

# BMJ Open Prevalence and incidence of dyslipidaemia among adults in Africa: a systematic review and meta-analysis protocol

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## ABSTRACT

**Introduction:** Cardiovascular disease (CVD) is the leading cause of death globally and disproportionately affects low-income and middle-income countries. Dyslipidaemia is an important modifiable risk factor for CVD. There are important knowledge gaps regarding the population levels of lipid variables and frequency of non-optimal levels in populations within Africa. We propose to conduct a systematic review to determine the prevalence and occurrence of dyslipidaemia in adult populations within countries in Africa.

**Methods and analysis:** We will perform a comprehensive search to identify all possible published and unpublished studies on the prevalence or incidence of dyslipidaemia in Africa reported from 1 January 1980, without language restriction. The scientific databases PubMed MEDLINE, EMBASE and ISI Web of Science will be searched, as well as Grey literature. Following study selection, full-text papers acquisition, and data extraction and synthesis, we will appraise the quality of studies and risk of bias, and assess heterogeneity. Prevalence/incidence data will be summarised by country and geographic regions and a meta-analysis will be conducted for variables defined identically across studies. Variance stabilising transformations will be applied as appropriate to the raw data before meta-analysis. This systematic review will be reported according to the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies.

**Ethics and dissemination:** The current study is based on published data and as such ethics consideration is not a requirement. This review is expected to provide relevant data to help in quantifying the magnitude of dyslipidaemia in African populations, to emphasise the need for appropriate prevention and control strategies, and to identify research gaps and remaining challenges. The final report of the systematic review in the form of a scientific paper will be published in peer-reviewed journals. Findings will further be presented at conferences and submitted to relevant health authorities.

**Trial registration number:** PROSPERO CRD42014015376.

## INTRODUCTION

Cardiovascular disease (CVD) including stroke, coronary heart disease and peripheral arterial disease is the leading cause of death globally.<sup>1</sup> An estimated 17.3 million people died from CVD worldwide in 2008, representing 30% of all deaths in that year.<sup>1</sup> Of these deaths, about 7.3 million and 6.2 million, respectively, were due to coronary heart disease and stroke.<sup>2</sup> Furthermore, CVD disproportionately affects low-income and middle-income countries (LMIC), where about 80% of the global CVD mortality occur.<sup>1</sup>

Dyslipidaemia is defined by the presence of non-optimal levels of blood lipids. In clinical practice guidelines, dyslipidaemia is mostly defined by elevated total cholesterol (TC) and/or low-density lipoprotein cholesterol (LDL-C), but the definition is also often extended to include non-optimal levels of high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), apolipoprotein B and apolipoprotein AI.<sup>3</sup> Dyslipidaemia is one the most important modifiable risk factors for CVD.<sup>4–6</sup> According to the WHO, globally, a third of ischaemic heart disease is attributable to high cholesterol. Overall, raised cholesterol is estimated to cause 2.6 million deaths (4.5% of total) and 29.7 million disability adjusted life years (DALYs), or 2% of total DALYs. In 2008, the global prevalence of raised total cholesterol among adults ( $\geq 5.0$  mmol/L) was 39% (37% for males and 40% for females).<sup>7</sup>

There is robust evidence that successful treatment of dyslipidaemia substantially reduces morbidity and mortality from CVD.<sup>8–11</sup> For instance, such treatment can reduce the risk of heart disease by 30% over 5 years.<sup>8</sup> Moreover, the benefits of lipid-lowering therapy are not only experienced by individuals with CVD, benefits also extend to individuals without clinically overt CVD.<sup>8</sup>

Although the burden of CVD is increasing in developing countries, including those within Africa, critical knowledge gaps on the epidemiology of the disease around the continent remain, including the lack of data regarding the distribution of key risk factors such as dyslipidaemia. We present the protocol for a systematic review to assess the distribution and occurrence of dyslipidaemia among adults within Africa. We are not aware of any previous effort to critically review existing published data on dyslipidaemia in this part of the world.

This protocol is prepared and presented according to the PRISMA-P 2015 guidelines.<sup>12</sup>

## OBJECTIVES

To conduct a systematic review and meta-analysis to determine the prevalence, incidence and characteristics of dyslipidaemia in populations within countries in Africa.

## REVIEW QUESTION

This systematic review will seek to address the following research question:

What are the prevalence and incidence of dyslipidaemia in adult populations within countries in Africa as reported in studies published from 1980 to 2015?

## CRITERIA FOR CONSIDERING STUDIES FOR THE REVIEW

### Inclusion criteria

1. We will include cross-sectional, case-control or cohort studies of adult participants residing in African countries reporting the prevalence or incidence of dyslipidaemia, or enough data to compute these estimates.
2. Diagnosis of dyslipidaemia will be based on doctor diagnosis, or measured lipid profile.

We will consider all published and unpublished studies reported from 1 January 1980, while accounting for changes in the definition of dyslipidaemia over time. No language restriction will be applied.

### Exclusion criteria

1. Studies conducted among populations of African origin residing outside Africa.
2. Studies not performed in human participants.
3. Studies in subgroups of participants selected on the basis of the presence of dyslipidaemia.
4. Studies in children and adolescents (ie, age <15 years).
5. Case series (sample size of less than 50 participants), letters, reviews, commentaries and editorials.
6. Studies lacking primary data and/or explicit method description.
7. Duplicates; for studies published in more than one report, the most comprehensive and up-to-date version will be used.
8. Studies with serious ethical issues.

## SEARCH STRATEGY FOR IDENTIFYING RELEVANT STUDIES

The methods for this systematic review have been developed according to the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies.<sup>13</sup> The search strategy will be implemented in two stages.

### Bibliographic database searches

- A. We will perform a comprehensive search of databases to identify all relevant articles published on dyslipidaemia in Africa between January 1980 and February 2015 without language restriction. A systematic search of PubMed MEDLINE, EMBASE and ISI Web of Science (Science Citation Index) will be undertaken using a predefined strategy based on the combination of relevant terms and the names of each of the 54 African countries and African subregions to capture the largest number of studies. We will use text words as well as medical subject heading (MeSH) terms; for example 'dyslipidemia', 'hyperlipidemia', 'lipid disorder', 'hypercholesterolemia' and 'hypertriglyceridemia'. These terms and their variants will be used in varying combinations. The literature search strategy will be adapted to suit each database. The main search strategy is shown in [table 1](#).
- B. We will manually search the reference lists of eligible articles and relevant reviews, and trace their citations using the ISI Web of Knowledge portal. Grey literature, from key conference proceedings and sources including the African regional database 'African Index Medicus', 'OpenSIGLE', the WHO International Clinical Trials Registry, the WHO Global Infobase and the meta-Register of Controlled Trials (mRCT) will also be reviewed for relevant information.

### Selection of studies for inclusion in the review

Two investigators will independently identify articles and sequentially screen their titles and abstracts for eligibility. Full text of articles deemed potentially eligible will be acquired. These investigators will further independently assess the full text of each study for eligibility, and consensually retain studies to be included. Disagreement will be solved by a third assessor. We will use a screening guide to ensure that the selection criteria are reliably applied by all assessors.

## APPRAISAL OF THE QUALITY OF INCLUDED STUDIES

We will evaluate included studies for quality and bias using an adapted version of the Risk of Bias Tool for Prevalence Studies developed by Hoy *et al*<sup>14</sup> (see online supplementary appendix S1), which will be applied to screened full-text articles. Assessment of the risk of selection and attrition bias will use the Cochrane guidelines available in Review Manager V.5.3 (<http://tech.cochrane.org/revman>). Furthermore, the reporting quality of each study will be assessed using the STROBE

**Table 1** Search history PubMed

Search	Search terms	Hits
1	Dyslipidemia [tw] OR lipid disorder [tw] OR lipid [tw] OR hypercholesterolemia [tw] OR hypertriglyceridemia [tw] OR hyperlipidemia [tw]	
2	Dyslipidemia [MeSH Terms]	
3	# 1 OR # 2	
4	(((((("Africa"[MeSH] OR Africa*[tw] OR Algeria[tw] OR Angola[tw] OR Benin[tw] OR Botswana[tw] OR "Burkina Faso"[tw] OR Burundi[tw] OR Cameroon[tw] OR "Canary Islands"[tw] OR "Cape Verde"[tw] OR "Central African Republic"[tw] OR Chad[tw] OR Comoros[tw] OR Congo[tw] OR "Democratic Republic of Congo"[tw] OR Djibouti[tw] OR Egypt[tw] OR "Equatorial Guinea"[tw] OR Eritrea[tw] OR Ethiopia[tw] OR Gabon[tw] OR Gambia[tw] OR Ghana[tw] OR Guinea[tw] OR "Guinea Bissau"[tw] OR "Ivory Coast"[tw] OR "Cote d'Ivoire"[tw] OR Jamahiriya [tw] OR Jamahiriya[tw] OR Kenya[tw] OR Lesotho[tw] OR Liberia[tw] OR Libya[tw] OR Libia[tw] OR Madagascar[tw] OR Malawi[tw] OR Mali[tw] OR Mauritania[tw] OR Mauritius[tw] OR Morocco[tw] OR Mozambique[tw] OR Mocambique[tw] OR Namibia[tw] OR Niger[tw] OR Nigeria [tw] OR Principe[tw] OR Reunion[tw] OR Rwanda[tw] OR "Sao Tome"[tw] OR Senegal[tw] OR Seychelles[tw] OR "Sierra Leone"[tw] OR Somalia[tw] OR "South Africa"[tw] OR "St Helena"[tw] OR Sudan[tw] OR Swaziland[tw] OR Tanzania[tw] OR Togo[tw] OR Tunisia[tw] OR Uganda[tw] OR "Western Sahara"[tw] OR Zaire[tw] OR Zambia[tw] OR Zimbabwe[tw] OR "Central Africa"[tw] OR "Central African"[tw] OR "West Africa"[tw] OR "West African"[tw] OR "Western Africa"[tw] OR "Western African"[tw] OR "East Africa"[tw] OR "East African"[tw] OR "Eastern Africa"[tw] OR "Eastern African"[tw] OR "North Africa"[tw] OR "North African"[tw] OR "Northern Africa"[tw] OR "Northern African"[tw] OR "South African"[tw] OR "Southern Africa"[tw] OR "Southern African"[tw] OR "sub Saharan Africa"[tw] OR "sub Saharan African"[tw] OR "subSaharan Africa"[tw] OR "subSaharan African"[tw]) NOT ("guinea pig"[tw] OR "guinea pigs"[tw] OR "aspergillus niger"[tw]))))))	
5	# 3 AND # 4	
6	#5 Limits: 1980/01/01 to 2015/02/28 and studies done in Humans	

checklist (see online supplementary appendix S2).<sup>15</sup> Risk of bias and quality scores will be presented in a table.

### DATA EXTRACTION AND MANAGEMENT

Two assessors will independently extract data regarding general information (authors, year, country, type of publication), study characteristics (study design, setting, sample size, response rate, mean or median age and proportions of female participants, diagnosis criteria for dyslipidaemia, possible disease specific to the study population), prevalence and incidence of dyslipidaemia. Where only primary data (sample size and number of outcomes) are provided, these will be used to calculate the prevalence or incidence estimates. Where prevalence/incidence rates or relevance for estimating them are not available, we will contact the corresponding author of the study to request the missing information. Data will be extracted using standardised data collection.

### DATA SYNTHESIS INCLUDING ASSESSMENT OF HETEROGENEITY

Prevalence/incidence data will be summarised by country and geographic region (central, eastern, northern, southern and western Africa). A meta-analysis will be conducted for variables defined identically across studies. SEs for the study-specific estimates will be determined from the point estimate and the appropriate denominators, assuming a binomial (or Poisson for incidence

data) distribution. We will pool the study-specific estimates using a random effects meta-analysis model to obtain an overall summary estimate of the prevalence/incidence across studies, after stabilising the variance of individual studies with the use of the Freeman-Tukey double arc-sine transformation.<sup>16</sup> Heterogeneity will be assessed using the  $\chi^2$  test on Cochrane's Q statistic<sup>17</sup> and quantified by calculating the I<sup>2</sup>.<sup>18</sup> Values of 25%, 50% and 75% for I<sup>2</sup> represent, respectively, low heterogeneity, medium heterogeneity and high heterogeneity. We will assess the presence of publication bias using funnel plots and Egger's test.<sup>19</sup> Where substantial heterogeneity is detected, we will perform subgroup analysis to investigate the possible sources of heterogeneity using the following grouping variables: age group, sex, study setting (rural vs urban; hospital vs community-based), geographical region (central, eastern, northern, southern and western Africa), study quality. We will assess inter-rater agreement for study inclusion using Cohen's  $\kappa$  coefficient.<sup>20</sup> Data will be analysed using the statistical software R (V.3.0.3 (2014-03-04), The R Foundation for statistical computing, Vienna, Austria).

### PRESENTING AND REPORTING THE RESULTS

The study selection process will be summarised using a flow diagram. Reasons for exclusion of studies will be described. This will follow the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies.<sup>13</sup> Quantitative data will be presented in



evidence tables of individual studies as well as in summary tables and forest plots where appropriate. We will examine prevalence/incidence by region, country, setting (rural or urban), time period and disease-specific populations depending on the data available. We plan to report on quality scores and risk of bias for each eligible study. This may be tabulated and accompanied by narrative summaries.

## CONCLUSIONS

CVD has reached epidemic proportions in Africa, driven mainly by hypertension, diabetes, obesity and dyslipidaemia.<sup>1</sup> The challenging first step to address the burden of CVD on the continent is to establish accurate epidemiological data on this condition and its risk factors. We anticipate that this review on dyslipidaemia in Africa will have implications for policy, practice and research. This review is expected to provide relevant data to help in quantifying the magnitude of dyslipidaemia in African populations and emphasise the need for appropriate prevention and control strategies. The review will also determine the characteristics of dyslipidaemia in the African populations, and may help to confirm some unique features of dyslipidaemia previously reported in a population of West Africans and African-Americans. Indeed, low HDL-C with normal triglyceride levels was found to be the most common lipid pattern in West Africans and African-Americans with metabolic syndrome, suggesting that the lipid profile associated with cardiovascular risk in populations of African ethnicity may differ from that in Caucasians.<sup>21</sup> Furthermore, this review may identify the research gaps and remaining challenges that may form the basis of future studies targeting various aspects of dyslipidaemia to tackle the burden of the disease in African populations.

The main possible limitations of this review could be the scarcity of studies on the subject and the predominance of clinic-based studies and poor quality data, as revealed by previous reviews on chronic non-communicable diseases in Africa,<sup>22–24</sup> which hampered definitive inferences and drawing relevant conclusions. Data presented would therefore be only general indicators of the epidemiology of dyslipidaemia on the continent.

## ETHICS AND DISSEMINATION

The current study is based on published data and as such ethics consideration is not a requirement. The final report of the systematic review in the form of a scientific paper will be published in peer-reviewed journals. Findings will further be presented at conferences and submitted to relevant health authorities. We also plan to update the review in future to monitor changes and guide health service and policy solutions.

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**Competing interests** None.

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## Appendix S1. Risk of bias assessment tool

Adapted from the Risk of Bias Tool for Prevalence Studies developed by Hoy et al. (2012)

<b>Risk of Bias Item</b>	<b>Answer: Yes (Low Risk) or No (High risk)</b>
<b>External Validity</b>	
1. Was the study target population a close representation of the national pregnant population in relation to relevant variables?	
2. Was the sampling frame a true or close representation of the target population?	
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	
4. Was the likelihood of non-participation bias minimal?	
<b>Internal Validity</b>	
5. Were data collected directly from the subjects (as opposed to medical records)?	
6. Were acceptable case definition of dyslipidemia used?	
7. Was a reliable and accepted diagnosis method for DN utilised?	
8. Was the same mode of data collection used for all subjects?	
9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	
10. Were the numerator(s) and denominator(s) for the calculation of the prevalence of dyslipidemia appropriate?	
<p>11. Summary item on the overall risk of study bias</p> <p>LOW RISK OF BIAS: 8 or more “yes” answers. Further research is very unlikely to change our confidence in the estimate.</p> <p>MODERATE RISK OF BIAS: 6 to 7 “yes” answers. Further research is likely to have an important impact on our confidence in the estimate and may change the estimate.</p> <p>HIGH RISK OF BIAS: 5 or fewer “yes” answers. Further research is very likely to have an important impact on our confidence in the estimate and is likely to change the estimate.</p>	

**Appendix S2. STROBE Statement: checklist of items that should be included in reports of observational studies**

	<b>Item No</b>	<b>Recommendation</b>
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed  <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed  <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed  <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy
		(e) Describe any sensitivity analyses
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest



		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<p><i>Cohort study</i>—Report numbers of outcome events or summary measures over time</p> <hr/> <p><i>Case-control study</i>—Report numbers in each exposure category, or summary measures of exposure</p> <hr/> <p><i>Cross-sectional study</i>—Report numbers of outcome events or summary measures</p>
Main results	16	<p>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</p> <hr/> <p>(b) Report category boundaries when continuous variables were categorized</p> <hr/> <p>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</p>
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalizability	21	Discuss the generalizability (external validity) of the study results
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.		

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

**Quality assessment score**

A quality assessment score out of 22 will be determined for each study by assigning a point per STROBE item addressed. Good/fair quality papers will be categorized as having a score of  $\geq 14/22$  and poor quality papers will be classified as having a score of  $< 14/22$ .