



A Systematic Review of Barriers and Facilitators to Long-Acting HIV Pre-Exposure Prophylaxis Uptake among Key Populations in Nigeria: Implications for Lenacapavir

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ABSTRACT

BACKGROUND

Long-acting injectable pre-exposure prophylaxis (LAI-PrEP) has emerged as a promising HIV prevention strategy by addressing adherence challenges associated with daily oral pre-exposure prophylaxis (PrEP). Lenacapavir, a twice-yearly subcutaneous capsid inhibitor, has demonstrated near-complete protection against HIV acquisition in clinical trials. However, evidence on its implementation among key populations (KPs) in Nigeria is currently lacking. This systematic review synthesized evidence from oral PrEP programmes and emerging LAI-PrEP studies to inform the future implementation of LAI-PrEP, including lenacapavir in Nigeria.

METHODS

This systematic review followed the PRISMA 2020 guidelines. PubMed, Scopus, ScienceDirect, Frontiers, BMC, African Journals Online (AJOL), relevant publisher platforms, and grey literature were searched for empirical studies published between 2020 and 2026. Methodological quality was assessed using the Mixed Methods Appraisal Tool, and findings were synthesized narratively.

RESULTS

Nine studies met the inclusion criteria. Evidence was derived primarily from oral PrEP programmes and emerging cabotegravir long-acting studies. Common barriers included low HIV risk perception, stigma, discrimination, provider bias, concerns about adverse effects, transportation costs, limited access to KP-friendly services, and health system constraints. Facilitators included peer-led education, differentiated service delivery, community-based KP-friendly services, and preference for long-acting injectable PrEP because of its convenience.

CONCLUSION

Current evidence suggests that successful future implementation of lenacapavir in Nigeria will require addressing multilevel barriers through equitable service delivery, provider preparedness, sustainable financing, and context-specific implementation research. Prospective implementation studies are needed to evaluate the real-world acceptability, feasibility, effectiveness, and cost-effectiveness of lenacapavir among Nigerian KPs.

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These implications are informed primarily by evidence from oral PrEP programmes and emerging cabotegravir long-acting studies.

INTRODUCTION

Human immunodeficiency virus (HIV) remains a major global public health challenge despite substantial advances in prevention, diagnosis, and treatment. In 2024, an estimated 1.3 million new HIV infections occurred worldwide, with sub-Saharan Africa continuing to account for approximately two-thirds of the global burden [1]. Although overall HIV incidence has declined in many settings, transmission remains disproportionately concentrated among key populations (KPs), including female sex workers (FSWs), men who have sex with men (MSM), people who inject drugs (PWID), transgender persons, and their sexual partners [2]. These populations experience intersecting social, legal, and structural vulnerabilities that limit equitable access to HIV prevention services and contribute to persistent disparities in HIV outcomes. Pre-exposure prophylaxis (PrEP) has become a cornerstone of global HIV prevention strategies, reducing the risk of HIV acquisition by more than 90% when used consistently [3]. However, the effectiveness of daily oral PrEP in routine practice has been limited by challenges such as suboptimal adherence, pill fatigue, stigma, concerns about adverse effects, forgetfulness, and difficulties maintaining long-term engagement in care, particularly in low- and middle-income countries (LMICs) [4]. These implementation challenges have stimulated the development of long-acting injectable pre-exposure prophylaxis (LAI-PrEP), which has the potential to reduce adherence burden and improve persistence in HIV prevention programmes.

Cabotegravir long-acting (CAB-LA), administered every two months, demonstrated superior efficacy to daily oral PrEP in Phase III clinical trials and has subsequently been incorporated into international HIV prevention recommendations [5, 6]. More recently, lenacapavir, a first-in-class capsid inhibitor administered as a subcutaneous injection every six months, demonstrated near-complete protection against HIV acquisition in the PURPOSE clinical trial programme. PURPOSE 1 reported 100% efficacy among cisgender women in South Africa and Uganda, while PURPOSE 2 demonstrated similarly high levels of protection among MSM, transgender persons, and gender-diverse individuals across multiple countries [7, 8]. These findings have generated considerable interest in the potential role of twice-yearly LAI-PrEP in strengthening HIV prevention. Nevertheless, evidence from clinical trials should not be equated with implementation success in routine healthcare settings. Effective rollout depends on multiple behavioural, community, organizational, and health system factors

that influence access, acceptability, and sustained use [9, 10].

Nigeria has one of the largest HIV epidemics in sub-Saharan Africa, with an estimated 1.9 million people living with HIV and approximately 100,000 new infections annually [11, 12]. HIV prevalence remains substantially higher among KPs than in the general population, with reported prevalence estimates of 14.4% among FSWs, 23% among MSM, 3.4% among PWID, and up to 25% among transgender persons [13]. The emergence of CAB-LA and the anticipated availability of lenacapavir provide an important opportunity to strengthen HIV prevention in Nigeria. Although oral PrEP was introduced nationally in 2016, programme evidence indicates persistently low uptake, poor continuation, and substantial attrition among KP programmes. A retrospective cohort involving 43,788 KP PrEP initiators between 2020 and 2023 reported only 11.5% continuation at six months, with continuation among transgender persons as low as 3.5% [14]. In addition, reductions in donor funding have affected programme sustainability and continuity of HIV prevention services [15]. Multiple barriers contribute to these implementation challenges. Studies conducted among Nigerian KPs consistently identify low HIV risk perception, stigma, discrimination, criminalization of same-sex relationships and sex work, provider bias, transportation costs, concerns regarding adverse effects, and limited access to KP-friendly healthcare services as important determinants of PrEP uptake and continuation [13, 16–18]. These barriers operate across multiple levels of the health system and social environment, indicating that successful implementation of HIV prevention interventions requires more than the availability of effective biomedical products.

Conversely, peer-led interventions, differentiated service delivery models, community-based HIV services, and culturally sensitive healthcare have been identified as important facilitators of PrEP uptake among underserved populations [14, 17, 18]. Although the emergence of LAI-PrEP offers new opportunities to strengthen HIV prevention, direct evidence regarding the implementation, acceptability, and uptake of lenacapavir among Nigerian KPs is currently unavailable. Consequently, implementation planning must rely on evidence generated from oral PrEP programmes together with emerging studies of CAB-LA and other analogous long-acting HIV prevention strategies. While CAB-LA and lenacapavir differ in dosing frequency, route of administration, and service delivery requirements, experiences from existing PrEP programmes provide valuable insights into the multilevel factors that may influence future implementation of twice-yearly LAI-PrEP in Nigeria. Given the limited direct evidence on lenacapavir implementation in Nigeria, this systematic review aimed to synthesize available evidence from oral PrEP

programmes and emerging LAI-PrEP studies to identify barriers and facilitators influencing HIV PrEP uptake among key populations in Nigeria and to examine their implications for the future implementation of LAI-PrEP, including lenacapavir.

OBJECTIVES OF THE STUDY

This systematic review aimed to:

1. Systematically synthesize evidence on barriers and facilitators influencing HIV PrEP uptake among key populations in Nigeria.
2. Identify individual, interpersonal, community, structural, and health system factors that may influence future implementation of LAI-PrEP.
3. Critically examine the applicability of evidence from oral PrEP programmes and emerging cabotegravir long-acting studies to the future implementation of lenacapavir in Nigeria.
4. Identify evidence gaps and implementation priorities to inform future research, policy, and equitable rollout of LAI-PrEP.

METHODS

STUDY DESIGN

This systematic review was conducted in accordance with a predefined review protocol and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement [20]. A review protocol was developed before commencement of the study to guide the review process. However, the protocol was not prospectively registered in PROSPERO before the review commenced. Nevertheless, the review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines [20], and all review methods were defined a priori to minimize methodological bias.

INFORMATION SOURCES

A comprehensive literature search was conducted in PubMed/MEDLINE, Scopus, ScienceDirect, African Journals Online (AJOL), and publisher platforms including Frontiers and BMC. Grey literature was also searched to identify implementation reports, policy documents, technical guidance, and programme evaluations published by the World Health Organization (WHO), Joint United Nations Programme on HIV/AIDS (UNAIDS), National Agency for the Control of AIDS (NACA), the United States President's Emergency Plan for AIDS Relief (PEPFAR), and other relevant organizations. Reference lists of all included studies and relevant review articles were manually screened to identify additional eligible publications.

SEARCH STRATEGY

The search was conducted to identify studies published between January 2020 and March 2026. January 2020 was selected as the starting point because it reflects the period during which implementation of oral PrEP programmes among Nigerian key populations expanded substantially and evidence relating to LAI-PrEP, particularly cabotegravir, began to emerge. Restricting the search to this contemporary period ensured that the review synthesized evidence most relevant to informing future implementation of LAI-PrEP, including lenacapavir, within current HIV prevention programmes.

Search terms combined Medical Subject Headings (MeSH) and free-text keywords relating to HIV prevention, pre-exposure prophylaxis, long-acting injectable PrEP, key populations, barriers, facilitators, implementation, and Nigeria. Boolean operators ("AND", "OR") were used to combine search terms appropriately. The principal search strategy included: ("Lenacapavir" OR "Cabotegravir" OR "Long-acting injectable PrEP" OR "LAI-PrEP") AND ("Pre-exposure prophylaxis" OR "PrEP") AND ("barriers" OR "facilitators" OR "acceptability" OR "uptake" OR "adherence" OR "implementation") AND ("Nigeria") AND ("key populations" OR "female sex workers" OR "men who have sex with men" OR "people who inject drugs" OR "transgender persons").

Grey literature was identified through structured searches of the official websites of WHO, UNAIDS, NACA, PEPFAR, and other relevant organizations. Reports were screened using the same eligibility criteria applied to peer-reviewed studies. Duplicate records were removed before title and document screening. Where multiple versions of the same report were identified, the most recent version was retained for review.

ELIGIBILITY CRITERIA

Inclusion criteria: Studies were eligible if they reported barriers, facilitators, acceptability, uptake, adherence, or implementation of oral PrEP or LAI-PrEP among Nigerian key populations; evaluated cabotegravir LAI or other LAI-PrEP modalities with findings relevant to sub-Saharan Africa; included female sex workers (FSWs), men who have sex with men (MSM), people who inject drugs (PWID), transgender persons, or other populations at substantial risk of HIV infection; employed qualitative, quantitative, or mixed-methods study designs; were published between January 2020 and March 2026; and were published in peer-reviewed journals or constituted relevant grey literature containing empirical data.

Exclusion criteria: Studies were excluded if they: focused exclusively on HIV treatment rather than prevention; examined general populations without reporting findings for key populations; lacked empirical data (e.g., commentaries, opinion articles, editorials);

were conference abstracts without sufficient methodological information; or were published before January 2020.

RISK OF BIAS ASSESSMENT

Methodological quality of the included studies was independently assessed by two reviewers using the Mixed Methods Appraisal Tool (MMAT), version 2018, which is appropriate for systematic reviews including qualitative, quantitative, and mixed-methods studies[21]. Each study was evaluated against the MMAT criteria relevant to its study design. Disagreements between reviewers were resolved through discussion and consensus. Where consensus could not initially be reached, the studies were re-examined jointly until

agreement was achieved. No study was excluded solely on the basis of methodological quality; rather, quality appraisal informed interpretation of the findings during narrative synthesis. The risk of bias assessment of the included studies are presented in **Table 2**.

STUDY SELECTION

Two reviewers independently screened titles and abstracts against the eligibility criteria. Potentially eligible articles subsequently underwent full-text review. Disagreements regarding study eligibility were resolved through discussion and consensus. The study selection process is presented in the PRISMA 2020 flow diagram (**Figure 1**).

TABLE 1 - Inclusion and exclusion criteria

S/N	Criterion	Inclusion	Exclusion
1	Study type	Empirical studies (quantitative, qualitative, mixed-methods) with primary data on hinderances/enablers	Editorials, commentaries, conference abstracts without full data, modelling studies without empirical component, systematic review, scoping review narrative review
2	Population	High-risk/key populations in Nigeria (FSW, MSM, PWID, transgender persons, young key populations) OR analogous LAI-PrEP acceptability studies from Nigeria	General population only; non-priority populations; studies outside Nigeria
3	Topic/Intervention	Hinderances and/or enablers to PrEP uptake, acceptability, initiation, or continuation; focus on oral PrEP, CAB-LA, or lenacapavir (or any long-acting injectable PrEP)	Studies solely on HIV treatment, post-exposure prophylaxis, or other non-PrEP interventions
4	Outcomes	Any data on individual, interpersonal, community, structural, or health-system factors influencing PrEP uptake	studies reporting only clinical efficacy or pharmacokinetic data without behavioural/ implementation outcomes
5	Setting	Nigeria (any state or national) countries for LAI-PrEP contextual evidence	Studies conducted exclusively outside Nigeria
6	Time period	Published or released January 2020 – March 2026	Pre-2020 publications
7	Language	English or with English abstract/translation	No English version available
8	Data availability	Full text available (peer-reviewed)	Abstracts only or inaccessible full text

TABLE 2 - Risk of Bias and Quality Assessment

S/N	Authors (Year)	Study Design	MMAT Category	MMAT Rating	Overall Quality Assessment	Risk of Bias
1	Olakunde et al. (2024) [13]	Secondary analysis	Quantitative	5/5	High	Low
2	Nwosu et al. (2025) [14]	Retrospective cohort analysis	Quantitative	5/5	High	Low
3	Emmanuel et al. (2025) [16]	Cross-sectional study	Quantitative	5/5	High	Low
4	Durosinmi-Etti et al. (2021) [17]	Mixed-methods	Mixed-methods	5/5	High	Low
5	Ogunbajo et al. (2022) [18]	Cross-sectional survey	Quantitative	5/5	High	Low
6	Abubakar et al. (2026) [23]	Qualitative	Qualitative	4/5	Moderate	Moderate
7	Abubakar et al. (2026) [25]	Phenomenological qualitative	Qualitative	4/5	Moderate	Moderate
8	Omenoba et al. (2025) [26]	Cross-sectional	Quantitative	5/5	High	Low
9	Emmanuel et al. (2020) [27]	Mixed-methods	Mixed-methods	4/5	Moderate	Moderate

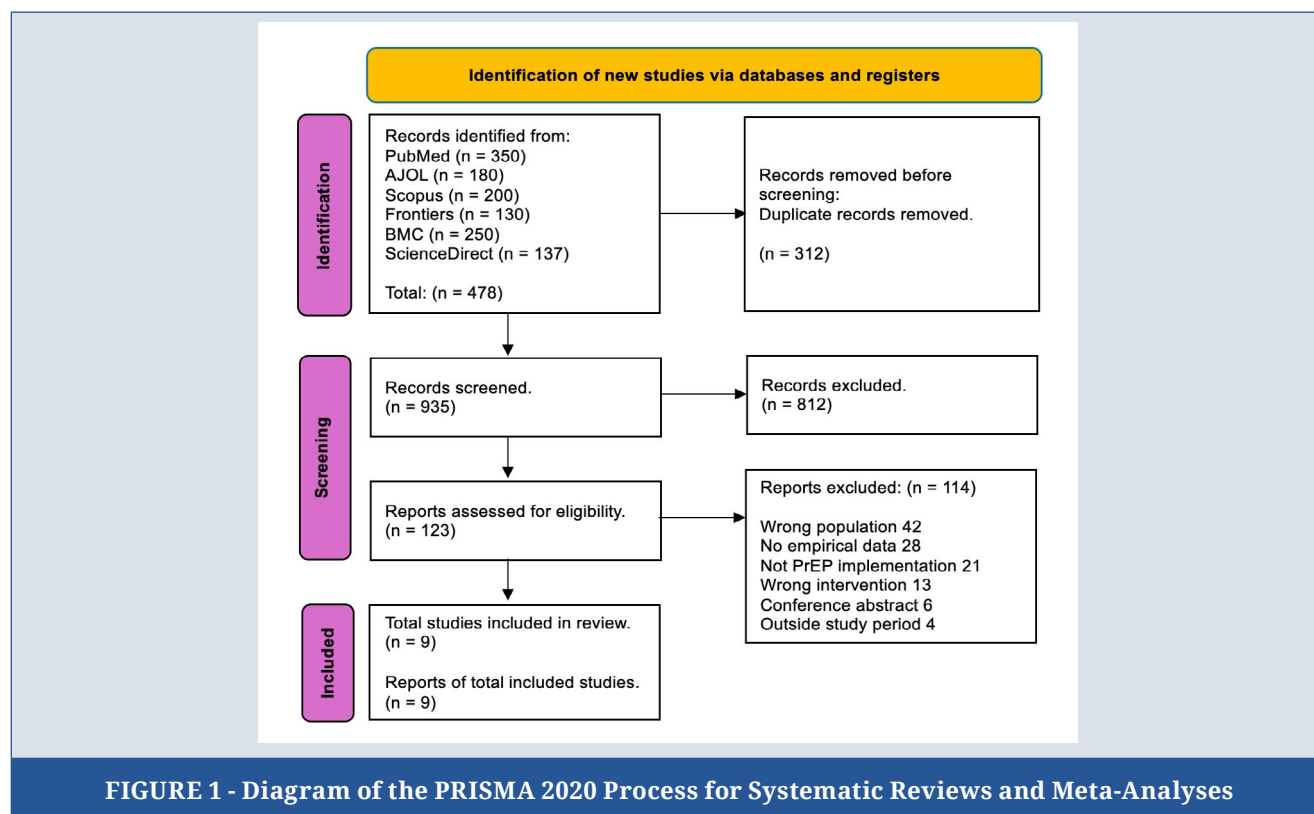


FIGURE 1 - Diagram of the PRISMA 2020 Process for Systematic Reviews and Meta-Analyses

DATA EXTRACTION

Data extraction and methodological quality assessment were independently performed by two reviewers using standardized forms. Any disagreements were resolved through discussion and consensus. The following information was extracted from each included study: author/year, objectives, design, sample/setting, key findings, and conclusions. Thematic synthesis identified recurring barriers and facilitators across individual, interpersonal, community, and structural levels [22]. Data extraction was independently verified to ensure completeness and consistency.

DATA SYNTHESIS

Given the methodological heterogeneity of the included studies, findings were therefore synthesized narratively using thematic analysis. Given the methodological heterogeneity of the included studies, findings were synthesized narratively using thematic analysis. Barriers and facilitators were organized according to the Socio-Ecological Model (SEM), which recognizes that health behaviours are influenced by interacting individual, interpersonal, community, organizational, and structural factors [22]. The SEM was selected because it provides a well-established framework for examining multilevel determinants of HIV prevention behaviours and has been widely applied in implementation research involving key populations. During synthesis, recurring barriers and facilitators were grouped into individual-level, interpersonal and community-level, and structural and health system-

level domains. In addition, the frequency with which each theme was reported across the included studies was documented to indicate the relative consistency of findings within the evidence base.

SCREENING PROCEDURE

The literature search identified 1,247 records. After removal of 312 duplicate records, 935 titles and abstracts were screened, of which 812 were excluded because they did not meet the eligibility criteria. A total of 123 full-text articles were assessed for eligibility. Following full-text review, 114 studies were excluded for reasons including wrong population (n = 42), no empirical data (n = 28), not PrEP implementation (n = 21), wrong intervention (n = 13), conference abstract (n = 6), and outside study period (n = 4). Ultimately, nine studies met the inclusion criteria and were included in the systematic review. Figure 1 presents the PRISMA 2020 flow diagram summarizing the study selection process.

QUALITY ASSESSMENT

The methodological quality of the included studies was assessed using the MMAT (2018) [21]. The appraisal evaluated the appropriateness of the research question, suitability of study design, participant selection, data collection methods, outcome measurement, completeness of outcome data, analytical rigor, and coherence between findings and conclusions, depending on the study design. Most included studies demonstrated moderate to high methodological

quality. Larger quantitative studies and retrospective programme analyses generally exhibited lower risk of bias because of robust sampling procedures and clearly defined analytical methods. Qualitative studies provided rich contextual evidence but were limited by purposive sampling and smaller sample sizes, reducing generalizability. Overall, the quality of evidence was considered sufficient to support thematic synthesis. **Table 2** presents the quality assessment of the included studies.

RESULTS

CHARACTERISTICS OF THE INCLUDED STUDIES

The nine included studies [13, 14, 16-18, 23, 25-27], published between 2020 and 2026, represent the current body of evidence on barriers and facilitators influencing HIV PrEP uptake among key populations (KPs) in Nigeria. No included study directly evaluated the implementation, acceptability, or uptake of lenacapavir following its introduction into the Nigerian HIV prevention programme. Consequently, the evidence synthesized in this review was derived primarily from studies evaluating oral PrEP implementation, programme data, and emerging evidence on LAI-PrEP, particularly cabotegravir long-acting (CAB-LA), which served as the closest available implementation model.

Most studies were conducted in Nigeria and included participants from high HIV burden settings such as Lagos, Abuja, Kano, and other programme-supported states. Study populations predominantly comprised female sex workers (FSWs), men who have sex with men (MSM), people who inject drugs (PWID), transgender persons (TG), healthcare providers, programme implementers, and community pharmacists. Sample sizes varied substantially, ranging from small qualitative studies involving 13 participants to large retrospective programme cohorts involving more than 43,000 PrEP users, reflecting considerable methodological diversity across the evidence base. The included studies employed qualitative, quantitative, mixed-methods, and retrospective cohort designs. Data sources included participant interviews, cross-sectional surveys, programme monitoring data, and national policy reports. Collectively, the included studies evaluated oral PrEP implementation, programme data, and emerging evidence relating to LAI-PrEP. **Table 3** presents the characteristics of the eligible included studies.

THEMATIC SYNTHESIS OF BARRIERS AND FACILITATORS

Thematic analysis identified barriers and facilitators operating across multiple levels of the socio-ecological framework. Four interrelated themes emerged from the included studies: (i) individual-level factors; (ii) interpersonal and community-level factors; (iii) structural and health system factors; and (iv) cross-

cutting implementation considerations relevant to the anticipated rollout of long-acting injectable PrEP in Nigeria. Although direct evidence relating to lenacapavir was unavailable, these findings provide important insights into implementation challenges and opportunities that are likely to influence the introduction and scale-up of long-acting PrEP among Nigerian KPs.

QUALITY APPRAISAL OF INCLUDED STUDIES

The methodological quality of the included studies was assessed using the Mixed Methods Appraisal Tool (MMAT), which is suitable for systematic reviews involving qualitative, quantitative, and mixed-methods designs [21]. The MMAT evaluates methodological rigor across study-specific criteria, including clarity of research questions, appropriateness of study design, sampling strategy, data collection methods, risk of bias, and coherence between findings and conclusions. Overall, the included studies demonstrated varying levels of methodological quality, reflecting heterogeneity in study designs, data sources, and analytical approaches. Most studies were judged to be of high to moderate quality, particularly large-scale quantitative studies and mixed-methods investigations that employed clear sampling frameworks, robust data collection procedures, and appropriate statistical or thematic analyses.

Studies categorized as high quality generally included large representative samples of key populations, national or multi-state coverage, and well-defined analytical strategies. These studies exhibited low risk of bias, particularly those based on secondary analysis of national surveys and large cohort datasets. Studies rated as moderate quality typically employed qualitative or mixed-methods designs with smaller sample sizes or limited geographic coverage. While these studies provided rich contextual insights into barriers and facilitators of PrEP uptake, some were limited by non-probability sampling techniques and reduced generalizability. One study was assessed as low quality, primarily due to its narrative review design and absence of primary empirical data collection, which limited its capacity to meet MMAT criteria for methodological rigor. Although this study contributed policy-relevant perspectives, its findings were interpreted cautiously in the synthesis due to its inherent methodological limitations.

Across all studies, common limitations included reliance on self-reported data, potential social desirability bias, and limited representation of rural key populations. Additionally, most studies were cross-sectional in nature, restricting the ability to infer causality or assess longitudinal PrEP uptake patterns. Despite these limitations, the overall quality of evidence was considered sufficient to support thematic synthesis. Importantly, no study was excluded on the basis of quality alone, consistent with systematic review

methodology. The quality assessment informed the interpretation of findings, particularly in distinguishing between robust empirical evidence and context-specific exploratory insights.

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the included studies: (i) individual-level factors; (ii) interpersonal and community-level factors; (iii) structural and health system factors; and (iv) cross-cutting implementation considerations relevant to the anticipated rollout of LAI-PrEP in Nigeria. Although no included study directly evaluated lenacapavir, the findings provide implementation insights derived from oral PrEP programmes and emerging CAB-LA evidence that may inform future rollout of LAI-PrEP in Nigeria.

TABLE 3 - Summary of Included Studies table

S/N	Authors (Year)	Objectives of the study	Study design	Sample size and study setting	Key Findings	Conclusion
1	Olakunde et al. (2024) [13]	Assess main barriers to oral PrEP uptake and variation among young KPs	Secondary analysis of 2020 IBBS survey (quantitative)	1,776 YKP (15-24 years) across 12 states; FSW, MSM, PWID, TG	Lack of access (28.3%) and fear of side effects (28.3%) highest for FSW; lack of interest (37.1%) for MSM; low risk perception (65.5%) for PWID; lack of access (34.4%) for TG. Significant differences by KP group.	Barriers vary by KP; KP-specific interventions urgently needed to improve PrEP uptake.
2	Nwosu et al. (2025) [14]	Investigate oral PrEP continuation rates among KPs	Retrospective cohort analysis	43,788 KP PrEP initiators (2020–2023); 7 states	6-month continuation 11.5% overall; FSW 13.7%, TG 3.5%. Age and employment associated with continuation.	Continuation critically low; need differentiated models and LAI options to improve retention.
3	Emmanuel et al. (2025) [16]	Assess the prevalence of HIV and the willingness to access HIV preventive services among key populations (KP)	Cross-sectional study	1,320 participants; three local government in Kano State; MSM, PWIDs, FSWs.	HIV prevalence: 10.8%; willingness to access HIV preventive services (57.7%) with significant influences from geographical location and sexual practices. Major barriers: stigma, lack of comprehensive services, limited knowledge of service providers.	Enhancing services accessibility and addressing stigma is essential for reducing HIV transmission.
4	Durosinmi-Etti et al. (2021) [17]	Explore communication needs, barriers, and facilitators for PrEP/HIVST uptake	Mixed-methods (survey + FGDs/IDs)	1,200 KPs (survey) + 48 qualitative; multiple states	Stigma, misinformation, access issues as barriers; peer education, trusted channels (social media) as facilitators.	Tailored, KP-led communication essential to boost uptake.
5	Ogunbajo et al. (2022) [18]	Examine acceptability and preferences for LAI-PrEP vs. other modalities among SMM	Cross-sectional survey (quantitative)	406 HIV-negative SMM; urban Nigeria (Lagos, Abuja)	High willingness for LAI-PrEP (73% preferred over daily oral when accessible); associated with higher HIV risk behaviours, health insurance, and primary care access.	LAI-PrEP highly acceptable; interventions should target high-risk SMM and address access barriers.
6	Abubakar et al. (2026) [23]	Explore multilevel barriers/enablers to PrEP among FSW	Qualitative (semi-structured interviews)	13 FSW + implementers; kano metropolis	Limited awareness, side-effect fears, partner stigma, packaging confusion with ART; peer sensitization and transport support as facilitators.	Discreet LAI-PrEP and community gatekeeper engagement critical.
7	Abubakar et al. (2026) [25]	Examine multilevel barriers/facilitators among MSM/PWID in Kano	Phenomenological qualitative	MSM and PWID; Kano State	Awareness gaps, stigma, transport costs, clinic times; peer support and OSS clinics as facilitators.	Holistic, KP-centred DSD required.

8	Omenoba et al. (2025) [26]	Assess community pharmacists' willingness to deliver PrEP	Cross-sectional survey	267 pharmacists; Abuja and Lagos	99.6% willing; training and logistical support needed; gender differences in serving MSM. Pharmacies closer to KP hotspots than hospitals.	Pharmacies offer scalable, accessible platform for PrEP/LAI delivery.
9	Emmanuel et al. (2020) [27]	Explore community perspectives on PrEP access barriers for MSM/FSW	Mixed-methods (survey + FGDs + workshop)	519 survey + 220 FGD + 65 workshop; Nigeria (14 states)	Stigma (60.7%), cost (53.4%), access/logistics primary barriers; peer education and free services key facilitators	Urgent need for community-led, stigma-free delivery models

OSS: One Stop Shops; FGDs: Focus Group Discussions; IDIs: In-Depth Interviews; AGYW: Adolescent Girls and Young Women; CAB-LA: Cabotegravir long-acting; DSD: Differentiated service delivery; FSW: Female sex workers; HIVST: HIV Self-Testing; HIV: Human Immunodeficiency Virus; IBBS: Integrated Biological and Behavioural Surveillance; KPs: Key populations; LAI-PrEP: Long-acting injectable pre-exposure prophylaxis; LMICs: Low- and middle-income countries; MSM: Men who have sex with men; NACA: National Agency for the Control of AIDS; PrEP: Pre-exposure prophylaxis; PEPFAR: President's Emergency Plan for AIDS Relief; PWID: People who inject drugs; TG: Transgender persons; YKP: Young key populations; SMM: Sexual Minority Men.

INDIVIDUAL-LEVEL BARRIERS AND FACILITATORS

The included studies consistently identified individual-level factors as important determinants of PrEP uptake among Nigerian key populations (KPs). Across studies, low HIV risk perception emerged as one of the most frequently reported barriers, particularly among people who inject drugs (PWID), where approximately 65.5% of participants identified perceived low personal risk as a reason for not initiating PrEP [13]. Similar findings were reported among female sex workers (FSWs), men who have sex with men (MSM), and transgender persons, indicating that inaccurate risk assessment remains a persistent obstacle despite the disproportionately high HIV burden within these populations [13, 18]. Concerns regarding adverse effects also influenced PrEP uptake. Fear of medication-related side effects, including anticipated injection-site reactions associated with long-acting injectable formulations, contributed to reluctance to initiate or continue HIV prevention services [18]. Among FSWs, approximately 28.3% expressed concerns about potential adverse effects, highlighting the importance of effective counselling and patient education during PrEP delivery [18]. In addition, misconceptions about PrEP, limited awareness of its preventive benefits, and distrust of newly introduced biomedical interventions contributed to low interest in PrEP uptake, particularly among MSM, where lack of interest was reported by 37.1% of respondents [17].

Conversely, several facilitators were consistently associated with increased willingness to use PrEP. Increased HIV risk awareness, particularly following peer education, community sensitization, or exposure to HIV infection within social networks, was associated with greater acceptance of HIV prevention services [14, 23]. Studies evaluating preferences for LAI-PrEP further suggested that many participants perceived injectable formulations as more convenient than daily oral medication. Among Nigerian MSM, approximately

73% expressed a preference for injectable PrEP over daily oral PrEP when cost and accessibility were comparable [18, 25-27]. Although these findings primarily relate to CAB-LA rather than lenacapavir, they suggest that reduced dosing frequency may improve acceptability among populations that experience challenges adhering to daily oral regimens. Overall, the evidence indicates that individual-level barriers extend beyond medication characteristics alone and reflect broader issues related to HIV risk perception, health literacy, and confidence in preventive interventions. These findings underscore the need for tailored educational strategies and culturally appropriate counselling to support informed decision-making during the implementation of LAI-PrEP in Nigeria.

INTERPERSONAL AND COMMUNITY-LEVEL BARRIERS AND FACILITATORS

The included studies consistently demonstrated that interpersonal relationships and community contexts substantially influence PrEP uptake among KPs. Stigma was the most consistently reported barrier, being identified in six of the eight included studies [13, 16-18, 25, 26]. Stigma and poor awareness of HIV service providers were key interpersonal barriers to HIV prevention service uptake among Nigerian KPs. In contrast, the high uptake of HIV self-testing (95.9%) suggests that confidential, user-centred approaches may facilitate acceptance of LAI-PrEP. Geographic differences in willingness to access services and variations according to sexual practices further indicate that community context and social norms influence engagement with HIV prevention services [16]. Experiences of anticipated, perceived, and enacted stigma discouraged engagement with HIV prevention services and contributed to concerns regarding confidentiality, discrimination, and involuntary disclosure of HIV risk behaviours [17, 25, 27]. Lack of access, fear of side effects, lack of

interest, and low risk perception limited opportunities to access HIV prevention services [13]. These findings illustrate how interpersonal relationships and broader community norms interact to influence healthcare-seeking behaviour.

Despite these barriers, several community-level facilitators were consistently reported. Peer-led education and community engagement were reported as facilitators in four studies [14, 17, 23, 26]. Peer-led education, community outreach, and KP-friendly counselling services were associated with greater awareness, improved trust in healthcare providers, and increased willingness to access PrEP [17]. Integration of HIV prevention into existing harm-reduction programmes for PWID and community-based outreach programmes for FSWs further enhanced service acceptability by delivering care through trusted community structures [14]. Collectively, these findings suggest that interventions developed in partnership with KP communities may be more effective than facility-based approaches alone in improving PrEP uptake. In addition, findings suggest that community-led education, peer navigation, stigma reduction interventions, and confidential service delivery models could facilitate the future uptake of LAI-PrEP such as lenacapavir.

STRUCTURAL AND HEALTH SYSTEM BARRIERS AND FACILITATORS

Structural and health system barriers represented the most consistently reported obstacles to PrEP implementation across the included studies. Transportation costs and geographical barriers were reported in three studies [13, 15, 26]. Limited geographical access to services, transportation costs, long waiting times, inconsistent commodity availability, and interruptions in medicine supply were frequently identified as barriers to both PrEP initiation and continuation [13]. These challenges were further exacerbated by dependence on donor-funded HIV programmes, with recent funding reductions substantially affecting service availability and continuity [15]. Provider stigma or bias was reported in four studies as a significant barrier to PrEP uptake [16, 18, 26, 27]. Healthcare provider factors also influenced service utilization. Several studies reported that provider stigma, limited knowledge of KP-specific healthcare needs, and inadequate training reduced the quality and acceptability of HIV prevention services [26]. In addition, structural barriers included limited access to comprehensive HIV prevention services and inadequate knowledge of available service providers. Although PrEP uptake reached 68.0%, strengthening integrated, accessible, and stigma-free health services remains essential to improve uptake of LAI-PrEP [16]. These findings demonstrate that health system readiness remains a critical determinant of successful implementation of both existing and emerging HIV

prevention interventions. The findings suggest that strengthening integrated HIV prevention programmes, expanding service delivery points, improving provider visibility, and ensuring non-discriminatory healthcare environments are essential health system facilitators. These system-level improvements would likely support successful implementation and equitable access to LAI-PrEP formulations, including lenacapavir.

Several structural facilitators were identified that may strengthen future implementation efforts. Differentiated service delivery models were identified as facilitators in five studies [14, 17, 18, 26, 27], including community pharmacies, one-stop centres, mobile outreach services, and community-based delivery platforms were associated with improved accessibility and acceptability of HIV prevention services among KPs [26]. Task-sharing with nurses and community health workers was also identified as a practical strategy for expanding service coverage, particularly in resource-constrained settings. Although few studies directly evaluated LAI-PrEP, these service delivery approaches may provide an appropriate foundation for future implementation of injectable HIV prevention strategies. The frequency of reported barriers and facilitators to HIV pre-exposure prophylaxis uptake among key populations in Nigeria is presented in Table 4.

DISCUSSION

This systematic review synthesized available evidence on barriers and facilitators influencing HIV PrEP uptake among key populations (KPs) in Nigeria and examined how these findings may inform the future implementation of LAI-PrEP, including lenacapavir [13, 14, 16-18, 23, 25-27]. None of the included studies directly evaluated lenacapavir implementation or uptake. Instead, the evidence was derived predominantly from oral PrEP programmes, supplemented by emerging evidence on cabotegravir long-acting (CAB-LA). Consequently, the introduction of an efficacious biomedical intervention alone is unlikely to achieve meaningful population-level impact without parallel investments in health system strengthening and equitable service delivery. The implications presented in this review should be interpreted as implementation insights rather than direct evidence of lenacapavir uptake or effectiveness within Nigerian healthcare settings. The findings demonstrate that barriers to PrEP uptake are multidimensional, extending beyond medication characteristics to encompass behavioural, social, legal, and health system determinants.

Although the Socio-Ecological Model provided an appropriate framework for organizing multilevel barriers and facilitators identified in the included studies, future implementation research evaluating LAI-PrEP may benefit from applying implementation science

TABLE 4 - Frequency of Reported Barriers and Facilitators

S/N	Theme	Number of studies reporting
1	Stigma and discrimination	6
2	Low HIV risk perception	4
3	Provider bias	4
4	Fear of adverse effects	4
5	Criminalization	3
6	Transportation costs	3
7	Commodity shortages	3
8	Peer-led education	4
9	Differentiated service delivery	5
10	Community-based services	5
11	Preference for injectable PrEP	3

frameworks such as the Consolidated Framework for Implementation Research (CFIR) or RE-AIM. These frameworks may facilitate more detailed evaluation of organizational readiness, implementation processes, intervention characteristics, and sustainability during future rollout of lenacapavir within routine healthcare systems.

INTERPRETATION OF THE FINDINGS IN THE CONTEXT OF EXISTING EVIDENCE

The PURPOSE clinical trials revealed that lenacapavir provides near-complete protection against HIV acquisition under controlled trial conditions [7, 8]. However, these findings should not be interpreted as evidence of successful implementation within routine healthcare systems in Nigeria. Participants enrolled in clinical trials generally receive intensive follow-up, adherence support, and uninterrupted access to healthcare services, conditions that differ considerably from those experienced by many Nigerian KPs. The consistently low continuation rates reported for oral PrEP programmes in Nigeria, including the 11.5% six-month continuation rate observed among more than 43,000 KP initiators, illustrate that implementation challenges frequently outweigh biomedical efficacy in determining real-world programme success [14]. The present review further revealed that many barriers identified during oral PrEP implementation are unlikely to disappear solely because a long-acting injectable formulation becomes available. Low HIV risk perception, misconceptions regarding PrEP, concerns about adverse effects, stigma, and criminalization were consistently reported across the included studies [13, 16-18]. While less frequent dosing may reduce some adherence-related challenges associated with daily oral medication, there is currently insufficient empirical evidence to conclude that lenacapavir alone

will overcome deeply rooted social and structural barriers. The evidence synthesized in this review suggests that successful future implementation of lenacapavir will likely depend on comprehensive strategies that combine biomedical innovation with community engagement, provider training, and supportive public health policies.

The significant finding of this review is the consistent preference for LAI-PrEP reported among several KP groups, particularly MSM [18, 34-36]. Participants frequently perceived injectable formulations as more convenient, more discreet, and easier to incorporate into daily life than oral PrEP. Although these findings are encouraging, they should be interpreted cautiously because they are based primarily on studies evaluating CAB-LA rather than lenacapavir. Differences in dosing schedules, service delivery requirements, medication costs, and implementation logistics may influence acceptability following wider deployment of lenacapavir. Consequently, direct extrapolation of CAB-LA findings to lenacapavir should be considered hypothesis-generating rather than conclusive, reinforcing the need for prospective implementation research in Nigerian settings.

IMPLICATIONS FOR HEALTH SYSTEMS AND EMERGENCY MEDICINE

The review highlights the central role of health systems in determining equitable access to HIV prevention. Structural barriers including limited service availability, transportation costs, provider stigma, workforce constraints, and dependence on external donor funding were among the most consistently reported challenges across the included studies [13, 15, 26]. These findings suggest that introducing lenacapavir into existing service delivery models without simultaneously strengthening health system

capacity may limit its potential public health impact. The findings are also relevant to emergency medicine. Emergency departments frequently provide care to individuals presenting with sexually transmitted infections, sexual assault, substance use disorders, and other conditions associated with elevated HIV acquisition risk.

For many underserved individuals, particularly members of KPs who experience stigma or limited engagement with routine healthcare services, emergency departments may represent one of the few points of contact with the health system. Incorporating HIV risk assessment, opportunistic HIV screening, brief prevention counselling, and referral pathways for oral or LAI-PrEP within emergency care may therefore strengthen linkage to prevention services. Although none of the included studies specifically evaluated emergency department-based PrEP delivery, emergency care settings may represent an additional opportunity for identifying individuals at substantial HIV risk and facilitating referral to HIV prevention services. This potential application should be regarded as a future implementation consideration rather than a finding of the present review and warrants evaluation through prospective implementation research.

TRANSFERABILITY OF EVIDENCE TO LENACAPAVIR

A key finding of this review is the limited direct evidence on lenacapavir implementation. Consequently, most conclusions are derived from oral PrEP and CAB-LA studies. While these provide useful insights into patterns of acceptability and service delivery challenges, important differences exist. Lenacapavir differs in dosing frequency (6-monthly vs monthly or daily), delivery requirements, pharmacological profile, and health system integration needs. Therefore, transferability of findings should be interpreted cautiously. This review suggests that while long-acting formulations may improve convenience, they are unlikely to overcome structural barriers such as stigma, criminalization, and health system fragmentation without targeted implementation strategies.

A major finding of this review is the absence of direct evidence evaluating lenacapavir implementation among Nigerian key populations. Consequently, the implementation implications presented throughout this review are inferred from oral PrEP programmes and emerging evidence on CAB-LA. While these interventions share the common objective of HIV prevention, differences in dosing frequency, administration route, health system requirements, and patient preferences mean that implementation experiences with CAB-LA cannot be assumed to translate directly to lenacapavir. Therefore, the findings should be interpreted as informing future implementation planning rather than predicting implementation outcomes.

Although cabotegravir and lenacapavir are both long-acting injectable PrEP agents, important implementation differences should be recognized. Cabotegravir is administered as an intramuscular injection every two months, whereas lenacapavir is administered as a subcutaneous injection every six months. These differences may influence patient preferences, clinic attendance requirements, workforce training needs, commodity logistics, cold-chain requirements where applicable, monitoring schedules, and programme costs. Consequently, implementation experiences with CAB-LA should be viewed as informative but not directly transferable to lenacapavir, reinforcing the need for prospective implementation research within Nigerian healthcare settings.

HEALTH EQUITY AND SYSTEM-LEVEL IMPLICATIONS

The findings reinforce that HIV prevention inequities are structurally driven. Key populations continue to experience intersecting vulnerabilities shaped by stigma, criminalization, and healthcare exclusion. Without deliberate equity-focused implementation strategies, there is a risk that lenacapavir rollout may reproduce existing disparities observed in oral PrEP programmes, where uptake remains lowest among the most marginalized groups. Ensuring equitable access will require integrating biomedical innovation with legal reform, community-led programming, and sustained health system investment.

STRENGTHS AND LIMITATIONS OF THE STUDY

This systematic review has several strengths. It followed the PRISMA 2020 reporting guideline and employed a comprehensive search strategy across multiple bibliographic databases, publisher platforms, and grey literature sources to identify relevant evidence. Methodological quality was assessed using the Mixed Methods Appraisal Tool (MMAT), and evidence from qualitative, quantitative, and mixed-methods studies was synthesized to provide a comprehensive understanding of multilevel factors influencing HIV PrEP uptake among key populations in Nigeria. By examining evidence from oral PrEP programmes alongside emerging studies of long-acting injectable PrEP, this review provides timely implementation insights relevant to the future introduction of lenacapavir in Nigeria.

Nevertheless, several limitations should be considered. First, none of the included studies directly evaluated the implementation or uptake of lenacapavir among Nigerian key populations. Consequently, conclusions regarding lenacapavir are inferred primarily from oral PrEP programmes and emerging evidence on cabotegravir long-acting, and should therefore be interpreted cautiously. Second, the relatively small number of eligible studies and their methodological heterogeneity precluded quantitative meta-analysis. Third, many included studies relied on self-reported

measures of PrEP awareness, acceptability, or uptake, introducing the possibility of recall and social desirability bias. Finally, most studies were conducted in urban or programme-supported settings, limiting the generalizability of findings to rural and underserved populations. Despite these limitations, the available evidence provides valuable insights to inform future implementation planning and research. Although the review focused on contemporary evidence (2020–2026), relevant studies published before 2020 may have been omitted. However, the selected timeframe was intended to capture evidence reflecting current PrEP implementation practices and the emergence of long-acting injectable HIV prevention strategies. Accordingly, all implementation implications for lenacapavir presented in this review should be interpreted as hypothesis-generating rather than confirmatory.

RESEARCH GAPS

This review identified several important gaps in the current evidence base. Most notably, no included study directly evaluated the real-world implementation of lenacapavir among Nigerian key populations. Consequently, there is an urgent need for prospective implementation studies assessing the acceptability, feasibility, uptake, adherence, implementation effectiveness, safety, and long-term sustainability of twice-yearly injectable PrEP within routine healthcare settings. Further research should evaluate health system readiness, including workforce capacity, procurement systems, supply chain resilience, pharmacovigilance, financing mechanisms, and digital monitoring systems required to support equitable rollout of long-acting injectable PrEP.

Comparative studies examining oral PrEP, cabotegravir long-acting, and lenacapavir under routine programme conditions would also provide valuable evidence regarding patient preferences, persistence in care, and service delivery requirements. Additional implementation research is needed among rural communities, adolescents, transgender persons, people who inject drugs, and other underserved populations that remain underrepresented in the current literature. Economic evaluations examining cost-effectiveness, budget impact, and sustainability under different financing models will also be essential for informing national HIV prevention policy. Finally, future studies should incorporate established implementation science frameworks, such as the Consolidated Framework for Implementation Research (CFIR) or RE-AIM, to strengthen evaluation of implementation processes, organizational readiness, scalability, and long-term programme outcomes.

IMPLICATIONS FOR POLICY AND IMPLEMENTATION

The findings suggest that successful future implementation of lenacapavir in Nigeria will require

a comprehensive approach (e.g. policy, health system, and community levels), extending beyond the introduction of a new biomedical intervention. Across the included studies, barriers to PrEP uptake were consistently influenced by broader health system, legal, and social determinants, suggesting that implementation strategies should be integrated within existing HIV prevention programmes rather than delivered as stand-alone interventions [13, 15, 16]. Strengthening differentiated service delivery (DSD) models, expanding community-based HIV prevention services, improving provider competency in KP-sensitive care, and ensuring uninterrupted commodity availability may improve the accessibility and acceptability of LAI-PrEP among populations at greatest risk of HIV acquisition. The review also highlights the importance of integrating LAI-PrEP within existing healthcare platforms. Community pharmacies, one-stop centres, sexually transmitted infection (STI) clinics, harm-reduction programmes, family planning clinics, and primary healthcare facilities have all showcase potential to improve access to HIV prevention services among KPs [26, 27].

Emergency departments may also contribute to these efforts by identifying individuals at substantial HIV risk during acute healthcare encounters and facilitating referral to appropriate prevention services. Such integrated service delivery models may reduce missed opportunities for HIV prevention while strengthening continuity of care across healthcare settings. Although modelling studies suggest that generic formulations of lenacapavir may become cost-effective within resource-limited settings, affordability alone is unlikely to ensure equitable uptake [10]. Sustainable implementation will require coordinated investment in procurement systems, workforce training, supply chain management, pharmacovigilance, and programme monitoring. In addition, implementation strategies should prioritize populations with the highest HIV incidence while ensuring equitable access for rural communities, adolescents, and other underserved groups that have historically experienced barriers to HIV prevention services.

CONCLUSION

This systematic review synthesized evidence from oral PrEP programmes and emerging LAI-PrEP studies to identify barriers and facilitators influencing HIV PrEP uptake among key populations in Nigeria and to explore their implications for the future implementation of lenacapavir. The evidence indicates that individual, community, structural, and health system factors collectively influence PrEP uptake and are likely to shape future implementation of long-acting injectable PrEP. Although direct evidence on lenacapavir implementation is currently unavailable, differentiated

service delivery, community engagement, provider training, sustainable financing, and strengthened health systems represent key priorities for equitable implementation. Prospective implementation research will be essential to determine how these findings translate into routine practice and to maximize the public health impact of long-acting HIV prevention in Nigeria.

Future implementation research should also examine whether emergency departments and other acute care settings can serve as effective entry points for referral to long-acting HIV prevention services among underserved populations. Overall, the evidence synthesized in this review suggests that future implementation of lenacapavir in Nigeria will likely require coordinated efforts combining biomedical innovation with health system strengthening, community engagement, sustainable financing, and equitable service delivery. Because these conclusions are derived primarily from oral PrEP and CAB-LA evidence, prospective implementation studies are needed to confirm their applicability to lenacapavir within routine healthcare settings.

RECOMMENDATIONS

Based on the findings of this systematic review, the following evidence-informed recommendations are proposed:

1. Strengthen differentiated service delivery (DSD).
2. Enhance healthcare workforce capacity.
3. Integrate HIV prevention across healthcare settings.
4. Support community-led implementation.
5. Strengthen procurement and supply chains.
6. Improve health system readiness.
7. Promote equitable policy implementation.
8. Increase domestic investment/financing in HIV prevention.
9. Conduct implementation research.
10. Strengthen monitoring and evaluation systems.

These recommendations should be interpreted alongside the current evidence base, recognizing that additional implementation research will be required as experience with lenacapavir expands within Nigeria.

FUTURE DIRECTIONS

Future research should prioritize;

1. Real-world implementation of lenacapavir.
2. Health system readiness.
3. Cost-effectiveness.
4. Rural and underserved populations.
5. Comparative studies of oral PrEP, CAB-LA, and lenacapavir.

KEYWORDS

HIV PREVENTION; PRE-EXPOSURE PROPHYLAXIS; LONG-ACTING INJECTABLE PrEP; INJECTABLE PrEP; LENACAPAVIR; IMPLEMENTATION SCIENCE; KEY POPULATIONS; NIGERIA

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BMO: Manuscript editing, Reference formatting.

DECLARATIONS

CONFLICTS OF INTERESTS

The Authors declare that there is no conflict of interest.

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REGISTRATION

No registration applicable.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

Ethical approval for this study was not required.

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