Anticoagulation in Atrial Fibrillation
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DOI:
10.33612/diss.132895541

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Jacobs, M. (2020). Anticoagulation in Atrial Fibrillation: Consideration for treatment and health economic aspects. University of Groningen. https://doi.org/10.33612/diss.132895541

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Chapter 3
Atrial fibrillation in Africa - an underreported and unrecognized risk factor for stroke: a systematic review

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Global Heart. 2019;14(3):269–279
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ABSTRACT

Over three-quarters of deaths from cardiovascular disease and diabetes occur in low- and middle-income countries, which include many African countries. Global studies showed that the prevalence of the cardiac arrhythmia atrial fibrillation (AF) appeared to be lower in Africa. A systematic search of PubMed and African Journals Online was conducted to determine the prevalence of AF and associated stroke risk factors in Africa and to quantify the need for screening. The publications search yielded a total of 840 articles of which 41 were included. AF was often not identified as the disease of primary interest with its own risks. Data on prevalence in the general population was scarce. The prevalence of stroke risk factors showed a large variation between studies, as well as within clustered subpopulations. AF in Africa is under-reported in published reports. The study types and populations are highly heterogeneous, making it difficult to draw a definitive conclusion on AF prevalence.
INTRODUCTION

Noncommunicable diseases cause more than one-half of the total burden of disease in Sub-Saharan Africa (SSA).[1-4] Cardiovascular diseases constitute a major part of this burden. Strokes and heart attacks are by far the most common cause of cardiovascular death.[1,5,6] For prevention of these conditions, a total-risk approach is recommended by the World Health Organization (WHO) with integrated management of hypertension, diabetes, high cholesterol, and other cardiovascular risk factors. WHO identified counselling and multidrug therapy for people with a high risk of developing heart attacks and stroke as being among the best-buy interventions.[7] Interestingly, targeting of cardiac arrhythmias such as atrial fibrillation (AF) is not mentioned in any of the best-buy strategies, although it is an established risk factor for stroke. AF increases the risk of stroke about 5-fold and it is associated with a 1.5- to 2.0-fold increase in all-cause mortality.[8] A global increase of 42.8% in AF-related deaths has been seen from 2006 to 2016, though a proportion may be attributable to an increased likelihood of reporting AF or atrial flutter as an underlying cause of death.[9] The disease has a high prevalence that can go up to at least 10% in people age 80 years and over in high-income countries.[10,11] The prevalence of AF is not clear in low- and middle-income countries (LMIC), including countries in Africa. It is uncertain if the low incidence and prevalence reported for the African region is due to poor surveillance, under-reporting, or genetic predisposition. [12] Underestimation could have resulted from poor access to health care and weak or nonexistent surveillance systems. We therefore conducted a systematic review of published reports to determine the prevalence of AF and associated stroke risk factors in Africa and to assess the need for appropriate screening and stroke prevention strategies.

METHODS

Search Strategy
We searched the PubMed database, which includes MEDLINE, for articles published between January 1, 2000, and April 15, 2018, on the epidemiology of AF in Africa. An additional search was performed in the African Journals Online (AJOL) database within the period January 1, 2000 (inserted as “1st of January 2004” as the earliest available date to choose) up to April 15, 2018.[13] For the initial identification of published studies, we used the following search terms: “atrial fibrillation,” “stroke,” and “anticoagulation” as Medical Subject Headings, or MeSH, terms. Details of the search are outlined in the Online Appendix. After the initial search phase in the databases, the secondary inclusion criterion was the term “atrial fibrillation” in the abstract combined with a number that could be the number of people with AF (n or %), the number of AF episodes, or prevalence
and/or incidence of AF. If there was no indication for an incidence and/or prevalence number in the abstract, but it did contain the term “atrial fibrillation,” the full text would be screened to see whether a number was included in the full-text manuscript. Articles that included the words “atrial fibrillation” in the abstract but did not provide any insight into incidence and/or prevalence were excluded. Articles were only included if the research described the African population living in Africa, the data were original (no duplicate publication), the full text was available, and the article was available in English. International articles were excluded if they did not provide country- and/or region-specific numbers for African countries [14]. All the articles were initially screened by 1 reviewer.

**Data extraction**

The following data, if available, was extracted from the included publications: country/location; study design; type of population; population size; proportion of female subjects, average age (mean or median); estimates of AF prevalence and/or incidence; method of diagnosis; type of AF (paroxysmal, persistent, permanent); CHADS2 (Congestive Heart Failure History, Hypertension History, Age ≥75 Years, Diabetes Mellitus History, Previous Stroke or Transient Ischemic Attack Symptoms) or CHA\(_2\)DS\(_2\)-VASc (Congestive Heart Failure of Left Ventricular Dysfunction, Hypertension, Age ≥75 [doubled], Diabetes, Thromboembolism or Stroke History [doubled], Vascular Disease, Age 65 to 74 Years, and Sex Category) score; HASBLED(Hypertension, Abnormal Renal or Liver Function, Stroke History, Bleeding History, Labile International Normalized Ratio, Elderly (Age >65), Drugs or Alcohol) score; presence of stroke risk factors including diabetes, hypertension, stroke history vascular disease, heart failure, and age ≥75 years old; anticoagulant and/or antiplatelet drug use in AF patients. The stroke risk factors included were based on the items included in the CHA\(_2\)DS\(_2\)-VASc score.[15] If specific numbers for the AF cohort were not available, we reported the information available for the whole population. Study country was the country where patient recruitment took place. The study types were coarsely classified as a retrospective cohort study, prospective cohort study, or a case-control study.

**Quality assessment**

Study quality was assessed using the checklist of Downs and Black. [16] This checklist is appropriate for both randomized and nonrandomized studies. The checklist item on power (item 27) was not taken into account; the maximum achievable score was therefore 27. Score ranges were given an overall quality level to qualify the available evidence included in the review: excellent (26 to 27); good (20 to 25); fair (15 to 19); and poor (≤14).
RESULTS

The systematic search identified 776 eligible articles from PubMed and 52 articles through the AJOL search. Two articles were indexed in both PubMed and AJOL. Of the identified articles, 115 were excluded because a full text was not available or the article was not in English. A total of 699 abstracts were screened and after exclusion of all articles that did not meet the predefined inclusion criteria, 41 original articles remained. The results are summarized in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart (Fig. 1).

Figure 1: PRISMA flow chart of systematic review article screening and reasons for exclusion
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Quality assessment
Overall, 14 studies had the quality score “poor,” 26 studies were scored “fair,” and only 2 were scored “good.” Low scores were partially due to the exploratory, nonrandomized nature of the studies. Study quality assessment results with a detailed summary of subscores for the questionnaire items can be found in Online Table 1.

Atrial fibrillation prevalence
The studies identified mainly focused on different patient subgroups and only 3 of the included articles described a population that would be representative for the general population. The results are summarized in Table 1. [17-57] AF prevalence in the older, general population was 0.30% to 0.70% [17-19]. The study of Dewhurst et al. [17] in a rural area calculated a crude prevalence of 0.67% and an age-adjusted prevalence of 0.64%. Prevalence was different between men (0.31%) and women (0.96%). Also, prevalence increased with age from 0.46% in people age 70 to 74 years up to 1.3% to those age 85 years and older.[17] The age limit for the prevalence number of 0.30% was 50 years and over, and for the higher prevalence of 0.70%, the age limit was 70 years and over.[17,18] In patients with known cardiovascular disease presenting at the hospital, the prevalence varied from 3.8% to 59.0%.[20-30] Patient inclusion for these studies on patients with cardiovascular disease was mainly carried out at a hospital and also described patients that were previously diagnosed with AF. The most frequently used method for AF diagnosis confirmation was a 12-lead electrocardiogram. In heart failure patients, the prevalence was higher and ranged from 15.7% up to 34.0% [31-35]. Four of the studies on heart failure patients were hospital-based and 1 included outpatients [32]. Patients who (recently) underwent cardiac surgery had an AF prevalence of 4.0% to 17.0% [36-40]. Stroke patients, which include patients who had an acute stroke or had a history of stroke, had an AF prevalence of 1.5% to 17.6% [41-47]. Patients with rheumatic heart disease (RHD), had a prevalence of 13.9% to 44.5% [27,48-52]. Patients with RHD represented a more heterogeneous population, including children as well as adults, and with 2 studies also including outpatient data [48,52]. Studies in anticoagulation clinics showed that 25.1% to 65.0% of the patients were using oral anticoagulation for nonvalvular AF as the indication [53-57]. Several studies had information on the type of AF, which is generally categorized as paroxysmal, persistent, or permanent [21,23,24,27,36,44]. Persistent AF was the most found type of AF, ranging from 21.2% to 81.0%. Permanent AF was seen in 5.0% to 58.8% of the patients, and paroxysmal AF accounted for 11.8% to 32.1% of the AF cases (see Table 2) [17-57]
**Table 1:** Study characteristics of included articles describing atrial fibrillation prevalence in Africa

| Author               | Year | Study type                      | Country               | Population                                                                 | No. pts | Female, % | Age, AF, % |
|----------------------|------|---------------------------------|-----------------------|---------------------------------------------------------------------------|---------|-----------|------------|
| **General population**                                                                                                                               |         |                       |                                                     |         |           |            |
| Dewhurst MJ          | 2012 | Prospective cohort study        | Tanzania              | People aged 70 years and over in a rural African community               | 2232    | 56·3      | 77·8 0·70  |
| Koopman JJ           | 2014 | Prospective cohort study        | Ghana                 | Individuals aged 50 years and over in a rural area                      | 924     | 48·1      | 66·0 0·30  |
| Gray WK              | 2016 | Prospective cohort study        | Tanzania              | People aged 70 years and over                                           | 2232    | 56·3      | 77·8 0·60  |
| **Patients with known cardiovascular disease**                                                                                                     |         |                       |                                                     |         |           |            |
| Nqayana T            | 2008 | Retrospective cohort study      | South Africa          | Patients with cardiac disease in pregnancy                              | 95      | 100·0     | - 9·5      |
| Ntep-Gweth M         | 2010 | Prospective cohort study        | Cameroon              | Patients >18 years with AF documented on an ECG during the index visit   | 172     | 56·4      | 65·8 100·0 |
| Sliwa K              | 2010 | Prospective cohort study        | South Africa          | Patients presenting to the Cardiology Unit (Heart of Soweto study)       | 5328    | 61·0      | 58·8 4·6   |
| Shavadia J           | 2013 | Retrospective cohort study      | Kenya                 | Patients with discharge diagnosis of either atrial fibrillation or flutter| 162     | 44·0      | 67·0 59·0  |
| Jardine RM           | 2014 | Prospective cohort study        | South Africa          | Patients with confirmed AF drawn from the private insured sector         | 302     | 40·1      | 67·0 100·0 |
| Gamra H              | 2014 | Cross-sectional observational study | Algeria, Egypt, Morocco, Tunisia | Patients with a history of AF documented by ECG                       | 1680    | 61·1      | 64·2 100·0 |
| Akpa MR              | 2015 | Retrospective cohort study      | Nigeria               | All patients referred to the Cardiology Unit or seen in the Cardiac Clinic with ECG evidence of AF | 228    | 42·6      | 59·8 29·8  |
| Bloomfield GS        | 2015 | Prospective cohort study        | Kenya                 | Patients aged 18 years and over with AF based on ruling out significant valvular heart disease | 298    | 53·0      | 68·0 24·0  |
| Ajayi EA             | 2016 | Prospective cohort study        | Nigeria               | Patients with an ECG at the hospital                                     | 1462    | 67·4*     | 67·3 3·8   |
| Yameogo AR           | 2016 | Retrospective cohort study      | Burkina Faso          | Patients at the Cardiology Department with non-valvular heart disease    | 970     | 44·6      | 65·5 7·0   |
| Temu TM              | 2017 | Prospective cohort study        | Kenya                 | AF patients in a teaching/ referral hospital: both nvAF as well as vAF | 146     | 55·0      | 69·4 47·3  |
### Table 1: Study characteristics of included articles describing atrial fibrillation prevalence in Africa (continued)

| Author          | Year | Study type                  | Country                                                                 | Population                                                                                           | No. pts | Female, % | Age, AF, % |
|-----------------|------|-----------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|---------|-----------|------------|
| **Patients with heart failure** |      |                             |                                                                         |                                                                                                       |         |           |            |
| Stewart S       | 2008 | Prospective cohort study    | South Africa                                                            | De novo presentation of patients with heart failure and related cardiomyopathies                     | 844     | 57·0      | 55·3 53·0  |
| Magaña-Serrano JA | 2011 | Prospective cohort study    | Tunisia, Algeria                                                         | Patients with heart failure and preserved ejection fraction                                          | 648     | 47·0      | 63·0 34·0  |
| Damasceno A     | 2012 | Prospective cohort study    | Cameroon, Ethiopia, Kenya, Mozambique, Nigeria, Senegal, South Africa, Sudan | Patients admitted to the hospital with diagnosed acute HF                                            | 1006    | 50·8      | 52·3 18·3  |
| Makubi A        | 2014 | Prospective cohort study    | Tanzania                                                                | Patients aged 18 years and over with heart failure attending a Cardiovascular Center                | 427     | 51·0      | 55·0 15·7  |
| Ogah OS         | 2015 | Prospective cohort study    | Cameroon, Ethiopia, Kenya, Mozambique, Nigeria, Senegal, South Africa, Sudan, Uganda | Patients with heart failure from Cardiology Units                                                    | 1006    | 50·8      | 52·4 18·4  |
| **Patients undergoing/who underwent cardiac surgery** |      |                             |                                                                         |                                                                                                       |         |           |            |
| Lorgat F        | 2012 | Prospective cohort study    | South Africa                                                            | Patients who underwent robotically assisted catheter ablation therapy in a hospital                | 95      | 25·0      | 59·4 100·0 |
| Mazibuko B      | 2012 | Retrospective cohort study  | South Africa                                                            | Pregnant patients with a prosthetic valve prostheses referred to a tertiary hospital               | 61      | 100·0     | 24·0 13·1  |
| Mansoor E       | 2014 | Retrospective cohort study  | South Africa                                                            | Post cardiac surgery patients                                                                      | 997     | 44·1      | 51·9 5·9   |
| Abdel-Salam Z   | 2016 | Prospective cohort study    | Egypt                                                                   | Patients scheduled for CABG with/without valve surgery                                             | 740     | 30·5      | 56·5 10·4  |
| Bun SS          | 2016 | Prospective cohort study    | Morocco                                                                  | Patients scheduled for radiofrequency catheter ablation or pacemaker implantation                 | 75      | 29·3      | 67·8 4·0   |
| Chtaou N        | 2016 | Retrospective cohort study  | Morocco                                                                  | All patients treated with rt-PA at a stroke unit                                                    | 52      | 50·5      | 63·0 17·0  |
Table 1: Study characteristics of included articles describing atrial fibrillation prevalence in Africa (continued)

| Author          | Year | Study type         | Country                  | Population                                                                 | No. pts | Female, % | Age, % | AF, % |
|-----------------|------|--------------------|--------------------------|----------------------------------------------------------------------------|---------|-----------|--------|-------|
| **Stroke patients** |      |                    |                          |                                                                            |         |           |        |       |
| Alkali NH       | 2013 | Prospective cohort study | Nigeria                  | Patients presenting with acute stroke                                        | 272     | 38·2      | 55·1   | 9·2   |
| Walker RW       | 2014 | Case-control study  | Tanzania                  | Incident stroke cases                                                        | 93      | 46·2      | 68·2   | 6·5   |
| Walker RW       | 2014 | Case-control study  | Tanzania, Dar-es-Salaam   | Incident stroke cases                                                        | 39      | 38·5      | 61·1   | 7·7   |
| Germain MD      | 2015 | Retrospective cohort study | Burkina Faso             | Hospitalized patients at the Cardiology and Neurology department with ischemic stroke | 391     | 62·3°     | 63·3   | 17·6  |
| Gomes J         | 2015 | Case-crossover study | Mozambique                | Patients admitted to the hospital for newly occurring ischemic and haemorrhagic stroke | 593     | 47·5      | 58·8   | 5·6   |
| Adeoye AM       | 2017 | Prospective cohort study | Nigeria, Ghana           | Acute stroke patients who had a 12-lead ECG recording within first 24h of admission | 890     | 58·3      | 58·3   | 4·2   |
| Lekoubou A      | 2017 | Retrospective cohort study | Cameroon                 | Stroke patients that were admitted to the hospital                         | 1678    | 50·2      | 62·0   | 1·5   |
| **Patients with rheumatic heart disease** |      |                    |                          |                                                                            |         |           |        |       |
| Sliwa K         | 2010 | Prospective cohort study | South Africa             | De novo cases of rheumatic heart disease presenting to the Cardiology Unit    | 344     | 68·0      | 43·0   | 34·0  |
| Okello E        | 2013 | Prospective cohort study | Uganda                   | Patients with newly diagnosed rheumatic heart disease                        | 309     | 63·5      | 30·0   | 13·9  |
| Zhang W         | 2013 | Prospective cohort study | Uganda                   | Patients with newly diagnosed rheumatic heart disease                        | 130     | 71·0      | 33·0   | 13·9  |
| Bloomfield GS   | 2015 | Prospective cohort study | Kenya                    | Patients aged 18 years and over with nvAF and vAF                           | 298     | 78·0      | 38·0   | 24·0  |
| Zühlke L        | 2016 | Prospective cohort study | LICs: Ethiopia, Kenya, Malawi, Rwanda, Uganda, and Zambia | Patients with symptomatic RHD visiting the hospital | 1110    | 65·8      | 24·0   | 18·2  |
**Table 1:** Study characteristics of included articles describing atrial fibrillation prevalence in Africa (continued)

| Author       | Year | Study type           | Country                                   | Population                                                                                   | No. pts | Female, % | Age, % | AF, % |
|--------------|------|----------------------|-------------------------------------------|------------------------------------------------------------------------------------------------|--------|----------|--------|-------|
| Zühlke L     | 2016 | Prospective cohort   | UMICs: Namibia and South Africa           | Patients with symptomatic RHD visiting the hospital                                           | 863    | 71.3     | 39.0   | 27.5  |
| Okello E     | 2017 | Prospective cohort   | Uganda                                    | Patient aged 5-60 years with established RHD                                                | 449    | 66.8     | 31.4   | 20.3  |
| Njovane XW   | 2013 | Retrospective cohort | South Africa                              | Patients using warfarin that attended a primary healthcare clinic                            | 111    | -        | -      | 44.5  |
| Anakwue RC   | 2014 | Retrospective cohort | Nigeria                                   | Patients that utilized anticoagulation services in a University Hospital                      | 26     | 53.4     | 53.8   | 30.8  |
| Sonuga BO    | 2016 | Retrospective cohort | South Africa                              | Patients attending the INR clinic                                                            | 136    | 56.6     | 64.0   | 65.0  |
| Schapkaitz E | 2017 | Prospective cohort   | South Africa                              | Patients attending the Anticoagulation Clinic                                                | 147    | 57.8     | 56.8   | 36.1  |
| Ebrahim I    | 2018 | Retrospective cohort | South Africa                              | Patient visiting the INR clinic                                                             | 363    | 65.6     | 55.0   | 25.1  |

Abbreviations: AF = Atrial Fibrillation; CHADS2 = Congestive heart failure, Hypertension, Age ≥75, Diabetes, Stroke or transient ischemic symptoms; CHA2DS2-VASc = Congestive heart failure of left ventricular dysfunction, Hypertension, Age ≥75, Diabetes, thromboembolism or Stroke history, Vascular disease, Age 65-74 years and Sex category; HAS-BLED = Hypertension, Abnormal renal or liver function, Stroke history, Bleeding history, Labile international normalized ratio, Elderly (age >65), Drugs or alcohol; HT = Hypertension; HF = Heart Failure; INR = International Normalized Ratio; OAC = Oral AntiCoagulation. ~Ischemic heart disease; * only myocardial infarction scored; ^Percentages for the AF sub-cohort; # 50% used an anticoagulant or aspirin; + Pulmonary hypertension; @ In patients with CHADS2 ≥2; $ 10% of these patients also used warfarin.
Stroke Risk Factors

The prevalence and presence of stroke risk factors were deducted from patients' characteristics tables of the included studies. The prevalence of stroke risk factors showed a large variation between studies but also within clustered subpopulations. Studies describing a population with known cardiovascular disease—AF or any other type of cardiovascular disease—included the most comprehensive information on stroke risk factors. Stroke history and the proportion of patients age 75 years and over were the factors that were least reported. The proportion of patients age 75 years and over was the least reported (nonmodifiable) factor, reported in only 4 studies, and in general <30% of the patients were age ≥75 years. Hypertension was the most frequently reported stroke risk factor, with prevalence at least around 60% to 70% for all studies. Prevalence seemed higher in the stroke subpopulation with a range of 31.0% to 93.8%, and it was lowest in RHD patients ranging from 5.2% to 53.3%. Diabetes prevalence ranged from as low as 8% in AF patients without valvular disease in Kenya up to 80.0% in coronary artery bypass surgery patients.[27,39] The definition of vascular disease varied between studies ranging from 6.0% up to 52.2% in post-cardiac surgery patients in South Africa.[38] Some studies only used a history of myocardial infarction, and other studies did not include a definition for vascular disease. Stroke history was reported in less than one-half of the included studies. For the subpopulation of stroke patients, the stroke history was scored prior to the admission. Overall, the reported stroke history showed a large variation ranging between 1.3% and 40.0% for the non-stroke patient subpopulation. Heart failure was present in 16.6% up to 60.3% of the population when excluding the subpopulation with known heart failure.
### Table 2: Stroke risk factors in patients with atrial fibrillation in Africa

| Author                  | Year | AF type                                  | CHADS$_2$ or CHA$_2$DS$_2$-VASc | Population | OAC use in AF patients (%) | Aspirin use in AF patients (%) |
|-------------------------|------|------------------------------------------|----------------------------------|------------|----------------------------|-------------------------------|
|                         |      | Paroxysmal; Persistent; Permanent        |                                  |            |                            |                               |
| General population      |      |                                          |                                  |            |                            |                               |
| Dewhurst MJ             | 2012 | -                                        | -                                | -          | -                          | 60·7                          |
| Koopman JJ              | 2014 | -                                        | -                                | 24·2       | 1·2*                       | -                             |
| Gray WK                 | 2016 | -                                        | -                                | 73·2       | 2·9                        | -                             |
| Patients with known cardiovascular disease | |                          |                                  |            |                            |                               |
| Nqayana T               | 2008 | -                                        | -                                | -          | -                          | -                             |
| Ntep-Gweth M            | 2010 | 22·7; 21·5; 55·8                         | 1·9 ± 1·1                        | 10·5       | 64·5                       | 17·4                          |
| Sliwa K                 | 2010 | 1·5 ± 0·9                                | -                                | -          | 60·0^                      | 6·5^                          |
| Shavadia J              | 2013 | 64·7% ≥2                                 | 33·0                             | 68         | -                          | 19·0                          |
| Jardine RM              | 2014 | 32·1; 21·2; 46·7                         | 3·08                             | 15·6       | 65·9                       | -                             |
| Gamra H                 | 2014 | 27·9; 21·6; 50·5                         | -                                | 22·7       | 54·7                       | -                             |
| Akpa MR                 | 2015 | 39·7%                                    | -                                | 58·8^      | -                          | -                             |
| Bloomfield GS           | 2015 | -                                        | 8·0                              | 67·0       | 25·0                       | -                             |
| Ajayi EA                | 2016 | 2·38                                     | -                                | 18·2^      | 87·3^                      | 40·0^                         |
| Yameogo AR              | 2016 | 11·8; -; 58·8                           | 3·9 ± 1·6                        | 3·5 ± 1·5  | -                          | -                             |
| Temu TM                 | 2017 | 2·2                                      | 8·7                              | 72·5       | 26·1                       | 49·0                          |
| Patients with heart failure | |                                      |                                  |            |                            |                               |
| Stewart S               | 2008 | -                                        | -                                | -          | 100·0                      | -                             |
Table 2: Stroke risk factors in patients with atrial fibrillation in Africa (continued)

| Author                  | Year | AF type          | CHADS₂ or CHA₂DS₂-VASc | Population            | Diabetes (%) | HT (%) | Stroke History (%) | Vascular Disease (%) | HF (%) | Age ≥75 (%) | OAC use in AF patients (%) | Aspirin use in AF patients (%) |
|-------------------------|------|------------------|-------------------------|-----------------------|--------------|--------|--------------------|----------------------|--------|-------------|-----------------------------|-------------------------------|
| Magaña-Serrano JA      | 2011 | -                | -                       | 42·0                  | 76·0         | 5·0    | 50·0               | 100·0                | -      | -           | -                           | -                             |
| Damasceno A            | 2012 | -                | -                       | 11·4                  | 55·5         | -      | -                  | 100·0                | 7·0    | 35·0        | -                           | -                             |
| Makubi A               | 2014 | -                | -                       | 45·0                  | -            | 3·7    | 9·0                | 100·0                | -      | -           | -                           | -                             |
| Ogah OS                | 2015 | -                | -                       | 11·4                  | 55·5         | 2·5    | 9·4                | 100·0                | -      | -           | -                           | -                             |
| Patients undergoing/who underwent cardiac surgery | | | | | | | | | | | | |
| Lorgat F              | 2012 | 14·0; 81·0; 5·0  | -                       | 9·0                   | 52·0         | 24·0   | -                  | -                    | -      | -           | -                           | -                             |
| Mazibuko B            | 2012 | -                | -                       | -                     | -            | -      | -                  | -                    | -      | -           | -                           | -                             |
| Mansoor E             | 2014 | -                | -                       | 40·7^                | 59·3         | -      | 52·2               | -                    | -      | -           | -                           | -                             |
| Abdel-Salam Z         | 2016 | -                | -                       | 80·0                  | 66·8         | -      | -                  | -                    | -      | -           | -                           | -                             |
| Bun SS                | 2016 | -                | -                       | -                     | -            | -      | -                  | -                    | -      | -           | -                           | -                             |
| Chtaou N              | 2016 | -                | -                       | 12·0                  | 31·0         | 10·0   | 6·0                | -                    | -      | -           | -                           | -                             |
| Stroke patients       |      |                  |                         |                       |              |        |                    |                      |        |             |                             |                               |
| Alkali NH             | 2013 | -                | -                       | 25·6                  | 83·7         | -      | -                  | -                    | -      | -           | -                           | -                             |
| Walker RW             | 2014 | -                | -                       | -                     | -            | -      | -                  | -                    | -      | -           | -                           | -                             |
| Walker RW             | 2014 | -                | -                       | -                     | -            | -      | -                  | -                    | -      | -           | -                           | -                             |
| Germain MD            | 2015 | 13·0; 52·1; 34·8 | 4·72                    | 39·1% ≥ 3            | 21·7^        | 85·5   | 100^               | 7·2^                 | 20·3   | 18·8        | 79·7                         | 14·0                          |
| Gomes J               | 2015 | -                | -                       | 13·4                  | 86·2         | 18·9   | -                  | -                    | -      | -           | -                           | -                             |
| Adeoye AM            | 2017 | -                | -                       | 32·9                  | 93·8         | -      | -                  | -                    | -      | -           | -                           | -                             |
| Lekoubou A           | 2017 | -                | -                       | 12·8                  | 67·9         | 14·5   | -                  | -                    | -      | -           | -                           | -                             |

Atrial fibrillation in Africa
| Author                  | Year | AF type       | CHADS$_2$ or CHA$_2$DS$_2$-VASc | Population | OAC use in AF patients (%) | Aspirin use in AF patients (%) |
|------------------------|------|---------------|---------------------------------|------------|---------------------------|-------------------------------|
|                        |      | Paroxysmal;   |                                 |            |                           |                               |
|                        |      | Persistent;   |                                 |            |                           |                               |
|                        |      | Permanent     |                                 |            |                           |                               |
|                        |      |               |                                 |            |                           |                               |
| **Patients with rheumatic heart disease** |      |               |                                 |            |                           |                               |
| Sliwa K$^{48}$          | 2010 | -             | -                               |            |                           |                               |
| Okello E$^{49}$         | 2013 | -             | -                               |            |                           |                               |
| Zhang W$^{50}$          | 2013 | -             | -                               |            |                           |                               |
| Bloomfield GS$^{57}$    | 2015 | -             | -                               |            |                           |                               |
| Zühlke L$^{52}$         | 2016 | -             | -                               |            |                           |                               |
| Zühlke L$^{52}$         | 2016 | -             | -                               |            |                           |                               |
| Okello E$^{52}$         | 2017 | -             | -                               |            |                           |                               |
| **Patients visiting an INR clinic** |      |               |                                 |            |                           |                               |
| Njovane XW$^{53}$       | 2013 | -             | -                               |            |                           |                               |
| Anakwue RC$^{54}$       | 2014 | -             | -                               |            |                           |                               |
| Sonuga BO$^{55}$        | 2016 | -             | -                               |            |                           |                               |
| Schapkaitz E$^{56}$     | 2017 | -             | -                               |            |                           |                               |
| Ebrahim I$^{57}$        | 2018 | -             | -                               |            |                           |                               |

Abbreviations: AF = Atrial Fibrillation; CHADS$_2$ = Congestive heart failure, Hypertension, Age ≥75, Diabetes, Stroke or transient ischemic symptoms; CHA$_2$DS$_2$-VASc = Congestive heart failure of left ventricular dysfunction, Hypertension, Age ≥75, Diabetes, thromboembolism or Stroke history, Vascular disease, Age 65-74 years and Sex category; HAS-BLED = Hypertension, Abnormal renal or liver function, Stroke history, Bleeding history, Labile international normalized ratio, Elderly (age >65), Drugs or alcohol; HT = Hypertension; HF = Heart Failure; INR = International Normalized Ratio; OAC = Oral AntiCoagulation. ~Ischemic heart disease; * only myocardial infarction scored; ^Percentages for the AF sub-cohort; # 50% used an anticoagulant or aspirin; + Pulmonary hypertension; @ In patients with CHADS$_2$ ≥2; $ 10\%$ of these patients also used warfarin.
Indication for Stroke Prevention, Anticoagulant Use, and Aspirin Use

Only 9 studies mentioned the CHADS₂ or CHA₂DS₂-VASc score. The reported CHADS₂ scores ranged from 1.5 to 2.4 and CHA₂DS₂-VASc scores ranged from 3.1 up to 3.9. The use of oral anticoagulation (OAC) and/or aspirin was reported in 10 studies, excluding the studies that focused on international normalized ratio (INR) clinics. All studies conducted in INR clinics described warfarin as the OAC being used. [53-57] Anticoagulants use showed a wide variation from 7.0% up to 81.2% of the patients, which included AF and non-AF patients. Aspirin was used in 14.0% to 94.1% of the patients. AF was the indication for OAC use in 25.1% to 65.0% of the patients that visited an INR clinic. Only 2 studies reported OAC and aspirin use for patients with a CHADS₂ score of 2 or higher; OAC use was 52.5% to 79.8% and aspirin use was 17.8% to 21.9% in these patients.[23,25] Patients with known AF had a mean OAC use between 8.8% and 81.2% and aspirin use ranging from 17.8% up to 94.1%. [21-27,29,30]

DISCUSSION

AF is under-reported in published reports from the African region. None of the included studies identify the extent of asymptomatic AF, which is crucial information to determine the overall prevalence and incidence. Underdiagnosis is most probably high and studies that focus on AF screening are lacking. This information is essential to determining the true AF burden and related severe consequences such as stroke. The study types and study populations are highly heterogeneous, making it difficult to draw definitive conclusions on AF prevalence in African populations. The focus of published studies seems to be on AF as a risk factor in other comorbid disease such as stroke, heart failure, or cardiovascular disease in general. AF is often not identified as the disease of primary interest with its own risks and complications. Data on prevalence in the general population was scarce; numbers that approached generalizable prevalence numbers ranged from 0.30% to 0.70% in patients ages 50 or 70 years and over, prevalence of ischemic stroke was lower and the prevalence of hemorrhagic stroke was higher in Africa and other LMIC than in high-income countries. In a SIREN (Stroke investigative research and educational network) study [61], a case-control study carried out in Ghana and Nigeria that aimed to identify and characterize stroke risk factors in SSA, 68% of the cases had ischemic stroke. However, this SIREN study [61] did not include data on AF as an individual factor and was only included in the combined risk factor “cardiac disease,” which had an odds ratio of 2.21 (99% confidence interval: 1.38 to 3.54) for ischemic stroke. A genetic component could play an important role in global and regional differences. The INTERSTROKE study [60] looked at global and regional effects of risk factors associated with acute stroke. AF was a significant predictor for ischemic stroke in Africa (odds ratio: 4.59; 99% confidence interval: 3.66 to 5.75; n= 1,364), and this effect was comparable in Western countries. [60] The population attributable risk of
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AF in stroke was lower in Africa than in the Western countries: 7.9% versus 17.1%.[60] The ORBIT-AF (Outcomes Registry for Better Informed Treatment for Atrial Fibrillation) study [62] found no difference in outcomes associated with AF, which included stroke, systemic embolism, transient ischemic attack, and various types of hospitalizations. Studies included in this review that described subpopulations of stroke patients showed an AF prevalence ranging from 1.5% to 17.6%, which was much lower than expected based on the knowledge that 20% to 30% of all strokes are due to AF.[8] The higher prevalence of RHD in African countries introduces an increase in complications related to AF, already at a young age. [63] Valvular heart disease can be associated with an increased thromboembolic risk, which probably also adds to the stroke risk in AF patients [64]. In the studies included in this systematic review, we found AF prevalence ranging from 13.9% up to 44.5% in the subpopulations describing RHD. The REMEDY (Global Rheumatic Heart Disease Registry) study [51], a large prospective registry in 12 African countries, India, and Yemen found AF as a comorbidity in 18.2% of the patients for the low-income countries (Ethiopia, Kenya, Malawi, Rwanda, Uganda, and Zambia), 22.6% for the LMIC (Egypt, India, Mozambique, Nigeria, Sudan, and Yemen), and 27.5% in the upper middle-income countries (South Africa and Namibia). Anticoagulant use in the populations studied was low and so was access to surgical interventions, especially in SSA. The included studies suggest that stroke prevention strategies in AF are suboptimal. WHO recommends aspirin as the drug of choice to reduce heart attacks and strokes in LMIC. It is understandable to choose a drug therapy that is affordable in these regions; however, this also implies that we would accept to provide suboptimal therapy. Analyses comparing the use of aspirin to OAC have shown that antiplatelet therapy is around 40.0% to 50.0% less effective in reducing the stroke burden in nonvalvular AF patients, though treatment benefit from vitamin K OAC is highly respectively. Remarkably, none of the studies included in this systematic review were used in the GBD (Global Burden of Disease) 2010 study. [12] The GBD estimates for AF seem not to be representative of the true AF burden in SSA and it is most likely an underestimation because studies with higher estimates and studies describing asymptomatic AF were not taken into account. This also illustrates that evidence on AF in this region is difficult to identify, even with a systematic approach, and search strategies need to be more tailored to the region. Based on published data, prevalence of AF in Africa seems low when compared with in the Western population where prevalence is at least 5.5% in people age 65 years and over.[10,58] AF patients in Africa are in general younger than AF patients in high-income countries.[59] Stroke also tends to occur at an earlier age in the African population when compared with age of occurrence in high-Income countries.[42-47] Reasons for an earlier presentation of the disease and its complications are not clear, though it seems that stroke type patterns are different for Africans. The INTERSTROKE (Global and Regional Effects of Potentially Modifiable Risk Factors Associated With Acute Stroke in
Atrial fibrillation in Africa

32 Countries) study [60] showed that the dependent on the time in therapeutic range.[65,66] Nonvitamin K antagonist OAC do not require routine monitoring and could therefore be a good alternative to vitamin K OAC therapy, with due consideration of prices that in all probability will drop the next couple of years because of expiring patents and also with possible inclusion on WHO's essential drug list. AF is not mentioned as a target for stroke prevention in any of the global actions plans or best-buy strategies of WHO. The World Heart Federation has published a very useful roadmap for nonvalvular AF in LMIC. One of the potential solutions includes optimization of AF detection, for example with a screening program by nonphysician health workers.[67] Screening for AF as a target for stroke prevention can be a cost-effective strategy depending on how the screening is arranged, the prevalence of AF and also the initiation of an appropriate stroke prevention strategy.[68–77] Opportunistic screening for AF is recommended in patients ≥65 years of age and systematic electrocardiogram screening may be considered to detect AF in patients age ≥75 years or those at high stroke risk according to the European Society of Cardiology guideline and the American Heart Association.[8,78] Systematic screening would be a good approach to determine the true prevalence of AF in the general population in Africa. In a low-resource region, it is very plausible that underdiagnosis is keeping the AF prevalence estimates artificially low. When taking into account that AF patients seem to be younger in Africa, one should consider screening at an earlier age to determine in which subpopulation this intervention would be most beneficial. Research has to be carried out to unravel racial differences in AF prevalence as well as consequential stroke severity and mortality. More attention needs to be paid to diagnosis and timely detection of AF in Africa. A broader prevention approach that also focuses on conditions predisposing to AF such as hypertension, heart failure, valvular heart disease, diabetes

CONCLUSIONS

AF is under-reported in published reports from the African region. Prevalence of AF seems lower and patients are generally younger compared with numbers found in high-income countries. Reasons for the earlier presentation of the disease and its complications are not clear. Numbers found most likely represent an underestimate because access to health care, use of routine monitoring electrocardiography, and patient surveillance is less common in Africa. Screening for AF would be an important approach to determine the true prevalence in the general population and to identify asymptomatic AF patients at risk for stroke.

SUPPLEMENTARY MATERIAL

Supplementary material is available online via https://doi.org/10.1016/j.gheart.2019.04.003
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