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INPLASY

Cardiometabolic risk stratification in treated individuals with perinatally acquired HIV: what to measure, when to measure

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

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 12 November 2025 and was last updated on 12 November 2025.

INTRODUCTION

Review question / Objective To systematically evaluate the prevalence, pattern, and determinants of cardiometabolic complications among individuals with perinatally acquired HIV (PHIV) receiving antiretroviral therapy (ART), and to propose age-stratified screening recommendations for early detection and prevention of cardiovascular disease in this population.

Condition being studied Cardiometabolic risk in perinatally acquired HIV.
This includes metabolic and vascular comorbidities such as dyslipidemia, insulin resistance, hypertension, metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), and subclinical atherosclerosis. These conditions contribute to premature cardiovascular disease despite virologic suppression in ART-treated PHIV youth.

METHODS

Participant or population Children, adolescents, and young adults (ages 0–30) with perinatally acquired HIV infection who are receiving ART. Studies enrolling mixed populations (perinatally and behaviorally acquired HIV) were included only if PHIV-specific data could be isolated. No restrictions were placed on sex, ethnicity, or geographic region.

Intervention Exposure to antiretroviral therapy (ART) — including first-generation (e.g., protease inhibitors, thymidine analogues) and newer regimens (e.g., integrase inhibitors). Interventions also encompass clinical management or monitoring strategies targeting metabolic and cardiovascular health in PHIV individuals.

Comparator Comparators included HIV-negative controls or reference values from age-matched general populations. In studies without external

controls, comparisons were made between different ART regimens, duration of HIV infection, or age strata within the PHIV cohort.

Study designs to be included Observational studies — including cross-sectional, retrospective, and prospective cohort studies — as well as interventional trials reporting cardiometabolic outcomes in PHIV populations. Systematic reviews were screened for reference mining but not included in quantitative synthesis.

Eligibility criteria
Inclusion criteria:
Studies published in English between January 2015 and August 2025.
Participants with perinatally acquired HIV receiving ART.
Reported outcomes on at least one cardiometabolic parameter (lipid profile, glucose/insulin indices, blood pressure, NAFLD, cIMT, or cardiovascular biomarkers).

Exclusion criteria:
Case reports, abstracts, reviews without original data.
Studies limited to HIV-exposed but uninfected participants.
Non-human or adult-only (behaviorally acquired HIV) cohorts.

Information sources Electronic databases: PubMed, Embase, Web of Science, and Scopus.
Manual screening of reference lists from relevant articles was performed. The search was initially completed in March 2025 and updated in August 2025.

Main outcome(s) Prevalence of metabolic abnormalities — dyslipidemia, insulin resistance, and metabolic syndrome — in PHIV youth.

Odds of NAFLD in PHIV versus HIV-negative peers.

Additional outcome(s) Subclinical vascular changes (e.g., carotid intima-media thickness, arterial stiffness).

Inflammatory and cardiovascular biomarkers.

Associations between ART exposure, age, or duration of infection and metabolic risk.

Quality assessment / Risk of bias analysis Quality was appraised using an adapted Newcastle–Ottawa Scale (NOS) appropriate for observational designs. Domains included participant selection, comparability, and outcome assessment. No study was excluded solely for high risk of bias; instead, bias ratings were used to inform interpretation of pooled results.

Strategy of data synthesis Data were summarized narratively and quantitatively by outcome domain.

Pooled prevalence estimates and odds ratios were calculated using random-effects meta-analysis (DerSimonian–Laird method).

Heterogeneity was quantified via I^2 and Cochran's Q statistics.

Forest plots were generated for dyslipidemia, metabolic syndrome, insulin resistance, NAFLD, and cIMT.

Narrative synthesis was applied when data were heterogeneous or insufficient for pooling.

Subgroup analysis Subgroup analyses were planned by:

Age group: children vs adolescents vs young adults.

Geographic region: high-income vs low/middle-income countries.

ART class exposure: protease inhibitor vs non-PI or integrase inhibitor-based regimens.

Study setting: resource-rich vs resource-limited environments.

Sensitivity analysis
Sensitivity analyses included:

Excluding outlier studies contributing to high heterogeneity.

Comparing results using fixed-effects vs random-effects models.

Assessing influence of study quality (excluding high-risk-of-bias studies).

Testing the stability of pooled estimates after removal of single studies ("leave-one-out" analysis).

Country(ies) involved Taiwan.

Other relevant information Authorship and author affiliations have been updated to reflect the current

contributing investigators. No changes have been made to the review question, eligibility criteria, outcomes, or analysis plan.

Keywords perinatally acquired HIV; cardiometabolic risk; dyslipidemia; screening; pediatrics.

Contributions of each author

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MCH and HW conceived the review. MCH and HW performed literature screening and data extraction, interpreted the data, and drafted and revised the manuscript. HW is the guarantor. Both authors approved the final version.

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