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Evaluating the combined use of ARVs and PrEP: Potential impact and challenges in high-risk populations

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Abstract

Human immunodeficiency virus (HIV) remains a significant public health challenge globally. While antiretroviral therapy (ARVs) and pre-exposure prophylaxis (PrEP) are proven interventions for prevention and treatment, their integration is hindered by barriers such as poor adherence, stigma, economic constraints, and limited healthcare infrastructure. This study aimed to explore the challenges and opportunities associated with integrating ARVs and PrEP into HIV prevention strategies. This narrative literature review synthesised evidence from multiple peer-reviewed studies addressing adherence challenges, stigma, healthcare access, and the economic implications of ARVs and PrEP. Data sources included global and regional research focused on low and middle-income settings. Findings revealed that adherence remains a critical concern, influenced by side effects, pill burden, stigma, and psychosocial factors. Economic barriers and limited healthcare access reduce uptake, particularly in resource-limited contexts.

Nevertheless, evidence suggests that integrating ARVs and PrEP could significantly reduce HIV transmission rates and healthcare costs. Public awareness and targeted education are essential in overcoming stigma and improving adherence. Strengthening the integration of ARVs and PrEP into HIV prevention requires community-based education, enhanced healthcare infrastructure, and innovative financing mechanisms. Policy interventions should prioritise stigma reduction and support for adherence. Future research should focus on long-term adherence strategies, cost-effective distribution models, and mitigating drug resistance to maximise the effectiveness of ARVs and PrEP in combating HIV/AIDS.

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Introduction

Globally, HIV/AIDS has remained a major global health issue and continues to represent a significant health burden worldwide, with millions of new infections reported each year. Combining antiretroviral therapy (ARVs) and pre-exposure prophylaxis (PrEP) offers a dual approach to reducing transmission rates and improving health outcomes among high-risk populations. While ARVs effectively manage HIV among diagnosed individuals, PrEP serves as a preventive measure for uninfected individuals at significant risk .[1,2] Understanding the synergies and challenges of this integration is critical to informing public health policies and interventions that can enhance access, adherence, and overall effectiveness.

Despite the proven benefits of both ARVs and PrEP, their combined use poses logistical and clinical challenges. Adherence is crucial in determining their effectiveness, as inconsistent use can lead to reduced efficacy and potential drug resistance.[3] Additionally, cost and accessibility remain significant barriers, particularly in low-income regions where the HIV burden is highest. Many countries struggle with securing adequate funding to provide widespread access to both treatments, further exacerbating disparities in HIV prevention and management.

The stigma surrounding HIV prevention and treatment significantly hinders the widespread adoption of these interventions. Many individuals hesitate to seek PrEP due to misconceptions and the fear of being labelled as high-risk. In contrast, others find it challenging to maintain consistent ARV use due to concerns about side effects and pill burden.[4] Furthermore, social determinants of health, such as discrimination, lack of adequate education, and cultural beliefs, contribute to the limited reach of these life-saving treatments. Overcoming these social and medical barriers is crucial for maximising the effectiveness of combined ARV and PrEP use. In this context, the study aims to examine the challenges and opportunities inherent in the concurrent use of ARVs and PrEP for HIV prevention, with a focus on adherence, healthcare access, stigma, and economic impact.

Literature review

The integration of antiretrovirals (ARVs) and pre-exposure prophylaxis (PrEP) has been widely explored as a strategy to reduce HIV transmission and improve population health outcomes.[1,2] ARVs have transformed the prognosis for people living with HIV by suppressing viral replication and lowering morbidity and mortality. At the same time, PrEP has proven highly effective in preventing new infections among populations at risk.[1,2] At first glance, combining these two interventions appears to be a straightforward way to achieve greater epidemic control.[5] Yet the literature reveals that the real challenge lies not in their clinical efficacy, but in the complex social, structural, and economic realities that shape how people access, use, and adhere to these interventions in everyday life.

Adherence is central to this challenge.[3] Irregular use of ARVs or PrEP undermines their protective benefits and increases the risk of drug resistance. Research across Kenya, Uganda, Zimbabwe, and South Africa show that while PrEP is generally acceptable among young people and women planning or experiencing pregnancy, sustaining adherence over time remains difficult.[6-8] Similarly, ARV adherence among people living with HIV is strongly influenced by socioeconomic conditions, including poverty, mental health, and access to healthcare.[9] What emerges from the literature is a complex picture. While individual factors such as side effects and pill burden play a role, they are often outweighed by structural and social determinants. Supportive social networks, perceived vulnerability to HIV, and access to confidential, convenient services can dramatically improve adherence, illustrating that adherence is less a matter of individual willpower and more a product of social and systemic context.

Stigma compounds these challenges, operating

as a persistent barrier to both PrEP uptake and ARV retention.[4] Misconceptions that PrEP encourages risky sexual behaviour, alongside fears of being labelled high-risk, discourage individuals from seeking preventive care. In contrast, HIV-positive individuals often face discrimination that erodes their engagement with treatment.[4] Despite this, much of the literature treats stigma descriptively, cataloguing its presence rather than interrogating how it functions across different communities and settings. Synthesising the available evidence suggests that stigma operates on multiple levels: at the service level, through breaches of confidentiality and judgmental attitudes from providers; in the community, through moralised narratives around sexuality; and through legal and policy environments that fail to protect privacy or criminalise certain behaviours. However, research evaluating which strategies effectively reduce stigma, particularly at scale, remains scarce.

Economic and system-level constraints further limit the effectiveness of integrated ARV–PrEP programs in the real world.[10] In the regions with the highest HIV burden, inconsistent drug supply, under-resourced health systems, and heavy reliance on donor funding restrict both reach and continuity of services. Global initiatives have subsidised costs, but access remains uneven, particularly for marginalised populations.[11] Technological innovations, such as long-acting injectable formulations, hold promise for improving adherence. Still, their potential is constrained by costs, regulatory hurdles, and the need for functional service-delivery platforms, conditions that many low-resource settings have yet to meet.

The literature suggests that technological solutions alone, without attention to social and systemic barriers, will not achieve the desired population-level impact. Taken together, the evidence points to a clear conclusion: structural determinants, including stigma, service design, and financing, are the primary factors shaping the effectiveness of integrated ARV–PrEP strategies, while individual biomedical barriers are often secondary or mediated by these broader forces. Interventions that focus solely on individual behaviour without addressing these social and systemic conditions are unlikely to be sustainable. Three critical gaps remain: the lack of comparative studies evaluating the relative influence of structural versus individual factors across different high-risk groups; limited evidence on scalable, community based stigma reduction interventions; and scarce research on cost-effective, equitable, and sustainable delivery models. While ARVs and PrEP are clinically effective, the literature makes it clear that efficacy alone is not enough. For integrated interventions to achieve meaningful population-level impact, biomedical innovation must be paired with context-sensitive delivery models, stigma reduction strategies, and sustainable financing mechanisms. Addressing these structural and social barriers is essential not only for improving adherence but for ensuring that interventions reach those who need them most and for achieving lasting progress in HIV prevention.

Synthesising the evidence reveals a clear pattern: structural determinants, including stigma, service design, and financing, emerge as the primary factors shaping real-world effectiveness of integrated ARV–PrEP strategies, while individual biomedical barriers are often secondary or mediated by these broader forces. Interventions targeting only individual behaviour, without addressing these systemic factors, are unlikely to produce sustainable outcomes. Critical gaps remain: a lack of comparative studies examining the relative influence of structural versus individual factors across high-risk populations; limited evidence on scalable stigma-reduction interventions; and scarce research on cost-effective, equitable, and sustainable delivery models.

The study aimed to explore how structural, social, and individual factors influence the uptake and sustained use of ARVs and PrEP among high-risk populations. Specifically, the study sought to identify the key determinants

of adherence and access, examine the influence of stigma and service-delivery barriers, and generate insights to inform strategies that enhance the effectiveness of integrated HIV prevention interventions.

Theoretical framework

This study was based on the Theory of Planned Behaviour (TPB), which explains how individual attitudes, subjective norms, and perceived behavioural control influence health-related decision-making.[12] TPB was particularly relevant in understanding the factors affecting adherence to ARVs and PrEP, as individuals' decisions to initiate and maintain these treatments were shaped by their beliefs about the benefits, societal pressures, and perceived ease or difficulty of adherence. The Social Ecological Model (SEM) highlights that PrEP and ARV uptake and adherence are shaped by individual, social, structural, and policy-level factors, underscoring the need for interventions that simultaneously address personal behaviour, community norms, healthcare system barriers, and broader policy contexts.[13] The SEM and TPB comparison highlights the multi-level influences on ARVs and PrEP use. While the SEM examines structural and social determinants at multiple levels, the TPB concentrates on individual decision-making factors, including attitudes, subjective norms, and perceived behavioural control.[2] Combining these frameworks provides a more holistic understanding of the barriers and facilitators influencing HIV prevention efforts, which can be achieved, as shown in Table 1.

Table 1. Comparison of the SEM and TPB in ARVs and PrEP use

SEM level	TPB construct	Integration / How they complement
Individual	Attitudes	Personal beliefs and knowledge (SEM) shape attitudes and perceived benefits (TPB), influencing willingness to use ARVs/PrEP.
Interpersonal	Subjective Norms	Family, peers, and partners (SEM) affect social pressures and perceived expectations (TPB), guiding intention and uptake.
Community	Perceived Behavioural Control	Community norms, stigma, and access (SEM) influence perceived ability to act (TPB), affecting adherence and engagement.
Organisational	Behavioural Intentions	Support from healthcare institutions (SEM) facilitates behavioural intentions (TPB) by improving accessibility and affordability.
Policy	External Influences	Policies and campaigns (SEM) shape the environment, indirectly affecting attitudes, norms, and perceived control (TPB), reinforcing uptake.

Research method

This study employed a narrative literature review to examine the challenges associated with implementing ARV and PrEP interventions for HIV prevention. A systematic search was conducted in PubMed, Scopus, Web of Science, and Google Scholar, focusing on peer-reviewed studies published between 2015 and 2025. The review targeted studies on adult populations, with particular attention to high-risk groups such as men who have sex with men (MSM), sex workers, and serodiscordant couples, especially in sub-Saharan Africa. Key search terms included “HIV prevention,” “ARVs,” “PrEP,” “adherence,” “uptake,” “stigma,” and “healthcare access,” enabling the identification of studies addressing both individual and structural determinants of intervention effectiveness.

Although the review prioritised contemporary

evidence, seminal theoretical works were deliberately included to provide historical and conceptual grounding. Foundational studies, such as Ajzen's theory of planned behaviour and Bronfenbrenner's ecological systems theory, offered critical frameworks for understanding how social, environmental, and individual factors interact to influence health behaviours.[12,13] Integrating these theoretical perspectives alongside empirical findings allowed the study to move beyond mere description of barriers and facilitators, enabling a more complex analysis of the mechanisms shaping ARV and PrEP uptake. This approach addresses a standard limitation in the field, where studies often report isolated findings without connecting them to broader behavioural or social theories.

The literature reviewed spans multiple periods, each contributing distinct insights. Early foundational studies (1979–1991) established theoretical models of health-related behaviours that continue to inform contemporary intervention design. Research from 2000–2010 explored stigma and adherence in the context of ART, revealing systemic and psychosocial barriers that persist today. Mid-period studies (2011–2020) examined the implementation of PrEP and ARV prophylaxis, including interventions targeting stigma reduction, while more recent literature (2021–2025) has focused on PrEP uptake, long-acting ART formulations, and barriers to HIV care in African contexts. Critically synthesising these findings revealed patterns across time: stigma, discrimination, and structural inequalities consistently impede adherence, while supportive social networks, confidentiality, and accessible services facilitate sustained engagement.[14-20]

The narrative review method was particularly suitable for this study because it enabled the integration of diverse evidence sources, including empirical research and theoretical frameworks, to identify overarching themes and knowledge gaps. Synthesising the literature in this way not only highlighted recurring barriers such as stigma, healthcare access, and systemic limitations but also illuminated where evidence remains sparse, including scalable interventions to reduce stigma and strategies to improve equitable access.[21] This method, therefore, enabled a critical examination of the interplay between social, structural, and individual determinants, moving beyond descriptive reporting to provide actionable insights for enhancing ARV and PrEP implementation.

Challenges and opportunities in the implementation of ARVs and PrEP

Adherence and its impact on efficacy

Adherence to ART and PrEP is influenced by a complex web of interrelated factors that operate across multiple levels, highlighting the need to understand not only individual behaviour but also the social and structural contexts in which treatment occurs. At the individual level, adherence is shaped by knowledge, beliefs, and perceptions of the medications, as well as practical considerations such as pill burden and side effects (e.g., gastrointestinal discomfort, nausea, fatigue).[22-24] Patients who understand the mechanism of action, appreciate the importance of consistent use, and are prepared to manage side effects are more likely to maintain adherence. In contrast, those facing poorly managed side effects or complex regimens are at higher risk of discontinuation.

Moving to the interpersonal level, social support, peer influence, and patient-provider relationships critically affect adherence behaviours. Patients with strong support networks and effective communication with healthcare providers demonstrate higher adherence, while social isolation or negative peer norms can reinforce non-adherence.

At the community level, stigma, cultural norms, and local health-seeking behaviours further complicate adherence. Fear of being perceived as HIV-positive may discourage uptake of PrEP or disclosure of ART use, while entrenched societal biases exacerbate barriers even for

patients with optimal clinical support. Community dynamics also mediate the effectiveness of educational and counselling interventions, indicating that adherence strategies cannot be purely individual-focused.

Structural determinants, including healthcare infrastructure, funding mechanisms, access to clinics, and policy environments, directly constrain or enable adherence.[10,20,26-30] For example, shortages of trained personnel, inadequate facilities, and reliance on donor funding in LMICs can disrupt medication supply chains, creating gaps in treatment continuity. Conversely, robust infrastructure and sustained financing support consistent access, monitoring, and long-term engagement with ART and PrEP programs.

Healthcare access and infrastructure

Healthcare access and infrastructure are critical factors influencing the effectiveness of ART and PrEP in both urban and rural settings. While high-income countries have successfully integrated these HIV prevention and treatment strategies into their healthcare systems, many resource-limited regions continue to face significant challenges. Rural areas often lack healthcare infrastructure, including insufficient healthcare facilities, limited access to trained medical professionals, and inadequate transportation networks for patients to access treatment.[20,26] This geographic disparity in healthcare access exacerbates the difficulty of providing continuous and reliable access to ART and PrEP, which are essential for HIV prevention and management. Urban areas, by contrast, typically have better healthcare infrastructure, though they face challenges, particularly with overcrowded clinics and healthcare staff shortages.[26,27]

The dependency of many low- and middle-income countries (LMICs) on donor funding has created additional challenges, particularly considering shifting global financial support. For example, a considerable portion of HIV-related financing in these regions comes from international organisations and foreign governments, including those from high-income countries. However, the 2025 freeze on foreign aid, primarily affecting global health programs, severely disrupted funding for ART and PrEP initiatives.[10] This freeze led to cuts in essential programs aimed at HIV prevention and treatment, leaving many countries struggling to maintain their healthcare services and meet the growing demand for ART and PrEP.[28] These funding cuts have further exacerbated the gaps in healthcare access and continued access to treatment, particularly in rural areas where services are already limited.

The reduction in funding, particularly for HIV-related programs, highlights the vulnerability of healthcare systems in LMICs that rely heavily on external financial support. The inability to secure continuous funding for ARVs and PrEP can result in stockouts, disrupted treatment regimens, and reduced quality of care.[26] Additionally, these financial constraints limit the ability to expand healthcare infrastructure, such as building new clinics or providing additional training for healthcare workers. This is crucial to ensure sustained access to HIV care.[27] With the global shift in funding priorities, many LMICs are forced to rely on increasingly limited resources, further exacerbating the disparities in healthcare access between urban and rural areas.

Moreover, the lack of funding for clinical trials in LMICs presents a significant limitation to advancing knowledge in ART and PrEP. The discovery of new formulations, alternative delivery models, and innovative treatment options that could enhance adherence and efficacy can be impeded by a lack of investment in research and development. Clinical trials are crucial for understanding these therapies' long-term impact and identifying strategies to overcome existing barriers.[29] Without adequate funding for such trials, the pace of innovation slows, and the ability to address emerging challenges in HIV prevention and treatment diminishes.[22] Investing in healthcare infrastructure and sustainable financing models that do not rely solely on external donors is essential to address these challenges.

Strategies to ensure equitable access to ART and PrEP should focus on improving healthcare delivery in rural areas, reducing geographical barriers, and building local capacity to maintain these programs.[10] Simultaneously, augmenting domestic funding and fostering robust collaborations between international organisations and governments in low- and middle-income countries can alleviate the effects of funding reductions and enhance the long-term viability of HIV prevention and treatment initiatives.[28]

Stigmatisation and social barriers

The HIV-related stigma continues to represent a significant barrier to the uptake of ARVs and PrEP, particularly among key populations such as sex workers, men who have sex with men, and serodiscordant couples. Concerns about being mistakenly perceived as HIV-positive contribute to reluctance in seeking PrEP, as individuals fear social exclusion, ostracization, and potential harm to personal and professional relationships. Evidence from multiple studies demonstrates that stigma and discrimination manifest across familial, community, and healthcare contexts adversely affect psychological well-being, adherence to treatment, and overall health behaviours, thereby diminishing quality of life. Importantly, research also highlights that interventions specifically designed to reduce HIV-related stigma can mitigate these adverse effects, enhancing health outcomes, fostering social support, and facilitating more equitable access to prevention and treatment services. This underscores the critical need for multilevel strategies that address stigma as both a social phenomenon and a determinant of public health effectiveness. [30-32] On the other hand, people living with HIV who are on effective ARV treatment continue to face significant stigma despite evidence that effective treatment reduces viral load and transmission risk.[33] This stigma, driven by misconceptions about HIV transmission and societal biases, contributes to the marginalisation of those who need these interventions the most.

The literature consistently identifies social stigma as a major impediment to the uptake and sustained use of ARVs and PrEP, as it diminishes individuals' willingness to seek care and compromises adherence to prescribed regimens, undermining the effectiveness of these essential interventions. Stigma within healthcare facilities has been shown to negatively impact patient diagnosis, treatment adherence, and overall health outcomes.[34] Although targeted interventions exist for conditions such as HIV, mental illness, and substance use, significant gaps remain, particularly regarding other medical conditions, multi-level staff engagement, the use of interactive technologies, and the stigma experienced by healthcare workers themselves, highlighting the need for comprehensive, systemic approaches to stigma reduction. While myriad studies highlight the negative impact of stigma on treatment uptake, the role of broader structural factors, such as economic inequality, legal frameworks, and cultural norms, has received less attention. These factors exacerbate stigma and limit access to care, especially in low-resource settings. For instance, individuals in impoverished or criminalised communities may face even greater barriers to care due to legal restrictions, poverty, and lack of healthcare infrastructure.[35] Additionally, while some studies have called for more widespread community-based education, there is insufficient emphasis on the need for comprehensive policy changes that could create safer environments for individuals seeking HIV prevention and treatment.[36]

An essential gap identified in the literature is the lack of long-term studies examining the impact of stigma-reduction interventions on the adoption of ARVs and PrEP. While community-based education and awareness campaigns are frequently recommended, limited empirical evidence demonstrates their effectiveness in reducing stigma over time.[37] Moreover, the scope of these programs often fails to account for the deep-rooted cultural attitudes and misconceptions perpetuating stigma. These programs must be tailored to local contexts, considering the specific cultural,

social, and economic barriers at-risk populations face. Additionally, while there is a growing body of research on healthcare providers' role in perpetuating stigma, more work is needed to explore how to train healthcare professionals better and empower them to provide non-judgmental, supportive care.[14, 38]

An opportunity exists to integrate stigma-reduction strategies into broader HIV prevention and care policies at both national and global levels. Governments and organisations should prioritise funding for comprehensive stigma-reduction initiatives encompassing community education, healthcare provider training, public policy advocacy, and legal reforms. Further research is needed to identify the most effective combinations of interventions to reduce stigma and improve PrEP and ARV uptake.[36] Additionally, interventions must go beyond reducing stigma within healthcare settings, addressing societal attitudes and the cultural dynamics that contribute to the marginalisation of at-risk populations.

A more integrated approach could include social media campaigns, peer-led education, and the involvement of influential community figures to challenge misconceptions and promote supportive attitudes toward HIV treatment and prevention. While there has been progress in recognising and addressing stigma as a barrier to HIV treatment and prevention, several gaps remain in terms of understanding its long-term impact and developing comprehensive, context-specific strategies for its reduction.

Economic impact

The combined use of ARVs and PrEP has the potential to yield substantial economic benefits. By significantly reducing new HIV infections, ART and PrEP can alleviate the financial burden on healthcare systems. Countries that have effectively implemented these programs have witnessed notable declines in new infections, demonstrating the potential cost savings.[26,39] The socioeconomic benefits of expanding access to ART and Prep include reduced healthcare costs, increased workforce productivity, and improved quality of life for those affected by HIV. However, challenges remain regarding the affordability and accessibility of these medications, particularly in low- and middle-income countries. Several studies have examined the economic benefits and combined use of ARVs and Prep. Expanding ART coverage to individuals in the early stages of HIV is more cost-effective than current guidelines, and targeted PrEP provision for high-risk populations in South Africa can yield cost savings.[27] This study highlights the potential cost savings for healthcare systems and significant socioeconomic advantages, including enhanced quality of life. Similarly, reducing HIV infections through the use of PrEP and ARVs in South Africa has been shown to lower healthcare costs and generate significant economic benefits, particularly by enhancing workforce productivity.[40] Furthermore, evidence from Lesotho indicates that widespread use of PrEP and ARVs among high-risk populations can generate economic savings by decreasing HIV-related health complications and enhancing workforce participation.[41]

Despite the clear economic benefits of ARVs and PrEP, significant challenges remain. High upfront costs, infrastructure needs, and ongoing adherence monitoring can strain health budgets, particularly in low-resource settings. Trade-offs exist between short-term investment and long-term savings, and the literature shows conflicting estimates of cost-effectiveness across populations and contexts. Blended funding models, combining domestic budgets, international aid, and outcome-based incentives, offer viable solutions to support sustainable and equitable access.

The combined use of ARVs and PrEP offers several economic benefits, such as reducing HIV transmission, lowering long-term healthcare costs, and improving workforce productivity. By preventing new HIV infections, PrEP helps reduce the number of people requiring ARV

treatment, saving healthcare expenses.[26, 39] It also serves as a cost-effective prevention strategy, promoting better health outcomes, life expectancy, and quality of life.[40]

Additionally, it empowers at-risk groups, such as sex workers, by keeping them healthy and productive, thereby improving their economic standing.[41] However, these benefits come with economic challenges, including high upfront medication costs (Table 2 below), healthcare personnel, and infrastructure.[39] Funding sustainability remains a concern, particularly in low-resource settings that rely heavily on international aid.[26] Ongoing adherence and monitoring requirements add to healthcare expenses, while stigma and discrimination can hinder PrEP uptake, leading to indirect costs like lost productivity.[40] Furthermore, inequality in access to ARVs and PrEP due to economic disparities may result in uneven health outcomes, and the high cost of medications remains a barrier.[41] Lastly, the potential for misuse of these treatments could lead to drug resistance or unnecessary costs, further complicating the economic landscape, Table 2.

Table 2. Economic benefits and challenges of combined use of ARVs and PrEP

Economic benefits	Economic challenges
Reduction in HIV transmission	**High upfront costs**
Preventing HIV infections through PrEP reduces the long-term costs associated with treating HIV.	Substantial initial costs for medications, healthcare personnel, and infrastructure.
Lower HIV-related healthcare costs	**Sustainability off funding**
PrEP reduces new HIV cases, minimising long-term treatment costs for ARV users.	Ongoing funding is required, especially in low-resource settings dependent on international aid.
Improved Workforce Productivity	**Adherence and monitoring costs**
Preventing new HIV infections helps maintain a healthier workforce, boosting economic productivity.	Regular health check-ups, HIV testing, and adherence monitoring add to the healthcare costs.
Cost-effective prevention strategy	**Stigma and discrimination**
PrEP is a cost-effective method to prevent HIV, reducing future medical expenses associated with treatment.	The stigma surrounding HIV and PrEP can decrease uptake, leading to indirect costs such as lost productivity.
Improved life expectancy and quality of life	**Inequality in access**
Using ARVs and PrEP improves health outcomes, reducing overall healthcare burdens.	Economic disparities may limit access to ARVs and PrEP, contributing to uneven health outcomes and higher costs in some regions.
Economic empowerment of at-risk groups	**Pharmaceutical costs**
People at risk (e.g., sex workers) can remain healthy and productive, improving their economic situation.	Costs of ARV and PrEP medications remain high, especially in areas without subsidies or low-cost alternatives.
	Potential for misuse
	Incorrect use or over-prescription of ARVs and PrEP may lead to drug resistance or unnecessary costs.

Drug resistance and long-term sustainability

The simultaneous use of ARVs and PrEP raises concerns about the risk of drug resistance, particularly when either medication is taken inconsistently. Several factors related to ARVs and PrEP raise concerns about the risk of drug resistance, particularly when either medication is taken inconsistently, as depicted in Figure 2 below. Resistance to these drugs could undermine both treatment and prevention efforts, making it critical to develop strategies that ensure adherence and minimise the emergence of resistant HIV strains.[42] Monitoring for drug resistance and developing smaller pill formulations and alternative delivery models are essential to sustain the effectiveness of both ARVs and PrEP in the

long term.[29] Ongoing research is needed to understand the long-term effects and sustainability of dual therapy, Figure 1.

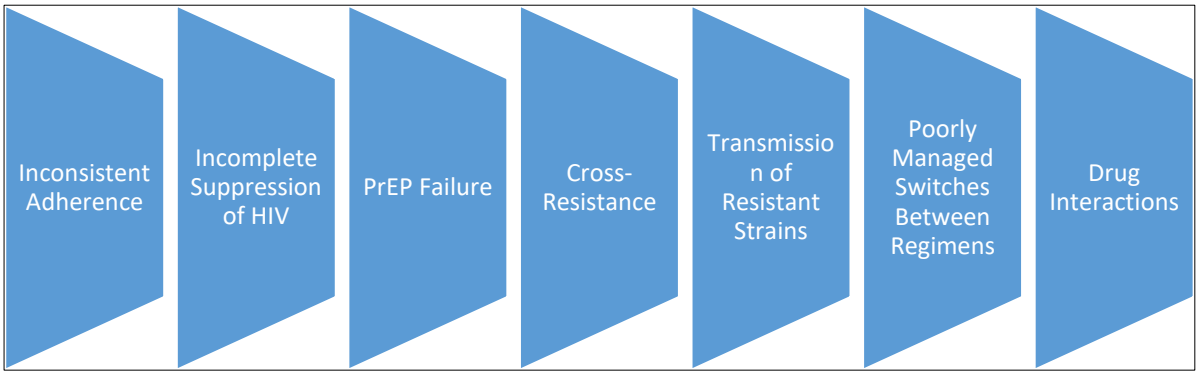

Figure 2: Factors increasing drug resistance risk with ARVs and PrEP

Key findings and discussion

The Adherence Paradox

Adherence to ART and PrEP is shaped by a complex interplay of individual, social, and structural factors. While pill burden and side effects influence individual behaviour, evidence shows that patients who understand how their medication works, the importance of consistent use, and the consequences of non-adherence are more likely to follow their regimens.[24] High-risk populations face additional challenges where misconceptions, stigma, and limited healthcare literacy reduce engagement.[24] Structural barriers, including restricted access to healthcare facilities, shortages of trained personnel, and reliance on donor funding, further complicate adherence, particularly in rural areas of LMICs.[20,26-28,39] Urban centres, although better resourced, still contend with overcrowded clinics and staff shortages, creating gaps in patient monitoring and continuity of care.[26,27] These findings suggest that adherence cannot be treated as an isolated behaviour; it emerges from a dynamic network of clinical, social, and systemic determinants. Evidence varies in strength, with some studies quantifying structural impacts and others relying on qualitative patient reports, highlighting the need for integrated, multi-method approaches.

The false economy of underfunding

Economic analyses indicate that combining ART and PrEP yields substantial long-term savings by preventing new infections, reducing chronic care costs, enhancing workforce productivity, and improving quality of life.[26,39,40,41] Targeted PrEP provision for high-risk populations and early ART initiation have demonstrated measurable cost benefits, particularly in South Africa.[27] Yet short-term funding limitations, especially in donor-dependent LMICs, create vulnerabilities. Disruptions in international support, such as the U.S. freeze on foreign aid in early 2025, have led to stockouts and disrupted treatment regimens, paradoxically generating long-term economic and health burdens by increasing transmission and complicating treatment.[10,28] Adherence monitoring, infrastructure development, and personnel training. However, costly upfront, they are economically justified when considering the avoidance of downstream healthcare burdens.[26,28,40] Blended funding models that integrate domestic financing, international aid, and performance-based incentives offer a pragmatic path to sustainable, equitable access, though evidence of their long-term effectiveness remains limited.[26, 28]

Stigma as a unifying barrier

Stigma constitutes a primary barrier to ART and PrEP uptake, directly undermining public health investments[30-32] It affects diverse populations, including sex workers, men who have sex with men, and serodiscordant couples. Individuals may avoid PrEP due to fear of being perceived

as HIV-positive, while persistent societal biases hinder ART adherence even when viral suppression is achieved.[33] Interventions such as community education, healthcare provider training, and policy advocacy show promise in reducing stigma.[34,35,37,38] Yet, they often fail to address structural and cultural factors poverty, criminalisation, and entrenched social norms that perpetuate exclusion.[34,25,36-38] Moreover, the long-term efficacy of stigma-reduction programs remains poorly understood, highlighting the need for sustained, context-specific strategies that integrate societal attitudes, healthcare practices, and supportive policies.

Resistance and clinical implications

Concurrent use of ART and PrEP raises concerns about drug resistance, particularly under inconsistent adherence.[42] Resistance can compromise both treatment and prevention efforts, emphasising the need for adherence strategies, smaller pill formulations, and alternative delivery models.[29] While existing studies provide valuable insights, long-term data on resistance patterns and the efficacy of combined therapy remain scarce, underscoring the need for longitudinal research to inform clinical and public health interventions.

Study limitations and future research

This study has several limitations that may affect interpretation and generalisability. Variations in study quality and context-specific findings, including conflicting evidence on adherence, stigma, and economic outcomes, limit the applicability of results across populations. Additionally, the sample may not fully represent diverse populations or contexts, determining the relevance of the findings to broader settings. The study relied primarily on secondary data from the literature. It did not incorporate quantitative studies, which limits insight into subjective experiences, social dynamics, and the barriers influencing ARV and PrEP use. Moreover, the study's cross-sectional design limits the ability to assess long-term behavioural changes or causality between the variables. To address these limitations, future research should adopt a mixed-methods approach, combining quantitative surveys with qualitative interviews or focus groups to provide a richer, more holistic view of the factors influencing ARV and PrEP use. Expanding the sample to include diverse populations from varied geographical, social, and economic backgrounds would improve the generalizability of the findings. Furthermore, undertaking longitudinal studies would provide insights into the evolution of attitudes and behaviours towards ARVs and PrEP, facilitating a more thorough understanding of the long-term efficacy of these interventions.

Governments and healthcare providers should consider these research recommendations to design more tailored and effective HIV prevention strategies, ensuring that interventions are accessible and contextually appropriate for different populations.

Study recommendations

To enhance the effectiveness of ART and PrEP, future interventions must prioritise patient education and health literacy. Educating patients about the importance of adherence, the risks associated with non-compliance, and how their treatment works can improve long-term outcomes. Regular counselling and ongoing education tailored to high-risk populations, where stigma and misconceptions abound, should be emphasised to ensure continuous adherence. Additionally, healthcare access and infrastructure should be strengthened, particularly in resource-limited and rural areas, to reduce geographical barriers to treatment. Investments in healthcare infrastructure, sustainable financing, and local capacity-building are necessary to support ART and PrEP programs, reduce reliance on external aid, and ensure long-term program viability.

Addressing the stigma surrounding HIV treatment and prevention is another critical area for improvement. Initiatives aimed at reducing stigma within healthcare settings and society should be integrated into national and

global HIV policies. Developing culturally relevant, community-driven stigma-reduction strategies, alongside training healthcare providers to offer non-judgmental care, could significantly improve uptake and adherence. Furthermore, more research on the long-term impact of stigma-reduction interventions and on the broader structural factors that perpetuate stigma is needed to inform future strategies.

Economically, the combined use of ARVs and PrEP can yield substantial benefits by reducing HIV transmission, lowering healthcare costs, and improving workforce productivity. However, challenges such as high medication costs, funding sustainability, and access inequalities must be addressed. Policymakers should explore innovative funding models and enhance access to affordable medications, especially in low-resource settings. Monitoring for drug resistance and developing alternative delivery methods could also ensure the long-term sustainability of these treatments while minimising the risk of resistance and enhancing overall treatment efficacy.

Conclusion

This study offers important insights into the various factors that affect the use of ARVs and PrEP, highlighting key implications for enhancing HIV prevention strategies. The findings underscore the importance of considering structural factors (such as healthcare access and community support) and individual behaviours (including attitudes and perceived control) when designing interventions. Although the study's limitations highlight the need for further research, addressing these gaps in future studies will help refine HIV prevention strategies and ensure that public health initiatives are comprehensive and practical. Enhancing research methodologies and incorporating varied perspectives will foster a more inclusive and sustainable approach for addressing HIV/AIDS.

Author contribution

Conception, design, literature search, drafting, revision, final version to be published and accountable for all aspects of the work: MMW

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Supplementary material

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