

Study data

We used data from the Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool), an online tool of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017. The database includes epidemiological data on 328 diseases from across 195 countries and territories across the world. GBD 2017 divided countries and regions into five super regions according to their sociodemographic index (SDI). The regions were as follows: low SDI, low–middle SDI, middle SDI, high–middle SDI and high SDI. SDI is a measure of the level of social development in a country or territory based on the per capita income at the national level, the average number of years of education for the population over the age of 15 and the fertility rate. The GBD 2017 also divided the world into 21 geographical regions.

Statistical analysis

We assessed the burden of AF/AFL using incidence, prevalence and DALYs obtained from GBD 2017. We calculated age-standardised rates (ASRs) of prevalence, incidence and DALYs. Age standardisation is essential when comparing different populations with distinct age structures or when the same population changes over time. The ASRs (per 100 000 population) were calculated by the direct method, which sums up the products of the age-specific rates and the number of persons in the same age subgroup of the standard population then divides them by the sum of the standard population weights.

DALYs were calculated as the sum of the years of life lost (YLLs) due to premature death in the population and the years lost due to disability (YLDs). To estimate YLLs, the number of deaths was multiplied by the standard life expectancy at the age at which death occurs. YLDs were estimated as the number of years lived with any short-term or long-term health loss, weighted for severity by the disability weights.

Trends in ASRs indicate changes in the disease patterns within populations. They also provide clues as to the changes in their risk factors. We

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assessed trends in the changes of incidence, prevalence and DALYs using percentage changes. We computed percentage changes based on the point estimates for the timepoints being compared. The ASR was considered to be increased if both boundaries of its 95% uncertainty intervals (UIs) are higher than 0. In contrast, if both boundaries of its 95% UIs are lower than 0, the ASR was considered to be decreased. Otherwise, the ASR was considered to be stable. The estimated annual percentage change is a measure of the ASR trend over a time interval, calculated following the method proposed by Hankey *et al*[9] (online supplemental materials).

Pearson's correlation coefficient was used to evaluate the relationship between ASRs and SDI. Locally weighted scatterplot smoothing was used in the regression analysis to create a smooth line to see the relationship between variables and foresee trends.

All analyses were performed using R programme V.3.5.3 (R Core Team). A p value of less than 0.05 was considered statistically significant.

RESULTS

Prevalence of AF/AFL

Globally, the estimated number of individuals with AF/AFL in 1990 was 19.1 million (95% UI 16.4 to 21.9 million), and that in 2017 was 37.6 million (95% UI 32.5 to 42.6 million): 19.8 million men (95% UI 17.2 to 22.4 million) and 17.8 million women (95% UI 15.3 to 20.2 million). The prevalence of AF/AFL decreased from 507.32 (95% UI 435.12 to 579.67) per 100 000 person-years in 1990 to 481.54 (95% UI 416.51 to 546.21) per 100 000 person-years in 2017 (table 1), resulting in a 5.08% decrease (95% UI −6.24% to −3.82%) (table 1 and figure 1C). In 2017, the highest prevalence of AF/AFL was observed in high-income North America (871.03, 95% CI 762.18 to 978.69, per 100 000 person-years). Contrary to this, the lowest prevalence was observed in high-income Asia Pacific (238.42, 95% CI 209.15 to 270.07, per 100 000 person-years) (table 1 and figure 1B). Over the same period, the largest increase in prevalence was observed in high-income North America (7.64%, 95% UI 3.59% to 11.69%) followed by East Asia and Eastern Europe (table 1 and figure 1C). The largest decrease was noted in west Europe (−9.57%, 95% UI −12.26% to −6.2%), followed by Southern Latin America and Australasia (table 1 and figure 1C).

Furthermore, ASRs of AF/AFL prevalence stratified by age and whether accompanied with symptoms are shown in figure 2. For both asymptomatic and symptomatic AFs/AFLs, prevalence rates increased with ageing in both 1990 and 2017. Across all the age groups, prevalence rates due to asymptomatic AF/AFL remained higher than those due to symptomatic AF/AFL. Both trends for ASRs of prevalence of asymptomatic and symptomatic AF/AFL were downwards from 1990 to 2017. Despite declining age-standardised AF/AFL prevalence, at all age groups, a net

Table 1 Age-standardised prevalence rates of AF/AFL in 1990 and 2017 and and its temporal trends from 1990 to 2017

Location	Prevalence (1990)	Prevalence[7]	Percentage change (prevalence), 1990–2017 (95% UI)	EAPC (prevalence) (95% CI)
Global	507.32 (435.12 to 579.67)	481.54 (416.51 to 546.21)	−5.08% (−6.24 to −3.82)*	−0.17 (−0.19 to −0.15)*
Low SDI	367.43 (314.45 to 423.08)	369.29 (315.87 to 425.1)	0.51% (−0.84 to 1.7)	0.01 (0.01 to 0.02)*
Low–middle SDI	383.84 (327 to 442.66)	391.93 (332.97 to 452.37)	2.11% (1.2 to 3.02)*	0.09 (0.08 to 0.1)*
Middle SDI	415.46 (356.4 to 475.12)	436.02 (373.72 to 498.62)	4.95% (4.24 to 5.64)*	0.2 (0.17 to 0.23)*
High–middle SDI	479.8 (411.08 to 548.35)	469.32 (402.67 to 535.94)	−2.19% (−3.19 to −1.14)*	−0.08 (−0.11 to −0.06)*
High SDI	642.61 (553.48 to 733.64)	598.57 (528.94 to 670.49)	−6.85% (−9.6 to −3.83)*	−0.22 (−0.24 to −0.2)*
Central Europe	616.95 (528.77 to 710.33)	608.37 (533.27 to 685.29)	−1.39% (−5.26 to 3.91)	0.03 (0 to 0.06)*
Australasia	864.27 (740.15 to 993.27)	799.52 (688.19 to 916.75)	−7.49% (−10.9 to −4.1)*	−0.3 (−0.34 to −0.26)*
Central Asia	498.05 (426.82 to 573.41)	524 (448.66 to 602.85)	5.21% (3.34 to 7.17)*	0.24 (0.22 to 0.26)*
Central Latin America	601.93 (524.29 to 687.45)	607.29 (526.38 to 692.27)	0.89% (−0.2 to 1.92)	0.05 (0.04 to 0.06)*
Tropical Latin America	620.7 (517.48 to 727.85)	642.04 (538.45 to 751.19)	3.44% (1.71 to 5.15)*	0.39 (0.23 to 0.56)*
Caribbean	531 (459.41 to 606.49)	540.28 (467.6 to 615.92)	1.75% (−0.09 to 3.75)	0.07 (0.07 to 0.08)*
Southern sub-Saharan Africa	377.86 (323.95 to 434.55)	371.14 (317.02 to 425.14)	−1.78% (−3.11 to −0.42)*	−0.06 (−0.08 to −0.05)*
Eastern Europe	540.36 (463 to 620.15)	580.82 (499.03 to 666.5)	7.49% (6.22 to 8.83)*	0.33 (0.3 to 0.35)*
Southern Latin America	618.63 (528.53 to 710.23)	571.26 (490.18 to 655.25)	−7.66% (−10.79 to −4.4)*	−0.33 (−0.37 to −0.28)*
Andean Latin America	508.5 (440.18 to 581.76)	532.23 (460.35 to 609.24)	4.67% (2.06 to 7.02)*	0.18 (0.17 to 0.2)*
Southeast Asia	383.1 (328.52 to 440.62)	394.61 (337.53 to 453.51)	3% (1.72 to 4.36)*	0.13 (0.12 to 0.14)*
Western Europe	668.38 (576.25 to 764.92)	604.42 (535.54 to 676.22)	−9.57% (−12.26 to −6.2)*	−0.31 (−0.34 to −0.28)*
High-income Asia Pacific	256.06 (219.55 to 296.45)	238.42 (209.15 to 270.07)	−6.89% (−0.61 to −2.76)*	−0.41 (−0.55 to −0.26)*
South Asia	392.71 (335.79 to 452.65)	393.7 (336.06 to 453.91)	0.25% (−0.63 to 1.21)	0 (0 to 0.01)
High-income North America	809.21 (691.94 to 927.2)	871.03 (762.18 to 978.69)	7.64% (3.59 to 11.69)*	0.35 (0.29 to 0.41)*
East Asia	383.3 (327.45 to 440.03)	412.18 (350.48 to 473.85)	7.53% (6.59 to 8.42)*	0.26 (0.19 to 0.32)*
North Africa and Middle East	321.46 (275.72 to 368.6)	311.85 (271.99 to 354.21)	−2.99% (−4.85 to −1.04)*	−0.19 (−0.22 to −0.16)*
Oceania	383.76 (327.43 to 443.08)	385.13 (330.37 to 442.84)	0.36% (−2.09 to 2.78)	−0.01 (−0.03 to 0)
Central sub-Saharan Africa	332.02 (284.24 to 383.21)	325.75 (278.91 to 375.85)	−1.89% (−5.03 to 1.24)	−0.08 (−0.1 to −0.05)*
Eastern sub-Saharan Africa	319.49 (273.18 to 366.6)	318.27 (271.53 to 364.94)	−0.38% (−1.49 to 0.81)	−0.04 (−0.05 to −0.03)*
Western sub-Saharan Africa	347.55 (296.73 to 399.29)	357.66 (305.72 to 411.51)	2.91% (0.62 to 5.1)*	0.09 (0.06 to 0.12)*

*<Significant difference.
AF/AFL, atrial fibrillation/atrial flutter; EAPC, estimated annual percentage change; SDI, sociodemographic index; UI, uncertainty interval.

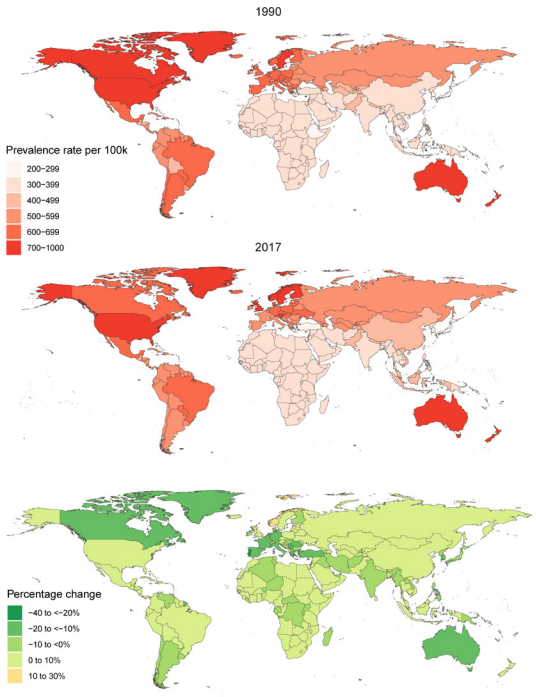

Figure 1 Global age-standardised prevalence of AF/AFL for both sexes in 195 countries and territories. (A) Age-standardised prevalence of AF/AFL in 1990, (B) age-standardised prevalence of AF/AFL in 2017 and (C) the relative change in prevalence of AF/AFL between 1990 and 2017. AF/AFL, atrial fibrillation/atrial flutter.

increase in the absolute number of patients who suffered with either asymptomatic or symptomatic AF/AFL was observed from 1990 to 2017.

Age-standardised AF/AFL prevalence stratified by SDI regions for both sexes is shown in figure 3. There was a positive, significant and moderate Pearson's product–moment correlation between SDI and prevalence for both men (ρ=0.66, 95% CI 0.62 to 0.7; p<0.001) and women (ρ=0.53, 95% CI 0.48 to

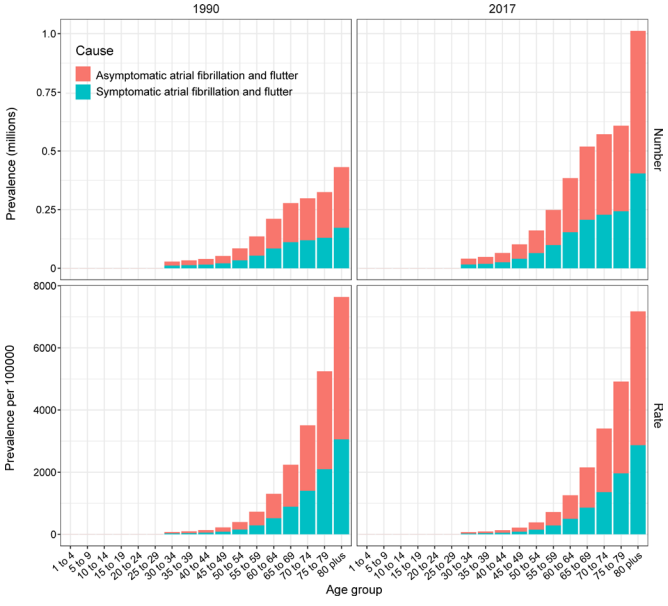

Figure 2 Number and rate of global prevalence for asymptomatic and symptomatic AF/AFL. AF/AFL, atrial fibrillation/atrial flutter.

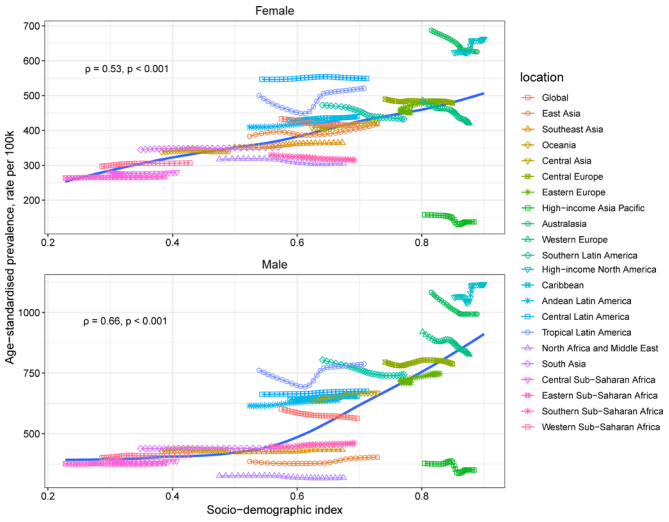

Figure 3 Age-standardised rate of prevalence for AF/AFL versus SDI for men and women by region, 1990–2017. The blue line, a LOWESS smoother, shows the expected value only on the SDI values of the global regions between 1990 and 2017. AF/AFL, atrial fibrillation/atrial flutter; LOWESS, locally weighted scatterplot smoothing; SDI, sociodemographic index.

0.58; p<0.001) from 1990 to 2017. In most regions, the prevalence rates increased with an increase in SDI values; high-income Asia Pacific is the exception. Between 1990 and 2017, a slight upward trend in the AF/AFL prevalence was observed for both sexes in regions with low and middle SDI values, except North Africa and Middle East, while a downward trend was observed for both sexes in regions with high SDI values (table 1), except high-income North America. For women, the largest increase in prevalence was observed in East Asia (11.94%, 95% UI 10.21% to 13.57%) followed by high-income North America and Eastern Europe. The greatest decrease in the prevalence was observed in western Europe (−13.26%, 95% UI −16.20% to −9.64%), followed by high-income Asia Pacific. For men, the largest increase in prevalence was observed in Eastern Europe (6.57%, 95% UI 4.77% to 8.35%) followed by high-income North America and East Asia, and the greatest decrease was observed in western Europe (−9.70%, 95% UI −12.62% to −6.01%) followed by Australasia. Men had a higher prevalence than women across all SDI regions, especially in regions with high SDI values, for all the calendar years from 1990 to 2017. Interestingly, only in China did women (424.18, 95% UI 361.19 to 489.77) have a higher prevalence than men (403.71, 95% UI 345.26 to 463.90, per 100 000) in 2017.

Incidence of AF/AFL

Globally, the estimated number of individuals with new-onset AF/AFL in 1990 was 1.59 million (95% UI 1.35 to 1.85 million) and 3.05 million (95% UI 2.6 to 3.5 million) in 2017, with 1.59 million men (95% UI 1.35 to 1.82 million) and 1.46 million women (95% UI 1.24 to 1.68 million). The total global age-standardised incidence changed from 39.89 (95% UI 33.73 to 46.33) per 100 000 person-years in 1990 to 38.16 (95% UI 32.56 to 43.9) per 100 000 person-years in 2017, showing a decline of 4.35% (95% UI −5.43% to −3.12%) (table 2), with the largest decrease observed in high-income Asia Pacific (−11.43%, 95% UI −15.47% to −7.07%) (table 2). In 2017, the highest incidence of AF/AFL was also observed in high-income North America (75.5, 95% UI 65.59 to 85.99, per

Table 2 Age-standardised incidence rates of AF/AFL in 1990 and 2017 and and its temporal trends from 1990 to 2017

Location	Incidence (1990)	Incidence (2017)	Percentage change (incidence), 1990–2017 (95% UI)	EAPC (incidence) (95% CI)
Global	39.89 (33.73 to 46.33)	38.16 (32.56 to 43.9)	−4.35% (−5.43 to −3.12)*	−0.15 (−0.18 to −0.12)*
Low SDI	30.13 (25.4 to 35.33)	30.33 (25.43 to 35.5)	0.64% (−0.69 to 1.94)	0.02 (0.01 to 0.02)*
Low–middle SDI	31.24 (26.18 to 36.45)	31.91 (26.73 to 37.2)	2.14% (1.17 to 3.21)*	0.09 (0.08 to 0.1)*
Middle SDI	32.74 (27.59 to 38.06)	34.42 (29.05 to 39.9)	5.14% (4.3 to 5.87)*	0.2 (0.17 to 0.24)*
High–middle SDI	36.9 (31.18 to 42.9)	36.37 (30.82 to 42.15)	−1.42% (−2.64 to −0.28)*	−0.06 (−0.09 to −0.03)*
High SDI	52.34 (44.46 to 60.59)	49.41 (42.94 to 55.99)	−5.6% (−8.55 to −2.36)*	−0.18 (−0.2 to −0.15)*
Central Europe	46.28 (39.28 to 53.54)	46.07 (40.25 to 52.38)	−0.44% (−4.3 to 5.01)	0.09 (0.05 to 0.13)*
Australasia	71.44 (60.31 to 83.33)	65.24 (55.19 to 75.74)	−8.68% (−12 to −5.3)*	−0.35 (−0.39 to −0.31)*
Central Asia	38.28 (32.45 to 44.56)	40.03 (33.92 to 46.58)	4.57% (2.49 to 6.72)*	0.21 (0.19 to 0.23)*
Central Latin America	42.65 (36.39 to 49.14)	43.07 (36.78 to 49.53)	0.98% (−0.13 to 2.18)	0.04 (0.04 to 0.05)*
Tropical Latin America	44.79 (36.51 to 53.86)	46.16 (37.68 to 55)	3.05% (1.13 to 4.93)*	0.41 (0.22 to 0.6)*
Caribbean	38.35 (32.66 to 44.21)	39.14 (33.24 to 45.12)	2.06% (−0.01 to 4.18)	0.08 (0.07 to 0.09)*
Southern sub-Saharan Africa	31.01 (26.1 to 36.2)	30.63 (25.74 to 35.82)	−1.22% (−2.64 to 0.11)	−0.04 (−0.05 to −0.03)*
Eastern Europe	40.8 (34.7 to 47.41)	43.48 (36.99 to 50.43)	6.58% (5.24 to 7.9)*	0.3 (0.27 to 0.32)*
Southern Latin America	51.27 (43.35 to 59.81)	47.3 (40.18 to 55.31)	−7.74% (−10.86 to −4.46)*	−0.33 (−0.37 to −0.29)*
Andean Latin America	36.88 (31.46 to 42.67)	38.56 (32.83 to 44.53)	4.54% (1.93 to 7.23)*	0.18 (0.17 to 0.19)*
Southeast Asia	31.41 (26.48 to 36.68)	32.33 (27.24 to 37.78)	2.92% (1.58 to 4.24)*	0.12 (0.12 to 0.13)*
Western Europe	55.16 (46.8 to 64)	49.35 (43.3 to 55.65)	−10.53% (−13.41 to −7.14)*	−0.35 (−0.38 to −0.32)*
High-income Asia Pacific	18.25 (15.35 to 21.39)	16.16 (13.84 to 18.43)	−11.43% (−15.47 to −7.07)*	−0.67 (−0.86 to −0.48)*
South Asia	32.42 (27.28 to 37.94)	32.53 (27.37 to 38.1)	0.34% (−0.55 to 1.31)	0.01 (0 to 0.01)*
High-income North America	68.97 (58.55 to 80.23)	75.5 (65.59 to 85.99)	9.47% (4.95 to 13.9)*	0.43 (0.36 to 0.49)*
East Asia	30.96 (25.96 to 36)	33.3 (27.98 to 38.77)	7.57% (6.59 to 8.46)*	0.26 (0.19 to 0.33)*
North Africa and Middle East	26.22 (22.11 to 30.53)	25.57 (21.92 to 29.52)	−2.46% (−4.36 to −0.45)*	−0.16 (−0.19 to −0.13)*
Oceania	31.34 (26.34 to 36.64)	31.49 (26.68 to 36.77)	0.48% (−2.35 to 3.49)	−0.01 (−0.02 to 0.01)
Central sub-Saharan Africa	27.15 (22.85 to 31.78)	26.93 (22.72 to 31.45)	−0.82% (−4.59 to 2.76)	−0.03 (−0.06 to −0.01)*
Eastern sub-Saharan Africa	26.01 (21.86 to 30.35)	26.11 (21.98 to 30.52)	0.39% (−0.77 to 1.68)	−0.01 (−0.02 to 0)
Western sub-Saharan Africa	28.53 (24.01 to 33.46)	29.17 (24.54 to 34.05)	2.23% (−0.03 to 4.49)	0.06 (0.03 to 0.09)*

*<Significant difference.
AF/AFL, atrial fibrillation/atrial flutter; EAPC, estimated annual percentage change;; SDI, sociodemographic index; UI, uncertainty interval.

100 000 person-years) followed by Australasia and Western Europe (table 2). By contrast, the lowest incidence was observed in high-income Asia Pacific (16.16, 95% UI 13.84 to 18.43, per 100 000 person-years) (table 2). Over the same period, the largest increase in incidence was observed in high-income North America (9.47%, 95% UI 4.95% to 13.9%) (table 2). Stratified by SDI regions, the high SDI region had the highest incidence, and the low SDI region had the lowest incidence in 2017 (table 2). Moreover, from 1990 to 2017, the largest increase in incidence was observed in the middle SDI region (5.14%, 95% UI 4.3% to 5.87%) and the greatest decrease was observed in the high SDI region (−5.6%, 95% UI −8.55% to −2.36%) (table 2).

DALYs of AF/AFL

The rate of age-standardised DALYs of AF/AFL declined from 80 (95% UI 67.59 to 95.25) per 100 000 person-years in 1990 to 77.97 (95% UI 66.14 to 92.05) per 100 000 person-years in 2017, showing a decrease of 2.53% (95% UI −4.16% to −0.29%) (table 3). In total, about 5.97 million (95% UI 5.04 to 7.09 million) DALYs were lost due to AF/AFL in 2017, while 2.87 million (95% UI 2.39 to 3.45 million) were lost in 1990. In 2017, the highest DALYs were observed in Australasia (126.25, 95% UI 104.5 to 151.2, per 100 000 person-years), showing a significant decline (−9.36%, 95% UI −14.05% to −4.55%) from 1990 (table 3). Besides Australasia, DALYs were also high in high-income North America (119.25, 95% UI 98.42 to 143.63, per 100 000 person-years) in 2017, where they increased by 19.46% (95% UI 14.66% to 26.56%) from DALYs in 1990 (table 3). The lowest DALYs in 2017 were in high-income Asia Pacific (45.58 per 100 000 person-years, 95% UI 39.13 to 53.54), with a significant decrease (−12.98%, 95% UI −16.58% to −9.27%) from DALYs in 1990 (table 3). Over the same period time, the greatest decrease in DALYs was shown in high-income Asia Pacific (−12.98%, 95% UI −16.58% to −9.27%), while the greatest increase was shown in Central Asia (21.18%, 95% UI 15.72% to 30.77%).

The estimated relation between SDI and ASRs of AF/AFL DALYs is generally positive, significant and moderate for men (ρ=0.63, 95% CI 0.59 to 0.67; p<0.001) and positive, significant and weak for women (ρ=0.28, 95% CI 0.22 to 0.35; p<0.001) (figure 4). AF/AFL DALY rates showed at stable trends at the lower end of the SDI scale, then increased rapidly for SDI values of 0.47 for men or 0.54 for women (figure 4). Andean Latin America, Oceania, central sub-Saharan Africa, Australasia and high-income North America had higher DALY rates than would be expected on the basis of comparisons of SDI for all years. Conversely, rates for high-income Asia Pacific and North Africa and Middle east were lower than expected based on SDI for all timepoints between 1990 and 2017. DALY rates in most regions showed a steady increase but was observed to have significantly declined in Australasia, western Europe and high-income Asia Pacific from 1990 to 2017. Generally, DALYs decreased in the high SDI region (−5.41%, 95% UI −7.98% to −2.64%) but increased in other SDI regions, with the largest increase observed in the low–middle SDI region (9.16%, 95% UI 4.66% to 14.93%) (table 3).

Table 3 Age-standardised rates of DALYs for AF/AFL in 1990 and 2017 and and its temporal trends from 1990 to 2017

Location	DALYs (1990)	DALYs (2017)	Percentage change (DALYs), 1990–2017 (95% UI)	EAPC (DALYs) (95% CI)
Global	80 (67.59 to 95.25)	77.97 (66.14 to 92.05)	−2.53% (−4.16 to −0.29)*	−0.1 (−0.27 to 0.07)
Low SDI	59.43 (48.24 to 72.76)	63.09 (51.51 to 76.39)	6.15% (1.76 to 11.7)*	0.2 (0.13 to 0.26)*
Low–middle SDI	62.67 (52.51 to 74.72)	68.42 (58.16 to 81.02)	9.16% (4.66 to 14.93)*	0.3 (0.25 to 0.34)*
Middle SDI	66.36 (55.91 to 79.41)	70.36 (59.65 to 83.48)	6.03% (3.1 to 9.65)*	0.16 (0.09 to 0.24)*
High–mmiddle SDI	75.73 (64.05 to 90.05)	75.67 (64.19 to 89.74)	−0.08% (−2.4 to 2.62)	−0.06 (−0.1 to −0.01)*
High SDI	98.85 (82.58 to 119.23)	93.5 (78.55 to 111.15)	−5.41% (−7.98 to −2.64)*	−0.2 (−0.68 to 0.29)
Central Europe	94.51 (79.58 to 113.34)	94.27 (78.96 to 111.89)	−0.25% (−4.22 to 3.23)	0.07 (−0.29 to 0.43)
Australasia	139.29 (116.59 to 166.42)	126.25 (104.5 to 151.2)	−9.36% (−14.05 to −4.55)*	−0.44 (−0.64 to −0.25)*
Central Asia	77.31 (64.22 to 93.07)	93.69 (80.44 to 109.66)	21.18% (15.72 to 30.77)*	0.71 (0.37 to 1.06)*
Central Latin America	91.18 (76.08 to 109.57)	91.65 (76.3 to 110.44)	0.51% (−2.21 to 2.63)	−0.05 (−0.08 to −0.02)*
Tropical Latin America	99.15 (82.47 to 118.96)	103.69 (86.36 to 124.05)	4.58% (1.73 to 7.35)*	0.33 (0.07 to 0.59)*
Caribbean	86.21 (72.37 to 103.32)	88.73 (75.45 to 104.64)	2.91% (−4.54 to 7.4)	0.07 (−0.15 to 0.29)
Southern sub-Saharan Africa	58.87 (48.45 to 70.18)	62.42 (53.21 to 73.58)	6.04% (1.97 to 11.64)*	0.29 (0.06 to 0.52)*
Eastern Europe	83 (69.79 to 99.02)	90.61 (76.33 to 107.85)	9.17% (6.14 to 14.77)*	0.32 (0.05 to 0.59)*
Southern Latin America	99.18 (82.71 to 119.1)	94 (78.83 to 112.3)	−5.23% (−10.88 to −0.06)*	−0.21 (−0.51 to 0.1)
Andean Latin America	82.41 (68.65 to 97.87)	86.36 (71.81 to 102.44)	4.79% (−1.86 to 12.08)	0.2 (−0.03 to 0.42)
Southeast Asia	60.46 (50.72 to 71.65)	66.17 (56.54 to 78.29)	9.44% (4.93 to 14.23)*	0.31 (0.26 to 0.35)*
Western Europe	108.47 (90.63 to 131.92)	101.72 (85.88 to 121.14)	−6.23% (−9.32 to −2.43)*	−0.2 (−0.65 to 0.25)
High-income Asia Pacific	52.37 (45.31 to 60.76)	45.58 (39.13 to 53.54)	−12.98% (−16.58 to −9.27)*	−0.71 (−1.56 to 0.15)
South Asia	57.77 (46.62 to 70.51)	65.73 (54.01 to 79.17)	13.78% (8.88 to 21.72)*	0.43 (0.36 to 0.5)*
High-income North America	108.63 (88.13 to 132.67)	119.25 (98.42 to 143.63)	9.78% (6.14 to 13.43)*	0.37 (−0.16 to 0.91)
East Asia	62.5 (52.34 to 74.48)	65.44 (54.95 to 77.92)	4.72% (0.4 to 9.24)*	0.12 (−0.11 to 0.34)
North Africa and Middle East	50.55 (42.32 to 60.72)	52.17 (43.95 to 61.91)	3.22% (−1.67 to 8.55)	0.11 (0.03 to 0.18)*
Oceania	88.6 (77.26 to 102.57)	92.47 (81.23 to 105.7)	4.37% (−3.53 to 11.65)	0.18 (0.07 to 0.29)*
Central sub-Saharan Africa	76.64 (62.43 to 93.67)	79.7 (64.38 to 97.47)	3.99% (−4.53 to 14.24)	0.06 (−0.01 to 0.14)
Eastern sub-Saharan Africa	72.33 (53.52 to 92.87)	66.21 (47.46 to 83.03)	−8.46% (−15.37 to −1.03)*	−0.48 (−0.56 to −0.4)*
Western sub-Saharan Africa	66.55 (53.95 to 80.24)	70.66 (58.74 to 84.49)	6.18% (−4.07 to 18.1)	0.18 (0.13 to 0.23)*

*<Significant difference.
AF/AFL, atrial fibrillation/atrial flutter; DALY, disability-adjusted life-year; EAPC, estimated annual percentage change; SDI, sociodemographic index; UI, uncertainty interval.

Globally, as the main exposure factor (figure 5), age-standardised population attributable fraction (PAF) for high systolic blood pressure accounted for 41.97% (95% UI 36.48% to 47.26%) in 1990, 40.09% (95% UI 34.67% to 45.43%) in 2007 and 39.80% (95% UI 34.41% to 45.13%) in 2017 of DALYs. PAF of high BMI accounted for 16.74% (95% UI 8.71% to 27.28%) in 1990, 20.54% (95% UI 11.63% to 31.84%) in 2007 and 21.82% (95% UI 12.55% to 33.29%) in 2017. Additionally, PAF of alcohol use, smoking and a high-sodium diet accounted for similar proportions for attributable DALYs. Interestingly, as an environmental risk factor, PAF of lead exposure accounted for a stable percentage from 1990 (2.98%, 95% UI 1.83% to 4.24%) to 2017 (3.18%, 95% UI 2.03% to 4.49%). PAF of high systolic blood pressure, alcohol use and smoking declined; that of high BMI increased; while that of a high-sodium diet remained relatively constant from 1990 to 2017.

PAFs for all risk factors stratified by age and sex are shown in figure 5. At all age groups, PAF trends for all risk factors were similar for men and women. PAFs for alcohol use and smoking for men were obviously higher than those for women. Conversely, PAF for high BMI was significantly lower for men than for women. For those aged 15–49 years, PAF for high systolic blood pressure increased slightly from 1990 to 2017 for both sexes. PAF for high systolic blood pressure in any single year from 1990 to 2017 for those aged 50–69 years was the highest compared with that of any other age group, at about 50%. After the age of 70 years, PAF of high systolic blood pressure showed a decreasing trend from 1990 to 2017. At all age groups, PAF of high BMI showed an increasing trend, whereas that of smoking showed a decreasing trend for both sexes from 1990 to 2017. With growing age, PAF of alcohol use and smoking decreased for both sexes. After the age of 70 years, PAFs for all risk factors declined.

DISCUSSION

The present study showed a comprehensive evaluation of the global burden of AF/AFL. Globally, about 37.6 million people suffered from AF/AFL in 2017. In 2014, there were approximately 33 million patients with AF/AFL,[10] showing an increase in the total number of individuals with AF/AFL. Despite a decline in the global prevalence and incidence rates, there were, on average, 2.86 million new cases of AF annually.

We identified specific differences in the global prevalence of AF/AFL by sex and SDI. Similar to the previous study,[6 11–13] we also observed that men had a higher prevalence rate of AF/AFL than women in most countries. For both sexes, we noted that across all timepoints, the prevalence rates of AF/AFL were higher with high SDI values. Furthermore, both the largest increase and the largest decrease in the prevalence rates across the years were observed in the high or high–middle SDI regions. The main components of SDI are years of schooling, per capital income levels and gross fertility rate. Therefore, social factors have an important impact on the prevalence rate of AF/AFL and its changes. It could be that better surveillance on the healthcare system was conducted in the high SDI regions, and there is a great untapped potential for improving

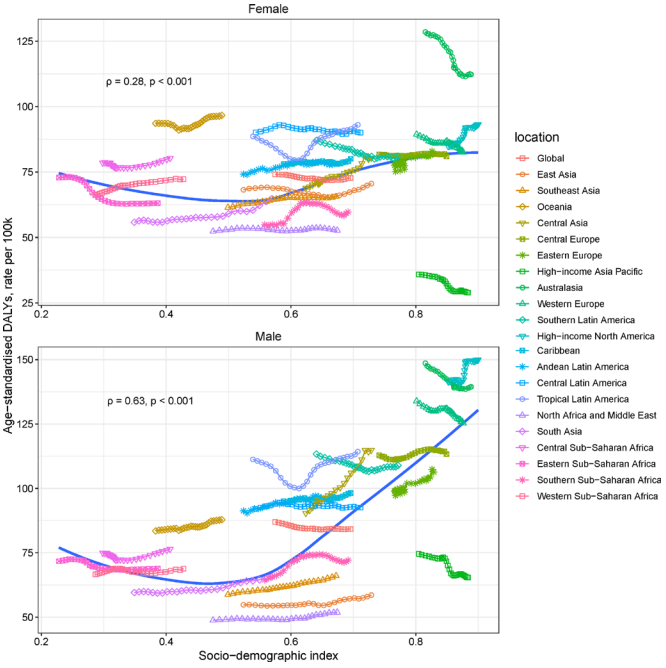

Figure 4 Age-standardised rate of DALYs for AF/AFL versus SDI for men and women, by region, 1990–2017. The blue line, a LOWESS smoother, shows the expected value only on the SDI values of the global regions between 1990 and 2017. AF/AFL, atrial fibrillation/atrial flutter; DALY, disability-adjusted life-year.; LOWESS, SDI, sociodemographic index.

the healthcare systems of the low, low–middle and middle SDI regions in order to accurately diagnose more patients with AF/AFL, especially those that are asymptomatic.

The overall burden of AF/AFL was quantified by age-standardised DALYs, which decreased by 2.53%. However, due to population growth and ageing, larger amounts of DALYs were lost due to AF/AFL from 1990 to 2017. Furthermore, DALY rates were higher with SDI values over about 0.5, showing a decline in most regions from 1990 to 2017. By contrast, DALY rates showed an increase in the regions with low and medium SDI values. This may be attributed to the treatment strategies, including use of new oral anticoagulants, left atrial appendage occlusion and catheter or cryogenic balloon ablation across regions, which varies across the different unequal

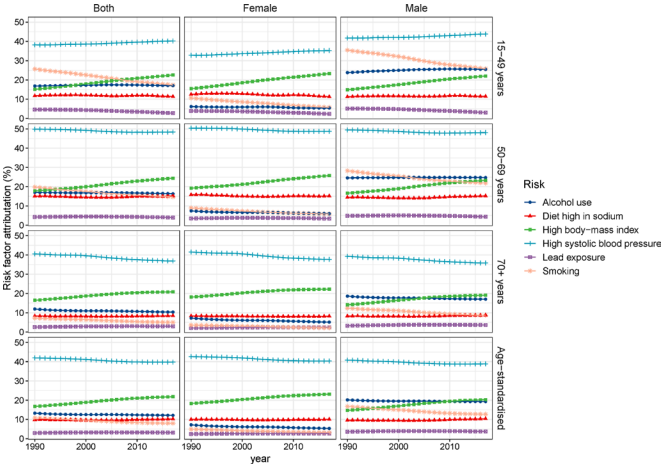

Figure 5 Population attributable fractions for risk factors attributed for disability-adjusted life-years stratified by age and sex.

distribution of socioeconomic circumstances regions. In addition, AF/AFL is a common entity, with over 70% of patients with AF/AFL having associated comorbidities.[2] The DALYs presented here should be interpreted with caution as various comorbidities associated AF/AFL, such as diabetes, pulmonary disease and atherosclerotic vascular disease, were not classified separately. Multiple risk factors influence the DALYs of AF/AFL. Our results highlight that in 2017, elevated systolic blood pressure ranked as the highest for attributable DALYs of AF/AFL. High BMI ranked second, followed by behavioural factors. Notably, lead exposure for attributable DALYs accounted for about 3% worldwide. Chronic exposure to low levels of lead, in food and drink, is still a significant public health issue, particularly in many developing and industrialising countries. More lead reduction programmes need to be implemented. Overall, the attributable burden for AF/AFL DALYs was generated by combining risk factors, with the final estimate being less than 100%. The remaining percentage is due to varying unknown or unmeasured risk factors, genetic predispositions and environmental exposures.

There are limitations to this study. First, majority of patients with paroxysmal AF/AFL can progress to permanent AF/AFL. The definitive factor that influenced AF/AFL progression was left atrial size.[14] Receiving antiarrhythmic drugs, pulmonary vein isolation, ablation of rotors, box isolation or cardioversion would reverse atrial substrate. Due to lack of data on these treatments and AF/AFL progressions, AF/AFL progression rate to permanent AF/AFL was absent in this study. Additionally, previous studies showed that prevalence AF/AFL without comorbidities varies since comorbidities are underdiagnosed[15] and multiple comorbid conditions raise the risk of AF/AFL-related complications.[16] Relevant data on comorbidity are also absent here, and the comorbidities associated with prevalent AF/AFL, incident AF/AFL as well as AF/AFL-related complications were therefore not included in the present analyses. Finally, the study is limited by all the general limitations described by the GBD collaboration group.[17–19] Differences in races, nationalities and socioeconomic structures within countries have an impact on the comprehensiveness of the database, which may affect the accuracy of the estimated results.

CONCLUSIONS

In summary, our results found that, although the ASRs of prevalence and DALYs decreased over time globally, the absolute number of individuals with AF/AFL and DALYs due to AF/AFL increased. This is probably due to population growth, which

Key messages

What is already known on this subject?

- Past observational studies showed that the incidence and prevalence rates of Atrial fibrillation/atrial flutter (AF/AFL) are increasing, with these increases differing among different regions.

What might this study add?

- Although rates of prevalence, incidence and disability-adjusted life-years (DALYs) decreased from 1990 to 2017, the absolute number of patients with AF/AFL, the annual number of new AF/AFL cases and DALYs increased.

How might this impact on clinical practice?

- The burden of AF/AFL is likely to remain high. Systematic surveillance is needed to better identify and manage AF/AFL so as to prevent its various risk factors and complications.

raises the healthcare costs needed to pay for treatment of AF/AFL across the world. The heterogeneous burden of exposures in different regions was mainly due to the imbalance of socioeconomic development, which indicated that systematic surveillance should be employed especially in the middle-income and low-income regions, for identifying and managing AF/AFL so as to prevent its various risk factors and complications.

Contributors LW, FZ and JL analysed the data, drafted and revised the paper. LM, BH and HN prepared and analysed the data. NZ conceived and designed the study, interpreted the results, drafted and revised the paper. All authors provided critical comments on the manuscript. All authors read and approved the final manuscript.

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Patient consent for publication Not required.

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Data availability statement Data are available in a public, open access repository. We retrieved data from the Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool), an online tool of the Global Burden of Diseases, Injuries, and Risk Factors Study 2017. The database is hosted by the Institute for Health Metrics and Evaluation at the Washington University.

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Supplemental materials

Estimated annual percentage changes (EAPC) is a measure of the ASR trend over a time interval, calculated as the method proposed by Hankey. The age-standardised rate (ASR) could be fitted in a regression model:

$$\ln(ASR) = \alpha + \beta x + \varepsilon.$$

where α is the intercept term, β is the annual change per 100,000 in the rates, x is the calendar year, ε is the error term.

EAPC is calculated as $100\times(\exp(\beta) - 1)$, and its 95% confidence interval (CI) can also be computed similarly from the linear regression model.

For example, if we want to calculate the EAPC of prevalence of global AF/AFL from 1990 to 2017, we can get the following raw data from GBD 2017. The name of the data frame in R is data:

measure_name	location_name	sex_name	cause_name	metric_name	year	ASR
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1990	507.3233189
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1994	499.4232023
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1998	493.2582504
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2002	489.3763761
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2006	487.7023255
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2010	486.2168861
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2014	483.5037373
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1993	501.3069835
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1997	494.6499164
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2001	489.8149858
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2005	488.310046
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2009	486.6468458
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2013	484.246483
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2017	481.5402806
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1992	503.2165201
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1996	496.1509016
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2000	490.6677486
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2004	488.7743747
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2008	487.0584908
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2012	484.864877
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2016	482.2168474

Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1991	505.2268778
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1995	497.7465089
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	1999	491.8607856
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2003	489.1214041
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2007	487.3211923
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2011	485.5297641
Prevalence	Global	Both	Atrial fibrillation and flutter	Rate	2015	482.9377298

The R code are like following:

```
######################

# First, fit a linear model to the year (from 1990 to 2017) and log(ASR):

fit_model <- glm(log(ASR)~ year, family = gaussian, data)

# Then we get β parameter of the fitted model:

coef <-  coefficients(fit_model)[2]

# And get the Confidence Intervals parameter:

lower25 <-  confint(fit_model)[2]

upper975 <-  confint(fit_model)[4]

# Thus, EAPC and its lower and upper boundary of 95% CI can be computed by:

eapc_mean <- (exp(coef) - 1)*100

eapc_lower <- (exp(lower25) - 1)*100

eapc_upper <- (exp(upper975) - 1)*100

# using paste0 to combine the result

EAPC <- paste0(round(eapc_mean,2),' (',round(eapc_lower,2),' to ',round(eapc_upper,2),')')

######################
```

Reference:

Hankey, B.F., Ries, L.A., Kosary, C.L., Feuer, E.J., Merrill, R.M., Clegg, L.X., Edwards, B.K., 2000. Partitioning linear trends in age-adjusted rates. Cancer Cause Control 11, 31-35.