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Prevalence of anaemia in children under five in Africa: a protocol for systematic review and meta-analysis

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Prevalence of anaemia in children under five in Africa: a protocol for systematic review and meta-analysis

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Abstract

Introduction: Anaemia, especially in children less than five years old, is a global health problem disproportionately affecting populations in low- 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 of anaemia in children less than five years residing in Africa.

Methods and analysis: This protocol was prepared using the 2015 Preferred Reporting Items for Systematic Reviews and Meta-analyses for Protocols (PRISMA-P) guidelines. Relevant citations will be identified by searching EMBASE, Web of Science, PubMed, Global Medicus Index, and African Journals Online from inception to 30 April 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 $\chi 2$ 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 account for 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.

Keywords: Anaemia, child, infant, Africa.

Word count: Abstract = 234; main text = 1460

Number of tables =1; Number of figures =0; supplementary files =2

Strengths and limitations of the study

1. This will be the first systematic review and meta-analysis on a serious developmental problem on the African continent.
2. We anticipate substantial heterogeneity in the prevalence of anaemia among published studies in Africa.
3. Nevertheless, appropriate systematic review and robust meta-analytic methods will be used to conduct the review and account for heterogeneity across studies, if any.

Introduction

Anaemia is a global public health problem associated with higher morbidity and mortality rates, increase 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]. The World Health Organisation (WHO) currently defines anaemia in children aged 6-59 months as a haemoglobin concentration less than 110g/l [6]. The aetiologies of anaemia could be multifactorial and vary globally depending on geography, age and gender [7]. Nonetheless, 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, B6, B12), haemoglobinopathies, parasitic infections, as well as acute and chronic inflammation [1, 6]. In a systematic analysis from 1990 to 2010, Kassebaum *et al* reported malaria, schistosomiasis and chronic kidney disease-related anaemia as the only conditions whose prevalence were found to be on the rise [7].

In 2010, the global prevalence of anaemia was estimated at 32.9% with the regions of South East Asia, Central, West and East sub-Saharan Africa bearing the greatest burden [7]. Though occurring at different stages in the life cycle, pregnant women and preschool age children have been found to be at greatest risk of having the disease [1], with children aged less than five years found to be the only age group with a negative trend from 1990 to 2010 [7]. The WHO estimates of 2011 suggest that about 273 million children and 42 million pregnant women have anaemia worldwide [6].

The prevalence of anaemia in children under five years in Africa varies from 9.7% in South eastern Nigeria to 78.4% in Ghana [8, 9]. Existing evidence suggests that severe anaemia, accounting for most anaemia-related deaths, mostly occurs among the under-five years age group, and generally in the rainy season (in the tropics) when the incidence of malaria is at its peak [8]. Furthermore, Brabin *et al* report that mortality due to severe anaemia from malaria is greater than that from iron deficiency anaemia in sub-Saharan Africa [10]. Besides malaria endemicity, poor nutrition, sickle cell disease, late arrival at health facilities, ignorance and poverty also account for high prevalence rates anaemia in this region [8, 11].

The prevalence of anaemia being an important health indicator coupled with the dearth of literature on the prevalence of anaemia in children under five 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 [12].

Objective

The aim of this systematic review is to determine the prevalence of anaemia in children under five years in Africa.

Review question

What is the prevalence of anaemia in children under five years in Africa?

Methods

Criteria for selection of studies for the review

Inclusion criteria

1. Cross-sectional and cohort studies published up to 30 April 2019 with available data to compute the prevalence of anaemia in children below five years
2. Studies which diagnosed anaemia using haemoglobin measurements
3. Studies which defined anaemia as haemoglobin levels below 110 g/l according to WHO and the United Nations Children Funds [13]
4. Age limit: children from 6 to 59 months of age

Exclusion criteria

1. Reviews, case reports and case series with less than 30 participants
2. Studies conducted in a population with haemoglobinopathies like as 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 under five published in EMBASE, Web of Science, PubMed, Global Medicus Index, and African Journals Online from inception to 30 April 2019. Medical subject headings and key text words like ‘anaemia’ OR ‘anemia’ 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 will also be screened for potential articles which we missed during our search.

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 upon for arbitration.

Data items and extraction

A pre-structured Google Form will be used for data abstraction by two authors after which the authors will then crosscheck each other's 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 region of Africa (northern, southern, eastern, western and central), the study area (urban, rural and suburbs), study design (cross sectional, cohort), study setting (hospital, school and community-based), sampling method (random sampling, consecutive, convenient), timing of data collection (prospective vs retrospective), male proportion, mean or median age in months, sample size, number of participants with anaemia, number of male participants, number of males with anaemia, number of female participants, number of females with anaemia, number of participants with mild anaemia, number of male participants with mild anaemia, number of female participants with mild anaemia, number of participants with moderate, number of male participants with moderate anaemia, number of female participants with moderate anaemia, number of participants with severe anaemia, number of male participants with severe anaemia, number of female participants with severe anaemia.

Where possible, data for multinational studies will be separated 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

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, to assess the risk of bias for prevalence studies, will be used to assess the study quality which will be scored on 10, **Supplementary Table 1**. Scores of 0 – 4, 5 – 7 and 8 – 10 will represent low moderate and high risk of bias, respectively

Data synthesis and analysis

The 'meta' package of the statistical software R (version 3.5.3, The R Foundation for statistical computing, Vienna, Austria) will be used for data analysis. The Cohen k statistics will be used to evaluate inter-rater agreement between authors for study inclusion [16]. The numerators and denominators 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 [17]. The χ^2 test on Cochrane's Q statistics, and I^2 will be used to assess and quantify heterogeneity across studies, respectively [18]. I^2 values of 70% or over will be consider to be evidence of substantial heterogeneity [19]. Prevalence estimates will be pooled according to the different Africa regions, the Q-test of analysis of variance will be used to compare the pooled estimates. Publication bias will be assessed visually funnel plots for asymmetry and confirmed statistically using the Egger's test [19]. 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), random sampling (Yes/No) and age groups.

A 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) and year of publication on the overall summary proportion. Only variables with p values <0.1 on bivariate analysis will be included in the multiple regression model. Two-sided p-values less than 5% will be considered statistically significant.

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 [20] 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. The 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.

Contributors: Study conception: VNA; Designed the protocol: LPS , VNA; Drafted the protocol: LPS, VNA; Protocol revision: EA, DSME, ENM, CEL, KNN, BAK Critical revision: DM. VNA is the guarantor of this review.

Competing interest: None.

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Data sharing statement

No additional data are available

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SN	Search Items	Hits

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List of tables

Table 1: Search Strategy for PubMed

Supplementary Table 1: Risk of bias assessment checklist for prevalence studies (adapted from Hoy et al)

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	

Table 1: Search Strategy for PubMed

Supplementary Table 1: Risk of bias assessment checklist for prevalence studies (adapted from Hoy et al)

Name of author(s):		
Year of publication:		
Study title:		
Risk of bias items	**Risk of bias levels**	**Points scored**
1. Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation?	**Yes** (**LOW RISK**): The study's target population was a close representation of the national population.	0
	No (**HIGH RISK**): The study's target population was clearly NOT representative of the national population.	1
2. Was the sampling frame a true or close representation of the target population?	**Yes** (**LOW RISK**): The sampling frame was a true or close representation of the target population.	0
	No (**HIGH RISK**): The sampling frame was NOT a true or close representation of the target population.	1
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	**Yes** (**LOW RISK**): A census was undertaken, OR, some form of random selection was used to select the sample (e.g. simple random sampling, stratified random sampling, cluster sampling, systematic sampling).	0
	No (**HIGH RISK**): A census was NOT undertaken, AND some form of random selection was NOT used to select the sample.	1
4. Was the likelihood of non-response bias minimal?	**Yes** (**LOW RISK**): The response rate for the study was ≥75%, OR, an analysis was performed that showed no significant difference in relevant demographic characteristics between responders and non- responders	0
	No (**HIGH RISK**): The response rate was <75%, and if any analysis comparing responders and non-responders was done, it showed a significant difference in relevant demographic characteristics between responders and non-responders	1
5. Were data collected directly from the subjects (as opposed to a proxy)?	**Yes** (**LOW RISK**): All data were collected directly from the subjects.	0
	No (**HIGH RISK**): In some instances, data were collected from a proxy.	1
6. Was an acceptable case definition used in the study?	**Yes** (**LOW RISK**): An acceptable case definition was used.	0
	No (**HIGH RISK**): An acceptable case definition was NOT used	1
7. Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)?	**Yes** (**LOW RISK**): The study instrument had been shown to have reliability and validity (if this was necessary), e.g. test-re- test, piloting, validation in a previous study, etc.	0
	No (**HIGH RISK**): The study instrument had NOT been shown to have reliability or validity (if this was necessary).	1
8. Was the same mode of data collection used for all subjects?	**Yes** (**LOW RISK**): The same mode of data collection was used for all subjects.	0
	No (**HIGH RISK**): The same mode of data collection was NOT used for all subjects.	1
9. Were the numerator(s) and denominato r(s) for the parameter of interest appropriate	**Yes** (**LOW RISK**): The paper presented appropriate numerator(s) AND denominator(s) for the parameter of interest (e.g. the prevalence of low back pain).	0
	No (**HIGH RISK**): The paper did present numerator(s) AND denominator(s) for the parameter of interest but one or more of these were inappropriate.	1
10. Summary on the overall risk of study bias	**LOW RISK**	0-4
	MODERATE RISK	5-7
	HIGH RISK	8-10

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments	4	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	11
Support:			
Sources	5a	Indicate sources of financial or other support for the review	13
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6-7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, Table 1
Study records:			
Data	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	8
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	8
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	8
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	9
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	9-10
	15b	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 (such as I^2, Kendall's τ)	9-10
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	10
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	10
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

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

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Paediatrics, Global health
Keywords:	Anaemia < HAEMATOLOGY, Child, Infant, Africa

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

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Abstract

Introduction: Anaemia, especially in children less than five years old, is a global health problem disproportionately affecting populations in low- 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 (PRISMA-P) 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 $\chi 2$ 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 account for 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.

Keywords: Anaemia, child, infant, Africa.

Word count: Abstract = 234; main text = 1460

Number of tables =1; Number of figures =0; supplementary files =2

Strengths and limitations of the study

1. 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.
2. We anticipate substantial heterogeneity in the prevalence of anaemia among published studies in Africa.
3. Nevertheless, appropriate systematic review and robust meta-analytic methods will be used to conduct the review and account for heterogeneity across studies, if any.

Introduction

Anaemia is a global public health problem associated with higher morbidity and mortality rates, increase 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]. The World Health Organisation (WHO) currently defines anaemia in children aged 6-59 months as a haemoglobin concentration less than 110g/l [6]. The aetiologies of anaemia could be multifactorial and vary globally depending on geography, age and gender [7]. Nonetheless, 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, B6, B12), haemoglobinopathies, parasitic infections, as well as acute and chronic inflammation [1, 6]. In a systematic analysis from 1990 to 2010, Kassebaum *et al* reported malaria, schistosomiasis and chronic kidney disease-related anaemia as the only conditions whose prevalence was found to be on the rise [7].

In 2010, the global prevalence of anaemia was estimated at 32.9% with the regions of South East Asia, Central, West and East sub-Saharan Africa bearing the greatest burden [7]. Though occurring at different stages in the life cycle, pregnant women and preschool age children have been found to be at greatest risk of having the disease [1], with children aged less than five years found to be the only age group with a negative trend from 1990 to 2010 [7]. The WHO estimates of 2011 suggested that about 273 million children and 42 million pregnant women had anaemia worldwide [6]. According to data by the World Bank, the global prevalence of anaemia in children under five years old 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 five years in Africa varies from 9.7% in South eastern Nigeria to 78.4% in Ghana [9, 10]. Existing evidence suggests that severe anaemia, accounting for most anaemia-related deaths, mostly occurs among the under-five years age group, and generally in the rainy season (in the tropics) when the incidence of malaria is at its peak [9]. Furthermore, Brabin *et al* report that mortality due to severe anaemia from malaria is greater than that from iron deficiency anaemia 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 five 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 as 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 to on the prevalence and determinants of anaemia in children between 6-59 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 hemoglobinometer, and defined anaemia as haemoglobin levels below 11.0 g/dl according to WHO and the United Nations Children Funds [6]
4. Studies which defined either mild, moderate or severe anaemia as haemoglobin values of 10.0-10.9, 7.0-9.9 or less than 7.0 g/dl, 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 less than 30 participants
2. Studies conducted in a population with haemoglobinopathies like as 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 which we 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 upon for arbitration.

Data items and extraction

A pre-structured Google Form will be used for data abstraction by two authors independently who will then crosscheck 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 region of Africa (northern, southern, eastern, western and central), the study area (urban, rural and suburbs), study design (cross sectional, cohort), 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, sample size, number of participants with anaemia, number of male participants, number of males with anaemia, number of female participants, number of females with anaemia, number of participants with mild anaemia, number of male participants with mild anaemia, number of female participants with mild anaemia, number of participants with moderate, number of male participants with moderate anaemia, number of female participants with moderate anaemia, number of participants with severe anaemia, number of male participants with severe anaemia, number of female participants with severe anaemia. In addition, we will extract data on the measure of association (adjusted odds ratio, relative risk, correlation coefficient) of the determinants of anaemia.

Where possible, data for multinational studies will be separated 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

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, **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, **Supplementary Table 2 and 3**.

Data synthesis and analysis

The 'meta' package of the statistical software R (version 3.5.3, The R Foundation for statistical computing, Vienna, Austria) will be used for data analysis. The Cohen k 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 consider to be evidence of substantial heterogeneity [20]. Prevalence estimates will be pooled according to the different Africa 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), random sampling (Yes/No), publication year (On or after 2009 vs before 2009), and age groups. 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, school 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 less than 5% will be considered statistically significant.

Data on the determinants of anaemia will be synthesized 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.

Contributors: Study conception: VNA; Designed the protocol: LPS, VNA; Drafted the protocol: LPS, VNA; Protocol revision: EA, DSME, ENM, CEL, KNN, BAK Critical revision: DM. VNA is the guarantor of this review.

Competing interest: None declared.

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Data sharing statement

No additional data are available

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List of tables

Table 1: Search Strategy for PubMed

Supplementary Table 1: Risk of bias assessment checklist for prevalence studies (adapted from Hoy et al)

Supplementary Table 2: Risk of bias assessment checklist for risk factor studies using the Newcastle Ottawa Scale.

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	

Table 1: Search Strategy for PubMed

Supplementary Table 1: Risk of bias assessment checklist for prevalence studies (adapted from Hoy et al)

Name of author(s): Year of publication: Study title:		
Risk of bias items	**Risk of bias levels**	**Points scored**
1. Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation?	**Yes** (**LOW RISK**): The study's target population was a close representation of the national population.	0
	No (**HIGH RISK**): The study's target population was clearly NOT representative of the national population.	1
2. Was the sampling frame a true or close representation of the target population?	**Yes** (**LOW RISK**): The sampling frame was a true or close representation of the target population.	0
	No (**HIGH RISK**): The sampling frame was NOT a true or close representation of the target population.	1
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	**Yes** (**LOW RISK**): A census was undertaken, OR, some form of random selection was used to select the sample (e.g. simple random sampling, stratified random sampling, cluster sampling, systematic sampling).	0
	No (**HIGH RISK**): A census was NOT undertaken, AND some form of random selection was NOT used to select the sample.	1
4. Was the likelihood of non-response bias minimal?	**Yes** (**LOW RISK**): The response rate for the study was ≥75%, OR, an analysis was performed that showed no significant difference in relevant demographic characteristics between responders and non- responders	0
	No (**HIGH RISK**): The response rate was <75%, and if any analysis comparing responders and non-responders was done, it showed a significant difference in relevant demographic characteristics between responders and non-responders	1
5. Were data collected directly from the subjects (as opposed to a proxy)?	**Yes** (**LOW RISK**): All data were collected directly from the subjects.	0
	No (**HIGH RISK**): In some instances, data were collected from a proxy.	1
6. Was an acceptable case definition used in the study?	**Yes** (**LOW RISK**): An acceptable case definition was used.	0
	No (**HIGH RISK**): An acceptable case definition was NOT used	1
7. Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)?	**Yes** (**LOW RISK**): The study instrument had been shown to have reliability and validity (if this was necessary), e.g. test-re- test, piloting, validation in a previous study, etc.	0
	No (**HIGH RISK**): The study instrument had NOT been shown to have reliability or validity (if this was necessary).	1
8. Was the same mode of data collection used for all subjects?	**Yes** (**LOW RISK**): The same mode of data collection was used for all subjects.	0
	No (**HIGH RISK**): The same mode of data collection was NOT used for all subjects.	1
9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	**Yes** (**LOW RISK**): The length of the shortest prevalence period for the parameter of interest was appropriate.	0
	No (**HIGH RISK**): the length of the shortest prevalence period for the parameter of interest was NOT appropriate.	1
10. Were the numerator(s) and denominator(s) for the parameter of interest appropriate	**Yes** (**LOW RISK**): The paper presented appropriate numerator(s) AND denominator(s) for the parameter of interest (e.g. the prevalence of low back pain).	0
	No (**HIGH RISK**): The paper did present numerator(s) AND denominator(s) for the parameter of interest but one or more of these were inappropriate.	1
Summary on the overall risk of study bias	**LOW RISK**	0-4
	MODERATE RISK	5-7
	HIGH RISK	8-10

Supplementary Table 2. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

No	Criterion	Decision rule	Score (*= 1, No* = 0)
	Selection		
1.	Is the case definition adequate?	a) yes, with independent validation * b) yes, eg record linkage or based on self reports c) no description	
2.	Representativeness of the cases	a) consecutive or obviously representative series of cases * b) potential for selection biases or not stated	
3.	Selection of Controls	a) community controls * b) hospital controls c) no description	
4.	Definition of Controls	a) no history of disease (endpoint) * b) no description of source	
	Comparability		
1.	Comparability of cases and controls on the basis of the design or analysis	a) study controls for age* b) study controls for gender *	
	Exposure		
1.	Ascertainment of exposure	a) secure record * b) structured interview where blind to case/control status * c) interview not blinded to case/control status d) written self report or medical record only e) no description	
2.	Same method of ascertainment for cases and controls	a) Yes * b) No	
3.	Non-Response rate	a) same rate for both groups * b) non respondents described c) rate different and no designation	
	Score		

Supplementary Table 3. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

No	Criterion	Decision rule	Score (✸= 1, No✸ = 0)
	Selection		
1.	Representativeness of the exposed cohort	a) Consecutive eligible participants were selected, participants were randomly selected, or all participants were invited to participate from the source population✸ b) Not satisfying requirements in part (a), or not stated.	
2.	Selection of the non-exposed cohort	a) Selected from the same source population✸ b) Selected from a different source population c) No description	
3.	Ascertainment of exposure	a) secure record (eg surgical records) ✸ b) structured interview ✸ c) written self report d) no description	
4.	Demonstration that outcome of interest was not present at start of study	a) Yes ✸ b) No	
	Comparability		
1.	Comparability of cohorts on the basis of the design or analysis	a) study controls for age✸ b) study controls for gender ✸	
	Outcome		
1.	Assessment of outcome	a) independent blind assessment ✸ b) record linkage ✸ c) self report d) no description	
2.	Was follow-up long enough for outcomes to occur	a) Yes ✸ b) No	
3.	Adequacy of follow up of cohorts	a) complete follow up - all subjects accounted for ✸ b) subjects lost to follow up unlikely to introduce bias - small number lost (< 15% follow up, or description provided of those lost) ✸ c) follow up rate < 85% and no description of those lost d) no statement	
	Score		

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments	4	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	11
Support:			
Sources	5a	Indicate sources of financial or other support for the review	13
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6-7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, Table 1
Study records:			
Data	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	8
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	8
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	8
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	9
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	9-10
	15b	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 (such as I^2, Kendall's τ)	9-10
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	10
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	10
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

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

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

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Abstract

Introduction: Anaemia, especially in children less than five years old, is a global health problem disproportionately affecting populations in low- 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 (PRISMA-P) 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 $\chi 2$ 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 account for 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.

Keywords: Anaemia, child, infant, Africa.

Word count: Abstract = 234; main text = 1460

Number of tables =1; Number of figures =0; supplementary files =2

Strengths and limitations of the study

1. 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.
2. We anticipate substantial heterogeneity in the prevalence of anaemia among published studies in Africa.
3. Nevertheless, appropriate systematic review and robust meta-analytic methods will be used to conduct the review and account for heterogeneity across studies, if any.

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]. The World Health Organisation (WHO) currently defines anaemia in children aged 6-59 months as a haemoglobin concentration less than 110g/l [6]. The aetiologies of anaemia could be multifactorial and vary globally depending on geography, age and gender [7]. Nonetheless, 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, B6, B12), 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, West and East sub-Saharan Africa bearing the greatest burden [7]. Though 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 less than five years found to be the only age group with a negative trend from 1990 to 2010 [7]. The 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 five 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 five years in Africa varies from 9.7% in South eastern 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-five, 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 iron deficiency anaemia 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 five 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 as 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 to on the prevalence and determinants of anaemia in children between 6-59 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 hemoglobinometer, and defined anaemia as haemoglobin levels below 11.0 g/dl according to WHO and the United Nations Children Funds [6]
4. Studies which defined either mild, moderate or severe anaemia as haemoglobin values of 10.0-10.9, 7.0-9.9 or less than 7.0 g/dl, 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 less than 30 participants
2. Studies conducted in a population with haemoglobinopathies like as 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 which we 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 upon for arbitration.

Data items and extraction

A pre-structured Google Form will be used for data abstraction by two authors independently who will then crosscheck 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 with mild anaemia, participants with moderate, males with moderate anaemia, females with moderate anaemia, participants with severe anaemia, males with severe anaemia, and females with severe anaemia. Finally, data on the measure of association (adjusted odds ratio, beta coefficient, and relative risk) of the determinants of anaemia will be extracted.

Where possible, data for multinational studies will be separated 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, **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, **Supplementary Table 2 and 3**.

Data synthesis and analysis

The 'meta' package of the statistical software R (version 3.5.3, The R Foundation for statistical computing, Vienna, Austria) will be used for data analysis. The Cohen k 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 Africa 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, school 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 less than 5% will be considered statistically significant.

Data on the determinants of anaemia will be synthesized 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.

Contributors: Study conception: VNA; Designed the protocol: LPS, VNA; Drafted the protocol: LPS, VNA; Protocol revision: EA, DSME, ENM, CEL, KNN, BAK Critical revision: DM. VNA is the guarantor of this review.

Competing interest: None declared.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data sharing statement

No additional data are available

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.

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List of tables

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	

Supplementary Table 1: Risk of bias assessment checklist for prevalence studies (adapted from Hoy et al)

Name of author(s): Year of publication: Study title:		
Risk of bias items	**Risk of bias levels**	**Points scored**
1. Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation?	**Yes** (**LOW RISK**): The study's target population was a close representation of the national population.	0
	No (**HIGH RISK**): The study's target population was clearly NOT representative of the national population.	1
2. Was the sampling frame a true or close representation of the target population?	**Yes** (**LOW RISK**): The sampling frame was a true or close representation of the target population.	0
	No (**HIGH RISK**): The sampling frame was NOT a true or close representation of the target population.	1
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	**Yes** (**LOW RISK**): A census was undertaken, OR, some form of random selection was used to select the sample (e.g. simple random sampling, stratified random sampling, cluster sampling, systematic sampling).	0
	No (**HIGH RISK**): A census was NOT undertaken, AND some form of random selection was NOT used to select the sample.	1
4. Was the likelihood of non-response bias minimal?	**Yes** (**LOW RISK**): The response rate for the study was ≥75%, OR, an analysis was performed that showed no significant difference in relevant demographic characteristics between responders and non- responders	0
	No (**HIGH RISK**): The response rate was <75%, and if any analysis comparing responders and non-responders was done, it showed a significant difference in relevant demographic characteristics between responders and non-responders	1
5. Were data collected directly from the subjects (as opposed to a proxy)?	**Yes** (**LOW RISK**): All data were collected directly from the subjects.	0
	No (**HIGH RISK**): In some instances, data were collected from a proxy.	1
6. Was an acceptable case definition used in the study?	**Yes** (**LOW RISK**): An acceptable case definition was used.	0
	No (**HIGH RISK**): An acceptable case definition was NOT used	1
7. Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)?	**Yes** (**LOW RISK**): The study instrument had been shown to have reliability and validity (if this was necessary), e.g. test-re- test, piloting, validation in a previous study, etc.	0
	No (**HIGH RISK**): The study instrument had NOT been shown to have reliability or validity (if this was necessary).	1
8. Was the same mode of data collection used for all subjects?	**Yes** (**LOW RISK**): The same mode of data collection was used for all subjects.	0
	No (**HIGH RISK**): The same mode of data collection was NOT used for all subjects.	1
9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	**Yes** (**LOW RISK**): The length of the shortest prevalence period for the parameter of interest was appropriate.	0
	No (**HIGH RISK**): the length of the shortest prevalence period for the parameter of interest was NOT appropriate.	1
10. Were the numerator(s) and denominator(s) for the parameter of interest appropriate	**Yes** (**LOW RISK**): The paper presented appropriate numerator(s) AND denominator(s) for the parameter of interest (e.g. the prevalence of low back pain).	0
	No (**HIGH RISK**): The paper did present numerator(s) AND denominator(s) for the parameter of interest but one or more of these were inappropriate.	1
Summary on the overall risk of study bias	**LOW RISK**	0-4
	MODERATE RISK	5-7
	HIGH RISK	8-10

Supplementary Table 2. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

No	Criterion	Decision rule	Score (*= 1, No* = 0)
	Selection		
1.	Is the case definition adequate?	a) yes, with independent validation * b) yes, eg record linkage or based on self reports c) no description	
2.	Representativeness of the cases	a) consecutive or obviously representative series of cases * b) potential for selection biases or not stated	
3.	Selection of Controls	a) community controls * b) hospital controls c) no description	
4.	Definition of Controls	a) no history of disease (endpoint) * b) no description of source	
	Comparability		
1.	Comparability of cases and controls on the basis of the design or analysis	a) study controls for age* b) study controls for gender *	
	Exposure		
1.	Ascertainment of exposure	a) secure record * b) structured interview where blind to case/control status * c) interview not blinded to case/control status d) written self report or medical record only e) no description	
2.	Same method of ascertainment for cases and controls	a) Yes * b) No	
3.	Non-Response rate	a) same rate for both groups * b) non respondents described c) rate different and no designation	
	Score		

Supplementary Table 3. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

No	Criterion	Decision rule	Score (✸= 1, No✸ = 0)
	Selection		
1.	Representativeness of the exposed cohort	a) Consecutive eligible participants were selected, participants were randomly selected, or all participants were invited to participate from the source population✸ b) Not satisfying requirements in part (a), or not stated.	
2.	Selection of the non-exposed cohort	a) Selected from the same source population✸ b) Selected from a different source population c) No description	
3.	Ascertainment of exposure	a) secure record (eg surgical records) ✸ b) structured interview ✸ c) written self report d) no description	
4.	Demonstration that outcome of interest was not present at start of study	a) Yes ✸ b) No	
	Comparability		
1.	Comparability of cohorts on the basis of the design or analysis	a) study controls for age✸ b) study controls for gender ✸	
	Outcome		
1.	Assessment of outcome	a) independent blind assessment ✸ b) record linkage ✸ c) self report d) no description	
2.	Was follow-up long enough for outcomes to occur	a) Yes ✸ b) No	
3.	Adequacy of follow up of cohorts	a) complete follow up - all subjects accounted for ✸ b) subjects lost to follow up unlikely to introduce bias - small number lost (< 15% follow up, or description provided of those lost) ✸ c) follow up rate < 85% and no description of those lost d) no statement	
	Score		

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments	4	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	11
Support:			
Sources	5a	Indicate sources of financial or other support for the review	13
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6-7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, Table 1
Study records:			
Data	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	8
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	8
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	8
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	9
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	9-10
	15b	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 (such as I^2, Kendall's τ)	9-10
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	10
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	10
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

BMJ Open

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

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Keywords:	Anaemia < HAEMATOLOGY, Child, Infant, Africa

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

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Abstract

Introduction: Anaemia, especially in children less than five years old, is a global health problem disproportionately affecting populations in low- 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 (PRISMA-P) 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 $\chi 2$ 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 account for 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.

Keywords: Anaemia, child, infant, Africa.

Word count: Abstract = 234; main text = 1460

Number of tables =1; Number of figures =0; supplementary files =2

Strengths and limitations of the study

1. 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.
2. We anticipate substantial heterogeneity in the prevalence of anaemia among published studies in Africa.
3. Nevertheless, appropriate systematic review and robust meta-analytic methods will be used to conduct the review and account for heterogeneity across studies, if any.

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]. The World Health Organisation (WHO) currently defines anaemia in children aged 6-59 months as a haemoglobin concentration less than 110g/l [6]. The aetiologies of anaemia could be multifactorial and vary globally depending on geography, age and gender [7]. Nonetheless, 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, B6, B12), 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, West and East sub-Saharan Africa bearing the greatest burden [7]. Though 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 less than five years found to be the only age group with a negative trend from 1990 to 2010 [7]. The 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 five 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 five years in Africa varies from 9.7% in South eastern 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-five, 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 iron deficiency anaemia 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 five 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 as 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 to on the prevalence and determinants of anaemia in children between 6-59 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 hemoglobinometer, and defined anaemia as haemoglobin levels below 11.0 g/dl according to WHO and the United Nations Children Funds [6]
4. Studies which defined either mild, moderate or severe anaemia as haemoglobin values of 10.0-10.9, 7.0-9.9 or less than 7.0 g/dl, 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 less than 30 participants
2. Studies conducted in a population with haemoglobinopathies like as 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 upon for arbitration.

Data items and extraction

A pre-structured Google Form will be used for data abstraction by two authors independently who will then crosscheck 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 with mild anaemia, participants with moderate, males with moderate anaemia, females with moderate anaemia, participants with severe anaemia, males with severe anaemia, and females with severe anaemia. Finally, data on potential measures of association (adjusted odds ratio 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, **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, **Supplementary Table 2 and 3**.

Data synthesis and analysis

The 'meta' package of the statistical software R (version 3.5.3, The R Foundation for statistical computing, Vienna, Austria) will be used for data analysis. The Cohen k 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 Africa 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, school 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 less than 5% will be considered statistically significant.

Data on the determinants of anaemia will be synthesized 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.

Contributors: Study conception: VNA; Designed the protocol: LPS, VNA; Drafted the protocol: LPS, VNA; Protocol revision: EA, DSME, ENM, CEL, KNN, BAK Critical revision: DM. VNA is the guarantor of this review.

Competing interest: None declared.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data sharing statement

No additional data are available

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.

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List of tables

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	

Supplementary Table 1: Risk of bias assessment checklist for prevalence studies (adapted from Hoy et al)

Name of author(s): Year of publication: Study title:		
Risk of bias items	**Risk of bias levels**	**Points scored**
1. Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation?	**Yes** (**LOW RISK**): The study's target population was a close representation of the national population.	0
	No (**HIGH RISK**): The study's target population was clearly NOT representative of the national population.	1
2. Was the sampling frame a true or close representation of the target population?	**Yes** (**LOW RISK**): The sampling frame was a true or close representation of the target population.	0
	No (**HIGH RISK**): The sampling frame was NOT a true or close representation of the target population.	1
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	**Yes** (**LOW RISK**): A census was undertaken, OR, some form of random selection was used to select the sample (e.g. simple random sampling, stratified random sampling, cluster sampling, systematic sampling).	0
	No (**HIGH RISK**): A census was NOT undertaken, AND some form of random selection was NOT used to select the sample.	1
4. Was the likelihood of non-response bias minimal?	**Yes** (**LOW RISK**): The response rate for the study was ≥75%, OR, an analysis was performed that showed no significant difference in relevant demographic characteristics between responders and non- responders	0
	No (**HIGH RISK**): The response rate was <75%, and if any analysis comparing responders and non-responders was done, it showed a significant difference in relevant demographic characteristics between responders and non-responders	1
5. Were data collected directly from the subjects (as opposed to a proxy)?	**Yes** (**LOW RISK**): All data were collected directly from the subjects.	0
	No (**HIGH RISK**): In some instances, data were collected from a proxy.	1
6. Was an acceptable case definition used in the study?	**Yes** (**LOW RISK**): An acceptable case definition was used.	0
	No (**HIGH RISK**): An acceptable case definition was NOT used	1
7. Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)?	**Yes** (**LOW RISK**): The study instrument had been shown to have reliability and validity (if this was necessary), e.g. test-re- test, piloting, validation in a previous study, etc.	0
	No (**HIGH RISK**): The study instrument had NOT been shown to have reliability or validity (if this was necessary).	1
8. Was the same mode of data collection used for all subjects?	**Yes** (**LOW RISK**): The same mode of data collection was used for all subjects.	0
	No (**HIGH RISK**): The same mode of data collection was NOT used for all subjects.	1
9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	**Yes** (**LOW RISK**): The length of the shortest prevalence period for the parameter of interest was appropriate.	0
	No (**HIGH RISK**): the length of the shortest prevalence period for the parameter of interest was NOT appropriate.	1
10. Were the numerator(s) and denominator(s) for the parameter of interest appropriate	**Yes** (**LOW RISK**): The paper presented appropriate numerator(s) AND denominator(s) for the parameter of interest (e.g. the prevalence of low back pain).	0
	No (**HIGH RISK**): The paper did present numerator(s) AND denominator(s) for the parameter of interest but one or more of these were inappropriate.	1
Summary on the overall risk of study bias	**LOW RISK**	0-4
	MODERATE RISK	5-7
	HIGH RISK	8-10

Supplementary Table 2. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

No	Criterion	Decision rule	Score (*= 1, No* = 0)
	Selection		
1.	Is the case definition adequate?	a) yes, with independent validation * b) yes, eg record linkage or based on self reports c) no description	
2.	Representativeness of the cases	a) consecutive or obviously representative series of cases * b) potential for selection biases or not stated	
3.	Selection of Controls	a) community controls * b) hospital controls c) no description	
4.	Definition of Controls	a) no history of disease (endpoint) * b) no description of source	
	Comparability		
1.	Comparability of cases and controls on the basis of the design or analysis	a) study controls for age* b) study controls for gender *	
	Exposure		
1.	Ascertainment of exposure	a) secure record * b) structured interview where blind to case/control status * c) interview not blinded to case/control status d) written self report or medical record only e) no description	
2.	Same method of ascertainment for cases and controls	a) Yes * b) No	
3.	Non-Response rate	a) same rate for both groups * b) non respondents described c) rate different and no designation	
	Score		

Supplementary Table 3. NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

No	Criterion	Decision rule	Score (✸= 1, No✸ = 0)
	Selection		
1.	Representativeness of the exposed cohort	a) Consecutive eligible participants were selected, participants were randomly selected, or all participants were invited to participate from the source population✸ b) Not satisfying requirements in part (a), or not stated.	
2.	Selection of the non-exposed cohort	a) Selected from the same source population✸ b) Selected from a different source population c) No description	
3.	Ascertainment of exposure	a) secure record (eg surgical records) ✸ b) structured interview ✸ c) written self report d) no description	
4.	Demonstration that outcome of interest was not present at start of study	a) Yes ✸ b) No	
	Comparability		
1.	Comparability of cohorts on the basis of the design or analysis	a) study controls for age✸ b) study controls for gender ✸	
	Outcome		
1.	Assessment of outcome	a) independent blind assessment ✸ b) record linkage ✸ c) self report d) no description	
2.	Was follow-up long enough for outcomes to occur	a) Yes ✸ b) No	
3.	Adequacy of follow up of cohorts	a) complete follow up - all subjects accounted for ✸ b) subjects lost to follow up unlikely to introduce bias - small number lost (< 15% follow up, or description provided of those lost) ✸ c) follow up rate < 85% and no description of those lost d) no statement	
	Score		

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments	4	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	11
Support:			
Sources	5a	Indicate sources of financial or other support for the review	13
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6-7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, Table 1
Study records:			
Data	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	8
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	8
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	8
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	9
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	9-10
	15b	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 (such as I^2, Kendall's τ)	9-10
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	10
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	10
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA