CLINTON HEALTH ACCESS INITIATIVE

2024 HIV MARKET REPORT

Issue 15, December 2024

The state of HIV treatment, testing, and prevention in low- and middle-income countries

BILL & MELINDA GATES foundation

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Foreign, Commonwealth & Development Office

DISCLAIMER

The data sources primarily used for analysis in the report include Clinton Health Access Initiative (CHAI) country teams, ministry of health counterparts, stakeholder resources and conversations (e.g. Global Fund, PEPFAR, UNAIDS, Unitaid, WHO, and civil society partners), and published research. CHAI has taken precautions to verify the information shared in the report. However, the analysis in the report is not exhaustive, and the responsibility for the interpretation and use of the material lies with the reader. The mention of specific companies or products does not imply CHAI's endorsement or recommendation.

ACKNOWLEDGMENT

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Front Cover: A clinician in Nigeria prepares a child for a blood draw to conduct viral load and CD4 testing.

HIV Market Report
CONTENTS

ACRONYMS

3HP	Three months of weekly RPT+INH for TPT
3TC	Lamivudine
5FC	Flucytosine
ABC	Abacavir
Africa CDC	Africa Centres for Disease Control and Prevention
AHD	Advanced HIV disease
AIDS	Acquired immunodeficiency syndrome
AP	Asia Pacific
APWG	ARV Procurement Working Group
ART	Antiretroviral therapy
ARV	Antiretroviral
ATV/r	Atazanavir/ritonavir
AZT	Zidovudine
BE	Bioequivalence
BIC	Bictegravir
bNAb	Broadly neutralizing antibody
CAB	Cabotegravir
CAB-LA	Long-acting cabotegravir
CAR	Caribbean
CE	Conformité Européenne (European Conformity)
CHAI	Clinton Health Access Initiative
CIFF	Children's Investment Fund Foundation
CLHIV	Children living with HIV
CM	Cryptococcal meningitis
CMD	Common mental health disorder
CrAg	Cryptococcal antigen
CROI	Conference on Retroviruses and Opportunistic Infections
CVD	Cardiovascular disease
DcNP	Drug-combination-nanoparticle
DPP	Dual prevention pill
DRV/r	Darunavir/ritonavir
DTG	Dolutegravir
DVR	Dapivirine vaginal ring
EECA	Eastern Europe and Central Asia
EFV	Efavirenz
EGPAF	Elizabeth Glaser Pediatric AIDS Foundation
EID	Early infant diagnosis
EOI	Expression of interest
ESA	East and Southern Africa
EXW	Ex-works
FDC	Fixed-dose combination
FTC	Emtricitabine
GA	Generic-accessible
GBP	Great Britain pound
GDP	Gross domestic product
GHSC-PSM	USAID Global Health Supply Chain Program - Procurement and Supply Management
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HIVST	HIV self-test

HPTN	HIV Prevention Trials Network
INH	Isoniazid
INSTI	Integrase strand transfer inhibitor
ISL	Islatravir
KP	Key population
LA	Latin America
L-AmB	Liposomal amphotericin B
LEN	Lenacapavir
LMIC	Low- and middle-income country
LPV/r	Lopinavir/ritonavir
MENA	Middle East and North Africa
MPTS	Multipurpose prevention technologies
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NCDS	Non-communicable diseases
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NRTTI	Nucleoside reverse transcriptase translocation inhibitor
NVP	Nevirapine
OI	Opportunistic infection
pALD	Pediatric ABC/3TC/DTG
pDRV/r	Pediatric darunavir/ritonavir
pDTG	Pediatric DTG
PEP	Post-exposure prophylaxis
PEPFAR	US President's Emergency Plan for AIDS Relief
PI	Protease inhibitor
PLHIV	People living with HIV
POC	Point-of-care
PQ	Prequalification
PREP	Pre-exposure prophylaxis
PRIMA	PrEP Implementation for Mothers in Antenatal Care
pTAF	Pediatric tenofovir alafenamide fumarate
RPT	Rifapentine
RPV	Rilpivirine
SC	Subcutaneous
SQ	Semiquantitative
SSA	Sub-Saharan Africa
TAF	Tenofovir alafenamide fumarate
TB	Tuberculosis
TDF	Tenofovir disoproxil fumarate
TLD	TDF/3TC/DTG
TPT	TB preventive therapy
UNAIDS	Joint United Nations Programme on HIV/AIDS
USD	United States dollar
US FDA	United States Food and Drug Administration
VL	Viral load
WCA	West and Central Africa
WCENA	Western and Central Europe and North America
WHO	World Health Organization
Wits RHI	University of the Witwatersrand Reproductive Health and HIV Institute
XTC	Emtricitibine (FTC) or lamivudine (3TC)

EXECUTIVE SUMMARY

Over the past decade, significant progress in HIV care optimization has increased treatment coverage and reduced AIDS-related deaths. The majority of people living with HIV on treatment in low- and middle-income countries (LMICs) are now on an optimal, dolutegravir (DTG)-based regimen. **But our work is not yet done.**

- More than nine million people living with HIV are not on treatment and many people cycle in and out of care, risking progressing to advanced HIV disease.[i]
- Outcomes for children and adolescents living with HIV continue to lag far behind outcomes for adults.
- New infections remain stubbornly high at 1.3 million in 2023, and progress has been unequal across regions and population groups.[i]
- Alongside improvements in life expectancy, increasing co-morbidities with non-communicable diseases present new health management challenges.
- Various political and economic contexts raise ever greater questions around future funding of and investment in essential HIV programs.

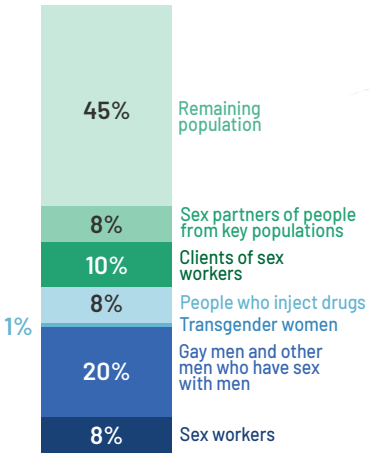
Despite these challenges, there is progress on the horizon. Groundbreaking updates in long-acting options for both treatment and prevention could enable transformation in the HIV space, offering person-centered and empowered choice. Synergies with sexual and reproductive health services are set to improve access to treatment and prevention options, including expanded access for pregnant people. Expanded use and development of HIV self-tests and multi-disease tests could help close the remaining identification gap and link individuals to care and prevention services. Momentum around integration of HIV services, including with primary health care, offers the opportunity to support client-centered, sustainable care.

However, affordable and widespread access to new innovations is not guaranteed and will require coordinated and urgent action from the global community. Improvements in care and access will also require adequate resourcing. Since 2017, HIV funding has declined, which alongside increasing resource needs will lead to an estimated US$9.5 billion financing gap for 2025.[i, ii] Donors such as PEPFAR and the Global Fund are precariously dependent on political will, with further uncertainty arising from recent US election results. HIV resourcing also competes with a growing list of global priorities, such as pandemic preparedness and response, climate change, and conflict management. Additionally, catastrophic debt in many LMICs means governments are spending significantly more on debt compared to health services.[iii, iv] Given the urgency to transition HIV programming to sustainable ownership by LMICs, debt distress will present a significant obstacle and conversations around debt relief are essential. Urgent and sustained resources are needed to meet international goals and end HIV as a public health threat.

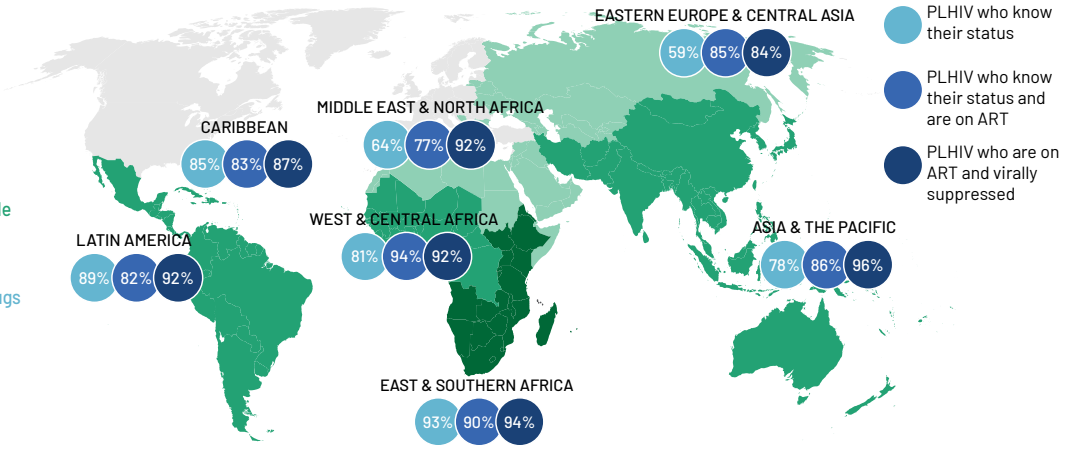
Reinvigorated commitment is essential to sustain gains, close gaps, and scale-up transformational interventions. Continued momentum is needed to achieve and sustain HIV epidemic control—failure to do so risks significant setbacks.

Global HIV Overview, 2023

ADULT HIV INFECTIONS BY KEY POPULATIONS[ii]



REGIONAL PROGRESS TOWARD UNAIDS 95-95-95 GOALS, 2023[i]



ADULT HIV TRENDS (15+)[i]

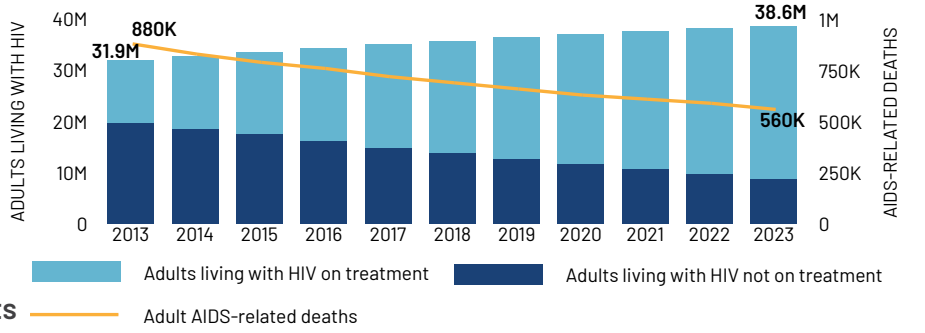
38.6M
adults living with HIV

77%
adult treatment coverage

560K
adult AIDS-related deaths

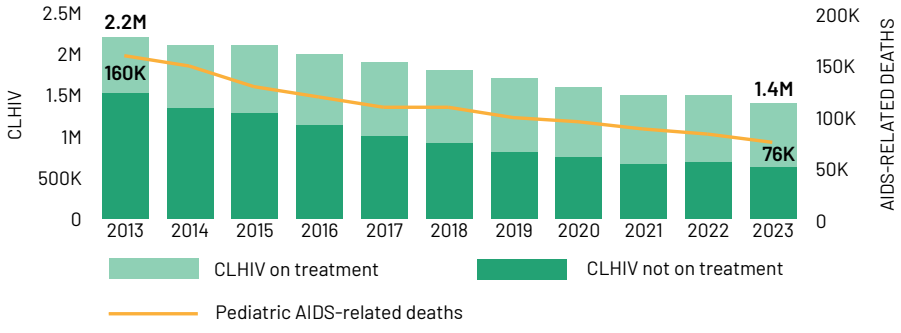
1.2M
new HIV infections among adults

GLOBAL ADULT PLHIV BY TREATMENT AND AIDS-RELATED DEATHS



PEDIATRIC HIV TRENDS (<15)[i]

GLOBAL CLHIV BY TREATMENT AND AIDS-RELATED DEATHS



1.4M
children living with HIV (CLHIV)

57%
pediatric treatment coverage

76K
pediatric AIDS-related deaths

120K
new HIV infections among children

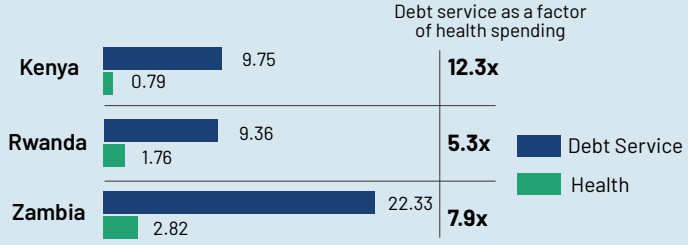
HIV FINANCING

$19.8B
in financing for HIV in LMICs in 2023 (USD)

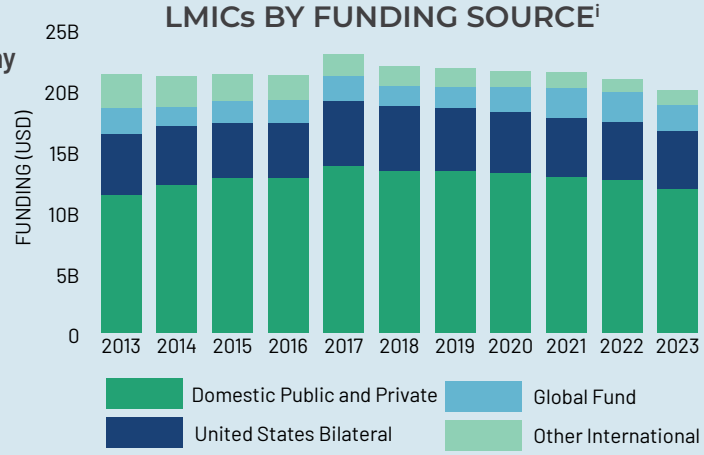
>5X
GDP spent on debt service in many LMICs as compared to health

FORECASTED DEBT SERVICE VS HEALTHCARE EXPENDITURE

(Percentage of GDP, 2026)[iii]



RESOURCE AVAILABILITY FOR HIV IN LMICs BY FUNDING SOURCE[i]



KEY HIV MARKET UPDATES

HIV PREVENTION

SUPERIOR EFFICACY

of twice-yearly subcutaneous lenacapavir for HIV PrEP demonstrated in PURPOSE 1 and 2 trials among diverse populations at elevated risk of HIV acquisition

GENERIC LICENSING

agreement signed between Gilead and 6 manufacturers to supply lenacapavir for select indications, opening up a pathway for access in 120 LMICs

HIV TESTING

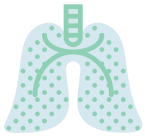
11+ COUNTRIES

with planned or ongoing adoption of blood-based HIV self-tests

~100K DECREASE

in early infant diagnosis tests run in LMICs between 2022 and 2023, highlighting the urgent need for global attention to ensure children are identified and initiated on treatment

ADVANCED HIV DISEASE



PEDIATRIC 3HP

for tuberculosis (TB) prevention now available as a dispersible tablet for children two years and older

AZITHROMYCIN

prequalified by the World Health Organization (WHO) in April 2024 for treatment of opportunistic infections

HIV TREATMENT

$1.6B

antiretroviral (ARV) market size in GA[1] LMICs, reflecting continued decreases in ARV costs (USD)[v]

1B+ PACKS

of TLD supplied as of June 2024, with 95% of adults on treatment in LMICs now on an optimal dolutegravir (DTG)-based regimen

<$40

PPPY for adult first-line treatment (USD)[vi]

14 COUNTRIES

have placed or received orders of pALD, the first triple-fixed dose combination product for children containing DTG

<$100

PPPY for pediatric first-line treatment[2] (USD)[vi]

HIV TREATMENT MONITORING

26M VIRAL LOAD TESTS

run in low- and middle-income countries in 2023

MINIMAL DTG RESISTANCE

and high viral load suppression according to observational data from a new WHO Report

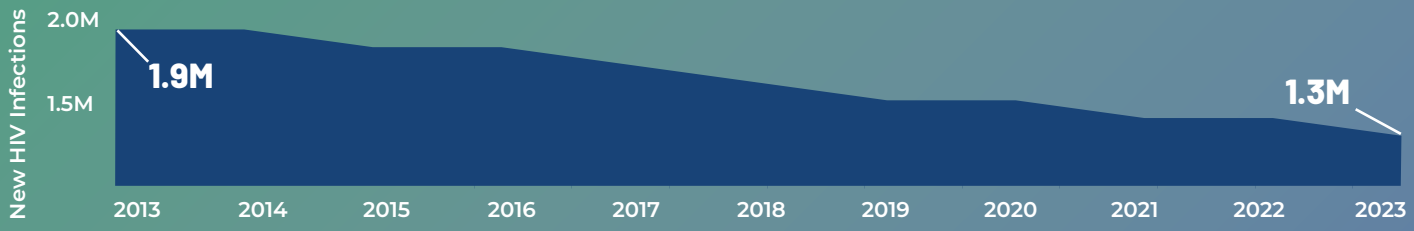
[1] *See Appendix C for a definition of generic-accessible (GA)*
[2] *Dosing for children weighing 10-13.9 kg*

PREVENTION

Developments in long-acting modalities for HIV prevention and multipurpose prevention technologies have the potential to pave the way for a transformed paradigm of increased choice and the expansion of person-centered care. Limited procurement and implementation studies have begun in the introduction of long-acting prevention products, but LMIC access remains inadequate. As efforts progress to ensure widespread, affordable generic access, continued innovations, such as differentiated service delivery and integration with sexual and reproductive health services, remain critical to expanding access to prevention services. With continued stagnation of new infections, and as the populations and regions most at risk continue to evolve, accelerating access at scale to these and expanded approaches is more important than ever.

Trends in Prevention

1.3M **new HIV infections globally in 2023, a 32% reduction in the last 10 years**[i]

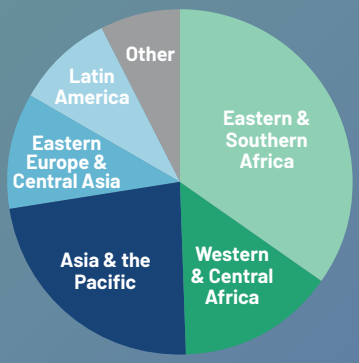


3 REGIONS **with increasing new HIV infections:** Eastern Europe/Central Asia, Middle East/North Africa, and Latin America[ii]

>50% **of new infections occurred outside of sub-Saharan Africa (SSA)** for the first time in the history of the HIV pandemic[ii]

21.2M **annual pre-exposure prophylaxis (PrEP) users needed in 2025 to reach prevention targets,** based on UNAIDS modeling[ii]

Geographic Distribution of New HIV Infections (2023)[ii]



Percent of New Infections Occurring Among KPs and their Partners (2022)[vii]

80% Outside of Sub-Saharan Africa

25% Within Sub-Saharan Africa

Key Updates

LEN	Two pivotal phase 3 trials demonstrate superior efficacy for twice-yearly subcutaneous LEN for HIV PrEP for cisgender women (PURPOSE 1), cisgender men, transgender people, and nonbinary individuals who have sex with partners assigned male at birth (PURPOSE 2).
CAB-LA	GBP 23.50 (EXW) per vial access price[viii]; Over 540K long-acting cabotegravir (CAB-LA) doses committed or delivered from 2023-2024 for implementation studies and limited programmatic use in LMICs[ix]; Positive safety data during pregnancy[x]
DVR	1,800 initiations in four countries in SSA as of June 2024[xi]; 150K rings will be made available for 2025-2026 through the CIFF and Global Fund Early Market Access Vehicle[xii]; The dapivirine vaginal ring (DVR) is safe for use during pregnancy, according to results from DELIVER study[xiii]
DPP	Viatris completed the pivotal BE study for its coformulated daily pill containing TDF, FTC, levonorgestrel, and ethinyl estradiol and is compiling a dossier for regulatory submission[xiv, xii]
Oral PrEP	2.1M oral PrEP initiations in 80 LMICs in 2023, a 25% increase from 2022[xi]
PEP	Updated WHO guidelines emphasize that timely post-exposure prophylaxis (PEP) access is the key determinant of effectiveness[xv]

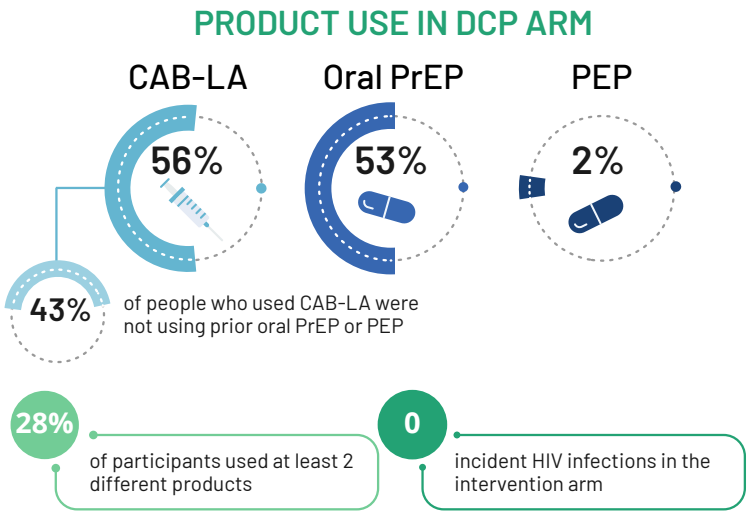
As the number of HIV prevention options increases, person-centered product choice alongside differentiated service delivery could drastically expand access, use, and impact

PRODUCT CHOICE

Results from several studies suggest that new prevention products and modalities entering the market could bolster current efforts to curb the epidemic while simultaneously better meeting the needs of people at risk of HIV acquisition.

- Findings from the SEARCH Dynamic Choice Prevention study found that offering multiple prevention options and allowing switches between options increased coverage and reduced HIV incidence.
- In CATALYST, among over two thousand participants in Kenya, Lesotho, South Africa, Uganda, and Zimbabwe offered the choice between oral PrEP and the DVR, 61 percent selected oral PrEP and only three percent of participants selected no method. The next phase of CATALYST will include CAB-LA, offering further insights into preferences for this product.
- Analysis from early CAB-LA implementation in Zambia found that among the first 609 clients who accessed PrEP, the majority (70 percent) had never used PrEP before. The analysis also reported high continuation, with 91 percent returning for their second injection.

FIGURE 1: SEARCH STUDY RESULTS



DIFFERENTIATED SERVICE DELIVERY

Alongside new products, increasing access to person-centered, differentiated service delivery systems has the potential to further expand choice and improve utilization of prevention services. Several innovative models have been trialed with this aim. A quasi-experimental study conducted across four public health clinics in Kenya evaluated the impact of an intervention package that included a direct-to-pharmacy PrEP refill, HIV self-testing, and pharmacist-led risk assessment and dispensing. Compared to the standard of care, the intervention reduced clinic visit time by 35 percent and improved PrEP continuation at one, three, and six months.

Highly efficacious, injectable, long-acting products could improve effective use and provide more acceptable, discreet HIV prevention options

LENACAPAVIR (LEN)

LEN is a novel capsid inhibitor under investigation as a twice-annual subcutaneous (SC) injectable for PrEP and already approved as treatment for highly treatment experienced PLHIV.

RESEARCH & DEVELOPMENT

- Groundbreaking results from the phase 3 PURPOSE 1 trial show 100 percent efficacy and superiority of twice- yearly LEN for PrEP over oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in cisgender women in South Africa and Uganda. In the more than two thousand participants in the LEN arm of the study, there were zero infections observed.

- 96 percent reduction in infections with LEN compared to background HIV incidence in the phase 3 PURPOSE 2 trial conducted among cisgender men, transgender people, and nonbinary individuals who have sex with partners assigned male at birth in Argentina, Brazil, Mexico, Peru, South Africa, Thailand, and the US. In this trial, there were only two incident cases among the over two thousand participants in the LEN arm.
- Additional studies in the PURPOSE portfolio are currently underway or planned, including among a range of populations.

ACCESS & IMPLEMENTATION

- In October 2024, Gilead announced royalty-free, voluntary licensing agreements with six generic manufacturers (Dr. Reddy's Laboratories Limited, Emcure, Eva Pharma, Ferozsons Laboratories Limited, Hetero, and Viatris) in 120 high-incidence, resource-limited countries. However, Gilead's license does not include Argentina, Brazil, Mexico, and Peru despite all four countries hosting PURPOSE 2 study sites.
- Gilead also stated that it plans to supply LEN until generic manufacturers can fully support demand and price at no profit.
- Gilead is expected to file LEN for PrEP with the United States Food and Drug Administration (US FDA) by the end of 2024.
- In November 2024, the WHO released an invitation to manufacturers to submit an expression of interest (EOI) in WHO prequalification (PQ) for an injectable and oral tablet formulation of LEN.
- In November 2024, Unitaid announced a US$22 million investment to accelerate the introduction and access to LEN. The investment will specifically focus on initiatives in South Africa and Brazil and aims to address the unique needs of at-risk populations.
- A long-acting, highly efficacious product like LEN could have a transformative impact on the prevention space by increasing user choice and decreasing the burden on users and health systems through less frequent clinic visits, but only if it is rapidly and affordably made available to those who need it most. To this end, several partners —including Unitaid, CHAI and Wits RHI— are currently undertaking initiatives to accelerate generic access.

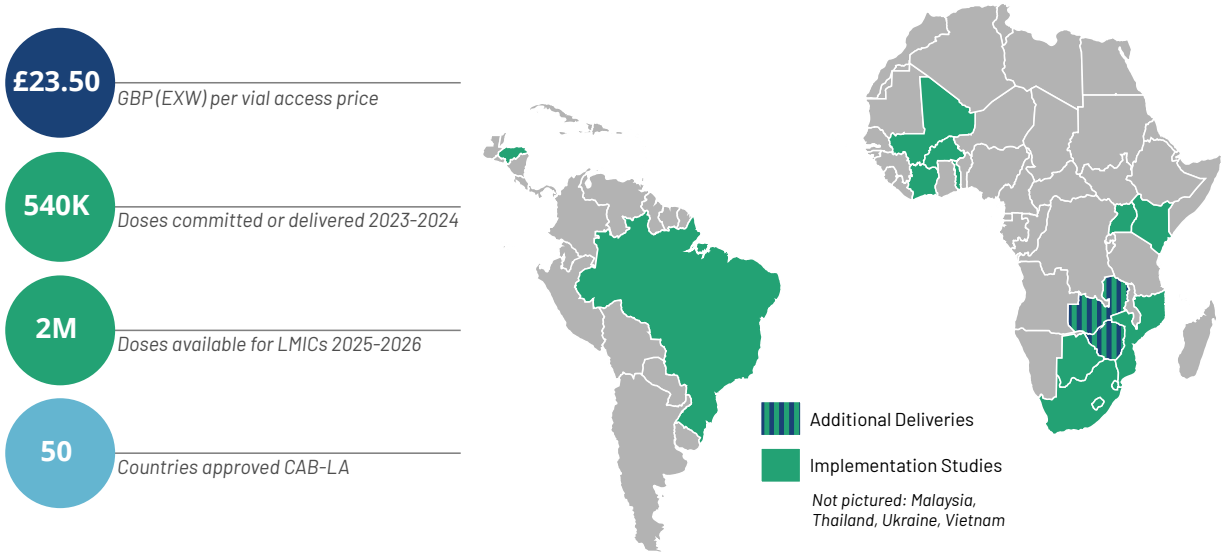
LONG-ACTING CABOTEGRAVIR (CAB-LA)

CAB-LA is a highly effective injectable PrEP administered intramuscularly every eight weeks, approved for use in adults and adolescents (over 35 kg).

APPROVALS & IMPLEMENTATION

- CAB-LA is the first long-acting injectable HIV prevention product on the market. CAB-LA received US FDA approval in December 2021 and WHO PQ in December 2023.[xvi] However, LMICs continue to face major access challenges three years after approval.

FIGURE 2: CAB-LA IMPLEMENTATION STUDIES AND ADDITIONAL DELIVERIES IN LMICs AS OF DECEMBER 2024[xvii, ix, viii]



- While ViiV announced increased supply for LMICs in October 2024 (at least 2 million doses for 2025-2026), access largely remains limited to implementation studies. Widespread, affordable access will not be possible until CAB-LA is readily available. Efforts are underway by Unitaid, Wits RHI, and CHAI to accelerate generic development of CAB-LA.
- Generic CAB-LA is under development via the licensees. Availability at the country level will depend on completion of development and resulting regulatory submissions; meanwhile, the only source of CAB-LA will be the originator product from ViiV Healthcare.[xviii]

RESEARCH & DEVELOPMENT

- A new formulation of cabotegravir, "ultra long-acting" CAB, given intramuscularly every four months, is also under investigation. Phase 1 trial outcomes presented at the Conference on Retroviruses and Opportunistic Infections (CROI) 2024 showed positive results with no adverse events.

Safety data in pregnancy and development of multipurpose technologies could improve integration with sexual and reproductive health services

PREGNANCY & PREVENTION

As new products enter the market, it is critical to generate safety data for pregnant and breastfeeding people to ensure access for these populations.

- New research from the HPTN 084 study on CAB-LA shows positive safety data for use during pregnancy. The global study included more than 300 pregnancies among cisgender women and found similar and low rates of adverse infant outcomes across study arms and reported no maternal deaths.
- Pregnant and lactating people were included in the PURPOSE 1 trial, allowing for earlier generation of data for this population and representing a novel approach to study design.
- The DELIVER study found that the dapivirine vaginal ring (DVR), a flexible self-inserted silicone ring for HIV PrEP, is safe for use during the second and third trimesters of pregnancy and, as demonstated previously in MTN 043 / B-PROTECTED, through breastfeeding.
- To increase access to the DVR, the Children's Investment Fund Foundation (CIFF), in partnership with the Global Fund and other partners, announced in July 2024 US$2 million over the 2024-2025 period for the purchase of approximately 150,000 DVRs in countries that implement Global Fund grants to fight HIV and AIDS.

Product access for pregnant and breastfeeding populations remains critical to prevent HIV acquisition and the possibility of vertical transmission during these crucial periods.

MULTIPURPOSE TECHNOLOGIES

There are several multipurpose prevention technologies (MPTs) under development that combine contraception with HIV PrEP.

RESEARCH & DEVELOPMENT

- Viatris is currently developing the dual prevention pill (DPP), a coformulated daily pill in a 28-pill blister pack with 21 pills containing TDF, FTC, levonorgestrel, and ethinyl estradiol, and seven pills containing only TDF/FTC.
  - Viatris completed the DPP's pivotal bioequivalence (BE) study in September 2024.[xiv]
  - In November 2024, the WHO released an invitation to manufacturers to submit an EOI for WHO PQ for the DPP.
  - As a result of the WHO EOI, Viatris is planning to submit for WHO PQ by the end of 2024.
  - AVAC and CHAI are working to accelerate commercialization and advance country-level preparation for DPP market entry in partnership with ministries of health as part of a consortium funded by CIFF.
- A three-month DVR combined with contraception is also currently under development.

- Further research is required to develop policies and tools that will support choice when offering MPTs.
- The development of products that combine HIV prevention with contraception offers further opportunities to integrate HIV and sexual and reproductive health services and expand access across populations.

In the interim before widespread access to new prevention modalities, research continues to explore approaches to maximizing impact of oral PrEP and PEP

ORAL PRE-EXPOSURE PROPHYLAXIS (PrEP)

Oral PrEP is a highly effective pill to prevent HIV.

- In the largest pooled analysis on global oral PrEP studies to date, researchers used prospective study data across 28 countries and over 17,000 participants to demonstrate TDF/FTC is highly effective even with less than daily dosing, in diverse clinical settings, geographies, populations, and routes of HIV exposure.
- As expected, lower adherence to oral TDF/FTC was associated with higher incidence of HIV, with the highest incidence seen among those who reported less than two doses per week.

POST-EXPOSURE PROPHYLAXIS (PEP)

PEP to prevent HIV acquisition contains two to three ARVs and should be started within 24 hours but no later than 72 hours after potential HIV exposure.

- In July 2024, the WHO released updated guidelines on HIV PEP, emphasizing that timely PEP access is the most important determinant of its effectiveness. The guidelines include two new recommendations, task shifting and community-based delivery, as essential strategies for ensuring timely access to PEP.

New research identifies opportunities for expansion of vertical elimination programs

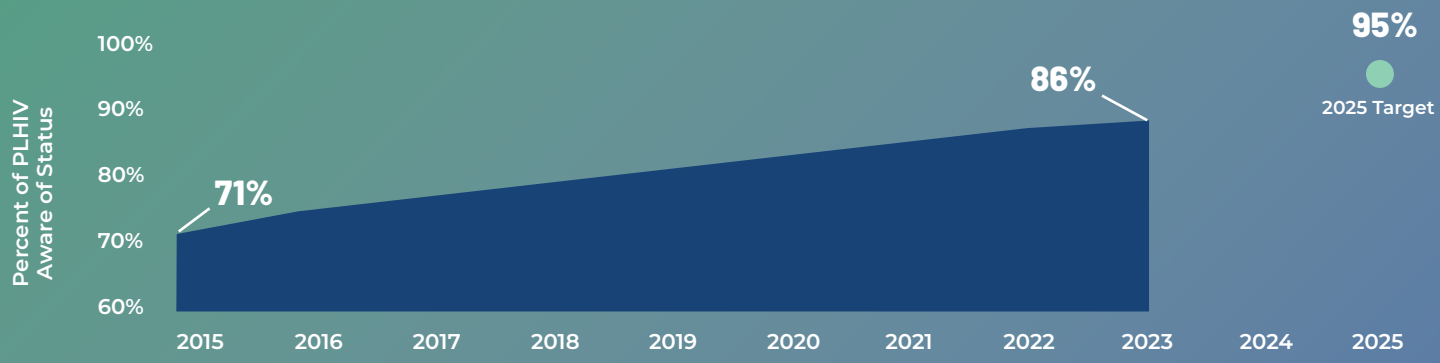
- **Solid dispersible pediatric fixed-dose combinations (FDCs) are safe for neonates for both HIV prevention and treatment**
  - Pediatric ABC/3TC fixed-dose dispersible tablets and LPV/r granules were shown to be safe for 24 HIV-exposed neonates, with drug exposures similar to those in young infants, according to results from the PETITE study conducted in South Africa.
  - While additional data on safety is required, this could potentially lead to improved treatment and prevention options for neonates via more child-friendly formulations.
- **Cost-effective vertical elimination interventions could significantly reduce infant infections**
  - A modelling study co-authored by CHAI evaluated the cost-effectiveness of nine intervention scale-up scenarios aimed at eliminating vertical transmission of HIV in Zambia.
  - Individually, maternal peer support groups, HIV retesting during late antenatal care, and infant prophylaxis were most effective in reducing vertical transmission.
  - In the three most cost-effective scenarios, infant infections reduced by 43.4 to 44.6 percent, averting 1,734 to 1,780 HIV infections and resulting in cost savings.
- **Universal approach to PrEP implementation in antenatal care may be the simplest and most effective option**
  - The PrEP Implementation for Mothers in Antenatal Care (PrIMA) study found that targeted PrEP using an HIV risk assessment tool was not superior to universal PrEP in Kenya.
  - Across the two scenarios, there was no difference in maternal HIV incidence and frequency of appropriate PrEP use, suggesting that offering PrEP counselling to all people in antenatal care may be better than targeted access.

TESTING

Rates of HIV status awareness lag behind UNAIDS targets, particularly outside of east and southern Africa. Many clients show an ongoing preference for HIV self-testing, which could help close this testing gap and improve access to services across the HIV cascade. For infants and young children, early infant diagnosis (EID) testing volumes have been stagnating and even declining, highlighting the urgent need for global attention to ensure children are not left behind. On the horizon, the development of additional multi-disease combination tests could improve identification and reduce rates of vertical transmission. To achieve these HIV testing service improvements, it will be critical to ensure community preferences are front and center in decision making.

Trends in Testing

86% **of PLHIV globally knew their HIV status in 2023[i]**

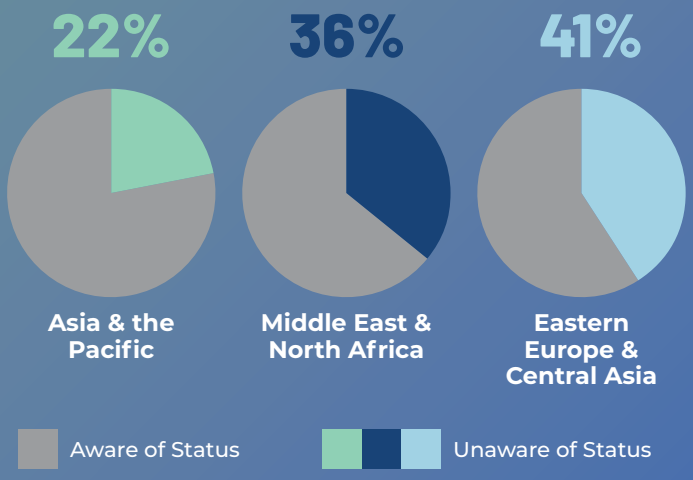


107 countries with HIV self-testing policies as of July 2024[xix]

1.8M EID tests estimated run in 2023, a decrease of ~100K from 2022[xx]

2X increased odds of HIV testing in countries in SSA where same-sex relationships are legal[xxi]

Regional Gaps in the Percent of PLHIV Unaware of Status[i]



Key Updates

HIVSTs	Increased procurement of blood-based self-tests, with adoption planned or underway in 11+ countries[xxii]
EID	Updated GeneXpert cartridge now with WHO PQ offers earlier detection and potential for simplification of waste management[xxii]
Combination Testing	Several combination tests in the development pipeline could simultaneously diagnose HIV, syphilis, and hepatitis B virus (HBV), helping to progress triple elimination goals[xxii]

Research and WHO guidance continues to support the expansion of HIV self-testing and network-based testing

HIV self-tests (HIVSTs) offer opportunities to reach diverse populations, including those not regularly interacting with clinics. They also have applications across the cascade such as use in prevention programs.

BLOOD-BASED HIVSTs

With several affordable blood-based HIVSTs now on the market, implementation continues to expand.

RESEARCH

Research continues to demonstrate user demand and preferences for both oral-fluid and blood-based HIVSTs, as well as the potential for expanded applications.

- A cross-sectional study conducted in Malawi found a strong preference among clients for HIV self-testing over provider-delivered testing, while demonstrating demand for both oral and blood-based products.
- Another cross-sectional study in Democratic Republic of the Congo found that blood-based HIVSTs were more acceptable than oral-fluid HIVSTs among key populations (71 percent compared to 28 percent).
- A modeling study in western Kenya found that scaling up the use of PrEP via HIVSTs provides similar health benefits, costs, and low risk of drug resistance, as those observed with provider-administered rapid diagnostic tests. This suggests that expanded use of self-testing in prevention settings could improve service uptake without sacrificing quality of service.

FIGURE 3: MAP OF COUNTRIES THAT HAVE ADOPTED WHO PQ'D BLOOD BASED HIVSTs[xxii]

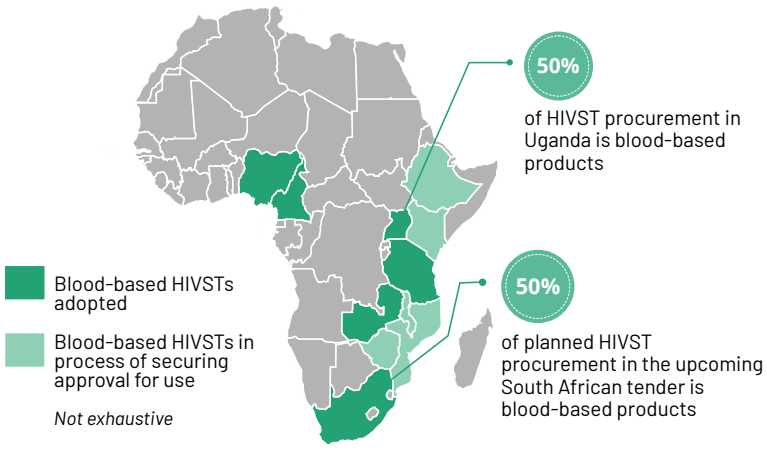
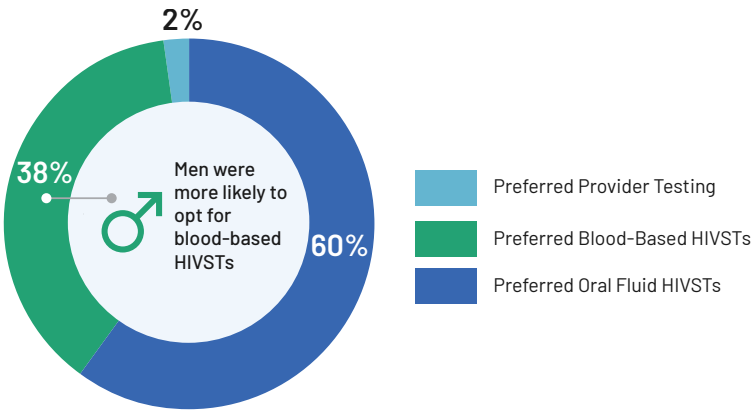


FIGURE 4: PREFERENCE FOR HIV SELF-TESTING IN MALAWI



GUIDELINES

Updated WHO guidelines on differentiated HIV testing services include several new recommendations that highlight the role of self-testing and network-based testing.[xxiii]

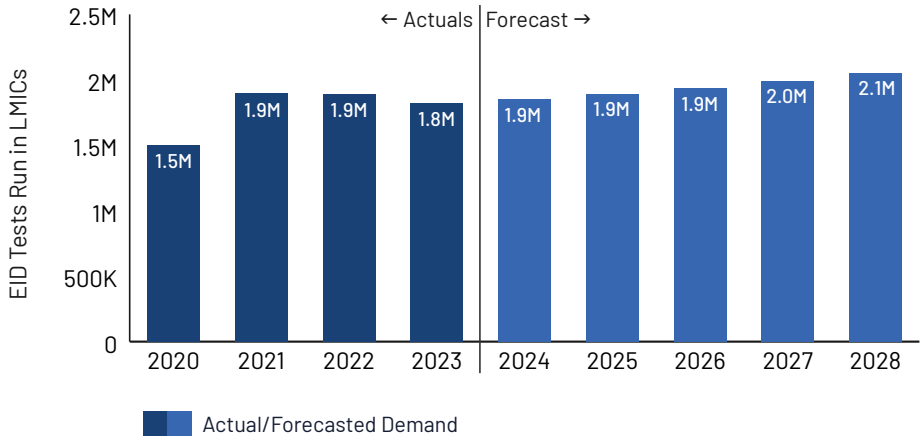
KEY UPDATES

- HIV self-testing may be offered as an additional option for testing at facilities
- HIV self-testing may be used to deliver PrEP, including for initiation, re-initiation and continuation
- Syphilis self-testing is suggested as an additional approach to syphilis testing services
- Network-based testing is recommended, including the use of social network testing, family and household testing, and partner services

Decreasing EID testing volumes highlight the increased global attention needed to ensure children are not left behind

Access to EID testing, specifically at the point-of-care (POC), is critical for HIV-exposed children to ensure rapid initiation into care for those testing positive.

FIGURE 5: LMIC EID TESTING DEMAND ACTUALS AND FORECAST[xx]



In 2023, estimated EID volumes in LMICs decreased to 1.8 million, highlighting the need for further global attention.

Availability of data continues to be a challenge in developing accurate POC forecasts, although historical trends indicate increasing use.

- Cepheid's updated EID test, the Xpert® HIV-1 Qual XC, received WHO PQ in March 2024 and has the potential to replace the legacy GX HIV-1 qual cartridge.
  - This new cartridge delivers results seven to ten days before seroconversion, a key attribute given that early identification is critical for this population.
  - It also does not require high-heat incineration, which will simplify waste management.
  - The test is available at the same cost as the legacy GX HIV-1 qual cartridge, enabling affordable access.

Ongoing development of combination tests offers opportunity to achieve triple elimination goals

Combination tests offer the potential for simultaneous identification of multiple diseases and serve as an important entry point to treatment and prevention services.

DUAL HIV/SYPHILIS TESTS

- There are currently three dual HIV/Syphilis tests with WHO PQ—Standard Q, First Response, and Bioline—with prices ranging from US$0.95 to US$1.50 (EXW).[xxiv]

TRIPLE ELIMINATION TESTS (HIV, SYPHILIS, AND HEPATITIS B)

Triple elimination initiatives aim to improve maternal and child health outcomes through the simultaneous elimination of vertical transmission of HIV, syphilis, and HBV.

TRIPLE ELIMINATION WORK IN WEST BENGAL, INDIA

The state government of West Bengal, India, in partnership with CHAI, conducted a demonstration pilot of targeted triple elimination interventions in four districts. Efforts focused on increasing the uptake of screening, improving data-sharing mechanisms for linkages, and training facility staff in integrated service flows. Initial results from the pilot found that these methods enhanced case finding and improved testing and treatment coverage of exposed infants. Further scale-up is planned across the entire state.

Enhanced case finding through introduction of behavioral risk screening in ANC:

0.1% of the total pregnant persons screened were found to be 'at-risk' and followed up for rescreening at third trimester/labor

1% testing yield for both HIV and syphilis within this cohort (compared to 0.02 percent and 0.04 percent testing yield for HIV and syphilis respectively in pregnant persons not identified as 'at-risk')

Enhanced coverage of exposed infants:

95%+ syphilis-exposed infants linked to care and testing and 95 percent of eligible infants received a prophylactic dose of benzathine penicillin G

95%+ HBV-exposed infants received a hepatitis B birth dose and more than 80 percent received hepatitis B immune globulin for prophylaxis

100% live births among pregnant people with HIV and 75 percent of infants received timely HIV prophylaxis

While there are safe, effective, and affordable tools to prevent transmission from mothers to children, diagnosis remains a critical access barrier. Triple combination rapid diagnostic tests could address some existing challenges by simplifying service delivery, reducing testing costs and time, and streamlining supply chains.

- Currently, there are several combination tests in the development pipeline aimed specifically at triple elimination.
- Products in development have various testing formats with single or multiple sample wells, buffers, and strips per test; these different combination test formats will contribute to varying degrees of workflow efficiency.

FIGURE 6: PRODUCTS UNDER DEVELOPMENT FOR HBV, HIV, AND SYPHILIS COMBINATION TESTING (NOT EXHAUSTIVE, SUBJECT TO CHANGE)[xxii]

MANUFACTURER	EXPECTED SAMPLE TYPES			TEST TYPE	
	WHOLE BLOOD	SERUM	PLASMA	LATERAL FLOW ASSAY	FLOW-THROUGH
ABBOTT[1]	X			X	
ACCUBIO[2]	X	X	X	X	
BIOLYTICAL	X			X	X
CTK BIOTECH[3]	X	X	X	X	
INTECH PRODUCTS	X	X	X	X	
SD BIOSENSOR	X	X	X	X	

[1]CE Marked, under WHO PQ Review
[2]CE-mark pending for 4-product test (HBV, HCV, HIV, syphilis) by Accubio
[3]CTK Biotech 4-product test (HBV, HCV, HIV, syphilis) commercialized in select countries

Key gaps and opportunities within the HIV testing space highlight the critical need for greater community engagement

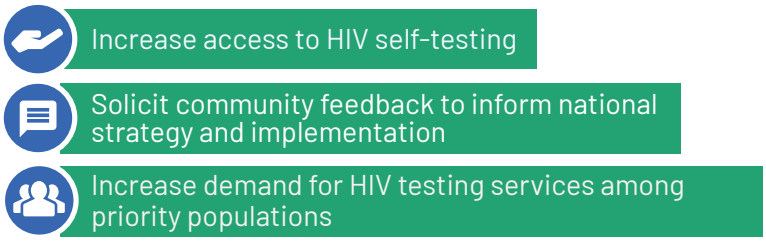
Across the HIV cascade, community engagement is critical to ensure services and products are fit-for-purpose to meet the needs of people living with or at risk of HIV. When client perspectives are not included, national strategies may not align with diverse population needs and people may not be effectively linked or retained in prevention or care services.

In recent years, the community voice has played an increasingly active role in the testing space through advocacy for direct engagement with community in the design and implementation of index testing programs to ensure ethical service delivery. Prior to this input on index testing delivery, programs documented harms including violence, coercion, and violations of confidentiality.

With support from the Bill & Melinda Gates Foundation, CHAI established a cross-country community advisory board with members from Malawi, Uganda, Zambia, and Zimbabwe to create an avenue for meaningful, sustained community engagement in national HIV testing services policies and decision making.

Meaningful, direct engagement with community in design and implementation aims to ensure ethical service delivery while expanding testing services to those who need it.

FIGURE 7: HIV TESTING SERVICES KEY COMMUNITY ADVISORY BOARD PRIORITIES

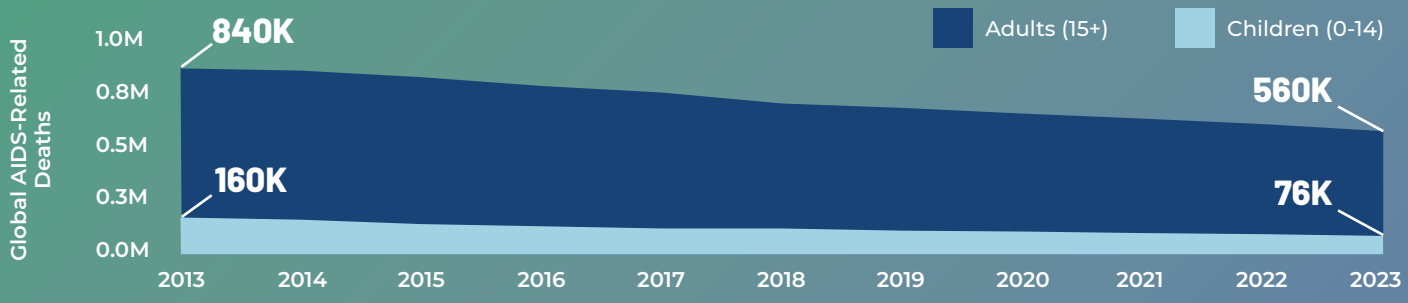


ADVANCED HIV DISEASE

While AIDS-related deaths have decreased by 50 percent since 2010, recent progress has stagnated, and the prevalence of advanced HIV disease (AHD) remains unacceptably high. Access to CD4 testing, a key entry point to the AHD package of care, remains inadequate, exacerbated by recent market shifts. Advancements in the prevention, diagnosis, and treatment of opportunistic infections (OIs) offer hope to further reduce mortality, though continued work is needed to ensure widespread access to these lifesaving products and services.

Trends in Advanced HIV Disease

~630K AIDS-related deaths, including 76K children 0-14 years[i]



1 IN 8 AIDS-related deaths was a child aged 0 to 14[i]

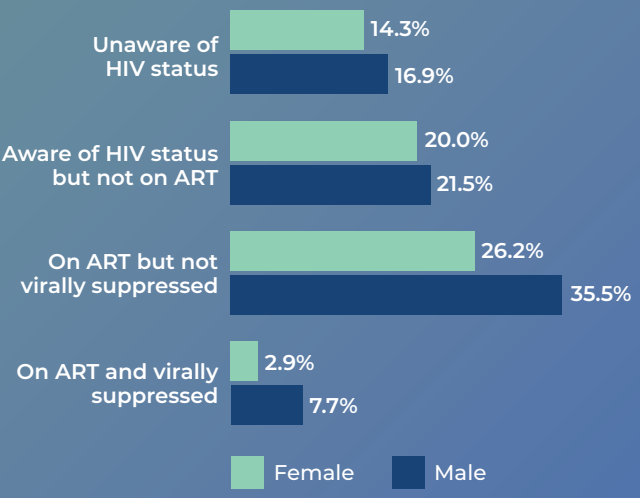
12.2M people with AHD globally in 2023, most common among people who received antiretroviral treatment (ART) and stopped[ii]

36% of virally unsuppressed people on ART had AHD[ii]

1.6X more likely for men to have AHD than women in SSA[xxv]

30–40% of PLHIV in LMICs present to care with AHD[xxvi]

Proportion of People with AHD by Sex across the HIV Cascade in 12 SSA Countries[xxv]



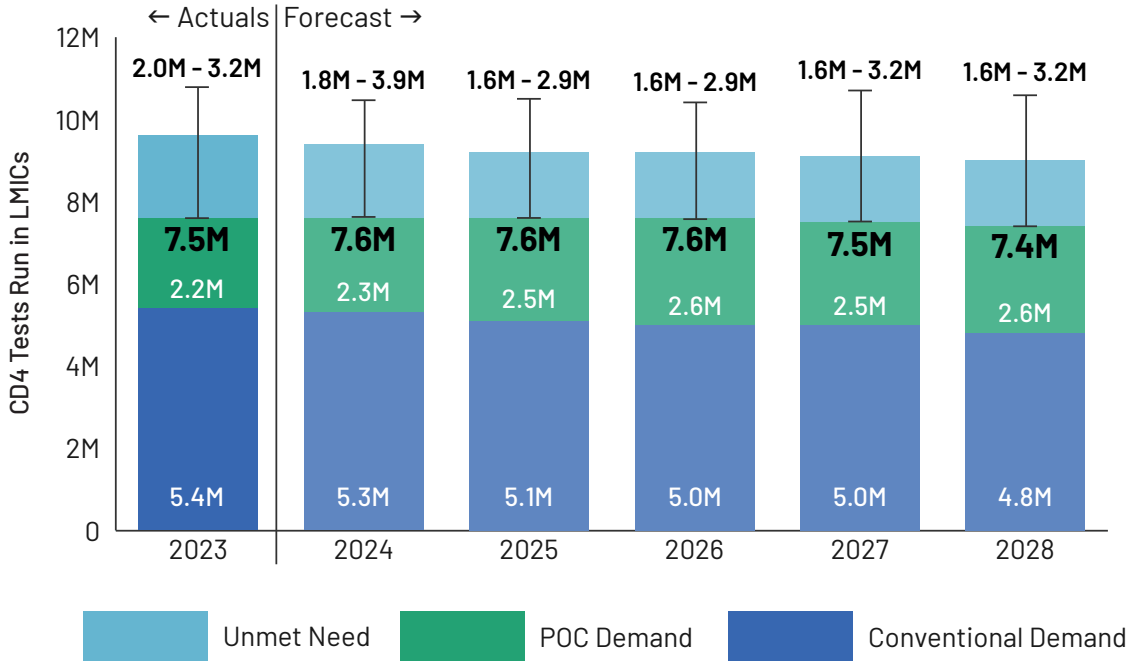
Key Updates

CD4 Testing	BD FACSCount and FACSPresto cartridges and analyzers for CD4 testing are no longer available for procurement; VISITECT® shelf-life has been extended from 12 months to 18 months, although WHO prequalification is yet to be updated[xxii]
Pediatric 3HP	Dispersible, pediatric formulation of 3HP (three months of weekly RPT+INH for TB preventive treatment) now available for children two years and older[xxvii]
CrAg Testing	First semiquantitative cryptococcal antigen (CrAg) test to be submitted to the US FDA for regulatory approval by the end of 2024[xxii]
L-AmB	Gilead, the sole supplier of liposomal amphotericin B (L-AmB) in LMICs, increased the access price from US$16.25 (EXW) per vial to US$23.00 (EXW) per vial in 2023[xxviii]
5FC	Continued expansion of flucytocine (5FC) use with introductions across 21 LMICs and a 23 percent increase in order volumes from 2022 to 2023[xxix]

Ensuring consistent access to CD4 testing remains critical amidst ongoing market changes and considerable unmet need

CD4 testing is a key entry point into the AHD package of care and an essential tool for the clinical management of people living with HIV.

FIGURE 8: LMIC CD4 TESTING DEMAND AND NEED (ACTUALS AND FORECAST)[xxx]



- In 2023, CHAI and Avenir Health estimate approximately 7.5 million CD4 tests were conducted in LMICs, with conventional tests accounting for 70 percent, and POC the remaining 30 percent. Over the next five years, CHAI forecasts stagnating demand for CD4 testing. However, there is considerable unmet need for CD4 testing,—which includes PLHIV who may not receive CD4 testing at (re)entry to HIV care, or those with an unsuppressed viral load (VL).[xxx, xxxi] CHAI aims to address this unmet need and improve CD4 demand through the Unitaid-funded THRIVE Project in collaboration with Afrocab and Penta. See Appendix C for more information on the methodology for this forecast.
- In a 2024 review of AHD screening policies in 147 countries, only 51 percent include the use of CD4 testing to determine AHD among PLHIV (re)entering care.[ii]
- Additional data from the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) indicates sub-optimal uptake of CD4 testing even when its available, with anywhere from less than one percent to 87 percent of eligible populations receiving CD4 testing across eight LMICs.

CHANGES TO THE CD4 MARKET

Supplier exits from the CD4 market further exacerbate limited access to this life-saving testing technology.[xxxii]

FIGURE 9: AVAILABILITY OF WHO PREQUALIFIED CD4 TESTING PLATFORMS AND ASSAYS[xxxii]

USE	BRAND	PRODUCT TYPE	CD4 TYPE	STATUS/UPDATES
POINT-OF-CARE (POC)	Accubio VISITECT® Advanced Disease	Rapid Diagnostic Test	Semi-quantitative (above or below 200 cells/µL)	• Available • Shelf life now 18 months, update to WHO PQ listing pending
	Abbott Pima	Platform & Cartridges	Quantitative	• New platforms no longer available as of May 2022 • Continued supply of cartridges and bead standards as well as service and refurbishment of existing analyzers • Cartridge price increase from US$6.60 (EXW) to US$7.60 (EXW) each[xxii]
NEAR POINT-OF-CARE	BD FACSPresto	Platform & Cartridges	Quantitative	• New platforms and cartridges no longer available as of June 2024
CONVENTIONAL	BD FACSCount	Platform & Cartridges	Quantitative	• New platforms no longer available as of December 2022 • Spare parts and service will be provided until December 2024, or until warranties expire in June 2026 • New cartridges will no longer be available after December 2024
	Sysmex Cyflow Counter	Platform & Cartridges	Quantitative	• Available, no anticipated changes to platform or cartridges
	Beckman Coulter Acquios CL Flowcytometer	Platform & Cartridges	Quantitative	• Available, no anticipated changes to platform or cartridges

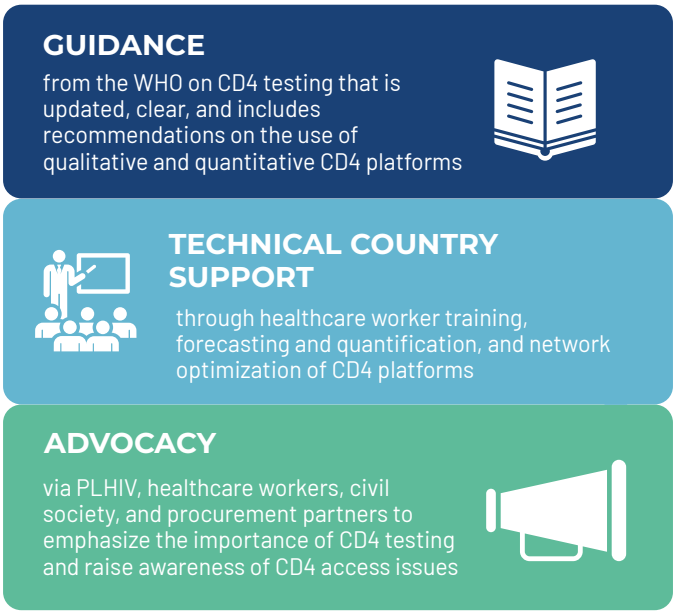
Available Devices discontinued; cartridges available Devices and cartridges discontinued

CD4 MARKET EXPANSION EFFORTS

The global community is working to address these CD4 challenges through engagements at global and national levels.

- These include demand-side interventions such as a CHAI- and Unitaid-supported CD4 roundtable held in February 2024, which brought together donors, national programs, and implementing partners to discuss issues contributing to suboptimal CD4 access and potential solutions.
- On the supply side, in June 2024, CHAI, the Aurum Institute, the Bill & Melinda Gates Foundation, and Unitaid issued a call for expressions of interest for suppliers who can provide a viable, accessible solution for CD4 testing in the LMIC market. In December 2024, suppliers who submitted an expression of interest were invited to partake in a formal request for proposals, which are due end of January 2025.

FIGURE 10: MARKET EXPANSION EFFORTS REQUIRED TO ADDRESS CD4 CHALLENGES



Not Exhaustive

QUALITY IMPROVEMENT INITIATIVE INCREASES ACCESS TO POC CD4 TESTING IN UGANDA

Between October 2022 and September 2023, the Uganda Ministry of Health, with support from partners, implemented quality-improvement initiatives aimed at addressing gaps in the delivery of the AHD package of care among PLHIV on ART with elevated viral loads.

Interventions included commodity management, the formation of facility-based AHD focal teams, improved data management, training on AHD identification and treatment, and the integration of CD4 testing into community-based HIV services using the VISITECT® POC test.

Access to CD4 testing among non-suppressed PLHIV on ART increased from 43 percent before the intervention to 60 percent by the end of the quality improvement initiative. While this is a significant increase, 40 percent of the eligible population was still not reached due to a national shortage of tests and limited integration of CD4 testing into lower-level facilities and community-led HIV services, indicating substantial need for CD4 testing remains in Uganda.

Suppliers of adult 3HP expand, while new approvals for child-friendly 3HP close an equity gap

In 2023, PLHIV accounted for more than six percent of the 10.8 million people with tuberculosis (TB) worldwide. At 161,000 deaths in 2023, TB is the leading cause of death among PLHIV.[xxxiii]

TB PREVENTION REGIMEN UPDATES

- In October 2024, Lupin's FDC of 3HP, a once-weekly, short course (12-weeks) regimen containing isoniazid (INH) and rifapentine (RPT) (300/300 mg), received WHO PQ, marking it as the second WHO prequalified FDC version of these drugs. Macleods is the other supplier of a WHO prequalified 3HP FDC formulation.[xvi]
- Pediatric 3HP is now available for children two years and above following the December 2023 approval of Lupin's child-friendly formulation of RPT by the Global Fund Expert Review Panel. This new 150 mg formulation is water-soluble and raspberry-mint flavored and will be available in more than 135 countries for US$6.53 to US$15.80 per course (EXW), depending on the weight of the child—narrowing an important equity gap between adult and pediatric TB preventive treatment (TPT) access and cost. The Unitaid-funded IMPAACT4TB Consortium has committed to catalyzing uptake of 85,000 patient courses through an Early Market Access Vehicle.[xxvii]
- Due to gaps in safety data, co-administration of 3HP with DTG-based ART in children living with HIV is not recommended. A South Africa-based phase 1/2 clinical trial aims to determine DTG dosing for children living with HIV undergoing TPT with 3HP. Initial results of this study are anticipated in late 2025. In adults, the DOLPHIN TOO study showed that co-administering 3HP with DTG in ART-naïve PLHIV did not require adjustments in DTG dosing, and the regimen was well tolerated, with no significant impact on viral load suppression.

Pipeline CrAg assay may simplify linkage to cryptococcal meningitis care, though access to the WHO-recommended treatment is still limited

After TB, cryptococcal meningitis (CM), a fungal infection of the brain and spinal cord, is the second-leading cause of death for PLHIV, accounting for 19 percent of global AIDS-related mortality.[xxxiv] In LMICs, diagnosing CM is challenging due to the requisite clinical training needed to perform lumbar punctures for cerebrospinal fluid analysis, but a new test may remedy this issue.

CM DIAGNOSTICS MARKET

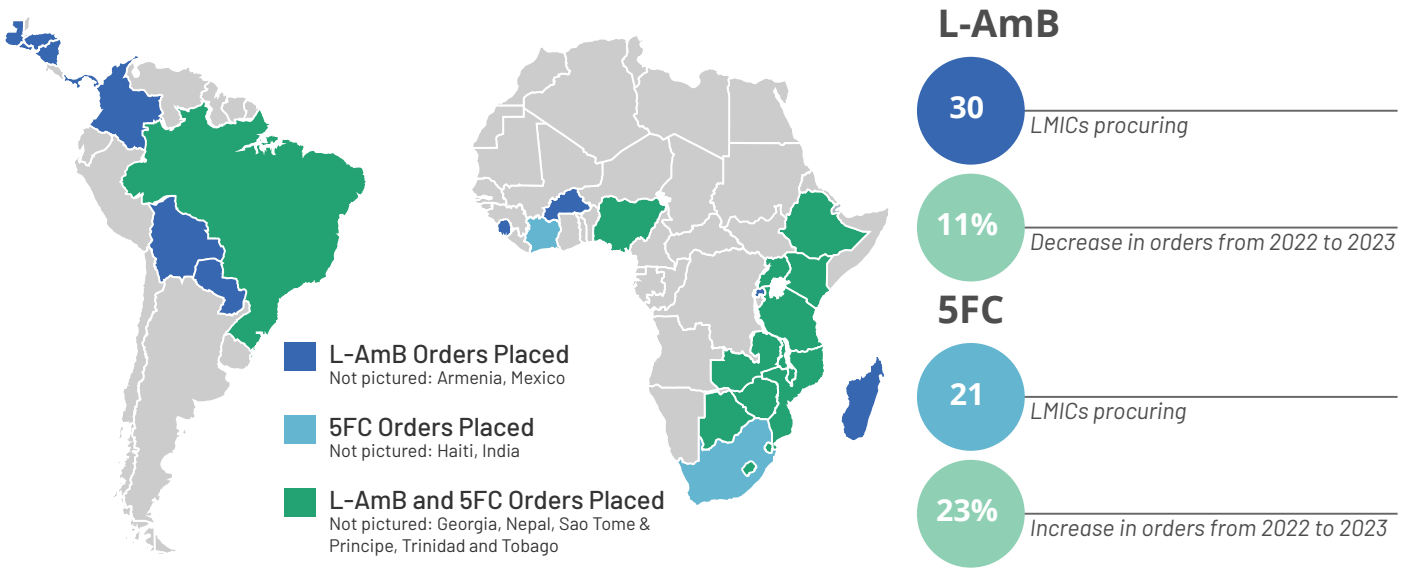
- A new semiquantitative (SQ) lateral flow cryptococcal antigen (CrAg) test by IMMY has the potential to simplify linkage to care by negating the need for a confirmatory lumbar puncture in a subset of patients. This SQ test can detect CrAg in serum, plasma, whole blood, and cerebrospinal fluid. IMMY anticipates submitting the CrAg SQ assay to the US FDA for regulatory approval before the end of 2024.[xxii]
- IMMY's existing US FDA approved CrAg lateral flow assay is now available in a 25-count pack in addition to the 50-count pack size. This smaller pack size has the potential to reduce wastage and is a better fit for decentralized, low volume sites.[xxii]

CM TREATMENT MARKET

Since 2022, a single high-dose of liposomal amphotericin B (L-AmB) administered alongside oral flucytosine (5FC) and fluconazole has been the WHO-recommended induction regimen for PLHIV with acute CM, however access to this treatment has historically been limited.[xxxv]

- As of 2023, 30 LMICs had procured L-AmB, though order volumes reduced by 11 percent between 2022 and 2023, which may be related to stock building in 2022.[xxix]
- Gilead is the sole supplier of L-AmB across LMICs and increased the access price from US$16.25 (EXW) per vial to US$23.00 (EXW) per vial in 2023.[xxviii]
- The market for 5FC remains stable with two generic suppliers, Strides and Viatris. 21 LMICs introduced this product as of 2023 and order volumes increased by 23 percent between 2022 and 2023.[xxix]

FIGURE 11: 5FC AND L-AMB ADOPTION MAP, AS OF 2023, AS SEEN BY THE APWG[xxix]



Expanded access to prevention and screening tools for opportunistic infections is needed to reduce AIDS-related morbidity and mortality

- **Generic, WHO prequalified azithromycin, alongside research into additional indications, could expand AHD prevention efforts**
  - An open-label trial conducted in Kenya, Malawi, Uganda, and Zimbabwe showed that administering a package of enhanced preventative treatment at the time ART is (re)started, including a five-day course of azithromycin, reduces mortality by nearly one third at 24 weeks among PLHIV with AHD.

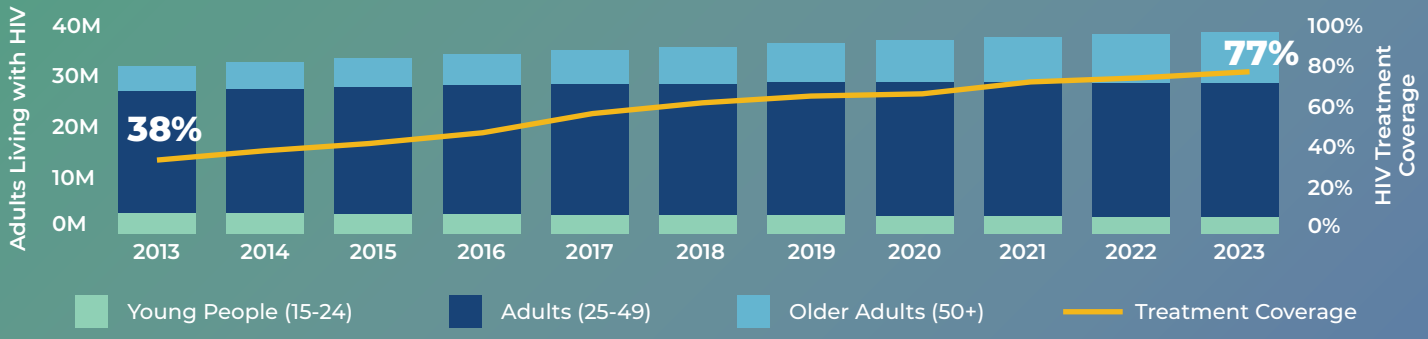
  - The phase 3 REVIVE trial aims to test whether once-daily azithromycin taken over four weeks can reduce mortality in adults with AHD. Funded by the Bill & Melinda Gates Foundation and led by African researchers, this trial will engage 8,000 participants across more than 100 sites in various African countries.
  - In April 2024, the WHO prequalified azithromycin (500 mg) manufactured by ACI HealthCare—allowing for wider procurement as a WHO-listed product and increased access to an essential component of an enhanced AHD package of care.
- **Decentralized testing may help expand rates of histoplasmosis screening**
  - Histoplasmosis is a lung infection caused by breathing in the histoplasma fungus. For PLHIV, this opportunistic infection can lead to high mortality rates, but decentralized POC testing is still not available in LMICs.
  - IMMY is currently developing a lateral flow assay for POC diagnosis of histoplasmosis, with submission for regulatory review anticipated in 2025.[xxii]
- **Limited mpox vaccine access in Africa may improve with new WHO prequalified vaccine**
  - In August 2024, the Africa Centres for Disease Control and Prevention (Africa CDC) declared mpox a public health emergency of continental security. Shortly thereafter, the WHO declared mpox a public health emergency of international concern. The virus, which spreads through close contact with an infected person, is endemic to some countries in West and Central Africa. Mpox cases continue to rise, posing a higher risk for PLHIV with AHD, who experience more severe mpox-related morbidity and mortality.[xxxvi]
  - The WHO has identified PLHIV as a priority population for mpox vaccines, though vaccine access is limited in Africa, which currently bears the largest burden of active mpox cases.[xxxvii] In September 2024, the WHO prequalified Bavarian Nordic's mpox vaccine, laying the foundation for more equitable access to mpox vaccines.
  - As of November 2024, several high-income countries, multilateral organizations, and pharmaceutical companies have pledged over 5.3 million vaccine doses for the mpox response in Africa. Nearly 300,000 mpox vaccines have arrived in the region to date, with the Democratic Republic of Congo, Nigeria, and Rwanda the first countries to receive deliveries of this urgently needed vaccine.[xxxviii]

ADULT TREATMENT

Access to optimal treatment continues to increase with approximately 95 percent of adults in generic-accessible (GA) LMICs on DTG-based regimens, and ongoing introduction of best-in-class protease inhibitor, darunavir, coformulated with ritonavir (DRV/r). As the epidemic matures, a focus on client retention and service integration is essential to providing person-centered, holistic care for PLHIV. PLHIV are living longer lives and increasingly experiencing co-morbidities with non-communicable diseases, which will require new management strategies. Further, new and pipeline products are set to transform the treatment paradigm with a shift toward product choice, including long-acting modalities. Additional research will be required to understand implementation considerations for long-acting injectable products in LMICs and ensure that these new products reach those who need them most.

Trends in Adult HIV Treatment

77% **global adult HIV treatment coverage in 2023**[i]



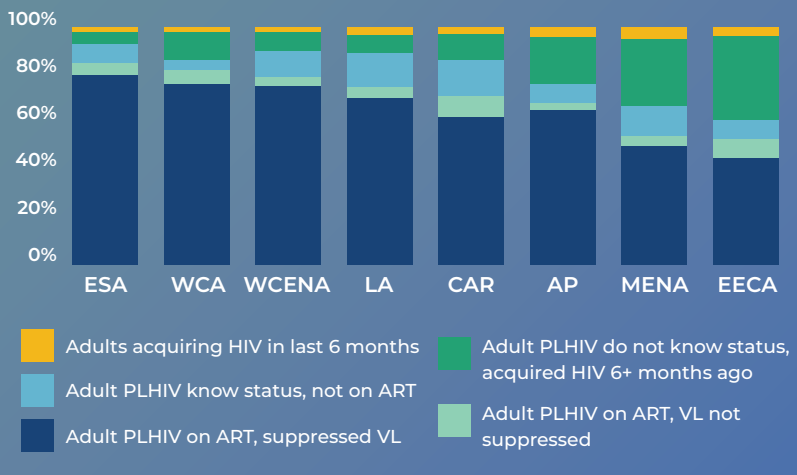
38.5M adults living with HIV globally in 2023[i]

64% global HIV treatment coverage for older adolescents (15 - 19 years)[ii]

65% of all adults living with HIV are in sub-Saharan Africa, 86% of whom are on treatment[i]

9.3M adults living with HIV were not on treatment globally in 2023[i]

Distribution of Adults Living with HIV by Infection and Treatment Cascade, 2023[i]



Key Updates

DTG	Over 23.5M PLHIV on DTG in generic-accessible (GA) LMICs, with over one billion packs of TDF/3TC/DTG (300/300/50 mg) (TLD) supplied as of June 2024[xxxix]
DRV/r	22 GA LMICs have procured or are planning to procure DRV/r[xl]
CAB+RPV	LATITUDE trial provides empirical evidence that the use of long-acting ART in people with adherence challenges improves treatment persistence and adherence and overall outcomes as compared to daily oral ART[xli]; Johnson and Johnson will not be manufacturing RPV for LMICs, significantly limiting drug access for research on CAB+RPV[xix]
LEN+CAB *(To be studied)*	US-based case series demonstrated viral suppression with six-monthly subcutaneous LEN and intramuscular CAB every four or eight weeks, supporting the need for a clinical trial to evaluate the use of a LEN+CAB combination[xlii]

Many PLHIV presenting for ART initiation are treatment experienced, suggesting new strategies are needed to improve retention in care

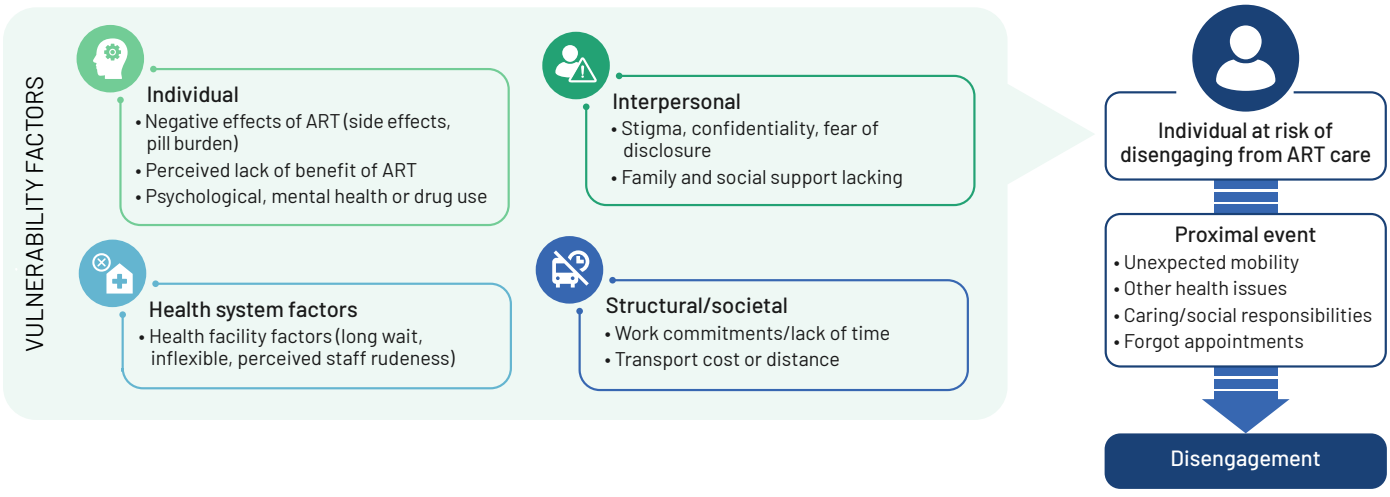
(RE)ENGAGEMENT RESEARCH

- Retain6, a three-year research project conducted by CHAI, Boston University's Department of Global Health, and the Health Economics and Epidemiology Research Office (HE²RO) in South Africa and Zambia found that most clients presenting for ART initiation were already treatment experienced.
  - This confirms findings from earlier systematic reviews from sub-Saharan Africa, which estimate between 20 and 50 percent of PLHIV are re-initiators.[xliii]
  - In South Africa, a cyclical pattern of engagement and treatment interruptions was common—with 68 percent of clients remaining continuously engaged in care either at the initiating facility or transferring to another facility, and 14 percent missing one or more months of care but re-engaging within the first six months on ART. The remaining 17 percent of PLHIV either died or disengaged from care.[xliv]
  - In Zambia, 87 percent of focus group discussion participants reported they were not offered a choice of service delivery location or dispensing duration in the first six months of care—though participants preferred longer multi-month dispensing intervals, facility-based care, and more frequent counselling.[xlv, xlvi, xlvii]
  - Early findings indicate enhanced counseling, differentiated service delivery, an assurance of privacy and confidentiality, and good provider-client relationships could improve early treatment outcomes.[xlviii]

(RE)ENGAGEMENT GUIDANCE

A new WHO policy brief outlines the complexities and challenges of people (re)engaging in HIV treatment services and highlights person-centered interventions that address the reasons for disengagement.

FIGURE 12: KEY REASONS FOR DISENGAGEMENT FROM HIV CARE[xlix]



As PLHIV age, service integration may address increasing co-morbidities with non-communicable diseases (NCDs)

Today, PLHIV are living longer lives due to the success of increasingly effective HIV treatment. In many high-income settings, the median age of PLHIV is over 50, and in East and Southern Africa, models estimate the median age to be above 40 years.[l, li] As PLHIV age, like the general population, they are likely to encounter several comorbidities, including non-communicable diseases such as cardiovascular disease (CVD) and

hypertension—chronic conditions that, similar to HIV, also require long-term care and management. An estimated 27 percent of PLHIV over age 50 in sub-Saharan Africa have elevated blood pressure, in line with rates among the general population.[lii, liii] The majority of people with hypertension never receive treatment, and only half of those treated will control their condition.[liv] Diagnosing and treating hypertension simultaneously with HIV has the potential to improve morbidity and mortality outcomes for PLHIV.

NCD/HIV GUIDANCE

- The WHO currently recommends integrating diabetes and hypertension care with HIV treatment and prevention services.
- Resolve to Save Lives developed a toolkit to provide guidance on how common differentiated service delivery treatment models for ART can be adapted to integrate hypertension management.
- In a 2024 addendum, PEPFAR stated that it encourages HIV programs to focus on implementing person-centered care and integrated services for hypertension.

RESEARCH AND IMPLEMENTATION SCIENCE

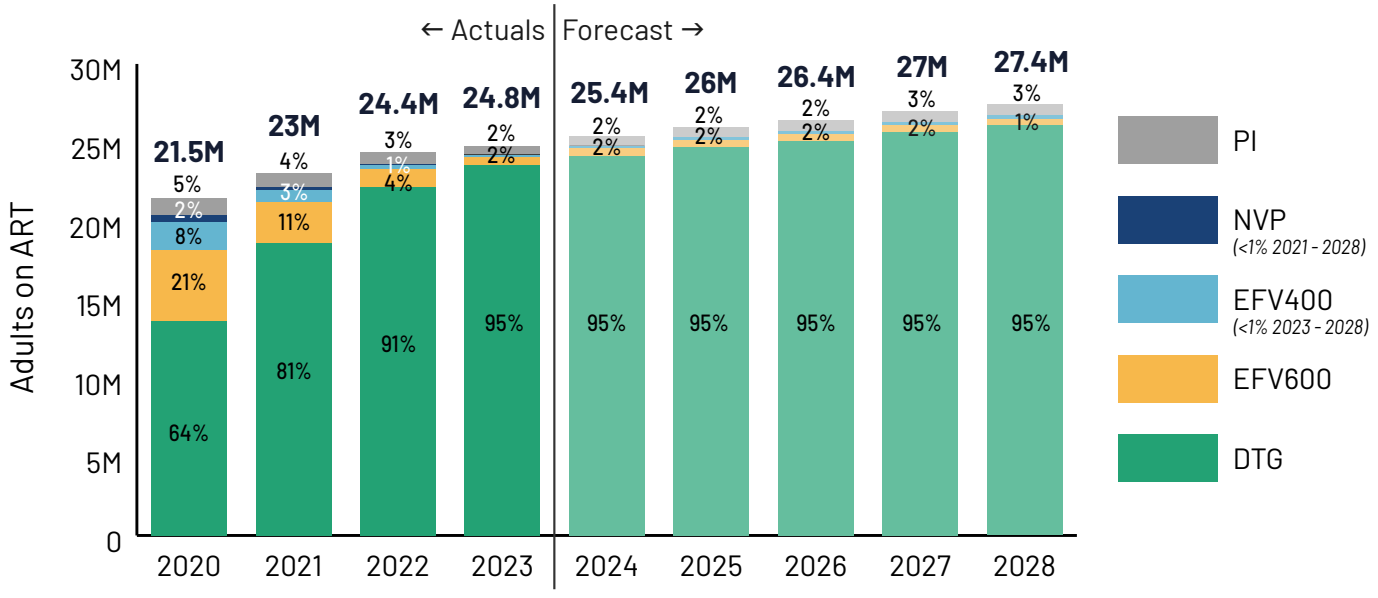
- Findings from the phase 3 REPRIEVE trial indicate that daily oral pitavastatin reduced major cardiovascular events among PLHIV by 35 percent.
- Follow-up research of the REPRIEVE trial, which included participants for a median 5.6 years, found that former and current use of abacavir (ABC) was associated with a 50 percent and 42 percent elevated risk of major adverse cardiovascular events, respectively. This association was not found with TDF, zidovudine (AZT), or protease inhibitors (PIs). More research is needed to inform these findings and better understand how they should be applied in the context of other risk factors for PLHIV.

Over 25 million adults in GA LMICs on ART as access to optimal treatment continues to increase

In 2023, nearly 25 million adults living with HIV in GA LMICs were on treatment, representing 80 percent treatment coverage, an increase of only three percentage points compared to 2022.[i, v] Treatment coverage is beginning to stagnate as case finding for undiagnosed PLHIV becomes more challenging.

In 2023, 95 percent of adults on treatment in GA LMICs were taking DTG-based regimens.[v] As of June 2024, over one billion 30-pack equivalents of the fixed-dose formulation, TLD, have been supplied to GA LMICs.[lv] CHAI forecasts that DTG use will remain steady over the next several years. Very minimal efavirenz (EFV) use is expected for individuals who cannot take DTG and marginal nevirapine (NVP) use may continue in select countries.

FIGURE 13: ADULT INSTI/NNRTI/PI USE IN GA LMICS[xxxix]



LESSONS LEARNED FROM GENERIC SECOND-LINE DRV/r ROLLOUT IN NIGERIA AND ZAMBIA TO INFORM WIDER UPTAKE

DRV/r is a best-in-class protease inhibitor with a high barrier to resistance, improved viral suppression, better tolerability, and lower pill burden compared to LPV/r. As a fixed-dose combination, DRV/r (400/50 mg) is formulated for second-line treatment among PLHIV who experience failure or intolerance to DTG-based ART.

DRV/r UPTAKE

- In 2023, CHAI estimates that approximately two percent of PLHIV on ART in GA LMICs were on regimens containing PIs.[xxxix]
- WHO guidelines currently list DRV/r as an alternative second-line treatment, although the WHO is currently evaluating the evidence of DRV/r and may consider elevating it as preferred in a guidelines update.[lvii, lviii] Should this guidance be updated, increased DRV/r uptake is expected.

LESSONS LEARNED IN DRV/r INTRODUCTION

- With support from Unitaid and CHAI, in July 2022 Nigeria and Zambia began introducing DRV/r (400/50 mg) for clients experiencing DTG-based failure or transitioning from ATV/r or LPV/r due to side effects.[lix]
- Supervision visits found that quality healthcare worker training, strengthened enhanced adherence counseling practices, expanded POC viral load testing, and early involvement of community groups improved DRV/r uptake and transition.[lx]
- PLHIV in Zambia who have transitioned to DRV/r report fewer side effects, reduced pill burden and better adherence compared to legacy PIs.[lxi]

FIGURE 14: DRV/r ADOPTION AS OF JUNE 2024, AS SEEN BY THE APWG[lvi]

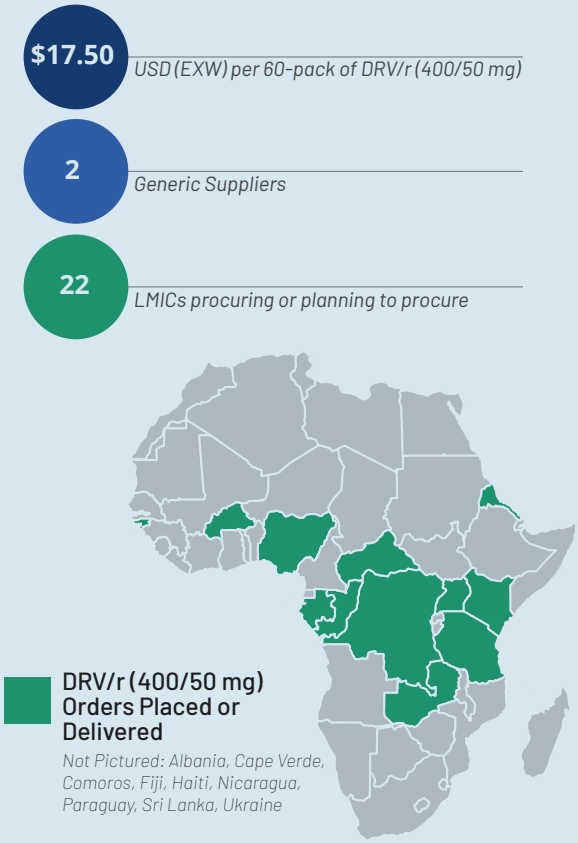
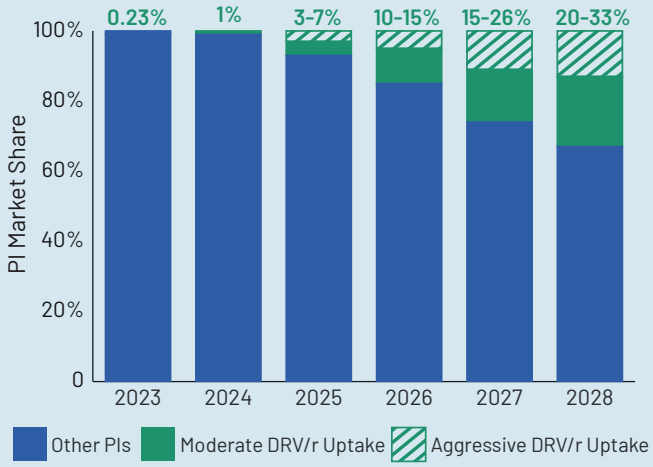


FIGURE 15: FORECASTED DRV/r UPTAKE (EXCLUDING SOUTH AFRICA)[v]



For me, I've never experienced side effects with the drug [DRV/r]. So far, I would say this is the best drug for me.

-17 Year-old PLHIV on ART in Central Province, Zambia[lxi]

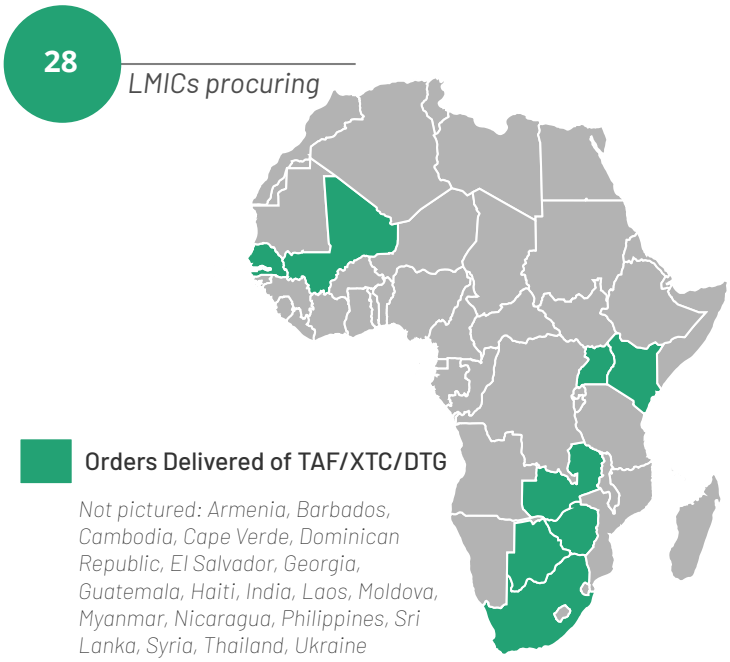
Growing interest in the use of TAF for special populations and shifting perspectives on its role in weight changes among PLHIV

Tenofovir alafenamide fumarate (TAF), a tenofovir pro-drug, is recommended by WHO as an alternative to TDF in children (>25 kg) and adolescents, and in special circumstances for adults with osteoporosis or impaired kidney function.[lvii] While TAF has benefits such as a smaller pill size and potentially lower risk profile as compared to TDF, several studies have found no statistically significant difference between TAF and unboosted TDF in terms of viral suppression and bone and renal safety.[lxii]

TAF UPTAKE

- Increasing interest in this product over the past year suggests the potential for future TAF use to expand, although programs will need to balance a slightly higher price (largely due to low volumes) with ongoing concerns about how TAF may impact weight.[xxii]

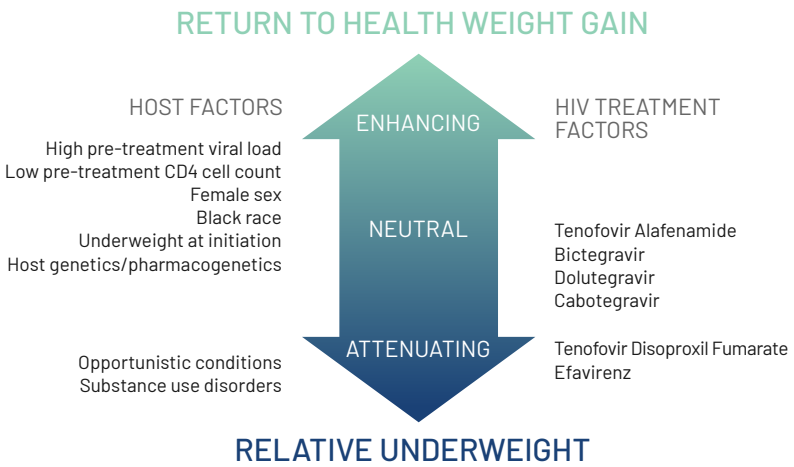
FIGURE 16: TAF UPTAKE AS OF JUNE 2024[lxiii, lxiv]



TAF AND WEIGHT GAIN

- Several studies suggest that regimens containing TAF are more likely to cause weight gain, with associated hypertension, and dyslipidemia than those with TDF or other drugs in the same class, particularly when co-administered with DTG.[lxv, lxvi]
- 48-week results from the PASO-DOBLE study found that the average weight gain for trial participants taking DTG/3TC was just under one kilogram, which mirrors weight gain in the general population. Conversely, participants in the BIC/FTC/TAF arm gained twice as much weight. Importantly, weight gain in the BIC/FTC/TAF arm was significantly higher when the pre-switch regimen included TDF.
- A recent review explored weight changes in major randomized trials of individuals on PrEP and ART as compared to the general population. The review found that DTG, BIC, and TAF are weight neutral, while TDF—especially when used with EFV—attenuates weight gain. The authors highlight other host factors mediate weight gain seen in PLHIV on ART and emphasize caution in attributing this to specific ARVs.
- Further, new research on PLHIV in Switzerland indicates that switching from TAF-based treatment to TDF results in decreased body weight and an improved lipid profile. However, these changes were not observed when individuals on TAF switched to two-drug regimens such as DTG/3TC and the long-acting injectable CAB+RPV, potentially signaling that the weight loss was associated with TDF.

FIGURE 17: FACTORS IMPACTING WEIGHT AMONG PLHIV ON ART[lxvii]



Long-acting HIV treatment represents a transformational step forward, but only if access is widespread and tailored for use in LMICs

The ongoing development of long-acting ARVs is a game-changing step forward in the global HIV response, with particular promise to improve adherence and retention in care. While global attention to-date has largely been focused on long-acting HIV prevention products, research and development is ongoing to make long-acting ART a reality in LMICs.

Currently, the only complete long-acting injectable regimen approved for a broad treatment indication is CAB+RPV, administered every eight weeks. While use of this product is growing in high-income settings, there are significant barriers to implementation in LMICs such as cold-chain requirements, RPV's low barrier to resistance, high rates of resistance due to historical EFV use, and limited drug availability, even for implementation research. Existing research on CAB+RPV has shown the feasibility of long-acting regimens in LMICS and demonstrated potential benefits especially for PLHIV with adherence challenges.

CARES

- A phase 3b randomized, multicenter, open-label trial that is the first to investigate CAB+RPV use in African populations.
- 48-week results show 96 percent of PLHIV in the CAB+RPV arm and 97 percent of PLHIV who remained on daily oral ART maintained viral suppression at follow-up, suggesting non inferiority of CAB+RPV to daily oral ART, even among populations with high levels of non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance.

LATITUDE

- A phase 3 prospective, randomized open-label trial, conducted among adult PLHIV in the US with suboptimal adherence (elevated viral load above 200 cells/µL), compared long-acting injectable treatment with CAB+RPV to daily oral ART. Notably, participants received cash incentives for viral suppression (<200 cells/µL) on daily oral ART for the first 24 weeks, and had to maintain viral suppression to be randomized into the CAB+RPV or continued daily oral ART arm.
- Interim findings indicate treatment with CAB+RPV demonstrated superior efficacy compared to daily oral ART—resulting in a lower cumulative probability of elevated viral load and treatment discontinuation and improved persistence and adherence to treatment.
- In February 2024, the Data Safety Monitoring Board recommended stopping randomization and offering CAB+RPV to all participants.
- Data from the LATITUDE trial, and similar findings from the US-based retrospective cohort study ABOVE, provide empirical evidence that long-acting ART can be used in people with adherence challenges.

In mid-2024, Johnson and Johnson told partners they will not be manufacturing RPV for LMICs and will no longer be enforcing their patent for RPV. However, they are not providing technology transfer to generic companies, which has resulted in extremely limited drug access impeding further research.[xix] Additional evidence generation is necessary to support the use of long-acting ARVs in GA LMICs, specifically safety and efficacy data, learnings from implementation studies, and research on community preferences.[lxviii]

Lenacapavir (LEN) demonstrates potential in populations with adherence challenges, however LMIC treatment access remains essentially nonexistent until generic licensees can support demand

In December 2022, the US FDA approved lenacapavir (LEN), the first ever capsid inhibitor, in combination with other ARVs as a twice-annual subcutaneous injection for treatment in highly experienced PLHIV, with a lead-in oral dose and optimized backbone. As mentioned in the prevention section, LEN is also being studied as a six-monthly injection for the prevention of HIV, with impressive results from phase 3 trials.[lxix]

LEN + CAB RESEARCH

In a US-based case series led by Monica Gandhi, clinical providers placed 34 PLHIV with ART adherence challenges on six-monthly subcutaneous LEN and intramuscular CAB every four or eight weeks, with or without RPV.

- Viral suppression increased from a baseline of 47 percent to 94 percent.
- Researchers indicate this data supports the need for a clinical trial to evaluate the use of a LEN+CAB combination.

LEN CLIENT EXPERIENCES

Gilead released data on experiences and quality of life from 72 PLHIV on LEN for treatment in their phase 2/3 CAPELLA study.

- Survey participants reported positive experiences with LEN regarding ease of integration into treatment regimens, efficacy, tolerability, discreteness of administration, and reduction in pill burden.
- After taking LEN, 64 percent agreed that their quality of life had improved and they had fewer negative feelings about their illness, and 92 percent agreed that LEN is well tolerated.

LEN ACCESS

As mentioned in the prevention section, in October 2024, Gilead stated it will supply LEN to GA LMIC countries for both treatment for highly treatment experienced PLHIV and prevention at no profit until the six generic manufacturers with voluntary licensing agreements are able to support demand. In October 2024, a meeting on *Accelerating Access Planning for Long-Acting HIV Treatment in LMICs* was convened in Washington, D.C. by the Bill & Melinda Gates Foundation, NIH, NIAID, PEPFAR, GHSC-PSM, the WHO, and CHAI. Meeting conveners brought together a group of leading experts in HIV treatment optimization to define a way forward to accelerating access to long-acting treatment. Excitement and momentum coming out of the meeting highlights the urgent need to expedite access to long-acting therapies in LMICs. Key outputs from the meeting include a Target Access Profile and ongoing coordination to accelerate development and introduction of fit-for-purpose long-acting HIV treatments for use in LMICs.

LONG-ACTING ART PREFERENCES

A discrete choice experiment conducted among PLHIV attending sex work outreach programs in Nairobi, Kenya found clients expressed a desire for long-acting ART over their daily ART. Among the hypothetical long-acting ART options, they preferred oral long-acting ART with no pain, followed by one-year implants with mild pain. Participants also preferred clinic-based administration and less frequent dosing.

The adult HIV treatment pipeline focuses on diversified delivery methods and combinations of long-acting products

PHASE 2 TRIALS

- **ISL + LEN:** 24-week results from a phase 2 study investigating weekly oral islatravir (ISL) and LEN demonstrated 94 percent viral suppression among participants and was well tolerated.
- **CAB + broadly neutralizing antibody (bNAb):** A phase 2 trial of once monthly intramuscular injectable CAB and a bi-monthly intravenous bNAb, VRC07-523LS, found the combination to be safe and well tolerated for maintenance ART in virally suppressed PLHIV.

PHASE 1 TRIALS

- **LEN + two bNAbs:** A phase 1b study of LEN with two bNAbs, teropavimab and zinlirvimab, demonstrated high levels of viral suppression among PLHIV with susceptibility to one or both bNAbs at 26 weeks.
- **GS-1614:** Calibr and Gilead have entered into a licensing agreement to develop GS-1614, a long-acting ARV for potential use in combination with LEN for HIV treatment. GS-1614 is a nucleoside reverse transcriptase translocation inhibitor (NRTTI) prodrug, and Gilead has initiated a phase 1 clinical study to determine the optimal dose, safety, and administration frequency. GS-1614 may also be explored for HIV PrEP in future.

PRECLINICAL TRIALS

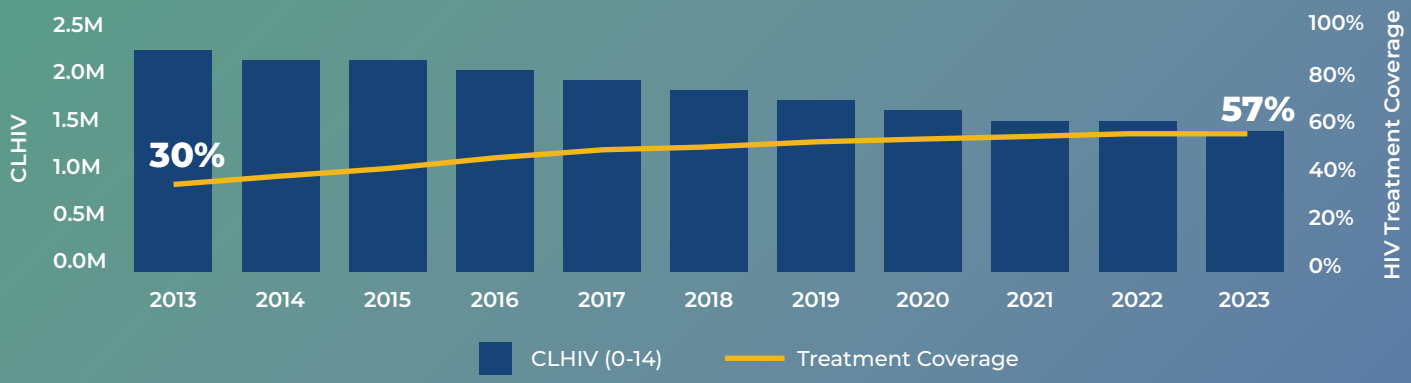
- **ISL Implant:** Results from a study of subdermal delivery of ISL via an implant in non-human primates showed higher antiviral potency than daily or weekly oral dosing of ISL. However, the emergence of resistance mutations with ISL monotherapy emphasizes the importance of combination ARV for effective viral suppression.
- **TLD in Drug-Combination-Nanoparticle (DcNP):** A preclinical study used DcNP technology to create a monthly injectable form of TLD. Following single-dose TLD-in-DcNP, all drugs exhibited long-acting profiles in non-human primates with levels that persisted above predicted viral-effective concentrations for four weeks.

PEDIATRIC TREATMENT

The new progress report on the Global Alliance to End AIDS in Children by 2030 reinforces a powerful message: we can end AIDS in children. While we are seeing a decrease in new childhood HIV infections and deaths, progress is not inclusive enough and far too slow. The majority of children in GA LMICs are now on a DTG-based regimen, the WHO-preferred treatment. However, considerable disparities remain between adults and children living with HIV, especially concerning treatment coverage. Among the 1.4 million CLHIV in 2023, only 57 percent were on treatment compared to 77 percent of adults. Children also account for a disproportionate percentage of AIDS-related deaths as a result of this and other inequities. While newly available, optimal, fixed-dose combination and pipeline ARVs may improve treatment outcomes for children, more work must be done to enhance case finding and improve treatment coverage, viral suppression, and retention in care.

Trends in Pediatric Treatment

57% **treatment coverage for CLHIV (0-14 years) globally in 2023**[i]

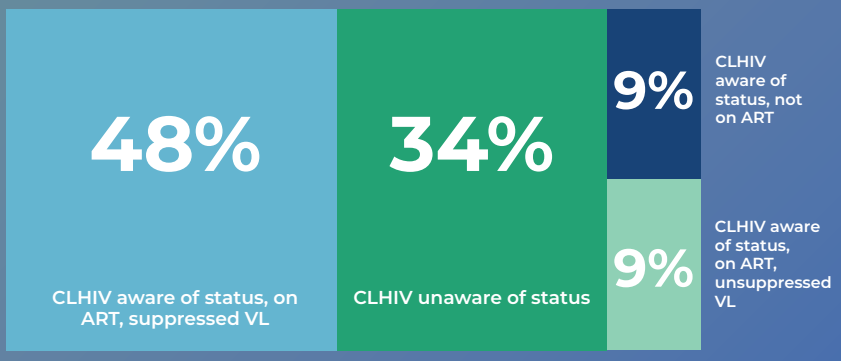


1.4M children living with HIV globally in 2023, 86% are in SSA[i]

84% of CLHIV ages 0-14 on ART had suppressed viral loads in 2023, a significant improvement compred to pre-DTG suppression rates below 70%[i]

12% of all AIDS-related deaths were children in 2023, despite constituting only 3% of PLHIV[i]

CLHIV by Testing and Treatment Cascade[i]



Key Updates

pALD	14 countries have placed or received orders of pediatric ABC/3TC/DTG (60/30/5 mg) disp. (pALD)[lvi]
pDTG	Over 25M 30-pack equivalents of pDTG supplied in 97 countries as of June 2024[lxiii, xxii]
pDRV/r	June 2024 US FDA regulatory filing for Laurus Labs, approval expected by end of year[xxii]
pTAF	Product development is on track and the bioequivalence studies have commenced[xxii]

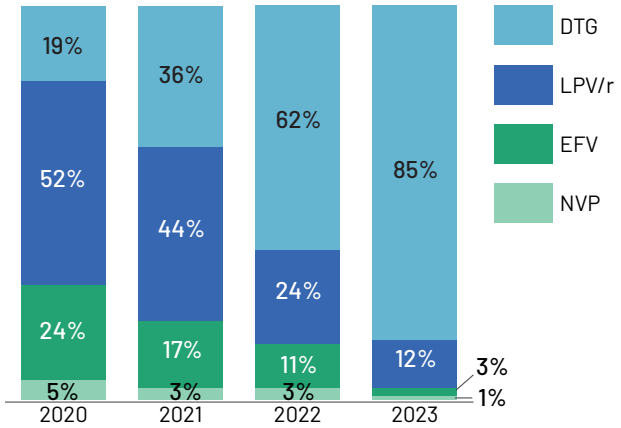
Research highlights opportunities to close pediatric testing and treatment gaps while supporting children to survive and thrive as they transition to adolescence

- **More efficient and effective testing for children is needed, especially amidst declining global HIV resources[lxx]**
  - This is particularly urgent in West and Central Africa, with high gaps in pediatric HIV diagnosis (~35 percent) and low overall HIV prevalence.[i]
  - Scaling country-specific mixes of testing strategies is essential, as different approaches vary in tests needed per positive child identified. Index testing can help increase diagnoses in countries with low pediatric and maternal ART coverage.[lxxi]
  - In South Africa, a mathematical model found that home-based and self-testing for adults yield the greatest impact and cost-effectiveness, at US$394 per life year saved. Application of this modelling is needed for children.
- **Evidence-based peer-support and mental health models can significantly improve outcomes for youth living with or at risk of HIV**
  - 50 percent of mental health conditions are established by age 14, and more than a quarter of young people living with HIV experience common mental health disorders (CMDs).[lxxii, lxxiii] There are significant bi-directional impacts of HIV and CMDs, and CMDs are greatly neglected.[lxxiv]
  - Cluster randomized trials have shown that peer-supported community-based HIV care delivery can improve HIV virological suppression, and symptoms of CMDs.[lxxv, lxxvi] An economic evaluation *(planned for publication in early 2025)* of this data (from pre-DTG era) showed that this intervention would lead to improved outcomes compared to the standard of care, including proportion of cohort with undetected viral load (65 percent vs 21 percent) and death (9 percent vs 57 percent). Estimated incremental cost-effectiveness ratios were US$372 per life-year gained and US$99 per quality-adjusted life-year gained.[lxxvii]
  - Economic modelling of selected interventions for adolescent mental health showed a return on investment of US$125.60 and cost per DALY averted at US$3.80 in the WHO African Region, with highest return on investment arising from treating mild depression with group-based cognitive behavioral therapy, prevention of suicide attempts among high-risk adolescents, and universal prevention of combined anxiety and depression in LMICs.

The majority of children in GA LMICs are now on a DTG-based regimen, ongoing transition to pALD will provide additional benefits

PEDIATRIC DTG OPTIMIZATION

FIGURE 18: ESTIMATED PEDIATRIC "THIRD POSITION" ARV USE IN GA LMICS[v]



In 2023, CHAI estimates that 85 percent of CLHIV on pediatric treatment were on DTG-based regimens, based on data from 14 GA LMICs representing 61 percent of CLHIV on ART in GA LMICs.[v] DTG use is anticipated to continue to grow given the scale-up of pDTG in high volume countries, including South Africa, where both pDTG and pALD were included in their most recent tender.[lxiv]

PEDIATRIC DTG (pDTG)

Dolutegravir (10 mg) dispersible and scored tablets (pDTG) are the WHO-preferred pediatric ARV for children at least four weeks of age and weighing at least three kg. Strawberry-cream flavored and dispersible in water, this once-daily optimal ARV is easy to administer, has a high barrier to resistance, and has a very favorable safety, tolerability, and efficacy profile.

RESEARCH

Real world studies of pDTG use indicate improvements in clinical outcomes among CLHIV, including increased rates of viral suppression.

- In Nigeria, a study explored the treatment outcomes of 180 children transitioning from LPV/r to pDTG. The percentage of CLHIV with suppressed viral load increased from 66 percent at baseline to 90 percent at 12 months.
- As of March 2024, South Africa had successfully transitioned nearly 50 percent of CLHIV under ten years of age to pDTG. Between April 2023 and March 2024 viral load suppression increased from 64 percent to 73 percent among CLHIV under ten years on ART.

PEDIATRIC ALD (pALD)

Pediatric ALD is a dispersible FDC of ABC/3TC/DTG (60/30/5 mg) recommended for children at least three months of age and at least six kg. This is the first ever pediatric FDC to include DTG, providing the complete WHO-recommended first-line regimen for children in one convenient pill.

pALD BENEFITS

- As a complete three-drug formulation, pALD eliminates the risk of mono or dual therapy that existed with legacy products, reducing the risk of poor viral suppression and drug resistance.
- pALD provides both caregiver and prescribing benefits as compared to separate DTG (10 mg) and ABC/3TC (120/60 mg) tablets—easing the administration burden and simplifying the guidance provided by pharmacists and clinicians.
- A Zambia-based analysis conducted by PEPFAR found pALD reduces the required number of bottles by 60 to 75 percent compared to separate products, thereby reducing the number of pallets and warehousing space and lowering air freight, in-country holding, and in-country distribution costs.[lxxviii]

FIGURE 19: BOTTLE DIFFERENCES FOR A 45-DAY SUPPLY pABC/3TC+pDTG vs pALD FOR ONE CHILD LIVING WITH HIV WEIGHING 10-13.9 KG[lxxviii]

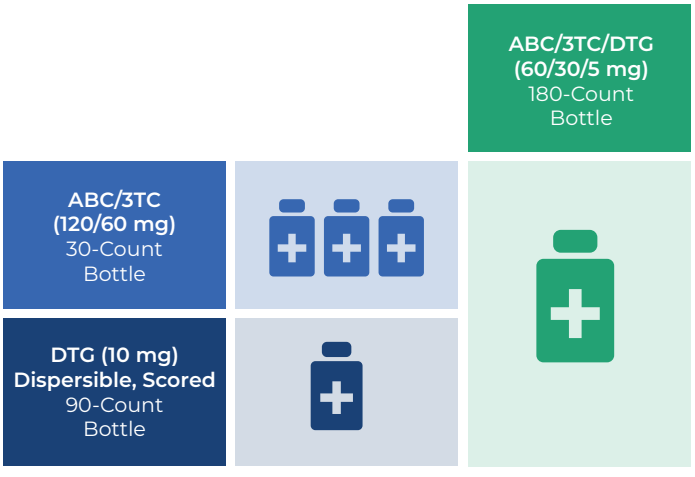
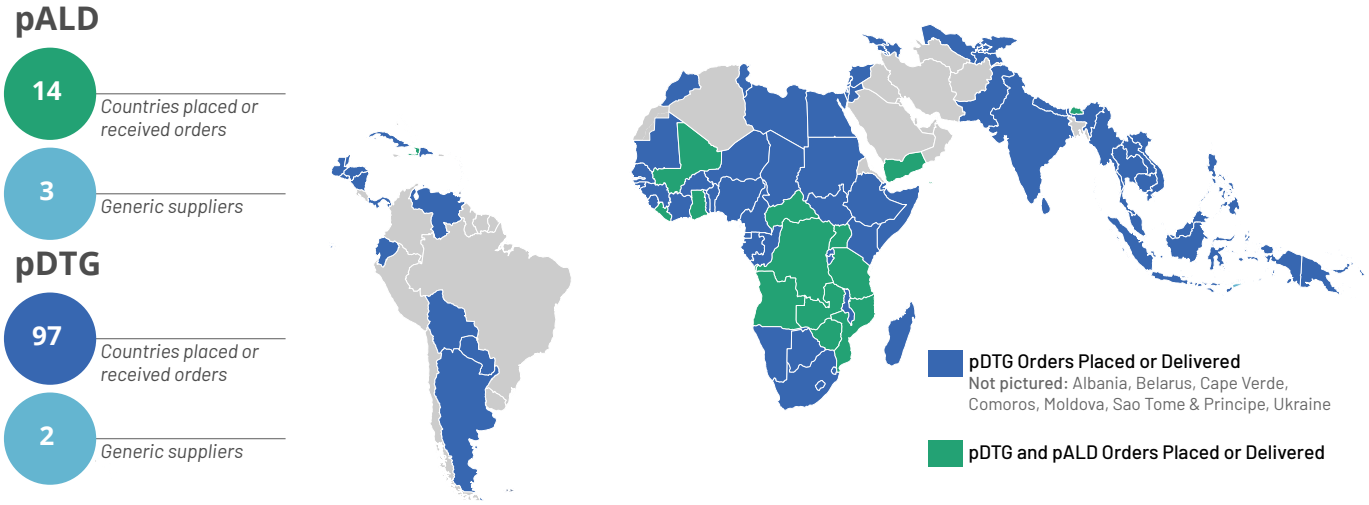


FIGURE 20: pDTG AND pALD ADOPTION AS OF JUNE 2024[lvi, lxiii]



IMPLEMENTATION

- Orders for pALD have been steadily increasing, although pDTG singles will need to be retained for children with TB co-infection, children between three and 5.9 kg and those under three months of age, and for some children who are on second- and third-line ART who have not previously taken DTG.
- Transition plans should account for existing and pipeline stocks of DTG (10 mg) and ABC/3TC (120/60 mg) and minimize wastage.
- Countries should prioritize procuring 180-count bottle sizes, which are preferred by PEPFAR to support multi-month dispensing.
- Additional guidance and resources to support pALD introduction can be found on the CHAI HIV New Product Introduction Toolkit website.

Pipeline pediatric ARVs provide further opportunities to optimize care and improve treatment outcomes

PEDIATRIC DRV/R (pDRV/R)

Darunavir is a best-in-class protease inhibitor, and currently under generic development with ritonavir as an FDC for children experiencing treatment failure on DTG-based regimens or who cannot tolerate DTG. DRV/r offers a number of benefits compared to LPV/r, including higher efficacy, significantly improved tolerability, and a higher barrier to resistance. With support from CHAI and funding from Unitaid for generic development, Laurus Labs filed with the US FDA in June 2024 for tentative approval of film coated pediatric DRV/r (120/20 mg), with approval expected by the end of 2024. More information about this key product and guidance to support early introduction planning can be found in CHAI's pediatric DRV/r resources.

PEDIATRIC TAF (pTAF)

CHAI continues to work as a formulation development partner with support from the UK Foreign, Commonwealth & Development Office, in collaboration with Penta Infectious Diseases Network and Gilead, to develop generic pTAF by Laurus Labs and Viatris.[lxxix] Product development on the triple fixed-dose combination containing TAF, FTC, and DTG is on track, and the bioequivalence studies have commenced. This TAF-containing product will enable children to access a tenofovir-containing regimen without the renal and bone toxicity concerns associated with TDF. Given these benefits and a higher barrier to resistance, pTAF could replace abacavir and become the primary backbone ARV for children.

BROADLY NEUTRALIZING ANTIBODIES (bNAbs)

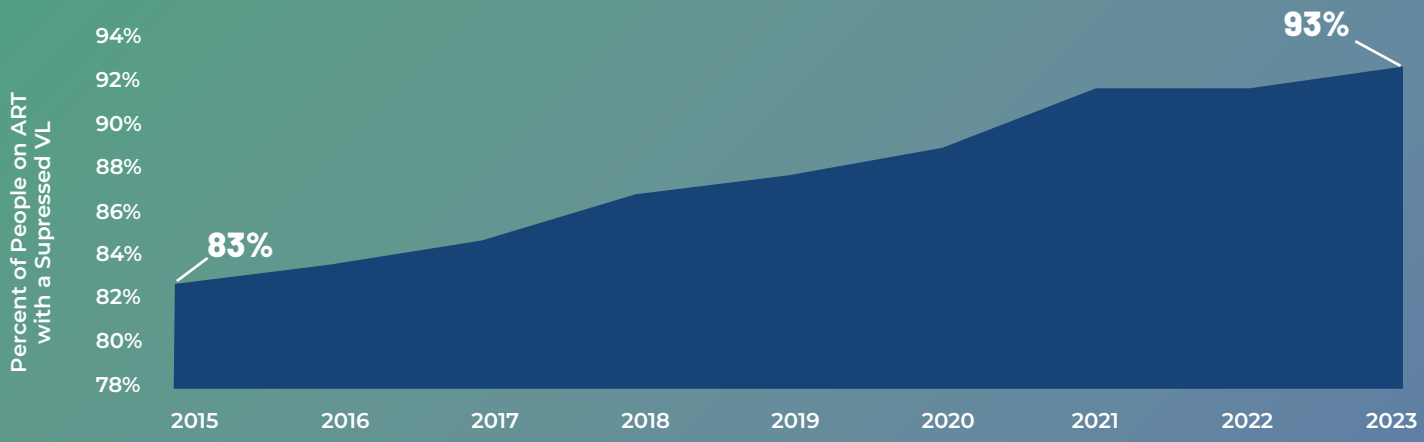
Broadly neutralizing antibodies are proteins that are injected intravenously or subcutaneously and are being studied for HIV treatment and prevention. Longer dosing intervals for bNAbs compared to daily oral ARVs could improve treatment adherence and ease administration burden for caregivers, although there are a number of potential challenges including cost, cold-chain requirements, and increased health system burdens for administration.[lxxx] New partnerships aim to accelerate the development of these options for CLHIV, including efforts from IAVI, Penta Child Health Research, and Achilles Vaccines. A recent study exploring the preferences of caregivers of CLHIV in Botswana indicated a preference for intravenously administered bNAbs over daily oral ART, and the CELEBRATE study aims examine the acceptability and feasibility of bNAbs for infant prophylaxis in Uganda and South Africa.

TREATMENT MONITORING

As access to optimal regimens scales-up, treatment monitoring remains critical to ensure continued viral suppression. New data shows low levels of DTG resistance, primarily driven by adherence challenges. However, expanded access to affordable drug resistance testing alongside continued expansion of viral load (VL) monitoring will help improve treatment outcomes and achieve epidemic control.

Trends in Monitoring

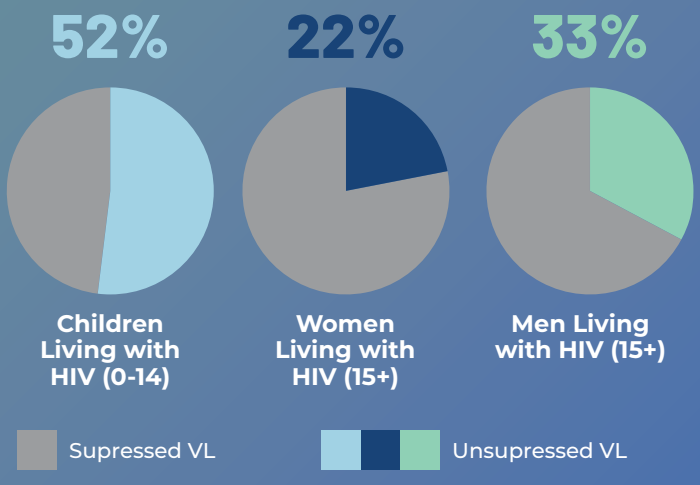
93% **of people on ART had a suppressed viral load in 2023**[i]



25% of HIV transmissions occur when partner is on ART but has an unsuppressed viral load, according to modelling[ii]

73% of 124 reporting LMICs were providing viral load monitoring in at least 95% of their HIV treatment facilities in 2024[ii]

Viral Suppression Rates among Children, Women, and Men Living with HIV (2023)[i]



Key Updates

Drug Resistance	Low levels of DTG resistance according to a new WHO report[lxxxi]
Viral Load	26.2M Viral load tests run in 2023 in LMICs[lxxxii]

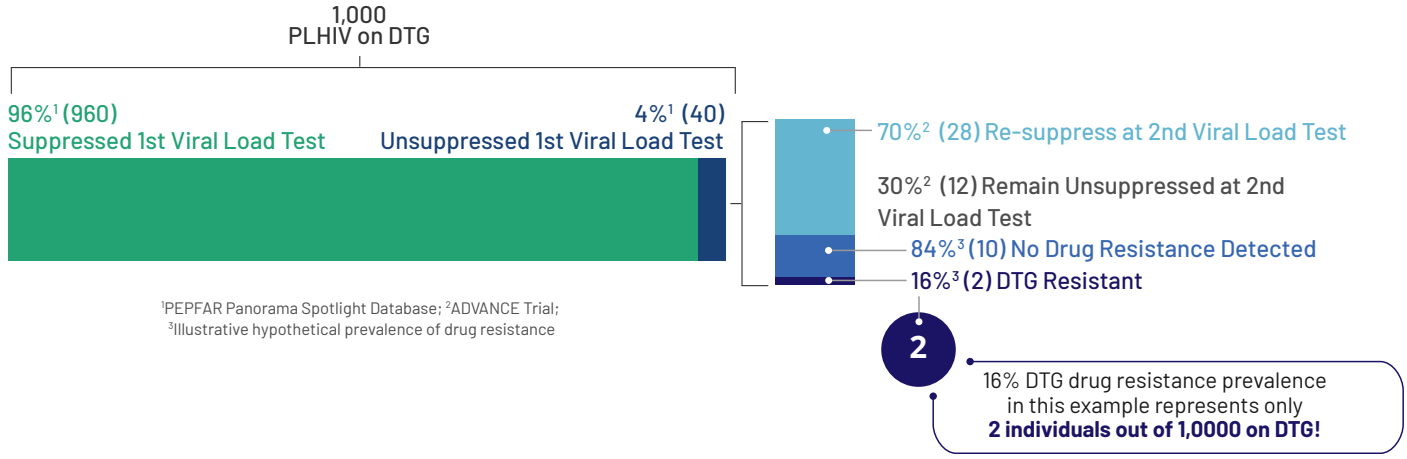
New data shows low levels of DTG resistance, but cost and limited normative guidance remains a barrier to expanded access to drug resistance testing when needed

Results from several studies and reports provide critical insights into levels of drug resistance in the era of expanded access to DTG.

2024 WHO HIV DRUG RESISTANCE REPORT

- DTG resistance in people newly initiating treatment was observed at 0.2 percent in only one country surveyed and was not present at all in any of the other ten.
- Viral suppression (and re-suppression) on DTG is high, and drug resistance is still very low as a proportion of the total number of PLHIV on DTG.
- Most PLHIV on DTG-based regimens do not have resistance to DTG at the time of failure to suppress viral load initially.
  - Clinical management of people with an unsuppressed viral load on DTG-based regimens should stress expanded access to high-quality and evidence-based adherence interventions.
- Levels of observed DTG resistance among those on treatment with *detectable viral loads* ranged from 3.9 percent to 19.6 percent. While this was reported as higher than anticipated, it is important to contextualize the size of this population compared to the broader population of people on ART as a whole.

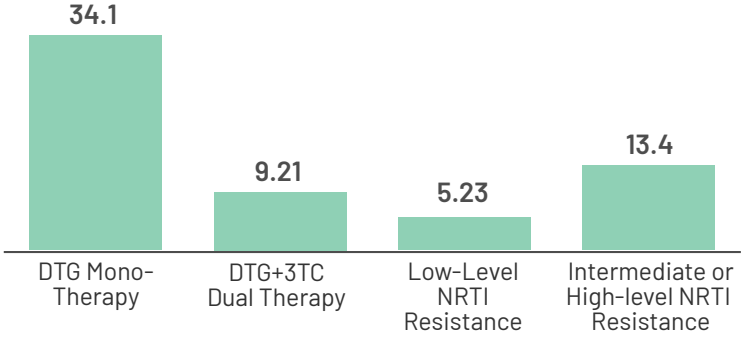
FIGURE 21: ILLUSTRATIVE EXAMPLE OF DRUG RESISTANCE PREVALENCE AMONG PEOPLE ON ART



DTG-RESIST STUDY

Among eight cohorts of PLHIV from Europe, North America, and South Africa who had unsuppressed viral loads while on DTG-based ART, DTG resistance was rare. Certain factors did contribute to a higher risk of resistance.

FIGURE 22: RISKS ASSOCIATED WITH HIGHER ODDS OF DTG RESISTANCE[lxxxiii]



EMERGING DOLUTEGRAVIR RESISTANCE AMONG CHILDREN BEING INVESTIGATED FOR TREATMENT FAILURE IN MALAWI

- In a cross-sectional survey of children two to 14 years old in Malawi, most children on ART with an elevated VL result resuppressed following adherence counselling.
- Rates of DTG resistance among those with VL failure were found to be higher among children (13.5 percent) compared to adults (8.5 percent).

Drug Resistance Testing

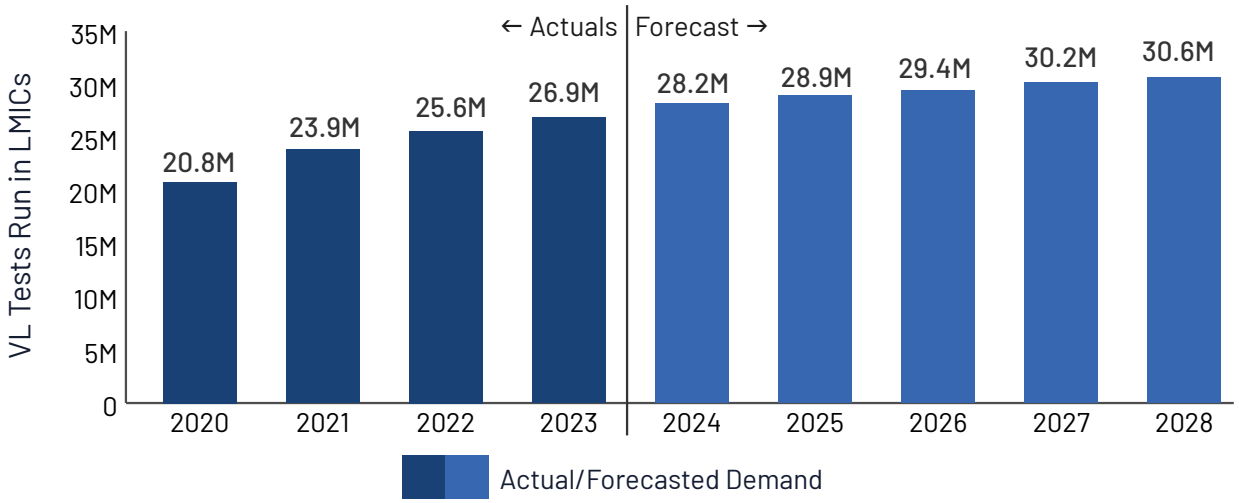
Even in the absence of WHO guidance, countries have begun to integrate drug resistance testing into national guidelines.

- Several countries, including Kenya, Malawi, Nigeria, and Zambia, have added drug resistance testing into their treatment algorithms following DTG failure.[lxxxiv]
- High costs remain a barrier to expanded implementation. Currently available HIV drug resistance tests range in price from US$40 per test (EXW floor price for the Thermo Fisher Sanger Assay Kit[xxii]) to over US$150 per test (EXW) for a conventional HIV drug resistance test.[lxxxv]
- While these costs may be high, drug resistance testing offers the potential to reduce the costs associated with unnecessary switches to more expensive regimens. Avoiding an unnecessary switch from DTG, which costs less than US$40 per person per year, to a protease inhibitor costing more than US$200, very quickly pays for the cost of resistance testing.[vi]
- To help support national HIV programs and ministries of health to estimate costs of expanding drug resistance testing, CHAI developed an HIV Drug Resistance Testing Costing Tool.

Viral load volumes and coverage continue to increase; continued efforts are needed to address ongoing disparities between adults and children

VL volumes are increasing, albeit at a slower rate than anticipated. In 2023, CHAI and Avenir estimate that almost 27 million VL tests were run in LMICs, an increase of 1.3 million tests.

FIGURE 23: VL TESTING DEMAND ACTUALS AND FORECAST[lxxxii]

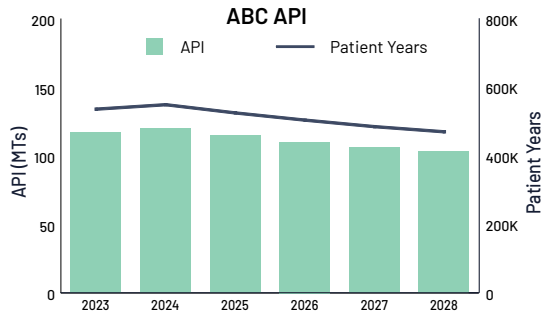


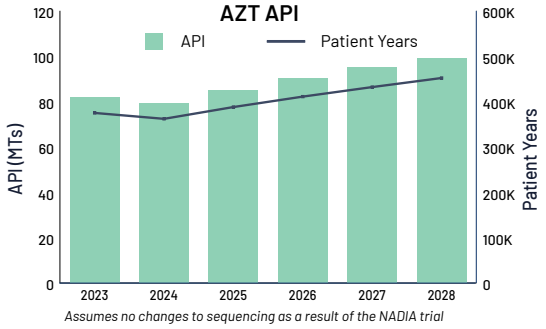
PEDIATRIC VL COVERAGE

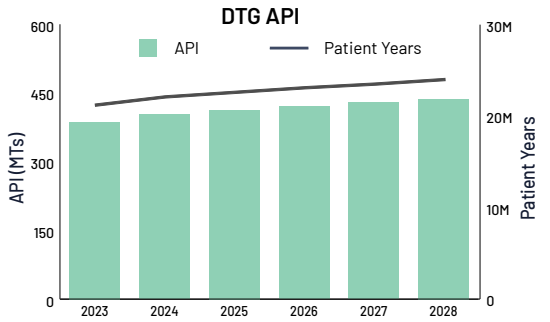
Pediatric viral load coverage and suppression is also increasing, according to data from PEPFAR-supported sites in Mozambique, Nigeria, Tanzania, and Zambia. Across the four countries, VL coverage increased from 78 percent in 2021 to 85 percent in 2023.[lxxxvi] However, countries experienced varied levels of progress, highlighting the continued need for targeted, country specific strategies to improve VL access for CLHIV.

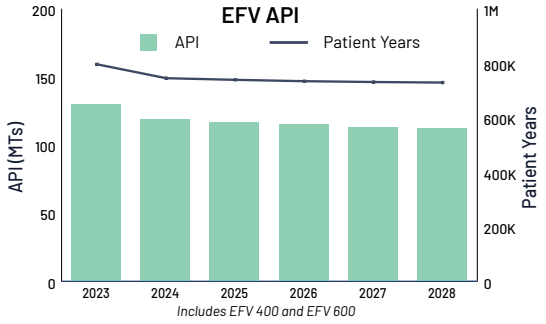
Appendix A:
Forecasted API Demand in GA LMICs

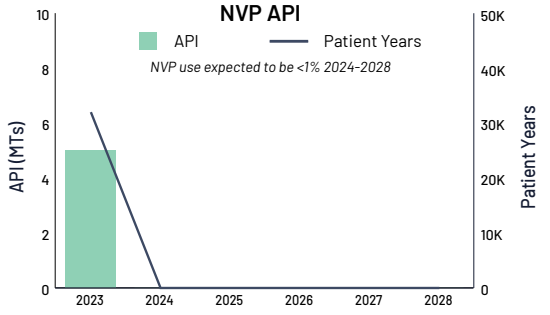
The graphs below show the estimated generic-accessible demand and active pharmaceutical ingredient (API) volume (in metric tons) for key adult ARVs. Patient years represent the effective number of clients on treatment for a full year and are used to calculate yearly API demand. Patient years are calculated by assuming newly-initiated clients are on treatment for six months on average in the year of initiation, and a 10 to 15 percent attrition rate is assumed to estimate yearly new initiations. Note that all figures are based on demand for adults only.

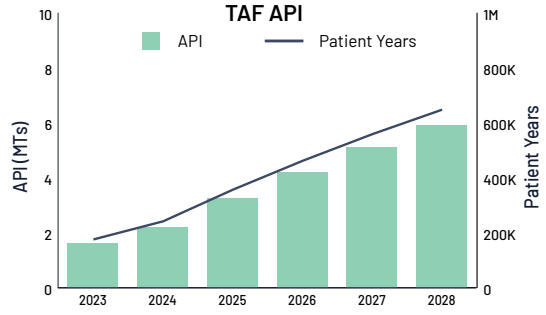


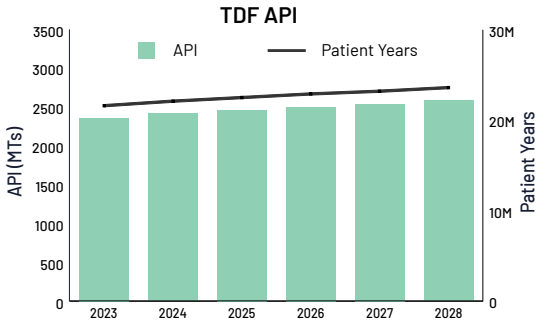


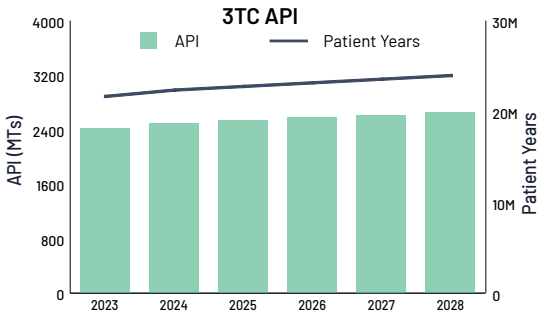












Appendix B:
CHAI ARV Benchmark Price Comparison List

The table below provides per pack or bottle prices (USD) for key adult and pediatric ARVs. Prices are Ex-Works (EXW).

PRODUCT	PACK SIZE*	GLOBAL FUND PPM PRICE OCT 2024[1]	GHSC-PSM E-CATALOG PRICE AUG 2024[2]	RSA WEIGHTED AVE TENDER PRICE 2022-2025[3,4]
Adult Products				
ABC/3TC (600/300 mg)	30 tablets	$7.85	$12.35	$5.85
ATV/r (300/100 mg)	30 tablets	$10.50	$10.95	$11.20
AZT/3TC (300/150 mg)	60 tablets	$5.35	$6.25	$4.37
DRV/r (400/50 mg)	60 tablets	$17.50	$17.50	$20.92
DTG (50 mg)	30 tablets	$1.21	$2.20	$1.50
DTG (50 mg)	90 tablets		$5.90	
LPV/r (200/50 mg)	120 tablets	$17.95		$13.68
RTV (100 mg) heat-stable	60 tablets		$7.00	$4.05
TAF/3TC/DTG (25/300/50 mg)	30 tablets	$4.75	$6.55	
TAF/3TC/DTG (25/300/50 mg)	90 tablets		$13.25	
TAF/FTC/DTG (25/200/50 mg)	30 tablets	$5.00	$5.43	
TAF/FTC/DTG (25/200/50 mg)	90 tablets		$18.65	
TDF (300 mg)	30 tablets	$2.40	$2.40	$1.94
TDF/3TC (300/300 mg)	30 tablets	$3.12	$3.09	
TDF/FTC (300/200 mg)	30 tablets	$3.32	$3.75	$2.89
TDF/3TC/DTG (300/300/50 mg)	30 tablets	$3.10		$3.75
TDF/3TC/DTG (300/300/50 mg)	90 tablets	$9.29	$10.60	$7.75
TDF/3TC/DTG (300/300/50 mg)	180 tablets	$18.50	$23.69	
TDF/3TC/EFV (300/300/400 mg)	30 tablets	$4.50		
TDF/3TC/EFV (300/300/400 mg)	90 tablets	$12.75	$12.65	
TDF/3TC/EFV (300/300/600 mg)	30 tablets	$5.25		
TDF/FTC/EFV (300/200/600 mg)	30 tablets			$4.38
Pediatric Products				
Optimal Formulary				
ABC/3TC (120/60 mg) disp. scored	30 tablets	$2.70	$2.70	$2.59
ABC/3TC (120/60 mg) disp. scored	60 tablets	$5.35	$5.35	
ABC/3TC/DTG (60/30/5 mg) disp.	90 tablets	$7.82		
ABC/3TC/DTG (60/30/5 mg) disp.	180 tablets	$14.85	$15.00	
AZT (50/5 mg/ml) oral solution	240 mL bottle	$2.50	$4.25	
AZT/3TC (60/30 mg) disp. scored	60 tablets	$1.90	$1.90	
DTG (10 mg) disp. scored	30 tablets		$1.45	$1.33
DTG (10 mg) disp. scored	90 tablets	$4.00	$4.22	
LPV/r (100/25 mg) heat-stable	60 tablets	$5.50		$3.63
LPV/r (40/10 mg) oral granules	120 sachets	$16.90	$17.95	
NVP (50/5 mg/ml) oral solution (with syringe)	100 mL bottle		$1.75	$0.95
Limited-Use List				
3TC (50/5 mg/ml) oral solution	240 mL	$2.25	$2.15	$1.19
DRV (75 mg)	480 tablets	$65.00	$54.00	$50.07
DRV (150 mg)	240 tablets		$54.54	$44.92
LPV/r (40/10 mg) oral pellets	120 capsules	$17.25		$11.71
NVP (50 mg) disp. scored	60 tablets		$1.60	
RAL (100 mg) granules	60 sachets		$57.00	
RTV (25 mg) heat-stable	30 tablets	$3.00	$3.25	

1) Global Fund Pooled Procurement Mechanism Reference Pricing: ARVs, October, 2024. Link
2) Global Health Supply Chain - Procurement and Supply Management (GHSC-PSM) E-Catalog: ARVs, August, 2024. Link
3) Republic of South Africa 2022 - 2025 Tender, weighted average price across awarded suppliers, 1 USD = 14.54 ZAR exchange rate used per tender documents
4) Republic of South Africa 2024-2025 Supplemental Tender, weighted average price across awarded suppliers, 1 USD = 18.67 ZAR exchange rate used per Tender documents
Note on 3-4: Ex-Works prices have been calculated by removing 15% VAT and 5% in shipping; prices subject to forex-based adjustments; some pack sizes differ slightly from those listed above, see tender for full details.

* For certain products, pricing on other pack sizes might be available (e.g., multi-month prescription pack sizes). Please refer to relevant price list for more information.

Appendix C:
Notes on Methodology

There are several CHAI analyses from which many figures in this report are derived:

ART Forecast: Each year, CHAI develops a forecast for the total number of PLHIV on ART in generic-accessible LMICs (GA LMICs). 'Generic-accessible' denotes countries where global generic manufacturers can register and supply a large proportion of that country's ARVs. For this purpose, CHAI defines GA countries as those LMICs that are covered under voluntary licenses for generic TDF/TAF, or for where there are no patents. The largest *generic-inaccessible* countries are Brazil, China, Mexico, and Russia.

CHAI compiles historic data on the number of PLHIV on ART from the UNAIDS AIDSinfo Database. For each country, CHAI assumes that the number of people receiving treatment will increase at the same rate as the linear trend observed in the last four years and will plateau as universal access (under a "Treat All" paradigm) is approached.

Historical ART coverage rates for GA LMICs are calculated based on data available in the UNAIDS AIDSinfo Database as of December 2024. The numerator and denominator are derived by only including countries with both ART and PLHIV data available for the age category in question (adults vs. children).

Adult ARV Demand Forecast: CHAI collects aggregate country data on regimens, formulations used, national guidelines, and anticipated future trends from CHAI country teams and published literature each year. CHAI uses that data, an internally developed forecasting model, and the ART forecast to project ARV demand in GA LMICs over the next five years at the global level. CHAI's 2024 ARV demand forecast for current drugs includes data from: Cambodia, Cameroon, Democratic Republic of the Congo, Ethiopia, Indonesia, Kenya, Laos, Lesotho, Malawi, Nigeria, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe. These countries represent approximately 67 percent of adult PLHIV on ART in GA LMICs in 2023.

ARV Market Sizing Analysis: Each year, CHAI combines known regimen splits by country with pricing data to estimate the size of the ARV market in dollar terms. The market size is an estimate of the cost of 1L and 2L treatment (drug costs only) in GA LMICs for all of 2023, and assumes that the countries CHAI has data for are representative of the remaining 33 percent of the market in GA LMICs. It is not an estimate of the cost of ARV procurement in 2023. The assumed price paid for ARVs comes from two sources: 1) South Africa procurement informs the price paid for each respective formulation within a given year for South Africa's regimens; 2) For all other countries, the Q2 Global Fund Pooled Procurement Mechanism (PPM) pricing from 2023 is used.

Diagnostics Forecasts: CHAI's VL, EID, and CD4 diagnostics forecasts have two primary components: 1) diagnostic testing demand, and 2) diagnostic testing need. While the exact methodology differs slightly between VL, EID, and CD4 tests, the general approach is as follows.

For *demand*, CHAI collects baseline (2023) testing volumes from CHAI country teams, uses publicly available dashboards, or other sources with supplemental data from Avenir Health and the WHO survey. For CD4 and EID, demand is forecasted by applying historical CAGRs to baseline data. CHAI forecasts VL demand by assigning countries to one of five growth analogs based on real-world viral load scale-up and hypothetical scenarios. CHAI assigns these analogs based on country intelligence around future scale-up plans. Testing need is forecasted based on the estimated number of PLHIV each year and country-level testing guidelines for each type of test. The estimated CD4 need is based on 1.1 CD4 tests at initiation (accounting for wastage/retesting) and 1-2 tests for those with an elevated VL result. National guidelines and implementation may differ from these assumptions. Need estimates do not include CD4 testing used for treatment monitoring. For all test types, CHAI forecasts at the country level and then aggregates globally across all LMICs.

Demand, need, and coverage are estimated at the test-level, and not the client-level (i.e., coverage is estimated as the number of tests run divided by the number of tests needed, not the number of peoplereceiving tests).

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