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Protocol for updated systematic review and meta-analysis on the burden of non-communicable diseases among people living with HIV in sub-Saharan Africa

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ABSTRACT

Introduction Sub-Saharan Africa (SSA) is faced with the dual epidemics of HIV/AIDS and non-communicable diseases (NCDs). Cardiovascular diseases, cancers, chronic respiratory diseases, diabetes and mental illnesses are the five major NCDs, causing death globally with low-income and middle-income countries, contributing 78% of all NCD deaths and 85% of premature deaths. There has been increased interest in the integration of HIV and NCDs care, especially in SSA that accounts for 55% of people living with HIV (PLHIV) globally. This systematic review and meta-analysis will estimate the overall prevalence or incidence of NCDs (or its risk factors) among adults living with HIV in SSA.

Methods and analysis The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines will be used. Two authors will independently screen the title and abstracts of the articles identified from the search. Study participants will be any adult (≥18 years old) living with HIV in SSA. Exposure of interest will be HIV (with or without ART). Outcomes of interest are prevalence or incidence of any NCD/NCD risk factors. A random-effects meta-analysis will be used to estimate pooled prevalence or incidence of the five major NCDs among PLHIV, using Stata software. χ^2 test and I^2 statistic will be used to measure statistical heterogeneity between studies. If there is significant heterogeneity, subgroup analysis will be used to investigate potential sources. Publication bias will be assessed using funnel plots and the Stata 'metabias' command.

Ethics and dissemination Ethical review will not be required because it is a systematic review. Data will be kept in the institutional data repository. Study findings will be disseminated through peer-reviewed publications and conference presentations.

PROSPERO registration number CRD42021258769.

Strengths and limitations of this study

⇒ The study aims to report the current burden of the five major non-communicable diseases (NCDs) and their respective risk factors among people living with HIV in sub-Saharan Africa.
⇒ Peer-reviewed studies published since 2010 will be reviewed.
⇒ PubMed/Medline, EBSCOhost and Scopus databases will be used to search for indexed publications.
⇒ Increased heterogeneity for some of the NCDs/risk factors may not allow for meta-analyses.

INTRODUCTION

Sub-Saharan Africa (SSA) is faced with the syndemic of HIV and non-communicable diseases (NCDs) that have been widely reported to be on the increase globally.[1–4] In 2016, NCDs accounted for 41 million deaths annually (71% of all deaths globally),[3] with over 85% of premature deaths (between the ages of 30 and 69 years) from NCDs, occurring in low-income and middle-income countries (LMICs).[3 5]

Cardiovascular diseases (CVDs), cancers, chronic respiratory diseases (CRDs) and diabetes are historically the four main groups of diseases that account for over 80% of all NCD-related deaths.[3 6 7] However, the WHO has recently classified mental illnesses as one of the main NCDs.[8] Moreover, in 2016, suicide was responsible for 800 000 deaths globally.[8] The NCDs are on the increase in LMICs that are also burdened with infectious diseases,[9–11] including COVID-19 pandemic, which is a current challenge. Furthermore, WHO has reported disruptions in NCD services due to the COVID-19 pandemic globally, including in 41 African countries. The main reasons for the disruption to the NCD services are the decrease in inpatient volume due to cancellation of elective services, closure of population-level screening, government or public transport lockdowns hindering access to the health facilities for patients, NCD-related clinical staff deployed to provide COVID-19 relief, closure of outpatient disease-specific consultation clinics, insufficient personal protective equipment available for healthcare providers to provide services, insufficient staff to provide services, closure of outpatient NCD services as per

government directive, decrease in outpatient volume due to patients not presenting and inpatient services/hospital beds not available and stock out of essential medicines, medical diagnostics or other health products at health facilities.[12] This disruption in NCD services has highlighted the need for poor resourced settings such as SSA to strengthen their health systems, also as a means of improving preparedness for future epidemics. Moreover, patients with pre-existing comorbidities were at a higher risk of severe disease due to the coronavirus, and hence a need to ensure that patients with NCD are well managed also as part of strengthening the health systems.

The increase in NCDs has been attributed to physical inactivity, unhealthy diets, harmful use of alcohol and tobacco in LMICs, just as in the developed countries.[3] Lifestyle changes in SSA due to the growth of urbanisation that entails more sedentary life style as urban work is often less physical, exposure to unhealthy diets that are high in salt, fat and sugar and pollution, among other factors have contributed to the NCD burden.[13] Among people living with HIV (PLHIV), there have been reports that HIV itself or antiretroviral therapy (ART) side effects predispose individuals further to NCDs.[14] In addition, the general increase in lifespan implies increased risk to age-related NCDs.

Modifiable behavioural risk factors for NCDs include, tobacco use (including secondhand smoke), physical inactivity, unhealthy diet and the harmful use of alcohol which consequently lead to raised blood pressure, overweight/obesity, hyperglycaemia and hyperlipidaemia.[7] Environmental air pollution has also been identified as a key risk factor for NCDs in general.[8]

Daily tobacco smoking has been associated with several morbidities, including CVDs and lung cancer.[15] Air pollution is also a major risk factor for NCD comparable to current tobacco use and is responsible for millions of deaths from ischaemic heart disease, chronic lung diseases and cancers.[8] Physical inactivity is also associated with CVD, type 2 diabetes, hypertension, obesity and high low density lipoprotein cholesterol and certain cancers such as colon and breast cancer.[16] Unhealthy diet is associated with obesity, increased risk of hypertension, diabetes, CVDs, cancers and CRDs. The harmful use of alcohol is also associated with CVDs, cancers and liver diseases.[2 7]

The NCDs are a challenge to economic development.[7 8 17] Globally, 37% of the deaths occur in people aged 30–69 years old, which is the working age group. As a result, employers face high staff turnover due to prolonged absenteeism and eventually deaths. Additionally, household costs associated with healthcare, increase in families that are already faced with financial difficulties in LMICs due to the chronic nature of the disease.[7 17] Indeed, NCDs tend to foster poverty as usually it is breadwinners whose lives are lost, thus leaving families in financial difficulties, especially in LMICs. According to WHO, NCDs threaten progress towards the 2030 Agenda for Sustainable Development that includes a target of reducing premature deaths from NCDs by one-third by 2030.[6 7] For example, in South Africa, NCDs remain the major cause of death in the young working population and was previously reported to have a loss of US$1.88 billion from its gross domestic product due to management of NCDs between 2006 and 2015.[17]

Among PLHIV, NCDs have equally been documented to be on the increase.[1 2 18 19] It has previously been reported that PLHIV are at risk of having NCDs from HIV infection itself, from ART and from the risk associated with increasing age. Individuals on ART are now able to live longer and therefore have an increased risk of chronic comorbidities, including CVD, diabetes, cancers, lipodystrophy and metabolic abnormalities.[2 18 20] SSA accounts for 55% of the 38 million PLHIV[21] globally. Therefore, it is imperative that NCDs among PLHIV are investigated and that public health systems in SSA implement integrated NCD/HIV care for PLHIV, allowing for comprehensive healthcare provision. Patel *et al*,[2] a systematic review, included articles published between 2010 and 2016 on the burden of NCDs among PLHIV in LMICs. However, it has not been updated and there have been several publications between 2017 and 2021. This systematic review will update the evidence from 2010 to the present date and report on changes in trends of NCD burden in the HIV population. The updated systematic review will include CRDs that were excluded in the previous systematic review.[2] The systematic review and meta-analysis will be conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of 2020.[22]

AIM

The aim of the systematic review and meta-analysis is to determine the burden of NCDs and NCD risk factors among PLHIV in SSA.

Objectives

1. To determine the prevalence or incidence of any NCD (five main NCDs) among PLHIV in SSA.
2. To determine the prevalence or incidence of risk factors of any NCD among PLHIV in SSA.
3. To determine if there is an association between being on ART and NCDs and/or NCD risk factors among PLHIV in SSA.

METHODS

Eligibility criteria

Any study published between 2010 to the current date, that focuses on the burden of any of the five major NCDs and their respective risk factors among PLHIV in SSA will be eligible. Two authors will independently screen the title and abstracts of the articles identified from the search. Study participants will be any adult (≥18 years old) living with HIV in SSA. The main exposure of interest will be HIV. Outcomes of interest are prevalence or incidence of any NCD or NCD risk factors in HIV populations. Study designs that will be reviewed are observational studies

(cross sectional and cohort), HIV and NCD reports, systematic reviews, Demographic and Health Surveys and other similar studies.

Information sources

The electronic databases that will be searched for eligible peer reviewed articles are PubMed/MEDLINE, Scopus and EBSCOhost online databases. A PubMed/MEDLINE search strategy will be developed and adapted for all other databases. Boolean operators, Medical Subject Heading terms and key words will be used as part of the search strategy. Where necessary, study authors will be contacted for verification of published data.

Grey literature will also be searched for relevant studies. A hand search for key HIV/AIDS and NCD journals will be conducted.

Bibliographies of the included studies will be checked as a measure to identify further eligible studies. Included studies will be corroborated with those included in the previously published systematic reviews.

All studies investigating NCDs and their associated risk factors among PLHIV since 2010 will be included. HIV studies that do not include any of the five main NCDs will be excluded. Clinical trials and systematic reviews will be included for bibliographic searches but will be excluded for the meta-analysis. Studies within the scope of this study that were published before 1 January 2010 will be excluded. The date of the last search will be documented.

Outcomes

Primary outcomes

- The prevalence or incidence of any NCD (five main NCDs) among PLHIV in SSA.
- The prevalence or incidence of NCD risk factors for any NCD among PLHIV in SSA.

Secondary outcomes

- ORs or risk ratios for association of exposure to ART and NCDs and NCDs risk factors among PLHIV in SSA.

  The keywords to be used in the search are HIV/AIDS, NCDs, CVD, hypertension, hyperlipidaemia, dyslipidaemia, diabetes, cancer, cervical cancer, mental illnesses, depression, CRDs and asthma.

Search strategy

A modified search strategy of Patel *et al*[2] will be used. Below is PubMed/Medline search strategy for 'cardiovascular disease' as indicated by Patel *et al*. A similar strategy will be employed for the other four NCDs and risk factors of interest.

Cardiovascular (PLWH* OR PLWHA* OR "people living with HIV" OR "people living with HIV/AIDS" OR "people living with" OR "people living with aids" OR "people living with hiv" OR "people living with hiv/aids" OR "people living with hiv/aids plwha" OR "people living with hiv/aids plwhas" OR "people living with hiv aids" OR "people living with hiv aids plwha" OR "people living with hiv aids plwhas" OR "people living with hiv and aids" OR "people living with hiv infection" OR "people living with hivs" OR "people living with human immunodeficiency virus" OR "people living with human immunodeficiency virus/acquired immunodeficiency syndrome" OR "people living with human immunodeficiency virus acquired immunodeficiency syndrome" OR "people living with hiv" OR "HIV Infections"[mesh] OR "HIV infection" OR "HIV infections" OR PLWHIV OR "HIV positive" OR "HIV-positive" OR "HIV+" OR "HIV infected" OR "HIV-infected" OR "HIV seropositivity"[mesh] OR "HIV seropositivity") AND OR Cote d'Ivoire[mesh] OR Ethiopia[mesh] OR Kenya[mesh] OR Malawi[mesh] OR South Africa[mesh] OR Uganda[mesh] OR Zambia[mesh] OR Ivory Coast[tiab] OR Cote d'Ivoire[tiab] OR Ethiopia[tiab] OR Kenya[tiab] OR Malawi[tiab] OR South Africa[tiab] OR Uganda[tiab] OR Zambia[tiab] OR "sub Saharan Africa" OR "sub-saharan Africa" OR Africa[tiab] OR Africa[mesh] OR "sub saharan Africa" OR "developing country" OR "developing countries" OR Cameroon[tiab] OR Central African Republic[tiab] OR Chad[tiab] OR Congo[tiab] OR Equatorial Guinea[tiab] OR Gabon[tiab] OR Democratic Republic of the Congo[tiab] OR Burundi[tiab] OR Djibouti[tiab] OR Ethiopia[tiab] OR Kenya[tiab] OR Rwanda[tiab] OR Somalia[tiab] OR Sudan[tiab] OR Tanzania[tiab] OR Uganda[tiab] OR Angola[tiab] OR Botswana[tiab] OR Lesotho[tiab] OR Malawi[tiab] OR Mozambique[tiab] OR Namibia[tiab] OR South Africa[tiab] OR Swaziland[tiab] OR Zambia[tiab] OR Zimbabwe[tiab] OR Benin[tiab] OR Burkina Faso[tiab] OR Cote D'ivoire OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR Liberia OR Mali OR Mauritania OR Niger[tiab] OR Nigeria[tiab] OR Senegal[tiab] OR Sierra Leone[tiab] OR Togo[tiab] OR Cameroon[mesh] OR Central African Republic[mesh] OR Chad[mesh] OR Congo[mesh] OR Equatorial Guinea[mesh] OR Gabon[mesh] OR Democratic Republic of the Congo[mesh] OR Burundi[mesh] OR Djibouti[mesh] OR Ethiopia[mesh] OR Kenya[mesh] OR Rwanda[mesh] OR Somalia[mesh] OR Sudan[mesh] OR Tanzania[mesh] OR Uganda[mesh] OR Angola[mesh] OR Botswana[mesh] OR Lesotho[mesh] OR Malawi[mesh] OR Mozambique[mesh] OR Namibia[mesh] OR South Africa[mesh] OR Swaziland[mesh] OR Zambia[mesh] OR Zimbabwe[mesh] OR Benin[mesh] OR Burkina Faso[mesh] OR Cote D'ivoire[mesh] OR Gambia[mesh] OR Ghana[mesh] OR Guinea[mesh] OR Guinea-Bissau[mesh] OR Liberia[mesh] OR Mali[mesh] OR Mauritania[mesh] OR Niger[mesh] OR Nigeria[mesh] OR Senegal[mesh] OR Sierra Leone[mesh] OR Togo[mesh] OR "Africa, Central"[Mesh] OR "Africa, Eastern"[Mesh] OR "Africa, Southern"[Mesh] OR "Africa, Western"[Mesh]) AND (Cardiovascular Diseases[mesh] OR Heart Diseases[mesh] OR hypertension[mesh] OR stroke[mesh] OR cardiovascular OR "heart disease" OR hypertension OR "high blood pressure" OR stroke OR "heart attack" OR "Coronary Disease"[Mesh] OR "Cerebrovascular Disorders"[Mesh] OR "Pulmonary Embolism"[Mesh] OR "Peripheral

Arterial Disease"[Mesh] OR "Peripheral Vascular Diseases"[Mesh] OR "Rheumatic Heart Disease"[Mesh] OR "Venous Thrombosis"[Mesh] OR "coronary disease" OR "pulmonary embolism" OR "cerebrovascular disorder" OR "cerebrovascular disease" OR "peripheral arterial disease" OR "rheumatic heart disease" OR "deep vein thrombosis" OR "ischemic heart disease" OR "heart failure" OR "coronary heart disease" OR "cardiovascular disease" OR "Inflammation"[Mesh] OR inflammation OR inflame* OR "Atherosclerosis"[Mesh] OR atherosclerosis OR "Metabolic Syndrome X"[Mesh] OR "metabolic cardiovascular syndrome" OR "metabolic syndrome" OR "metabolic syndrome X" OR "insulin resistance syndrome X" OR "metabolic X syndrome" OR "cardiovascular biomarker" OR "inflammation biomarker" OR "endothelial function" OR "Interleukin-6"[Mesh] OR IL-6 OR "C-Reactive Protein"[Mesh] OR "C Reactive Protein" OR "C-Reactive Protein" OR "Carotid Intima-Media Thickness"[Mesh] OR "carotid intima media thickness" OR "carotid intima-media thickness" OR "Cholesterol"[Mesh] OR cholesterol OR "Angiography"[Mesh] OR angiography OR "HydroxymethylglutarylCoA Reductase Inhibitors"[Mesh] OR "Hydroxymethylglutaryl CoA Reductase Inhibitors" OR "HMG-CoA Statins" OR "HMG-CoA Reductase Inhibitors" OR "Fluorodeoxyglucose F18"[Mesh] OR 18F-FDG OR "18F FDG" OR "Fluorodeoxyglucose F 18" OR "2-Fluoro-2-deoxy-D-glucose" OR "Venous Thromboembolism"[Mesh] OR "venous thromboembolism" OR cardiometabolic OR "Myocardial Infarction"[Mesh] OR "myocardial infarction" OR "myocardial infarct" OR "Vascular Diseases"[Mesh] OR "vascular disease" OR "Coronary Artery Disease"[Mesh] OR "coronary artery disease" OR "Myocarditis"[Mesh] OR myocarditis OR "Cardiomyopathies"[Mesh] OR cardiomyopathy OR cardiomyopathies OR "cardiac disease" OR "cardiac arrhythmias" OR "Arrhythmias, Cardiac"[Mesh] OR arrhythmia* OR "myocardial disease" OR "myocardial diseases" OR myocardiopathy OR myocardiopathies OR carditis OR "dyslipidemias"[MeSH] OR dyslipidemia OR hyperlipidemia OR hypercholesterolemia OR hypertriglyceridemia OR triglyceride OR triglycerides OR HDL OR LDL OR VLDL OR "Lipoproteins, HDL"[Mesh] OR "Lipoproteins, LDL"[Mesh] OR "Lipoproteins, VLDL"[Mesh] OR hyperlipoproteinemia OR lipoprotein(a) OR hyperlipidaemia OR hypercholesterolaemia OR hypertriglyceridaemia OR "Blood Pressure"[MeSH] OR "blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure" OR SBP[tiab] OR DBP[tiab])

Study selection

Two independent review authors will screen the potentially relevant titles and abstracts according to the pre specified eligibility criteria. Selected articles from the respective databases will be transferred to EndNote V.20 (https://endnote.com/). These articles will then be transferred to Rayyan software (https://www.rayyan.ai/) for screening of titles and abstracts. Full-text articles will be retrieved after screening the titles and abstracts. Any disagreements arising from record screening will be resolved through discussion.

Data extraction

A predesigned data extraction form will be used by two review authors who will independently extract data on prevalence or incidence of any NCD (CVD, cancer, mental illness (specifically, depression), CRD and diabetes) among PLHIV, prevalence or incidence of NCD risk factors (hypertension, hyperlipidaemia, dyslipidaemia, physical inactivity, obesity, smoking and pollution) in PLHIV, study design, sample size, participants' age, recruitment methods, study country and date of study publication. The same review authors will independently assess each included study for risk of bias with respect to sequence generation, incomplete outcome data, selective reporting and other potential sources of bias.

Discrepancies will be resolved by discussion or by consulting with a third review author. Data will beexported to Stata V.16 (Stata IC/V.16.0, StataCorp) for meta-analysis.

The strength of the body of evidence will be assessed using the Grading of Recommendations, Assessment, Development and Evaluations framework.

Missing data

Study authors will be contacted concerning missing data on either outcomes or risk of bias.

Data synthesis

Meta-analysis will be performed using the 'metan' and 'metaprop' commands in Stata V.16. A random-effects meta-analysis will be used to estimate pooled prevalence or incidence of the five major NCDs among PLHIV. The pooled prevalence or incidence of hypertension, hyperlipidaemia, obesity, overweight and waist circumference in addition to the prevalence of modifiable risk factors (tobacco use, alcohol intake, diet and physical activity) will be determined. The main outcome of interest will be the prevalence of NCD and NCD risk factors among PLHIV with respective 95% CIs. Forest plots will be constructed to display meta-analysis results. χ^2 test and I^2 statistic will be used to measure statistical heterogeneity between studies. If there is significant heterogeneity, subgroup analysis will be used to investigate potential sources; this may include the type of NCD, country or gender (male/female). Publication bias will be assessed using funnel plots and the Stata 'metabias' command.

As part of the analysis, we will compare the systematic review results with Patel *et al*[2] and note any differences in the cumulative prevalence/incidence of NCDs among PLHIV post 2016.

The study is scheduled to start in December 2021 and end by June 2022.

Patient and public involvement

No patient involved.

Contributors MM: conception of the study, writing-original draft and editing; AM: conception and design of the study, writing-reviewing and editing, supervision. All authors approved the final version to be submitted.

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Competing interests None declared.

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

Patient consent for publication Not applicable.

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