

Supplementary Materials: SUPPLEMENTARY FILE S3: GLOBAL IMPLEMENTATION

Supplementary File S3

Global Implementation

Policy

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Supplementary File S3: Global Implementation Considerations

This supplementary file expands on global implementation complexities referenced in Section 3.6 of the main manuscript. The bridge period barrier is not unique to the United States but represents a fundamental implementation challenge with region-specific variations.

S3.1: Global Scale of LAI-PrEP Implementation Challenge

UNAIDS estimates that 25 million people globally are eligible for PrEP (defined as people with substantial HIV exposure risk who are HIV-negative) [1]. Current PrEP coverage is approximately 10% of those eligible, meaning 2.5 million people access PrEP globally. However, these 2.5 million are concentrated in well-resourced healthcare systems (primarily high-income countries), while the majority of global HIV burden is in low- and middle-income countries with limited healthcare infrastructure.

As WHO recommends LAI-PrEP and lenacapavir for prevention, and as the UNAIDS 2025 target calls for 21.2 million people to access PrEP (increasing from 2.5 million currently), LAI-PrEP deployment at global scale means bridge period support in contexts where healthcare systems are fragile, testing infrastructure is limited, and supply chains are complex. The bridge period challenge scales to unprecedented proportions.

S3.2: Sub-Saharan Africa: Highest Burden Region

Sub-Saharan Africa accounts for 62% of global HIV infections (approximately 20 million people) and 70% of annual new infections [1]. The region has lowest resources for health system strengthening, lowest healthcare worker density (1.4 physicians per 1,000 population in low-income sub-Saharan Africa vs. 4.3 in high-income countries), and greatest structural barriers to healthcare access.

Cold Chain and Supply Chain Challenges

Lenacapavir requires refrigeration at 2-8°C; cabotegravir requires room temperature but still requires appropriate storage. In resource-limited settings, maintaining cold chain across transportation, storage in clinics, and secure inventory management presents substantial challenges. This is not new (existing vaccines and some antiretrovirals face similar challenges), but it does add to bridge period complexity: if lenacapavir is unavailable

at local clinic, patients may need to travel to district or regional facility for first injection,
adding transportation barriers.

Healthcare Worker Capacity

Sub-Saharan Africa faces profound healthcare worker shortages. The bridge period requires training healthcare workers (nurses, physicians, counselors, pharmacists) in LAI-PrEP protocols, testing algorithms, and addressing structural barriers. In countries where healthcare workers are already stretched across multiple health programs (HIV treatment, tuberculosis, malaria, maternal health), integrating new LAI-PrEP protocols requires substantial training investment.

Testing Infrastructure and Turnaround Time

Conservative bridge period protocols require HIV testing with adequate window period (18-45 days for standard testing). In settings where testing is centralized (e.g., large laboratories in capital cities), turnaround time for results can be 2-4 weeks, extending bridge period beyond clinical necessity. Strengthening point-of-care or rapid testing capacity is essential for sub-Saharan Africa, but requires investment in both equipment and training.

Financial Barriers

While UNAIDS and donor funding are supporting LAI-PrEP introduction in sub-Saharan Africa, out-of-pocket costs remain barriers in many settings. Additionally, healthcare access itself (transportation to clinics, meals while attending appointments, childcare for appointments) creates financial barriers during bridge period, particularly for poorest populations who carry highest HIV burden.

S3.3: Southeast Asia and Southern Asia: Hidden Epidemic

Southeast Asia and Southern Asia account for approximately 4 million people with HIV (7% of global burden), but epidemiology is concentrated among key populations (PWID, men who have sex with men, sex workers). Healthcare access varies enormously: wealthier areas (Bangkok, Manila, Delhi) have reasonable HIV services; rural and remote areas have minimal services. Additionally, drug use criminalization in many countries creates barriers to PWID accessing harm reduction and PrEP services.

Bridge period challenges include: concentrated access to testing in urban centers (requiring travel from rural areas), limited PWID healthcare engagement due to criminalization, and competing public health priorities (drug-resistant tuberculosis, dengue, hepatitis C) limiting resources for HIV prevention.

S3.4: Eastern Europe and Central Asia: Opioid Epidemic Context

Eastern Europe and Central Asia face concentrated HIV epidemiology driven by opioid epidemics. Russia, Ukraine, and Central Asian countries have high PWID-related HIV burden, and countries have generally NOT implemented comprehensive harm reduction (limited SSP, limited MAT). Bridge period support for PWID in these settings requires integration with harm reduction expansion AND criminalization reform—challenging advocacy agendas in some contexts.

S3.5: Resource-Limited Settings: Systemic Barriers

Healthcare Infrastructure Challenges

In resource-limited settings, healthcare systems focus on treatment of active disease rather than prevention. HIV clinics may exist for treatment but not PrEP services. Testing capacity is essential but limited. Record-keeping may be paper-based rather than electronic,

limiting ability to track individuals through bridge period or identify gaps. Appointment systems may be informal, relying on paper-based scheduling without reminder capacity.

Workforce Capacity

Beyond training, healthcare workers in resource-limited settings are overburdened. A nurse managing a clinic may see 100-200 patients daily; adding LAI-PrEP counseling and bridge period support to their workload is unrealistic without additional staffing and resources.

Financial Sustainability

In high-income countries, LAI-PrEP is increasingly covered by insurance. In low- and middle-income countries, funding depends on global health initiatives (PEPFAR, Global Fund, UNAIDS). If funding shifts or programs end, previously achieved coverage gains can be lost. Bridge period support programs (navigation, testing, transportation support) require sustained funding; they cannot be sustained as one-time interventions.

S3.6: High-Income Countries with Gaps

Even in high-income countries (US, Europe, Australia), implementation gaps exist. Rural populations may lack access to LAI-PrEP providers. Racial and ethnic disparities in LAI-PrEP access exist (White MSM have higher access than Black and Latino MSM despite higher HIV burden in latter groups). Housing instability and criminalization affect PWID and incarcerated populations similarly to low-income countries.

S3.7: Evidence-Based Global Implementation Strategies

Community Partnership and Co-Design

Global LAI-PrEP programs should be designed in partnership with communities most affected by HIV, not imposed by external actors. Co-design of testing protocols, navigation support, and supply chain management ensures programs address actual barriers rather than theoretical ones.

Task-Shifting and Community Health Worker Models

WHO recommendations support task-shifting (training community health workers, nurses, pharmacists in PrEP provision) to overcome healthcare worker shortages [2]. Integrating LAI-PrEP delivery with community health worker networks (already established in many settings for vaccination, maternal health, HIV treatment) leverages existing infrastructure.

Integration with Existing Services

Rather than creating standalone LAI-PrEP clinics, integrating LAI-PrEP with existing HIV treatment clinics, primary care, reproductive health, and harm reduction services reduces barriers for individuals. In some settings, integrating with tuberculosis (TB) clinics makes sense (high co-infection risk); in others, integrating with maternal health services (for women).

Strengthening Testing Infrastructure

Global investment in rapid testing capacity (point-of-care, laboratory rapid turnaround) benefits not only LAI-PrEP programs but strengthens overall health system capacity. Supporting local manufacturing of rapid tests (where appropriate) improves accessibility and sustainability.

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| Financial Support for Access | 122 |
| Comprehensive programs provide not only medications but also financial support for bridge period access: transportation vouchers, childcare support, lost wages compensation. This recognizes that bridge period is not only clinical but economic barrier. | 123 |
| 124 | 125 |
| Procurement and Supply Chain Optimization | 126 |
| For large-scale global access, procurement efficiency (pooled purchasing, regional manufacturing where appropriate) and supply chain optimization (predictable supply, local storage capacity) are essential. Countries should plan on deploying both cabotegravir (room temperature, every 8 weeks) and lenacapavir (cold chain, twice-yearly) initially, then potentially once-yearly as Phase 3 data emerge. | 127 |
| 128 | 129 |
| 130 | 131 |
| Monitoring and Equity Focus | 132 |
| Global programs should explicitly monitor bridge period completion rates by geography, population, and program type. Are urban users completing bridge period at higher rates than rural? Are men completing at higher rates than women? Is one program model (integrated vs. standalone) more effective? Monitoring equity gaps enables targeted investments. | 133 |
| 134 | 135 |
| 136 | 137 |
| 1. Joint United Nations Programme on HIV/AIDS (UNAIDS). The Urgency of Now: AIDS at a Crossroads (Global AIDS Update 2024), 2024. Accessed 2025-12-12. | 138 |
| 2. World Health Organization. Task Shifting: Global Recommendations and Guidelines, 2008. Accessed 2025-12-12. | 139 |
| | 140 |
| | 141 |