BMJ Open

The prevalence of Type 2 diabetes in South Africa: a systematic review protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021029
Article Type:	Protocol
Date Submitted by the Author:	06-Dec-2017
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Keywords:	Type 2 Diabetes Mellitus, Prevalence, South Africa, Impaired glucose tolerance, Impaired fasting glucose, Undiagnosed diabetes

The prevalence of Type 2 diabetes in South Africa: a systematic review protocol

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Abbreviations

GRADE: Grading of Recommendations Assessment, Development and Evaluation; IDF: International Diabetes Federation; PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols; TB: Tuberculosis; HIV: human immunodeficiency virus

Keywords

Prevalence, South Africa, Type 2 Diabetes Mellitus, Impaired glucose tolerance, Impaired fasting glucose, Undiagnosed diabetes

Abstract

Introduction

Type 2 diabetes mellitus is a major source of morbidity and mortality in South Africa, spurred by increased urbanization and unhealthy lifestyle factors. Urgent action is required to halt the burgeoning diabetes epidemic, however, such initiatives are hampered by the lack of national prevalence data. Although studies have estimated the prevalence of diabetes in South Africa, these are not suitable to estimate the national diabetes burden. The purpose of this review is estimate the prevalence of Type 2 diabetes by collating and synthesizing all studies reporting the prevalence of diabetes in South Africa. A secondary aim is to estimate the prevalence of impaired glucose tolerance and impaired fasting glucose, conditions which are associated with an increased risk of progression to overt diabetes. Lastly, the prevalence of undiagnosed diabetes will be assessed.

Methods and analysis

Multiple databases will be searched for diabetes prevalence studies conducted in South Africa between 1997 and 2017. Two authors will independently select studies that meet the inclusion criteria, extract data and appraise studies using the risk of bias tool for prevalence studies and the Newcastle-Ottawa Scale for assessing the quality of non-randomized studies. Heterogeneity across studies will be calculated using the χ^2 test and the inconsistency statistic (I^2). A pooled estimate will be calculated using the fixed-effects or random-effects model. If a meta-analysis is not possible, articles will be described narratively. Sources of heterogeneity will be explored using subgroup analysis. Publication bias will be assessed using funnel plots and the Egger and Begg's test.

Ethics and dissemination

The systematic review does not require ethics clearance since published studies with non-identifiable data will be used. This review will provide accurate epidemiological data to inform the Second National Global Burden of Disease study, which will help guide health and policy planning.

PROSPERO registration number: CRD42017071280

Strengths of the study

- First systematic review to collate and synthesize all studies reporting the prevalence of diabetes in South Africa.
- A comprehensive synthesis of available South African diabetes prevalence data using robust systematic review methods, which will provide accurate epidemiological data for the Second National Global Burden of Disease study to inform health and policy planning.
- Adheres to Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines.
- Studies with a high risk of bias will be excluded and the quality of the review will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

Limitations of the study

- Heterogeneity of population. South Africa is comprised of different population groups with varied risks for diabetes.

Introduction

Diabetes mellitus, a condition characterized by raised blood glucose levels, is a major source of morbidity, mortality and health costs worldwide. The International Diabetes Federation (IDF) estimates that in 2013, 382 million people worldwide had diabetes, with projections of 592 million cases by 2035 [1]. Africa is expected to bear the brunt of the diabetes increase, with the prevalence of diabetes increasing by 109% between 2013 and 2035. These numbers are probably grossly underestimated due to high rates of undiagnosed diabetes in Africa, estimated at 46% for middle income countries and 75.1% for low income countries [2]. The IDF estimates that in 2015, 79% of the 321,000 deaths due to diabetes occurred in individuals younger than 60 years of age [3], emphasizing the magnitude of the diabetes epidemic in Africa. In Africa, as in other parts of the world, Type 2 diabetes represents over 90% of diabetes cases [4,5].

South Africa is at the forefront of the war against diabetes in Africa. In 2009, approximately 2 million (9%) people aged 30 years and older had diabetes [6], increasing almost two-fold since 2000 when Bradshaw et al. reported a prevalence of 5.5% [7]. Several factors such as the aging population, economic transition, and urbanization associated with nutrition transition and obesity have contributed to the increased diabetes prevalence [8–11]. Indeed, in 2000 it was estimated that 90% of diabetes cases in South Africa were attributed to excess body weight [12]. This is concerning since in 2013 ~38% of men and ~69% of women in South Africa were considered overweight or obese [13]. In 2015 the global burden of disease study estimated that high body mass index and hyperglycemia, ranked as the second and third-leading risk factors, respectively, after unsafe sex, for early death and disability in South Africa [14].

Diabetes, due to its association with several micro- and macrovascular complications, places a significant burden on the South African health system. In 2009 it was estimated that diabetes caused about 8,000 new cases of blindness and 2,000 new cases of amputations annually [6]. A national burden of disease study in 2000 reported that diabetes accounted for approximately 14% of cases of ischemic heart disease (IHD), 10% of stroke, 12% of hypertensive disease and 12% of renal disease [7]. Furthermore, the indirect costs of diabetes are high. Diabetes in Africa affect mainly working-aged people between 40 and 60 years old [11] placing an added burden on the economy due to work absenteeism and decreased productivity. South Africa is battling a quadruple burden of disease due to high rates of infectious diseases, non-communicable disease, maternal and child mortality, and injury-related disorders, thus have limited resources to meet the increased health and economic costs of diabetes [15].

Rationale

Urgent action is required to halt the burgeoning diabetes epidemic in South Africa. The feasibility of population-level interventions, particularly those aimed at prevention is widely reported [16]. However, such initiatives are hampered by the lack of national prevalence data, a challenge faced by all countries in Africa [17]. Several studies have measured the prevalence of diabetes in South Africa [18–28], although they were conducted in different geographical areas (urban vs. rural), amongst different population

groups, and are generally too small to individually give reliable national prevalence data. Pooling of existing data is considered an effective strategy to generate representative and robust prevalence figures [10]. Bertram et al. calculated the national prevalence of diabetes in 2009 [6], however, their estimate was not comprehensive, including only four studies measuring the diabetes prevalence in black South Africans in two rural, one urban and one metro urban population [23–26]. The study did not account for the racial variations in diabetes prevalence in South Africa [18,21,22,25], and focused on estimating the disability burden of diabetes rather than characterizing the different levels of hyperglycemia in these populations.

Objective

The purpose of this systematic review is to collate and synthesize all existing studies reporting the prevalence of diabetes in South Africa so as to estimate the overall prevalence of Type 2 diabetes. A secondary aim is to estimate the prevalence of impaired glucose tolerance and impaired fasting glucose, conditions which are associated with an increased risk of progression to overt diabetes. Lastly, the prevalence of undiagnosed diabetes will be assessed. These findings will be used to inform the Second National Global Burden of Disease study, which will help guide health and policy planning.

METHODS

Study selection

Published population-based surveys, cross-sectional studies and prospective or retrospective cohort studies that report the prevalence of diabetes in South Africa.

Inclusion criteria

Studies will be included if they were published between January 1997 and December 2017, include more than 100 participants regardless of age, gender, ethnicity, socioeconomic and educational background and study setting, and report the primary outcome using a case definition according to the 2006 World Health Organization diagnostic criteria [29], where Type 2 diabetes is diagnosed either by a physician, fasting blood glucose concentrations more than or equal to 7.0 mmol/L, two-hour oral glucose tolerance test values more than or equal to 11.1 mmol/L or self-reported use of oral diabetes drugs. In addition, glycosylated hemoglobin more than or equal to 6.5 % will also be used for case definition [30]. Due to limitations that hamper the differentiation between Type 1 diabetes and Type 2 diabetes, diabetes in individuals older than 25 years of age will be classified as Type 2 diabetes. Impaired glucose tolerance will be defined by fasting blood glucose concentrations less than 7.0 mmol/L and two-hour oral glucose tolerance values more than or equal to 7.8 mmol/L, but less than 11.1 mmol/L. Impaired fasting glucose will be defined as fasting blood glucose concentrations between 6.1 mmol/L and 6.9 mmol/L, and, if available, two-hour oral glucose tolerance values less than 7.8 mmol/L [29].

Exclusion criteria

Studies will be excluded if they were not conducted in South Africa, do not report the primary outcome, have no clear description of the case definition, and contain data for refugees in camps since they may not be representative of the South African population.

Primary Outcome

Prevalence of Type 2 diabetes.

Secondary Outcome

Prevalence of impaired glucose tolerance, impaired fasting glucose and undiagnosed Type 2 diabetes.

Search strategy

A search of articles written in English and indexed in PubMed, Scopus, Web of Science and African Index Medicus between January 1997 and December 2017 will be conducted. An experienced librarian and disease content experts will be consulted to ensure that the search terms are relevant and optimally arranged, and will include keywords and medical subject headings (MeSH) terms. An example of the search strategy in PubMed is illustrated in Table 1. The search will be modified to each database. References will be managed in EndNote.

Table 1. PubMed search strategy.

Search	Query
#4	Search ((#3 NOT (animals[mh] NOT humans[mh]))) AND ("1997/01/01"[Date-Publication] : "2018/02/28"[Date-Publication])
#3	Search (#1 AND #2)
#2	Search (South Africa[mh]OR"South Africa*"[tiab] OR RSA[tiab] OR Africa, Southern[mh:noexp] OR Southern Africa[tiab])
#1	Search (Diabetes[Mesh] OR Diabetes mellitus[Mesh] OR Type 2 diabetes mellitus[Mesh] OR Type 2 diabetes[Mesh] OR Diabetes mellitus, type 2[Mesh] OR Diabetes, type 2[Mesh] OR hyperglycemia[Mesh] OR Blood glucose[Mesh] OR Hemoglobin A, glycosylated[Mesh] OR Glycosylated hemoglobin OR Impaired glucose tolerance OR Impaired fasting glucose OR Undiagnosed diabetes

Study selection

The titles and abstracts of articles from the electronic search outputs will be screened independently by two reviewers to identify eligible studies. Disagreements or uncertainties will be resolved by discussion and consensus between the two reviewers, or with a third reviewer if disagreement persists. Full-text copies of the eligible articles will be retrieved and reviewed by two independent reviewers for inclusion. Additional information will be requested from the study authors if required. Reasons for exclusion will be recorded.

Data extraction

After the final decision to include studies into the review, two authors will independently extract and record data using the Burden of Disease (BOD) Review Manager developed by the South African Medical Research Council [31]. The following data will be extracted:

- Study details: date of publication, study title, study design, study period and study purpose.
- Study population: province/district of study, study setting (community or health facility based), setting (urban or rural) and sample size.
- Case definition as reported in the study.
- Prevalence of Type 2 diabetes, impaired glucose tolerance, impaired fasting glucose and undiagnosed Type 2 diabetes.
- Characteristics of cases: age, sex, population group, and comorbid disease (tuberculosis (TB) or human immunodeficiency virus (HIV) status).

After completion, data will be compared and discrepancies will be resolved through consensus between the two reviewers, or in consultation with a third reviewer.

Risk of bias assessment

Two reviewers will independently appraise the study quality and risk of bias using a checklist adapted from the risk of bias tool for population-based studies [32] and the Newcastle-Ottawa Scale for assessing the quality of non-randomized studies [33,34], and standardized in the BOD Review Manager [31]. Parameters assessed will include: external validity (whether the target population is representative of South Africa, representativeness of sample, selection criteria, non-response bias) and internal validity (case definition, validity and reliability of test instruments, consistency of case measurement, appropriateness of time period, and appropriateness of numerators and denominators in estimation). Disagreements between the reviewers over the risk of bias will be resolved by discussion with a third review reviewer where necessary.

Data synthesis

Studies with a moderate or low risk of bias will be included in the analysis. If suitable, a meta-analysis will be conducted for quantitative data using STATA v14 (StataCorp, College Station, Texas, USA). The study-specific estimates will be pooled to obtain the overall summary estimate and 95% confidence interval across studies. Standard errors (SEs) will be calculated for studies using the crude corresponding denominators and numerators. Clinical heterogeneity will be investigated by looking at the type of participants and case definitions in the study, while statistical heterogeneity will be calculated using the $\chi 2$ test with a p value ≤ 0.10 indicating statistically significant heterogeneity. The degree of heterogeneity across studies will be assessed using the I^2 statistic, with <25% indicating low heterogeneity, 25-50% moderate heterogeneity, and >75% high heterogeneity [35,36]. Statistically homogenous studies ($\chi 2$ $p > 0.10$) will be pooled using the fixed-effect or random-effect meta-analysis. Clinically and statistically heterogeneous studies will be evaluated using tables and figures. A narrative description will be conducted for data not suitable for the meta-analysis, and will include information about sample size, publication date and effect size. The symmetry of funnel plots will be visually inspected to assess publication bias, while the Egger and Begg's tests will be conducted to statistically assess publication bias [37,38].

Subgroup analysis

Subgroup analyses for study population (province/district, community or health facility based, urban or rural) and characteristics of cases (age, sex, population group, and comorbid disease TB or HIV) if sufficient data exists.

Confidence in cumulative evidence

The strength of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method [39], which scores studies as very low, low, moderate, or high based on methodological flaws within the included studies, consistency of results across diverse studies, precision of estimates and publication bias.

Ethics and Dissemination

The systematic review does not require ethics clearance since published studies with non-identifiable data will be used. This review is the first to collate and synthesize all the available studies reporting the prevalence of diabetes in South Africa and will provide accurate epidemiological data to inform the Second National Global Burden of Disease study, which will help guide health and policy planning. Findings from the review will be disseminated in a peer-reviewed journal article and academic reports according to the PRISMA guidelines [40].

Authors' contributions

CP, VPvW, JJ and DB conceived the idea and design of the study and drafted the protocol.
NL and MN helped to draft the protocol.
All authors wrote and approved the final manuscript.

Acknowledgements

The authors would like to thank Eunice Turawa of the Burden of Disease unit, South African Medical Research Council for her assistance with the development of the search strategy.

Funding

This work was supported by the South Africa Medical Research Council (SAMRC).

Conflict of interest

The authors have no competing interests.

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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	Pheiffer et al. manuscript Page No.
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	1
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	9
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	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	9
Sponsor	5b	Provide name for the review funder and/or sponsor	
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)	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	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
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	6,7

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7
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	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	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5,6
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	8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	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)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	8

*** 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.

BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021029.R1
Article Type:	Protocol
Date Submitted by the Author:	24-May-2018
Complete List of Authors:	Pheiffer, Carmen; South African Medical Research Council, Biomedical Research and Innovation Platform; Stellenbosch University, Division of Medical Physiology, Faculty of Health Sciences, Pillay-van Wyk, Victoria; South African Medical Research Council, Burden of Disease Research Unit, Tygerberg Joubert, Jané; South African Medical Research Council, Burden of Disease Research Unit, Tygerberg Levitt, Naomi; University of Cape Town , Medicine Nglazi, Mweete; South African Medical Research Council, Burden of Disease Research Unit Bradshaw, Debbie; South African Medical Research Council, MRC Burden of Disease Research Unit
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology
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Abbreviations

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ABSTRACT

Introduction

Type 2 diabetes mellitus is a major source of morbidity and mortality in South Africa, spurred by increased urbanization and unhealthy lifestyle factors. Local epidemiological data are required to inform health planning and policy. The purpose of this systematic review is to identify, collate and synthesize all studies reporting the prevalence of diabetes in South Africa. A secondary aim is to report the prevalence of impaired glucose tolerance and impaired fasting glucose, conditions which are associated with an increased risk of progression to overt diabetes, and the prevalence of undiagnosed diabetes.

Methods and analysis

Multiple databases will be searched for diabetes prevalence studies conducted in South Africa between 1997 and 2018. Two authors will independently select studies that meet the inclusion criteria, extract data and appraise studies using a risk of bias tool for prevalence studies. Studies with low or moderate risk of bias will be included. Sources of heterogeneity will be explored using subgroup analysis.

Ethics and dissemination

The systematic review does not require ethics clearance since published studies with non-identifiable data will be used. This review will provide best estimates to inform the Second National Burden of Disease study, which can guide health and policy planning.

PROSPERO registration number: CRD42017071280

Strengths and limitations of the study

- The first ever systematic review of Type 2 diabetes prevalence in South Africa.
- A comprehensive synthesis of all available diabetes prevalence data in South Africa using a standardized risk of bias tool.
- The protocol adheres to Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines.
- The quality of the review will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE).
- The heterogeneity in diagnostic criteria, study dates, age of study participants, and population groups may limit comparison across studies.

INTRODUCTION

Diabetes mellitus, a condition characterized by raised blood glucose levels, is a major source of morbidity, mortality and health costs worldwide. The International Diabetes Federation (IDF) estimates that in 2017, 451 million adults worldwide had diabetes, with projections of 693 million cases by 2045 [1]. Globally, approximately 50% of diabetes cases are undiagnosed, with the majority of these occurring in low and middle income countries. In Africa, the proportion of undiagnosed diabetes is 69.2%. Furthermore, 77% of deaths due to diabetes in Africa occurred in individuals younger than 60 years of age [1], emphasizing the magnitude of the diabetes epidemic. In Africa, as in other parts of the world, Type 2 diabetes represents over 90% of diabetes cases [2,3].

The prevalence of diabetes is rapidly increasing in South Africa. In 2009, approximately 2 million (9%) people aged 30 years and older had diabetes [4], increasing almost two-fold since 2000 when Bradshaw et al. reported a prevalence of 5.5% [5]. Several factors such as the aging population, economic transition, and urbanization associated with nutrition transition and obesity have contributed to the increased diabetes prevalence [6–9]. In 2000 it was estimated that 90% of diabetes cases in South Africa were attributed to excess body weight [10]. This is concerning since in 2013 ~38% of men and ~69% of women in South Africa were considered overweight or obese [11]. In 2015 the global burden of disease study estimated that high body mass index and hyperglycemia, ranked as the second and third-leading risk factors, respectively, after unsafe sex, for early death and disability in South Africa [12].

Diabetes, due to its association with several micro- and macrovascular complications, places a significant burden on the South African health system. In 2009 it was estimated that diabetes caused about 8,000 new cases of blindness and 2,000 new cases of amputations annually [4]. A national burden of disease study in 2000 reported that diabetes accounted for approximately 14% of cases of ischemic heart disease (IHD), 10% of stroke, 12% of hypertensive disease and 12% of renal disease [5]. Furthermore, the indirect costs of diabetes are high. Diabetes in Africa affect mainly working-aged people between 40 and 60 years old [9] placing an added burden on the economy due to work absenteeism and decreased productivity. South Africa is battling a quadruple burden of disease due to high rates of infectious diseases, non-communicable disease, maternal and child mortality, and injury-related disorders, thus have limited resources to meet the increased health and economic costs of diabetes [13].

Rationale

Urgent action is required to halt the burgeoning diabetes epidemic in South Africa. The feasibility of population-level interventions, particularly those aimed at prevention is widely reported [14]. However, such initiatives are hampered by the lack of epidemiological data, a challenge faced by all countries in Africa [15]. Several studies have measured the prevalence of diabetes in South Africa [16–26], although they were conducted in different geographical areas (urban vs. rural), amongst different population groups, and are generally too small to individually give generalizable prevalence data. Pooling of existing data is considered an effective strategy to generate representative and robust prevalence figures [8]. Bertram et al. calculated the national prevalence of

diabetes in 2009 [4], however, their estimate included only four studies measuring the diabetes prevalence in black South Africans in two rural, one urban and one metro urban population [21–24]. The study did not account for population variation in diabetes prevalence in South Africa [16,19,20,23], and focused on estimating the disability burden of diabetes rather than characterizing the different levels of hyperglycemia in these populations. This review explores availability and quality of diabetes prevalence data for South Africa.

Objective

The purpose of this systematic review is to identify, collate and synthesize all studies reporting the prevalence of diabetes in South Africa. A secondary aim is to report the prevalence of impaired glucose tolerance and impaired fasting glucose, conditions which are associated with an increased risk of progression to overt diabetes, and the prevalence of undiagnosed diabetes. These findings will be used to inform the Second National Burden of Disease study, which can inform health and policy planning.

METHODS

Study selection

Published population-based surveys, cross-sectional studies and prospective or retrospective cohort studies that report the prevalence of diabetes in South Africa.

Inclusion criteria

Studies will be included if they were published between January 1997 and February 2018, include more than 100 participants regardless of age, gender, ethnicity, socioeconomic and educational background and study setting, and report the primary outcome using a case definition according to the 2006 World Health Organization diagnostic criteria [27], where Type 2 diabetes is diagnosed either by a physician, fasting blood glucose concentrations more than or equal to 7.0 mmol/L, two-hour oral glucose tolerance test values more than or equal to 11.1 mmol/L or self-reported use of oral diabetes drugs. In addition, glycosylated hemoglobin more than or equal to 6.5 % will also be used for case definition [28]. Due to limitations that hamper the differentiation between Type 1 diabetes and Type 2 diabetes, diabetes in individuals older than 25 years of age will be classified as Type 2 diabetes. Impaired glucose tolerance will be defined by fasting blood glucose concentrations less than 7.0 mmol/L and two-hour oral glucose tolerance values more than or equal to 7.8 mmol/L, but less than 11.1 mmol/L. Impaired fasting glucose will be defined as fasting blood glucose concentrations between 6.1 mmol/L and 6.9 mmol/L, and, if available, two-hour oral glucose tolerance values less than 7.8 mmol/L [27].

Exclusion criteria

Studies will be excluded if they were not conducted in South Africa, do not report the primary outcome, have no clear description of the case definition, and contain data for refugees in camps since they may not be representative of the South African population.

Primary Outcome

Prevalence of Type 2 diabetes.

Secondary Outcome

Prevalence of impaired glucose tolerance, impaired fasting glucose and undiagnosed Type 2 diabetes.

Search strategy

A search of articles written in English and indexed in PubMed, Scopus, Web of Science and African Index Medicus between January 1997 and February 2018 will be conducted. An experienced information scientist and disease content experts will be consulted to ensure that the search terms are relevant and optimally arranged, and will include keywords and medical subject headings (MeSH) terms. An example of the search strategy in PubMed is illustrated in Table 1. The search will be modified to each database. References will be managed in EndNote.

Table 1. PubMed search strategy.

Search	Query
#4	Search ((#3 NOT (animals[mh] NOT humans[mh]))) AND ("1997/01/01"[Date-Publication] : "2018/02/28"[Date-Publication])
#3	Search (#1 AND #2)
#2	Search (South Africa[mh]OR"South Africa*"[tiab] OR RSA[tiab] OR Africa, Southern[mh:noexp] OR Southern Africa[tiab])
#1	Search (Diabetes[Mesh] OR Diabetes mellitus[Mesh] OR Type 2 diabetes mellitus[Mesh] OR Type 2 diabetes[Mesh] OR Diabetes mellitus, type 2[Mesh] OR Diabetes, type 2[Mesh] OR hyperglycemia[Mesh] OR Blood glucose[Mesh] OR Hemoglobin A, glycosylated[Mesh] OR Glycosylated hemoglobin OR Impaired glucose tolerance OR Impaired fasting glucose OR Undiagnosed diabetes

Study selection

The titles and abstracts of articles from the electronic search outputs will be screened independently by two reviewers to identify eligible studies. Disagreements or uncertainties will be resolved by discussion and consensus between the two reviewers, or with a third reviewer if disagreement persists. Full-text copies of the eligible articles will be retrieved and reviewed by two independent reviewers for inclusion. Additional information will be requested from the study authors if required. Reasons for exclusion will be recorded.

Data extraction

After the final decision to include studies into the review, two authors will independently extract and record data using the Burden of Disease (BOD) Review Manager developed by the South African Medical Research Council [29]. The following data will be extracted:

- Study details: date of publication, study title, study design, study period and study purpose.
- Study population: province/district of study, study setting (community or health facility based), setting (urban or rural) and sample size.
- Response rate.
- Case definition as reported in the study.
- Prevalence of Type 2 diabetes, impaired glucose tolerance, impaired fasting glucose and undiagnosed Type 2 diabetes.
- Characteristics of study population: age, sex, population group (ethnicity) and comorbid disease (tuberculosis (TB) or human immunodeficiency virus (HIV) status).

After completion, data will be compared and discrepancies will be resolved through consensus between the two reviewers, or in consultation with a third reviewer.

Risk of bias assessment
Two reviewers will independently appraise the study quality and risk of bias using a checklist for observational epidemiological studies that was adapted from the risk of bias tool for population-based studies [30] and the Newcastle-Ottawa Scale for assessing the quality of non-randomized studies [31,32], and standardized in the BOD Review Manager [29]. Parameters assessed will include: external validity (whether the target population is representative of South Africa, representativeness of sample, selection criteria and non-response bias) and internal validity (case definition, validity and reliability of test instruments, consistency of case measurement, appropriateness of time period, and appropriateness of numerators and denominators in estimation). Disagreements between the reviewers over the risk of bias will be resolved by discussion with a third review reviewer where necessary.

Data synthesis
A narrative description will be conducted for studies with a low or moderate risk of bias. Clinical heterogeneity will be investigated by looking at the characteristics of participants, method of diagnosis and case definitions in the study.
Subgroup analyses for study population (province/district, community or health facility based, urban or rural) and characteristics of cases (age, sex, population group, and comorbid disease TB or HIV) will be done if sufficient data exists. If possible, a meta-regression to explore possible sources of variability in prevalence reported between studies will be conducted. Review findings will be displayed using tables and forest plots as appropriate.

Confidence in cumulative evidence
The strength of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method [33], which scores studies as very low, low, moderate, or high based on methodological flaws within the included studies, consistency of results across diverse studies, precision of estimates and publication bias.

Patient and Public Involvement
Patients and the public were not involved.

ETHICS AND DISSEMINATION

The systematic review does not require ethics clearance since published studies with non-identifiable data will be used. This review is the first to collate and synthesize all the available studies reporting the prevalence of diabetes in South Africa and will provide local epidemiological data to inform the Second National Burden of Disease study, which can guide health and policy planning. Findings from the review will be disseminated in a peer-reviewed journal article and academic reports according to the PRISMA guidelines [34].

Authors' contributions

CP, VPvW, JJ and DB conceived the idea and design of the study, and drafted the protocol.
NL and MN helped to draft the protocol.
All authors wrote and approved the final manuscript.

Acknowledgements

The authors would like to thank Eunice Turawa of the Burden of Disease unit, South African Medical Research Council for her assistance with the development of the search strategy.

Funding

This research and the publication thereof were funded by the South African Medical Research Council's (SAMRC) Flagship Awards Project SAMRC-RFA-IFSP-01-2013/SA CRA 2 and by SAMRC baseline funding.

Conflict of interest

The authors have no competing interests.

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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	Pheiffer et al. manuscript Page No.
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	1
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	9
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	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	9
Sponsor	5b	Provide name for the review funder and/or sponsor	
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)	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	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
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	6,7

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7
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	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	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5,6
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	8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	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)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	8

*** 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.