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Hypertension prevalence, incidence and risk factors among children and adolescents in Africa: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction: The African adult population is facing a growing epidemic of hypertension. Establishment of accurate epidemiological data on hypertension in African children and adolescents may have important implications for hypertension preventive strategies in Africa.

Methods and analysis: This systematic review and meta-analysis will follow the MOOSE Guidelines. Relevant abstracts published in English/French from 1 January 1985 to 31 July 2015 will be searched in PubMed, Google Scholar and Online African journals. Full texts of eligible studies will then be accessed through PubMed, Google Scholar, HINARI and the respective journals' websites. Relevant unpublished papers and conference proceedings will also be checked. Data will be analysed using R statistical software. The study-specific estimates will be pooled through a random-effects meta-analysis model to obtain an overall summary estimate of the prevalence/incidence of hypertension across studies. Also, we will assess the association between risk factors and hypertension. Heterogeneity of studies will be evaluated by the χ^2 test on Cochrane's Q statistic. Funnel plots analysis and Egger's test will be done to detect publication bias. Results will be presented by geographic region (central, eastern, northern, southern and western Africa). A p value less than 0.05 will be considered significant for factors that predicted hypertension.

Ethics and dissemination: The current study is based on published data, and thus ethical approval is not required. This systematic review and meta-analysis is expected to serve as input for designing early life preventive and control strategies, and as a guide for future research based on existing gaps. The final report of the systematic review in the form of a scientific paper will be published in peer-reviewed journals. Findings will further be presented at conferences and submitted to relevant health authorities.

Trial registration number: CRD42015019029.

INTRODUCTION

Low-and-middle income countries (LMICs) are facing concurrent epidemics of communicable and non-communicable diseases.[1] Unlike high-income countries, the prevalence of non-communicable diseases has rapidly and continuously risen in the past decades in LMICs.[2] This increasing burden of non-communicable diseases is particularly true for cardiovascular diseases (CVD), including stroke, coronary heart disease, peripheral arterial disease and heart failure.[2 3] The high CVD-related morbidity and mortality observed in LMICs are paralleled by the increasing prevalence of lifestyle risk factors in these countries, especially hypertension.[4] Hypertension, once rare in traditional African societies,[5 6] has become a major public health problem because of high prevalence rates contrasting with low awareness, treatment and control rates.[7–9] The high prevalence of hypertension in Africa is due to both urbanisation and a shift towards western habits such as smoking, unhealthy diets with excess salt and fat intake, physical inactivity and consequential increased adiposity, and increasingly recognised non-traditional risk factors such as air pollution.[5–7 10 11]

High blood pressure (BP) tracks from childhood to adulthood, such that children presenting with high BP (HBP) are at high risk of becoming hypertensive at an adult age.[5 12–14] Emerging data from developed populations also suggest that, as in adults, primary hypertension is more common than secondary hypertension in the paediatric population.[6 15] Furthermore, the presence of HBP has been linked to end-organ damage (particularly left ventricular hypertrophy and kidney failure) and subclinical atherosclerosis.[6 16 17] Hence, in western countries, it is strongly recommended to measure BP in all children ≥3 years of age in the course of routine healthcare, [18] in order to promote cardiovascular health in adults.

It is difficult to estimate the prevalence of hypertension in the paediatric population

because BP relates to sex, age and height during childhood, making it complicated to consider a single BP value as in adults.[14 16 18 19] Nevertheless, many epidemiological studies summarised in systematic reviews have attempted this issue in high-income countries, and reported an increasing burden of hypertension in children and adolescents,[16] with prevalence rates of 1–5%.[20 21] This is not the case for African countries where there is a considerable variability of the estimated prevalence among studies conducted in South Africa and certain West African countries (0–22.3%).[5 6 19 22 23] Additionally, there is no reported incidence of hypertension among children in Africa, to the best of our knowledge, as well as limited evidence for its risk factors.

Thus, it is unclear whether the growing epidemic of hypertension in the African adult population is reflected in children and adolescents. The fast transition towards CVD in Africa, together with the increasing awareness of hypertension in children by African health professionals involved in paediatric care, stresses the need to build an accurate epidemiology of hypertension in children and adolescents in this part of the world. Along these lines, we present the protocol for a systematic review and meta-analysis to estimate the prevalence and incidence rates of hypertension among African children and adolescents, as well as its risk factors. Results are intended to provide an essential basis for designing cost-effective interventions that can be introduced early in life to prevent the burden of CVD in adulthood.

OBJECTIVE

To conduct a systematic review and meta-analysis to estimate the prevalence and the incidence of hypertension among children and adolescents in Africa, as well as its risk factors.

Review question

This review of studies published in the past 30 years, from 1 January 1985 to 30 April 2015, should answer the following questions:

1. What is the prevalence of HBP among African children and adolescents residing in Africa?
2. What is the incidence of HBP among African children and adolescents?
3. Which factors are associated with HBP among African children and adolescents?

Criteria for considering studies for the review

Inclusion criteria

We will include:

1. Cross-sectional, case–control or cohort studies of children and adolescents aged 1–18 years residing in African countries reporting the prevalence or incidence of HBP, or enough data to compute these estimates.
2. Studies including assessment of office and/or ambulatory and/or home BP, as well as those evaluating risk factors for hypertension in African children and adolescents.
3. Studies with a diagnosis of hypertension based on BP ≥95th centile.
4. Studies published in English or French, unpublished studies and conference proceedings.

Exclusion criteria

1. Studies on non-systemic hypertension (intracranial hypertension, pulmonary hypertension).
2. Studies conducted among populations of African origin residing outside of Africa.
3. Studies in subgroups of participants selected on the basis of the presence of hypertension (eg, clinical trials).
4. Studies including adult and paediatric populations in which it will not be possible to extract data of children and/or adolescents.
5. Case series with small sample size (less than 50 participants), letters, reviews, commentaries and editorials.
6. Studies lacking primary data and/or explicit method description.
7. Duplicates: for studies published in more than one paper, the most comprehensive one reporting the largest sample size will be considered.
8. Studies with serious ethical issues.
9. Studies whose full data will not be accessible even after request from the authors.

Search strategy for identifying relevant studies

This systematic review and meta-analysis will follow the guidelines set out by MOOSE.[24] The search strategy will be implemented in two stages:

Bibliographic database searches

A. Relevant abstracts published in English or French on the prevalence, the incidence and the risk factors for HBP in children and adolescents in Africa will be identified via searching PubMed, Google Scholar and online African journals. The search will be limited to studies published between 1 January 1985 and 31 July 2015. Both text words and medical subject heading terms will be used. Key search terms will be: Africa, children, adolescents, prevalence, incidence, risk factors and hypertension. We will also use individual country names for the 53 African countries and hypertension as additional key search terms for more abstracts on the subject. Conference proceedings of the study period will also be identified through Medline and checked. The main search strategy is shown in table 1.

B. The abstracts of all eligible papers will be reviewed and full articles will be accessed through PubMed, Google Scholar, HINARI or journals' websites. The references of all the relevant research articles will also be scrutinised for additional potential data sources, and their full texts will be accessed in a similar way. The authors whose full text papers will

Table 1 Search method in PUBMED

Search	Search terms
1	Hypertension [tw] OR high blood pressure [tw] OR systolic hypertension [tw] OR diastolic hypertension [tw]
2	Hypertension [MeSH terms]
3	# 1 OR # 2
4	(Child [tw] OR Child [MeSH terms] Children [tw] OR childhood [tw] OR adolescent [MeSH terms] OR adolescent [tw] OR adolescent* [tw] OR pediatric [tw] OR teens [tw] OR teen [tw] OR Teenage* [tw] OR Youth* [tw] OR Infan* [tw])
5	# 3 AND # 4
6	(((((“Africa"[MeSH] OR Africa* [tw] OR Algeria[tw] OR Angola[tw] OR Benin[tw] OR Botswana[tw] OR “Burkina Faso"[tw] OR Burundi [tw] OR Cameroon [tw] OR “Canary Islands” [tw] OR “Cape Verde” [tw] OR “Central African Republic” [tw] OR Chad [tw] OR Comoros [tw] OR Congo [tw] OR “Democratic Republic of Congo” [tw] OR Djibouti [tw] OR Egypt [tw] OR “Equatorial Guinea” [tw] OR Eritrea [tw] OR Ethiopia [tw] OR Gabon [tw] OR Gambia [tw] OR Ghana [tw] OR Guinea [tw] OR “Guinea Bissau” [tw] OR “Ivory Coast” [tw] OR “Cote d’Ivoire” [tw] OR Jamahiriya [tw] OR Jamahiryia [tw] OR Kenya [tw] OR Lesotho [tw] OR Liberia [tw] OR Libya [tw] OR Libia [tw] OR Madagascar [tw] OR Malawi [tw] OR Mali [tw] OR Mauritania [tw] OR Mauritius [tw] OR Morocco [tw] OR Mozambique [tw] OR Mocambique [tw] OR Namibia [tw] OR Niger [tw] OR Nigeria [tw] OR Principe [tw] OR Reunion [tw] OR Rwanda [tw] OR “Sao Tome” [tw] OR Senegal [tw] OR Seychelles [tw] OR “Sierra Leone” [tw] OR Somalia [tw] OR “South Africa” [tw] OR “St Helena” [tw] OR Sudan [tw] OR Swaziland [tw] OR Tanzania [tw] OR Togo [tw] OR Tunisia [tw] OR Uganda [tw] OR “Western Sahara” [tw] OR Zaire [tw] OR Zambia [tw] OR Zimbabwe [tw] OR “Central Africa” [tw] OR “Central African” [tw] OR “West Africa” [tw] OR “West African” [tw] OR “Western Africa” [tw] OR “Western African” [tw] OR “East Africa” [tw] OR “East African” [tw] OR “Eastern Africa” [tw] OR “Eastern African” [tw] OR “North Africa” [tw] OR “North African” [tw] OR “Northern Africa” [tw] OR “Northern African” [tw] OR “South African” [tw] OR “Southern Africa” [tw] OR “Southern African” [tw] OR “sub Saharan Africa” [tw] OR “sub Saharan African” [tw] OR “subSaharan Africa” [tw] OR “subSaharan African” [tw]) NOT (“guinea pig” [tw] OR “guinea pigs” [tw] OR “aspergillus niger” [tw]))))
7	# 5 AND # 6
8	#7 Limits: 1985/01/01 to 2015/04/30 and studies done in Humans, in English and French

not be accessible by the numerous internet-based sources will be directly contacted to provide them. In case of no feedback from these authors, the corresponding studies will be excluded.

Selection of studies for inclusion in the review

Assessment of eligible papers will be done by three members of the team independently, and using an assessment guide to ensure that the selection criteria are reliably applied by all the investigators. They will also consensually retain the studies that will be included in the review, and any disagreement will be solved by a fourth assessor.

Assessment of methodological quality and data reporting

The Risk of Bias Tool for Prevalence Studies developed by Hoy *et al*[25] (see online supplementary material appendix S1), and the Cochrane guidelines available in Review Manager V.5.3 (http://tech.cochrane.org/revman) will be used to assess the methodological quality and risk of bias for each study. The STROBE checklist (see online supplementary material appendix S2)[26] will be used to evaluate the reporting methodology in each paper. Risk of bias and quality scores will be presented in a table.

Data extraction and management

A data extraction sheet will be used to collect information about the country, the year of publication, the language of publication, the type of publication, the study design, the number of participants, the mean age of the population, the diagnostic criteria for hypertension, the prevalence and the incidence of hypertension, as well as its predictive factors when available. Where prevalence/incidence rates or information for calculating them (eg, sample size, number of outcomes) are lacking, we will directly contact the corresponding author to request the information. In case of multinational studies, we will separate the results to show the prevalence, the incidence and risk factors within individual countries. Where it will not be possible to disaggregate the data by country, the study will be presented as one and the countries in which the study was done will be shown.

Statistical analysis

Data will be analysed using Stata software (Stata Corp V.13, Texas, USA). A meta-analysis will be conducted for data obtained from studies in which hypertension was defined identically. SEs for the study-specific estimates will first be determined from the point estimate and the appropriate denominators, assuming a binominal (or Poisson for incidence data) distribution. Then the study-specific estimates will be pooled through a random-effects meta-analysis model, to obtain an overall summary estimate of the prevalence/incidence across studies, after stabilising the variance of individual studies using the Freeman-Tukey double arc-sine transformation.[27] A meta-analysis will be

performed to assess the association between risk factors and hypertension.

Heterogeneity will be evaluated by the χ^2 test on Cochrane[28]'s Q statistic, which is quantified by I^2 values,[29] assuming that I^2 values of 25%, 50% and 75%, respectively, represent low, medium and high heterogeneity. Where substantial heterogeneity will be detected, a subgroup analysis will be performed to detect its possible sources using the following grouping variables: age group, sex, study setting (hospital vs community-based), geographical area (central, eastern, northern, southern and western Africa), study quality. Inter-rater agreement for study inclusion will be assessed using Cohen's κ coefficient.[30] Funnel plots analysis and Egger's test[31] will be done to detect publication bias.

Results will be presented by geographic region (central, eastern, northern, southern and western Africa). A p value less than 0.05 will be considered significant for factors that predicted hypertension.

Results reporting and presentation

The study selection process will be summarised using a flow diagram. Reasons for studies' exclusion will be described. This will follow the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies.[24] Quantitative data will be presented in evidence tables of individual studies as well as in summary tables and funnel plots where appropriate. We will examine prevalence/incidence and risk factors by region, setting (hospital or community), time period and disease-specific populations depending on the data available. We plan to report on quality scores and risk of bias for each eligible study. This may be tabulated and accompanied by narrative summaries.

Conclusion

Hypertension, a major driver of the CVD burden in Africa, has reached epidemic proportions in the adult population. Given that children and adolescents presenting with HBP have a major risk of becoming hypertensive adults, specific cost-effective interventions need to be introduced early in life to prevent CVD in adulthood. Prior to these strategies, accurate epidemiological data should be obtained. We wish that this review will guide policy, practice and research by providing information on the magnitude of hypertension among African children, as well as its risk factors, and the remaining gaps that may form the basis for future studies.

A major possible limitation of this study could be the limited data with predominance of hospital-based studies and poor quality data when available. Another possible limitation may be the heterogeneity of studies, making further analysis difficult. In addition, there may be a predominance of cross-sectional studies, making it difficult to obtain reliable incidence estimates and to determine risk factors for hypertension. Other drawbacks might include the non-random selection of participants, and the under-representation of some geographical areas such as Central Africa. These problems have already been noted by previous reviews on non-communicable diseases in Africa,[1–3 8 32] and might be reinforced by the fact that BP is still not routinely recorded in paediatric consultations in many African countries. Finally, since we will include only studies published in English or French, we may lose relevant data from countries where these languages are not spoken.

ETHICS AND DISSEMINATION

This study is based on published data, and therefore ethical approval is not a requirement. This systematic review and meta-analysis is expected to serve as a basis for designing preventive and control strategies early in life, and as a guide for future research based on the remaining gaps. The final report of this study in the form of a scientific paper will be published in peer-reviewed journals. Findings will further be presented at conferences and submitted to relevant health authorities. We also plan to update the review in the future to monitor changes and guide health service and policy solutions.

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Contributors JJNN, ME and JJRB conceived and designed the protocol, and ME drafted the manuscript. JJNN, JJRB, JRNN, AMJ, LNA and JZ critically revised the manuscript for methodological and intellectual content. JJNN is the guarantor of the review. All authors approved the final version.

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Appendix S1: Risk of bias assessment tool
Adapted from the Risk of Bias Tool for Prevalence Studies developed by Hoy et al. (2012)

Risk of bias Item	Answer: Yes (Low Risk) or No (High risk)
External Validity	
1. Was the study target population a close representation of the national pregnant population in relation to relevant variables?	
2. Was the sampling frame a true or close representation of the target population?	
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	
4. Was the likelihood of non-participation bias minimal?	
Internal Validity	
5. Were data collected directly from the subjects (as opposed to medical records)?	
6. Were acceptable case definition of hypertension used?	
7. Was a reliable and accepted diagnosis method for hypertension utilized?	
8. Was the same mode of data collection used for all subjects?	

9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	
10. Were the numerator(s) and denominator(s) for the calculation of the prevalence of dyslipidemia appropriate?	
11. Summary item on the overall risk of study bias **Low Risk of Bias**: 8 or more "yes" answers. Further research is very unlikely to change our confidence in the estimate. **Moderate Risk of Bias**: 6 to 7 "yes" answers. Further research is likely to have an important impact on our confidence in the estimate and may change the estimate. **High Risk of Bias**: 5 or fewer "yes" answers. Further research is very likely to have an important impact on our confidence in the estimate and is likely to change the estimate.	

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

	Item N°	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objective	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection

Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe

		comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity

		analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure

		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives,

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalizability	21	Discuss the generalizability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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

Quality assessment score

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