BMJ Open

Incidence and prevalence of type 1 diabetes in Africa: a systematic review and meta-analysis protocol

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To cite: Katte JC, Agoons BB, Akem Dimala C, *et al*. Incidence and prevalence of type 1 diabetes in Africa: a systematic review and meta-analysis protocol. *BMJ Open* 2022;**12**:e061605. doi:10.1136/bmjopen-2022-061605

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-061605).

Received 31 January 2022
Accepted 12 August 2022

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ABSTRACT

Introduction Type 1 diabetes is reported to have significant mortality in Africa. However, there is a paucity of data on pooled estimates of its incidence and prevalence in Africa. This first systematic review and meta-analysis will be conducted to determine the incidence and prevalence of this condition in Africa.

Methods Based on predefined criteria, electronic databases, including PubMed, Excerpta Medica database, Africa Journal Online and Web of Science, will be searched for relevant studies involving paediatric and adult patients, with no language restrictions. Quality assessment of the individual studies will be performed, and the Q-statistic test and I^2 statistic test will be used to assess statistical heterogeneity. Appropriate meta-analysis will then be used to pool studies judged to be clinically homogenous. Egger's test will be used to detect publication bias. The planned search dates for the eligible articles are from 1 September to 30 September 2022.

Ethics and dissemination Since this review will use previously published studies, it will not require the consent of an ethics committee. The results will be prepared and disseminated through a peer-reviewed journal and will be presented in relevant conferences.

PROSPERO registration number CRD42021278227.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We will employ robust methods and statistical analyses to determine the burden of type 1 diabetes mellitus, providing evidence for public health strategies.
⇒ The review will include primary studies without language restrictions, allowing the maximum inclusion of studies published on the topic.
⇒ The review uses an inclusive search in large databases, with a long-time range.
⇒ Methodological biases in the primary studies included may cause uncertainty in the final results obtained.
⇒ This study will also assess the quality of published incidence and prevalence data of type 1 diabetes in Africa.

INTRODUCTION

The true epidemiological feature of type 1 diabetes is unknown in Africa despite recent reports suggesting an increase in the number of persons with the condition in the continent.[1 2] In 2013, the International Diabetes Federation (IDF) reported that about 39 000 individuals were living with type 1 diabetes in Africa, with an incidence of 6.4/1 000 000 among those less than 14 years old.[3] In 2017, the IDF reported an estimated 50 600 children and adolescents below 20 years living with type 1 diabetes in Africa.[4] Interestingly, these IDF reports are limited to a cohort of subjects aged less than 20 years old. It is therefore necessary to provide supplementary data on type 1 diabetes in all age categories in Africa.

A previous narrative review of some early population-based studies across different countries in Africa stated that the prevalence of type 1 diabetes was <1/1000, with incidence rates ranging from 1.5 to 10.1/100 000 per year.[5] This was not a systematic review and only presented results in ranges, reporting conflicting findings regarding the prevalence of type 1 diabetes in sex-specific groups across east to west Africa.

Type 1 diabetes is reported to have high mortality in Africa. It stands out as an almost neglected disease in the continent, receiving very little scientific attention and funding for research.[1] A possible reason for this neglect is the high cost of confirmatory diagnostic tests for type 1 diabetes (dosage of islet autoantibodies), potentially underestimating true prevalence estimates. Therefore, in this context, there is a need for accurate, evidence-based epidemiological data summarising the trends of the condition, which may serve as a basis for developing adequate public health strategies, health service organisations and interventions in the African continent.[6] To our knowledge, this is the first systematic review and meta-analysis aiming to summarise available data on the incidence and prevalence of type 1 diabetes in Africa. We will also

examine the epidemiology of the condition with regard to age, sex, geographical region and temporal trends.

The findings of this study are intended to serve as a supplement to the recent IDF atlas reports on the incidence and prevalence of type 1 diabetes in Africa. While the results of the IDF are based on a single study per African country available and are limited to data in the 0–20 years age group, this study will aim to provide estimates using multiple studies available per given African country, and also inform on epidemiological estimates of type 1 diabetes in adults aged 20 years and above.

REVIEW QUESTION

What are the epidemiological features of type 1 diabetes on the African continent?

OBJECTIVES

The objective of the present systematic review and meta-analysis is to estimate the prevalence and incidence of type 1 diabetes in patients (of any age, including paediatrics or adults) in Africa.

Secondary objectives

1. Assess the quality of published incidence and prevalence data of type 1 diabetes in Africa.
2. Estimate the incidence and prevalence of type 1 diabetes by gender, age and geographical delimitations.
3. Determine the temporal trend of the prevalence and incidence of type 1 diabetes in Africa.
4. Compare incidence and prevalence of type 1 diabetes between North Africa and sub-Saharan Africa.

METHODS AND DESIGN

The Preferred Reporting Items for Systematic Reviews and Meta-analysis for Protocols (PRISMA-P) guidelines served as the template for reporting this protocol.[7] This systematic review and meta-analysis will be conducted as recommended in the Joanna Briggs Institute (JBI) reviewer's manual for prevalence and incidence review.[8] The PRISMA-P checklist is attached (see online supplemental file 1).

Patient and public involvement

Patients and the public will not be involved in the design or planning of the study.

Criteria for considering studies for the review

Types of studies

This study shall select all hospital-based and population-based observational studies that correctly provide data estimates on the incidence and prevalence of type 1 diabetes in Africa. These observational studies will include population-based cross-sectional studies for estimating the prevalence and prospective, population-based cohort studies for estimating the incidence.

Population

We will consider studies involving children, adolescents and adults with no particular age limit with a clinical diagnosis of type 1 diabetes. This refers to all children/adolescents/adults with diabetes on insulin therapy, and confirmed by the treating physician as 'type 1 diabetes'.

Outcome

Studies included in this review will be studies reporting on the prevalence and/or incidence of type 1 diabetes or insulin dependent diabetes mellitus (IDDM) or juvenile diabetes conducted in Africa. Studies lacking explicit method descriptions will be excluded if the information was not provided after contacting authors twice. The minimum acceptable sample size for the preliminary studies is 30 participants from the general population. This is to ensure that we recruit studies with large sample sizes, in order to provide accurate estimates on type 1 diabetes incidence and prevalence.

Research strategy for identifying relevant studies

The search strategy will be conducted as discussed below.

Bibliographic database searches

A comprehensive search of PubMed, Excerpta Medica database, Africa Journal Online and Web of Science will be conducted to identify all published relevant articles without any language and period of publication restriction. A search strategy based on the combination of relevant terms will be designed and applied. This search strategy was built according to PRESS guidelines.[9] The primary search strategy in PubMed is shown in online supplemental file 2. This search strategy will be adapted for search in other databases. The search strategy will be applied in all databases on 3 January 2022. A manual search consisting of scanning reference lists of eligible studies and relevant reviews will be performed to identify missed studies during the review process or by search strategy or for studies not indexed in the five targeted electronic databases. For articles published in a language other than English and French, an experienced translator in the concerned language will be contacted for translation. Studies published from 1 January 1980 to 31 December 2021 will be deemed eligible for assessment.

Searching for other sources

We will scan the references of all selected articles for additional data sources missed during our search, and their full texts obtained. All studies that meet our selection criteria will be included for analyses.

Selection of studies to include in the review

Two investigators (JCK and JJB) will independently screen records for eligibility based on titles and abstracts. Full texts of articles deemed potentially eligible will be retrieved. Further, these investigators will independently assess the full text of each study for eligibility and consensually retained studies to be included. Disagreements will be resolved by consensus and following an

independent review by a third reviewer in case of unresolved disagreements.

Data extraction and management

Data will be extracted using a preconceived, piloted and standardised data abstraction form. Two investigators (JCK and BBA) will independently extract data, including the name of the first author, year of publication, study design, period of inclusion of participants, recruitment site (country, number of locations), sampling method, sample size, number of cases, age distribution, proportion male and presence of specific conditions/disease. After article extraction and data collection, the authors will unanimously decide if it is necessary to implement the study protocol, if the data appears to be limited.

Methodological quality assessment

We will use an adapted version of the tool developed by the JBI to assess the risk of bias in included studies.[8] All selected full-text articles will be critically appraised by two investigators after comparing it to the nine elements found in the JBI checklist for studies reporting prevalence data. Any unanimous decision by the both investigators on article inclusion/exclusion on the basis of quality is final, with a third investigator needed, in case of any decision discrepancy (CAD).

Data synthesis and analysis

Meta-analyses will be conducted using the *meta* packages of the R statistical software (V.3.6.0, The R Foundation for Statistical Computing, Vienna, Austria). Only populations with the same clinical profile (specific disease or condition) will be pooled together. The aim of pooling data from patients/population with the same clinical profile is to reduce clinical heterogeneity. With *metaprop* function, we will use the reference method to synthesise prevalence data as recommended by Barendregt and colleagues.[10] All prevalence estimates will be reported with their 95% CI; alongside their 95% prediction intervals that can help better understand the uncertainty.[11] The prediction interval predicts the range in which a future individual observation will fall, while the CI will show the likely range of values associated with a statistical parameter of the epidemiological data of interest. To minimise the effect of studies with extremely small or extremely large prevalence estimates on the overall estimate, the variance of study-specific prevalence will be stabilised with the Freeman-Tukey double arcsine transformation before pooling the data with the random effects meta-analysis model.[10]

Heterogeneity will be assessed by the χ^2 test on Cochrane's Q statistic,[12] and quantified by I^2 values, assuming I^2 values of 25%, 50% and 75%, representing low, medium and high heterogeneity.[13] The Egger test will be used to assess the presence of publication bias.[14] A p value <0.10 will be considered indicative of a statistically significant publication bias.[15] It was decided a priori that if publication bias were present, it would not be adjusted for since we believed that the prevalence estimates of interest would likely be published even if substantially different from previously reported estimates. We will conduct subgroup analyses according to subregions in Africa (Northern, Southern, Western, Central and Eastern), level of country human development index, age group and sex. We will calculate R^2 through meta-regression analysis (with *metareg* function) to identify covariates that explain the heterogeneity in the overall estimate and quantify the heterogeneity. Inter-rater agreements between investigators for study inclusion and methodological quality assessment will be assessed using Cohen's κ.

Presentation and reporting of results

The study selection process will be summarised using a flow diagram. Quantitative data will be presented in tables of individual studies and in summary tables or forest plots where appropriate. The quality scores of bias for each eligible study will be reported accordingly.

Potential study amendments

We do not plan to modify the protocol to avoid reporting bias. However, if necessary, any amendment in the review process will be reported for transparency.

Ethics and dissemination

Since primary data will not be collected in this study, ethical approval is not required. This review is expected to provide accurate data on the incidence and prevalence of type 1 diabetes in Africa. The final report will be published in an international peer-reviewed journal.

Contributors JCK and ES developed the idea, design for this protocol. JCK, BBA, CAD wrote the first draft of the manuscript. CAD and JJB developed the search strategy. All authors critically revised this manuscript. JCK and ES are the guarantors of the review. All authors critically revised the methodology and intellectual content and approved the final version of this manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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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 Number
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	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
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	7
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	7
Support:			
Sources	5a	Indicate sources of financial or other support for the review	
Sponsor	5b	Provide name for the review funder and/or sponsor	7
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
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)	4,5
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
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	6

		coverage	
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	5, 6 and supplementary
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
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)	6
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	6, 7
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	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
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	6,7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6
	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)	6
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	6
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	7

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Incidence and prevalence of type 1 diabetes in Africa: a systematic review and meta-analysis

Search	Search terms
#1	"type 1 diabetes" OR "type 1 diabetes mellitus" OR "juvenile diabetes" OR "juvenile diabetes mellitus" OR "insulin dependent diabetes mellitus" or "insulin-dependent diabetes mellitus" OR "early-onset diabetes mellitus" OR "young-onset diabetes mellitus" OR "childhood diabetes"
#2	Africa* OR Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR "Canary Islands" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Democratic Republic of the Congo" OR Djibouti OR "Equatorial Guinea" OR Eritrea OR Eswatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR "Guinea Bissau" OR "Ivory Coast" OR "Cote d'Ivoire" OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Mozambique OR Namibia OR Niger OR Nigeria OR Réunion OR Rwanda OR "Sao Tome and Principe" OR Senegal OR Seychelles OR "Sierra Leone" OR Somalia OR "South Africa" OR "South Sudan" OR "Saint Helena" OR Togo OR Uganda OR "United Republic of Tanzania" OR Zambia OR Zimbabwe OR "Eastern Africa" OR "Middle Africa" OR "Southern Africa" OR "Western Africa" OR "East Africa" OR "East African" OR "Eastern Africa" OR "South African" OR "Southern African" OR "West Africa" OR "West African" OR "Western African" OR "Central Africa" OR "Central African" OR "Western Sahara" OR "sub Saharan Africa" OR "sub Saharan African" OR "subSaharan Africa" OR "subSaharan African"
#3	Incidence* OR Prevalence*
#4	#1 AND #2 AND #3
#5	#Limit [1980/01/01 to 2021/12/31

Table 1: Search Strategy for PubMed

Search strategy for Embase (Excerpta Medica)

Search	**Search terms**
#1	'type 1 diabetes'/exp OR 'type 1 diabetes' OR 'type 1 diabetes mellitus'/exp OR 'type 1 diabetes mellitus' OR 'juvenile diabetes'/exp OR 'juvenile diabetes' OR 'juvenile diabetes mellitus'/exp OR 'juvenile diabetes mellitus' OR 'insulin dependent diabetes mellitus'/exp OR 'insulin dependent diabetes mellitus' OR 'insulin-dependent diabetes mellitus'/exp OR 'insulin-dependent diabetes mellitus' OR 'early-onset diabetes mellitus'/exp OR 'early-onset diabetes mellitus' OR 'young-onset diabetes mellitus' OR 'childhood diabetes'
#2	africa* OR angola OR benin OR botswana OR 'burkina faso' OR burundi OR 'cabo verde' OR cameroon OR 'canary islands' OR 'central african republic' OR chad OR comoros OR congo OR 'democratic republic of the congo' OR djibouti OR 'equatorial guinea' OR eritrea OR eswatini OR ethiopia OR gabon OR gambia OR ghana OR guinea OR 'guinea bissau' OR 'ivory coast' OR 'cote ivoire' OR kenya OR lesotho OR liberia OR madagascar OR malawi OR mali OR mauritania OR mauritius OR mayotte OR mozambique OR namibia OR niger OR nigeria OR réunion OR rwanda OR 'sao tome and principe' OR senegal OR seychelles OR 'sierra leone' OR somalia OR 'south africa' OR 'south sudan' OR 'saint helena' OR togo OR uganda OR 'united republic of tanzania' OR zambia OR zimbabwe OR 'middle africa' OR 'southern africa' OR 'western africa' OR 'east africa' OR 'east african' OR 'eastern africa' OR 'south african' OR 'southern african' OR 'west africa' OR 'west african' OR 'western african' OR 'central africa' OR 'central african' OR 'western sahara' OR 'sub saharan africa' OR 'sub saharan african' OR 'subsaharan africa' OR 'subsaharan african'
#3	incidence* OR prevalence*
#4	#1 AND #2 AND #3
#5	#1 AND #2 AND #3 AND [1980-2021]/py

Search strategy of Web of Science

Search	**Search terms**
#1	(type 1 diabetes OR juvenile diabetes OR insulin dependent diabetes mellitus OR insulin-dependent diabetes mellitus OR early-onset diabetes mellitus OR young-onset diabetes mellitus OR childhood diabetes)
#2	africa* OR angola OR benin OR botswana OR burkina faso OR burundi OR cape verde OR cameroon OR central african republic OR chad OR comoros OR congo OR democratic republic of the congo OR djibouti OR equatorial guinea OR eritrea OR eswatini OR ethiopia OR gabon OR gambia OR ghana OR guinea OR guinea bissau OR ivory coast OR cote ivoire OR kenya OR lesotho OR liberia OR madagascar OR malawi OR mali OR mauritania OR mauritius OR mayotte OR mozambique OR namibia OR niger OR nigeria OR réunion OR rwanda OR sao tome and principe OR senegal OR seychelles OR sierra leone OR somalia OR south africa OR south sudan OR saint helena OR togo OR uganda OR united republic of tanzania OR zambia OR zimbabwe OR middle africa OR southern africa OR western africa OR east africa OR east african OR eastern africa OR south african OR southern african OR west africa OR west african OR western african OR central africa OR central african OR western sahara OR sub saharan africa OR sub saharan african OR subsaharan africa OR subsaharan African OR north africa
#3	incidence OR prevalence OR epidemiology
#4	#1 AND #2 AND #3
#5	#1 AND #2 AND #3 AND [1980-2021]/py

Search strategy of AJOL

Search	Search terms
#1	(type 1 diabetes OR type 1 diabetes mellitus OR juvenile diabetes OR juvenile diabetes mellitus OR insulin-dependent diabetes mellitus OR insulin dependent diabetes mellitus OR early-onset diabetes OR early-onset diabetes mellitus OR young-onset diabetes OR childhood diabetes)
#2	africa* OR angola OR benin OR botswana OR 'burkina faso OR burundi OR cape verde OR cameroon OR central african republic OR chad OR comoros OR congo OR democratic republic of the congo OR djibouti OR equatorial guinea OR eritrea OR eswatini OR ethiopia OR gabon OR gambia OR ghana OR guinea OR guinea bissau OR ivory coast OR cote ivoire OR kenya OR lesotho OR liberia OR madagascar OR malawi OR mali OR mauritania OR mauritius OR mayotte OR mozambique OR namibia OR niger OR nigeria OR réunion OR rwanda OR sao tome and principe OR senegal OR seychelles OR sierra leone OR somalia OR south africa OR south sudan OR togo OR uganda OR united republic of tanzania OR zambia OR zimbabwe OR middle africa OR southern africa OR western africa OR east africa OR east african OR eastern africa OR south african OR southern african OR west africa OR west african OR western african OR central africa OR central african OR western sahara OR sub-saharan africa OR sub saharan african OR subsaharan africa OR subsaharan African OR north africa
#3	incidence OR prevalence OR epidemiology
#4	#1 AND #2 AND #3
#5	#1 AND #2 AND #3 AND [1980-2021]/py