Prevalent diabetes mellitus in patients with heart failure and disease determinants in sub-Saharan Africans having diabetes with heart failure: a protocol for a systematic review and meta-analysis

Leopold Ndemnge Aminde,1,2 Anastase Dzudie,1,3,4 Andre Pascal Kengne1,4,5

ABSTRACT

Introduction: Heart failure (HF) is the final common pathway for most cardiovascular disease (CVDs). Diabetes mellitus (DM) is a major contributor to CVD burden and an independent predictor of mortality in patients with HF. However, the epidemiology of DM in African patients with HF is less well described. The current proposal is for a systematic review to assess the prevalence of DM in HF and the determinants of disease in patients with diabetes and HF in sub-Saharan Africa (SSA).

Methods and analysis: A systematic search of published literature will be conducted for observational studies on the prevalence of DM in HF and risk factors of HF in these patients in SSA. Databases including MEDLINE, Google Scholar, SCOPUS and Africa Wide Information will be searched from January 1995 to February 2016. Screening of identified articles and data extraction will be conducted independently by two investigators. Risk of bias and methodological quality of the included studies will be assessed using a Risk of Bias tool and STROBE checklist. Appropriate meta-analytic techniques will be used to pool prevalence estimates from studies with similar features, overall and by major subgroups. Heterogeneity of the estimates across studies will be assessed and quantified and publication bias investigated. This protocol is reported according to Preferred Reporting Items for Systematic reviews and Meta-Analysis protocols (PRISMA-P) 2015 guidelines.

Ethics and dissemination: The proposed study will utilise published data; as such there is no requirement for ethical approval. The resulting manuscript will be published in a peer-reviewed journal. This review will identify the knowledge gaps as well as inform policymakers in the region on the contemporary burden of DM in patients with HF.

Trial registration number: CRD42015026410.

INTRODUCTION

Rationale

Sub-Saharan Africa (SSA) continues to face rapid epidemiological transition from communicable diseases to chronic non-communicable diseases (NCD) owing to the growing burden of risk factors such as high-blood pressure, obesity, diabetes mellitus (DM), physical inactivity and unhealthy eating habits. NCDs are the number one cause of death around the world and second leading cause of mortality in SSA accounting for 30% of the 9.5 million deaths in 2011. According to the 2013 Global Burden of Disease Study (GBD), cardiovascular disease (CVD) accounted for 38.3% of NCD deaths in SSA, and recent increases in global deaths due to CVD have been attributed to population growth and ageing. In a recent comprehensive review on aetiologies, epidemiology and clinical characteristics of heart failure in SSA, highlighted that this syndrome was largely due to non-ischaemic causes, the majority being hypertensive heart disease, rheumatic heart disease and the cardiomyopathies. This was similarly observed in THESUS-HF, the first heart failure registry on the continent.

It was, however, suggested that, though atherosclerotic heart disease (to which diabetes is a major contributor) was apparently rare, these conclusions were based on only a few studies and hence its contribution cannot be totally ruled out. DM is a major contributor to CVD burden. Recent estimates from the International Diabetes Federation (IDF) suggest that global population of individuals with diabetes will increase from 382 million in 2013 to 592 million by 2035.
million in 2035, with the highest relative increase at 109% occurring in SSA where it is estimated that the number of people with diabetes will double from 19.8 million to 41.5 million.9 Kengne et al10 recently estimated that diabetes was accounting for 8.6% of total mortality in SSA in 2013. Several studies have shown that the risk of developing CVD is more than twice in patients with diabetes over those without diabetes and about 80% of the mortality in patients with diabetes occurs through CVD.11 12

Besides atherosclerotic CVDs, cardiac failure is a recognised CVD complication in diabetes, where it is over two times more frequent than in people without diabetes.12 Via several mechanisms including diabetic cardiomyopathy and coronary heart disease, DM has been shown to play a significant role in the pathogenesis and outcome of heart failure (HF).13 Besides conventional cardiovascular risk factors leading to the development of HF, individuals with diabetes are more vulnerable via the contributing influence of diabetes-related risk factors including chronic hyperglycaemia, insulin resistance and collagen deposition in the myocardium eventually leading to the so called ‘diabetic cardiomyopathy’, causing abnormal left ventricular and diastolic function.14 In an in-depth literature review on HF in people with diabetes, it was suggested that the determinants of heart failure documented in other parts of the world are similar to those in African patients, however, the contribution of diabetic cardiomyopathy was still somewhat discordant.15 Moreover, several reports have shown DM to be an independent predictor of mortality in HF.16 17 In spite of these observations, the epidemiology of DM in patients with HF has been less well described. Hence, we propose this protocol for a systematic review and meta-analysis to estimate the current prevalence of diabetes among individuals with HF in SSA as well as the determinants of disease in those patients having diabetes with HF. Results will provide evidence on the current burden of diabetes in this vulnerable population and inform health authorities on major risk factors for which control interventions should be tailored in the region, to curb this burden.

Objectives
We aim to conduct a systematic review and meta-analysis to ascertain the prevalence of DM among patients with HF as well as the determinants of disease in sub-Saharan Africans having diabetes with HF.

Review questions
The proposed review will strive to address the following research questions:
1. What is the prevalence of DM among adult sub-Saharan Africans with HF as documented in studies reported between 1995 and 2015?
2. What are the determinants of HF among sub-Saharan Africans having diabetes with HF in those studies?

METHODS
Eligibility criteria
Inclusion criteria
A. Study designs: cross-sectional, case–control and cohort studies conducted on HF in SSA, with data available on prevalent diabetes and risk factors for HF among patients with diabetes.
B. Study participants: adult (age ≥18 years) human participants residing in SSA, regardless of their ethnic background.
C. The final diagnosis will be based on physician-made diagnosis or as defined by the WHO/IDF18 for DM and European Society of Cardiology (ESC)19/American Heart Association (AHA)20/Framingham criteria21 for HF diagnosis at the time of study (table 1), or self-reported.
D. Time-period: we intend to consider all published and unpublished data found between 1 January 1995 and 29 February 2016, while considering changes in definition of diabetes and HF over time.
E. Study settings: health facilities or community-based settings; rural or urban SSA.
F. Language: all studies reported in the English or French languages and conducted on human subjects will be considered.

Exclusion criteria
A. Studies conducted among populations of African origin but residing outside Africa.
B. Studies lacking prevalence rates and risk factors with absence of data to compute them.
C. Case series with small sample sizes (sample less than 30 participants).
D. Letters to editors, reviews, commentaries, editorials and any publication without primary data.
E. Studies in subgroups of participants selected based on the presence of diabetes.
F. Duplicate publications from the same study. For studies published in more than one journal/conference, the most recent and comprehensive publication will be used.
G. Studies not performed in human participants or published in languages other than English and French.

Source of information
The methods of this systematic review are reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis protocols (PRISMA-P) 2015 Guidelines.22 See table 2 for checklist.

Search strategy for study identification
Electronic searches
We will search PubMed MEDLINE, Google Scholar, SCOPUS, ISI Web of Science (Science Citation Index), Africa Wide Information, African Index Medicus (AIM) and AFROLIB databases, from 1 January 1995 to 31 August 2015, for published studies on DM in patients...
with heart failure in SSA. This search shall be conducted using a predefined comprehensive and sensitive search strategy combining relevant terms with names of countries in SSA, to obtain the maximum possible number of studies. This search will be guided by the African search filter, which has been reported to have good sensitivity (and improved precision) of 74% (1.3–9.4%) and 73% (5–28%) for MEDLINE and EMBASE, respectively.23 This search filter includes names of each African country and shortened terms to capture studies from regions. Countries with official names in a language other than English will also be entered in the official form, and for countries that have changed names over time, both names shall be included in the search. Table 3 depicts the main search strategy to be employed.

Reference lists
We will search reference lists of relevant citations for articles of interest.

Grey literature
We will contact authors, experts in the field, research organisations, conference websites and proceedings, for any relevant material. This shall be carried out via emails. If, after repeated attempts to contact authors via email for relevant information, no response is gotten, the said study shall be excluded.

Study records
Data management
All identified search results will be entered into RevMan V.5 software for de-duplication of records. These shall be subsequently uploaded into Eppi-Reviewer, which is an internet-based software program to facilitate collaboration between investigators during the selection of studies to be included in the review. Prior to screening of studies, investigators shall create standardised and pre-tested questions following the inclusion criteria. These questions together with abstracts and full texts of articles will be uploaded into Eppi-Reviewer for eventual piloting of the test questions.

Screening
Two investigators (LNA and AD) will independently select studies that meet inclusion criteria. Citations and abstracts will be screened for relevance, and duplicate citations will be excluded. Titles and abstracts shall then be screened following inclusion criteria stipulated earlier, following which the full texts of potentially eligible articles will be obtained. These full texts will be screened using a standardised and pre-tested form to include eligible studies. Disagreements will be resolved by consensus, with consultation of a third author (APK) when resolution cannot be achieved. Corresponding authors will be contacted in the event that the publication (1) is

Table 1 Definitions of diabetes mellitus and heart failure

<table>
<thead>
<tr>
<th>Disease</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus (IDF/WHO) 2006</td>
<td>Fasting plasma glucose ≥7.0 mmol/l (126 mg/dL) or 2 h plasma glucose ≥11.1 mmol/l (200 mg/dL)</td>
</tr>
<tr>
<td>Heart failure definition</td>
<td>HF is defined, clinically, as a syndrome in which patients have typical symptoms (eg, breathlessness, ankle swelling and fatigue) and signs (eg, elevated jugular venous pressure, pulmonary crackles and displaced apex beat) resulting from an abnormality of cardiac structure or function (cardiomegaly, third heart sound, abnormality on echocardiogram, raised natriuretic peptide concentration)</td>
</tr>
<tr>
<td>1. European Society of Cardiology (ESC) guidelines 2012</td>
<td>A complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. The cardinal manifestations are dyspnoea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary and/or splanchnic congestion and/or peripheral oedema</td>
</tr>
<tr>
<td>2. American Heart Association/American College of Cardiology Foundation (AHA/ACCF) 2013</td>
<td>A. Major criteria: paroxysmal nocturnal dyspnoea; neck vein distension; crackles; radiographic cardiomegaly; acute pulmonary oedema; S3 gallop; central venous pressure &gt;16 cm H2O; circulation time 25 s; hepatojugular reflux; pulmonary oedema, visceral congestion or cardiomegaly at autopsy; weight loss—4.5 kg in 5 days in response to treatment of congestive heart failure. B. Minor criteria: bilateral ankle oedema; nocturnal cough; dyspnoea on ordinary exertion; hepatomegaly; pleural effusion; decreased vital capacity by one-third from maximal value recorded; tachycardia (&gt;120 bpm)</td>
</tr>
</tbody>
</table>

The diagnosis of congestive heart failure requires that two major only or one major and two minor criteria be present concurrently. Minor criteria are acceptable only if they are not attributed to another medical condition.

IDF, International Diabetes Federation.
### Table 2 PRISMA-P 2015 checklist for systematic review and meta-analysis protocol on prevalent diabetes mellitus in patients with heart failure in sub-Saharan Africa

<table>
<thead>
<tr>
<th>Section/topic</th>
<th>Item No</th>
<th>Checklist item</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title</td>
<td>1a</td>
<td>Identify the report as a protocol of a systematic review</td>
<td>Done (page 1)</td>
</tr>
<tr>
<td>Identification</td>
<td>1b</td>
<td>If the protocol is for an update of a previous systematic review, identify as such</td>
<td>NAP</td>
</tr>
<tr>
<td>Update</td>
<td>2</td>
<td>If registered, provide the name of the registry (eg, PROSPERO) and registration number</td>
<td>Done (page 2)</td>
</tr>
<tr>
<td>Registration</td>
<td>3a</td>
<td>Provide name, institutional affiliation, and email address of all protocol authors, provide physical mailing address of corresponding author</td>
<td>Done (page 1)</td>
</tr>
<tr>
<td>Authors</td>
<td>3b</td>
<td>Describe contributions of protocol authors and identify the guarantor of the review</td>
<td>Done (page 11)</td>
</tr>
<tr>
<td>Contributions</td>
<td>4</td>
<td>If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments</td>
<td>Done (page 10)</td>
</tr>
<tr>
<td>Amendments</td>
<td>5a</td>
<td>Indicate sources of financial or other support</td>
<td>Done (page 11)</td>
</tr>
<tr>
<td>Sources</td>
<td>5b</td>
<td>Provide name of the review funder and/or sponsor</td>
<td>NAP</td>
</tr>
<tr>
<td>Sponsor</td>
<td>5c</td>
<td>Describe role(s) of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol</td>
<td>NAP</td>
</tr>
<tr>
<td>Support</td>
<td>6</td>
<td>Describe the rationale for the review in the context of what is already known</td>
<td>Done (page 2)</td>
</tr>
<tr>
<td>Rationale</td>
<td>7</td>
<td>Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators and outcomes (PICO)</td>
<td>Done (page 4)</td>
</tr>
<tr>
<td>Methods</td>
<td>8</td>
<td>Specify the study characteristics (eg, PICO, study design, setting, time frame) and report characteristics (eg, years considered, language, publication status) to be used as criteria of eligibility for the review</td>
<td>Done (pages 4 and 5)</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>9</td>
<td>Describe all intended information sources (eg, electronic databases contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage</td>
<td>Done (page 6)</td>
</tr>
<tr>
<td>Information sources</td>
<td>10</td>
<td>Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated</td>
<td>Done (page 17)</td>
</tr>
<tr>
<td>Search strategy</td>
<td>11a</td>
<td>Describe the mechanism(s) that will be used to manage data throughout the review</td>
<td>Done (page 7)</td>
</tr>
<tr>
<td>Data management</td>
<td>11b</td>
<td>State the process that will be used for selecting studies (eg, two independent reviewers) through each phase of the review (ie, screening, eligibility and inclusion in meta-analysis)</td>
<td>Done (page 7)</td>
</tr>
<tr>
<td>Study Records</td>
<td>11c</td>
<td>Describe planned method of extracting data from reports (eg, piloting forms, carried out independently, in duplicate), any process for obtaining and confirming data from investigators</td>
<td>Done (page 7)</td>
</tr>
<tr>
<td>Data collection process</td>
<td>12</td>
<td>List and define all variables for which data will be sought (eg, PICO items, funding sources), any pre-planned data assumptions and simplifications</td>
<td>Done (page 8)</td>
</tr>
<tr>
<td>Data items</td>
<td>13</td>
<td>List and define all outcomes for which data will be sought, including prioritisation of main and additional outcomes, with rationale</td>
<td>–</td>
</tr>
<tr>
<td>Outcomes and prioritisation</td>
<td>14</td>
<td>Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be carried out at the outcome or study level, or both; state how this information will be used in data synthesis</td>
<td>Done (page 8)</td>
</tr>
</tbody>
</table>

Continued
where study was conducted, the year study was carried out and year of publication, the language of publication, demographic characteristics of participants (mean age, sex proportions), study design, setting (rural or urban, health-facility or community-based), sample size, number and proportion with diabetes, known duration of diabetes, diagnostic criteria for diabetes and HF, respectively, cardiovascular as well as diabetes-specific risk factors of patients and measures of association (χ², ORs, risk ratios, p values and CIs) will be recorded.

Assessment of methodological quality and risk of bias
Two reviewers (LNA and AD) will independently score the quality of included studies. The STROBE checklist⑥ will be used to evaluate reporting methodology in each paper while risk of bias in individual studies will be assessed using the Risk of Bias Tool for Prevalence

Data extraction
Two investigators (LNA and AD) will independently extract data from included studies, using a standardised and pre-tested data extraction form. Any inconsistencies or disagreement shall be resolved by consensus or consultation with the third investigator (APK).

Data items
Data will include the geographic region and country where study was conducted, the year study was carried out and year of publication, the language of publication, demographic characteristics of participants (mean age, sex proportions), study design, setting (rural or urban, health-facility or community-based), sample size, number and proportion with diabetes, known duration of diabetes, diagnostic criteria for diabetes and HF, respectively, cardiovascular as well as diabetes-specific risk factors of patients and measures of association (χ², ORs, risk ratios, p values and CIs) will be recorded.

Assessment of methodological quality and risk of bias
Two reviewers (LNA and AD) will independently score the quality of included studies. The STROBE checklist⑥ will be used to evaluate reporting methodology in each paper while risk of bias in individual studies will be assessed using the Risk of Bias Tool for Prevalence

<table>
<thead>
<tr>
<th>Section/topic</th>
<th>Item No</th>
<th>Checklist item</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data synthesis</td>
<td>15a</td>
<td>Describe criteria under which study data will be quantitatively synthesised</td>
<td>Done (page 9)</td>
</tr>
<tr>
<td></td>
<td>15b</td>
<td>If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (eg, I², Kendall’s τ)</td>
<td>Done (page 9)</td>
</tr>
<tr>
<td></td>
<td>15c</td>
<td>Describe any proposed additional analysis (eg, sensitivity or subgroup analysis, meta-regression)</td>
<td>Done (page 9)</td>
</tr>
<tr>
<td></td>
<td>15d</td>
<td>If quantitative synthesis is not appropriate, describe the type of summary planned</td>
<td>Done (page 9)</td>
</tr>
<tr>
<td>Meta-bias(es)</td>
<td>16</td>
<td>Specify if any planned assessment of meta-bias(es) (eg, publication bias across studies, selective reporting within studies)</td>
<td>–</td>
</tr>
<tr>
<td>Confidence in cumulative evidence</td>
<td>17</td>
<td>Describe how the strength of the body of evidence will be assessed (eg, GRADE)</td>
<td>Done (pages 9 and 10)</td>
</tr>
</tbody>
</table>

PRISMA-P, Preferred Reporting Items for Systematic reviews and Meta-Analysis protocols.
Studies developed by Hoy et al\textsuperscript{25} (table 4) and the Cochrane guidelines available in Review Manager V.5.3 (http://tech.cochrane.org/revman). Discrepancies will be resolved by consensus or by consulting the third investigator (APK). Inter-rater agreement on screening, data abstraction and methodological quality will be assessed using Cohen’s $\kappa$ coefficient.\textsuperscript{26} We intend to present risk of bias and quality scores in a table.

### Data synthesis, analysis and assessment of heterogeneity

Data will be synthesised to answer both research questions. Prevalence data will be summarised by country and geographic regions. In a situation where a population is reported at both regional level and with national estimates, we shall consider the most comprehensive and updated national estimates. Any other material will be excluded or considered as duplicate. A meta-analysis will be performed for the prevalence across studies with similar characteristic. Further to this purpose, the study-specific estimates will be pooled through a random-effects meta-analysis model, to obtain the overall summary estimate of the prevalence across studies, after stabilising the variance of individual studies with the use of Freeman-Tukey double arc-sine transformation.\textsuperscript{27} Such a transformation is required to reduce the effect of extremely high or extremely low prevalence rates on the pooled estimate. Heterogeneity will be evaluated by the $\chi^2$ test on Cochrane’s $Q$ statistic, which is quantified by $I^2$ values,\textsuperscript{28} assuming that $I^2$ values of 25%, 50% and 75% represent low, medium and high heterogeneity, respectively. Funnel plots supplemented by the Egger test\textsuperscript{29} of bias will be used to investigate the publication bias. When statistical data pooling does not yield meaningful results, such as in the presence of considerable clinical heterogeneity, we will conduct a narrative synthesis. Meta-analysis will be conducted overall, that is, across all possible eligible studies. However, we will also conduct subgroup analysis to compare the estimate across major predictive characteristics and assess the consistency of the effects across those subgroups. Major grouping characteristics will include gender (gender-specific analysis where possible; and below vs at or above the median proportion of men across study), age (below vs at or above the median), geographic region, time the study was conducted/published (below vs at or above the median); duration of diabetes (below at or above the median), diagnostic methods; study design, etc. For determinants of HF, in anticipation of the large variability in their investigation and reporting across studies, only a narrative synthesis of the evidence will be conducted. We will report the total number of determinants investigated across all studies, and for each determinant, the number of times it was reported to be associated with the outcome. We will further report on the range of measure association used for each determinant across studies, with indication of whether those measures were adjusted for confounders or not.
The data will be analysed using the statistical software R (V.3.0.3 (2014–03–04), The R Foundation for statistical computing, Vienna, Austria).

Sensitivity analysis
We will perform subgroup analysis where substantial heterogeneity will be detected to identify possible sources with the following grouping variables; age group, gender, study setting (rural vs urban, health-facility vs community-based), geographical region (central, west, east and southern Africa) and study quality. Any subgroup differences identified will be described, and our findings will be interpreted in the light of these differences.

Confidence in cumulative evidence
We intend to assess the strength of evidence provided by studies included in the review, using the Grading of recommendations Assessment, Development and Evaluation (GRADE) approach. This assessment of the quality of evidence would include risk of bias, consistency and publication bias. Studies in which further research is, respectively, unlikely to change effect estimates, or likely to have a considerable impact on effect estimates, or capable of changing the effect estimates, or those in which there is uncertainty in effect estimates, will be described as ‘high’, ‘moderate’, ‘low’ or ‘very low’ qualities.

Reporting of this review
The proposed systematic review will be reported following the PRISMA guidelines. We intend to publish a PRISMA checklist alongside the final report.

Potential amendments
We do not intend to make any amendments to the protocol, to avoid the possibility of outcome reporting bias. However, any amendments that do prove necessary will be documented and reported transparently.

Conclusion
Cardiovascular disease continues to be a daunting problem in SSA and is projected to worsen in the coming decades if no action is taken. DM is a major contributor to the CVD burden and studies among Caucasians suggest it is an independent predictor of mortality in HF (the final endpoint for most CVDs). The epidemiology and burden of diabetes in this group of patients with HF has been less well documented in Africa. We intend to describe the current prevalence of DM among patients with HF and the determinants of HF among patients with diabetes in SSA. Determining this current burden will be important for clinicians providing care to this vulnerable group of patients. If diabetes is found to be as common among patients with heart failure in SSA as those elsewhere, clinicians in this setting would have to be alert when managing these patients and, more especially, aggressively control identified modifyable risk factors. This would reduce the morbidity and mortality associated with CVD, as well as the economic burden in an already financially-constrained setting plagued with communicable diseases as well. Possible limitations of this study would include a predominance of poor quality studies and significant heterogeneity of studies precluding further analysis. In addition, a predominance of cross-sectional studies would make it difficult to obtain or determine risk factors for diabetes. Finally, including only studies published in the English or French languages, we may lose relevant data from studies published in other languages. This review will, however, identify gaps in the current literature on this topic and provide direction for future research in people with diabetes and cardiomyopathy.

Ethics and dissemination
The current study is based on published data, and hence does not require ethical approval. The final report of this review in the form of a scientific paper will be published in a peer-reviewed journal. Findings will also be presented at conferences and submitted to relevant health and policy authorities. We also plan to update the review in the future to monitor any progressive changes on the subject.

Author affiliations
1Clinical Research Education, Networking and Consultancy (CRENC), Douala, Cameroon
2School of Public Health, Faculty of Medicine & Biomedical Sciences, University of Queensland, Brisbane, Australia
3Faculty of Health Sciences, Department of Internal Medicine, General Hospital Douala, University of Buea, Buea, Cameroon
4Faculty of Health Sciences, Department of Medicine, University of Cape Town, Cape Town, South Africa
5Non-communicable Diseases Research Unit, South African Medical Research Council, Cape Town, South Africa

Contributors AD and LNA conceived and designed the protocol. LNA was responsible for manuscript drafting. APK and AD took part in critical revision for methodological and intellectual content. LNA is the guarantor of this review. All the authors read and approved the final version of the manuscript.

Competing interests None declared.

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, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

REFERENCES


19. McMurray JJV, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 2012;14:803–69.


