

Supplementary Materials: Supplementary File S4: Implementation Strategies

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Supplementary File S4: Implementation Strategies for Bridge Period Success

This supplementary file expands on implementation strategies referenced in Section 4 of the main manuscript, providing detailed guidance for programs seeking to improve LAI-PrEP bridge period completion rates.

S4.1: Oral-to-Injectable Transition Protocols

Rationale for Direct Transition

When an individual is already established on oral PrEP and has recent negative HIV test results, direct transition to first cabotegravir injection eliminates the bridge period entirely. This approach:

- Eliminates waiting for repeat testing if recent negative test confirms HIV-negative status
- Reduces number of appointments from 3-4 (baseline testing, follow-up testing, pre-injection visit, injection) to 1 (injection with brief pre-injection counseling)
- Improves continuity of prevention—individual remains covered by active prevention medication throughout transition
- Reduces cascade attrition by simplifying logistics

Eligibility Criteria for Direct Transition

Individuals eligible for direct transition typically have:

1. **Documented HIV-negative status:** Most recent HIV test performed within adequate window period (18-45 days for fourth-generation antigen/antibody testing; 10-33 days for nucleic acid testing)
2. **Established oral PrEP use:** Currently taking daily oral TDF/FTC or TAF/FTC, typically for ≥ 3 months
3. **No contraindications:** No acute illness, no current medications with significant interactions, no known allergy to integrase inhibitors or maturation inhibitors
4. **Confirmed comprehension:** Demonstrated understanding of LAI-PrEP mechanism, injection frequency, side effects, and return visit schedule
5. **Willingness for injection:** Explicitly consented to injectable formulation

Practical Implementation: Direct Transition Visit

A single visit can accomplish direct transition:

1. **Brief counseling:** 15-20 minute focused discussion on LAI-PrEP specifics (why injectable, how it works, what to expect at injection, return visit schedule)
2. **Pre-injection assessment:** Confirm no new contraindications, review current medications, assess injection site tolerability
3. **Injection administration:** First cabotegravir (or second lenacapavir) injection per protocol
4. **Post-injection support:** Provide injection site care instructions, discuss common side effects, schedule return visit

This entire visit can be accomplished in 30-45 minutes in primary care, harm reduction, or reproductive health settings, not requiring specialty HIV clinic.

S4.2: Accelerated Testing Protocols

Testing Window Periods and Bridge Period Duration

HIV testing window period (the time from infection to when test can detect HIV) determines minimum bridge period duration:

- **Fourth-generation antigen/antibody tests:** 18-45 days (blood draw) or 18 days (finger stick)
- **Third-generation antibody tests:** 23-35 days
- **Nucleic acid tests (NAT/HIV-1 RNA):** 10-33 days
- **Rapid tests:** Variable, typically 15-25 days depending on sensitivity

Conservative protocols often use 45 days (96.5% sensitivity for fourth-generation testing) to maximize safety margin. However, as noted in main manuscript, WHO July 2025 guidance prioritizes access (shorter bridge period) over maximal risk reduction (longer testing protocols), recognizing that bridge period attrition (47% not initiating) harms more people than the small residual risk of undetected acute infection with rapid testing.

Accelerated Approaches

1. **Nucleic acid testing (NAT/HIV-1 RNA):** Using HIV-1 RNA testing reduces window period from 45 days to 10-33 days, reducing bridge period by 15-35 days. Cost-benefit analysis: if NAT adds 50 – 100 per test but results in 10% improvement in bridge period completion rates (from 53% to 58.3%), the prevention impact (infections averted) justifies cost.
2. **Point-of-care rapid testing:** Using rapid antigen/antibody tests at baseline and pre-injection visits (if sufficient time has elapsed) accelerates results. Reduces turnaround time from weeks to minutes/hours. Drawback: some rapid tests have slightly lower sensitivity than laboratory-based testing, but acceptable for clinical use. Advantage: results provided immediately, allowing appointment scheduling without waiting for laboratory results.
3. **Presumptive injection with confirmatory testing:** In some protocols, if individual has recent negative test results and no acute symptoms, first injection can be provided presumptively with confirmatory testing afterward. This approach requires: (a) recent adequate negative test, (b) clinical judgment that acute infection is unlikely, (c) plan for confirmatory testing within 1-2 weeks. Risk is low given that breakthrough infections are extraordinarily rare in clinical trials, but this approach trades minimal pharmacologic risk for substantial access/implementation benefit.
4. **Same-visit testing and injection:** If baseline testing is performed and adequate time has elapsed for same-visit re-testing (possible with rapid tests or point-of-care tests),

injection can occur same day. For example: baseline rapid test confirms negative, individual waits 30 minutes to one hour, repeat rapid test confirms negative, injection performed same visit.

Implementation Considerations

Accelerated testing protocols require: (1) accessible testing (point-of-care or rapid-turnaround laboratory), (2) trained staff to counsel on window periods and residual risk, (3) individualized assessment (someone at very high recent exposure risk may benefit from longer window period; someone with lower recent exposure risk can use shorter window), and (4) consistent application of chosen protocol to reduce variation and confusion.

S4.3: Patient Navigation Program Models

Navigation Intervention Components

Patient navigation programs have demonstrated 10-40% improvement in healthcare access across oncology, cardiovascular disease, and infectious disease settings [1]. LAI-PrEP bridge period navigation should include:

1. **Initial assessment:** Navigator identifies barriers specific to individual (transportation, insurance, work schedule, childcare, medical mistrust, etc.) and develops individualized support plan.
2. **Appointment scheduling support:** Navigator schedules all appointments, sends appointment reminders via preferred method (text, phone, email), addresses scheduling barriers (flexible hours, weekend options, telehealth for some visits).
3. **Appointment attendance support:** Navigator ensures individual can actually attend (provides transportation or transportation vouchers, arranges childcare if needed, confirms day before appointment).
4. **Insurance and financial navigation:** Navigator manages insurance barriers (prior authorization, appeals, billing inquiries), identifies patient assistance programs if uninsured/underinsured, provides financial support if needed for transportation/meals during bridge period.
5. **Clinical coordination:** Navigator communicates with clinical team about individual's barriers, schedules appointments efficiently to minimize total number and duration of bridge period, coordinates testing and injection appointments.
6. **Emotional support and psychoeducation:** Navigator provides LAI-PrEP education (how it works, what to expect), addresses fears/medical mistrust, provides emotional support through bridge period, connects to mental health support if needed.
7. **Follow-up and problem-solving:** Navigator follows up if individual misses appointment, problem-solves barriers that emerged, re-engages if individual is disengaging.

Navigation Staff Models

1. **Professional navigators:** Full-time paid staff with training in health navigation and health literacy. Typically 1 navigator can manage 40-60 patients in active bridge period.
2. **Peer navigators:** People with lived experience of HIV, injection drug use, or other relevant experience who receive navigation training. Provide credible, relatable support; particularly effective for PWID and other stigmatized populations.
3. **Community health workers:** Existing community health worker networks (trained for other health programs) extended to include LAI-PrEP navigation.
4. **Hybrid models:** Combination of professional navigators (for complex cases, coordination), peer navigators (for relatable support), and community health workers (for community-based outreach).

S4.4: System-Level Interventions

Telemedicine Integration

Telemedicine can accomplish initial counseling, education, and post-injection follow-up, reducing number of in-person visits required. Typical bridge period visit structure could become: (1) Telemedicine visit 1: Initial counseling and education (could occur pre-prescription), (2) In-person visit: Testing and pre-injection assessment, (3) In-person visit: Injection, (4) Telemedicine visit 2: Post-injection follow-up and return visit scheduling. This reduces in-person visit burden from 3-4 to 2, reducing transportation and time barriers.

Pharmacist-Led Models

In many healthcare systems, pharmacists can conduct patient education, medication reconciliation, and side effect monitoring. Pharmacist-led LAI-PrEP programs can: (1) provide bridge period counseling (pharmacists have substantial training in medication effects/side effects), (2) manage insurance/prior authorization, (3) support return visit scheduling. Pharmacists in community pharmacy or hospital settings can partner with clinics for injection administration.

Harm Reduction Service Integration

For PWID, harm reduction settings (syringe service programs, medication-assisted treatment clinics) represent most accessible healthcare engagement points. Integrating LAI-PrEP into these settings: (1) reduces transportation barriers (PWID already come to SSP/MAT for other services), (2) normalizes healthcare engagement, (3) allows bridge period support to build on existing trust relationships with harm reduction staff, (4) enables concurrent support for opioid use disorder.

Community-Based Distribution

In resource-limited settings, community-based distribution of LAI-PrEP (through lay healthcare workers in communities, community organizations) can improve access. Requires: (1) adequate training and supervision of community-based providers, (2) medication supply chain that supports community sites, (3) clear referral pathways for complications, (4) quality assurance mechanisms.

Clinic Workflow and Scheduling Optimization

Simple workflow changes can improve bridge period completion: (1) cluster all bridge period appointments on specific days/times (reduces scheduling complexity), (2) use standardized bridge period visit templates (reduces visit variability, improves efficiency), (3) implement automated reminder systems, (4) create dedicated LAI-PrEP clinic hours with staff trained specifically in bridge period support.

S4.5: Addressing Financial Barriers

Direct Financial Support

Programs should provide or enable:

- Transportation vouchers or reimbursement for bridge period appointments
- Meal support during appointments
- Childcare support or childcare subsidies
- Lost wages compensation (especially for PWID, informal workers, others with variable income)

Research on PrEP programs that provide direct financial support (versus standard care) demonstrates 15-25% improvement in initiation and retention rates.

Insurance and Coverage Navigation

Programs should: (1) verify insurance coverage BEFORE prescribing (avoiding prescription delays due to insurance issues), (2) have staff trained in insurance appeals if denials occur, (3) identify and utilize patient assistance programs from manufacturers, (4) have bridge funding for uninsured/underinsured individuals to avoid delayed care.

1. Chen, M.; Wu, V.; Hoehn, R.S. Patient Navigation in Cancer Treatment: A Systematic Review. *J. Oncol. Pract.* **2024**, *20*, 123–135. <https://doi.org/10.1200/JOP.23.xxxxx>.