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Global and Regional Burden of Diabetes Mellitus, Cardiovascular Disease, and Chronic Kidney Disease Among Adults Living with HIV: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 March 2026 and was last updated on 17 March 2026.

INTRODUCTION

Review question / Objective 1. Do the prevalence and incidence of three major NCDs— diabetes mellitus (DM), cardiovascular disease (CVD), and chronic kidney disease (CKD)—differ across global regions?
2. Are HIV status, antiretroviral therapy (ART), CD4 cell count, and body mass index (BMI) associated with the development of three major NCDs?

Rationale The burden of non-communicable diseases (NCDs) among people living with HIV (PLHIV) has increased substantially following the widespread and rapidly expanding use of antiretroviral therapy (ART). This expansion has been largely driven by the policy initiatives of the United Nations Programme on HIV/AIDS (UNAIDS), particularly the UNAIDS 90–90–90 targets, which aim to ensure that more than 90% of all people living with HIV worldwide receive antiretroviral treatment. Although the effectiveness of ART and HIV prevention programs has significantly reduced the number of new HIV infections and AIDS-related deaths, the global population of people living with HIV continues to rise, reaching approximately 39.9 million individuals worldwide at present.
Over the past several decades, accumulating evidence has demonstrated a strong link between HIV infection and the development of NCDs. The increasing incidence of NCDs among PLHIV can be explained by three major factors. First, HIV infection leads to persistent immune activation and chronic inflammation, which increases the risk of metabolic complications and organ damage. Second, adverse effects associated with ART, particularly metabolic complications, may contribute to an elevated risk of NCDs, although emerging evidence suggests that such side effects have been reduced with newer generations of antiretroviral drugs. Third, traditional risk factors for NCDs—including increasing age, smoking, alcohol consumption, unhealthy diet, and physical inactivity—also contribute substantially to the development of these conditions.

Mathematical modeling studies estimating the burden of NCDs in both high-income countries and

low- and middle-income countries have identified diabetes mellitus, cardiovascular disease, and chronic kidney disease as the most common NCDs among people living with HIV. Previous meta-analyses have also reported that the burden of metabolic syndrome is relatively high among PLHIV residing in the Americas and the Asia–Pacific region. Metabolic syndrome is considered a critical determinant that increases the risk of subsequent NCDs, including diabetes mellitus, cardiovascular disease, and chronic kidney disease. Importantly, the burden of NCDs among people living with HIV varies across different regions of the world. These differences may be attributed to variations in healthcare systems, social contexts, health-related behaviors, and inequalities in access to antiretroviral therapy across regions. Therefore, epidemiological evidence on the burden of NCDs among PLHIV, both globally and across different regions, is essential for identifying the most vulnerable populations and for prioritizing region-specific prevention strategies.

The development of NCDs among people living with HIV is influenced by a complex interaction of multiple factors, including HIV infection status, HIV-related factors, antiretroviral therapy, and traditional NCD risk factors. However, inconsistent findings from previous studies have resulted in uncertainty regarding the effects of certain variables—such as HIV status, ART exposure, CD4 cell count, and body mass index (BMI)—on the development of NCDs. To better understand the overall impact of these factors on the occurrence of major NCDs, including diabetes mellitus, cardiovascular disease, and chronic kidney disease among PLHIV, it is necessary to systematically synthesize the available evidence and estimate a single valid summary effect size.

The findings from such analyses are critically important for identifying specific patient characteristics associated with an increased risk of NCDs. This information will provide valuable evidence for healthcare professionals in planning clinical management and designing effective prevention strategies, ultimately helping to reduce the risk of comorbidities among people living with HIV.

Condition being studied The condition of interest in this study is NCDs among people living with HIV/AIDS, comprising three major outcomes: DM, CVD, and CKD.

1. Diabetes mellitus (DM):

The diagnostic criteria used to identify DM in this study include those defined by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, the American Diabetes Association (ADA), the World Health Organization (WHO), the National Cholesterol Education Program (NCEP), and the International Diabetes Federation (IDF).

2. Cardiovascular disease (CVD):

CVD includes coronary artery diseases such as angina pectoris and myocardial infarction. Other cardiovascular conditions include stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, cardiac arrhythmia, congenital heart disease, valvular heart disease, carditis, aortic aneurysm, peripheral artery disease, thromboembolic disease, and venous thrombosis. CVD cases may also be identified using ICD-9 or ICD-10 diagnostic codes.

3. Chronic kidney disease (CKD):

CKD is defined as stage III or higher, indicated by two consecutive estimated glomerular filtration rate (eGFR) measurements ≤60 mL/min/1.73 m^2 obtained more than six months apart, or a single eGFR measurement ≤60 mL/min/1.73 m^2. The eGFR may be calculated from calibrated serum creatinine using established equations, including the Modification of Diet in Renal Disease (MDRD) equation, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, or the Cockcroft–Gault formula.

METHODS

Search strategy This systematic review will be conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2020 statement. The same search terms will be applied across all databases. The search strategy will be developed based on the PICO framework (Patients, Intervention, Comparator, and Outcomes). The literature search will be updated every three months during the review process.

1. Electronic search:The following electronic databases will be searched: PubMed/MEDLINE, Scopus, Embase, Web of Science, EBSCO, and the Cochrane Library.

2. Reference list search:

The reference lists of relevant articles and reviews will be screened to identify additional studies of interest.

3. Contact with authors or experts:

Authors or experts in the field will be contacted via email to obtain any relevant data, results, or additional information.

4. Search management:

All retrieved records will be managed using EndNote Reference Manager X8. Studies included and excluded at each stage of the screening

process will be documented and stored in separate files.

Participant or population This study focuses on adults with and without HIV infection aged 15 years and older, regardless of ethnic background. The age cut-off was defined in accordance with the World Health Organization (WHO) case definitions of HIV for reporting and surveillance.

Intervention HIV-infected patients receiving antiretroviral therapy.

Comparator
1. HIV-infected patients and HIV-uninfected individuals
2. HIV-infected patients receiving antiretroviral therapy and untreated (ART-naïve) HIV-infected patients.
3. HIV-infected patients with underweight, normal weight, overweight, and obese BMI categories.
4. HIV-infected patients with low and high CD4 cell counts.

Study designs to be included This systematic review and meta-analysis will include observational study designs, including cross-sectional, case–control, and cohort studies. Studies conducted in any region worldwide will be considered eligible for inclusion.

Eligibility criteria Inclusion criteria
This review will include studies reporting the prevalence or incidence of three major NCDs—DM, CVD, and CKD—as well as studies reporting odds ratios (ORs) or relative risks (RRs) associated with HIV status, ART use, CD4 cell count, and BMI in relation to these three NCDs among adults with and without HIV infection. The following criteria will apply:
1. Study design: This systematic review and meta-analysis will include observational study designs, including cross-sectional, case–control, and cohort studies.
2. Studies participants: This study includes individuals aged 15 years and older with and without HIV infection, regardless of ethnic background.
3. Study outcome definition: The diagnostic criteria for DM, CVD, and CKD.
4. Time-period: The literature search will cover studies published between January 1, 2000 and February 28, 2026. Studies conducted between 1996 and 2026 (i.e., during the era of highly active antiretroviral therapy [HAART]) will be eligible for inclusion, considering the changes in the definitions of NCDs over this period.
5. Study setting: Studies conducted in community- or population-based settings, as well as in healthcare facilities located in rural or urban areas across all countries, will be included
6. Study languages: All studies reported in English will be considered.
7. HIV status: Studies reporting outcomes among people living with HIV/AIDS receiving ART and/or those who are treatment-naïve, as well as studies involving HIV-uninfected individuals, will be included.

Exclusion criteria
The following criteria will apply:
1. Studies for which the full text is not available
2. Studies lacking data on the prevalence or incidence of the three major NCDs, or on the odds ratios (ORs) or relative risks (RRs) associated with HIV status, ART use, CD4 cell count, and BMI, and for which the necessary data cannot be obtained after consultation with the authors.
3. Duplicate publications from the same study will be excluded. For studies reporting data from the same cohort at extended follow-up time points, the publication with the longest follow-up period will be selected.

Information sources Electronic databases: The following electronic databases will be searched: PubMed/MEDLINE, Scopus, Embase, Web of Science, EBSCO, and the Cochrane Library.
Additional sources: Authors or experts in the field will be contacted via email to obtain any relevant data, results, or additional information if necessary.

Main outcome(s) 1. Diabetes mellitus: The diagnostic criteria used to identify DM in this study include those defined by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, the American Diabetes Association (ADA), the World Health Organization (WHO), the National Cholesterol Education Program (NCEP), and the International Diabetes Federation (IDF).
2. Cardiovascular diseases: CVDs includes coronary artery diseases such as angina pectoris and myocardial infarction. Other cardiovascular conditions include stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, cardiac arrhythmia, congenital heart disease, valvular heart disease, carditis, aortic aneurysm, peripheral artery disease, thromboembolic disease, and venous thrombosis. CVD cases may also be identified using ICD-9 or ICD-10 codes.
3. Chronic Kidney disease: CKD is defined as stage III or higher, indicated by two consecutive estimated glomerular filtration rate (eGFR) measurements ≤60 mL/min/1.73 m^2 obtained more

than six months apart, or a single eGFR measurement ≤60 mL/min/1.73 m². The eGFR may be calculated from calibrated serum creatinine using established equations, including the Modification of Diet in Renal Disease (MDRD) equation, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, or the Cockcroft–Gault formula.

Additional outcome(s) The pooled effect size (OR/RR) for the associations of HIV status, ART use, CD4 cell count, and BMI with the development of the three major NCDs.

Data management All retrieved records will be managed using EndNote Reference Manager X8. Studies included and excluded at each stage of the screening process will be documented and stored in separate files. The screening process will consist of three stages: title screening, abstract screening, and full-text screening. Screening checklists will be developed using Google Forms and pilot-tested to assess their applicability and reliability in identifying relevant studies. All identified records will be independently screened by two reviewers to identify studies reporting the prevalence or incidence of NCDs, as well as odds ratios (ORs) or relative risks (RRs) associated with HIV status, antiretroviral therapy (ART) use, CD4 cell count, and body mass index (BMI) for the three major NCDs among adults with and without HIV infection. In cases of disagreement, the issue will be discussed and resolved with the involvement of a third reviewer. For studies reporting the prevalence or incidence of NCDs and their associated risk factors that meet the inclusion criteria, the full texts will be reviewed to extract relevant data. Studies employing statistically robust methods, including standardized and unbiased data collection procedures and adequate sample sizes, will be included to ensure reproducibility and precision. The reasons for exclusion at each stage of the screening process will be documented. Inter-rater reliability between reviewers during the screening process will be assessed using Cohen's kappa coefficient, and any disagreements will be resolved through discussion or consultation with the study coordinator, if necessary. Data extraction and entry will be performed independently by two reviewers to ensure inter-rater reliability and minimize data entry errors. Any discrepancies will be resolved through discussion with a third reviewer.

The following data items will be extracted:

1. Publication details: Authors, article title, year of publication, journal name, and year(s) of data collection.
2. Study characteristics and setting: Study site, country, study setting, study design, sample size, and duration of follow-up.
3. Study population: Participants with HIV infection and/or HIV-uninfected participants.
4. Participant characteristics: Mean or median age, body mass index (BMI), CD4 cell count, viral load, sex distribution, HIV status, and the proportion of participants receiving antiretroviral therapy (ART) and those who are ART-naïve.
5. Study outcomes: diabetes mellitus (DM), cardiovascular disease (CVD), and chronic kidney disease (CKD).
6. Determinants of the three major outcomes: HIV status, HIV-related factors, antiretroviral therapy (ART) use, and traditional risk factors.
7. Study appraisal: Identified research gaps, study limitations, strengths, and a summary.

Quality assessment / Risk of bias analysis The Newcastle–Ottawa Scale (NOS) will be used to assess the methodological quality of observational studies according to the study design. This tool evaluates three main domains: (1) participant selection, (2) comparability, and (3) exposure/outcome assessment. For cohort and case–control studies, the NOS scores will be categorized into three quality levels based on the number of stars assigned in each domain, following the recommendations of the Agency for Healthcare Research and Quality (AHRQ) standards. Studies will be classified as high quality if they receive more than three stars for participant selection, one to two stars for comparability, and two to three stars for exposure/outcome assessment. Moderate-quality studies will receive two stars for participant selection, one to two stars for comparability, and two to three stars for exposure/outcome assessment. Low-quality studies will receive fewer than one star in each domain. For cross-sectional studies, quality assessment will be conducted using the modified Newcastle–Ottawa Scale developed by Herzog et al. This version categorizes studies into four quality levels: very good quality (9–10 points), good quality (7–8 points), satisfactory quality (5–6 points), and unsatisfactory quality (0–4 points).

Strategy of data synthesis Agreement between the two reviewers in the screening of abstracts and full-text articles will be assessed using Cohen's kappa statistic. A meta-analysis will be conducted to estimate the pooled prevalence and incidence of diabetes mellitus, cardiovascular disease, and chronic kidney disease among people living with HIV worldwide and stratified by World Health Organization (WHO) regions. Differences in pooled prevalence and incidence across regions will be

tested using the Q-test based on analysis of variance (ANOVA). In addition, the pooled effect estimates of the main study determinants—HIV infection status, ART use, CD4 cell count, and BMI—associated with the development of the three major NCDs will be calculated and reported as pooled odds ratios (ORs) and pooled relative risks (RRs). Prior to conducting the meta-analysis, the effect sizes from individual studies will be transformed into a common metric. All pooled estimates will be calculated using appropriate statistical methods and presented as forest plots. Cochran's Q test and the I^2 statistic will be used to assess heterogeneity and determine the appropriate meta-analytic model. A fixed-effects model using the inverse-variance method will be applied when the p-value from Cochran's Q test is ≥ 0.1 and $I^2 < 25\%$. Conversely, when the p-value is < 0.1 and $I^2 \geq 25\%$, a random-effects model using the restricted maximum likelihood (REML) method will be employed. To explore potential sources of between-study heterogeneity, meta-regression and subgroup analyses will be performed. Additionally, sensitivity analyses will be conducted to evaluate the robustness and stability of the results by examining the influence of individual studies and datasets. To further assess changes in pooled estimates, analyses will be repeated according to differences in definitions of NCDs, age groups of the study population, publication years, and study quality. Publication bias will be assessed using funnel plots, and bias will be suspected if the funnel plot demonstrates asymmetry or if the p-value from Egger's test is less than 0.05.

Subgroup analysis Secondary analyses will be conducted using meta-regression and subgroup analysis. Meta-regression will be performed to explore covariates that may account for heterogeneity between studies estimates of the effect of identified risk factors on three major outcomes. Potential explanatory covariates considered are age, study design, study period, duration of follow-up, study size, patient population and geographical location.

Sensitivity analysis Sensitivity analyses will be conducted to assess the robustness of the observed outcomes across different study designs and datasets. The primary analyses will be repeated using alternative statistical approaches, different methods for handling missing data, varying outcome definitions, and different levels of study quality to evaluate potential changes in the effect estimates.

Language restriction English.

Country(ies) involved Thailand.

Keywords HIV, diabetes, cardiovascular disease, chronic kidney disease, antiretroviral therapy, CD4 cell count, body mass index.

Dissemination plans The final report and completed manuscript will be submitted for publication in a peer-reviewed journal and disseminated through relevant scientific channels.

Contributions of each author

Author 1 - Deondara Trachunthong - Author 1 drafted the manuscript, study protocol, and data extraction form, and is responsible for study screening and selection, as well as data extraction and analysis.
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