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## Prevalence and associated factors of active smoking among patients with hypertension and/or diabetes mellitus in Africa: a systematic review and meta-analysis protocol

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# Prevalence and associated factors of active smoking among patients with hypertension and/or diabetes mellitus in Africa: a systematic review and meta-analysis protocol

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## Abstract

**Introduction:** Tobacco use significantly increases cardiovascular complications in hypertension and/or diabetes. Summarizing data on the prevalence of active smoking in these conditions in Africa may therefore be useful to develop strategies for prevention of these complications.

**Method and analysis**: This systematic review and meta-analysis will be reported according to the PRISMA guidelines. We will search PubMed, Embase, Google Scholar and Online African journals for relevant abstracts of studies on active smoking in diabetes and/or hypertensive patients published from inception to December 31, 2016, with no language restriction. Additionally, relevant unpublished papers and conference proceedings will be checked, as well as references of included articles. Two investigators will independently screen, select studies, extract data and assess the risk of bias in each study. Data will be analysed using Stata software (Stata Corp V.14, Texas, USA). The study-specific estimates will be pooled through a random-effects meta-analysis model to obtain an overall summary estimate of the prevalence of smoking across studies. Also, we will assess factors associated to smoking. Heterogeneity of studies will be evaluated by the $\chi 2$ 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 associated to smoking.

**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 cost-effective interventions to reduce and prevent smoking

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in diabetes and/or hypertensive patients, 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. Results are intended to help in emphasizing on the need to control and prevent smoking among those patients, and to serve as basis for designing effective interventions for that purpose.

**Review registration number:**

**Funding:** None.

## Strengths and limitations of this study

- This review would be limited by the predominance of clinic-based studies, the poor quality data and the heterogeneity of diagnostic method of pulmonary hypertension.

- For determining risk factors associated with active smoking, cross sectional studies are not best design. The review would be therefore limited for this specific purpose since most of studies could have cross sectional design.

- This will be the first systematic review and meta-analysis summarizing the prevalence of active smoking among hypertensive and diabetes patients in Africa.

- Strong and robust statistical methods will be used for summarizing data.

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## Introduction

In 2015, cardiovascular diseases (CVD) were responsible for approximately 18 million deaths worldwide, representing the leading cause of death. That figure is increasing in both developing and developed countries as risk factors for the disease continue to increase in both contexts [1]. In sub-Saharan Africa especially, CVD caused nearly 1 million deaths in 2013, representing 38.3% of non-communicable disease-related deaths and 11.3% of all-cause mortality [2]. Intriguingly, these deaths due to CVD in SSA occur at a younger age as compared to the rest of the world [3].

Hypertension, diabetes mellitus, hypercholesterolemia and smoking are the four major modifiable traditional cardiovascular risk factors [4]. In fact, almost 80% to 95% of patients who experienced a fatal or non-fatal cardiovascular event had at least 1 of these 4 major cardiovascular risk factors [5,6]. In 2010, the two leading risk factors for global disease burden were high blood pressure (7 % of global disability-adjusted life years) and tobacco smoking (6.3% of global disability-adjusted life years) [7]. In hypertensive or diabetes patients, smoking appears to be a significant and independent risk factor for all-cause, cardiovascular, and non-cardiovascular disease morbidity and mortality [8]. Its remains the cause of 6 million preventable deaths per year globally[9].

According to the World Health Organization, tobacco use is increasing all over the world, particularly in the African region. In 2012, the global prevalence of current tobacco smoking among adults was 22% [9]. Tobacco use increases the risk of cardiovascular disease and premature death, and smoking cessation is an important part of hypertension and diabetes management [9–11]. However, the burden and magnitude of active tobacco

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smoking is not well known in Africans suffering from hypertension and diabetes, which could inform on how much efforts should be made to reduce/lessen these growing threats. We present here the protocol for a systematic review and meta-analysis to estimate the prevalence of active smoking among African hypertensive and/or diabetes patients, as well as associated factors. Results are intended to help in emphasizing on the need to control and prevent smoking among those patients, and to serve as basis for designing effective interventions accordingly. The results may also provide a robust basis for monitoring future trends.

## Objective

To conduct a systematic review and meta-analysis in order to estimate the prevalence of active smoking among hypertensive and/or diabetes patients in Africa, as well as its associated factors.

## Review question

This review of studies should answer the following question: what are the prevalence and associated factors of active smoking among African hypertensive and/or diabetes adults patients?

## Criteria for considering studies for the review

### Inclusion criteria

We will include:

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1. Cross-sectional, case–control or cohort studies of hypertensive and/diabetes patients aged more than 15 years residing in African countries reporting the prevalence of active smoking, or enough data to compute this estimate. Active smoking will be defined as current use of any tobacco product in either smoked or smokeless form[9].

2. Studies published in any language and unpublished studies (trial registries, conference proceedings, dissertations, monographs, and reports held by government agencies, academics).

**Exclusion criteria**

1. Studies on non-systemic hypertension (intracranial hypertension, pulmonary hypertension) or studies on gestational diabetes.

2. Studies conducted among populations of African origin residing outside of Africa.

3. Studies including adult and paediatric populations in which it will not be possible to extract data for adults after contacting the corresponding authors.

4. Case series with small sample size (less than 50 participants), letters, reviews, commentaries and editorials.

5. Studies lacking key data and/or explicit method description.

6. Duplicates: for studies published in more than one paper, the most comprehensive one reporting the largest sample size will be considered.

7. Studies with serious ethical issues.

8. Studies whose full data will not be accessible even after request from the authors.

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## Search strategy for identifying relevant studies

This systematic review and meta-analysis will follow the Institutes of Medicine Standards for Systematic Reviews[12]. Reporting will align to the guidelines set out by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group[13]. The search strategy will be implemented in two stages:

### Bibliographic database searches

A. Relevant abstracts published on the prevalence and associated factors of active smoking in African hypertensive and/or diabetes patients will be identified after searching PubMed, Embase, and online African journals. The search will include studies from inception to December 31, 2016. Both text words and medical subject heading (MeSH) terms will be used. Key search terms will be: Africa, adults, hypertensive, diabetes, prevalence, risk factors, determinants and smoking. We will also use individual country names for the 54 African countries and ''hypertensive + smoking'', ''diabetes + smoking'' as additional key search terms in order to obtain more abstracts on the subject. 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 relevant research articles and review papers 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 not be accessible by the numerous internet-based sources will

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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 independently conducted by two review authors; using an assessment guide to ensure that the selection criteria are reliably applied by each of these authors. The same authors will independently assess the full-texts of records deemed relevant or potentially relevant for eligibility; any disagreement between them will be resolved by a third author. Agreement between review authors will be measured using the Cohen's Kappa statistic [14].

## Data extraction and management

A data extraction sheet will be used to collect information about the country, the African sub-region, year of publication, type of publication, study design, study population, number of participants, mean/median age of participants, male proportion, prevalence of active smoking and predictive factors whenever available, the frequency of different forms of tobacco (cigarettes, chew, bidis, chew, cigars, E-cigarette, hookah, pipe, snuff, waterpipe). Where prevalence of smoking or information for calculating it (eg, sample size, number of smokers) 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 and associated 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.

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## Assessment of methodological quality and data reporting

The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses will be used to assess the quality of case-control and cohort studies [15]. A modified version of the NOS will be used for cross-sectional studies. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement checklist will be used to measure completeness of reporting methodology in each paper [16]. Risk of bias and quality scores will be presented in a table

## Data synthesis and analysis

Data will be analysed using Stata software (Stata Corp V.14, Texas, USA). A stratified meta-analysis will be conducted for data obtained from studies depending on the definition of active smoking in those studies. Standard Errors for the study-specific estimates will first be determined from the point estimate and the appropriate denominators, assuming a binominal distribution. Then the study-specific estimates will be pooled through a random-effects meta-analysis model, to obtain an overall summary estimate of the across studies, after stabilising the variance of individual studies using the Freeman-Tukey double arc-sine transformation [17]. Score method will be used to compute the study specific confidence interval [18]. A meta-regression will be performed to assess factors associated to smoking. If it is not possible to summarize data, a narrative review will be conducted for associated factors. A p value less than 0.05 will be considered significant for factors associated to smoking.

Heterogeneity will be evaluated by the $\chi2$ test on Cochrane's Q statistic [19], which is quantified by $I^2$ values [20], assuming that $I^2$ values of 25%, 50% and 75%, represent

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low, medium and high heterogeneity respectively. 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, geographical area (central, eastern, northern, southern and western Africa), study quality, baseline disease (diabetes vs hypertension), and definition of smoking. Subgroups comparisons then used the Q-test based on the Analysis of the Variance. Inter-rater agreement for study inclusion will be assessed using Cohen's κ coefficient [21]. Funnel plots analysis and Egger's test will be done to detect publication bias. A p-Egger test < 0.1 will be consider indicative of statistically significant publication bias [22]. Results will be presented by geographical region (central, eastern, northern, southern and western Africa).

## Results reporting and presentation

The study selection process will be summarised using a flow diagram. Reasons for studies' exclusion will be described. This review will follow the guidelines set out by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group [13]. 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 of active smoking and associated factors by region, 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.

## Ethics and dissemination

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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 cost-effective interventions to reduce and prevent smoking in diabetes and/or hypertensive patients, 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. Additionally, findings will 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.

## Conclusions

Smoking is a major risk factor for cardiovascular diseases which are actually rising in Africa. In hypertensive and/or diabetes patients, active smoking independently and significantly increase the risk for complications. It is therefore necessary to introduce cost-effective interventions in order to reduce smoking in those populations, remembering that it has been projected an increase in tobacco smoking burden in Africa. Prior to these strategies, accurate epidemiological data should be obtained. We anticipate that this review will guide policy, practice and research by providing information on the magnitude of smoking among hypertensive and/or diabetes patients and associated factors.

There are some possible limitations to this review, among which the poor quality of data when available, the heterogeneity of studies which will make further analysis difficult, the predominance of cross-sectional studies, making it difficult to determine smoking associated factors. Other draw-backs could include the non-random selection of

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participants and the under-representation of African sub-regions. These problems have already been highlighted by previous studies on non-communicable diseases in Africa [23,24].

## Author's Contributions

JJNN, GSW, ATT and FTEA conceived and designed the protocol. GSW drafted the manuscript. ATT, JJRB, JRNN, FTEA, ADK and JJNN critically revised the manuscript for methodological and intellectual content. JJNN is the guarantor of the review. All authors approved the final version of this manuscript.

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## Competing interests

None

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**Table 1**: Search strategy in PubMed

| Search | Search terms |
|--------|--------------|
| 1 | Smoking [tw] OR tobacco  [tw] OR snuff [tw] OR cigarette [tw] OR Cigar [tw] OR pipe [tw] OR chewing [tw] OR Smoking [MeSH terms] OR nicotine [tw] OR tabacum [tw] OR nicotiana [tw] OR waterpipe [tw] OR e-cig [tw] OR e-cigarette [tw] |
| 2 | (Hypertension [tw] OR Hypertension [MeSH terms] OR high blood pressure [tw] OR systolic hypertension [tw] OR diastolic hypertension [tw] OR Hypertensive patients OR Raised blood pressure [tw]) |
| 3 | (Diabetes mellitus [tw] OR diabetes mellitus [MeSH terms] OR high blood sugar [tw] OR hyperglycemia [tw] OR diabetes patients OR Glucose intolerance [tw]) |
| 4 | (# 1 AND # 3) OR (# 2 AND # 3) |

| | |
|---|---|
| 5 | (((((("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]))))) |
| 6 | # 4 AND # 5 |

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**Prevalence and associated factors of active smoking among patients with hypertension and/or diabetes mellitus in Africa: a systematic review and meta-analysis protocol**

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 check list:

| Section and topic | Item No | Checklist item | |
|---|---|---|---|
| ADMINISTRATIVE INFORMATION | | | |
| Title:<br>   Identification | 1a | Prevalence and associated factors of active smoking among patients with hypertension and/or diabetes mellitus in Africa: a systematic review and meta-analysis protocol | |
|    Update | 1b | This is not an update of a previous review | |
| Registration | 2 | In accordance with the guidelines, our systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 01 December 2016 (registration number  52 560) | |
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| Contributions | 3b | JJNN, GSW, ATT and FTEA conceived and designed the protocol. GSW drafted the manuscript. ATT, JJRB, JRNN, FTEA, ADK and JJNN critically revised the manuscript for methodological and intellectual content. JJNN is the guarantor of the review. All authors approved the final version of this manuscript. |
| Amendments | 4 | This protocol is not an amendment of a previously completed or published protocol. |
| Support Sources | 5a | This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors |
| Sponsor | 5b | This review has no funder and/or sponsor |
| Role of sponsor | 5c | None |

| INTRODUCTION | | |
|---|---|---|
| Rationale | 6 | Cardiovascular diseases are the major cause of mortality worldwide, and the mortality rate linked to those diseases is increasing in both developing and developed countries as risk factors for the disease continue to increase in both contexts. Among these factors, the four major modifiable are hypertension, diabetes mellitus, hypercholesterolemia and smoking. Smoking is increasing all over the world, particularly in the African region and remains the cause of 6 million preventable deaths per year globally. In hypertensive or diabetes patients, it appears to be a significant and independent risk factor for all-cause cardiovascular, and non-cardiovascular disease morbidity and mortality. However, the burden and magnitude of active tobacco smoking is not well known in Africans suffering from hypertension and/or diabetes. |
| Objectives | 7 | This review of studies should answer the following question: what are the prevalence and associated factors of active smoking among African hypertensive and/or diabetes adults patients? |
| METHODS | | |
| Eligibility criteria | 8 | We will include: 1. Cross-sectional, case–control or cohort studies of hypertensive and/diabetes patients aged more than 15 years residing in African countries reporting the prevalence of active smoking, or enough data to compute this estimate. 2. Studies published in any language and unpublished studies (trial registries, conference proceedings, dissertations, monographs, and reports held by government agencies, academics). 3. Study from inception to December 31, 2016. |
| Information sources | 9 | Relevant abstracts published on the prevalence and associated factors of active smoking in African hypertensive and/or diabetes patients will be identified after searching PubMed, Embase, and online African journals. The search will include studies from inception to December 31, 2016. 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 relevant research articles and review papers 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 not be accessible by the numerous internet-based sources will be directly contacted to provide them. |
| Search strategy | 10 | Only quantitative studies will be sought. No language limits |

| | | |
|---|---|---|
| | | will be imposed on the search, but it will be limited to research done in African countries. Medline, Embase and online African journals will be searched. The Medline strategy will be developed with input from the project team, and a draft Medline search strategy is include in Appendix 1. After Medline strategy is finalized, it will be adapted to the syntax and subject headings of the other databases. |
| Study records: Data management | 11a | Literature search will be perform by a member of the research team with expertise in systematic review searching, and results will be transfer in an EndNote file to two members of the team. They will develop and test screening questions, and assess studies based on the inclusion and exclusion criteria. Prior to the formal screening process, a calibration exercise will be undertaken to pilot and refine the screening questions. |
| Selection process | 11b | Assessment of eligible papers will be independently conducted by two review authors; using an assessment guide to ensure that the selection criteria are reliably applied by each of these authors. The same authors will independently assess the full-texts of records deemed relevant or potentially relevant for eligibility; any disagreement between them will be resolved by a third author. |
| Data collection process | 11c | Data extraction will be carried out by one reviewer with verification by another in order to reduce bias and reduce errors in data extraction. Discrepancies will be solve through discussion with a third author. A data extraction sheet will be used to collect information about the country, the African sub-region, year of publication, type of publication, study design, study population, number of participants, mean/median age of participants, male proportion, prevalence of active smoking and predictive factors whenever available, the frequency of different forms of tobacco (cigarettes, chew, bidis, chew, cigars, E-cigarette, hookah, pipe, snuff, waterpipe). Where prevalence of smoking or information for calculating it (eg, sample size, number of smokers) 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 and associated 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. |
| Data items | 12 | We will extract information about the country, the African sub-region, year of publication, type of publication, study design, study population, number of participants, mean/median age of participants, male proportion, prevalence of active smoking and predictive factors whenever available, the frequency of different forms of tobacco (cigarettes, chew, bidis, chew, cigars, E-cigarette, hookah, pipe, snuff, waterpipe). Where prevalence of smoking or information for calculating it (eg, sample size, number of smokers) are lacking, we will directly contact the corresponding author to request the information. |
| Outcome and prioritization | 13 | As this is a descriptive review, there is no outcome. |
| Risk of bias in individual studies | 14 | The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses will be used to assess the quality of case-control and cohort studies. A modified version of the NOS will be used for cross-sectional studies. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement checklist will be used to measure completeness of reporting methodology in each paper. Risk of bias and quality scores will be presented in a table. This bias assessment will be undertaken by two separate reviewers. Where there is disagreement, a third reviewer will be used as an arbitrator. |
| Data synthesis | 15a | We will conduct meta-analyses using a random-effects model. |
| | 15b | A stratified meta-analysis will be conducted for data obtained from studies depending on the definition of active smoking in those studies. Standard Errors for the study-specific estimates will first be determined from the point estimate and the appropriate denominators, assuming a binominal distribution. Then the study-specific estimates will be pooled through a random-effects meta-analysis model, to obtain an overall summary estimate of the across studies, after stabilising the variance of individual studies using the Freeman-Tukey double arc-sine transformation. Score method will be used to compute the study specific confidence interval. If it is not possible to summarize data, a narrative review will be conducted for associated factors. Heterogeneity will be evaluated by the $\chi 2$ test on Cochrane's Q statistic, which is quantified by $I^2$ values, assuming that $I^2$ values of 25%, 50% and 75%, represent |

| | | |
|---|---|---|
| | | low, medium and high heterogeneity respectively. |
| | 15c | 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, geographical area (central, eastern, northern, southern and western Africa), study quality, baseline disease (diabetes vs hypertension), and definition of smoking. Subgroups comparisons then used the Q-test based on the Analysis of the Variance. A meta-regression will be performed to assess factors associated to smoking. |
| | 15d | If it is not possible to summarize data, a narrative review will be conducted for associated factors. |
| Meta-bias | 16 | Funnel plots analysis and Egger's test will be done to detect publication bias. A p-Egger test < 0.1 will be consider indicative of statistically significant publication bias. |
| Confidence in cumulative evidence | 17 | No strength of evidence assessment will be done. |

Appendix 1: Search strategy in Medline

| Search | Search terms |
|---|---|
| 1 | Smoking [tw] OR tobacco [tw] OR snuff [tw] OR cigarette [tw] OR Cigar [tw] OR pipe [tw] OR chewing [tw] OR Smoking [MeSH terms] OR nicotine [tw] OR tabacum [tw] OR nicotiana [tw] OR waterpipe [tw] OR e-cig [tw] OR e-cigarette [tw] |
| 2 | (Hypertension [tw] OR Hypertension [MeSH terms] OR high blood pressure [tw] OR systolic hypertension [tw] OR diastolic hypertension [tw] OR Hypertensive patients OR Raised blood pressure [tw]) |
| 3 | (Diabetes mellitus [tw] OR diabetes mellitus [MeSH terms] OR high blood sugar [tw] OR hyperglycemia [tw] OR diabetes patients OR Glucose intolerance [tw]) |
| 4 | (# 1 AND # 3) OR (# 2 AND # 3) |
| 5 | ((((("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]))))) |
| 6 | # 4 AND # 5 |

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# Prevalence and associated factors of active smoking among people with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol

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# Prevalence and associated factors of active smoking among people with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol

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## Abstract

**Introduction:** Tobacco use significantly increases cardiovascular complications in people with hypertension and/or diabetes. We aim to summarize data on the prevalence and factors associated with active smoking in these conditions in Africa.

**Method and analysis**: We will search PubMed, Embase, Google Scholar and African Journals Online for relevant abstracts of studies on active smoking in patients with diabetes and/or hypertension published from January 1st 2000 to December 31st, 2016, with no language restriction. Additionally, relevant unpublished papers and conference proceedings will be checked, as well as references of included articles. Two investigators will independently screen, select studies, extract data and assess the risk of bias in each study. Data will be analysed using Stata software (Stata Corp V.14, Texas, USA). The study-specific estimates will be pooled through a random-effects meta-analysis model to obtain an overall summary estimate of the prevalence of smoking across studies. Also, we will assess factors associated to smoking. Heterogeneity of studies will be evaluated by the $\chi 2$ 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 associated to smoking.

**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 cost-effective interventions to reduce and prevent smoking in patients with diabetes and/or hypertension, 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

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published in peer-reviewed journals. Findings will further be presented at conferences

and submitted to relevant health authorities.

**Review registration number:** CRD42016052560

## Strengths and limitations of this study

- This will be the first systematic review and meta-analysis summarizing the prevalence of active smoking among patients with hypertension and/or diabetes in Africa.

- Strong and robust statistical methods will be used for summarizing data.

- This review would be limited by the predominance of clinic-based studies and the poor quality data.

- For determining risk factors associated with active smoking, cross sectional studies are not best design. The review would be therefore limited for this specific purpose since most of studies could have cross sectional design.

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## Introduction

In 2015, cardiovascular diseases (CVDs) were responsible for approximately 18 million deaths worldwide, representing the leading cause of death[1]. That figure is increasing in both developing and developed countries as risk factors for the disease continue to increase in both contexts [1]. In Sub-Saharan Africa (SSA) especially, CVDs caused nearly 1 million deaths in 2013, representing 38.3% of non-communicable disease-related deaths and 11.3% of all-cause mortality [2]. Intriguingly, these deaths due to CVDs in SSA occur at a younger age as compared to the rest of the world [3].

Hypertension, diabetes mellitus, hypercholesterolemia and smoking are the four major modifiable traditional cardiovascular risk factors [4]. In fact,  80% to 95% of patients who experienced a fatal or non-fatal cardiovascular event had at least 1 of these 4 major cardiovascular risk factors [5,6].  In 2010, the two leading risk factors for global disease burden were high blood pressure (7 % of global disability-adjusted life years) and tobacco smoking (6.3% of global disability-adjusted life years) [7]. In patients with hypertension or diabetes, smoking appears to be a significant and independent risk factor for all-cause, cardiovascular, and non-cardiovascular disease morbidity and mortality [8]. It remains the cause of 6 million preventable deaths per year globally[9].

World Health Assembly endorsed a voluntary global target of a 30% relative reduction in tobacco use worldwide among people aged 15 years or older by 2025 (with 2010 levels as baseline) [9]. From 2000-2010, prevalence of tobacco smoking fell in more than 70% of countries, mostly in those with high-incomes. In 2012, the global prevalence of current tobacco smoking among adults was 22% [9]. Furthermore, rapid increase is projected by 2025 in African and eastern Mediterranean low-income and middle-income countries[10].  Tobacco use increases the risk of cardiovascular disease and premature

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death, and smoking cessation is an important part of hypertension and diabetes management [9,11,12]. However, the burden and magnitude of active tobacco smoking is not well known in Africans suffering from hypertension and diabetes, which could inform on how much efforts should be made to reduce/lessen these growing threats. We present here the protocol for a systematic review and meta-analysis to estimate the prevalence of active smoking among African patients with hypertension and/or diabetes, as well as associated factors. Results are intended to help in emphasizing on the need to control and prevent smoking among those patients, and to serve as basis for designing effective interventions accordingly. The results may also provide a robust basis for monitoring future trends.

## Objective

To conduct a systematic review and meta-analysis in order to estimate the prevalence of active smoking among patients with hypertension and/or diabetes in Africa, as well as its associated factors.

## Criteria for considering studies for the review

### Inclusion criteria

1. Population: persons with hypertension and/or diabetes aged more than 15 years residing in Africa continent. Hypertension will be considered in the presence of systolic blood pressure $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg or any antihypertensive treatment [13]. Diabetes will be considered using the following diagnostic criteria: A1c hemoglobin $\geq$ 6.5% or fasting plasma glucose $\geq$ 126 mg/dl (7.0

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mmol/l) or 2-hours Plasma Glucose $\geq$ 200 mg/dl (11.1 mmol/l) or random plasma glucose $\geq$ 200 mg/dl (11.1 mmol/l) in presence of classic symptoms of hyperglycemia [14]. All types of diabetes will be considered.

2. Type of studies: cross-sectional, case-control or cohort studies.

3. Outcome: active smoking which will be defined as current use of any tobacco product in either smoked or smokeless form [9].

4. Type of data: prevalence of active smoking or enough data to compute this estimate and factors associated with active smoking.

5. Studies published in any language and unpublished studies (trial registries, conference proceedings, dissertations, monographs, and reports held by government agencies, academics).

**Exclusion criteria**

1. Studies on non-systemic hypertension (intracranial hypertension, pulmonary hypertension) or studies on gestational diabetes.

2. Studies conducted among populations of African origin residing outside of Africa.

3. Studies including adult and paediatric populations in which it will not be possible to extract data for adults after contacting the corresponding authors.

4. Case series with small sample size (less than 50 participants), letters, reviews, commentaries and editorials.

5. Studies lacking key data and/or explicit method description.

6. Duplicates: for studies published in more than one paper, the most comprehensive one reporting the largest sample size will be considered.

7. Studies with serious ethical issues.

8. 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 Institutes of Medicine Standards for Systematic Reviews[15]. Reporting will align to the guidelines set out by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group[16]. The search strategy will be implemented in two stages:

**Bibliographic database searches**

A. Relevant abstracts published on the prevalence and associated factors of active smoking in African patients with hypertension and/or diabetes will be identified after searching PubMed/Medline, Excerpta Medica Database (EMBASE), and African Journals Online. The search will include studies from January 1st, 2000 to December 31st, 2016. Both text words and medical subject heading terms will be used. Key search terms will be ''Africa'', ''hypertension'', ''diabetes'', and ''smoking''. We will also use individual country names for the 54 African countries as additional key search terms in order to obtain more abstracts on the subject. The main search strategy is shown in Table 1. An expert Liberian will conduct searches in different databases.

B. The titles and 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 relevant research articles and review papers 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 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.

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**Selection of studies for inclusion in the review**

Assessment of eligible papers will be independently conducted by two review authors; using an assessment guide to ensure that the selection criteria are reliably applied by each of these authors. The same authors will independently assess the full-texts of records deemed relevant or potentially relevant for eligibility; any disagreement between them will be resolved by a third author. Records resulting from search strategy will be transferred to EndNote X7 for selection of studies based on title and abstract and removing of duplicates. Eligible studies in other languages will be translated using Google Translate and considered for inclusion. Agreement between review authors will be measured using the Cohen's Kappa statistic [17].

**Data extraction and management**

A data extraction sheet will be used to collect information about the country, the African sub-region, year of publication, type of publication, study design, study population, number of participants, mean/median age of participants, male proportion, prevalence of active smoking and predictive factors whenever available, the frequency of different forms of tobacco (cigarettes, chew, bidis, chew, cigars, E-cigarette, hookah, pipe, snuff, waterpipe). Where prevalence of smoking or information for calculating it (eg, sample size, number of smokers) 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 and associated factors within individual countries. Where it will not

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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.

## Assessment of methodological quality and data reporting

The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses will be used to assess the quality of case-control and cohort studies [18]. A modified version of the NOS will be used for cross-sectional studies. Risk of bias and quality scores will be presented in a table.

## Data synthesis and analysis

Data will be analysed using Stata software (Stata Corp V.14, Texas, USA). A stratified meta-analysis will be conducted for data obtained from studies depending on the definition of active smoking in those studies. Standard Errors for the study-specific estimates will first be determined from the point estimate and the appropriate denominators, assuming a binominal distribution. Then the study-specific estimates will be pooled through a random-effects meta-analysis model, to obtain an overall summary estimate of the across studies, after stabilising the variance of individual studies using the Freeman-Tukey double arc-sine transformation [19]. Score method will be used to compute the study specific confidence interval [20]. A meta-regression will be performed to assess factors associated to smoking. If it is not possible to summarize data, a narrative review will be conducted for associated factors. A p value less than 0.05 will be considered significant for factors associated to smoking.

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Heterogeneity will be evaluated by the $\chi 2$ test on Cochrane's Q statistic [21], which is quantified by $I^2$ values [22], assuming that $I^2$ values of 25%, 50% and 75%, represent low, medium and high heterogeneity respectively. 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, geographical area (central, eastern, northern, southern and western Africa), study quality, baseline disease (diabetes vs hypertension), and definition of smoking. Subgroups comparisons then used the Q-test based on the Analysis of the Variance. Inter-rater agreement for study inclusion will be assessed using Cohen's $\kappa$ coefficient [23]. Funnel plots analysis and Egger's test will be done to detect publication bias. A p-Egger test < 0.1 will be consider indicative of statistically significant publication bias [24]. Results will be presented by geographical region (central, eastern, northern, southern and western Africa).

## Results reporting and presentation

The study selection process will be summarised using a flow diagram. Reasons for studies' exclusion will be described. This review will follow the guidelines set out by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group [16]. 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 of active smoking and associated factors by region, 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.

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## 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 cost-effective interventions to reduce and prevent smoking in patients with hypertension and/or diabetes, 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. Additionally, findings will 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.

## Conclusions

Smoking is a major risk factor for cardiovascular diseases which are actually rising in Africa. In patients with hypertension and/or diabetes, active smoking independently and significantly increase the risk for complications. It is therefore necessary to introduce cost-effective interventions in order to reduce smoking in those populations, remembering that it has been projected an increase in tobacco smoking burden in Africa. Prior to these strategies, accurate epidemiological data should be obtained. We anticipate that this review would guide policy, practice and research by providing information on the magnitude of smoking among patients with hypertension and/or diabetes and associated factors.

There are some possible limitations to this review, among which the poor quality of data when available, the heterogeneity of studies which will make further analysis difficult,

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the predominance of cross-sectional studies, making it difficult to determine smoking associated factors. Other draw-backs could include the non-random selection of participants and the under-representation of African sub-regions. These problems have already been highlighted by previous studies on non-communicable diseases in Africa [25,26].

## Author's Contributions

JJNN, GSW, ATT and FTEA conceived and designed the protocol. GSW drafted the manuscript. ATT, JJRB, JRNN, FTEA, ADK and JJNN critically revised the manuscript for methodological and intellectual content. JJNN is the guarantor of the review. All authors approved the final version of this manuscript.

## Funding

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## Competing interests

None

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**Table 1**: Search strategy in PubMed

| Search | Search terms |
|--------|--------------|
| 1 | Smoking [tw] OR tobacco  [tw] OR snuff [tw] OR cigarette [tw] OR Cigar |

| | |
|---|---|
| | [tw] OR pipe [tw] OR chewing [tw] OR Smoking [MeSH terms] OR nicotine [tw] OR tabacum [tw] OR nicotiana [tw] OR waterpipe [tw] OR e-cig [tw] OR e-cigarette [tw] |
| 2 | (Hypertension [tw] OR Hypertension [MeSH terms] OR high blood pressure [tw] OR systolic hypertension [tw] OR diastolic hypertension [tw] OR Hypertensive patients OR Raised blood pressure [tw]) |
| 3 | (Diabetes mellitus [tw] OR diabetes mellitus [MeSH terms] OR high blood sugar [tw] OR hyperglycemia [tw] OR diabetes patients OR Glucose intolerance [tw]) |
| 4 | (# 1 AND # 3) OR (# 2 AND # 3) |
| 5 | (((((("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]))))) |
| 6 | # 4 AND # 5 |

# Prevalence and associated factors of active smoking among people with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 check list:

| Section and topic | Item No | Checklist item | |
|---|---|---|---|
| ADMINISTRATIVE INFORMATION | | | |
| Title: | | | |
|    Identification | 1a | Prevalence and associated factors of active smoking among people with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol | |
|    Update | 1b | This is not an update of a previous review | |
| Registration | 2 | In accordance with the guidelines, our systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 01 December 2016 (registration number: CRD42016052560) | |
| Authors: | | | |
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|---|---|---|---|
| Contributions | 3b | JJNN, GSW, ATT and FTEA conceived and designed the protocol. GSW drafted the manuscript. ATT, JJRB, JRNN, FTEA, ADK and JJNN critically revised the manuscript for methodological and intellectual content. JJNN is the guarantor of the review. All authors approved the final version of this manuscript. | |
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| Sponsor | 5b | This review has no funder and/or sponsor | |
| Role of sponsor | 5c | None | |

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| Data collection process | 11c | Page 9 |
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| Outcome and prioritization | 13 | As this is a descriptive review, there is no outcome |
| Risk of bias in individual studies | 14 | Page 10 |
| Data synthesis | 15a | We will conduct meta-analyses using a random-effects model |
| | 15b | Page 10 and 11 |
| | 15c | Page 10 and 11 |
| | 15d | If it is not possible to summarize data, a narrative review will be conducted for associated factors. |
| Meta-bias | 16 | Funnel plots analysis and Egger's test will be done to detect publication bias. A p-Egger test < 0.1 will be consider indicative of statistically significant publication bias |
| Confidence in cumulative evidence | 17 | No strength of evidence assessment will be done |

Appendix 1: Search strategy in Medline

| Search | Search terms |
|--------|--------------|
| 1 | Smoking [tw] OR tobacco [tw] OR snuff [tw] OR cigarette [tw] OR Cigar [tw] OR pipe [tw] OR chewing [tw] OR Smoking [MeSH terms] OR nicotine [tw] OR tabacum [tw] OR nicotiana [tw] OR waterpipe [tw] OR e-cig [tw] OR e-cigarette [tw] |
| 2 | (Hypertension [tw] OR Hypertension [MeSH terms] OR high blood pressure [tw] OR systolic hypertension [tw] OR diastolic hypertension [tw] OR Hypertensive patients OR Raised blood pressure [tw]) |
| 3 | (Diabetes mellitus [tw] OR diabetes mellitus [MeSH terms] OR high blood sugar [tw] OR hyperglycemia [tw] OR diabetes patients OR Glucose intolerance [tw]) |
| 4 | (# 1 AND # 3) OR (# 2 AND # 3) |
| 5 | (((((("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]))))) |
| 6 | # 4 AND # 5 |

# BMJ Open

# Prevalence and associated factors of active smoking among individuals living with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol

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| <b>Primary Subject Heading</b>: | Cardiovascular medicine |
| Secondary Subject Heading: | Smoking and tobacco, Diabetes and endocrinology |
| Keywords: | Hypertension < CARDIOLOGY, General diabetes < DIABETES & ENDOCRINOLOGY, Active smoking, Africa |

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Manuscripts

**Prevalence and associated factors of active smoking among individuals living with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol**

**Review registration number:** CRD42016052560

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**Author's Contributions**

JJNN, GSW, ATT and FTEA conceived and designed the protocol. GSW drafted the manuscript. ATT, JJRB, JRNN, FTEA, ADK and JJNN critically revised the manuscript for methodological and intellectual content. JJNN is the guarantor of the review. All authors approved the final version of this manuscript.

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## Abstract

**Introduction:** Tobacco use significantly increases cardiovascular complications in people living with hypertension and/or diabetes. We aim to summarize data on the prevalence and factors associated with active smoking in these conditions in Africa.

**Method and analysis**: We will search PubMed, Embase, Google Scholar and African Journals Online for relevant abstracts of studies on active smoking in individuals living with diabetes and/or hypertension published from January 1$^{st}$ 2000 to December 31$^{st}$, 2016, with no language restriction. Additionally, relevant unpublished papers and conference proceedings will be checked, as well as references of included articles. Two investigators will independently screen, select studies, extract data and assess the risk of bias in each study. Data will be analysed using Stata software (Stata Corp V.14, Texas, USA). The study-specific estimates will be pooled through a random-effects meta-analysis model to obtain an overall summary estimate of the prevalence of smoking across studies. Also, we will assess factors associated to smoking. Heterogeneity of studies will be evaluated by the $\chi 2$ 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 associated to smoking.

**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 cost-effective interventions to reduce and prevent smoking in patients with diabetes and/or hypertension, 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.

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## Strengths and limitations of this study

- This will be the first systematic review and meta-analysis summarizing the prevalence of active smoking among individuals living with hypertension and/or diabetes in Africa.

- Strong and robust statistical methods will be used for summarizing data.

- This review would be limited by the predominance of clinic-based studies and the poor quality data.

- For determining risk factors associated with active smoking, cross sectional studies are not best design. The review would be therefore limited for this specific purpose since most of studies could have cross sectional design.

## Introduction

### Rationale

In 2015, cardiovascular diseases (CVDs) were responsible for approximately 18 million deaths worldwide, representing the leading cause of death[1]. That figure is increasing in both developing and developed countries as risk factors for the disease continue to increase in both contexts [1]. In Sub-Saharan Africa (SSA) especially, CVDs caused nearly 1 million deaths in 2013, representing 38.3% of non-communicable disease-related deaths and 11.3% of all-cause mortality [2]. Intriguingly, these deaths due to CVDs in SSA occur at a younger age as compared to the rest of the world [3].

Hypertension, diabetes mellitus, hypercholesterolemia and smoking are the four major modifiable traditional cardiovascular risk factors [4]. In fact, 80% to 95% of patients who experienced a fatal or non-fatal cardiovascular event had at least 1 of these 4 major cardiovascular risk factors [5,6]. In 2010, the two leading risk factors for global disease burden were high blood pressure (7 % of global disability-adjusted life years) and tobacco smoking (6.3% of global disability-adjusted life years) [7]. In patients with hypertension or diabetes, smoking appears to be a significant and independent risk factor for all-cause, cardiovascular, and non-cardiovascular disease morbidity and mortality [8]. It remains the cause of 6 million preventable deaths per year globally[9].

World Health Assembly endorsed a voluntary global target of a 30% relative reduction in tobacco use worldwide among people aged 15 years or older by 2025 (with 2010 levels as baseline) [9]. From 2000-2010, prevalence of tobacco smoking fell in more than 70% of countries, mostly in those with high-incomes. In 2012, the global prevalence of current tobacco smoking among adults was 22% [9]. Furthermore, rapid increase is projected by 2025 in African and eastern Mediterranean low-income and middle-income

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countries[10]. Tobacco use increases the risk of cardiovascular disease and premature death, and smoking cessation is an important part of hypertension and diabetes management [9,11,12]. However, the burden and magnitude of active tobacco smoking is not well known in Africans suffering from hypertension and diabetes, which could inform on how much efforts should be made to reduce/lessen these growing threats. We present here the protocol for a systematic review and meta-analysis to estimate the prevalence of active smoking among African patients with hypertension and/or diabetes, as well as associated factors. Results are intended to help in emphasizing on the need to control and prevent smoking among those patients, and to serve as basis for designing effective interventions accordingly. The results may also provide a robust basis for monitoring future trends.

**Objective**

To conduct a systematic review and meta-analysis in order to estimate the prevalence of active smoking among individuals living with hypertension and/or diabetes in Africa, as well as its associated factors.

**Methods**

**Eligibility criteria**

Inclusion criteria

1. Population: persons living with hypertension and/or diabetes aged more than 15 years residing in Africa continent. Hypertension will be considered in the presence of systolic blood pressure $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg or any antihypertensive treatment [13]. Diabetes will be considered using the following

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diagnostic criteria: A1c hemoglobin ≥ 6.5% or fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/l) or 2-hours Plasma Glucose ≥ 200 mg/dl (11.1 mmol/l) or random plasma glucose ≥ 200 mg/dl (11.1 mmol/l) in presence of classic symptoms of hyperglycemia [14]. All types of diabetes will be considered.

2. Type of studies: cross-sectional, case-control or cohort studies.

3. Outcome: active smoking which will be defined as current use of any tobacco product in either smoked or smokeless form [9].

4. Type of data: prevalence of active smoking or enough data to compute this estimate and factors associated with active smoking.

5. Studies published in any language and unpublished studies (trial registries, conference proceedings, dissertations, monographs, and reports held by government agencies, academics).

Exclusion criteria

1. Studies on non-systemic hypertension (intracranial hypertension, pulmonary hypertension) or studies on gestational diabetes.

2. Studies conducted among populations of African origin residing outside of Africa.

3. Studies including adult and paediatric populations in which it will not be possible to extract data for adults after contacting the corresponding authors.

4. Case series with small sample size (less than 50 participants), letters, reviews, commentaries and editorials.

5. Studies lacking key data and/or explicit method description.

6. Duplicates: for studies published in more than one paper, the most comprehensive one reporting the largest sample size will be considered.

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7. Studies with serious ethical issues.

8. Studies whose full data will not be accessible even after request from the authors.

**Information sources and search strategy**

This systematic review and meta-analysis will follow the Institutes of Medicine Standards for Systematic Reviews[15]. Reporting will align to the guidelines set out by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group[16]. The search strategy will be implemented in two stages:

A. Relevant abstracts published on the prevalence and associated factors of active smoking in African individuals living with hypertension and/or diabetes will be identified after searching PubMed/Medline, Excerpta Medica Database (EMBASE), and African Journals Online. The search will include studies from January 1st, 2000 to December 31st, 2016. Both text words and medical subject heading terms will be used. Key search terms will be ''Africa'', ''hypertension'', ''diabetes'', and ''smoking''. We will also use individual country names for the 54 African countries as additional key search terms in order to obtain more abstracts on the subject. The main search strategy is shown in Table 1. An expert Liberian will conduct searches in different databases.

B. The titles and 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 relevant research articles and review papers 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 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.

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**Selection process**

Assessment of eligible papers will be independently conducted by two review authors; using an assessment guide to ensure that the selection criteria are reliably applied by each of these authors. The same authors will independently assess the full-texts of records deemed relevant or potentially relevant for eligibility; any disagreement between them will be resolved by a third author. Records resulting from search strategy will be transferred to EndNote X7 for selection of studies based on title and abstract and removing of duplicates. Eligible studies in other languages will be translated using Google Translate and considered for inclusion. Agreement between review authors will be measured using the Cohen's Kappa statistic [17].

**Data collection process and data items**

A data extraction sheet will be used to collect information about the country, the African sub-region, year of publication, type of publication, study design, study population, number of participants, mean/median age of participants, male proportion, prevalence of active smoking and predictive factors whenever available, the frequency of different forms of tobacco (cigarettes, chew, bidis, chew, cigars, E-cigarette, hookah, pipe, snuff, waterpipe). Where prevalence of smoking or information for calculating it (eg, sample size, number of smokers) 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 and associated factors within individual countries. Where it will not

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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.

**Assessment of methodological quality and data reporting**

The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses will be used to assess the quality of case-control and cohort studies [18]. A modified version of the NOS will be used for cross-sectional studies. Risk of bias and quality scores will be presented in a table.

**Data synthesis and analysis**

Data will be analysed using Stata software (Stata Corp V.14, Texas, USA). A stratified meta-analysis will be conducted for data obtained from studies depending on the definition of active smoking in those studies. Standard Errors for the study-specific estimates will first be determined from the point estimate and the appropriate denominators, assuming a binominal distribution. Then the study-specific estimates will be pooled through a random-effects meta-analysis model, to obtain an overall summary estimate of the across studies, after stabilising the variance of individual studies using the Freeman-Tukey double arc-sine transformation [19]. Score method will be used to compute the study specific confidence interval [20]. A meta-regression will be performed to assess factors associated to smoking. If it is not possible to summarize data, a narrative review will be conducted for associated factors. A p value less than 0.05 will be considered significant for factors associated to smoking.

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Heterogeneity will be evaluated by the χ2 test on Cochrane's Q statistic [21], which is quantified by $I^2$ values [22], assuming that $I^2$ values of 25%, 50% and 75%, represent low, medium and high heterogeneity respectively. 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, geographical area (central, eastern, northern, southern and western Africa), study quality, baseline disease (diabetes vs hypertension), and definition of smoking. Subgroups comparisons then used the Q-test based on the Analysis of the Variance. Inter-rater agreement for study inclusion will be assessed using Cohen's κ coefficient [23]. Funnel plots analysis and Egger's test will be done to detect publication bias. A p-Egger test < 0.1 will be consider indicative of statistically significant publication bias [24]. Results will be presented by geographical region (central, eastern, northern, southern and western Africa).

## Results reporting and presentation

The study selection process will be summarised using a flow diagram. Reasons for studies' exclusion will be described. This review will follow the guidelines set out by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group [16]. 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 of active smoking and associated factors by region, 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.

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## 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 cost-effective interventions to reduce and prevent smoking in patients with hypertension and/or diabetes, 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. Additionally, findings will 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.

## Conclusions

Smoking is a major risk factor for cardiovascular diseases which are actually rising in Africa. In patients with hypertension and/or diabetes, active smoking independently and significantly increase the risk for complications. It is therefore necessary to introduce cost-effective interventions in order to reduce smoking in those populations, remembering that it has been projected an increase in tobacco smoking burden in Africa. Prior to these strategies, accurate epidemiological data should be obtained. We anticipate that this review would guide policy, practice and research by providing information on the magnitude of smoking among patients with hypertension and/or diabetes and associated factors.

There are some possible limitations to this review, among which the poor quality of data when available, the heterogeneity of studies which will make further analysis difficult,

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the predominance of cross-sectional studies, making it difficult to determine smoking associated factors. Other draw-backs could include the non-random selection of participants and the under-representation of African sub-regions. These problems have already been highlighted by previous studies on non-communicable diseases in Africa [25,26].

## Funding

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## Competing interests

None

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**Table 1**: Search strategy in PubMed

| Search | Search terms |
|---|---|
| 1 | Smoking [tw] OR tobacco [tw] OR snuff [tw] OR cigarette [tw] OR Cigar [tw] OR pipe [tw] OR chewing [tw] OR Smoking [MeSH terms] OR nicotine [tw] OR tabacum [tw] OR nicotiana [tw] OR waterpipe [tw] OR e-cig [tw] OR e-cigarette [tw] |
| 2 | (Hypertension [tw] OR Hypertension [MeSH terms] OR high blood pressure [tw] OR systolic hypertension [tw] OR diastolic hypertension [tw] OR Hypertensive patients OR Raised blood pressure [tw]) |

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| 3 | (Diabetes mellitus [tw] OR diabetes mellitus [MeSH terms] OR high blood sugar [tw] OR hyperglycemia [tw] OR diabetes patients OR Glucose intolerance [tw]) |
|---|---|
| 4 | (# 1 AND # 3) OR (# 2 AND # 3) |
| 5 | ((((("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] |

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|---|---|
| | 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]))))) |
| 6 | # 4 AND # 5 |

# Prevalence and associated factors of active smoking among people with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 check list:

| Section and topic | Item No | Checklist item | |
|---|---|---|---|
| ADMINISTRATIVE INFORMATION | | | |
| Title:<br>　Identification | 1a | Prevalence and associated factors of active smoking among people with hypertension and/or diabetes in Africa: a systematic review and meta-analysis protocol | |
| 　Update | 1b | This is not an update of a previous review | |
| Registration | 2 | In accordance with the guidelines, our systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 01 December 2016 (registration number:  CRD42016052560) | |
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|---|---|---|
| Contributions | 3b | JJNN, GSW, ATT and FTEA conceived and designed the protocol. GSW drafted the manuscript. ATT, JJRB, JRNN, FTEA, ADK and JJNN critically revised the manuscript for methodological and intellectual content. JJNN is the guarantor of the review. All authors approved the final version of this manuscript. |
| Amendments | 4 | This protocol is an amendment of a previously completed or published protocol. |
| Support Sources | 5a | This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors |
| Sponsor | 5b | This review has no funder and/or sponsor |
| Role of sponsor | 5c | None |

| INTRODUCTION | | |
|---|---|---|
| Rationale | 6 | Page 5 and 6 |
| Objectives | 7 | Page 6 |
| METHODS | | |
| Eligibility criteria | 8 | Page 6 and 7 |
| Information sources | 9 | Page 8 |
| Search strategy | 10 | Page 8 |
| Study records:<br>  Data management | 11a | Page 9 |
| Selection process | 11b | Page 9 |
| Data collection process | 11c | Page 9 |
| Data items | 12 | Page 9 |
| Outcome and prioritization | 13 | As this is a descriptive review, there is no outcome |
| Risk of bias in individual studies | 14 | Page 10 |
| Data synthesis | 15a | We will conduct meta-analyses using a random-effects model |
| | 15b | Page 10 and 11 |
| | 15c | Page 10 and 11 |
| | 15d | If it is not possible to summarize data, a narrative review will be conducted for associated factors. |
| Meta-bias | 16 | Funnel plots analysis and Egger's test will be done to detect publication bias. A p-Egger test < 0.1 will be consider indicative of statistically significant publication bias |
| Confidence in cumulative evidence | 17 | No strength of evidence assessment will be done |

Appendix 1: Search strategy in Medline

| Search | Search terms |
|--------|-------------|
| 1 | Smoking [tw] OR tobacco  [tw] OR snuff [tw] OR cigarette [tw] OR Cigar [tw] OR pipe [tw] OR chewing [tw] OR Smoking [MeSH terms] OR nicotine [tw] OR tabacum [tw] OR nicotiana [tw] OR waterpipe [tw] OR e-cig [tw] OR e-cigarette [tw] |
| 2 | (Hypertension [tw] OR Hypertension [MeSH terms] OR high blood pressure [tw] OR systolic hypertension [tw] OR diastolic hypertension [tw] OR Hypertensive patients OR Raised blood pressure [tw]) |
| 3 | (Diabetes mellitus [tw] OR diabetes mellitus [MeSH terms] OR high blood sugar [tw] OR hyperglycemia [tw] OR diabetes patients OR Glucose intolerance [tw]) |
| 4 | (# 1 AND # 3) OR (# 2 AND # 3) |
| 5 | (((((("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])))))

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| 6 | # 4 AND # 5 |