Supplement S1: Mathematical Foundations

The Prevention Theorem, Nested Barrier Framework,
and Signal-to-Noise Ratio Analysis

Supporting the manuscript:

Structural barriers drive near-zero population-level effectiveness of HIV prevention among people who inject drugs:
A Computational Modeling Study

AC Demidont, DO
Independent Researcher, Nyx Dynamics LLC

December 27, 2025

Contents

This supplement provides formal mathematical derivations and methodological foundations underlying the main analysis. All results here are intended to support, not extend, the conclusions of the primary manuscript.

1 Epidemiological Foundations

1.1 The Basic Reproductive Number

Definition 1.1 (Basic Reproductive Number). The basic reproductive number R_0 is defined as the expected number of secondary infections produced by a single infected individual in a completely susceptible population:

$$R_0 = \beta \cdot c \cdot D \tag{1}$$

where β = transmission probability per contact, c = contact rate, and D = duration of infectiousness.

For injection-related HIV transmission, β ranges from 0.0063 to 0.0080 per needle-sharing event—approximately 10-fold higher than receptive anal intercourse (0.0014) and 100-fold higher than insertive vaginal intercourse (0.0004).

1.2 The Epidemic Threshold

Theorem 1.1 (Epidemic Threshold). An infectious disease spreads in a population if and only if $R_0 > 1$. When $R_0 < 1$, the disease dies out. When $R_0 = 1$, the system is at critical equilibrium.

Proof. Let $I(t)$ denote infected individuals at time t:

$$\frac{dI}{dt} = R_0 \cdot I - \gamma I = I(R_0 - \gamma) \tag{2}$$

When $R_0 > 1$, $\frac{dI}{dt} > 0$ (epidemic grows). When $R_0 < 1$, $\frac{dI}{dt} < 0$ (epidemic declines). $\square$

1.3 Effective Reproductive Number Under Intervention

Definition 1.2 (Effective Reproductive Number). When intervention reduces transmission:

$$R_e = R_0 \cdot (1 - \varepsilon \cdot p) \tag{3}$$

where ε = intervention efficacy and p = proportion covered.

Corollary 1.2 (Elimination Threshold). Complete elimination ($R_e = 0$) requires either $\varepsilon = 1$ (perfect efficacy) or $\varepsilon \cdot p = 1$.

2 The Prevention Theorem

2.1 Statement

Theorem 2.1 (The Prevention Theorem). For any infectious disease with transmission dynamics governed by R_0, the only closed-form solution to prevention is:

$$R_0 = 0 \tag{4}$$

Any policy permitting $R_0 > 0$ accepts ongoing transmission as a structural feature.

Proof. The steady-state prevalence equation is:

$$I^* = S^* \cdot \left(1 - \frac{1}{R_0}\right) \tag{5}$$

For any $R_0 > 0$:

- If $R_0 > 1$: Endemic equilibrium with $I^* > 0$

- If $R_0 = 1$: Critical equilibrium (unstable)

- If $0 < R_0 < 1$: Declining epidemic, but $I^* = 0$ only asymptotically

Only at $R_0 = 0$ does $I^* = 0$ hold exactly and immediately. $\square$

2.2 Drug-Mediated Prevention

Proposition 2.2. Let $\varepsilon_{\text{drug}}$ denote drug efficacy. For LAI-PrEP:

$$\varepsilon_{\text{drug}} = 0.999 \quad \text{(PURPOSE-1)} \tag{6}$$

For $\varepsilon_{\text{drug}} = 0.999$, achieving $R_e < 0.01$ requires: [1]

$$\pi_{\text{cascade}} > \frac{R_0^{\text{baseline}} - 0.01}{0.999 \cdot R_0^{\text{baseline}}} \tag{7}$$

For $R_0^{\text{baseline}} = 2$:

$$\pi_{\text{cascade}} > \frac{1.99}{1.998} \approx 0.996 \tag{8}$$

Thus, cascade completion of $\sim$99.6% achieves effective elimination. The problem is cascade completion, not drug efficacy.

2.3 Policy-Dependent Decomposition

Definition 2.1. Decompose the reproductive number:

$$R_0^{\text{effective}} = R_0^{\text{drug}} + R_0^{\text{policy}} \tag{9}$$

4

where:

$$R_0^{\text{drug}} = R_0^{\text{baseline}} \cdot (1 - \varepsilon_{\text{drug}}) \approx 0.002 \tag{10}$$

$$R_0^{\text{policy}} = R_0^{\text{baseline}} \cdot (1 - \pi_{\text{cascade}}) \cdot \varepsilon_{\text{drug}} \tag{11}$$

Theorem 2.3 (Policy Dominance). For $\varepsilon_{\text{drug}} \geq 0.96$:

$$\frac{R_0^{\text{policy}}}{R_0^{\text{drug}}} = \frac{(1 - \pi_{\text{cascade}}) \cdot \varepsilon_{\text{drug}}}{1 - \varepsilon_{\text{drug}}} \approx \frac{1 - \pi_{\text{cascade}}}{0.001} \tag{12}$$

For PWID cascade completion $\pi_{\text{cascade}} = 0.0006$:

$$\frac{R_0^{\text{policy}}}{R_0^{\text{drug}}} \approx \frac{0.9994}{0.001} = 999 \tag{13}$$

Policy barriers contribute $\sim$1000$\times$ more to transmission than drug limitations.

3 The Prevention Cascade

3.1 Cascade Structure

Definition 3.1 (Prevention Cascade). The prevention cascade is a multiplicative sequence describing conditional attrition across sequential stages of prevention and care, consistent with established HIV treatment and prevention cascade frameworks.[2, 3]

$$\pi_{\text{cascade}} = \prod_{i=1}^{n} P(S_i | S_{i-1}) \tag{14}$$

where S_i denotes reaching stage i and $S_0 \equiv$ "at risk."

3.2 Eight-Stage Model for PWID

$$\pi_{\text{cascade}} = P(\text{aware}) \times P(\text{willing}|\text{aware}) \times P(\text{access}|\text{willing}) \times \ldots \times P(\text{sustain}|\text{start}) \tag{15}$$

3.3 Parameter Estimates

Parameter estimates were derived from U.S. National HIV Behavioral Surveillance data, systematic reviews of the PrEP care cascade among people who inject drugs, and observational studies of PrEP initiation and persistence in low-threshold settings.[4, 3, 5, 6, 7]

Parameters reflect empirically observed attrition across the PrEP prevention cascade among PWID, synthesised from surveillance data, qualitative studies, and implementation research. Point estimates were selected conservatively; uncertainty is explored in sensitivity analyses.[4, 3, 5, 8]

Table 1: Prevention cascade parameters for PWID

Stage	Parameter	Estimate
Awareness	$P(\text{aware})$	0.10
Willingness	$P(\text{willing}|\text{aware})$	0.30
Healthcare access	$P(\text{access}|\text{willing})$	0.35
Disclosure	$P(\text{disclose}|\text{access})$	0.25
Provider offer	$P(\text{provider}|\text{disclose})$	0.35
Testing complete	$P(\text{test}|\text{provider})$	0.45
First injection	$P(\text{start}|\text{test})$	0.45
Sustained	$P(\text{sustain}|\text{start})$	0.25
Product	π_{cascade}	**0.000047**

3.4 Comparison with MSM

MSM cascade parameters were derived from randomized PrEP trials and subsequent implementation analyses in populations explicitly included in prevention trial design.[9, 10, 11, 12]

$$\pi_{\text{cascade}}^{\text{MSM}} = 0.90 \times 0.80 \times 0.85 \times 0.85 \times 0.90 \times 0.95 \times 0.90 \times 0.75 \approx 0.21 \tag{16}$$

$$\frac{\pi_{\text{cascade}}^{\text{MSM}}}{\pi_{\text{cascade}}^{\text{PWID}}} = \frac{0.21}{0.000047} \approx 4,468 \tag{17}$$

MSM achieve ~4,500-fold higher cascade completion with identical drug efficacy.

4 The Nested Barrier Framework

4.1 Formal Definition

Definition 4.1 (Nested Barrier Structure). A nested barrier structure is a hierarchical sequence $\{B_k\}_{k=0}^{K}$ where:

1. Each barrier B_k has transmission probability $\tau_k = P(\text{pass } B_k|\text{passed } B_{k-1})$

2. Overall transmission: $\Pi = \prod_{k=0}^{K} \tau_k$

3. Barriers are nested: B_k depends on B_{k-1}

4. Root barrier B_0 determines existence of subsequent barriers

4.2 Root Node Dominance

Theorem 4.1 (Root Node Dominance). If $\tau_0 \to 0$ (population excluded at root), then $\Pi \to 0$ regardless of downstream improvements.

Proof.

6

$$\Pi = \tau_0 \cdot \prod_{k=1}^{K} \tau_k \qquad (18)$$

$$\lim_{\tau_0 \to 0} \Pi = \lim_{\tau_0 \to 0} \tau_0 \cdot \prod_{k=1}^{K} \tau_k = 0 \quad \square \qquad (19)$$

Corollary 4.2 (Intervention Hierarchy). Interventions at barrier B_j can only improve outcomes for populations that passed $B_0, \ldots, B_{j-1}$. Downstream interventions cannot compensate for upstream exclusion.

5 Signal-to-Noise Ratio Analysis

5.1 Training Data SNR Definition

Definition 5.1 (Training Data SNR). For ML algorithms trained on HIV prevention literature:

$$\text{SNR} = \frac{n \times \tau \times \pi}{\epsilon \times \mu} \qquad (20)$$

where:

- n = number of trial participants

- τ = evidence tier (1.0 for direct RCT, 0.5 for extrapolated)

- π = precision (inverse of CI width)

- ϵ = extrapolation required

- μ = population mismatch factor

5.2 Population-Specific SNR Calculation

For MSM:

Population-level signal-to-noise parameters for MSM were derived from large randomized and implementation trials evaluating oral and long-acting PrEP, with direct applicability to contemporary LAI-PrEP deployment and minimal extrapolation.[9, 10, 12, 11, 13]

$$n_{\text{MSM}} = 10{,}800 \quad \text{(HPTN 083 + iPrEx + PROUD + PURPOSE-2)} \qquad (21)$$

$$\tau_{\text{MSM}} = 1.0 \quad \text{(direct LAI-PrEP RCT evidence)} \qquad (22)$$

$$\pi_{\text{MSM}} = 0.85 \quad \text{(narrow CIs from large trials)} \qquad (23)$$

$$\epsilon_{\text{MSM}} = 1.0 \quad \text{(no extrapolation needed)} \qquad (24)$$

$$\mu_{\text{MSM}} = 1.0 \quad \text{(population matches training)} \qquad (25)$$

$$\boxed{\text{SNR}_{\text{MSM}} = \frac{10,800 \times 1.0 \times 0.85}{1.0 \times 1.0} = 9,180} \tag{26}$$

For PWID:

Signal-to-noise parameters for PWID were derived from the sole randomized PrEP trial enrolling PWID and supplemented by observational and qualitative evidence, requiring multiple layers of extrapolation across formulation, geography, and implementation context.[14, 6, 3]

$$n_{\text{PWID}} = 2,413 \quad \text{(Bangkok TDF Study only)} \tag{27}$$

$$\tau_{\text{PWID}} = 0.5 \quad \text{(oral PrEP, extrapolated to LAI)} \tag{28}$$

$$\pi_{\text{PWID}} = 0.38 \quad \text{(wide CI: 9.6\%–72.2\%)} \tag{29}$$

$$\epsilon_{\text{PWID}} = 3.0 \quad \text{(oral} \rightarrow \text{LAI extrapolation)} \tag{30}$$

$$\mu_{\text{PWID}} = 2.0 \quad \text{(Thai} \rightarrow \text{US population mismatch)} \tag{31}$$

$$\boxed{\text{SNR}_{\text{PWID}} = \frac{2,413 \times 0.5 \times 0.38}{3.0 \times 2.0} = \frac{458.5}{6.0} = 76.4} \tag{32}$$

5.3 Disparity Ratio

$$\boxed{\text{Disparity} = \frac{\text{SNR}_{\text{MSM}}}{\text{SNR}_{\text{PWID}}} = \frac{9,180}{76.4} = 120.2} \tag{33}$$

ML algorithms receive **120-fold more reliable signal** about MSM than PWID.

5.4 LAI-PrEP Specific SNR

For LAI-PrEP agents:

Signal-to-noise parameters for LAI-PrEP were derived from the randomized PrEP trials enrolling MSM and the absence of any trials enrolling PWID.[10, 11, 8, 15]

For LAI-PrEP specifically:

$$\text{SNR}_{\text{MSM}}^{\text{LAI}} = \frac{7,770 \times 1.0 \times 0.85}{1.0 \times 1.0} = 6,605 \tag{34}$$

$$\text{SNR}_{\text{PWID}}^{\text{LAI}} = \frac{0 \times \cdot \times \cdot}{\cdot \times \cdot} = \text{undefined} \tag{35}$$

For LAI-PrEP, the PWID SNR is **undefined** (division by zero participants).

5.5 Algorithmic Access Probability

Definition 5.2. Let $P(\text{alg}|G)$ denote probability that ML systems do not systematically deprioritize population G:

$$P(\text{alg}|G) = \frac{n_G}{n_{\text{total}}} \times q_G \tag{36}$$

where n_G/n_{total} is representation ratio and q_G is evidence quality factor.

For MSM:

$$P(\text{alg}|\text{MSM}) = \frac{10,800}{13,213} \times 1.0 = 0.82 \approx 0.92 \text{ (adjusted)} \tag{37}$$

For PWID:

$$P(\text{alg}|\text{PWID}) = \frac{2,413}{13,213} \times 0.38 = 0.07 \approx 0.15 \text{ (adjusted)} \tag{38}$$

5.6 Multiplicative Effect

Theorem 5.1 (Algorithmic Attenuation). The algorithmic barrier operates multiplicatively:

$$\pi_{\text{effective}} = \pi_{\text{cascade}} \times P(\text{alg}) \tag{39}$$

For PWID with $P(\text{alg}) = 0.15$:

$$\pi_{\text{effective}}^{\text{PWID}} = 0.000047 \times 0.15 = 0.000007 = 0.0007\% \tag{40}$$

This represents 85% additional reduction from algorithmic mediation alone.

6 Leave-One-Out Cross-Validation Interpretation

Definition 6.1 (Inadvertent LOOCV). HIV prevention research has created a leave-one-out cross-validation framework at population scale:

- **Training set:** MSM, cisgender women, heterosexual couples (9+ trials, $>$10,800 participants)

- **Held-out test set:** PWID (1 trial, 2,413 participants, no FDA approval)

Proposition 6.1. Under LOOCV interpretation, poor algorithmic performance for PWID is not "bias" but expected generalization failure to an out-of-distribution population.

The algorithm performs correctly on its training distribution. PWID outcomes reflect test-set performance on a population systematically excluded from training.

7 Intervention Mathematics

Proposition 7.1 (Removing Root Barrier). If the root barrier B_0 is neutralized (e.g., regulatory and trial-design requirements mandating inclusion of PWID), downstream data generation, guideline incorporation,

and algorithmic performance improve deterministically based on established evidence from HIV prevention trials and clinical guidance.[14, 16, 17, 18, 19]

$$\tau_0 \to 1 \quad \text{(PWID included in trials)} \tag{41}$$

$$\tau_1 \to 1 \quad \text{(data generated)} \tag{42}$$

$$\tau_2 \to 1 \quad \text{(guidelines include)} \tag{43}$$

$$\tau_3 \to 0.92 \quad \text{(algorithm trained on inclusive data)} \tag{44}$$

Theorem 7.2 (Failure of Downstream-Only Intervention). Interventions targeting downstream barriers without addressing upstream exclusion cannot achieve $R_0 = 0$.

Proof. Let $\Pi' = \prod_{k=3}^{5} \tau_k$ be downstream-only effect. Even if $\Pi' \to 1$:

$$\Pi_{\text{total}} = \tau_0 \cdot \tau_1 \cdot \tau_2 \cdot \Pi' \leq \tau_0 \cdot \tau_1 \cdot \tau_2 < \pi^* \tag{45}$$

when $\tau_0 \cdot \tau_1 \cdot \tau_2 < \pi^*$.

For PWID: $\tau_0 \cdot \tau_1 \cdot \tau_2 \approx 0.18 \times 0.1 \times 0.1 = 0.0018 \ll 0.996 = \pi^*$.

Therefore, $R_0 > 0$ persists regardless of downstream improvements. $\square$

8   Summary of Mathematical Results

1. $R_0 = 0$ is the unique closed-form solution to HIV prevention

2. LAI-PrEP efficacy ($\varepsilon = 0.999$) is sufficient for elimination

3. PWID cascade completion ($\pi = 0.000007$) is $>$140,000-fold below threshold

4. The cascade deficit is policy-constructed, not biologically determined

5. SNR disparity is 120-fold (MSM: 9,180; PWID: 76.4)

6. For LAI-PrEP, PWID SNR is undefined (zero participants)

7. Algorithmic barriers amplify deficit by 85% through training exclusion

8. Downstream interventions cannot compensate for upstream exclusion

8.1   The Central Equation

The complete probability model for achieving sustained HIV protection:

$$\boxed{P(R_0 = 0) = \varepsilon_{\text{drug}} \times \pi_{\text{cascade}} \times P(\text{no incarceration})^T \times P(\text{alg})} \tag{46}$$

For PWID under current policy:

$$P(R_0 = 0|\text{PWID}) = \underbrace{0.999}_{\varepsilon} \times \underbrace{0.000047}_{\pi} \times \underbrace{0.168}_{(0.7)^5} \times \underbrace{0.15}_{P(\text{alg})} = 0.0000012 \qquad (47)$$

For MSM under current policy:

$$P(R_0 = 0|\text{MSM}) = \underbrace{0.999}_{\varepsilon} \times \underbrace{0.21}_{\pi} \times \underbrace{0.774}_{(0.95)^5} \times \underbrace{0.92}_{P(\text{alg})} = 0.149 \qquad (48)$$

Disparity:

$$\frac{P(R_0 = 0|\text{MSM})}{P(R_0 = 0|\text{PWID})} = \frac{0.149}{0.0000012} \approx 124,000 \qquad (49)$$

Identical drug efficacy produces **124,000-fold disparity** in sustained protection probability.

References

[1] L.-G. Bekker, M. Das, Q. Abdool Karim, K. Ahmed, J. Batting, W. Brumskine, K. Gill, I. Harkoo, M. Jaggernath, G. Kigozi, N. Kiwanuka, P. Kotze, L. Lebina, C. E. Louw, M. Malahleha, M. Manentsa, L. E. Mansoor, D. Moodley, V. Naicker, L. Naidoo, M. Naidoo, G. Nair, N. Ndlovu, T. Palanee-Phillips, R. Panchia, S. Pillay, D. Potloane, P. Selepe, N. Singh, Y. Singh, E. Spooner, A. M. Ward, Z. Zwane, R. Ebrahimi, Y. Zhao, A. Kintu, C. Deaton, C. C. Carter, J. M. Baeten, F. Matovu Kiweewa, Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women, New England Journal of Medicine 391 (13) (2024) 1179–1192. `doi:10.1056/NEJMoa2407001`.
URL `http://www.nejm.org/doi/10.1056/NEJMoa2407001`

[2] S. E. Rutstein, C. J. Sellers, J. Ananworanich, M. S. Cohen, The HIV treatment cascade in acutely infected people: informing global guidelines, Current Opinion in HIV and AIDS 10 (6) (2015) 395–402. `doi:10.1097/COH.0000000000000193`.
URL `http://journals.lww.com/01222929-201511000-00003`

[3] C. B. Mistler, et al., PrEP awareness, uptake and use among people who inject drugs: a systematic review, AIDS Behav (2021). `doi:10.1007/s10461-020-02988-x`.

[4] A. R. Baugher, C. Wejnert, D. Kanny, D. Broz, J. Feelemyer, R. B. Hershow, J. Burnett, J. Chapin-Bardales, M. Haynes, T. Finlayson, J. Prejean, NHBS Study Group, Are we ending the HIV epidemic among persons who inject drugs?: key findings from 19 US cities, AIDS 39 (12) (2025) 1813–1819. `doi:10.1097/QAD.0000000000004249`.

[5] A. R. Bazzi, D. L. Biancarelli, E. Childs, M.-L. Drainoni, A. Edeza, P. Salhaney, M. J. Mimiaga, K. B. Biello, Limited Knowledge and Mixed Interest in Pre-Exposure Prophylaxis for HIV Prevention

Among People Who Inject Drugs, AIDS Patient Care and STDs 32 (12) (2018) 529–537. `doi: 10.1089/apc.2018.0126`.
URL `https://www.liebertpub.com/doi/10.1089/apc.2018.0126`

[6] K. B. Biello, A. R. Bazzi, M. J. Mimiaga, D. L. Biancarelli, A. Edeza, P. Salhaney, E. Childs, M. L. Drainoni, Perspectives on HIV pre-exposure prophylaxis (PrEP) utilization and related intervention needs among people who inject drugs, Harm Reduct J 15 (1) (2018) 55. `doi:10.1186/s12954-018-0263-5`.

[7] H. Rozansky, P. J. Christine, M. Younkin, J. M. Fox, Z. M. Weinstein, S. Suarez, J. Stewart, N. Farrell, J. L. Taylor, Addiction consult service involvement in PrEP and PEP delivery for patients who inject drugs admitted to an urban essential hospital, Addict Sci Clin Pract 19 (1) (2024) 77. `doi:10.1186/s13722-024-00502-5`.

[8] K. B. Biello, A. Edeza, P. Salhaney, D. L. Biancarelli, M. J. Mimiaga, M. L. Drainoni, E. S. Childs, A. R. Bazzi, A missing perspective: injectable pre-exposure prophylaxis for people who inject drugs, AIDS Care 31 (10) (2019) 1214–1220. `doi:10.1080/09540121.2019.1587356`.

[9] R. M. Grant, J. R. Lama, P. L. Anderson, et al., Preexposure chemoprophylaxis for HIV prevention in men who have sex with men, N Engl J Med 363 (27) (2010) 2587–2599. `doi:10.1056/NEJMoa1011205`.

[10] R. J. Landovitz, D. Donnell, M. E. Clement, B. Hanscom, L. Cottle, L. Coelho, R. Cabello, S. Chariyalertsak, E. F. Dunne, I. Frank, et al., Cabotegravir for hiv prevention in cisgender men and transgender women, N. Engl. J. Med. 385 (2021) 595–608. `doi:10.1056/NEJMoa2101016`.

[11] C. F. Kelley, et al., Lenacapavir for HIV prevention in cisgender women, N Engl J Med (2024). `doi:10.1056/NEJMoa2411858`.

[12] K. H. Mayer, J.-M. Molina, M. A. Thompson, P. L. Anderson, K. C. Mounzer, J. J. De Wet, E. DeJesus, H. Jessen, R. M. Grant, P. J. Ruane, P. Wong, R. Ebrahimi, L. Zhong, A. Mathias, C. Callebaut, S. E. Collins, M. Das, S. McCallister, D. M. Brainard, C. Brinson, A. Clarke, P. Coll, F. A. Post, C. B. Hare, Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial, The Lancet 396 (10246) (2020) 239–254. `doi:10.1016/S0140-6736(20)31065-5`.
URL `https://linkinghub.elsevier.com/retrieve/pii/S0140673620310655`

[13] S. McCormack, D. T. Dunn, M. Desai, D. I. Dolling, M. Gafos, R. Gilson, A. K. Sullivan, A. Clarke, I. Reeves, G. Schembri, N. Mackie, C. Bowman, C. J. Lacey, V. Apea, M. Brady, J. Fox, S. Taylor, S. Antonucci, S. H. Khoo, J. Rooney, A. Nardone, M. Fisher, A. McOwan, A. N. Phillips, A. M. Johnson, B. Gazzard, O. N. Gill, Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial, The

Lancet 387 (10013) (2016) 53–60. doi:10.1016/S0140-6736(15)00056-2.
URL https://linkinghub.elsevier.com/retrieve/pii/S0140673615000562

[14] K. Choopanya, M. Martin, P. Suntharasamai, U. Sangkum, P. A. Mock, M. Leethochawalit, S. Chi-amwongpaet, P. Kitisin, P. Natrujirote, S. Kittimunkong, R. Chuachoowong, R. J. Gvetadze, J. M. McNicholl, L. A. Paxton, M. E. Curlin, C. W. Hendrix, S. Vanichseni, Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial, Lancet 381 (9883) (2013) 2083–2090. doi:10.1016/S0140-6736(13)61127-7.

[15] O. Sued, N. Nardi, L. Spadaccini, Key population perceptions and opinions about long-acting antiretro-virals for prevention and treatment: a scoping review, Current opinion in HIV and AIDS 17 (3) (2022) 145–161. doi:10.1097/COH.0000000000000734.

[16] J. K. Brody, et al., The systematic exclusion of people who inject drugs from HIV prevention trials, Int J Drug Policy (2021). doi:10.1016/j.drugpo.2021.103284.

[17] M. R. Tanner, J. G. O'Shea, K. M. Byrd, M. Johnston, G. G. Dumitru, J. N. Le, A. Lale, K. K. Byrd, P. Cholli, E. Kamitani, W. Zhu, K. W. Hoover, A. P. Kourtis, Antiretroviral postexposure prophy-laxis after sexual, injection drug use, or other nonoccupational exposure to HIV – CDC recommen-dations, United States, 2025, MMWR Recomm Rep 74 (1) (2025) 1–56. doi:10.15585/mmwr.rr7401a1.

[18] R. R. Patel, K. W. Hoover, A. Lale, J. Cabrales, K. M. Byrd, A. P. Kourtis, Clinical recommendation for the use of injectable lenacapavir as hiv preexposure prophylaxis — united states, 2025, MMWR. Mor-bidity and Mortality Weekly Report 74 (35) (2025) 541–549. doi:10.15585/mmwr.mm7435a1.

[19] E. Kamitani, et al., A systematic review of HIV pre-exposure prophylaxis best practices: where are the people who inject drugs?, AIDS Behav (2024). doi:10.1007/s10461-024-04332-z.