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Prevalence of Metabolic Syndrome in People Living with HIV Receiving Integrase Strand Transfer Inhibitors: A Systematic Review and Meta-Analysis

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Abstract

Introduction: Integrase strand transfer inhibitor (INSTI)-based antiretroviral therapy (ART) has substantially improved HIV treatment outcomes and is now the cornerstone of HIV care globally. However, there have been concerns that INSTI-based regimens may contribute to weight gain and other metabolic disturbances that increase the risk of metabolic syndrome (MetS) and its associated cardiometabolic complications. We conducted a systematic review and meta-analysis to estimate the pooled prevalence of MetS among people living with HIV (PLHIV) receiving INSTI-based ART.

Methods: This systematic review and meta-analysis followed PRISMA 2020 guidelines. Studies reporting the prevalence of MetS among PLHIV receiving INSTI-based ART were identified through a systematic literature search. Pooled prevalence estimates were calculated using random-effects meta-analysis with Freeman–Tukey double-arcsine transformation. Subgroup and sensitivity analyses were conducted to investigate heterogeneity and evaluate the robustness of findings.

Results: A total of 15 studies involving 6,385 PLHIV receiving INSTI-based ART were included. The pooled prevalence of MetS was 24.6% (95% CI: 19.7%–29.8%), with substantial heterogeneity across studies. Prevalence varied significantly according to diagnostic criteria ($p = 0.041$), ranging from 15.9% using Modified ATP III criteria to 28.6% using JIS criteria. Higher prevalence estimates were observed in studies from the African Region (32.5%) and low-income countries (33.4%). Prevalence also varied across INSTI regimens, with the highest estimates reported in DTG-based studies (28.7%; 95% CI: 22.7%–35.1%). No clear differences were observed according to study design or risk-of-bias category.

Conclusion: Approximately one in four PLHIV receiving INSTI-based ART have MetS, indicating a substantial cardiometabolic burden in the contemporary HIV treatment era. Prevalence varied across geographic regions, income settings, diagnostic criteria, and INSTI regimens, with particularly high

estimates observed in African and low-income settings. These findings underscore the need to strengthen cardiometabolic prevention, screening, and management within HIV care programmes as INSTI-based ART continues to expand globally.

Key Words: Metabolic Syndrome , Integrase Strand Transfer Inhibitors , HIV, Systematic Review, Meta-analysis

1. Introduction

Human immunodeficiency virus (HIV) infection remains a major global public health concern, with millions of people living with HIV (PLHIV) requiring lifelong antiretroviral therapy (ART) to achieve sustained viral suppression and improved survival [1]. Over the past years, integrase strand transfer inhibitors (INSTIs) have become the cornerstone of first-line ART due to their high efficacy, tolerability, and strong resistance profile [2]. The widespread adoption of INSTI-based regimens, combined with earlier ART initiation and improved treatment access, has substantially increased life expectancy among PLHIV, shifting the focus of HIV care from opportunistic infections to long-term cardiometabolic comorbidities [2].

Metabolic syndrome (MetS) is a cluster of interconnected metabolic abnormalities characterized by the presence of at least three of the following conditions: abdominal obesity, elevated triglycerides, low HDL cholesterol, elevated blood pressure, and elevated fasting glucose [3, 4]. These abnormalities substantially increase the risk of cardiovascular disease and type 2 diabetes [3]. PLHIV experience a disproportionately high burden of MetS due to chronic inflammation, persistent immune activation, lifestyle factors, and ART-related metabolic effects [5]. A recent global meta-analysis reported that the prevalence of MetS

among PLHIV ranges from 16.7% to 31.3% across different populations and settings [6]. Furthermore, studies have reported a higher incidence of MetS among PLHIV receiving combination ART compared with ART-naïve individuals, suggesting an important role of treatment-related metabolic effects in the development of cardiometabolic risk [7].

Accumulating evidence suggests that INSTI-based regimens, while highly effective virologically, may be associated with weight gain and other metabolic disturbances that could contribute to the development of MetS [8–12]. Despite their efficacy and safety profiles, concerns have emerged regarding the cardiometabolic consequences of INSTI use. Some studies have reported a higher prevalence of obesity and insulin resistance associated with INSTI use, particularly with agents such as dolutegravir, while others have found minimal or no significant metabolic impact [9, 10]. As INSTI-based regimens become increasingly utilized worldwide, understanding their potential contribution to cardiometabolic risk has become an important clinical and public health priority.

Despite increasing recognition of these metabolic effects, current research presents inconsistent findings regarding both the magnitude and clinical significance of MetS among PLHIV receiving INSTIs. Reported prevalence estimates vary considerably across studies because of differences in populations, geographic settings, diagnostic criteria, ART exposure history, and treatment duration. This variability has made it difficult to establish the overall burden of metabolic syndrome among individuals receiving INSTI-based ART. Furthermore, while previous studies and reviews have examined metabolic syndrome among PLHIV more broadly, evidence specifically focused on INSTI-treated populations remains fragmented. Consequently, the burden of MetS among PLHIV receiving INSTI-based ART remains unclear. Therefore, we conducted a systematic review and meta-analysis to determine the pooled prevalence of metabolic syndrome among people living with HIV receiving INSTI-based ART.

METHODS

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines and was prospectively registered with PROSPERO (CRD420251176677) [13].

Search Strategy and Information Sources

A comprehensive literature search was performed across PubMed/MEDLINE, Embase, and Web of Science from database inception to March 26, 2026. The search strategy combined controlled vocabulary terms, including Medical Subject Headings (MeSH) in PubMed and Emtree terms in Embase, with free-text terms related to three key concepts: (i) HIV infection and antiretroviral therapy, (ii) integrase strand transfer inhibitors (dolutegravir, raltegravir, bictegravir, elvitegravir, and cabotegravir), and (iii) metabolic syndrome. No language or publication type restrictions were applied. Reference lists of included studies and relevant reviews were hand-searched for additional eligible records. Full database-specific strategies are provided in Supplementary Table S1.

Eligibility Criteria

Studies were eligible for inclusion if they: (i) included adults aged 18 years or older living with HIV and receiving INSTI-based ART regimens; (ii) reported the prevalence of metabolic syndrome using a validated diagnostic criterion, including the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), International Diabetes Federation (IDF), Joint Interim Statement (JIS), modified Adult Treatment Panel III (modified ATP III), or World Health Organization (WHO) definitions; and (iii) were observational studies (cross-sectional, cohort) or randomized controlled trials.We excluded case reports, narrative reviews, editorials, systematic reviews, letters without primary data, studies with sample size less than 30 participants and studies reporting only individual metabolic syndrome components without a composite metabolic syndrome prevalence. When studies included mixed ART populations, they were considered only if data for the INSTI-exposed group could be extracted separately.

Where multiple publications reported overlapping cohorts, the study with the largest sample size or most recent data was included.

Study Selection and Data Extraction

Three reviewers independently screened titles and abstracts for eligibility, followed by full-text assessment of potentially eligible articles. Disagreements at each stage were resolved through consensus among the three reviewers. Data extraction was performed collaboratively by the review team using a standardized, pilot-tested form, with all extracted items agreed upon through joint review of the included studies. Extracted data included first author, publication year, country, study design, clinical setting, sample size, INSTI type (dolutegravir, raltegravir, bictegravir, or mixed), metabolic syndrome diagnostic criteria, number of participants assessed, number meeting metabolic syndrome criteria, prevalence estimate, participant age (mean or median), proportion of female participants, and individual MetS component frequencies where available.

Risk of Bias Assessment

Methodological quality was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data[14]. This tool evaluates nine domains: appropriateness of the sample frame, recruitment methods, adequacy of sample size, description of study subjects and setting, sufficient coverage of the identified sample, use of valid methods for condition identification, standardized and reliable measurement, appropriateness of statistical analysis, and adequacy of response rate. The three reviewers assessed each included study together and reached consensus on every item. Each domain was scored as “yes” (1 point), “no” (0 points), “unclear” (0 points), or “not applicable.” Studies scoring 7–9 were classified as low risk of bias, 5–6 as moderate risk, and ≤4 as high risk of bias.

Statistical Analysis

All analyses were conducted in R version 4.5.1 using the meta and metafor packages. Pooled prevalence estimates with 95% confidence intervals (CIs) were calculated using using a random-effects meta-analysis of single proportions with the Freeman-Tukey double arcsine transformation as the primary analysis [15]. Study-specific 95% CIs were calculated using the Clopper-Pearson exact method, and between-study variance was estimated using the DerSimonian-Laird method.

Between-study heterogeneity was quantified using the I^2 statistic (interpreted as low [<25%], moderate [25–75%], or high [>75%]), Cochran's Q test, and the between-study variance (τ^2). Prediction intervals were calculated to estimate the range within which the true prevalence of a future comparable study would be expected to fall. Pre-specified subgroup analyses were conducted by metabolic syndrome diagnostic criteria, INSTI type, WHO region, World Bank income classification, study design, and risk-of-bias category. Univariable meta-regression analyses were performed to explore study-level sources of between-study heterogeneity where sufficient data were available.

Sensitivity analyses included: (i) re-estimation of pooled prevalence using a generalized linear mixed model (GLMM) with logit transformation [16, 17]; (ii) leave-one-out analysis to assess the influence of individual studies on the pooled estimate; (iii) exclusion of studies rated as high risk of bias; and (iv) restriction to observational studies. Influential diagnostics, including Baujat plots, were used to identify studies contributing disproportionately to between-study heterogeneity and to the pooled estimate [18]. Publication bias and small-study effects were explored using a Doi plot with the LFK index, a contour-enhanced funnel plot, Egger's regression test (with significance set at $p < 0.10$) [19, 20], and Duval and Tweedie's trim-and-fill analysis [21].

RESULTS

Study Selection

A total of 2,340 records were identified via database searching. After deduplication, we screened the titles and abstracts of 1,305 articles. Of these, 84 articles were assessed in full text, and 15 studies met the eligibility criteria and were included in the synthesis (Figure 1).

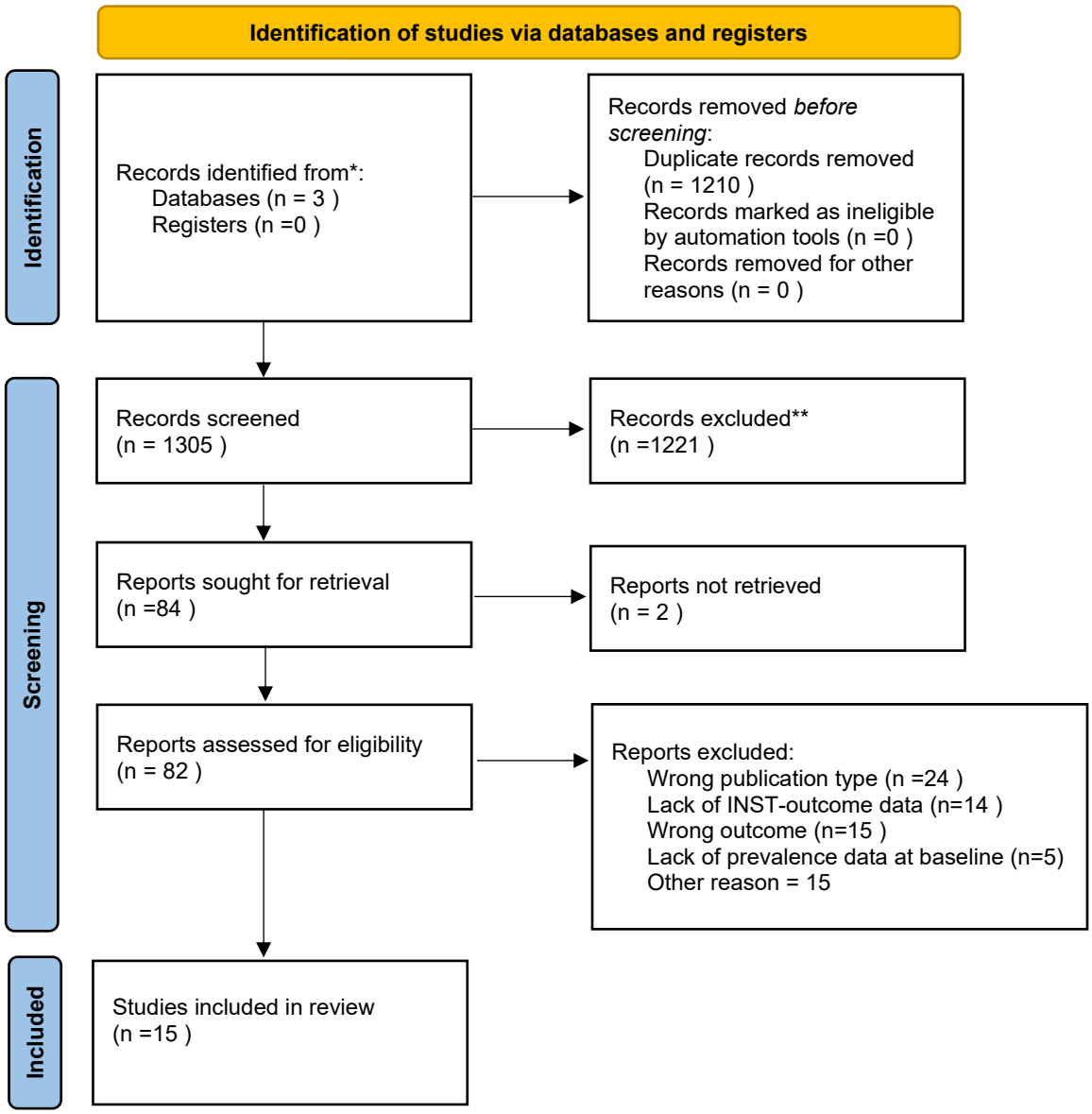


Figure 1. PRISMA 2020 flow diagram of study selection.

Characteristics of Included Studies

The included 15 studies were published between 2013 and 2026, and contributed data from 6,385 participants, including 1,541 metabolic syndrome cases. Of the included studies, 9 (60.0%) were cross-sectional, 4 (26.7%) were randomized controlled trials, and 2 (13.3%) were prospective cohort studies (Table 1; Supplementary Table S2).

Geographically, 7 studies (46.7%) were from the African region, including 3 from Ethiopia. A further 4 (26.7%) were multinational, 2 (13.3%) were from the Western Pacific region, 1 (6.7%) from Europe, and 1 (6.7%) from the Americas. By World Bank income classification, 6 studies (40.0%) were conducted in low-income countries, 5 (33.3%) in high-income settings, 2 (13.3%) in upper-middle-income countries, and 2 (13.3%) spanned multiple income settings (Supplementary Table S2).

Dolutegravir (DTG) was the predominant INSTI exposure, represented in 9 studies (60.0%); mixed INSTI regimens accounted for 4 (26.7%), while BIC and RAL were each represented in 1 study (6.7%). MetS definitions also varied, with JIS used in 6 studies (40.0%), IDF in 4 (26.7%), modified ATP III in 3 (20.0%), and NCEP ATP III in 2 (13.3%). Sample sizes ranged from 71 to 1,848 (median: 298), participant age ranged from 30 to 54 years (median: 41.1) across studies, and the proportion of female participants ranged from 2.3% to 100.0% (median: 56.2) (Table 1; Supplementary Table S2). Treatment duration was inconsistently reported across studies. Duration of INSTI exposure was available in 4 studies, with a median of 1.3 years (IQR 1.0-4.2), while overall ART duration was reported in 7 studies, with a median of 5.6 years (IQR 3.2-10.5).

Risk of Bias Assessment

The JBI critical appraisal scores ranged from 3 to 9 (Table 1). Overall, 7 studies (46.7%) were rated as low risk of bias (JBI score 7–9), 3 (20.0%) as moderate risk (score 5–6), and 5 (33.3%) as high risk (score ≤4) (Supplementary Table S2). The most common methodological limitations among high-risk studies included inadequate sample size justification, suboptimal sampling strategies (convenience sampling), and insufficient description of study subjects and settings (Supplementary Figure 1).

Table 1. Characteristics of included studies on metabolic syndrome prevalence among PLHIV on INSTI-based ART.

Author, Year	Country	Study Design	N	INSTI Type	MetS Criteria	Age	% Female	Prevalence (%)	JBI	Risk of Bias
Tu 2025[22]	Taiwan	Cross-sectional	658	Mixed	Modified ATP III	39.4 (mean)	2.3	10.0	6	Moderate
Kileel 2021[23]	Multinational	RCT	1848	Mixed	JIS	51 (median)	20.0	26.8	6	Moderate
Ang 2021[24]	Singapore	Cross-sectional	286	Mixed	Modified ATP III	41 (median)	6.1	23.8	3	High
Hirigo 2025[25]	Ethiopia	Cross-sectional	433	DTG	JIS	41.1 (mean)	58.2	36.0	8	Low
Bengtson 2024[26]	South Africa	Prospective cohort	71	DTG	JIS	30 (median)	100.0	23.9	6	Moderate
Batterham 2023[27]	Multinational	RCT	298	DTG	IDF	40 (median)	7.0	14.4	8	Low
Tan 2025[28]	Multinational	RCT	681	BIC	NCEP ATP III	37 (median)	17.6	16.6	9	Low
Bagenda 2025[29]	Uganda	Cross-sectional	377	DTG	NCEP ATP III	44 (median)	56.2	35.3	8	Low
Hamooya 2021[30]	Zambia	Cross-sectional	133	DTG	JIS	41 (median)	60.1	30.1	4	High
Borjesson 2023[31]	Italy	Prospective cohort	599	Mixed	Modified ATP III	51.2 (median)	33.0	15.2	3	High
Mirai TE 2024[32]	Tanzania	Cross-sectional	312	DTG	IDF	54 (median)	77.6	42.3	8	Low
Jemal M 2024[33]	Ethiopia	Cross-sectional	86	DTG	IDF	NR	61.6	25.6	7	Low
Ortiz 2022[34]	Guatemala	Cross-sectional	74	DTG	JIS	44 (median)	43.2	21.6	3	High
Martin 2013[35]	Multinational	RCT	107	RAL	IDF	38.9 (median)	58.3	29.0	4	High
Jemal 2026[36]	Ethiopia	Cross-sectional	422	DTG	JIS	43 (mean)	73.2	27.7	9	Low

Abbreviations: ATP III, Adult Treatment Panel III; BIC, bictegravir; DTG, dolutegravir; IDF, International Diabetes Federation; JBI, Joanna Briggs Institute (score out of 9); JIS, Joint Interim Statement; MetS, metabolic syndrome; NCEP, National Cholesterol Education Program; NR, not reported; RAL, raltegravir; RCT, randomized controlled trial.

Pooled Prevalence of Metabolic Syndrome

Overall, the pooled prevalence of metabolic syndrome among PLHIV on INSTI-based ART across 15 studies was 24.6% (95% CI: 19.7% to 29.8%; Figure 2). Between-study heterogeneity was considerable (I^2 = 95.0%; τ = 0.1097; p < 0.001). The 95% prediction interval ranged from 7.3% to 47.9%.

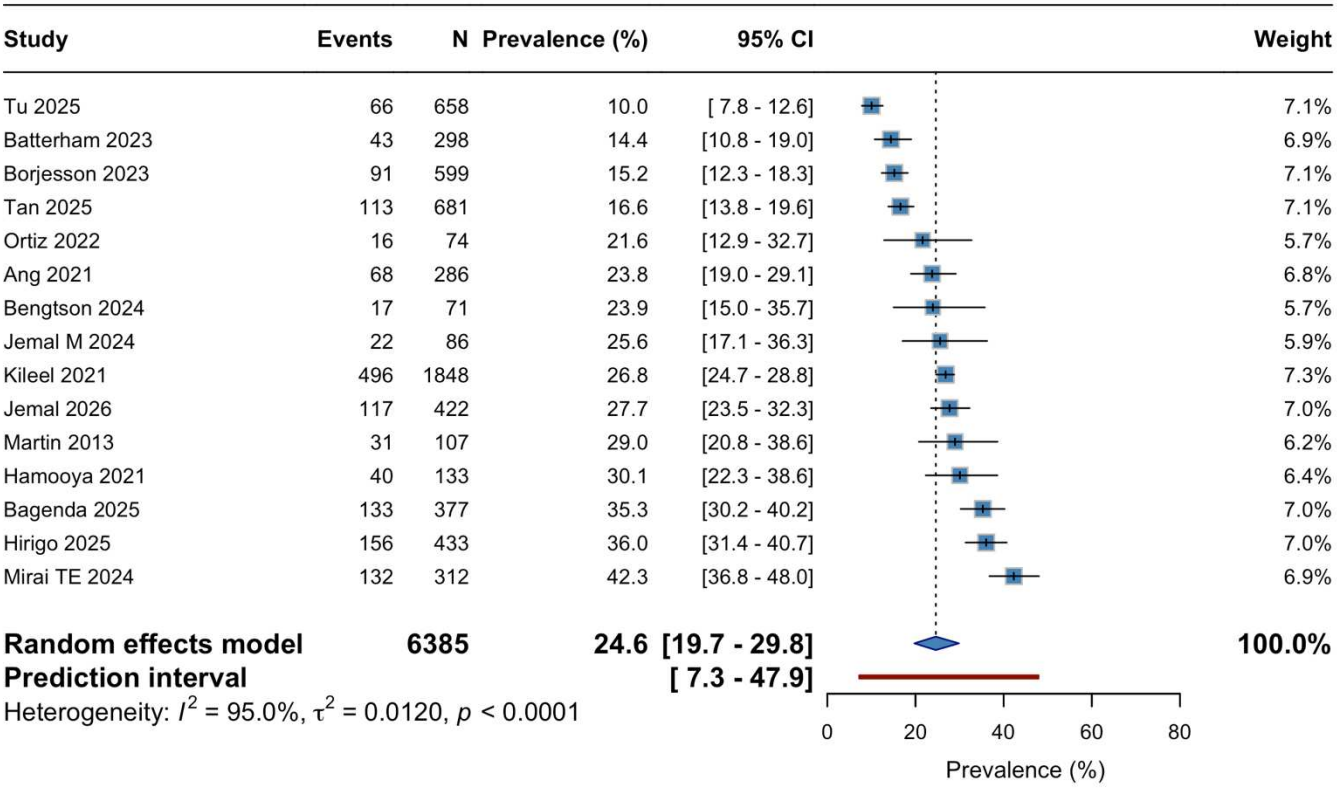


Figure 2. Forest plot of the prevalence of metabolic syndrome in people living with HIV receiving integrase strand transfer inhibitor-based antiretroviral therapy.

By metabolic syndrome diagnostic criteria: Pooled prevalence differed significantly according to the diagnostic criteria used (Figure 3; p = 0.041). Estimates ranged from 15.9% (95% CI 9.4-23.5%) in 3 studies using modified ATP III criteria to 28.6% (95% CI 24.9-32.6%) in 6 studies using JIS criteria. The corresponding pooled prevalence estimates were 27.4% (95% CI 14.2-43.1%) in 4 studies using IDF criteria and 25.3% (95% CI 9.6-45.4%) in 2 studies using NCEP ATP III criteria.

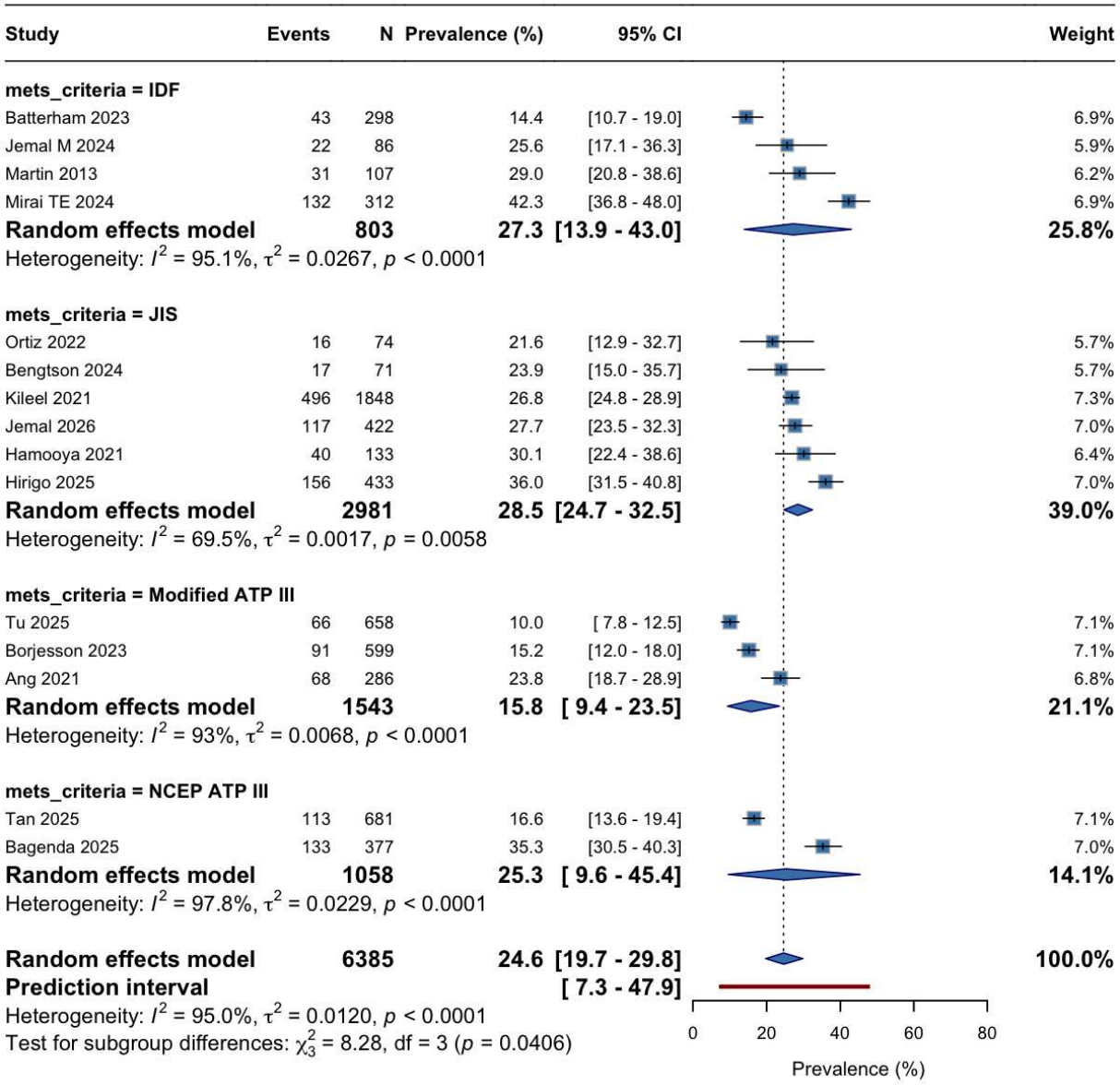


Figure 3. Forest plot of pooled metabolic syndrome prevalence by diagnostic criteria.

By INSTI type: Studies evaluating DTG-based regimens reported a pooled prevalence of 28.7% (95% CI 22.7-35.1%) across 9 studies, compared with 18.5% (95% CI 10.7-28.0%) across 4 studies including mixed INSTI regimens ($p < 0.001$). Single-study estimates were 16.6% (95% CI 13.9-19.5%) for BIC and 29.2% (95% CI 21.0-38.1%) for RAL (Table 2).

By WHO region: The highest pooled prevalence was observed in the African Region, at 32.5% (95% CI 27.9-37.2%) across 7 studies. This compared with 16.3% (95% CI 5.3-31.8%) across 2 studies from the

Western Pacific Region and 21.2% (95% CI 14.5-28.8%) across 4 multinational studies; subgroup differences were significant ($p < 0.001$) (Table 2)..

By income setting: Prevalence differed significantly by country income category ($p < 0.001$). The pooled prevalence was 33.4% (95% CI 28.7-38.2%) across 6 studies from low-income settings and 15.7% (95% CI 11.9-19.9%) across 5 studies from high-income settings. The corresponding pooled estimates were 23.1% (95% CI 16.7-30.3%) across 2 studies from upper-middle-income settings and 27.0% (95% CI 25.0-29.0%) across 2 studies spanning multiple income settings (Table 2)..

By study design: There was no evidence that pooled prevalence differed by study design ($p = 0.296$). The pooled prevalence was 27.7% (95% CI 19.7-36.5%) across 9 cross-sectional studies, 21.2% (95% CI 14.5-28.8%) across 4 randomized controlled trials, and 18.5% (95% CI 10.9-27.7%) across 2 prospective cohort studies (Table 2)..

By risk of bias Estimates did not differ significantly across risk-of-bias strata ($p = 0.554$). The pooled prevalence was 27.8% (95% CI 19.9-36.5%) across 7 low risk-of-bias studies, 19.6% (95% CI 8.1-34.7%) across 3 moderate risk-of-bias studies, and 23.5% (95% CI 17.2-30.4%) across 5 high risk-of-bias studies (Table 2).

Table 2. Subgroup analyses of metabolic syndrome prevalence in people living with HIV receiving INSTI-based ART.

Variable	Subgroup	k	Prevalence (95% CI)	I^2 (%)	p-value for subgroup differences
MetS Criteria	JIS	6	28.6 (24.9 – 32.6)	69.5	0.041
	IDF	4	27.4 (14.2 – 43.1)	95.1	
	Modified ATP III	3	15.9 (9.4 – 23.5)	93.0	
	NCEP ATP III	2	25.3 (9.6 – 45.4)	97.8	
INSTI Type	DTG	9	28.7 (22.7 – 35.1)	90.1	<0.001
	Mixed	4	18.5 (10.7 – 28.0)	97.3	
	BIC	1	16.6 (13.9 – 19.5)	–	
	RAL	1	29.2 (21.0 – 38.1)	–	
WHO Region	African Region	7	32.5 (27.9 – 37.2)	75.8	<0.001
	Multiple	4	21.2 (14.5 – 28.8)	93.8	
	Western Pacific	2	16.3 (5.3 – 31.8)	96.4	
	European Region	1	15.2 (12.5 – 18.2)	–	

	Region of the Americas	1	22.0 (13.4 – 32.0)	–	
Income Level	Low income	6	33.4 (28.7 – 38.2)	76.9	<0.001
	High income	5	15.7 (11.9 – 19.9)	86.9	
	Upper-middle income	2	23.1 (16.7 – 30.3)	0.0	
	Multiple	2	27.0 (25.0 – 29.0)	0.0	
Study Design	Cross-sectional	9	27.7 (19.7 – 36.5)	95.9	0.3
	RCT	4	21.2 (14.5 – 28.8)	93.8	
	Prospective cohort	2	18.5 (10.9 – 27.7)	70.1	
Risk of Bias	Low	7	27.8 (19.9 – 36.5)	95.5	0.55
	High	5	23.5 (17.2 – 30.4)	83.6	
	Moderate	3	19.6 (8.1 – 34.7)	97.9	

k = number of studies contributing to the subgroup; ART = antiretroviral therapy; INSTI = integrase strand transfer inhibitor; MetS = metabolic syndrome; WHO = World Health Organization.

Meta-regression

Univariable meta-regression analyses identified female proportion as the only significant study-level moderator of metabolic syndrome prevalence ($p < 0.001$). Publication year ($p = 0.757$), mean/median age ($p = 0.278$), JBI quality score ($p = 0.445$), and sample size ($p = 0.625$) were not significantly associated with prevalence. Detailed meta-regression results are presented in Supplementary Table S3, and corresponding bubble plots are shown in Supplementary Figures S14–S18.

Sensitivity Analyses

Sensitivity analyses showed that the pooled estimate was stable across alternative approaches. In the secondary GLMM with logit transformation, the pooled prevalence was 24.1% (95% CI 19.6-29.1%), compared with 24.8% (95% CI 19.9-29.9%) in the primary Freeman-Tukey analysis (Figure 3). Excluding studies at high risk of bias yielded a pooled prevalence of 25.3% (95% CI 19.0-32.2%), while restriction to observational studies yielded 26.1% (95% CI 19.2-33.7%). Leave-one-out analysis and influence diagnostics similarly indicated that the overall result was not driven by any single study, although Tu (2025) and Mirai TE (2024) contributed relatively more to between-study variability than the remaining studies (Supplementary Figures S14-S18).

Publication Bias and small-study effects

There was no clear evidence of marked asymmetry. The LFK index was -0.18, indicating no asymmetry, and Egger's regression test was not statistically significant (p = 0.681). Exploratory trim-and-fill analysis imputed 2 studies, with the pooled prevalence attenuating slightly from 24.8% (95% CI 19.9-29.9%) to 22.6% (95% CI 17.9-27.7%). The contour-enhanced funnel plot, trim-and-fill funnel plot, and Doi plot are shown in Supplementary Figures S11-S13.

DISCUSSION

To our knowledge, this is the first systematic review and meta-analysis to quantify the burden of MetS among contemporary populations receiving INSTI-therapy in the DTG era. Our findings indicate that approximately one in four individuals receiving INSTI-based therapy meet criteria for MetS. Prevalence estimates varied considerably across studies, reflecting differences in geographic region, country income classification, diagnostic criteria, and study populations. As INSTI-based regimens continue to form the backbone of HIV treatment globally, addressing this metabolic burden will become increasingly important for long-term HIV care.

The prevalence observed in this review was broadly consistent with that reported in the wider HIV literature. Our pooled estimate of 24.6% closely matched the 25.3% prevalence reported among all PLHIV and the 25.6% prevalence reported among ART-treated PLHIV in a recent 2024 global meta-analysis [37]. It also falls within the range reported in contemporary studies of the general population, including a global prevalence estimate of 28.4% in 2023 [38], prevalence estimates ranging from 12.5% to 31.4% in a 2022 global meta-analysis [39], and modelled global prevalence estimates of 31.0% among women and 25.7% among men in 2023 [38]. These observations suggest that the burden of MetS among INSTI-treated PLHIV largely mirrors the broader cardiometabolic burden already reported among treated HIV populations rather than indicating a markedly different epidemiological profile. Nonetheless, the consistently high prevalence observed across HIV-specific and general populations underscores the

growing importance of metabolic health as a major component of chronic disease management in the era of increased longevity.

The subgroup analyses provide additional insight into factors that may underlie the observed variation in prevalence estimates. Differences were evident according to geographic region, country income classification, diagnostic criteria, and INSTI regimen, whereas variation according to study design and risk-of-bias category was less apparent. This pattern suggests that differences in MetS burden may be driven more by population characteristics, healthcare contexts, and diagnostic approaches than by methodological differences between studies. Although prevalence also differed across INSTI regimens, this finding should be interpreted cautiously because most included studies evaluated DTG-based regimens, whereas evidence for other INSTIs was comparatively limited.

Among the subgroup findings, the higher prevalence observed in studies from Africa and low-income countries is particularly noteworthy. These findings likely reflect overlapping rather than independent influences, given the substantial representation of low-income countries within the African region. The observed pattern is consistent with ongoing epidemiological transitions across many low- and middle-income countries, where increasing rates of obesity, hypertension, and diabetes coexist with expanded access to ART and improved survival among PLHIV. These trends may contribute to a growing population of PLHIV at risk of chronic cardiometabolic conditions. The regional findings are also notable when viewed in the context of previous evidence. A recent systematic review from sub-Saharan Africa reported pooled MetS prevalences of 21.0% using NCEP ATP III criteria and 23.4% using IDF criteria among PLHIV [40], both lower than the estimates observed in the African subgroup of the present review. One possible explanation is that our review focused specifically on INSTI-treated populations and included several DTG-based cohorts from East and Southern Africa. However, differences in treatment histories, sex distributions, underlying cardiometabolic risk profiles, healthcare infrastructure, and screening practices are also likely to have contributed to the observed variation. Given that sub-Saharan Africa bears

the largest global burden of HIV, these findings highlight the importance of strengthening cardiometabolic surveillance and prevention within HIV programmes across the region.

Diagnostic criteria also emerged as an important source of variability in prevalence estimates. Studies using the Modified ATP III criteria reported lower prevalence estimates than those using the IDF and JIS definitions, consistent with findings from previous reviews among PLHIV [6]. These findings highlight the influence of case definitions on estimates of disease burden and suggest that part of the heterogeneity observed across studies may reflect differences in classification rather than true differences in underlying disease risk. The magnitude of these differences suggests that prevalence estimates should not be compared directly without considering the underlying case definition. This reinforces the importance of accounting for diagnostic criteria when interpreting and comparing MetS prevalence estimates across populations.

The findings of this review have important implications for HIV care programmes. The convergence of widespread INSTI use, improved survival among PLHIV, and rising rates of obesity and other non-communicable diseases means that metabolic health is likely to become an increasingly important determinant of long-term outcomes. Potential mechanisms linking INSTI exposure and MetS may include, weight gain after INSTI initiation, adipocyte differentiation, insulin resistance, visceral adiposity, endothelial dysfuction and chronic inflammation but also the rising of cardiometabolic risk factors in a genetically diverse and ageing African population. Consequently, integrating routine assessment of cardiometabolic risk factors into HIV care may facilitate earlier identification of individuals at increased risk of cardiovascular morbidity. This specifically implies body mass index and waist circumference measurement, blood pressure, fasting glucose/HbA1c and lipid screening, particularly after DTG initiation. In Africa where resources are limited, leveraging existing HIV care infrastructure to support integrated chronic disease management may represent an efficient strategy for addressing this growing burden.

This review has several strengths and limitations. It focused specifically on INSTI-treated PLHIV, followed a prespecified protocol, incorporated formal risk-of-bias assessment, and demonstrated robust findings across multiple sensitivity analyses. However, because of the substantial heterogeneity, our pooled estimate should be viewed as an average burden across diverse settings rather than a single universally applicable prevalence. Several subgroup analyses, particularly for non-DTG INSTIs and some regions, were based on few studies and should be interpreted cautiously. INSTI-specific treatment duration was poorly reported, limiting assessment of exposure-response relationships, and the predominantly observational nature of the evidence precludes causal inference. Finally, differences in MetS definitions across studies likely contributed to the observed variability, and residual publication bias cannot be completely excluded.

Conclusion

This first pooled estimate of MetS prevalence in the contemporary INSTI-treated populations showed that approximately one in four PLHIV receiving INSTI-based ART has MetS, indicating a substantial cardiometabolic burden in this population. While the overall prevalence was comparable to that reported in broader HIV populations, important variation was observed across geographic regions, income settings, and diagnostic criteria. The particularly high prevalence observed in African and low-income settings underscores the need to strengthen cardiometabolic prevention, screening, and management within HIV care programmes. As INSTI-based regimens continue to expand globally, addressing MetS will be critical to improving long-term health outcomes among PLHIV.

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Author Contributions

The conception and design of the study were developed by P.V., M.J. and E.G. The literature search and the extraction of data were carried out M.J., E.G. , and P.V. The synthesis of the data and drafting of manuscript was done by M.J. and P.V . All authors (M.J, P.V. , E.G., J.C., S.K. ,M.Y., A.P., A.D.) read, provided feedback, and approved the final version of the manuscript.

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Data availability

All data generated or analysed during this study are included in this article and its supplementary information files. The datasets used for the meta-analysis were extracted from published studies cited in the reference list.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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