No One Left Behind
HIV Prevention Across the Life Course

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Disclosures

- Site investigator for Merck EXPrESSIVE-10 clinical trial
- Consultant for Merck, Inc.

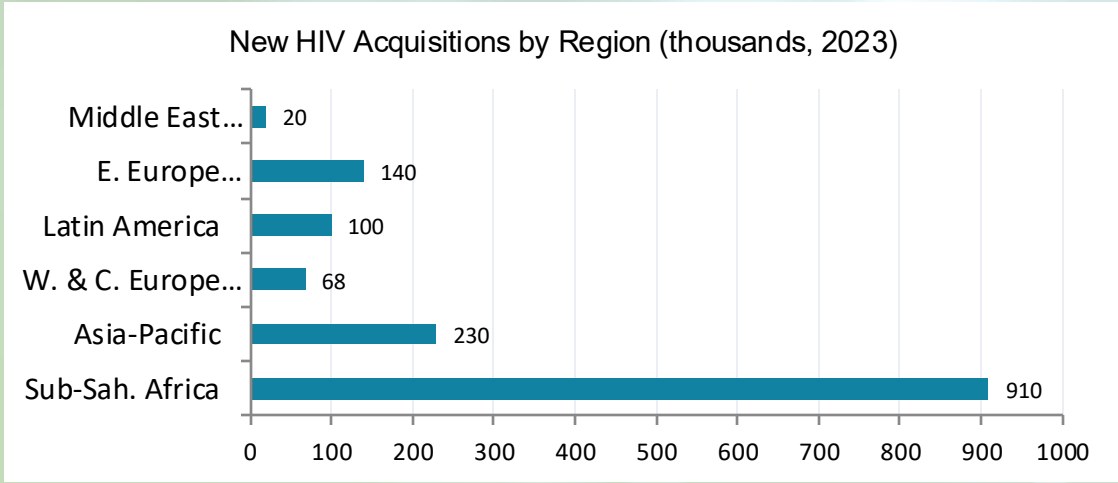
The Unfinished Epidemic: Global HIV Burden in 2025

40.8M
people living with HIV globally

1.3M
new HIV acquisitions in 2024

630K
AIDS-related deaths in 2024

29.8M
on antiretroviral therapy



Despite Progress…

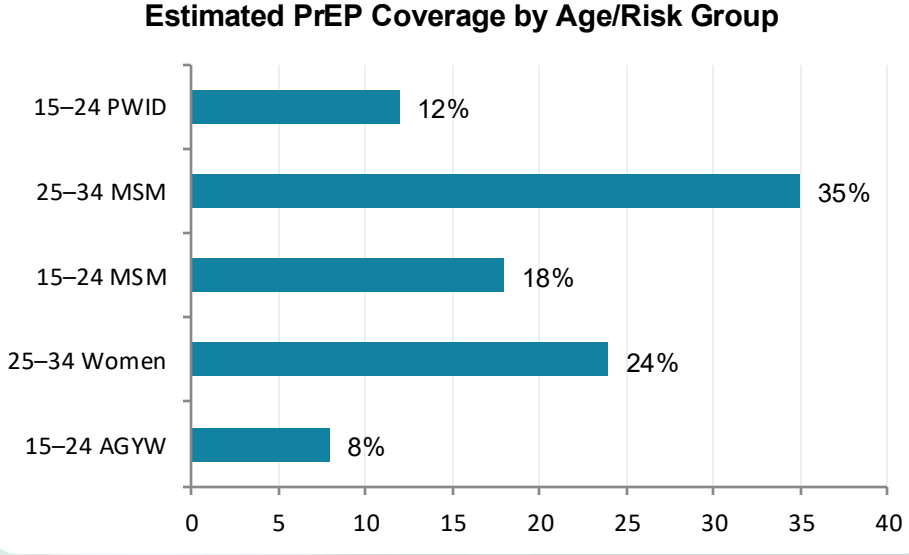
- 4,000+ new acquisitions daily
- Prevention coverage remains deeply inequitable
- Young people account for 1 in 3 new HIV acqusitions
- Key populations carry disproportionate burden
- Older adults are a rapidly growing PLHIV group

Source: UNAIDS Global HIV & AIDS Statistics — 2025 Fact Sheet

Adolescents and Young Adults: Highest Risk, Lowest Coverage

The Prevention Gap

- Individuals 15–24 years old account for ~35% of new HIV acqusitions globally
- Only 29% of adolescent girls and 19% of adolescent boys aged 15–19 in Eastern and Southern Africa know their HIV status
- PrEP coverage among adolescent girls and young women (AGYW) in sub-Saharan Africa remains <10%
- Structural barriers: stigma, cost, parental consent, provider bias, school-based exclusions



Evidence Gap

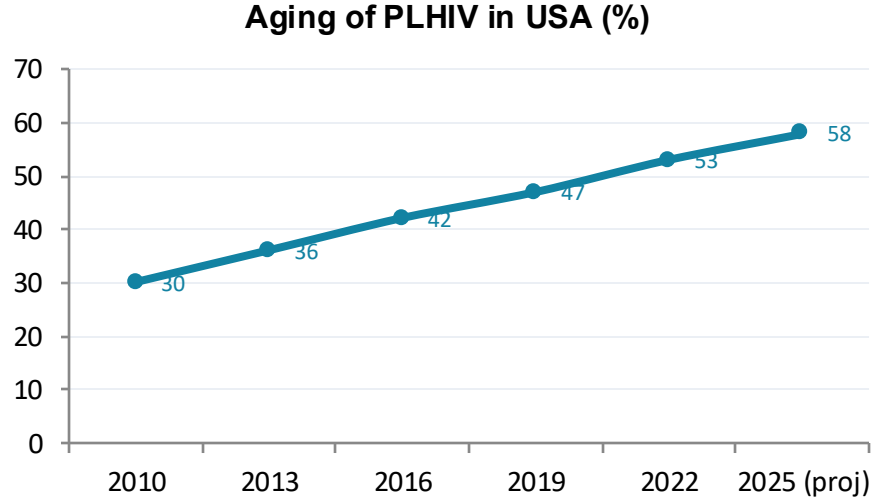
Few RCTs of long-acting PrEP have enrolled adolescents <18 yrs. Regulatory approvals lag behind evidence. Dedicated adolescent pharmacokinetic studies urgently needed.

Sources: UNICEF 2025 | UNAIDS 2024

Older Adults: The Invisible Prevention Population

Why Older Adults Are at Risk

- >50% of PLHIV in high-income countries are now aged ≥50 (CDC 2023)
- New acquisitions among ≥50s account for 16% of diagnoses in USA
- Lower condom use post-menopause; reduced perceived risk
- Clinicians rarely offer HIV testing or PrEP to older patients (assumed low risk)
- Widowhood and new partnerships in later life increase exposure
- Erectile dysfunction medications associated with condomless sex



Evidence Gap & Implementation Challenge

PrEP trials have systematically excluded or under-enrolled older adults. Polypharmacy, renal function, and bone density concerns require dedicated PK/PD data for long-acting agents in this group. PrEP prescribing rates among ≥50s remain extremely low.

Source: CDC HIV Surveillance Report 2023 | hivinfo.nih.gov

Median HIV prevalence: Key populations vs. other adults

Transgender people

8.5%

Highest per-capita burden globally

MSM

7.6%

HIV prevalence vs general population (global)

PWID

7.1%

Overlap with HCV, mental health, sex work

Sex workers

2.7%

Higher risk in LMICs; criminalization limits care

People in prison

1.4%

Higher prevalence; PrEP access near-zero

Adults aged 15-49 years

0.7%

Low PrEP utilization

Key Implementation Challenge:

Criminalization of same-sex relationships (67+ countries), sex work, and drug use structurally blocks PrEP access. Long-acting modalities may reduce stigma by eliminating visible pill-taking, but require clinic access, a barrier for key populations.

Source: UNAIDS Global AIDS Update 2025

Other Overlooked High-Risk Groups Worldwide

Migrants and Refugees

Disrupted care, documentation requirements limit PrEP access. Conflict zones = surveillance void.

Women Who Inject Drugs

Double marginalisation. Maternal HIV risk. Excluded from most trials.

Incarcerated Women

High coercive sex risk; few PrEP programs in prisons globally.

Serodifferent Couples

U=U messaging under-utilised; sub-optimal PrEP coverage in seronegative partners.

Bisexual Men

Bridge population. Often excluded from MSM-targeted prevention programs.

Rural and Indigenous

Structural barriers: supply chain gaps, limited provider training, cultural barriers to PrEP, few harm reduction services.

Common Thread: Low prioritization in national HIV strategies, sparse prevention data, and structural exclusion from biomedical prevention programs

#CONTINUUM2026

Who Is Still Being Left Behind?

Estimated PrEP coverage vs. need by population group; persistent prevention gaps remain

MSM

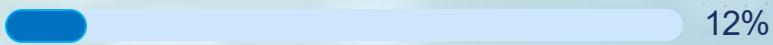
78% unmet need

Transgender Women

85% unmet need

People Who Inject Drugs

92% unmet need



Adolescent Girls and Young Women

88% unmet need

Sex Workers

82% unmet need

Older Adults (50+)

95% unmet need

Sources: Zhao Int J Infect Dis 2025 | UNAIDS 2024 | Global AIDS Report 2025

Monthly or Weekly Oral PrEP: The Next Frontier

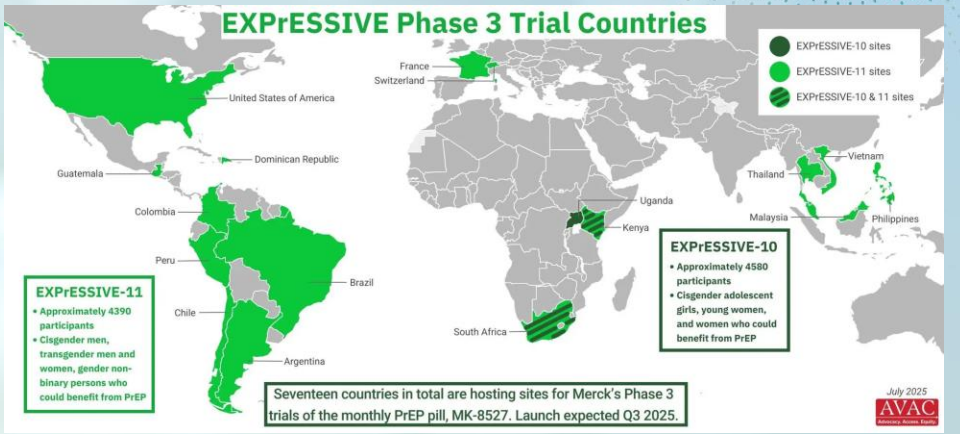
MK-8527

Mechanism: Nucleoside reverse transcriptase translocation inhibitor (NRTTI)

Dosing: 11 mg once monthly (oral)

Status: Phase 3 trials underway

Key note: CD4 count decline signal halted ISL monotherapy; no safety signal in MK-8527 phase 1/2 trials



June 15, 2026

U.S. FDA Accepts Gilead's Application for Investigational Once-Weekly Oral Yeztugo, Potentially the First Long-Acting Pill for HIV Prevention

⚠ Evidence Gap: No Phase 3 efficacy data yet for monthly oral PrEP. Implementation advantage (no injections, private dosing) could be transformative if efficacy confirmed.

One-and-Done PEP: Revolutionising Post-Exposure Prophylaxis

The Problem with Current PEP

- Requires timely access (within 72 hours); hard in remote/LMIC settings
- Limited availability in community settings and for sexually abused children and adolescents
- 28-day daily pill course; high non-completion rates (30–50%)
- Stigma around presentation to health services
- Multiple healthcare visits required
- Cost and supply barriers in LMICs

The Vision: Single-Dose or Once-Weekly PEP

- Single dose injectable PEP: 66.7% (95% CI: -3.4%, 89.3%) efficacy of CAB LA/RPV LA in macaque model
- Single dose oral PEP: MK8527 being evaluated in phase 3 trials for PrEP (could reduce PEP dosing from 28 pills to 1, but concerns about monotherapy)
- Once-weekly PEP: Lenacapavir 300 mg qw; islatravir/lenacapavir weekly dosing being evaluated in Phase 3 trial for treatment (could reduce PEP from 28 pills to 4)
- Potential for pharmacist or community dispensing without 28-day course

Sources: Srinivasan EBioMedicine. 2026; Ford AIDS 2014; ClinicalTrials.gov NCT06630286 , NCT06630299

Self-Start PEP – Bringing Forward the 72 Hour Window

PEP starter packs dramatically reduce time to first dose. A simple intervention with major impact.

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Median time from exposure to first PEP dose (HOME PEPSE study baseline)

AFTER (ADVANCE PACK)

7.3 hours

Median time from exposure to first PEP dose with self-start advance supply

74% reduction in time to first dose

- Pharmacist-dispensed advance packs shown feasible in UK and other settings
- mHealth reminders and telehealth follow-up improve adherence and reduce LTFU
- Reduces dependence on emergency department attendance; reduces stigma exposure

Fox, Sex Transm Infect. 2024 | Kennedy, J Int AIDS Soc. 2025

Broadly Neutralising Antibodies (bNAbs) and HIV Vaccines

bNAbs for Prevention

- VRC01 (CD4-binding site): (HVTN 703/HPTN 081 and HVTN 704/HPTN 085); proof-of-concept for bNAb PrEP
- 3BNC117 and 10-1074 (V3 loop): IAVI C100 Phase 1/2 trial completed
- Combination antibodies: HVTN 140/HPTN 101 (VRC07-523LS [CD4 binding site], PGT121.414.LS [V3-glycan loop], and PGDM1400LS [V2-apex] safe and well tolerated
- Challenge: strain diversity limits universal protection
- Long-acting bNAb formulations (half-life extension) in development

HIV Vaccine Landscape

- RV144 (Thai trial, 2009): 31.2% efficacy; only vaccine showing partial protection
- HVTN 702 (modified RV144 in Africa): NO efficacy (trial halted for futility in 2020)
- HVTN 705/HPX2008 Phase 2b halted in 2021 for futility
- HVTN 706/HPX3002/Mosaico - Ad26.Mos4.HIV + gp140-mosaic gp140; stopped for futility in 2023
- T-cell therapeutic vaccines (HIV-CORE 005.2; HIV-CORE 006) completed Phase 1 trials
- Timeline to licensed HIV vaccine: likely 2030s at earliest

Sources: Buchbinder Lancet HIV 2025; Borthwick Lancet Microbe 2025; Chanda Lancet Microbe 2025; Corey NEJM 2021; Gray NEJM 2021; Rerks-Ngarm NEJM 2009

Reaching the Unreached through Community-Based Delivery

Decentralised delivery models are essential to overcome structural barriers and reach key populations

Pharmacist-Initiated PrEP/PEP

- Reduces clinic barriers and wait times
- Shown feasible in multiple settings
- Advance PEP supply dramatically cuts time to first dose

Evidence: Ortblad 2024, Kareithi 2025

Lay Health Workers

- Systematic review supports task sharing for PEP delivery
- Community health workers reduce stigma at point of care
- Quality of evidence: low-moderate; more trials needed

Evidence: Kennedy 2025

mHealth and Telehealth

- SMS reminders improve adherence to 28-day PEP
- Virtual consultations reduce clinic attendance burden
- Chatbots and apps increase PEP/PrEP awareness

Evidence: Multiple implementation studies

Advance Supply (Self-Start)

- Dramatically reduces time to first dose (28.5 to 7.3 hours)
- Appropriate uptake increased with advance supply
- Suitable for frequent PEP users and high-risk individuals

Evidence: Fox 2022

Kennedy, J Int AIDS Soc. 2025 | Fox Sex Transm Infect. 2024 Nov 11

Evidence Gaps: What We Still Don't Know

Adolescents	Limited LEN, CAB-LA PK safety data for <18 yrs or weighing<35 kg (<77 lbs); regulatory pathway for minors; school and community delivery models
Older Adults	Renal and bone safety of LA agents; polypharmacy interactions; PK in >65 yrs; cognitive, adherence considerations
Pregnant/ Lactating Women	LA-PrEP safety data in pregnant and breastfeeding adolescents and women
PWID	LA PrEP integrated with opioid agonist therapy; drug-drug interactions with methadone, buprenorphine
One-dose PEP	No human trial data; optimal agent; window period coverage; resistance selection risk
Monthly Oral PrEP	Phase 3 efficacy pending; no safety concerns in phase 1/2 MK-8527 studies; long-term safety
Real-world LA PrEP	Effectiveness beyond RCT settings; LTFU from injection programs; patient-reported outcomes

Implementation Challenges: Bridging Efficacy to Impact

Cost & Affordability

CAB-LA ~$3,700/yr USA; lenacapavir >$40,000/yr treatment price. Gilead voluntary licensing for generics in 120 LMICs — critical but implementation lagging. Cost-effectiveness models needed.

Health System Capacity

LA PrEP requires trained injectors, cold chain, biowaste disposal. Limited PrEP-experienced providers in LMICs. Task-shifting to nurses, community health workers essential.

Resistance and Drug Resistance

Cabotegravir resistance if HIV acquired during low-level drug exposure ('tail effect'). Baseline INSTI resistance testing required. Lenacapavir resistance patterns still emerging (N74D, K70R, Q67H).

Regulatory and Policy Gaps

CAB-LA approved in >60 countries. Lenacapavir PrEP being rolled out. National PrEP programs are updating guidelines.

Community Trust and Demand Creation

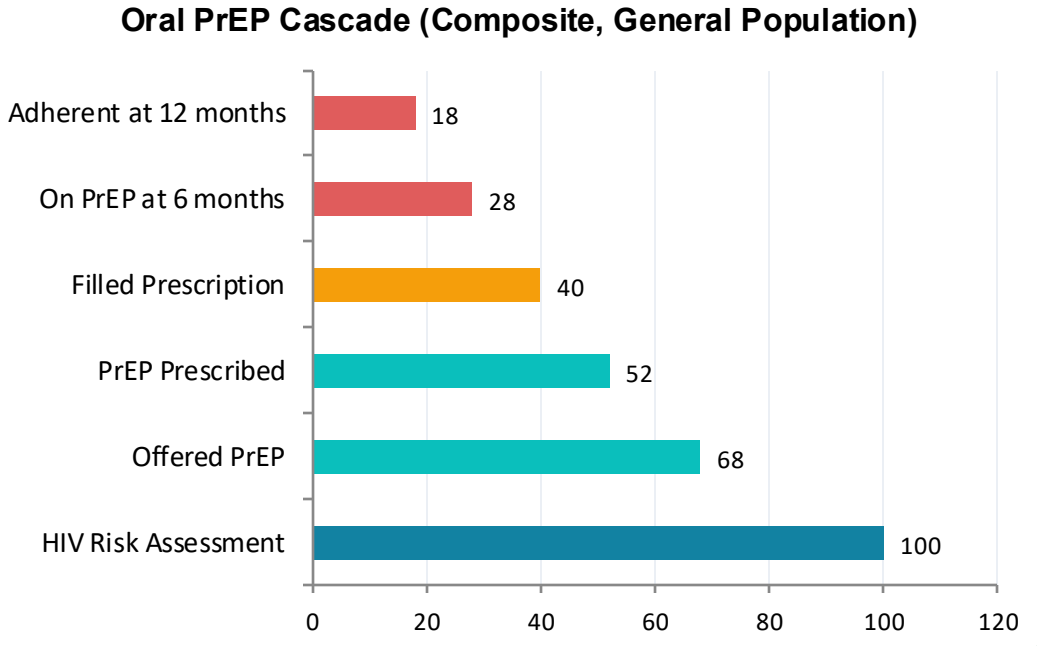
Injection hesitancy documented in trials. Concerns about equitable LA-PrEP access and ‘pharmacokinetic tail' period. Community-led research and demand creation critical.

Equity and Access

Biomedical advances risk widening prevention inequities. Priority settings (SSA) and AGYW have highest burden but least access. LA PrEP must be designed for community delivery and not be clinic-dependent.

Equity-Centred Implementation: Reaching Those Left Behind

The Prevention Cascade — Where People Fall Out



Closing the Gap

- Community-based LA PrEP delivery (mobile units, AGYW clubs)
- Pharmacy-based initiation without physician gatekeeping
- PrEP navigation by community health workers
- Demand creation through peer networks & social media
- Reduce clinic visits — LA PrEP inherently reduces burden
- PEPFAR & GFATM integration with LA PrEP programs
- Patient-centred outcome measurement

Sources: Miller AJPM 2025 | Tang IAS 2023 | Smith Lancet HIV 2023 | Mistler 2021

Future Directions: The Next Decade of HIV Prevention

01

Accelerate Access to Lenacapavir PrEP

Accelerate generic manufacturing (India, South Africa, etc). Community delivery models, e.g., pharmacies

02

Monthly/weekly Oral PrEP Efficacy

Complete EXPrESSIVE-10 and 11 trials. Monthly or weekly oral PrEP could be transformative for privacy and equity in LMIC settings.

03

Develop One-and-Done PEP

Prioritise community pharmacy dispensing. Integrate with sexual health services and emergency departments.

04

Inclusive Trial Designs

Mandate adolescent sub-studies. Enrol older adults, pregnant women, PWID. Sex-stratified analyses. Community advisory boards in study governance.

05

Combination Prevention 2.0

Co-located LA PrEP + STI services + contraception + harm reduction. Integrate HIV prevention with reproductive health, mental health, and harm reduction at community level.

06

Structural and Social Enablers

Decriminalize same-sex relationships and drug use. Remove consent barriers for adolescents. Finance community-led HIV prevention at scale.

Key Conclusions and Messages for the Field

1. Long-acting PrEP is here. Lenacapavir's PURPOSE trials represent a historic breakthrough, with high efficacy in real-world populations. Equitable access is a critical next step.

2. Cabotegravir-LA bridges the gap; already approved and with limited availability, but cost, clinic burden, and resistance management require urgent systems solutions.

3. Weekly or monthly oral PrEP and one-dose PEP are transformational in concept; evidence gaps must be closed urgently, particularly for populations that cannot access injections.

4. Prevention disparities are structural; adolescents, key populations, older adults, and overlooked groups carry disproportionate risk but benefit least from current programs. Equity must be designed in, not retrofitted.

5. The next era of HIV prevention demands combination: biomedical innovation + community delivery + structural reform + political will. Long-acting tools only reach their potential when paired with access.

"Science has given us the tools. The question now is whether we have the will, equity, and systems to use them."