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Prevalence and determinants of anaemia in children aged 6–59 months in Africa: a protocol for systematic review and meta-analysis

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ABSTRACT

Introduction Anaemia, especially in children aged <5 years, is a global health problem disproportionately affecting populations in low-income and middle-income countries. It is associated with high disability and death rates and has a negative effect on development. This study seeks to evaluate the prevalence and determinants of anaemia in children aged 6–59 months residing in Africa.
Methods and analysis This protocol was prepared using the 2015 Preferred Reporting Items for Systematic Reviews and Meta-analyses for Protocols guidelines. Relevant citations will be identified by searching EMBASE, Web of Science, PubMed, Global Medicus Index and African Journals Online from inception to 30 September 2019 with no language restrictions. Two authors will independently screen and select eligible studies for the review. Random-effect meta-analytic methods will be used to pool study-specific estimates and heterogeneity will be assessed and quantified using the χ^2 test on Cochrane's Q and I^2 statistics, respectively. Publication bias will be evaluated using funnel plots and Egger's test. Subgroup analysis and multiple meta-regression using backward elimination will be performed to investigate sources of substantial heterogeneity.
Ethics and dissemination No ethical approval is required for this study as it is based on already published data. The findings of the review will be published in a peer-reviewed journal and presented at conferences.

INTRODUCTION

Anaemia is a global public health problem associated with high morbidity and mortality rates, increased hospitalisation and a reverse effect on socioeconomic development.[1–3] Anaemia in infancy is associated with long-lasting effects on the brain and behaviour leading to poorer motor, cognitive and social-emotional functions.[4 5] WHO currently defines anaemia in children aged 6–59 months as a haemoglobin concentration <110 g/L.[6] The aetiologies of anaemia could be multifactorial and vary globally depending on geography, age and gender.[7] Nonetheless,

Strengths and limitations of this study

► This will be the first systematic review and meta-analysis to estimate the burden of anaemia in children aged 6–59 months living on the African continent.
► We anticipate substantial heterogeneity in the prevalence of anaemia among published studies in Africa.
► Nevertheless, appropriate systematic review and robust meta-analytic methods will be used to conduct the review and account for heterogeneity across studies, if any.

iron deficiency anaemia (IDA) is known to be the most important contributing factor to the global burden of the disease.[6] Other aetiologies of anaemia include other nutritional deficiencies (folate, B_6, B_{12}), haemoglobinopathies, parasitic infections as well as acute and chronic inflammation.[1 6] In a systematic analysis from 1990 to 2010, Kassebaum *et al* reported a rising prevalence of anaemia from malaria, schistosomiasis and chronic kidney disease.[7]

In 2010, the global prevalence of anaemia was estimated at 32.9% with the regions of South East Asia, central, western and eastern sub-Saharan Africa bearing the greatest burden.[7] Although occurring at different stages in the life, pregnant women and preschool age children have been found to be at greatest risk of developing anaemia,[1] with children aged <5 years found to be the only age group with a negative trend from 1990 to 2010.[7] WHO estimates of 2011 suggested that about 273 million children and 42 million pregnant women had anaemia worldwide.[6] According to data from the World Bank, the global prevalence of anaemia in children below 5 years reduced steadily from 41.5% in

1990 and then remained steady around 41.5% between 2013 and 2016.[8]

The prevalence of anaemia in children under 5 years in Africa varies from 9.7% in southeastern Nigeria to 78.4% in Ghana.[9 10] Existing evidence suggests that severe anaemia, accounting for most anaemia-related deaths, mostly occurs among children under 5, and generally in the rainy season (in the tropics) when the incidence of malaria is at its peak.[9] Furthermore, mortality from malaria-associated severe anaemia is greater than that from IDA in sub-Saharan Africa.[11] Besides malaria endemicity, poor nutrition, sickle cell disease, late arrival at health facilities, ignorance and poverty also account for high prevalence rates of anaemia in this region.[9 12]

The dearth of current estimates on the prevalence of anaemia in children under 5 residing in Africa, prompted the need for this study to assess the burden of anaemia among this age group and inform policies aimed at achieving the sustainable development goal 3.2 which has an aim to 'end preventable deaths of newborns and children under 5 years of age by 2030'.[13] The aim of this systematic review is to summarise the prevalence and determinants of anaemia in children aged 6–59 months residing in Africa.

METHODS
Criteria for selection of studies for the review
Inclusion criteria
1. Cross-sectional, control arm of randomised controlled trials, case-control and cohort studies published up to 30 September 2019 with available data on the prevalence and determinants of anaemia in children between 6 and 59 months residing in Africa will be considered.
2. For studies which assessed the determinants of anaemia, only those where adjustment for at least one exposure variable was done will be eligible for inclusion in our study.
3. Studies which diagnosed anaemia by measuring haemoglobin concentration using a complete blood count or haemoglobinometer, and defined anaemia as haemoglobin levels <110.0 g/L according to WHO and UNICEF.[6]
4. Studies which defined either mild, moderate or severe anaemia as haemoglobin values of 100.0–109.0, 70.0–99.0 or <70.0 g/L, respectively.[6]
5. Age limit: children from 6 to 59 months of age.
6. For duplicate publications, only the most recent, comprehensive publication with the largest sample will be included.

Exclusion criteria
1. Reviews, commentaries, letters, case reports and case series with fewer than 30 participants.
2. Studies conducted in a population with haemoglobinopathies like sickle cell anaemia.

3. Studies with no information on the tool used to diagnose anaemia.

Information sources
Search strategy
We will search for relevant titles and abstracts on anaemia in children aged 6–59 months published in EMBASE, Web of Science, PubMed, Global Medicus Index and African Journals Online from inception to 30 September 2019. Medical subject headings and key text words like 'anaemia' OR 'anaemia' OR 'haemoglobin' will be combined to a list of the 54 African nations to optimise the sensitivity of our search (table 1). The references of eligible full text and relevant reviews will also be screened for potential articles missed during our search. We will also search the World Hematology Congress, International Pediatrics Association Congress, International Conference on Pediatrics & Primary Care and International Conference on Pediatrics Health conference proceedings. Furthermore, ResearchGate will be searched for conference abstracts and articles not cited in the aforementioned databases.

Study records
Data management and study screening
The titles and abstracts of from database searches will be exported to EndNote X9 for removal of duplicates. The remaining titles and abstracts will then be exported to the application Rayyan QCRI[14] for screening of titles and abstracts. The full text of selected abstracts will be downloaded and assessed using the eligibility criteria for final inclusion. The full texts of citations identified through bibliographic screening will also be assessed for eligibility before final inclusion. The screening process will be independently conducted by two authors and any discrepancies will be resolved through discussion until a consensus is reached, otherwise a third author will be called on for arbitration.

Data items and extraction
A pre-structured Google Form will be used for data abstraction by two authors independently who will then cross-check each other's constituted database for completeness and correctness. Data will be extracted on the surname of the first author and the year of publication, the country of study, the study area (urban, rural and suburbs) and study design (cross-sectional, cohort). The region of Africa where the study was conducted will be deduced from the country where the study was conducted. We will also extract data on the study setting (hospital, school and community-based), sampling method (random sampling, consecutive, convenient), timing of data collection (prospective vs retrospective), test used to diagnose anaemia (complete blood count or haemoglobinometer), male proportion, mean or median age in months and sample size. In addition, we will extract data on number of: participants with anaemia, males, males with anaemia, females, females with anaemia, participants with mild anaemia, males with mild anaemia, females

Table 1 Search strategy for PubMed

SN	Search items	Hits
1.	(((Africa* (tiab) OR Algeria (tiab) OR Angola (tiab) OR Benin (tiab) OR Botswana (tiab) OR 'Burkina Faso' (tiab) OR Burundi (tiab) OR Cameroon (tiab) OR 'Canary Islands' (tiab) OR 'Cape Verde' (tiab) OR 'Central African Republic' (tiab) OR Chad (tiab) OR Comoros (tiab) OR Congo (tiab) OR 'Democratic Republic of Congo' (tiab) OR Djibouti (tiab) OR Egypt (tiab) OR 'Equatorial Guinea' (tiab) OR Eritrea (tiab) OR Ethiopia (tiab) OR Gabon (tiab) OR Gambia (tiab) OR Ghana (tiab) OR Guinea (tiab) OR 'Guinea Bissau' (tiab) OR 'Ivory Coast' (tiab) OR 'Cote d'Ivoire' (tiab) OR Jamahiriya (tiab) OR Kenya (tiab) OR Lesotho (tiab) OR Liberia (tiab) OR Libya (tiab) OR Madagascar (tiab) OR Malawi (tiab) OR Mali (tiab) OR Mauritania (tiab) OR Mauritius (tiab) OR Mayotte (tiab) OR Morocco (tiab) OR Mozambique (tiab) OR Namibia (tiab) OR Niger (tiab) OR Nigeria (tiab) OR Principe (tiab) OR Reunion (tiab) OR Rwanda (tiab) OR 'Sao Tome' (tiab) OR Senegal (tiab) OR Seychelles (tiab) OR 'Sierra Leone' (tiab) OR Somalia (tiab) OR 'South Africa' (tiab) OR 'South Sudan' (tiab) OR 'St Helena' (tiab) OR Sudan (tiab) OR Swaziland (tiab) OR Tanzania (tiab) OR Togo (tiab) OR Tunisia (tiab) OR Uganda (tiab) OR 'Western Sahara' (tiab) OR Zaire (tiab) OR Zambia (tiab) OR Zimbabwe (tiab) OR 'Central Africa' (tiab) OR 'Central African' (tiab) OR 'West Africa' (tiab) OR 'West African' (tiab) OR 'Western Africa' (tiab) OR 'Western African' (tiab) OR 'East Africa' (tiab) OR 'East African' (tiab) OR 'Eastern Africa' (tiab) OR 'Eastern African' (tiab) OR 'North Africa' (tiab) OR 'North African' (tiab) OR 'Northern Africa' (tiab) OR 'Northern African' (tiab) OR 'South African' (tiab) OR 'Southern Africa' (tiab) OR 'Southern African' (tiab) OR 'sub Saharan Africa' (tiab) OR 'sub Saharan African' (tiab) OR 'subSaharan Africa' (tiab) OR 'subSaharan African' (tiab)) NOT ('guinea pig' (tiab) OR 'guinea pigs' (tiab) OR 'aspergillus niger (tiab)')))	
2.	('anemia' OR 'anaemia' OR 'anemias' OR 'anaemias' OR 'hemoglobin' OR 'haemoglobin')	
3.	#1 AND #2	
4.	(('Child, Preschool'(Mesh)) AND 'Infant'(Mesh))	
5.	#3 AND #4	
6.	Publication date limits: from database inception to 30 September 2019, with no language restrictions	

with mild anaemia, participants with moderate anaemia, males with moderate anaemia, females with moderate anaemia, participants with severe anaemia, males with severe anaemia and females with severe anaemia. Finally, data on measures of association (adjusted OR and relative risk) of the determinants of anaemia will be extracted.

Where possible, data for multinational studies will be reported according to the country where the study was conducted. Else, they will be reported as a single study, and the countries where the study was conducted will be highlighted.

Assessment of methodological quality and risk of bias

The two authors who performed data extraction will assess the quality of the included studies. Quality assessment of the included studies will be conducted simultaneously with the process of data abstraction. An adapted version of the Hoy *et al*[15] tool will be used to assess the risk of bias of prevalence studies (online supplementary table 1). Risk of bias will be totalled on 10 and scores of 0–4, 5–7 and 8–10 will represent low, moderate and high risk of bias, respectively. The Newcastle Ottawa Scale[16] will be used to assess the quality of case-control and cohort studies (online supplementary table 2,3).

Data synthesis and analysis

The 'meta' package of the statistical software R (V.3.5.3, The R Foundation for statistical computing, Vienna, Austria) will be used for data analysis. The Cohen's kappa statistics will be used to evaluate inter-rater agreement between authors for study inclusion, data abstraction and

assessment of study quality.[17] The numerators and denominators of variables of interest from each individual study will be used to calculate the study-specific prevalence estimates before pooling using random-effect models. Before pooling, the Freeman-Tukey double arcsine transformation will be used to stabilise the variance of each study-specific estimate.[18] The χ^2 test on Cochrane's Q statistics, and I^2 will be used to assess and quantify heterogeneity across studies, respectively.[19] I^2 values of 70% or over will be considered as evidence of substantial heterogeneity.[20] Prevalence estimates will be pooled according to the different African regions, and the Q-test of analysis of variance will be used to compare the pooled estimates. Publication bias will be assessed visually using funnel plots for asymmetry and confirmed statistically using the Egger's test.[20] P values below 10% on Egger's test will be considered statistically significant for publication bias.

In case of substantial heterogeneity across studies, a subgroup analysis will be conducted with the following variables: study region (North Africa (northern) vs sub-Sahara Africa (southern, western, central and eastern)), study setting (hospital-based, school-based and community-based), gender (male vs female) study area (rural, urban, suburb) and random sampling (yes/no). A sensitivity analysis including only studies with low risk of bias will be performed to estimate the prevalence of anaemia.

Multiple meta-regression analysis using backward elimination will be used to assess the impact of age, gender, publication year, study region (North Africa

(northern) vs sub-Sahara Africa (southern, western, central and eastern)), study area (rural, urban, suburb), study sampling (random vs non-random), study setting (hospital-based, school-based and community-based) and year of publication on the overall summary proportion. Only variables with p values <0.25 on bivariate analysis will be included in the multiple regression model. Two-sided p values <5% will be considered statistically significant.

Data on the determinants of anaemia will be synthesised using narrative summaries and tables.

Patient and public involvement

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

Presentation and reporting of results

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 statement[21] will be used to publish this review. The process of study screening and selection will be reported with the aid of a flow diagram depicting the reason(s) of study exclusion. Prevalence measures will be displayed using forest plots and tables, while the determinants of anaemia and risk of bias assessment will be presented as narrative summaries and using tables.

Protocol amendments

The authors do not plan to modify this protocol. Nevertheless, subsequent revisions in the study review will be carefully reported.

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