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## **Epidemiology of atrial fibrillation**

**Running title:** Epidemiology of AF

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## **Abstract**

**Background:** The most common type of arrhythmia in the United States and in the European countries is atrial fibrillation (AF). The prevalence of AF is increasing worldwide with advances in technology, better prediction methods and increased awareness among healthcare physicians and patients. **Methods:** This article summarises the literature on the epidemiology of AF worldwide according to continents, age and ethnicity/race, and also includes the prevalence of AF in stroke patients. **Results:** In Australia, Europe and the USA, the current estimated prevalence of AF is about between 1-4%, with lower prevalence evident in Asia (0.49%-1.9%). AF prevalence is highest among Whites. In Western Europe, Australia and North America 70% of people with AF are aged >65 years whereas the average age of AF patients in other geographical regions is often lower. **Conclusions:** Although the prevalence of AF worldwide is increasing steadily, large variation can be seen between studies and countries. Further epidemiological studies should be undertaken globally, especially in Asian and African countries so that a better and more accurate picture of the incidence and prevalence of AF can be captured, to enable stroke prevention strategies to be appropriately implemented to prevent or reduce the risk of stroke, the most severe consequence of AF.

**Keywords:** atrial fibrillation, epidemiology, prevalence, worldwide, continents, ethnicity, age, stroke

## Introduction

Atrial fibrillation (AF), the most common form of arrhythmia with clinical significance is a major global health burden worldwide.<sup>1</sup> In the United States (US) and European countries, one in every four middle-aged adults will develop AF. Most importantly, AF is associated with a five-fold greater risk of stroke, increased risk of death and development of heart failure, and a greater risk of hospital admission, with 10-40% of AF patients hospitalised annually. Additionally, irrespective of other cardiovascular-related conditions, AF patients have poorer quality of life and unfortunately, despite anticoagulation for stroke prevention, they can still develop vascular dementia and a decline in cognitive function.<sup>2</sup>

According to the Global Burden of AF,<sup>3</sup> worldwide, the projected number of people with AF in 2010 was 33.5 million, consisting of 20.9 million males (UI, 19.5-22.2 million) and 12.6 million females (UI, 12.0-13.7 million), with higher incidence and prevalence rates in developed countries (**Table 1**). Mortality associated with AF globally is higher in females, primarily driven by higher mortality among females in developing countries. (**Figure 1**). This article summarises the literature on the epidemiology of AF worldwide according to continents, age and ethnicity/race, and also includes the prevalence of AF in stroke patients.

## Methods

A literature search was performed on PubMed using the following keywords alone or in combination: ‘atrial’, ‘fibrillation’, ‘incidence’, ‘prevalence’, ‘stroke’, ‘worldwide’, ‘epidemiology’, ‘Asian’, ‘race’, ‘ethnicity’. The bibliography from Rahman et al<sup>1</sup> was checked and additional studies on the prevalence of AF worldwide were included. The studies were collated according to the year of publication and country, and summarised in Tables 2 and 3.

## Worldwide prevalence of AF by continents

In Europe, AF currently affects eight million people and is expected to rise drastically, 2.3-fold by 2060.<sup>4, 5</sup> In the United Kingdom projections from the Clinical Practice Research Database suggest that AF will affect between 1.3 and 1.8 million people by 2060.<sup>6</sup> In the United States, about 3-5 million people are currently affected by AF and by 2050 this figure is expected to be greater than 8 million people.<sup>7</sup> In Australia, Europe and the USA, the current estimated prevalence of AF is about between 1-4%.<sup>1, 4</sup> **Table 2** and **Figure 2** illustrates the prevalence of AF in nine countries, stratified by continents worldwide. Australia has the highest prevalence of AF i.e., 5.4% followed by Africa 4.6%, although the prevalence was lower (0.7%) in another African study by Shavadiwa et al<sup>8</sup>, followed by Iceland (2.4%) and lowest in Asian countries (0.49%-1.9%).

A recent review<sup>9</sup> on AF epidemiology of 58 studies from five Asian (China, Japan, South Korea, India, Malaysia) and eight Middle Eastern countries (Turkey, Bahrain, Qatar, Kuwait, Saudi Arabia, Oman, United Arab Emirates and Yemen)<sup>9</sup> reported the annual incidence of AF to be 5.38 per 1000 person-years mainly from Chinese, Japanese and Korean studies (10 studies in total)<sup>10-19</sup> conducted from 1991-2012, with study populations ranging from 1485<sup>14</sup> to 471,446.<sup>12</sup> Prevalence of AF varies between hospital-based and community-based studies; being higher in the latter (0.37%-3.56% vs 2.8%-15.8%).<sup>9</sup>

Differences in the incidence and prevalence rates between studies is likely dependent on the time the study was conducted, the design (nationwide studies, medical insurance databases etc., retrospective, prospective, cross-sectional) and the study population (age of patients, urban compared to remote areas as their risk factors may vary, for example the prevalence of rheumatic heart disease is higher in rural populations in India)<sup>20</sup> which in turn effects the quality of data obtained.<sup>4</sup>

## Ethnicity, age and prevalence of AF

The prevalence of AF across different ethnic groups differs, although most of the studies investigating these differences have been conducted in the United States. For the purpose of this review, ethnicity is classified as White, (European, American) Afro-Caribbean, (Blacks, Black British, African-American) East Asian, (Chinese, Japanese, Malaysian and other Asians) South Asian (Indian, Pakistani, Bangladeshi), Hispanics (Hispanic or Latino), and others, as reported in individual studies.<sup>21, 22</sup>

**Table 3** shows the prevalence of AF by race and ethnicity according to 11 studies,<sup>23-33</sup> conducted in the United States and one<sup>23</sup> multicentre study conducted in North America, Europe and Asia. In all studies, the prevalence of AF was highest among the Whites compared to Afro-Caribbeans, East Asians and Hispanics, ranging from 42%<sup>32</sup> to 2.5%<sup>31</sup> among the Whites, and 21%<sup>31</sup> to 1.7%<sup>30</sup> among Afro-Caribbeans. Only three studies<sup>23, 25, 33</sup> reported AF prevalence among East Asians which ranged from 3.9%<sup>25</sup> to 10.1%,<sup>23</sup> while only one study reported AF prevalence among Hispanics (3.9%).<sup>25</sup> A meta-analysis of 10 studies examining the prevalence of AF among African-Americans in the United States compared to Whites, concluded that being African-American was associated with a ‘protective effect’ from AF (OR 0.51, 95% CI 0.44-0.59,  $p < 0.001$ ). Despite the lower prevalence of AF, African-Americans in the US have twice the risk of first ever stroke compared to Whites.<sup>34</sup>

In addition to ethnic differences, age distribution of AF diagnosis may also differ between regions. More than 70% of AF patients in Western Europe, Australia and North America were aged  $>65$  years.<sup>1</sup> A different pattern in the average age of AF diagnosis is evident from other regions whereby AF patients are younger, for example; the mean age of AF patients was  $57 \pm 16$  years in the Gulf-SAFE registry from Arabic population,<sup>35</sup>  $41 \pm 13$  years in an Ethiopian study,<sup>36</sup>  $<65$  years in 43% of the South Korean population detected with AF<sup>1</sup> and  $<50$  years in 38% of patients from one South-African hospital.<sup>37</sup> Results from the

RE-LY AF registry which enrolled AF patients from the 164 emergency departments worldwide to evaluate the differences in the presentation and management of AF, also shows some regional variation in terms of age at AF diagnosis; patients from America and Europe countries were on average 10-12 years older than those from Africa, India and the Middle East.<sup>38</sup>

### **Incidence and prevalence of AF in stroke patients**

AF increases the risk of stroke approximately 5 times compared to those without AF.<sup>2</sup> An Italian study has shown<sup>39</sup> the presence of AF in 24.6% of patients (mean age  $78.8 \pm 13.3$  years) with ischemic stroke in a population based study, where AF is more frequent in women and patients 80 years or older. In this study, AF was an independent predictor of 30-day and 1-year mortality in Cox regression analysis.<sup>39</sup>

Another prospective study in Germany reported an overall prevalence of AF slightly higher than the Italian study, i.e., 28.6% in 692 patients with ischemic stroke or transient ischemic attack, with prevalence increasing with age.<sup>40</sup> Hanchate et al reported a similar prevalence of AF in the USA in 2013 (i.e., 23% in acute ischaemic stroke patients from eight states),<sup>41</sup> in two European studies (24.6 and 28.6% respectively)<sup>20, 42</sup> and an Australian study (25%; study population 26,960).<sup>43</sup> However, the prevalence of AF was reportedly lower in some Asian countries, approximately 10% in China,<sup>44</sup> 5.8-6% in India,<sup>45, 46</sup> but higher in Japan (32%).<sup>47</sup>

Sposato et al conducted a meta-analysis of 50 studies in 2015<sup>48</sup> to estimate the proportion of newly diagnosed AF patients experiencing stroke or TIA after undergoing four sequential phases of cardiac monitoring; phase 1: ECG at admission, phase 2: continuous inpatient ECG, phase 3: Holter monitoring and phase 4: mobile cardiac outpatient telemetry. In this study, they reported an overall presence of AF in 23.7% (95% CI 17.2-31.0) of their

post-stroke patients and an estimated prevalence of AF in post-stroke patients with either known or newly diagnosed AF of about 39.0%, higher than previously reported studies.<sup>48</sup>

## **Conclusion**

The prevalence of AF worldwide is increasing steadily although large variation can be seen between studies and countries. A larger proportion of ischemic stroke patients are also found to have AF either during admission or upon investigation post- discharge that becomes a major concern as AF related to stroke has poorer outcomes and prognosis.<sup>2, 4</sup> This increase in the prevalence of AF may be explained by the fact that better prediction methods have been used to detect AF<sup>1, 2, 49</sup> and also greater awareness among physicians and other healthcare providers who are able to detect patients with AF during routine check-ups, flu injections and also during hospital admissions.

More epidemiological studies should perhaps be undertaken globally, especially in Asian and African countries, in urban and rural areas, so that a more accurate picture of the incidence and prevalence of AF can be captured, thereby allowing appropriate implementation of stroke prevention strategies to reduce stroke risk and burden.



**Authors contributions:**

All authors contributed to the data interpretation, drafting the article and critical revision.

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Table 1: Incidence and prevalence of AF and AF- associated mortality rate with 95% uncertainty intervals (UI) (per 100,000) for males and females (data extracted from Chugh 2014) <sup>3</sup>

	1990	2010	1990	2010
	Male		Female	
<b>Incidence of AF</b>				
Globally, all ages	60.7 (49.2-78.5)	77.5 (65.2-95.4)	43.8 (35.9-55.0)	59.5 (49.9-74.9)
Developed Countries	78.4 (67.5-91.9)	123.4 (107.6-141.5)	52.8 (45.0-62.9)	90.4 (77.8-104.5)
Developing Countries	50.0 (33.8-76.8)	53.8 (38.7-79.8)	36.0 (24.5-54.7)	40.0 (27.2-62.6)
<b>Prevalence of AF</b>				
Globally, all ages	569.5 (532.8-612.7)	596.2 (558.4-636.7)	359.9 (334.7-392.6)	373.1 (347.9-402.2)
Developed Countries	608.2 (547.0-693.5)	660.9 (597.1-738.2)	362.5 (329.3-422.3)	387.7 (343.8-450.0)
Developing Countries	546.6 (503.0-599.6)	656.7 (522.9-617.6)	358.2 (329.8-393.0)	366.1 (337.4-400.8)
<b>Mortality rate</b>				
Globally, all ages	0.8 (0.5-1.1)	1.6 (1.0-2.4)	0.9 (0.7-1.2)	1.7 (1.4-2.2)
Developed Countries	1.3 (0.9-1.9)	2.7 (1.9-4.3)	1.1 (1.0-1.3)	2.4 (2.0-3.0)
Developing Countries	0.4 (0.2-0.8)	0.7 (0.4-1.3)	0.7 (0.4-1.4)	1.0 (0.6-1.7)

AF= atrial fibrillation

Table 2: Worldwide prevalence of AF by continent

Country	Study	Years data obtained Study design	Sample size	Study population		Prevalence (%) total, (men and women)
				Data source	Age (SD) [Men, women (%)]	
Africa						
Africa	Sliwa et al 2010 <sup>37</sup>	2006-2008 Prospective	5328 cardiac cases	Hospital-based, single centre, urban population	59 (18) [39, 61% AF]	4.6 (†)
Kenya	Shavadia et al 2013 <sup>8</sup>	2008-2010 Retrospective	44, 144	One hospital admission in Nairobi	≥18 [56, 44% AF]	0.7 (†)
Asia						
Malaysia	Lim et al 2016 <sup>50</sup>	2007-2014 Prospective	10,805	18 urban, 22 rural communities across Malaysia	52.6 (11.6)	0.49 (†)
Singapore	Yap et al 2008 <sup>51</sup>	† Prospective	1,839	Community-based study	≥55	1.4 (†)
Thailand	Phrommintikul et al 2016 <sup>52</sup>	† Prospective	1,277	Cross section of Maerim District, Chiang Mai	≥65 [45.8, 54.2% AF]	1.9 (†)
Australia						
Australia	Ball et al 2015 <sup>53</sup>	June 2014	6,140,651	7 international epidemiology study	≥ 55 years	5.35 (5.97, 4.79)

Australia	Sturn et al 2002 <sup>54</sup>	2000 Prospective	14, 194	50 consecutive patients at 321 general practices	≥30	4.0 (6.0, 4.0)
<b>Europe</b>						
England	Health & Social Care Information Centre 2014-2015 <sup>55</sup>	2014-2015 Retrospective	56,939,507	National primary care practice database	†	1.6 (†)
United Kingdom	Lane et al 2017 <sup>6</sup>	1998-2010 Retrospective	57, 818	UK Clinical Practice Research Datalink (CPRD)	≥18 years [51.7, 48.3% AF]	1.26 (1.33, 1.18) per 1000 pt- yrs [age-adjusted incidence]
Iceland	Stefansdottir et al 2011 <sup>5</sup>	1987 -31 December 2008 Retrospective	4905-AF cases	The National University Hospital of Iceland	20–99 years	2.4-age and sex standardised
<b>North America</b>						
USA	Naccarelli et al 2009 <sup>56</sup>	2004-2005 Retrospective	242, 903	National databases of employer-funded insurance and Medicare	≥20	1.1 (†)
<b>South America</b>						
Brazil	Marcolino et al 2015 <sup>42</sup>	Jan-December 2011 Retrospective	262 685	658 municipalities, primary Care	50.3 (19.3) [40.4, 59.6]	1.8 (2.4, 1.3)
† Not reported						

Table 3 Prevalence of AF by ethnicity and race

Country/State	Study	a) Study design b) Follow up c) Sample size	Mean age study population (SD)	Prevalence of AF (%)			
				Whites	Afro-Caribbeans	East Asians	Hispanics
North America, Europe, Asia	Lau et al 2013 <sup>23</sup>	a) Prospective b) 2.5 years c) 2580	Europeans: 76.2 (6.6) Black African: 75.2 (6.2) Chinese: 76.2 (6.7) Japanese: 78.4 (7.0)	18	8.3	10.1 Chinese, 9.5 Japanese	N/A
Michigan, USA	Lahiri et al 2011 <sup>24</sup>	a) Retrospective b) N/A c) 1001	African American: 33.0% ≥70 European American: 35.4% ≥70	29	19	N/A	N/A
USA	Winkelmayer et al 2011 <sup>33</sup>	a) Cross sectional b) 15 years c) 2,483,199	70.9 (11.8)	14	6.5	9.0*	N/A
California, USA	Shen et al 2010 <sup>25</sup>	a) Cross-sectional b) N/A c) 430, 317	White: 70 (64-77) Black: 68 (64-74) Asian: 67 (63-73) Hispanic: 67 (61-71)	8	3.8	3.9	3.6
15 U.S states, Washington, DC	Marcus et al 2010 <sup>26</sup>	a) Combination of CHS and ARIC study b) – c) 19, 784	<b>CHS</b> African American: 73 (6) Whites: 73 (6) <b>ARIC</b> African Americans: 53 (6) Whites: 54 (6)	23	15	N/A	N/A



Maryland, Minnesota, Mississippi, N. Carolina, USA	Alonso et al 2009 <sup>27</sup>	a) Prospective b) 228,976 person-years c) 15, 407	Whites: 54.4 (5.7) African Americans: 53.6 (5.8)	7.9	4.8	N/A	N/A
Ohio, USA	Smith et al 2006 <sup>28</sup>	a) Prospective b) - c) 9671	-	24	17	N/A	N/A
California, USA	Ruo et al 2004 <sup>29</sup>	a) Retrospective and prospective b) - c) 1373	73 overall	38	20	N/A	N/A
Georgia, USA	Upshaw et al 2002 <sup>30</sup>	a) Retrospective b) - c) 2123	14% age 70-79	7.8	2.5	N/A	N/A
California, USA	Go et al 2001 <sup>31</sup>	a) Cross sectional b) N/A c) 17, 974	71.2 (12.2) whole cohort	2.5	1.7	N/A	N/A
Michigan, USA	Afzal et al 1999 <sup>32</sup>	a) Prospective b) 6 months c) 163	Blacks: 63.8 (13.7) Whites: 70.8 (13.1)	42	21	N/A	N/A

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Pt-yrs = patient years; \*Asian Americans; N/A = not applicable

## **Figure legends**

**Figure 1:** AF associated mortality stratified by sex and region (developed and developing countries)

**Figure 2:** Prevalence of AF by continents



