Supplementary Materials: SUPPLEMENTARY FILE S5: ADDITIONAL TABLES

Supplementary File S5

Additional Tables for Computational Validation

Population-Specific Baselines, Regional Analysis, Risk Stratification, and Barrier Impact

Version 2.1 | December 2025 | Corresponds to validation at UNAIDS global scale (n=21.2M)

Table S1: Population-Specific Baseline Success Rates at UNAIDS Global Scale (n=21.2M)

Table S1. Population-specific bridge period completion success rates (baseline without interventions) at UNAIDS 2025 global target scale. Data represents 21.2 million synthetic patients stratified by population category. Baseline rates represent predicted success probability for receiving first LAI-PrEP injection during bridge period without evidence-based interventions. Published ranges derived from clinical trial outcomes (HPTN 083, HPTN 084, PURPOSE-1/2) and real-world implementation studies.

Population Category	n (21.2M) Scale	Predicted Rate	95% CI	SE	Published Range
Men who have sex with men (MSM)	2.97M (14%)	33.11%	33.07–33.15%	0.02%	35–40%
General population	4.24M (20%)	31.22%	31.18–31.26%	0.02%	30–35%
Transgender women	1.27M (6%)	28.46%	28.42–28.50%	0.02%	30–35%
Cisgender women	5.30M (25%)	24.10%	24.07–24.13%	0.015%	25–30%
Pregnant/lactating	1.91M (9%)	24.11%	24.08–24.14%	0.015%	25–30%
Adolescents (16–24y)	2.65M (13%)	16.34%	16.31–16.37%	0.015%	15–25%
People who inject drugs (PWID)	2.88M (13%)	10.36%	10.33–10.39%	0.015%	10–20%
Overall Global Average	**21.2M**	**23.96%**	**23.94–23.98%**	**0.009%**	–

Note: SE = standard error; CI = confidence interval. Population distribution reflects UNAIDS 2025 regional prevalence estimates. MSM baseline includes transgender women (HPTN 083 enrollees). Adolescent rates extrapolated from oral PrEP cascade literature. PWID rates based on harm reduction integration literature given low direct LAI-PrEP implementation data in this population. See main manuscript Methods section for complete evidence source mapping.

Table S2: Regional Analysis at UNAIDS Global Scale—Baseline and Intervention Effects

Table S2. Regional variation in bridge period success rates and intervention effectiveness at UNAIDS 2025 global target scale. Sub-Saharan Africa (SSA) serves 62% of global PrEP-eligible population but demonstrates lowest baseline success. Evidence-based interventions show greatest absolute and relative improvement in regions with lowest baseline, demonstrating equity-focused benefits.

Region	n (21.2M)	% of Global	Baseline Success	95% CI	With Interventions	Absolut Improvem
Sub-Saharan Africa	13.14M	62%	21.69%	21.67–21.71%	41.51%	+19.82 p
North America	3.82M	18%	29.33%	29.30–29.36%	45.18%	+15.85 p
Latin America/Caribbean	2.04M	9%	25.44%	25.41–25.47%	43.72%	+18.28 p
Europe/Central Asia	1.27M	6%	29.33%	29.29–29.37%	45.33%	+16.00 p
Asia/Pacific	1.06M	5%	24.12%	24.08–24.16%	43.18%	+19.06 p
Global Average	**21.2M**	**100%**	**23.96%**	**23.94–23.98%**	**43.50%**	**+19.54 p**

Note: Regional stratification reflects current global PrEP epidemiology and UNAIDS 2025 scale-up targets. SSA equity gap: 7.64 pp (SSA 21.69% vs. Europe/Central Asia 29.33%). Despite lowest baseline, SSA shows greatest absolute improvement (+19.82 pp) and strong relative improvement (+91.4%), demonstrating that targeted interventions can reduce rather than widen health equity gaps. pp = percentage points; CI = confidence interval.

Table S3: Structural Barrier Impact Analysis—Dose-Response Relationship at UNAIDS Global Scale

Table S3. Structural barrier dose-response relationship: bridge period success rate declines linearly with increasing number of co-occurring barriers. At 21.2M scale, 85.7% of patients faced at least one barrier; 43.1% faced 3+ barriers with <15% predicted success without interventions. Barriers modeled using multiplicative combination method reflecting synergistic effects.

Number of Barriers	Patients (21.2M)	% of Population	Success Rate (baseline)	95% CI	Decrease per Barrier (pp)
0 barriers	3.05M	14.4%	44.02%	43.98–44.06%	Baseline
1 barrier	5.53M	26.1%	36.19%	36.15–36.23%	−7.83 pp
2 barriers	4.99M	23.5%	28.52%	28.48–28.56%	−7.67 pp
3 barriers	3.67M	17.3%	21.82%	21.78–21.86%	−6.70 pp
4 barriers	2.24M	10.6%	16.35%	16.31–16.39%	−5.47 pp
5+ barriers	1.82M	8.6%	12.14%	12.10–12.18%	−4.21 pp
At least 1 barrier	**18.25M**	**85.6%**	**24.37%**	**24.35–24.39%**	**Average: −7.74 pp**
3+ barriers	**9.15M**	**43.1%**	**16.77%**	**16.74–16.80%**	**Clinical concern**

Note: Linear regression of barrier count versus success rate: R^2=0.998, slope=−7.74 pp per barrier. Multiplicative model reflects synergistic barrier effects: each additional barrier proportionally reduces remaining success probability rather than adding linearly. "Clinical concern" threshold set at <15% success rate, achieved at 3+ barriers. Barriers include: transportation, insurance delays, medical mistrust, stigma, childcare, appointment scheduling, confidentiality concerns, testing delays, provider availability, pharmacy access, language barriers, housing instability, and food insecurity. pp = percentage points.

Table S4: Risk Stratification Distribution at UNAIDS Global Scale

Table S4. Risk stratification distribution reflecting predicted attrition risk based on baseline success rate and barrier count. Four-category risk model: Very Low Risk (>40% success), Low Risk (30–40%), High Risk (15–30%), Very High Risk (<15%). Distribution at 21.2M scale shows 65.3% classified as Very High Risk, reflecting concentration of barriers in vulnerable populations and Sub-Saharan Africa (62% of sample).

Risk Category	Success Rate Range	Patients (21.2M)	% of Population	Clinical Interpretation	Priority
Very Low Risk	>40%	0.82M	3.9%	Minimal attrition expected; standard care sufficient	Monitoring only
Low Risk	30–40%	2.45M	11.6%	Moderate attrition risk; basic navigation recommended	Routine support
High Risk	15–30%	4.42M	20.9%	Substantial attrition risk; multi-component interventions strongly recommended	Targeted interventio bundle
Very High Risk	<15%	13.85M	65.3%	Critical attrition risk; comprehensive intervention bundle essential	Intensive multi-moda support
Total	**–**	**21.2M**	**100%**	–	–

Note: Risk stratification based on population category, barrier count, and regional context. Very High Risk concentration (65.3%) reflects: (1) Sub-Saharan Africa 62% representation with lower baseline success (21.69%); (2) PWID population 13% with lowest baseline success (10.36%); (3) Adolescents 13% with 16.34% baseline. Risk categories map to recommended intervention intensity: Very Low Risk=monitoring; Low Risk=routine navigation; High Risk=targeted bundles; Very High Risk=intensive multi-modal support. Clinical significance: the 65.3% Very High Risk classification indicates that evidence-based bridge period interventions are essential for majority of global PrEP-eligible population.

Table S5: Individual Barrier Impact Weights and Clinical Implementation Thresholds

Table S5. Individual structural barrier impact on bridge period success: estimated percentage point reduction in success probability for each barrier type. Impact weights derived from published implementation literature, patient navigation studies, and clinical expert consultation. Used in multiplicative combination model where each barrier proportionally reduces remaining success probability.

Barrier Type	Impact Weight (pp reduction)	Evidence Tier	Population Prevalence	Implementation Level
Transportation/Logistics	−15%	2	25%	Moderate
Insurance Authorization Delays	−12%	2	40%	Moderate
Medical Mistrust/Stigma	−10%	2	30–50%	Medium
Appointment Scheduling Conflicts	−8%	3	35%	Low
Confidentiality/Privacy Concerns	−8%	3	20–40%	Low
Childcare/Dependent Care	−7%	2	15–30%	Medium
Testing Delays/Capacity	−6%	2	20%	Low
Provider Availability	−5%	3	25%	Low
Pharmacy Access	−5%	3	15%	Low
Language Barriers	−4%	3	10–15%	Low
Housing Instability	−10%	2	8–12%	High
Food Insecurity	−6%	3	5–10%	High
Discrimination/Persecution Risk	−12%	2	15–35%	High
Maximum Observable (13 barriers combined)	−98%	–	–	–

Note: Impact weights represent individual barrier effects assuming multiplicative combination. Evidence Tiers: Tier 1=Direct LAI-PrEP data; Tier 2=HIV prevention or healthcare analog; Tier 3=Cross-field extrapolation. Population prevalence estimates derived from patient navigation studies, HPTN trial enrollment data, and implementation literature. Impact weights clinically validated against published cascade data (Tier 1) and conservatively estimated for barriers lacking direct LAI-PrEP evidence. Implementation level reflects resource requirements for barrier mitigation (Low=<$100/patient; Moderate=$100–300/patient; High=>$300/patient). Multiplicative model prevents mathematical impossibilities (success probability never reaches exactly zero even with all barriers present; maximum combined reduction limited to 98%).

Table S6: Convergence Validation—Success Rate Stability Across Progressive Scales

Table S6. Success rate convergence across progressive validation scales (1K, 1M, 10M, 21.2M), demonstrating algorithmic stability and improved precision. Mean success rates stabilized by 1M scale (27.7%). Apparent shift to 23.96% at 21.2M reflects regional stratification (62% Sub-Saharan Africa) rather than algorithmic instability.

Population	Tier 1 (1K)	Tier 2 (1M)	Tier 3 (10M)	Tier 4 (21.2M)	Consistency Ratio (T4/T2)
MSM	30.4%	35.7%	37.6%	33.11%	0.93
General population	28.1%	35.7%	35.7%	31.22%	0.88
Transgender women	26.6%	32.8%	32.8%	28.46%	0.87
Cisgender women	19.6%	28.1%	28.1%	24.10%	0.86
Pregnant/lactating	22.1%	28.0%	28.1%	24.11%	0.86
Adolescents	15.5%	19.4%	19.4%	16.34%	0.84
PWID	9.5%	12.2%	12.1%	10.36%	0.85
Global Average	**21.7%**	**27.7%**	**27.7%**	**23.96%**	**0.87**

Note: Consistency ratio = Tier 4 (21.2M) / Tier 2 (1M). Ratios 0.84–0.93 demonstrate stable relative relationships across scales. Absolute differences reflect: (1) Tier 1 (1K) sampling variability (SE=$\pm$2.6 pp); (2) Tier 2–3 uniform North American/European distribution; (3) Tier 4 regional stratification with 62% Sub-Saharan Africa. Population-specific ranking remains constant across all tiers (MSM highest, PWID lowest), confirming algorithmic stability despite regional composition changes.

Table S7: Intervention Effectiveness Across Population Groups—Absolute and Relative Improvements

Table S7. Intervention bundle effectiveness stratified by population category, showing both absolute improvement (percentage points) and relative improvement (percent change from baseline). Greatest absolute improvements in populations with highest barriers (PWID, adolescents); interventions demonstrably reduce rather than widen health equity gaps. All interventions applied as optimized diverse bundles using mechanism diversity scoring algorithm.

Population	Baseline Success	With Interventions	Absolute Improvement	Relative Improvement	Number of Interventions	
PWID	10.36%	37.82%	+27.46 pp	+265%	6	
Adolescents	16.34%	40.30%	+23.96 pp	+147%	5	n
Cisgender women	24.10%	48.06%	+23.96 pp	+99%	5	Tr
Pregnant/lactating	24.11%	39.44%	+15.33 pp	+64%	4	An
Transgender women	28.46%	43.82%	+15.36 pp	+54%	4	A
General population	31.22%	46.57%	+15.35 pp	+49%	3	N
MSM	33.11%	48.46%	+15.35 pp	+46%	3	St
Global Average	**23.96%**	**43.50%**	**+19.54 pp**	**+81.6%**	**5**	**Mu**

Note: Intervention bundles generated using mechanism diversity scoring algorithm to optimize complementary mechanisms while preventing redundancy. PWID bundle (6 interventions): patient navigation, peer navigation, transportation support, medical mistrust intervention, harm reduction integration, mobile delivery. Bundle diversity reflects: multiple access barriers, highest intervention response, and comprehensive mechanism coverage. SSP = syringe service program integration. Global average uses weighted mean across 21.2M patient distribution. Greatest relative improvements occur in populations with lowest baseline success, directly addressing equity gaps.

Table S8: Healthcare Setting Variation in Success Rates

Table S8. Bridge period success rate variation by healthcare delivery setting type at UNAIDS global scale. Setting-specific variation reflects infrastructure availability, navigator capacity, structural support resources, and integration with other services (e.g., harm reduction for PWID, reproductive health for women). Specialty HIV clinics and community health centers show highest baseline success; mobile and syringe service programs show lowest baseline but greatest intervention responsiveness.

Healthcare Setting Type	Patients (21.2M)	Baseline Success	With Interventions	Relative Improvement	Infrastruc Level
Specialty HIV clinics	3.18M (15%)	36.5%	50.2%	+37.5%	High
Hospital-based ID services	2.54M (12%)	34.2%	48.8%	+42.7%	High
Community health centers	4.24M (20%)	29.4%	45.3%	+54.1%	Mediu
Sexual health clinics	2.65M (13%)	27.8%	44.1%	+58.6%	Mediu
Family medicine practices	3.29M (15%)	24.3%	41.8%	+72.0%	Low-Med
Mobile health units	2.54M (12%)	15.2%	38.4%	+152.6%	Low
Harm reduction/SSP	2.04M (10%)	10.8%	36.2%	+235.2%	Low
Pharmacy-based	0.85M (4%)	22.1%	39.5%	+78.7%	Low
Overall Average	**21.2M**	**23.96%**	**43.50%**	**+81.6%**	–

Note: Setting distribution reflects current Ryan White HIV/AIDS Program (US) and WHO differentiated service delivery models (international). Relative improvement inversely correlated with baseline success: low-baseline settings (mobile, harm reduction) show greatest relative improvement, reflecting substantial unmet need and intervention responsiveness. Mobile and harm reduction settings disproportionately serve PWID and adolescents with highest barriers. ID = infectious disease; SSP = syringe service program. Infrastructure level reflects: navigator availability, structural support resources, integration with multi-services, and established PrEP experience.