

Methodological Inconsistencies in Nigerian HPV Systematic Reviews: A Meta- Epidemiological Analysis for Evidence-Based Policy

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Abstract

Background:

Reliable estimates of human papillomavirus (HPV) prevalence are essential for informing vaccine policy, screening strategies, and resource allocation in high-burden settings like Nigeria. However, systematic reviews of HPV prevalence among Nigerian women have produced methodologically inconsistent and geographically contradictory results, limiting their utility for health economic and policy decision-making.

Objective:

This meta-epidemiological analysis critically evaluates systematic reviews published between 2020 and 2024, comparing methodological quality, diagnostic approaches, geographic coverage, HIV stratification, and genotype reporting.

Methods:

Systematic reviews were assessed using AMSTAR-2, and key epidemiological and methodological variables were extracted. Comparisons focused on pooled prevalence estimates, confidence intervals, heterogeneity metrics, and regional representation. Particular attention was paid to HIV co-infection stratification and genotype-specific prevalence.

Results:

Pooled HPV prevalence estimates ranged from 20.7–42%, with confidence interval widths varying more than tenfold across reviews. Geographic findings were inconsistent, with different regions identified as having the highest prevalence and contradictory estimates for the same zones (e.g., North West: 73% vs. 6.8%). Genotype distributions showed major inconsistencies, especially for high-risk types not covered by current vaccines. HIV-positive populations were either excluded, aggregated without stratification, or inadequately analyzed. AMSTAR-2 ratings ranged from high to critically low.

Conclusion:

Substantial methodological heterogeneity undermines the reliability of current HPV prevalence data for informing cost-effectiveness analyses, vaccine selection, and national cervical cancer prevention planning. This meta-epidemiological analysis critically evaluates the existing literature and is a roadmap for developing standardized surveillance protocols. It aims to create a more reliable evidence base to inform equitable, value-driven public health decisions.

Background

Human papillomavirus (HPV) infection is the primary cause of cervical cancer in sub-Saharan Africa (SSA). Sub-Saharan Africa bears a disproportionate burden, accounting for 24.55% of global cervical cancer deaths, and in 2020, an estimated 84% of the worldwide burden and 88% of related deaths occurred in low-resource nations, including SSA.[1, 2]. The pooled prevalence of high-risk HPV (hrHPV) among women in SSA is consistently reported as very high.[3, 4]

Nigeria is Africa's most populous country.

Systematic reviews and meta-analyses play a central role in evidence-based health planning. In Nigeria, where resource constraints demand high-impact interventions, accurate and reliable HPV prevalence data are essential for cost-effective public health programming. Such data underpin vaccine policy development, guide screening strategies, and support the optimal allocation of limited healthcare resources. However, a critical comparative assessment of the systematic review literature on HPV prevalence among Nigerian women reveals profound methodological inconsistencies and contradictory findings. These inconsistencies are not just a limitation of the existing literature; they are a critical barrier to sound health, economic, and policy decision-making.

This meta-epidemiological critique examines these methodological limitations and assesses their direct implications for economic modeling, vaccine policy, and resource allocation in Nigeria's cervical cancer prevention landscape. Our contribution is not to produce a new pooled prevalence estimate from a flawed evidence base, but rather to identify the specific sources of heterogeneity and demonstrate

how this evidence chaos fundamentally undermines the reliability of health economics and outcomes research (HEOR). We conclude by proposing a roadmap for strengthening the evidence base to enable more reliable HEOR applications and inform equitable, value-driven public health decisions.

Methods

Study Design and Framework

This meta-epidemiological critique employed a systematic comparative analytical framework to examine methodological variations and their implications across systematic reviews of HPV prevalence in Nigerian women. The study was guided by established meta-epidemiological and comparative effectiveness research principles.

Search Strategy and Study Selection

A comprehensive literature search was conducted across PubMed, Proquest Central, covering January 2020 to December 2024. Search terms included: ("human papillomavirus" OR "HPV") AND ("systematic review" OR "meta-analysis") AND "Nigeria" AND ("prevalence" OR "epidemiology"). A supplementary search of the Cochrane Library (Issue 7 of 12, July 2025) found no Cochrane Reviews or Protocols related to HPV prevalence or epidemiology in Nigeria.

From an initial pool of 208 potentially relevant articles, systematic reviews were included if they:

1. Employed a systematic review methodology with a clearly reported search strategy.
2. Included primary studies with HPV prevalence data among Nigerian women.
3. Provided either pooled prevalence estimates or comprehensive narrative synthesis.
4. Were published between January 2020 and December 2024.
5. Addressed topics relevant to public health policy (e.g., vaccination, screening, or health economics).

Reviews were excluded if pooled prevalence was not reported or lacked systematic methodology (e.g., narrative reviews).

Two reviewers (A.K. and O.O.) independently screened titles and abstracts. Disagreements were resolved by consensus. Full-text reviews followed the same procedure, resulting in the inclusion of four systematic reviews.

Quality Assessment

Methodological quality was assessed using A Measurement Tool to Assess Systematic Reviews Version 2 (AMSTAR-2) tool.[5] Two reviewers (A.K.S. and O.M.T.) independently assessed each review across the 16 AMSTAR-2 domains, with particular attention to the seven critical elements. To measure the reliability of our quality assessment, we calculated Cohen's Kappa (κ) for the inter-rater agreement on all 16 items. While we achieved perfect agreement ($\kappa = 1.00$) for several items, like the explanation of study designs and the list of exclusions, we observed a κ of 0.00 for three critical elements: the protocol, the duplication of study selection, and the assessment of risk-of-bias impact on the meta-analysis. This lack of initial agreement was likely due to the small sample size ($n = 4$). Therefore, we discussed resolving every discrepancy and reached a final consensus for the grading of each systematic review. This process was essential for ensuring our grading of each systematic review was valid [see appendices].

Subsequently, each article was then graded on its appraisal for decision making from critically low to high.[5]

Data Extraction and Standardization

A standardized template was used for data extraction. Extracted variables included:

- **Methodological features:** Protocol registration, number of databases searched, inclusion/exclusion criteria, quality assessment tools, and synthesis methods.
- **Epidemiological metrics:** Pooled prevalence estimates, 95% confidence intervals, I^2 statistics, and subgroup analyses.
- **Population details:** Age ranges, sample sizes, sampling frames (hospital-based, community-based), and geopolitical representation.
- **Clinical parameters:** HPV detection methods (e.g., PCR platforms, primer sets), genotype-specific prevalence, and HIV co-infection analysis.

- **Geographic data:** Geopolitical regional prevalence breakdown.

Two reviewers (A.K.S. and O.O.O.) independently extracted data. Discrepancies were resolved through discussion and reference to original texts.

Insert Fig. 1 here

Statistical Analysis and Visualization

Descriptive statistics were calculated for all extracted parameters. Regional prevalence maps were developed using R statistical software (version 4.3.2), employing sf and ggplot2 packages with publicly available shapefiles from the Database of Global Administrative Areas (GADM).

Ethical Considerations

This study relied solely on previously published systematic reviews and did not involve individual patient data; therefore, ethical approval was not required. All data analyzed were publicly available.

Result

Insert Fig. 1. Here immediately after Result Heading

Flowchart illustrating the identification and selection of systematic reviews included in the meta-epidemiological analysis. The process followed adapted PRISMA methodology for transparency and rigor.

Insert Table 1 here Immediately after Fig. 2.

Table 1 Methodological Characteristics of Systematic Reviews on HPV Prevalence in Nigeria									
Author	Year	Time Frame	No. of Studies	Population	HIV Stratification	Sampling	Diagnostic Method	HPV Types Tested	Geographic Coverage
Anoruo et al.	2022	1999–2021	17	Women (15–49)	No	Mixed (Random/Convenience)	PCR & Serology	20–30	All Zones
Kabuga et al.	2020	1999–2019	18	Women (15–86)	Subgroup: Yes	Mostly Hospital-Based	PCR	13–30	Multiple Zones
Emeribe et al.	2021	2000–2020	18	Women (15–65)	Not Reported	Varied	PCR GP5+/GP6+	~ 20	Multiple zone
Ezechi et al.	2023	2001–2022	18	Women (25–65), incl. HIV+	Yes (Primary Focus)	Mixed (Clinical & community)	PCR, HC, GP5+	12 HR types	Multiple zones

The four systematic reviews varied widely in methodological approaches: all focused on Nigerian women aged 15–86, with differences in HIV stratification (only Ezechi et al. focused primarily on HIV status), sampling methods (ranging from random to hospital-based), diagnostic tools (mostly PCR-based), and geographic coverage including multiple geopolitical zones.

Insert Table 2 here Immediately after Table 1.

Table 2
Key Findings from Systematic Reviews on HPV Prevalence in Nigeria

Author	Pooled Prevalence (%)	95% CI	Heterogeneity (I^2)	Most Common Genotypes	Highest Regional Prevalence	Lowest Regional Prevalence	AMSTAR-2 Appraisal Grade
Anoruo et al.	32%	23–42%	High $I^2 = 99.04$, $P < 0.001$.	HPV-16, 18	South East (71.1%)	South South (4.9%)	Low
Kabuga et al.	42%	30–54%	High $I^2 = 99.2$, $p < 0.01$	HPV-16 (27%), HPV-18 (23%)	North West (73%)	South East (6.0%)	Low
Emeribe et al.	21%	19.7–21.7%	-	HPV-31 (70.8%), HPV-35 (69.9%)	North East (48.1%)	North West (6.8%)	Critically Low
Ezechi et al.	25%	19–32%	High	HPV-18 (10%), HPV-16 (9%)	North (32%)	East (no Data)	High

The four reviews reported widely divergent pooled HPV prevalence estimates (21–42%) with high heterogeneity ($I^2 > 99\%$ for most), notable variation in dominant HPV genotypes (HPV-16, 18, 31, 35), regional prevalence extremes (e.g., 73% in NW vs 4.9% in SS), and differing methodological quality, with AMSTAR-2 ratings ranging from high (Ezechi et al.) to critically low (Emeribe et al.).

Comparative Analysis of Prevalence Estimates and Methodological Heterogeneity

Systematic reviews examining HPV prevalence among Nigerian women present divergent epidemiological estimates, most notably reflected in the wide range of pooled prevalence figures and associated confidence intervals (CIs). Emeribe et al. (2021) reported the lowest prevalence at 20.7% with a narrow 95% CI of 19.7–21.7% (CI width: 2%), suggesting high internal consistency and minimal statistical uncertainty.[6] These findings, regardless, require careful consideration because the reliability of the evidence is critically low.

In stark contrast, Kabuga et al. (2020) reported the highest pooled prevalence at 42% with a wide CI of 30–54% (CI width: 24%), reflecting substantial heterogeneity in the included studies—likely due to varied diagnostic tools, sampling frames (mostly hospital-based), and HIV stratification.[7] The 2.03-fold difference in point estimates and 12-fold difference in CI widths between these two reviews exemplify the methodological divergence that complicates comparative interpretation.

A closer inspection of CI overlap provides further insight into statistical compatibility across reviews. Emeribe et al.’ narrow CI shows no meaningful overlap with Kabuga et al. and only marginal overlap with Anoruo et al. (2022), whose pooled prevalence was 32% (CI: 23–42%).[8] This suggests Emeribe’s findings may represent a substantively different population, methodology, or both.

In contrast, Anoruo et al., Ezechi et al. (2023; 25%, CI: 19–32%), and Kabuga et al. exhibit moderate CI overlap, with the lower bound of Kabuga (30%) overlapping the upper bound of Ezechi (32%) and aligning with Anoruo’s estimate.[7–9] This convergence suggests that, despite differing central estimates, the true national prevalence may plausibly lie within the 25–35% range—an important consideration for policymakers and modellers.

These variations are not merely academic. In health economic modelling, such discrepancies can dramatically shift incremental cost-effectiveness ratios (ICERs), changing the interpretation of HPV vaccination programs from highly cost-effective to marginal. This inconsistency undermines HEOR tools—such as CEAs and BIAs—which rely on stable prevalence inputs to estimate disease burden and cost per QALY or DALY averted.[10, 11] For countries like Nigeria, where budget constraints make marginal investments unsustainable, such uncertainty undermines the reliability of policy recommendations.

Diagnostic Method Variations

Building on the discrepancies in pooled prevalence and confidence intervals, a key driver of heterogeneity across the systematic reviews is the variation in diagnostic methods used to detect HPV. These differences have a direct bearing on the reliability, comparability, and policy utility of prevalence estimates.

High-sensitivity molecular techniques such as polymerase chain reaction (PCR), Hybrid Capture (HC), and SPF10/LiPA25 were the most employed methods, particularly in Kabuga et al. (2020) and Ezechi et al. (2023), who reported relatively high prevalence rates.[7, 9] In contrast, Emeribe et al. (2021), who reported the lowest prevalence, utilized a mix of molecular and immunological assays with narrower

genotype detection scopes.[6] Anoruo et al. (2022) further highlighted that studies using serological assays produced higher prevalence estimates than those using genotyping, likely due to serology's ability to detect both current and past infections.[8]

These methodological discrepancies are not trivial—they introduce substantial variation in sensitivity and specificity, directly influencing pooled estimates. Assays that differ in their ability to detect latent versus active infections or high-risk genotypes will yield inconsistent prevalence figures, even within similar populations.

From a health economic and policy perspective, such inconsistencies undermine the integrity of cost-effectiveness models. If prevalence estimates are inflated or deflated based on assay sensitivity rather than true disease burden, subsequent outputs—such as ICERs and budget impact estimates—become unreliable. This, in turn, affects resource allocation decisions, priority setting, and donor confidence in national HPV prevention strategies.

As Nigeria continues to scale up its cervical cancer control efforts, the standardization of diagnostic methods across surveillance and research is essential. Without this, decision-makers lack a stable foundation of epidemiologic evidence upon which to base vaccination rollout, screening strategies, and long-term investment in HPV control programs.

Geographic Contradictions

The geographic findings across the systematic reviews reveal striking contradictions, highlighting both methodological inconsistencies and regional disparities in Nigeria's HPV research landscape. Each review identified a different geopolitical zone as having the highest prevalence: Kabuga et al. reported 73% in the North West, Anoruo et al. found 71.1% in the South East (based on a single study), and Emeribe et al. estimated 48.1% in the North East.[6–8] Similarly, the lowest prevalence estimates ranged widely—from 4.9% in the South South (Anoruo et al.) to 6.0% in the South East (Kabuga et al.) and 6.8% in the North West (Emeribe et al.).

Such variation is unlikely to reflect true epidemiological differences. More plausibly, it results from differences in study selection criteria, diagnostic techniques, HIV stratification, and uneven regional research representation. This imbalance is further exemplified by Ezechi et al. (2023), who found no eligible studies on high-risk HPV among HIV-positive women in the Eastern region.[9] These discrepancies point to a systemic research coverage bias—where some regions are overrepresented by outlier studies while others remain under-researched or entirely absent from the evidence base. [12–14]

Perhaps the most striking contradiction appears in the North West, where Kabuga et al. reported a prevalence of 73%, while Emeribe et al. found just 6.8%—a nearly tenfold disparity within the same geopolitical zone. This extreme divergence cannot be explained by regional variation and instead highlights serious methodological inconsistencies, including differences in diagnostic platforms, inclusion criteria, and study settings. The fact that Emeribe et al.'s review was rated *critically low* on AMSTAR-2 further raises concerns about underestimation, while Kabuga et al.'s hospital-based data may have inflated prevalence due to referral bias. Therefore, inaccurate regional estimates compromise health equity, reduce efficiency, and threaten the long-term sustainability of Nigeria's cervical cancer prevention programs.

Color-coded representation of Nigeria's geopolitical zones based on systematic review findings (Fig. 1). The map illustrates stark geographic inconsistencies in HPV prevalence data across Nigeria, with some regions showing contradictory estimates and others lacking data entirely, highlighting critical gaps in evidence for equitable policy planning.

HIV Co-infection Gap

A persistent limitation across systematic reviews of HPV prevalence in Nigeria is the insufficient stratification by HIV status, despite well-established links between HIV co-infection and increased hrHPV persistence and progression to cervical cancer.[4] This omission undermines accurate burden estimation and weakens the evidence base for cost-effective, targeted interventions

Anoruo et al. (2022) excluded HIV-positive women entirely, aiming to avoid inflating prevalence estimates due to immunosuppression—but at the cost of reduced generalizability and the exclusion of a high-risk subgroup.[8] Conversely, Emeribe et al. included both HIV-positive and negative women but failed to stratify prevalence estimates, obscuring critical differences by immunological status.[6]

Ezechi et al. (2023) offered more detailed insights, reporting a 71% (95% CI: 69–73) hrHPV prevalence among HIV-positive women, and examining predictors such as CD4 count and ART use.[9] However, they did not present pooled prevalence for HIV-negative women or conduct stratified analyses, limiting comparative effect size estimation. Kabuga et al. (2020) reported a lower pooled prevalence of 37% (95% CI: 25–50%) in HIV-positive women, with subgroup analysis yielding an odds ratio of 2.34 (95% CI: 1.36–4.02), confirming the elevated risk.[7]

Without robust stratification and adjusted analyses (e.g., meta-regression by ART status or CD4 count), it's difficult to model the marginal benefit of targeting HIV-positive women—an urgent gap in a country where over 1.3 million people live with HIV, many within the screening age range. [15] Future reviews must prioritize comparative analyses to inform integrated HPV-HIV screening strategies and optimize value-based cervical cancer prevention.

Genotype Distribution Challenges

Genotype distribution data from Nigerian systematic reviews reveal major inconsistencies that complicate HPV vaccine policy and weaken the value proposition of current immunization strategies. Ezechi et al. (2023), a highly reliable evidence reported nearly equal prevalence of HPV-18 (10%, 95% CI: 8–27%) and HPV-16 (9%, 95% CI: 7–26%)—a pattern that diverges from global norms where HPV-16 is consistently dominant.[9] By contrast, Kabuga et al. (2020) more closely reflected international trends, identifying HPV-16 as most prevalent (27%, 95% CI: 18–35%), followed by HPV-18 (23%, 95% CI: 15–31%).[7]

Even greater discordance appears with other high-risk types. Emeribe et al. (2021) reported extremely high prevalence of HPV-31 (70.8%) and HPV-35 (69.9%), while Kabuga et al. found much lower rates—15% and 19%, respectively, among HIV-positive women.[6, 7] Such discrepancies likely reflect differences in diagnostic assays, population selection, and inclusion criteria, further complicating the interpretation of genotype-specific risk.

These inconsistencies have serious implications for vaccine planning. HPV-31 and HPV-35 are high-risk types not covered by Nigeria's currently deployed bivalent and quadrivalent vaccines; only the nonavalent vaccine includes HPV-31, and even it does not cover HPV-35.[16] If these genotypes are indeed highly prevalent, existing vaccine strategies may offer limited protection, compromising both health impact and cost-effectiveness.

Economic models assuming HPV-16 and 18 dominance may overstate the benefits of narrower-spectrum vaccines, while underestimating the potential value of broader-coverage alternatives. Although the nonavalent vaccine offers improved protection, its higher cost poses a major barrier to widespread adoption in resource-constrained settings. Without reliable, representative genotype data, policymakers cannot make evidence-based choices between vaccine options or accurately assess their budget impact.

These data gaps demand urgent attention. A re-evaluation of Nigeria's vaccine selection strategy—grounded in standardized, multi-site genotyping studies—is essential to align prevention efforts with local epidemiology. Only through consistent and context-specific surveillance can vaccine investments be optimized for equity, effectiveness, and long-term sustainability.

Limitations of Current Evidence for Policy and Economic Modeling

Despite the growing number of systematic reviews on HPV prevalence in Nigeria, the overall evidence base remains methodologically fragile and poorly suited to guide robust health policy. Many of the included reviews scored poorly on the AMSTAR-2 appraisal, with most receiving low or critically low confidence ratings, primarily due to non-transparent study selection processes, lack of pre-registered protocols, and inadequate assessment of risk of bias. These methodological shortcomings raise serious concerns about the validity of pooled estimates and their utility in informing national strategies.

In addition, the reliance on cross-sectional primary studies limits the depth of epidemiological inference. While cross-sectional data offer snapshots of HPV prevalence, they do not capture incidence, persistence, or progression, all of which are critical for long-term modeling and evaluating vaccine or screening impact. The absence of longitudinal data undermines the development of dynamic models required for robust cost-effectiveness and budget impact analyses.

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Conclusion and Call to Action

This meta-epidemiological analysis reveals substantial methodological heterogeneity across systematic reviews assessing HPV prevalence in Nigeria. Discrepancies in diagnostic platforms, inconsistent HIV stratification, contradictory genotype profiles, and pronounced regional gaps in study coverage have produced divergent prevalence estimates that undermine their policy utility. AMSTAR-2 assessments further highlight serious limitations in review conduct and reporting quality, with only one review rated high and others falling into low or critically low confidence categories.

These inconsistencies have profound implications for health economics modeling. With pooled prevalence estimates ranging from 20.7–42% and regional figures differing by over 60 percentage points, cost-effectiveness analyses for HPV vaccination, screening, or surveillance become unstable and unreliable. The absence of disaggregated data for high-risk populations such as HIV-positive women—and inconsistent inclusion criteria across reviews—further weakens the evidence base required for targeted intervention planning.

To support value-based cervical cancer prevention in Nigeria, a nationally coordinated HPV surveillance system is urgently needed. This system should implement harmonized diagnostic protocols, ensure stratified reporting by HIV status and region, and include representative sampling across Nigeria's geopolitical zones. Such data infrastructure is not only critical for accurate health economic evaluation but also essential for equitable policy design that reflects the true burden of HPV-related disease.

Closing these evidence gaps is both a methodological priority and a public health imperative. Without rigorous, standardized prevalence data, HPV control efforts risk perpetuating inequities, misallocating scarce resources, and undermining the long-term success of national cervical cancer elimination strategies. This analysis serves as a roadmap for future research and policy by identifying key methodological gaps and proposing a framework for a nationally coordinated HPV surveillance system. By embracing this proactive strategy, Nigeria can develop a strong evidence base that guarantees its cervical cancer prevention programs are equitable, effective, and sustainable.

Declarations

Ethics approval and consent to participate

Not applicable. This study is a meta-epidemiological analysis of previously published systematic reviews and did not involve direct human participants or new data collection.

Consent for publication

Not applicable.

Competing interests

The author declares no competing interests.

Author's contributions

A.K.S. conceived the study, conducted data extraction and quality assessment, performed the meta-epidemiological comparisons, created the figures, and drafted the manuscript. The author read and approved the final manuscript. O.O.O. conducted data extraction, performed the meta-epidemiological comparisons and drafted the manuscript. The author read and approved the final manuscript. O.M.T conducted data extraction and quality assessment, performed the meta-epidemiological comparisons, created and drafted the manuscript. The author read and approved the final manuscript. A.A.T. drafted the manuscript. The author read and approved the final manuscript.

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Author Contribution

A.K.S. conceived the study, conducted data extraction and quality assessment, performed the meta-epidemiological comparisons, created the figures, and drafted the manuscript. The author read and approved the final manuscript. O.O.O. conducted data extraction, performed the meta-epidemiological comparisons and drafted the manuscript. The author read and approved the final manuscript. O.M.T. conducted data extraction and quality assessment, performed the meta-epidemiological comparisons, and created and drafted the manuscript. The author read and approved the final manuscript. A.A.T. drafted the manuscript. The author read and approved the final manuscript.

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Not applicable.

Availability of data and materials

All data used in this study were extracted from publicly available systematic reviews. Full references to all included studies are provided in the manuscript. Additional datasets generated during the current study (e.g., maps, AMSTAR-2 appraisals) are available from the corresponding author upon reasonable request.

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Figures

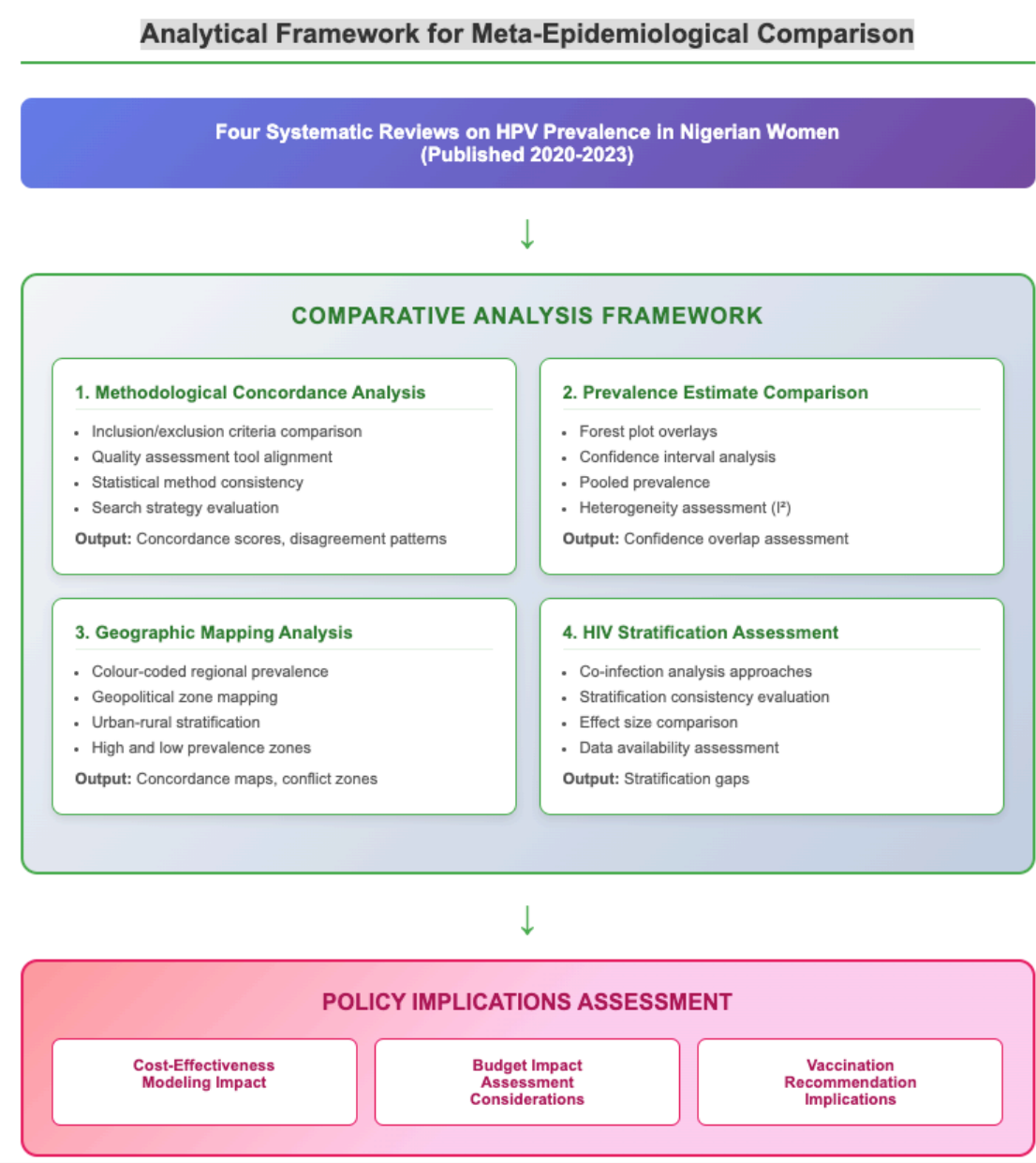


Figure 1

Analytical framework for the comparison of systematic reviews

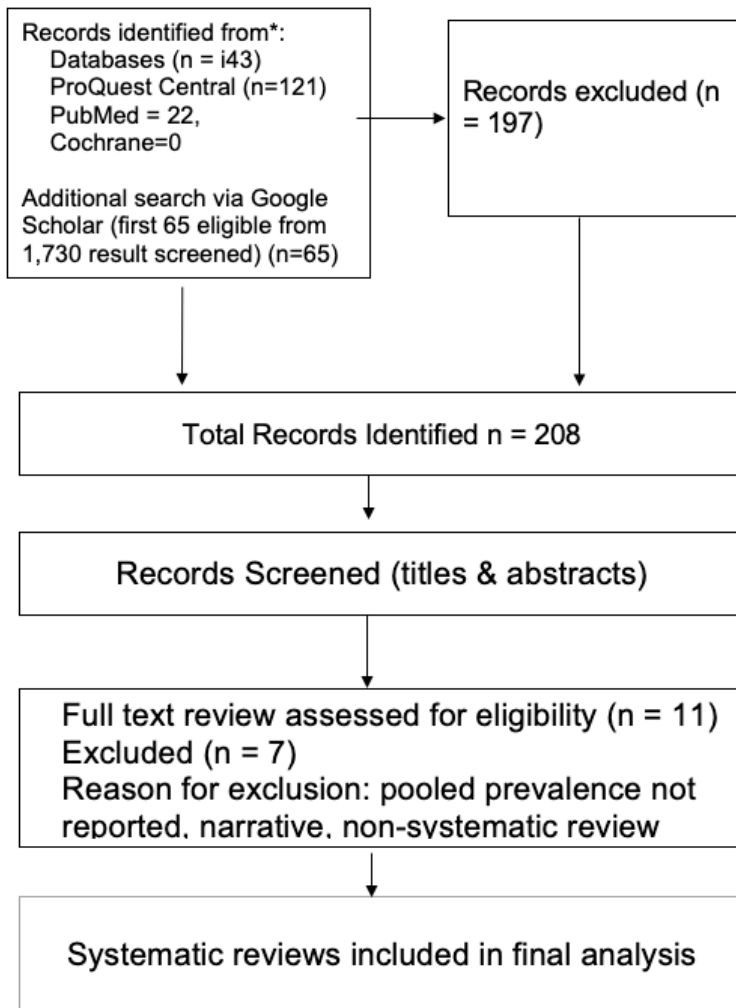


Figure 2

Selection Process for Systematic Reviews Included in Meta-Epidemiological Analysis

Flowchart illustrating the identification and selection of systematic reviews included in the meta-epidemiological analysis. The process followed adapted PRISMA methodology for transparency and rigor.

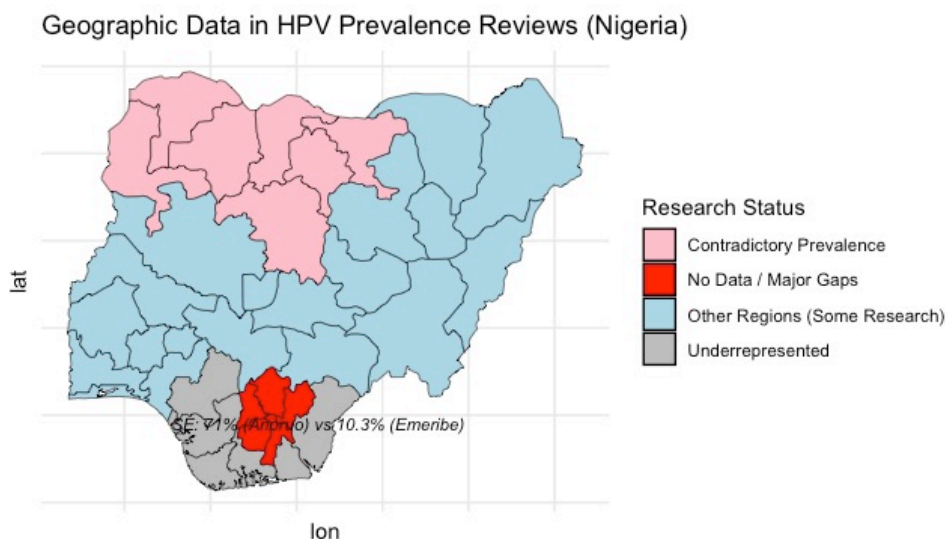


Figure 3

Geographic Data Gaps and Inconsistencies in Nigerian HPV Research

Color-coded representation of Nigeria's geopolitical zones based on systematic review findings (Figure 1). The map illustrates stark geographic inconsistencies in HPV prevalence data across Nigeria, with some regions showing contradictory estimates and others lacking data entirely, highlighting critical gaps in evidence for equitable policy planning.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [appendixA.docx](#)