Atrial fibrillation among adults with heart failure in sub-Saharan Africa — prevalence, incidence and all-cause mortality: a systematic review and meta-analysis protocol

Valerie Ndip Agbor,1,2 Leopold Ndemnge Aminde,3,4 Frank-Leonel Tianyi,5 Clarence Mvalo Mbanga,6 Saint-Just N Petnga,7 Chobufo Ditah,8 Jean Jacques Noubiap9

ABSTRACT
Introduction Heart failure (HF) remains a major non-communicable disease in sub-Saharan Africa (SSA) associated with high rates of readmission, mortality and loss of economic productivity as it affects mostly young and economically active adults. Atrial fibrillation (AFib) is a major determinant of mortality among patients with HF in SSA. Meanwhile, the use of anti-arrhythmic medications in the region remains unacceptably low. This review aims to evaluate the prevalence and incidence of AFib in adult patients with HF in SSA, and the all-cause mortality rate among patients with HF and AFib.

Methods and analysis The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols 2015 statement was used to prepare this protocol. All eligible studies from database inception to December, 31 2018 in MEDLINE, Embase, Google Scholar, Web of science and Africa-specific databases (AFROLIB, African Index Medicus and African Journals Online) will be included without language restrictions. The process of study screening, selection, data extraction and assessment of risk of bias will be conducted independently by two reviewers. Disagreements will be arbitrated by a third reviewer. Study-specific estimates will be pooled using random-effect meta-analysis and summary measures obtained will be presented in forest plots. The $\chi^2$ test on Cochrane’s Q and the I$^2$ statistics will be used to assess and quantify heterogeneity, respectively. The Egger’s test and funnel plots will be used to assess publication bias.

Ethics and dissemination Since our review will be based on already published data, an ethical approval is not required. The findings of this review will be presented in conferences and peer-reviewed journals and shared on social media such as Researchgate, Facebook, WhatsApp and Twitter.

PROSPERO registration number CRD42018087564.

INTRODUCTION
The rapid transition in disease epidemiology from communicable to chronic non-communicable diseases (NCDs) in sub-Saharan Africa (SSA) has been particularly linked to the increasing prevalence of cardiovascular risk factors such as hypertension, diabetes, obesity and dyslipidaemia, and poor dietary and sedentary lifestyles owing to the-breeze of westernisation and urbanisation.1-3 Cardiovascular disease (CVD) is the leading cause of death globally and is said to overtake the Human Immunodeficiency Virus as the top killer in SSA in the next two decades.4

Heart failure (HF) is a major public health threat in SSA. It is the leading cause of admission into cardiology units and is associated with longer duration of hospital stay, high rates of readmissions and mortality, and a huge economic burden.5,6 On the other hand,
atrial fibrillation (AFib) remains the most common cardiac arrhythmia globally, and its prevalence in Africa is expected to rise due to increasing prevalence of risk factors such as rheumatic heart disease, hypertension, diabetes, obesity, cardiomyopathy and ageing population. It is associated with a high risk of thromboembolic events, especially stroke, morbidity and mortality. About 16%–20% of HF patients in SSA are diagnosed with AFib. Patients with HF in SSA are particularly prone to AFib and its complications due to the significant contributions of hypertension, cardiomyopathy and rheumatic valvular disease in the development of HF in the region. In addition to being a complication of HF, AFib can be the aetiology of HF through the development of atrial cardiomyopathy. AFib is a major decompensating factor and predictor of mortality among HF patients in SSA and elsewhere. In fact, HF patients with AFib are 1.3–3.4 times at risk of death compared to their counterparts without AFib. Atrial fibrillation is associated with more than 25% of all-cause mortality among patients with HF in SSA. Moreover, HF patients with AFib are at risk of higher readmissions rates, longer hospital stay and mortality compared with those without AFib. Meanwhile, the integration of anticoagulants and antiarrhythmic drugs such as beta-blockers and digoxin in the treatment of HF in SSA remains unacceptably low. This is aggravated by the unavailability of these drugs in the local pharmacies.

This systematic review and meta-analysis will focus on AFib as a complication of HF. Therefore, it seeks to summarise data on the prevalence and incidence of AFib in adults with HF in SSA, and all-cause mortality of patients with HF and AFib in the same population. The result of this study will go a long way to inform healthcare professionals and policymakers on the burden of AFib among HF patients in SSA so that adequate measures can be implemented to curb the morbidity and mortality associated with AFib among patients with HF in the region.

OBJECTIVE
To estimate the prevalence and incidence of AFib among adult patients with HF in SSA, and the mortality rate of patients with HF and AFib in the same population.

REVIEW QUESTIONS
1. What is the prevalence of AFib among patients with HF in SSA?
2. What is the incidence of AFib among patients with HF in SSA?
3. What is the proportion of all-cause mortality rate among HF patients with AFib in SSA?

METHODS AND ANALYSIS
Criteria for considering studies for the review
Inclusion criteria
1. Observational studies reporting on the prevalence (cross-sectional and cohort studies), incidence (cohort and randomised controlled trials) of AFib in patients with heart failure and all-cause mortality rates (cross-sectional, cohort and randomised controlled trials) among patients with HF and AFib in SSA.
2. Age limit: participants must be at least 15 years of age.
3. For duplicate studies: we shall include only the most recent and comprehensive study with the largest sample.
4. Publication date: from database inception to December 31, 2018.

Exclusion criteria
We shall exclude
1. Letters to the editor, editorials, commentaries, review articles and case series with fewer than 30 participants.
2. Studies conducted in participants with an initial diagnosis of AFib without HF.
3. Studies with incomplete data that could not be recovered even after a reasonable request from the corresponding author of the study.

Information sources
Search strategy for identifying relevant studies
MEDLINE, Embase, Google Scholar, Web of science and Asia-specific databases (AFROLIB, African Index Medicus and African Journals Online) will be searched from the inception date of each database to December 31, 2018 for relevant abstracts with information on the prevalence and/or incidence of AFib in HF, and/or mortality rate among HF patients with AFib in SSA. Medical subject headings and key text words like ‘atrial fibrillation’ and ‘heart failure’ will be used to build the search strategy. A validated search filter will be used to increase the geographical precision of our search. Table 1 depicts the main strategy for MEDLINE. This strategy will be adapted to suit other databases.

The full texts of eligible abstracts will be retrieved and assessed for final inclusion in this review. Database searches will be supplemented by scrutinising the reference lists of eligible articles and relevant reviews for additional studies. In case the full text of an article cannot be retrieved online, the corresponding authors will be contacted via their emails or other social platforms like Researchgate and a fortnightly reminder will be scheduled. If no response is received after eight reminder emails or before the end of the data extraction process, the study will be automatically excluded.

Study records
Data management
Titles and abstracts retrieved from database searches will initially be imported to the software EndNote V.7.4 for removal of duplicates. The unduplicated titles and abstracts will then be uploaded to Rayyan QCRI, a mobile and web-based application that facilitates collaboration between authors involved in study screening and selection for final inclusion in a systematic review. The process of study selection will
Table 1 Search strategy for PubMed

<table>
<thead>
<tr>
<th>SN</th>
<th>Search items</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>‘Heart failure’ [Mesh] OR ‘Cardiac failure’ [tiab] OR ‘Cardiac insufficiency’ [tiab] OR ‘heart failure’ [tiab]</td>
</tr>
<tr>
<td>2.</td>
<td>‘Atrial fibrillation’ [Mesh] OR ‘Atrial fibrillation’ [tiab]</td>
</tr>
<tr>
<td>3.</td>
<td>#1 AND #2</td>
</tr>
</tbody>
</table>
| 4. | benin/or burkina faso/or cape verde/or cote d’ivoire/or gambia/or ghana/or guinea/or guinea-bissau/or liberia/or mali/or mauritania/or niger/or senegal/or sierra leone/or togo/or (africa adj2 west* or benin* or burkina fas* or cape verde* or cabo verde* or ivory coast or cote d’ivoire* or gambia* or ghana* or (guinea* not pig*) or bissau or liberia* or (mali not fowl) or malian or mauritania* or nigeria* or senegal* or sierra leone* or togo*)
| 5. | mp. or (lagos or accra or abidjan or dakar or abobo or abuja or freetown or ouagadougou or conakry or lome or bamako or cotonou or kumasi or monrovia or ibadan or kano or port harcourt or benin city or porto novo or niamey or yamoussoukro or banjul or timbuktu or djenne or abomey or zaria or tamale or jos or cape coast or maisigui or abja or gao or calabar or warri or maiduguri or bobo dioulasso or parakou or sokoto or djouge or bohicon or sekondi takoradi or sunyani or obuasi or teshie or tema or sissou or kakariko or nouakchott or dakhat nouadhibou or benin city or port harcourt or ilorin or kaduna or enugu or ikorodu or onitsha or bauchi or akure or obea or abekuta or ibadan or ilorin or sosogbo or osogbo or gombe or ilse or badagry or makurdi or sagamu or iseyin or obbomosho or awka or ado ekiti or nsukka or ikeja or katsina or okene or lagos or ife or ilorin or oyo or osun or osun state or oyo state or benin state or kogi or kwara or edo or lagos or ibadan or ilorin or kwara or osun or osun state or edo state or benin state or kogi state or kwara state or edo state or lagos state or ibadan state or ilorin state or kwara state or osun state or osun state state or edo state state or lagos state state or ibadan state state or ilorin state state or kwara state state or osun state state or osun state state |
| 6. | Publication date limits: from database inception to December 31, 2018 with no language restrictions

be guided by a tool developed a priori based on the eligibility criteria.

Study screening

Two reviewers (CMM and FLT) will independently screen the titles and abstracts retrieved from the searches. Discrepancies in the screening of abstracts will be resolved through discussion and consensus. If disagreement persists, a third reviewer (VNA) will be consulted. Two reviewers (CMM and FLT) will then download and independently screen the full texts of selected records for final inclusion. Discrepancies and disagreements will be handled as mentioned above.

Data items and extraction

Using a pre-established Google data abstraction form, two reviewers (CMM and SNP) will independently extract data (online) depending on the outcomes of interest: prevalence, incidence and all-cause mortality rates of AFib among patients with HF in SSA. Generally, data will be extracted on: the surname of the first author and year of study publication; the country in which the study was conducted; the region (western, central, southern and eastern); study setting (hospital- vs community-based); study design (cross-sectional, cohort, case-control or randomised controlled trials); sampling method (random, consecutive or exhaustive); data collection (prospective or retrospective); male proportion; mean or median age in years; age range in years; proportion of anticoagulant use; proportion of beta-blocker use and sample size. Additional data will be extracted on (1) the characteristics of HF such as the mean or median duration of HF in years, causes of HF (like hypertensive heart
disease, cardiomyopathy, rheumatic heart disease or isch- 
amic heart disease) and severity of HF (according to the 
New York Heart Association [NYHA] classification and left 
ventricular ejection fraction [EF] on echocardiography) 
and (2) the characteristics of AFib: mean or median dura-
tion since diagnosis in years, type of AFib (paroxysmal, 
persistent or permanent) and proportion of participants 
on any anticoagulation therapy.

In addition to the aforementioned data items to be 
extracted, we shall extract data on the number of AFib 
cases in patients with HF. To determine the incidence of 
AFib in HF patients, data will be extracted on the number 
of new cases of AFib among patients with HF. Finally, data 
will be extracted on the mean or median duration of 
follow-up, the number of death due to any cause among 
patients with HF, and the number of deaths due to any 
cause among HF patients with AFib in order to determine 
proportion of all-cause mortality among HF patients with 
AFib.

For multinational studies, data on the outcome of 
interest will be disaggregated according to the coun-
tries in which the study was conducted. Otherwise, these 
studies will be presented as a single study and the coun-
tries where the study was conducted in will be highlighted. 
The extracted data will be cross-checked at least once by 
two authors (LNA and VNA) for consistency and obvious 
errors.

A duplicate of the online data abstraction form will be 
created for both authors who will be responsible for data 
 extraction (CMM and SNP), while the consistency of the 
extracted data will be monitored online by a third author 
(LNA) who will conduct the statistical analysis. Disagree-
ments among authors will be resolved through consensus.

Assessment of methodological quality and risk of bias
Two reviewers (CMM and SNP) will independently assess 
the included full texts for bias. The risk of bias and quality 
of included studies reporting on prevalence and inci-
dence measures will be assessed using the risk of bias tool 
for prevalence studies proposed by Hoy et al., adapted 
for the purpose of this study (online supplementary file 1). 
Also, the Quality In Prognosis Studies (QUIPS) tool 
(see online supplementary file 2) will be used to eval-
uate the risk of bias or quality of studies reporting on the 
mortality rate among HF patients with AFib. Disagree-
ments during this process will be arbitrated by a single 
reviewer (CD).

Data synthesis and analysis
The author, LNA, will conduct the statistical analysis. The 
‘meta’ package of the statistical software R (V.3.3.3, The 
R Foundation for statistical computing, Vienna, Austria) 
will be used to analyse the extracted data. Study-specific 
prevalence, incidence and mortality estimates will be 
recalculated using crude numerators and denominators 
from the individual studies. Using the Freeman-Tukey 
arc-sine transformation, the variance of study-specific esti-
mates will be stabilised before pooling with random effect 
meta-analysis model. Heterogeneity across studies will 
be assessed and quantified using the Cochrane’s Q and 
I² statistics, respectively. Low, medium and substantial 
heterogeneity will be represented by I² values of 25%, 50% 
and 75%, respectively. A subgroup analysis using the 
following variables will be performed in case of substan-
tial heterogeneity: region (western, central, southern 
and eastern); study type (hospital- vs community-based); 
study design; study area (urban, rural or both); random 
sampling (yes vs no); data collection (prospective vs ret-
rospective); gender (male vs female); age group (below vs 
at or above the median age); cause of HF (valvular vs 
non-valvular); severity of HF (NYHA stage I and II vs III 
and IV; and EF <35% vs >35%); type of AFib (paroxysmal, 
persistent or permanent); proportion of anticoagulants 
and beta-blocker use (as continuous variables) and study 
quality.

Estimates of the prevalence, incidence and all-cause 
mortality rates will be pooled according to the SSA region 
and compared using the Q-test on analysis of variance. 
Publication bias will be assessed with the aid of a symmetry 
of forest and funnel plots and Egger’s test. A p value 
below 10% on Egger’s test will be considered statistically 
significant.

Presentation and reporting of results
This review will be published in accordance with the 
Preferred Reporting Items for Systematic Reviews and 
Meta-Analyses statement. With the aid of a flow diagram, 
the process of study screening, selection, final inclusion 
and reasons for study exclusion will be demonstrated. 
Where necessary, summary tables and forest plots will 
be used to display quantitative data. The risk of bias for 
all the included studies will be presented using narrative 
summaries and tables.

The prevalence and incidence of AFib among HF 
patients, and the mortality rate of HF patients with AFib 
will be reported according to the SSA region (western, 
eastern, southern and central), cause of HF (valvular vs 
non-valvular), HF severity (NYHA stage I and II versus III 
and IV; and EF <35% vs >35%) and study type (hospital- 
vs community-based).

Protocol amendments
We do not plan to modify the present protocol. However, 
any modification will be succinctly described in the final 
review.

Patient and public involvement
Patients and/or the public were not directly involved in 
this study.

Ethics and dissemination
Since the review is based on already published data, an 
ethical approval is not required. The findings of this 
review will be presented in conferences and peer-reviewed 
journals and shared on social media such as Research-
Gate, Facebook, WhatsApp and Twitter.
Author affiliations
1General Practice, Ibal Sub-Divisional Hospital, Ibal, Northwest Region, Cameroon
2Department of Clinical Research, Health Education and Research Organisation (HERO), Buea, Cameroon
3Non-communicable disease unit, Clinical Research Education, Networking and Consultancy (CRENC), Douala, Cameroon
4School of Public Health, Faculty of Medicine, University of Queensland, Brisbane, Australia
5Department of Medicine, Groote Schuur Hospital and University of Cape Town, South Africa
6Clinical Medicine, Interfaith Medical Center, Brooklyn, New York, USA
7Public Health, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Central, Cameroon
8School of Public Health, Faculty of Medicine, University of Yaoundé I, Yaoundé, Northwest Region, Cameroon
9Department of Medicine, Ibal Sub-Divisional Hospital, Ibal, Northwest Region, Cameroon

Twitter @ValerieAgbor

Contributors VNA conceived the study. VNA LNA and JJJ designed the study protocol. VNA drafted the initial manuscript. LNA, FLT CMM, SNP, CD and JJJ critically revised the protocol for methodological and intellectual content. All authors read and approved the final version of the manuscript prior to submission. VNA is the guarantor of the review.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES