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# 2021 HIV MARKET REPORT

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

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BILL & MELINDA  
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The data sources primarily used for analysis in the report include CHAI country teams, Ministry of Health counterparts, stakeholder resources and conversations (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.

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# ACRONYMS

<b>1L</b>	First-line	<b>INH</b>	Isoniazid
<b>2L</b>	Second-line	<b>INSTI</b>	Integrase strand transfer inhibitor
<b>3HP</b>	Three months of weekly RPT+INH for TPT	<b>ISL</b>	Islatravir
<b>3L</b>	Third-line	<b>LA</b>	Long-acting
<b>3TC</b>	Lamivudine	<b>L-Amb</b>	Liposomal amphotericin B
<b>5FC</b>	Flucytosine	<b>LEN</b>	Lenacapavir
<b>ABC</b>	Abacavir	<b>LMIC</b>	Low- and middle-income country
<b>AGYW</b>	Adolescent girls and young women	<b>LPV/r</b>	Lopinavir/ritonavir
<b>AHD</b>	Advanced HIV Disease	<b>LTFU</b>	Lost to follow up
<b>AIDS</b>	Acquired immunodeficiency syndrome	<b>MMD</b>	Multi-month dispensing
<b>AmB-d</b>	Amphotericin B deoxycholate	<b>MPT</b>	Multipurpose prevention technology
<b>ARV</b>	Antiretroviral	<b>MSM</b>	Men who have sex with men
<b>ATV/r</b>	Atazanavir/ritonavir	<b>NNRTI</b>	Non-nucleoside reverse transcriptase inhibitor
<b>ART</b>	Antiretroviral therapy	<b>NRTI</b>	Nucleoside reverse transcriptase inhibitor
<b>AZT</b>	Zidovudine	<b>NRTTI</b>	Nucleoside reverse transcriptase translocation inhibitor
<b>BMGF</b>	Bill & Melinda Gates Foundation	<b>NVP</b>	Nevirapine
<b>CAB</b>	Cabotegravir	<b>OBR</b>	Optimized background regimen
<b>CLHIV</b>	Children living with HIV	<b>OI</b>	Opportunistic infection
<b>CM</b>	Cryptococcal meningitis	<b>PADO</b>	Pediatric ARV Drug Optimization
<b>COP</b>	Country operating plan	<b>pDGT</b>	Pediatric DTG (10 mg) scored, dispersible
<b>CrAg</b>	Cryptococcal antigen	<b>PEPFAR</b>	President's Emergency Plan for AIDS Relief
<b>CROI</b>	Conference on Retroviruses and Opportunistic Infections	<b>PI</b>	Protease inhibitor
<b>DPP</b>	Dual prevention pill	<b>PLHIV</b>	People living with HIV
<b>DRV/r</b>	Darunavir/ritonavir	<b>PMTCT</b>	Prevention of mother-to-child transmission
<b>DSD</b>	Differentiated service delivery	<b>POC</b>	Point-of-care
<b>EFV</b>	Efavirenz	<b>PrEP</b>	Pre-exposure prophylaxis
<b>DTG</b>	Dolutegravir	<b>RPT</b>	Rifapentine
<b>EID</b>	Early infant diagnosis	<b>RPV</b>	Rilpivirine
<b>EMAV</b>	Early market access vehicle	<b>RTV</b>	Ritonavir
<b>DVR</b>	Dapivirine vaginal ring	<b>SOC</b>	Standard of care
<b>ERP</b>	Expert Review Panel for Diagnostics	<b>TAF</b>	Tenofovir alafenamide fumarate
<b>EXW</b>	Ex-works	<b>TB</b>	Tuberculosis
<b>FDC</b>	Fixed-dose combination	<b>TDF</b>	Tenofovir disoproxil fumarate
<b>FTC</b>	Emtricitabine	<b>TLD</b>	TDF+3TC+DTG
<b>GA</b>	Generic-accessible	<b>TPT</b>	TB preventive therapy
<b>GF</b>	Global Fund to Fight AIDS, Tuberculosis and Malaria	<b>UNAIDS</b>	Joint United Nations Programme on HIV/AIDS
<b>HIV</b>	Human immunodeficiency virus	<b>US FDA</b>	United States Food and Drug Administration
<b>HIVST</b>	HIV self-test	<b>VL</b>	Viral load
<b>HTS</b>	HIV testing services	<b>VMMC</b>	Voluntary medical male circumcision
<b>IAS</b>	International AIDS Society	<b>WHO</b>	World Health Organization

# 2021 CHAI HIV Market Report

## AT-A-GLANCE

### HIV Data Overview, 2020

**37.7M** People Living with HIV (PLHIV)

**27.5M** People on Treatment



### COVID-19 disruptions led to service delivery innovations:



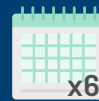
Increased Use of HIV Self-Testing



Tele-Medicine



Virtual Training



Multi-Month Dispensing

### Test Smart



**16%** of PLHIV globally did not know their HIV status in 2020



**1.46M** early infant diagnosis tests run in low- and middle- income countries (LMICs) in 2020



**3** HIV self-tests available for US \$2 or less

### Treat Right

#### By Addressing Advanced HIV Disease



**>100K** VISITECT® CD4 Advanced HIV Disease tests ordered through the Early Market Access Vehicle



**High Single Dose** of L-AmB non-inferior to AmB-d in AMBITION trial for cryptococcal meningitis

#### With Optimal ARVs for Adults



**~67%** of first-line adults in generic-accessible LMICs on TLD by end of 2020



**NADIA Trial**  
TDF/3TC may potentially be reused in second-line treatment



**US \$17.50/pk** for newly available generic DRV/r (400/50 mg) in a fixed-dose for second-line treatment

#### With Optimal ARVs for Children



**25x Faster** receipt of tentative US FDA approval of pDTG than average generic pediatric HIV treatment



**25+ Countries** have placed or received orders for optimal product pDTG

### Stay Negative



**1.5M** new global HIV infections in 2020



**~1M** cumulative oral PrEP initiations in LMICs, with 82% occurring in 2020 and 2021



**Phase III Trials** have commenced investigating long-acting formulations of lenacapavir and islatravir for PrEP

# GENERAL TRENDS

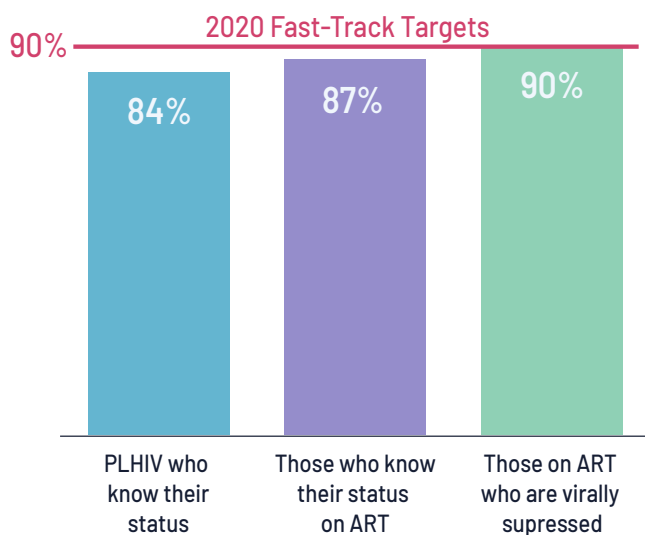
## Progress in HIV treatment, prevention, and diagnostics in a year defined by COVID-19

With the close of the 90-90-90 era, new 95-95-95 targets aim to further galvanize the HIV community to end HIV as a public health threat by 2030 despite additional challenges posed by the COVID-19 pandemic. Although there have been some COVID-19-related setbacks, national HIV programs have shown remarkable resilience in sustaining access to lifesaving HIV care.

### UNAIDS updates global HIV targets as 90-90-90 era ends with mixed success

The 90-90-90 era came to a close at the end of 2020. Although all three targets were not met at the global level, the third 90 was achieved and significant progress was made toward the first two targets [Figure 1]. Additionally, a number of countries, including some high-burden low- and middle-income countries (LMICs), were able to reach all three targets either on time or ahead of schedule.<sup>i</sup>

Figure 1: Global 90s Progress at the End of 2020<sup>i</sup>

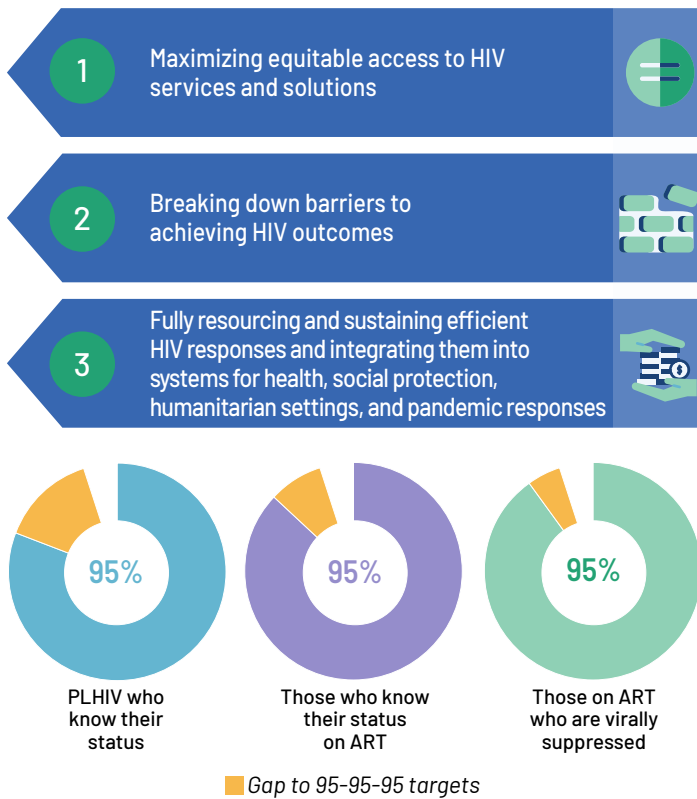


While targets can serve as important calls to action, they alone do not tell the full story of the HIV response. Behind every global target, even missed ones, are important successes. For example, despite missing the second 90 target at the global level, the scale up of antiretroviral (ARV) therapy (ART) has averted an estimated 16.2M AIDS-related deaths since 2001.<sup>ii</sup>

Recognizing that new targets are needed to continue to push the global HIV response to achieve epidemic control, UNAIDS adopted a new Global AIDS Strategy in 2021. The strategy outlines strategic directions and priority actions, along with a new set of targets, to implement by 2025 to end HIV as a public health threat by 2030 [Figure 2].<sup>iii</sup>

This strategy and the new 95-95-95 targets [Figure 2] were adopted by the United Nations member states and build on the previous 90s targets with the aim to bring comprehensive HIV services to 95 percent of people in need. Models estimate that, if achieved, the targets will result in fewer than 370K new infections and 250K AIDS-related deaths annually by 2025.<sup>ii</sup>

Figure 2: Updated Strategic Priorities and New 95-95-95 Targets<sup>ii, iii</sup>



Updated WHO consolidated guidelines emphasize the importance of differentiated and integrated services

The World Health Organization (WHO) released updated consolidated HIV guidelines in July 2021. Since the release of the last consolidated guidelines in 2016, much has changed in the HIV response: DTG is now recommended as the preferred treatment for all people living with HIV (PLHIV) over 3kg, managing advanced HIV disease (AHD) is a priority for many country programs, and differentiated service delivery models are being scaled nationally in many LMICs [Figure 3].<sup>iv</sup>

The COVID-19 pandemic has added urgency to many of the recommendations in the guidelines, such as the need to scale up HIV self-testing (HIVST), the importance of integrating psychosocial support into HIV care, and the benefits of implementing multi-month dispensing (MMD) for all patient populations, including children.

New research shows PLHIV to be particularly at-risk of serious COVID-19 outcomes and mortality

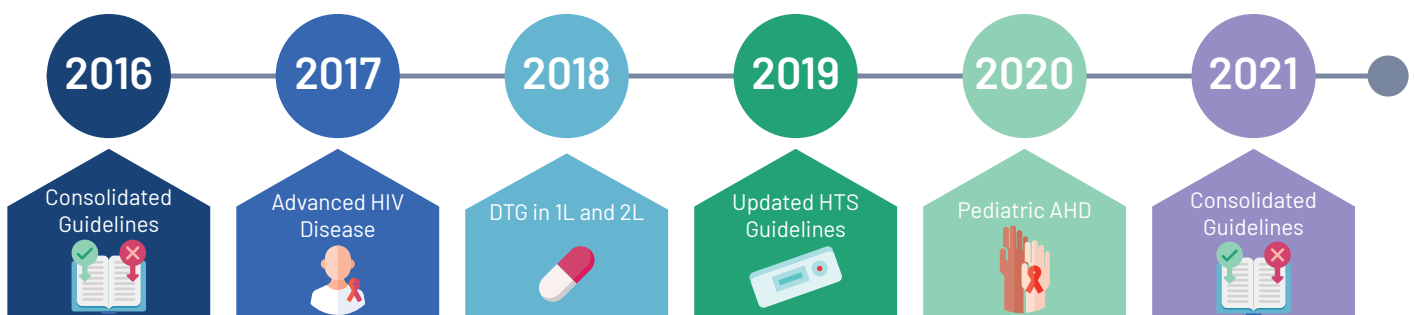
The impact of COVID-19 infection on PLHIV was hotly debated during the COVID-19 pandemic’s first year, with mixed study results complicating decision-making. However, data released in July 2021 from a WHO study including over 15,000 COVID-19 cases among PLHIV found that hospitalization was 13 percent more likely and death 30 percent more likely among PLHIV compared to those who were HIV negative. Additionally, the study found that HIV was a significant, independent risk factor for severe or critical COVID-19 symptoms and mortality.<sup>v</sup>

The WHO now recommends that PLHIV be prioritized for COVID-19 vaccination, and a rapid WHO survey recently showed that only 40 of 100 countries considered PLHIV a priority population for COVID-19 vaccination.<sup>vi, vii</sup>

“All people living with HIV should be prioritized for early [COVID-19] vaccination.”

World Health Organization on COVID-19 Vaccines

Figure 3: Selected WHO Guidelines Updates



However, global COVID-19 vaccine access remains inequitable. Compared to high-income countries where 46 percent of people have received one dose, only one percent of people in low-income countries and 11 percent of people in lower-middle income countries received at least one dose by the end of June 2021.<sup>i</sup>

### Ongoing COVID-19 waves complicate service delivery, but national programs show resilience

In many countries, the COVID-19 pandemic has added enormous pressure to already strained health systems and revealed that historical investments in public health have been inadequate.<sup>i</sup> As subsequent COVID-19 waves have swept across the globe, measures to reduce the spread of the pandemic disrupted some HIV services and commodity supply chains, with many countries reporting dips in new HIV diagnoses and other HIV service access in 2020.<sup>viii</sup>

However, COVID-19 has also demonstrated the resilience and innovative spirit of the HIV response, especially that of community-led initiatives supplying essential services under difficult circumstances. Details of the COVID-19 pandemic's impact on HIV services, and resulting program resilience, are included throughout this report.

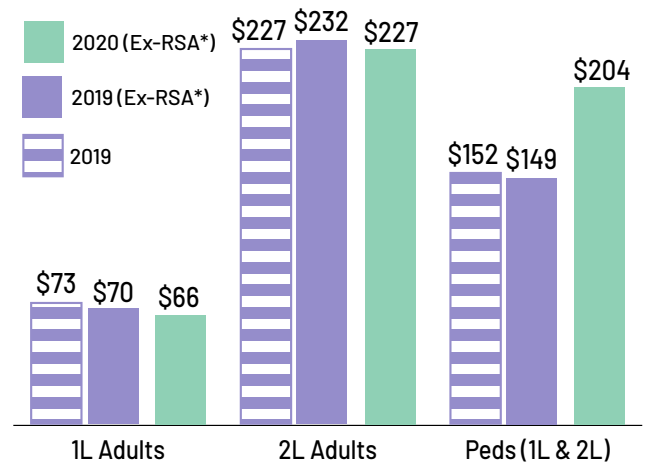
### Fears of widespread COVID-19-related HIV commodity price increases not realized

When lockdowns across the globe hampered international travel and trade, the global community feared that HIV commodity prices would rise. While there have been some fluctuations in prices since the COVID-19 pandemic began, and logistics and shipping prices did increase significantly, fears concerning widespread product pricing increases have not been realized.

Between 2019 and 2020, adult first-line (1L) treatment costs in generic-accessible<sup>1</sup> (GA) LMICs (excluding

<sup>1</sup> See Appendix D (p. 35) for a definition of generic-accessible.

Figure 4: Weighted Avg. GA LMIC Regimen Prices<sup>ix</sup>



\*South Africa (RSA) excluded from pricing analysis

South Africa) declined by US \$4 per patient per year, reflecting a continued drop in the price of TLD and optimization away from more expensive regimens.<sup>ix</sup> Adult second-line (2L) treatment costs also continue to decline as both DTG and ATV/r increasingly gain share over LPV/r. At the same time, pediatric treatment costs rose as country programs switched patients to more expensive LPV/r-based formulations [Figure 4]. However, with the introduction in 2021 of DTG 10 mg scored, dispersible tablets at just US \$4.50/pack, CHAI expects that annual pediatric ART costs will begin to decline sharply.<sup>ix</sup>

CHAI estimates that the approximate ARV market size in GA LMICs in 2020 was US \$1.9B (based on weighted average treatment costs and formulations in-use in 2020). This increase in the ARV market size occurred as more PLHIV initiate treatment despite continued decreases in ARV prices.<sup>ix</sup>



# TEST SMART

## Testing programs focus on increasing accessibility amidst challenges presented by COVID-19

Country programs found ways to adapt testing services during the COVID-19 pandemic, including increasing use of HIVST, which was complemented by HIVST pricing deals and new products. For HIV-exposed infants, use of point-of-care technologies for early infant diagnosis is expected to increase following updated guidance from the WHO and continued evidence on improved linkage to care over laboratory based testing.

### The COVID-19 pandemic disrupted HIV testing services in 2020, catalyzing a shift toward HIV self-testing and other adaptations

The COVID-19 pandemic has significantly disrupted HIV testing services (HTS). Reallocation of resources toward the COVID-19 response, suspension of in-person activities, and other impediments such as lockdowns and travel restrictions led to decreases in HIV testing volumes and HIV diagnoses.<sup>i</sup>

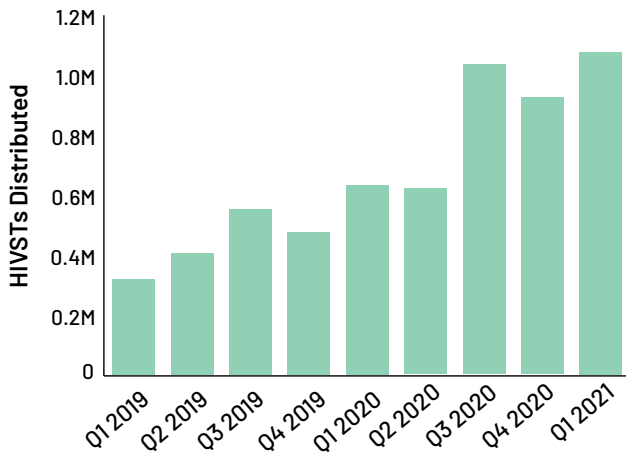
A Global Fund analysis of data from over 500 health facilities in 32 countries found that HIV testing volumes fell 41 percent in 2020 (April to September) compared to the same months in 2019, accelerating overall trends of declining volumes.<sup>x</sup> A similar South African analysis found that testing volumes and the proportion of positive tests decreased early in the pandemic (April to July 2020) compared to pre-lockdown volumes. This was largely the result of a corresponding decrease in outpatient attendance at healthcare facilities, where most clients are tested. However, by July 2020, HIV testing volumes

had increased to over 80 percent of pre-lockdown levels, suggesting a potentially transient impact of the COVID-19 pandemic's first wave in South Africa.<sup>xi</sup>

The COVID-19 pandemic has also heavily affected pediatric identifications. PEPFAR data from 14 countries in sub-Saharan Africa showed that overall pediatric HIV testing declined by 40 percent, and diagnoses declined by 29 percent, during the early stage of the pandemic (April to June 2020) compared to the months prior.<sup>xii</sup> Even within this analysis, however, country level impact varied significantly. Pediatric testing and diagnosis increased in Cameroon, and index testing for adolescents increased in Cameroon, Nigeria, and Côte d'Ivoire.<sup>xiii</sup>

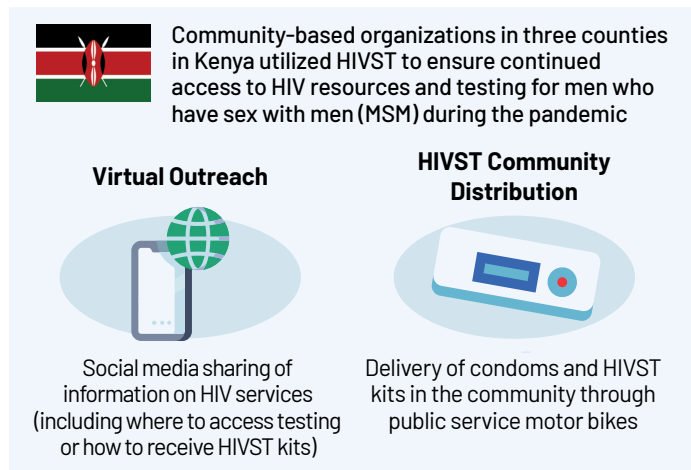
In light of these challenges, innovative service delivery approaches are increasingly important to ensure continuity of care as COVID-19 continues to impact essential HIV services. HIVST became a critical tool to help countries maintain testing services while following COVID-19 prevention protocols. For example, in PEPFAR-supported countries, HIVST increased significantly in the second half of 2020 and continues to play a significant role in 2021 [Figure 5].<sup>xiii</sup>

**Figure 5: HIV Self-Test Distribution in PEPFAR-Supported Countries, Q1 2019 to Q1 2021\***<sup>xiii</sup>

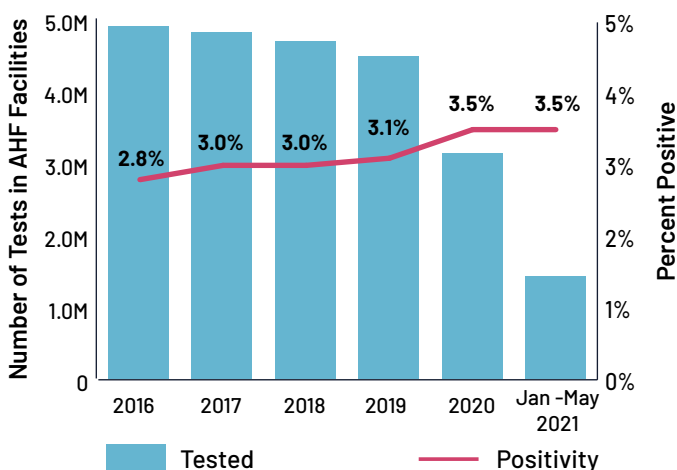


\*Data reported through the PEPFAR Dashboard may not be inclusive of all HIVST distribution in a country

**Figure 6: Adaptations to HIV Testing Services in Kenya During COVID-19 to Reach MSM**<sup>xiv</sup>



**Figure 7: Number of People Tested for HIV and Avg. Positivity Rates in AHF Facilities, 2016 to 2021**<sup>xv</sup>



Further, during the pandemic, partners and national governments have relied on a combination of virtual and in-person HIVST distribution models to reach those most in need [Figure 6].<sup>xiv</sup>

Despite these innovations, the continued impact of the pandemic remains variable. Initial data from 2021 indicate that testing volumes are still below 2019 levels in AIDS Healthcare Foundation (AHF) facilities, suggesting COVID-19 concerns and restrictions continue to impact testing access [Figure 7].<sup>xv</sup> Additionally, as countries experience resurgences in COVID-19 cases, the continued impact on HIV testing services in 2021 and beyond is still to be determined.

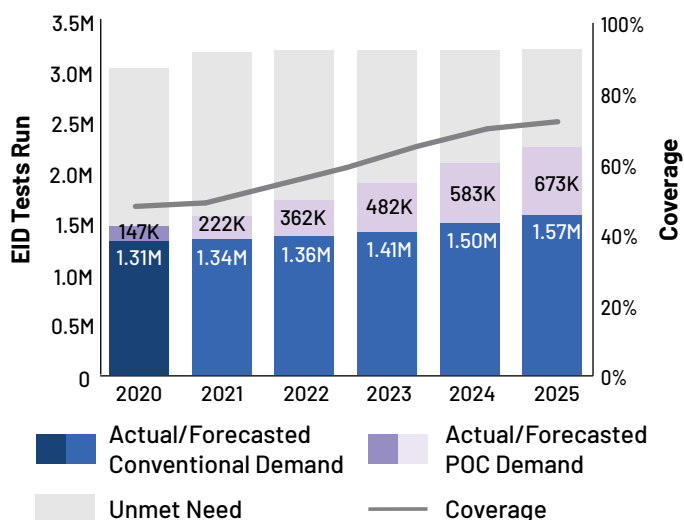
**Early infant diagnosis also impacted by the COVID-19 pandemic, but increased use of POC could improve testing and linkage rates**

The COVID-19 pandemic continues to affect early infant diagnosis (EID) despite prioritization by many countries during lockdowns. CHAI estimates that EID testing volumes declined for the first time in LMICs in 2020 with only 1.46M tests run compared to 1.63M in 2019.<sup>xvi</sup> UNAIDS data from 2020 also shows that some regions were particularly impacted, exacerbating existing regional differences in EID testing coverage. In West and Central Africa in 2020, only 25 percent of HIV-exposed infants received an EID test within two months of birth, a decrease from 33 percent in 2019. In contrast, 74 percent of HIV-exposed infants in Eastern and Southern Africa received an EID test in 2020, an increase from 69 percent in 2019.<sup>xvii</sup>

However, even in the face of these challenges, the use of point-of-care (POC) EID continues to scale up across LMICs. In 2020, CHAI estimated there were approximately 147K POC EID tests run in LMICs, an increase from the 123K estimated to be run in 2019.<sup>xvi</sup> However, despite this increase in the use of POC, it only accounted for 10 percent of all EID testing in 2020, although this number will likely increase over the next five years as POC EID is further scaled up [Figure 8].

Supporting the scale-up of POC EID, updated WHO guidance now strongly recommends the use of POC nucleic acid testing to diagnose HIV in infants and children under 18 months given robust evidence

Figure 8: LMIC EID Demand Forecast<sup>\*xvi</sup>



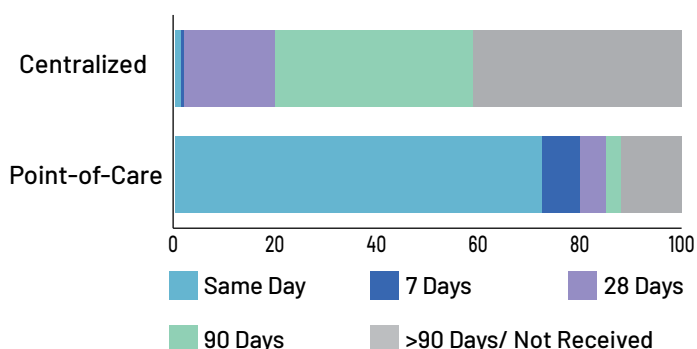
\*The COVID-19 pandemic may continue to impact forecasted EID testing volumes.

showing that POC EID improves treatment initiation rates.<sup>iv</sup> More details on this recommendation and further updates are available in the full 2021 [WHO consolidated guidelines](#).

A CHAI-led evaluation of POC EID in six African countries found that 72 percent of caregivers received infant test results on the same day as sample collection with the use of POC testing compared with only one percent with centralized testing [Figure 9].<sup>xviii</sup> Furthermore, the HIV-positive infants who received their test results on the same day were six times more likely to start treatment within the 90 days of the study than those diagnosed one or more days after sample collection.<sup>xviii</sup>

This mounting body of evidence underscores the importance of POC EID to ensure rapid identification and linkage to treatment for HIV-positive infants.

Figure 9: Proportion of EID Test Results Received by Caregiver by Number of Days<sup>xviii</sup>



### Additional suppliers and new pricing deals make HIVST more accessible

The Global Fund’s Expert Review Panel for Diagnostics (GF ERPD) approved two new blood-based HIVSTs, bringing the total number of WHO prequalified or GF ERPD-approved HIVSTs on the market to six.<sup>xix</sup>

PRODUCT NAME	MANUFACTURER	SAMPLE	REGULATORY STATUS
CheckNOW	Abbott	Blood	ERPD (WHO PQ Pending)
EXACTO	Biosynex	Blood	ERPD (WHO PQ Pending)
Sure Check HIV Self-Test	Chembio Diagnostics	Blood	WHO PQ
Mylan HIV Self-Test	Viartis Inc / Atomo Diagnostics	Blood	WHO PQ
INSTI HIV Self-Test	bioLytical Laboratories	Blood	WHO PQ
OraQuick	OraSure Technologies	Saliva	WHO PQ

As the supply base expands, prices for HIVSTs continue to fall. Through a recent -led pricing agreement, the Mylan HIVST will now be available for US \$1.99 (EXW) in 135 countries.<sup>xxi</sup> Abbott’s CheckNOW HIVST is also expected to enter the market at US \$1.50 (EXW).<sup>xxii</sup> Additionally, HIVST market-leader OraSure has announced that it will maintain the US \$2.00 (EXW) price for its OraQuick HIVST, initially established via the BMGF subsidy, and expand access to that price to all purchasers of the WHO prequalified version intended for public health distribution.<sup>xxiii</sup>

As the supply and affordability of HIVST increase, research continues to demonstrate its benefits. Results from 14 randomized clinical trials found that HIVST is safe, increases testing uptake, and results in positivity and linkage rates comparable to professional HIV testing.<sup>xx</sup> Further, these results were consistent across distribution models for the general population. This review found that the proportion of patients linked to treatment or care following HIVST was similar to the standard of care, independent of the provision of linkage support.<sup>xx</sup> However, other studies have found that the addition of linkage-focused interventions can improve linkage compared to HIVST alone. Ultimately, this study underscores the opportunity presented by self-testing to reach PLHIV and link them to care.

# TREAT RIGHT

## Major advances toward HIV treatment optimization achieved alongside new and upcoming improvements to AHD care

Significant treatment optimization milestones were achieved over the past year, with widespread adoption of WHO-preferred DTG for adults, a generic DTG formulation now available for children, and the approval of a generic adult DRV/r co-formulation. AHD care continues to improve with several new and upcoming commodities set to increase patient identification and simplify diagnosis and treatment of opportunistic infections.

### TREAT RIGHT

#### By Addressing Advanced HIV Disease

#### Progress to eliminate AIDS-related deaths is still slow, particularly for children living with HIV

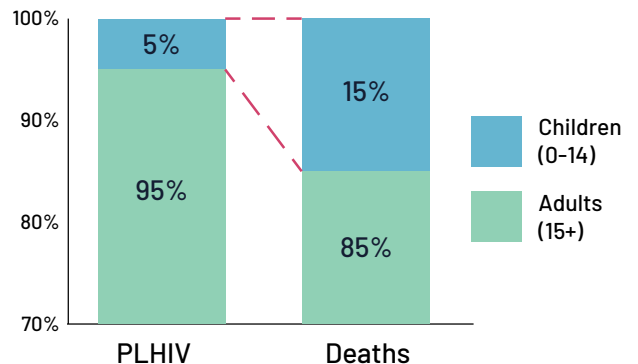
Despite progress toward reducing AIDS-related mortality over the past decade, there were still 680K AIDS-related deaths in 2020, only a six percent decrease from 2019.<sup>xvii</sup> For adults, while improvements in treatment options and increases in ART coverage have correlated with declining deaths, mortality remains stubbornly high. ART coverage remains low among children and, as a result, they account for a disproportionate share of AIDS-related mortality. In 2020, children accounted for only five percent of all people living with HIV, but represented 15 percent of all AIDS-related deaths [Figure 10].<sup>xvii</sup>

Across both adult and pediatric populations, increases in ART coverage are important but not sufficient alone to address AHD and related opportunistic infections (OIs). Updated WHO consolidated guidelines published

in 2021 include a dedicated section specifically on managing AHD, emphasizing the need for a complete package of care including screening, treatment, and prophylaxis for OIs.

Given the disproportionate burden of AIDS-related deaths on children living with HIV (CLHIV), interventions for this population are particularly important. To this end, PEPFAR's 2021 COP guidance highlights the importance of pediatric AHD care, complementing the 2020 WHO technical brief on interventions specifically focused on children with AHD.<sup>xxiv,xxv</sup> These recommendations represent a critical step toward a holistic approach to addressing AHD and reducing AIDS-related mortality in all populations.

Figure 10: PLHIV and AIDS-Related Deaths in 2020 by Age Group<sup>xvii</sup>





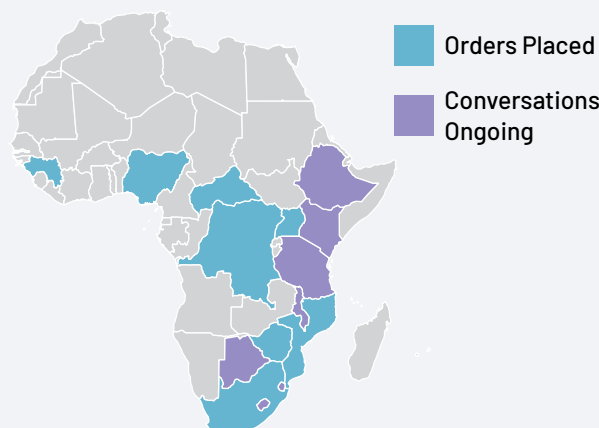
## Device-free, same-day CD4 testing set to increase identification of people with AHD

Unitaid and CHAI initiated the Early Market Access Vehicle (EMAV) in April 2020 to expand access to the Omega VISITECT® CD4 Advanced Disease test. The EMAV supports initial procurement of this device-free, same-day CD4 test, enabling over 130 LMICs to have access to the test at US \$3.98 (EXW).<sup>xxvi</sup> By providing same-day results, the VISITECT® test allows for rapid identification of people with AHD, enabling prompt access to services as required. The EMAV aims to give implementers early experience using this test and enable best practice sharing to support broader adoption in the future.

Eight countries have already placed or received orders and conversations around adoption are ongoing in several additional countries [Figure 11]. As of publication, over 100K VISITECT® tests have been ordered through the EMAV.<sup>xxii</sup>

In addition to procurement via the EMAV, PEPFAR explicitly supports adoption of the VISITECT® CD4 Advanced Disease test with 2021 COP guidance recommending the product as an inexpensive option to improve AHD identification rates.<sup>xxiv</sup>

Figure 11: VISITECT® CD4 Advanced HIV Disease Test Adoption Map



“This [VISITECT® CD4 Advanced Disease test] and other CD4 point-of-care approaches with similar characteristics and implementation considerations should be given highest priority”

PEPFAR Country Operational Plan Guidance 2021

### TB remains a leading cause of AIDS-related deaths; screening and accurate diagnosis critical to treatment access

To reduce AIDS-related deaths, prevention, diagnosis, and treatment of OIs are ultimately required. While tuberculosis (TB) is the most common OI in PLHIV, the WHO estimates that only 55 percent of global incident TB cases among PLHIV were diagnosed and notified in 2019.<sup>iii</sup> Further, despite accessibility of TB treatment in most LMICs, TB still accounts for roughly one in three deaths among PLHIV.<sup>iii</sup>

Consequently, TB screening is critical to find and treat patients in need of care. A study presented at CROI 2021 found that TB screening for everyone with

HIV and others at high risk of TB increased diagnosis rates by 17 percent compared to symptom-based screening alone.<sup>xxvii</sup> Updated WHO guidelines also now include several key recommendations on TB screening and treatment initiation for PLHIV co-infected with TB [Figure 12].

Figure 12: Key Recommendations on TB/HIV from 2021 WHO Consolidated HIV Guidelines<sup>iv</sup>



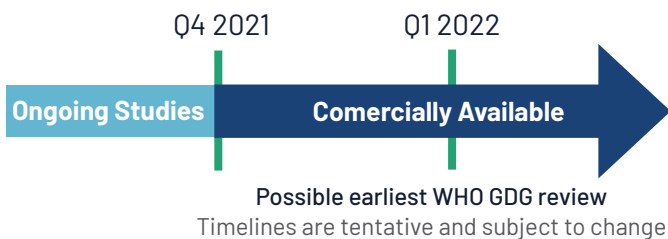
- 1 PLHIV should be systematically screened for TB disease at each visit to a health facility 
- 2 ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 cell count, among PLHIV 

Figure 13: SILVAMP Development Timelines



In addition to expanded screening, new diagnostic products could also improve TB diagnosis rates among PLHIV. SILVAMP, a new urine-based TB LAM test in development by FujiFilm, aims to increase testing sensitivity over existing options. SILVAMP clinical trials are ongoing at 60 sites across 20 countries, with initial results expected by the end of 2021. Once completed, FujiFilm plans to submit the study results to the WHO with the goal of being reviewed by a WHO-convened Guideline Development Group (GDG) as early as the first half of 2022 [Figure 13].

Current TB LAM assays have only moderate sensitivity and (WHO) recommended use is limited to PLHIV with low CD4 counts, signs or symptoms of TB, or hospitalized with severe illness. Consequently, most SILVAMP studies focus on HIV-positive adults with signs and symptoms of TB. However, better than expected results from HIV-negative and pediatric populations suggest the potential for SILVAMP to be used outside of immunocompromised individuals.

### Supply issues continue in 2021 for rifapentine, a key drug used for TB preventive therapy; supply capacity is expected to increase into 2022

Ensuring access to TB preventive therapy (TPT) for PLHIV can help prevent TB infection. However, rifapentine (RPT), a key drug for the optimal TPT regimen 3HP, experienced significant supply disruptions over the last year, although supply is expected to increase into 2022.

In 2020, nitrosamine impurity issues and quality control clearances affected the supply of both Sanofi’s RPT (150 mg) tablets and Macleods’ INH/RPT (300/300 mg) fixed-dose combination (FDC), a complete 3HP regimen.<sup>xxviii</sup> Further, the COVID-19 pandemic delayed launch and scale up of Macleods’ 3HP FDC.

In addition to supply security, pricing also remains an important consideration for widespread adoption of 3HP. Sanofi’s RPT (150 mg) tablets currently cost US \$15 per patient course; however, this may increase to US \$18 per patient course once backlog orders are filled.<sup>xxix</sup>

To improve 3HP access, in August 2021 Macleods committed to scale up 3HP production capacity and continue the US \$15 per pack access price through 2023 as part of a MedAccess, CHAI, and Unitaid-led volume guarantee.<sup>xxix</sup> Demand for the Macleods FDC currently outpaces supply, and the ARV Procurement Working Group (APWG) is allocating orders to country programs who are ready to implement 3HP. Resolving existing supply issues and increasing the supply base remains a priority to ensure continued access to 3HP in LMICs.

### Fight against cryptococcal meningitis (CM) gains steam with calls to end CM deaths by 2030 and positive trial results supporting treatment optimization

Cryptococcal meningitis is responsible for an estimated 15 percent of all AIDS-related deaths,<sup>xxx</sup> and access to CM screening and treatment commodities historically has been limited in LMICs due to supply and cost concerns. The 2021 publication of the first strategic framework to end cryptococcal meningitis deaths by 2030 outlines key strategic approaches and considerations to improve access to diagnosis and treatment [Figure 14].<sup>xxxi</sup>

As identified in the strategic framework, access to optimal medicines has been a historical barrier to CM care. The current standard of care for treatment induction consists of one week of flucytosine (5FC) and amphotericin B followed by one week of fluconazole.

Figure 14: Highlights from the Updated Cryptococcal Meningitis Strategic Framework<sup>xxxi</sup>

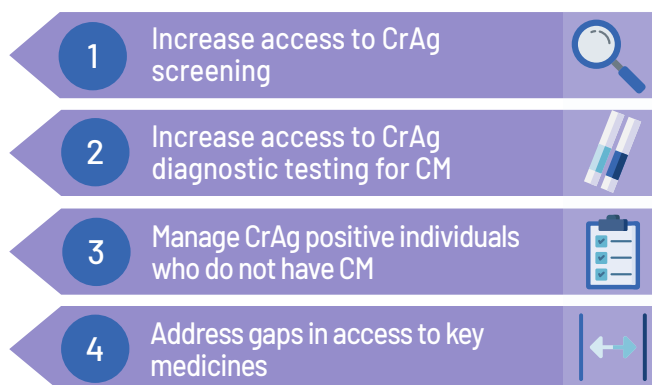
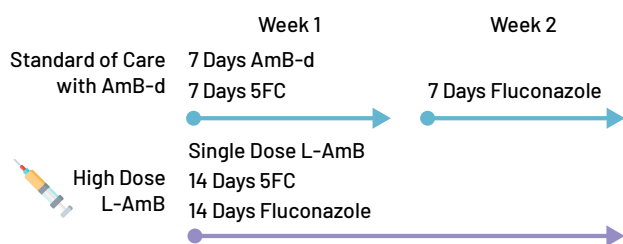


Figure 15: AMBITION-cm Trial Results<sup>xxxiii</sup>



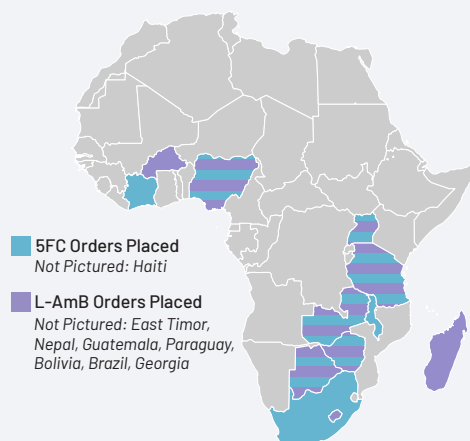
While access to amphotericin B deoxycholate (AmB-d) is more widespread, this formulation has significant toxicities requiring extensive resources to monitor and manage complications.

Liposomal amphotericin B (L-AmB) is considerably easier to administer and is associated with significantly fewer drug-related adverse events compared to AmB-d.<sup>xxxii</sup> Recent results from AMBITION-cm, a phase III trial conducted in sub-Saharan Africa, showed that one high dose of L-AmB is non-inferior to the standard of care with AmB-d [Figure 15].<sup>xxxiii</sup>

Since 2019, the Unitaid-CHAI AHD Initiative has been working to increase the accessibility of CM treatment in nine countries. Early work from the initiative resulted in a 30 percent reduction in the price of 5FC from US \$120 to US \$75, which has now further decreased to US \$65 (EXW) per pack.<sup>cxvi</sup> Current work focuses on country adoption and scale-up of both 5FC and L-AmB [Figure 16].



Figure 16: 5FC and L-AmB Adoption Map<sup>cxvii</sup>



For more information and tools to support the introduction of AHD products, see the AHD toolkit at [www.differentiatedcare.org/Resources/Resource-Library/Global-Advanced-HIV-DiseaseToolkit](http://www.differentiatedcare.org/Resources/Resource-Library/Global-Advanced-HIV-DiseaseToolkit).

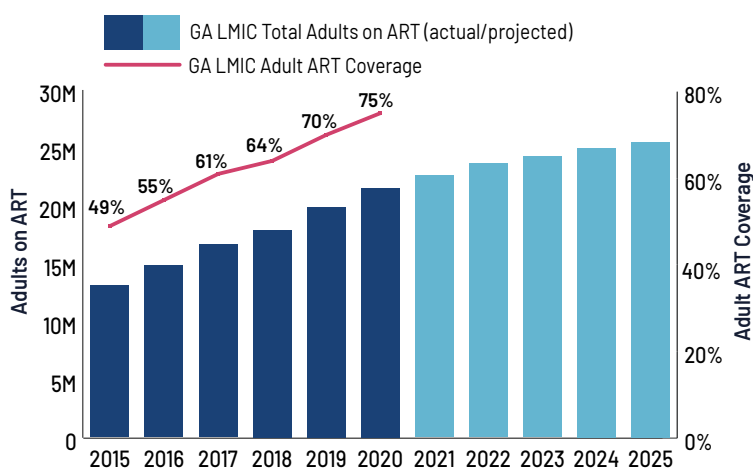
## TREAT RIGHT

### With Optimal ARVs for Adults

Over 26 million adults on treatment globally in 2020, with more than 21 million in GA LMICs<sup>xvii</sup>

Over two million adults (re-)initiated on ART globally in 2020 despite fears that the COVID-19 pandemic would hamper treatment initiation. In GA LMICs, adult ART coverage reached 75 percent in 2020, a five percentage point increase from 2019 [Figure 17].<sup>xxxiv</sup>

Figure 17: Adults on ART and Coverage in GA LMICs<sup>xxxiv</sup>



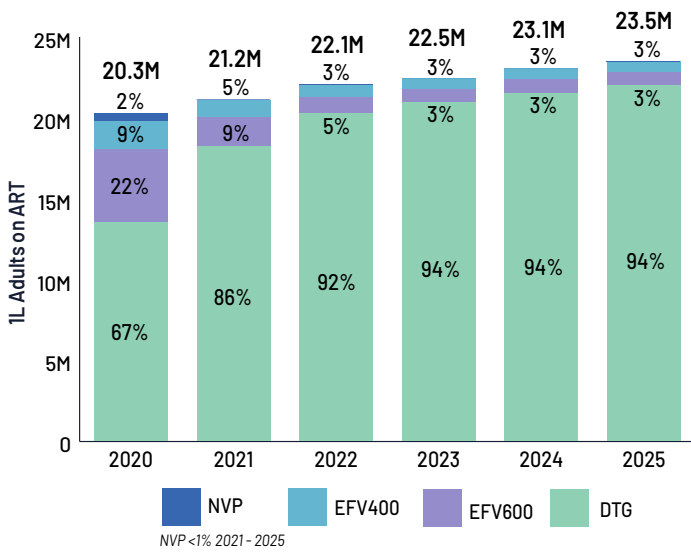
### Country programs plan 2L transitions to DTG as 1L TLD rollouts near completion

Since 2018, when the WHO released interim HIV treatment guidelines recommending DTG-based regimens as the preferred treatment in 1L and 2L for all patient populations,<sup>xxxv</sup> most high-burden countries have adopted DTG in their national guidelines and many have transitioned the majority of their 1L adult cohorts to TLD [Figure 18].<sup>xxxvi</sup>

Figure 18: Countries with Greater than 90 percent of 1L Adults on DTG-Based Regimens<sup>xxii</sup>



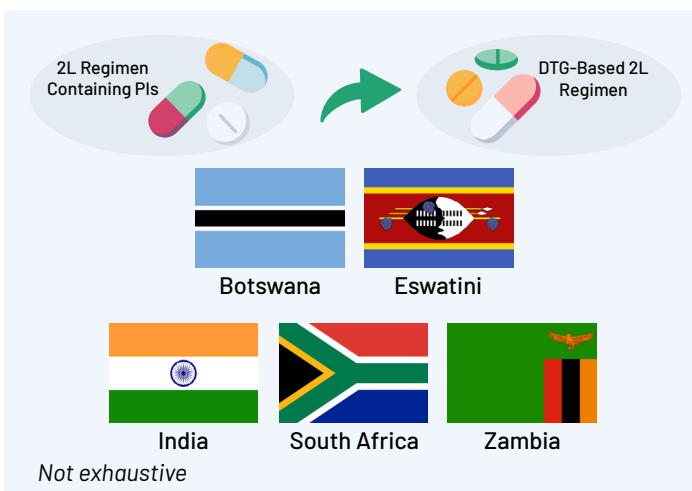
**Figure 19: 1L Adult INSTI/NNRTI Use in GA LMICs, Growth and Share (Includes Use as FDC and Singles)<sup>xxxiv</sup>**



Country programs and donors have procured over 350 million 30-pack equivalents of TLD since the United States Food and Drug Administration (US FDA) tentatively approved the first generic product in August 2017.<sup>xxxvii</sup> In 2020, CHAI estimates that 67 percent of 1L adults in GA LMICs were on DTG-based regimens, a 38 percentage point increase in DTG use from 2019. CHAI projects DTG-based regimens will compose over 90 percent of 1L adult INSTI/NNRTI use by 2022 [Figure 19].<sup>xxxiv</sup>

Given the clinical benefits, convenience, and affordability of DTG over protease inhibitors (PIs),

**Figure 20: Countries Planning to Implement Active Switching from PIs to DTG in 2L<sup>xxxviii</sup>**



access to DTG in 2L should be a priority for country programs—including switching existing 2L patients stable on PIs. Currently, WHO guidance recommends viral load (VL) testing prior to transitioning to DTG in 2L, however, this should not be a requirement for switching to optimal regimens.<sup>iv</sup> At the time of publication, several country programs are actively switching or planning to switch 2L PLHIV on PIs to DTG-based regimens [Figure 20].<sup>xxxviii</sup>

96-week results from the NADIA trial—a large, randomized study in three African countries—demonstrate that DTG is non-inferior to DRV/r in 2L treatment.<sup>xxxix</sup> These data support the utility of using DTG in 2L as a cost-effective alternative to PIs, and proactive switching of patients from inferior PIs such as LPV/r. Additionally, the trial found that TDF is non-inferior to AZT in 2L therapy even when recycled from 1L, suggesting the potential for TDF/3TC to be successfully reused in 2L treatment even in PLHIV with high levels of NRTI resistance.<sup>xxxix</sup> Although this evidence supports the potential use of TLD in 2L among PLHIV failing TDF+3TC+NNRTI-based 1L regimens, the WHO has not updated their guidelines and national programs will need to evaluate these findings prior to local adoption.

### New research revisits the potential clinical benefits of TAF

TDF has formed part of the WHO-recommended adult ART backbone since 2013, with TDF composing the largest share of NRTI use in GA LMICs for the past several years. TDF is efficacious, generally very safe, and well tolerated, but has been associated with reductions in bone mineral density and kidney abnormalities in younger and elderly patients, primarily when used in combination with a boosted PI.<sup>xi</sup>

TAF, another tenofovir pro-drug, minimizes these side effects by achieving high intercellular concentrations while reducing exposure of the kidneys and bone to tenofovir. However, a recent systematic review and meta-analysis has updated previous findings to include additional clinical trials and found no statistically significant difference between unboosted TAF and TDF in terms of viral suppression and bone and renal safety.<sup>xii</sup>



## Further evidence of weight gain seen in patients on DTG- and TAF-containing regimens

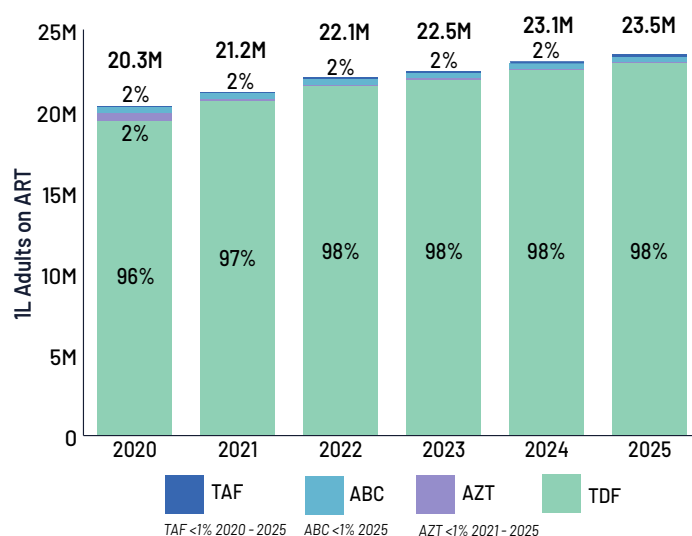
While weight gain is common following initiation on most ARV regimens, studies continue to show greater incidence of weight gain with DTG and TAF.

To date, some of the most striking data on weight gain and DTG-containing regimens comes from the ADVANCE trial, which found an average weight gain of 7.1kg in men and women on TAF/FTC/DTG, 4.3kg among PLHIV taking TDF/FTC/DTG, and 2.3kg for those on TDF/FTC/EFV at 96 weeks, though weight gain was more pronounced in women than men.<sup>xiii</sup> A supplementary genotyping study among ADVANCE trial participants found that PLHIV metabolize EFV at different rates. Among PLHIV who metabolize EFV slowly, weight gain was impaired due to increased toxicity and side effects from EFV. PLHIV who metabolized EFV more quickly were found to gain weight at similar rates to patients on DTG-containing regimens, which was in line with weight gain trends more broadly in South Africa.<sup>xiii</sup>

CHAI also conducted an analysis in Laos that found statistically significant weight gain in patients on TLD after 18 months,<sup>xiv</sup> and a potential weight gain plateau by 24 months among ART-experienced patients in a Nigerian analysis.<sup>xiv</sup> These real-world findings show that weight gain should be monitored in patients on TLD, especially in the first two years on treatment.

VESTED, an open-label phase III trial—one of few randomized trials to compare the safety and efficacy of HIV treatment regimens started in pregnancy—found women on TAF/FTC/DTG gained weight at rates comparable to gestational standards, while women on TDF/FTC/DTG and TDF/FTC/EFV were consistently underweight. Further analysis found low prenatal weight among participants was associated with adverse pregnancy outcomes. Women in the TAF/FTC/DTG study arm gained the most weight and experienced a lower proportion of neonatal deaths. These findings suggest a potential use case for TAF+DTG among women initiating ART in pregnancy, although questions on the impact of intrapartum weight gain remain.<sup>xvi</sup>

Figure 21: 1L Adult NRTI Use in GA LMICs, Growth and Share<sup>xxxiv</sup>



TAF was also linked to weight gain in three large studies of treatment-experienced PLHIV changing regimens, but the studies produced conflicting findings on the role of integrase inhibitors.<sup>xlvii, xlviii, xlix</sup> How TAF leads to weight gain, and why there might be an interaction with integrase inhibitors—especially DTG—requires further investigation.

With uncertainty about broader TAF rollout, CHAI predicts that TAF will constitute a very small proportion of adult NRTI use in the coming years [Figure 21].<sup>xxxiv</sup> This is a lower proportion than previous forecasts, which assumed that TAF would become a 1L alternative regimen in the updated WHO guidelines.<sup>1</sup>

## Generic DRV/r (400/50 mg) now available at an affordable price in a fixed-dose for 2L use

Despite first receiving US FDA approval in 2006, the lack of an affordable generic FDC of DRV co-formulated with RTV for use in 2L has limited uptake of this optimal product in LMICs and posed a serious equity issue. Longstanding clinical evidence highlights the key benefits of DRV, including a high barrier to resistance and improved viral suppression and tolerability compared to LPV/r and ATV/r.<sup>li, liii</sup> However, despite these clinical benefits, DRV/r is currently listed as an alternative 2L option by the WHO given the historic lack of an affordable, generic FDC.

To address inequitable access to DRV, CHAI and Unitaid implemented an incentive program to secure a highly competitive yet sustainable price for DRV/r (400/50 mg). In July 2021, Hetero received WHO prequalification for a DRV/r (400/50 mg) co-formulated, heat-stable tablet, which launched at an EXW price of US \$17.50 per pack, slightly lower than LPV/r.<sup>cxviii</sup> With an affordable FDC now on the market, country programs should now consider adoption and implementation of DRV/r for use in adult 2L treatment.

**Unitaid**  
Innovation in Global Health

US \$17.50 per 60 pack (EXW)

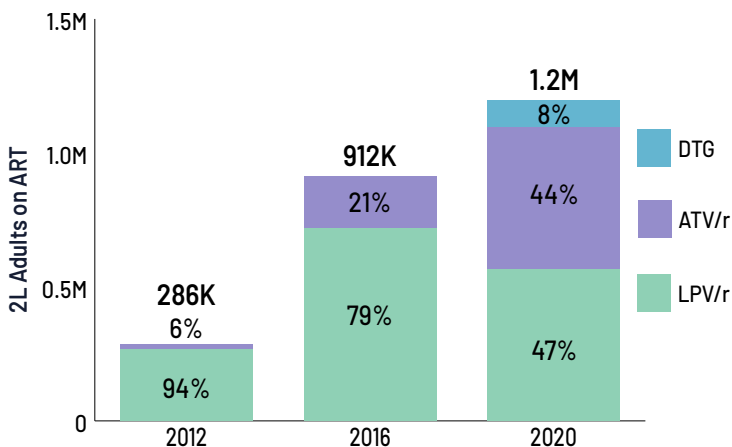
US \$210 per patient per year (EXW)

DRV/r 400/50 mg

Although DRV is often thought of as a third-line (3L) drug, its use in 2L has multiple benefits. Its improved efficacy, especially compared to LPV/r, means that wider use in 2L may reduce the number of patients who fail 2L and ultimately need expensive and hard-to-procure 3L products. Additionally, DRV's high genetic barrier to resistance means that it can potentially be reused in 3L at a higher dose.

Moving forward, widespread adoption of DRV/r as a preferred 2L PI in country guidelines is critical to ensure rapid access for patients in need of a PI.

Figure 22: Adult 2L PI/INSTI Market Share in GA LMICs<sup>xxxiv</sup>



In GA LMICs, CHAI estimates that DTG comprised eight percent of 2L treatment in 2020, while PIs made up the remaining market [Figure 22]. The share of DTG in 2L is expected to increase dramatically as countries complete 1L transitions and accelerate use in 2L. Within the PI market, ATV/r has been steadily gaining share against LPV/r. With an affordable FDC of DRV/r now on the market, DRV/r is anticipated to make up a larger share of the PI market moving forward.<sup>xxxiv</sup>

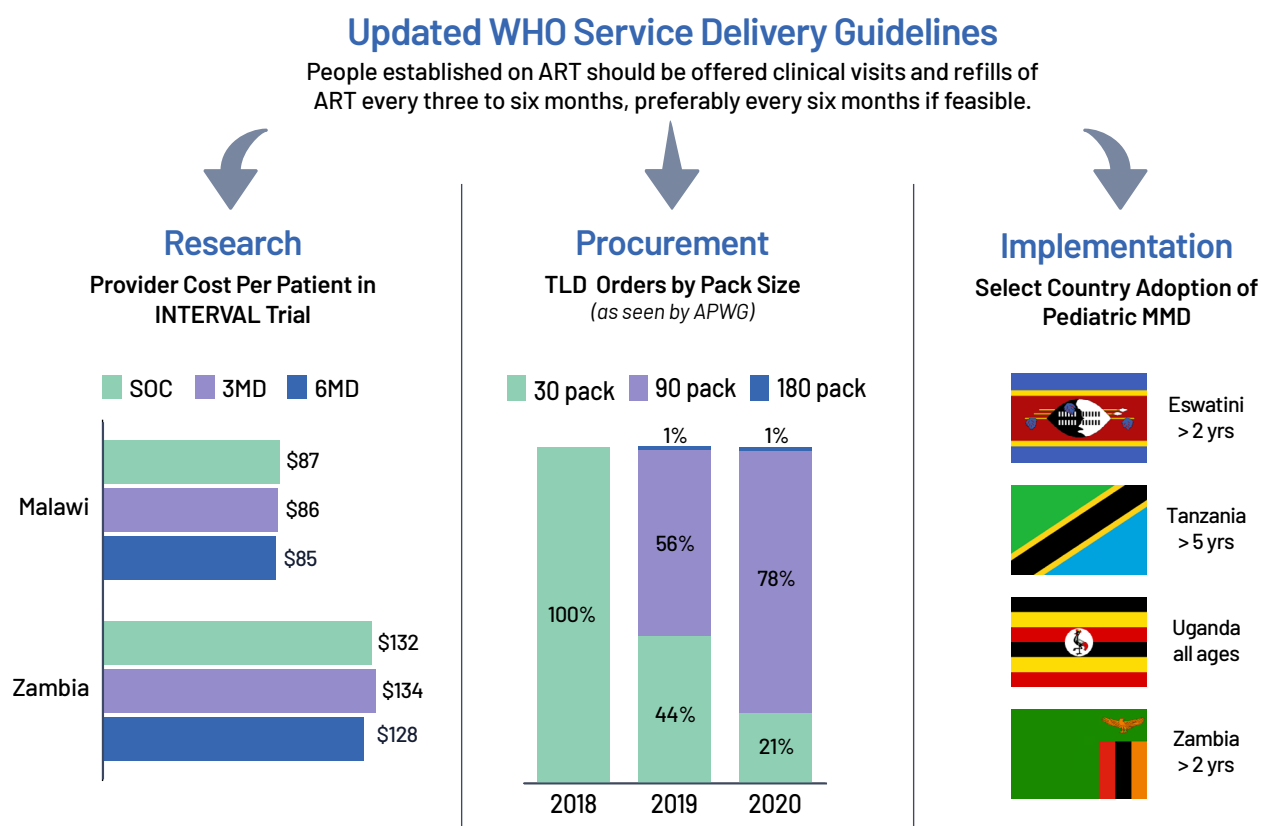
### The updated WHO service delivery guidelines emphasize benefits of MMD for all PLHIV

While the COVID-19 pandemic has presented unique challenges for HIV care continuity, it also led to widespread rollout of differentiated service delivery (DSD) practices such as MMD to limit exposure to COVID-19.

Updated WHO guidelines recommend both adults and children living with HIV and stable on ART be offered clinical visits and ART refills every three to six months, with a preference for six months if feasible.<sup>iv</sup> Existing efforts supporting the widespread adoption of MMD can be seen in recently published research, historical procurement trends, and country implementation [Figure 23].<sup>liii, xxii, xxxviii</sup> Moving forward, countries are advised to formally update national guidance and implement policies in line with WHO recommendations to better serve PLHIV.

In Malawi and Zambia, the INTERVAL trial demonstrated that six month ARV refills were associated with better retention in care and lower provider costs than three month refills.<sup>liii</sup> Similarly, a retrospective study found that patients in Zambia receiving four to six month MMD and simultaneously enrolled in other DSD models such as group-based or fast-track care had the lowest loss to follow up after a year.<sup>liv</sup> In Uganda and Kenya, DSD—such as patient-centered care, increased appointment spacing, improved clinic access, and patient reminders—was associated with higher viral suppression among ART-experienced patients with viremia in the SEARCH study.<sup>lv</sup>

Real world studies estimating the cost of DSD in sub-Saharan Africa found provider costs for community-based care to be equivalent to traditional facility-based treatment, however DSD offers significant benefits to PLHIV, including convenience and fewer out of pocket costs to access care.<sup>lvi</sup>

Figure 23: Research, Procurement, & Implementation Supporting Updated WHO Service Delivery Guidelines<sup>liii, xxii, xxxviii</sup>

## A robust treatment pipeline moves away from daily oral therapy

With the availability of a generic, affordable FDC of DRV/r, and widespread adoption of TLD, the access gap between LMICs and high-income countries for optimal treatments has shrunk considerably. The pipeline of next generation treatment products is moving away from daily oral therapy and toward a future of long-acting agents.

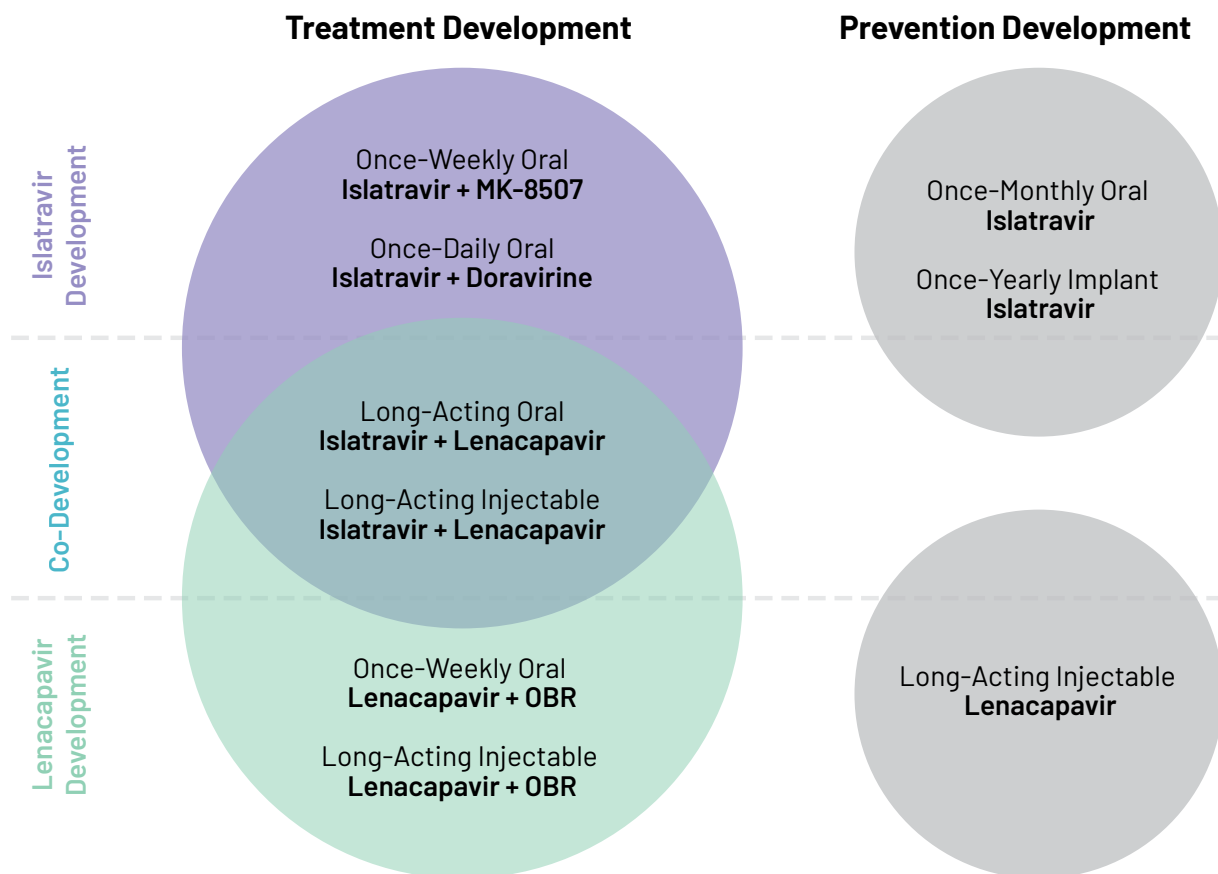
PRODUCT AND FORMULATION		FREQUENCY
Islatravir + Doravirine	Oral	Once-Daily
Islatravir + MK-8507	Oral	Once-Weekly
Lenacapavir + Optimized Background Regimen (OBR)	Injectable (plus oral OBR)	Every Six Months
	Oral	Once-Daily
Lenacapavir + Islatravir	Oral	TBD
	Injectable	TBD

## Lenacapavir and Islatravir

Lenacapavir (LEN) and islatravir (ISL) are two pipeline products with long-acting potential generating considerable excitement in the HIV space for both treatment and prevention [Figure 24]. Both drugs are prospective first-in-class medicines in late-stage clinical trials, with significant data generated to-date.

Gilead is developing lenacapavir, an HIV-1 capsid inhibitor showing promise for both treatment-experienced and treatment-naïve PLHIV. In the CALIBRATE trial, subcutaneous LEN in combination with oral TAF/FTC was found to be safe and tolerable, and led to over 90 percent viral suppression in treatment-naïve PLHIV by week 28.<sup>lvii</sup> Data from the CAPELLA study presented at IAS 2021 showed that 81 percent of heavily treatment-experienced PLHIV with multi-drug resistance who received LEN alongside their failing regimen were virally suppressed at week 26.<sup>lviii</sup> In June 2021, Gilead submitted a new drug application to the US FDA seeking approval of lenacapavir for treatment in multi-drug resistant, heavily treatment-experienced PLHIV.<sup>lix</sup> If approved, lenacapavir would be the first capsid inhibitor and the only HIV treatment option administered every six months.

Figure 24: Islatravir and Lenacapavir Development for HIV Treatment and Prevention



Merck is developing islatravir, a first-in-class nucleoside reverse transcriptase translocation inhibitor (NRTTI) that continues to demonstrate high potency and tolerability at 96-weeks when combined with doravirine as indicated in phase IIb trials. These results suggest the potential for a potent two-drug regimen warranting further studies.<sup>lx, lxi</sup> Phase III studies among treatment-naïve, virologically suppressed, and heavily pretreated PLHIV are currently underway.<sup>lxii</sup>

In March 2021, Gilead and Merck entered into an agreement to co-develop and co-commercialize a long-acting two-drug HIV treatment combining lenacapavir and islatravir. The collaboration will focus on long-acting oral and injectable formulations with clinical studies expected to begin in the second half of 2021.<sup>lxiii</sup> Islatravir and lenacapavir have also demonstrated success in prevention applications, which are outlined later in this report.

**Cabotegravir + Rilpivirine**

In January 2021, the US FDA approved ViiV’s once-monthly *Cabenuva* (CAB+RPV)—the first injectable

ART—for use in virally suppressed, treatment-experienced patients. The approval was based on the results of the FLAIR and ATLAS studies, which demonstrated that monthly injections maintained viral suppression as well as a standard oral regimen.<sup>lxiv</sup> Follow-up results from ATLAS-2M showed that administration every other month works as well as monthly injections.<sup>lxv</sup> In February 2021, ViiV submitted a supplemental application to the US FDA to allow for use of *Cabenuva* every two months, which was still under review at the time of publication.<sup>lxvi</sup>

In the United States, ViiV launched *Cabenuva* at a wholesale acquisition cost of approximately US \$4,000 per monthly injection among select health facilities where they are also providing clinician education and training on the long-acting injectable.<sup>lxvii, lxviii</sup> While injectable ART represents an exciting paradigm shift in the HIV treatment space, there are a number of concerns limiting the applicability of *Cabenuva* in LMICs, including cost, cold-chain storage requirements, a lack of cross-treatment for Hepatitis B, RPV’s low barrier to resistance, and others.<sup>lxix</sup>

# TREAT RIGHT

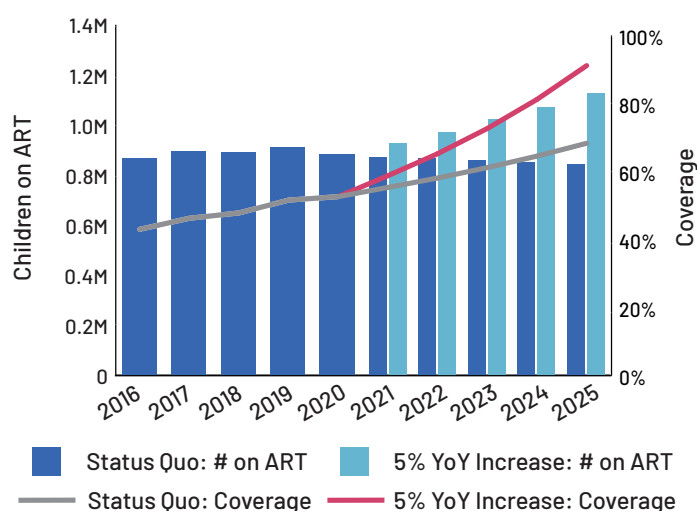
## With Optimal ARVs for Children

The number of children on ART globally declined in 2020, but slight improvements in case finding could drastically increase coverage

For the first time ever, the number of children on ART globally has declined, leaving almost 800K children living with HIV (CLHIV) without lifesaving ART in 2020.<sup>i</sup> While this is in part due to children aging out of the pediatric cohort, pediatric case finding declined in 2020 due in large part to the COVID-19 pandemic, as discussed in the Test Smart section. Further, a concerning number of children are not retained in care once initiated on ART. According to an analysis in 16 countries in sub-Saharan Africa, one in five children under the age of five on ART are lost to follow-up.<sup>bx</sup> To make meaningful improvements in pediatric ART coverage, all children identified as HIV-positive need to be rapidly linked to and retained in care.

Between 2019 and 2020, pediatric ART coverage in GA LMICs remained flat at 53 percent as both the number of CLHIV and the number of children on ART decreased.<sup>xxxiv</sup> CHAI estimates that, with current trends in case finding, pediatric coverage will increase to approximately 70 percent over the next five years with the number of children on ART remaining relatively stable. However, by achieving only a five percent year-over-year (YoY) increase in the number of CLHIV on ART, pediatric coverage

Figure 25: Actual and Forecasted Children on ART and Pediatric ART Coverage in GA LMICs<sup>xxxiv</sup>



could increase to over 90 percent by 2025 [Figure 25]. Adopting innovative approaches to achieve this goal over the next five years remains a priority.

## Optimal pediatric formulation of DTG now available from two suppliers at a price well below the previous standard of care

Given its favorable safety, tolerability, and efficacy profiles, and its high barrier to resistance, DTG has been part of the WHO-preferred regimen for children above four weeks of age weighing at least 3kg since 2018. However, until recently, the lack of availability of a generic formulation for children below 20kg delayed access to this optimal drug for the youngest children living with HIV.

To expedite access, CHAI and Unitaid selected Viatris and Macleods for an incentive program to develop a generic DTG 10 mg scored, dispersible tablet. Viatris and Macleods received technical knowledge transfer from ViiV and engaged in an innovative US FDA filing strategy that allowed them to file while ViiV's innovator product was still under US FDA review. Through this filing strategy, Viatris received US FDA tentative approval under the PEPFAR review process in November 2020, just five months after ViiV received US FDA approval [Figure 26].

Figure 26: Timeline of Pediatric DTG Approvals

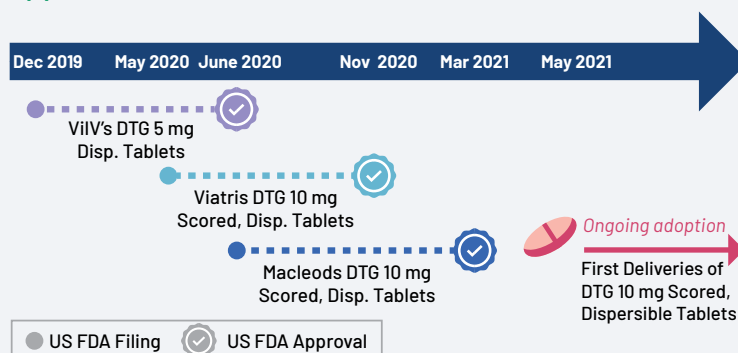
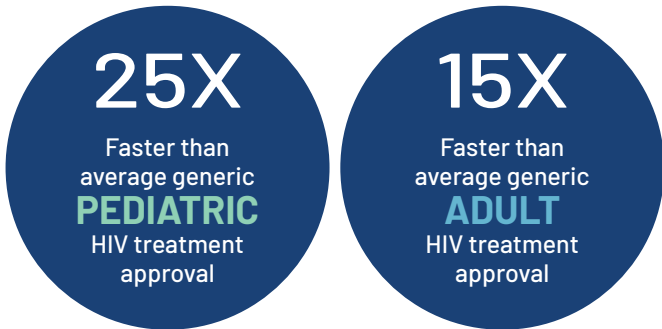


Figure 27: pDTG US FDA Tentative Approval Metrics<sup>ix</sup>




Based on US FDA tentative approval under the PEPFAR program or full US FDA approval where patent protections had expired.

The tentative approval of DTG 10 mg scored, dispersible tablets, also known as pediatric DTG (pDTG), is the fastest ever regulatory approval of a generic pediatric ARV.<sup>lxxi</sup> Development and commercialization of pDTG took only two years from initiation to US FDA tentative approval, a significant improvement over the historical average for pediatric products of approximately eight to ten years.<sup>ix</sup> Due to this expedited development timeline, children in LMICs are now accessing optimal treatment years before it would have otherwise been available [Figure 27].


Further, both suppliers of pDTG have reported sufficient capacity to meet demand with no supply issues anticipated.

In complement to this expedited development timeline, CHAI and Unitaid negotiated a price of US \$4.50 per 90-count pack (EXW) of pDTG for all public procurers for use in over 123 countries covered in ViiV's license with the Medicines Patent Pool (MPP).<sup>lxxix</sup> This agreement significantly lowers the cost for annual pediatric HIV treatment from over US \$480 per child for the historic, LPV/r-based standard of care, to under US \$120 per child with pDTG.<sup>lxxx</sup> This price reduction of approximately 75 percent could generate US \$60–260 million in global health savings over five years.<sup>lxxx</sup>

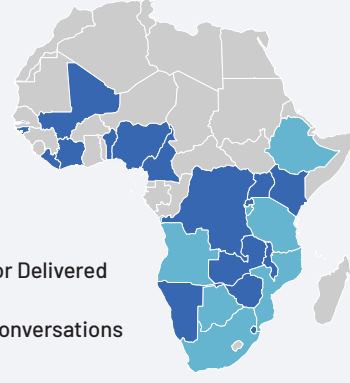


pDTG adoption picks up speed with supportive partner guidance and further data on clinical superiority and cost savings

Following US FDA tentative approval of pDTG, rapid rollout is a top priority to ensure that CLHIV are put on the best available HIV treatment as soon as possible. To this end, CHAI and Unitaid initiated procurement of pDTG in six early adopter countries to build preliminary experience with the product and catalyze broader interest. As of publication, there have been confirmed pDTG deliveries in 17 countries, which includes these early adopters, with orders placed or conversations ongoing in over seven additional countries [Figure 28].



**Figure 28: Current Generic pDTG Tablet Procurement, as of Q3 2021<sup>lxxvii</sup>**



**Orders Placed or Delivered**  
**Procurement Conversations Ongoing**  
**No data**

*\*Orders placed but not pictured: Cambodia, Haiti, Papua New Guinea, and Venezuela*

Partner guidance also supports rapid adoption with a joint statement issued in December 2020 from global partners, including the WHO, the Global Fund, and PEPFAR, calling for urgent country scale up of pDTG.<sup>lxxii</sup> Further, PEPFAR, via COP 2021 guidance, expects rapid adoption of pDTG with a full transition within 12 months of the arrival of the first shipment.<sup>lxxiv</sup>

Resources to support the introduction of pDTG, including customizable healthcare worker resources, transition planning templates, community-facing literacy materials, and further information are available on CHAI's HIV New Product Introduction Toolkit at <https://www.newhivdrugs.org/featured-product-pdtg>.

Given the significant benefits of pDTG, guidance has also stressed that obtaining a recent viral load test should not be a barrier to access. The WHO emphasizes that while VL monitoring remains a good practice, it should not be considered a precondition to pDTG transitions.

“Children should not have their transition to DTG delayed due to lack of documented viral load.”

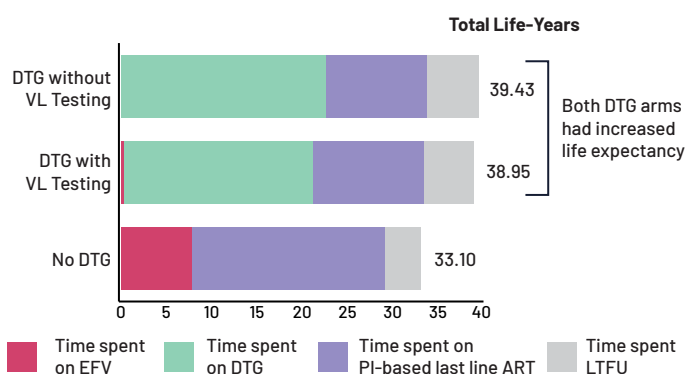
2021 Optimal Formulary and Limited-Use List for Antiretroviral Drugs for Children<sup>lxxiii</sup>

Supporting this guidance, recent data from a South African CEPAC modelling study presented at IAS 2021 examined life expectancy outcomes and cost implications across children switched to DTG with and without VL tests [Figure 29].<sup>lxxiv</sup>

The results showed that the groups switched to DTG, with and without a pre-transition viral load test, had a higher life expectancy compared to those not switched at all.<sup>lxxiv</sup> The study also found that both DTG groups had cost savings compared to the non-DTG group.<sup>lxxiv</sup>

Recent data from the ODYSSEY trial released at CROI 2021 also found that DTG-based ART is superior to the standard of care for children over 3kg starting 1L and 2L treatment, clearly supporting WHO recommendations.<sup>lxxv</sup>

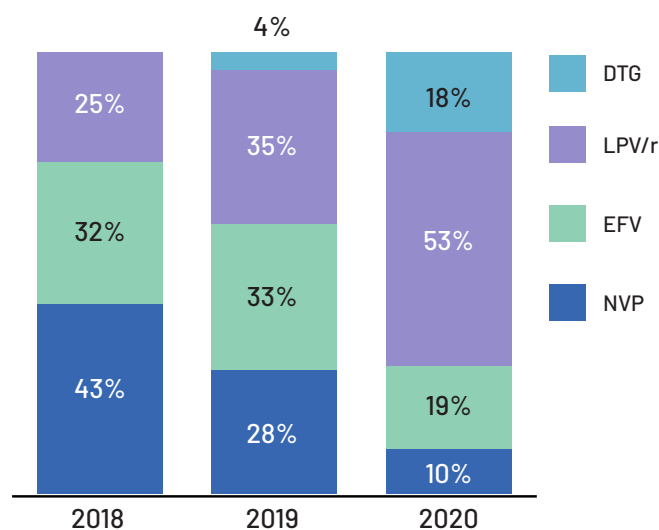
Figure 29: Impact of DTG and VL Testing on Child Life Expectancy in CEPAC Modelling Study<sup>lxxiv</sup>



## DTG expected to rapidly dominate pediatric treatment and replace LPV/r as the new standard of care

Prior to the availability of pDTG, LPV/r-based products comprised the majority of pediatric regimens in 2020 after NVP use rapidly reduced following a global push in 2019 [Figure 30].

Figure 30: Estimated Pediatric NNRTI/PI/INSTI Use in GA LMICs<sup>lxxxiv</sup>



\*Regimens with backbones comprised of pediatric formulations only.

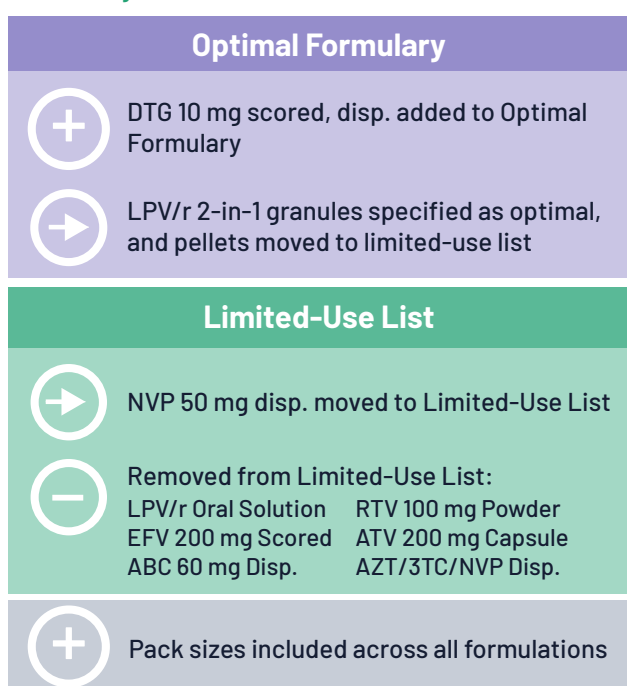
In 2020, given pDTG was not yet available, DTG use in pediatric patients was limited to CLHIV above 20kg who are able to take DTG 50 mg tablets. This transition is ongoing and in Ethiopia and Nigeria over 70 percent of eligible children have transitioned.<sup>lxxxii</sup> Moving forward, DTG will play a major role in pediatric treatment with LPV/r-based regimens only used for the minority of children unable to tolerate DTG. Data from the ODYSSEY trial suggest that fewer than five percent of children will need non-DTG-based regimens.<sup>lxxxv</sup>

## Updated WHO Optimal Formulary reinforces prioritization of pDTG and national formulary simplification

In April 2021, the WHO released an updated Optimal Formulary and Limited-Use List outlining the minimum number of pediatric formulations required for WHO-recommended regimens (Appendix C). The

updated formulary includes pDTG, underscoring the importance of this product as part of the WHO-preferred 1L and 2L regimen for children [Figure 31]. The WHO Limited-Use List was also significantly shortened, encouraging simplification of national formularies and promoting optimization efforts. Pack sizes were also included for all products to encourage harmonization across countries and suppliers. The full list of products is available on the [WHO website](#) and in Appendix C of this report.

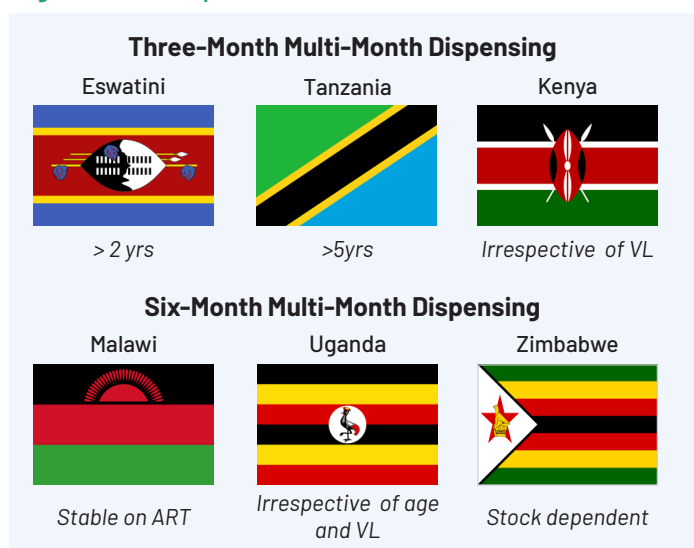
**Figure 31: Major Changes to WHO Optimal Formulary and Limited-Use List**



### WHO expands MMD recommendations to include pediatric and adolescent patients

Updated WHO guidelines recommend pediatric clinical visits and ART refills every three to six months, with a preference for six months, in line with historic recommendations for adults.<sup>iv</sup> As discussed in the adult section, MMD offers significant clinical and cost savings benefits for patients and providers. It also represents an opportunity to reduce exposure to COVID-19 by minimizing clinic visits. Due to these benefits, a number of countries have already begun adoption of MMD for pediatric patients [Figure 32].

**Figure 32: Adoption of MMD in Select Countries**



The WHO also now recommends that country programs provide psychosocial interventions to all adolescents and young adults living with HIV. Psychosocial interventions can improve adherence to ART and lead to increased rates of viral suppression, according to a WHO review of 30 randomized controlled trials [Figure 33].<sup>iv</sup>

**Figure 33: Psychosocial Interventions<sup>iv</sup>**



### Additional pediatric products in the pipeline, but countries should continue to prioritize pDTG adoption

Several pipeline pediatric products are currently in development, but are still likely a few years away from commercial availability in LMICs.

#### Fixed-Dose Pediatric ABC/3TC/DTG (pALD)

Development of a pediatric, dispersible, triple FDC of ABC/3TC/DTG (pALD) is ongoing as another collaboration between CHAI, Unitaid, and ViiV. However, national programs should not delay optimization with pDTG to await an FDC formulation.



### Pediatric DRV/r 120/20 mg (pDRV/r)

Development of pediatric ritonavir-boosted darunavir (pDRV)/r, a best-in-class protease inhibitor, is a priority for children failing DTG-based treatment and has been listed as a PADO priority since 2013. However, high startup costs and a relatively low number of children who need the product have historically been barriers to product development.

## TREAT RIGHT

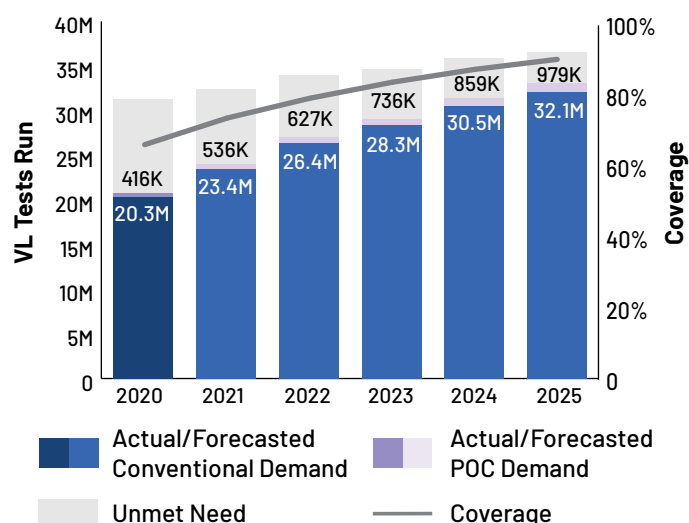
### With Appropriate Treatment Monitoring

LMIC VL volumes stagnant from 2019 to 2020 while suppression rates remain stable, pointing to sustained access to ART in the COVID-19 pandemic's first year

As COVID-19 surged across the globe in 2020, its ultimate impact on treatment success and monitoring was closely monitored. CHAI estimates that VL volumes in LMICs remained mostly unchanged from 2019 to 2020, at almost 21M tests annually [Figure 34].<sup>lxxvii</sup>

However, like most global estimates, this data masks vast differences at the facility, regional, and country levels. Some countries, such as Nigeria, were able to continue scaling up their VL volumes from 2019 to 2020. Whereas in others, such as Kenya, VL volumes decreased. Despite the varied impact of the COVID-19 pandemic on VL volumes, viral suppression rates remained virtually unchanged across countries. Data from PEPAR-supported countries from October 2019 to June 2020 found that viral suppression rates stayed at just over 90 percent throughout the period, suggesting that ART access and adherence remained high.<sup>lxxviii</sup>

Figure 34: LMIC VL Forecast<sup>lxxvii</sup>



In September 2020, in partnership with Unitaid and under the Optimal grant, CHAI launched an RFP for an incentive program to catalyze the development of pDRV/r to improve access for CLHIV.<sup>lxxxi</sup> In June 2021, Laurus Labs was awarded the incentive contract as the generic development partner and is developing the pDRV/r 120/20 mg tablets.<sup>lxxxi</sup>



### Pediatric TAF (pTAF)

Planning for development of pediatric-friendly, dispersible TAF-containing products has started through the UNIVERSAL grant that Penta received from the European & Developing Countries Clinical Trials Partnership (EDCTP), in which CHAI is listed as the formulation development partner. The aim of the grant is to develop fixed-dose combinations for infants and children initiating on ART, and to monitor the long-term efficacy and safety of other pediatric formulations as they enter the market across Africa.<sup>lxxvi</sup>

## 2021 WHO consolidated HIV guidelines conditionally recommend POC VL testing and update the treatment monitoring algorithm

While the benefits of POC EID are now well-established, ideal use cases for POC VL monitoring remain the subject of debate. However, as part of their 2021 consolidated HIV guidelines, the WHO now conditionally recommends the use of POC VL testing to monitor treatment among PLHIV on ART. The guidelines also identify six priority populations most likely to receive the greatest benefit from rapid VL result return [Figure 35].<sup>iv</sup> CHAI estimates that over 20 percent of PLHIV on ART in sub-Saharan Africa are eligible for POC VL under these guidelines based on available data for these priority populations.

CHAI supported the rollout and evaluation of near-POC VL testing across 57 public sector facilities in Cameroon, DRC, Kenya, Malawi, Senegal, Tanzania, and Zimbabwe from 2017 to 2019. In this large multi-country assessment, near-POC testing decreased the median time from sample collection to patient result return from 68 to six days compared to conventional devices in centralized laboratories. Time to clinical action for individuals with an elevated VL also decreased to three days with near-POC testing compared to 49 days with centralized testing. Overall, 37 percent of the patients with elevated VL results tested on near-POC devices had documented clinical action compared to only seven percent of those tested via centralized labs, highlighting that additional systems strengthening is needed to ensure that all patients received timely clinical follow-up based on test results.<sup>lxxix</sup>

In addition to the conditional recommendation on the use of POC VL, the WHO also updated the treatment monitoring algorithm [Appendix E]. Updates to the algorithm include clarifying that results from the first viral load test should be available within six months after starting ART and that the second viral load test should be performed three months after the initial test. The updated algorithm also now differentiates between undetectable viral loads ( $\leq 50$  copies/ml) and suppressed but detectable viral loads ( $>50$  to  $\leq 1,000$  copies/ml). For patients with unsuppressed viral loads on NNRTI-based regimens, the WHO now recommends a regimen switch after a single elevated viral load result due to high levels of pretreatment drug resistance.<sup>iv</sup>

Figure 35: POC VL Priority Populations<sup>iv</sup>

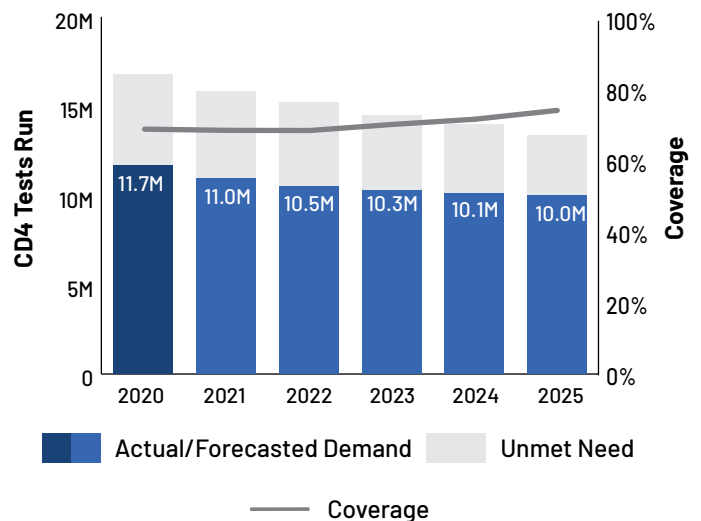


## Access to CD4 testing growing more important as programs implement the WHO AHD package of care

CHAI estimates that 11.7M device-based CD4 tests were conducted in 2020 [Figure 36].<sup>lxxx</sup> Although viral load remains the gold standard for treatment monitoring, CD4 testing still has an important role to play in identifying patients with AHD and for immunological monitoring in patients with elevated viral loads.

CHAI expects the overall need and demand for CD4 testing to decrease as national viral load programs mature and optimal regimens improve suppression rates. However, with a growing number of programs implementing the WHO AHD package of care, and with increasing adoption of the VISITECT® CD4 Advanced Disease test, CD4 testing rates will likely increase in many countries over the next few years.

Figure 36: LMIC CD4 Forecast<sup>lxxx</sup>



# STAY NEGATIVE

## An upcoming paradigm shift in prevention products aims to address stagnation in progress toward eliminating new HIV infections

Despite considerable progress toward reducing HIV infections in the last decade, and innovative changes to service delivery during COVID-19, global HIV infections in 2020 were three times the UNAIDS target. A robust and diverse product pipeline for HIV prevention aims to curb the HIV epidemic by offering longer-acting products and increasingly diverse formulations that give users greater choice.

### HIV prevention progress is stalling with new infections in 2020 significantly off-track from global goals

Globally, there were 31 percent fewer HIV infections in 2020 compared to 2010. While countries around the world have made considerable progress toward HIV prevention goals, momentum has slowed. 1.5 million people acquired HIV in 2020, representing only a slight reduction in new infections over the past four years, and three times the target for 2020 [Figure 37].<sup>xvii</sup>

The proportion of new global HIV infections among key populations and their sexual partners increased from 62 percent in 2019 to 65 percent in 2020, though distribution varies across geographies. Key populations and their partners accounted for 93 percent of new HIV infections outside of sub-Saharan Africa, and 39 percent within sub-Saharan Africa (up from just 20 percent in 2014).<sup>lxxxix</sup> In the past year, many regions where the HIV epidemic is concentrated among key populations and their partners, such as Latin America and Eastern Europe and Central Asia, have seen stagnating declines in or increasing rates of new infections overall.<sup>lxxxii</sup>

Achieving the new UNAIDS 2025 targets, which aim to reduce annual HIV infections to less than 370,000 by 2025, will require a renewed focus on effective and equitable rollout of combination prevention approaches, increased focus on key populations and their partners, and introduction of new, effective prevention products that give users greater choice.

**Figure 37: Progress Toward UNAIDS Targets on HIV Infection<sup>xvii</sup>**

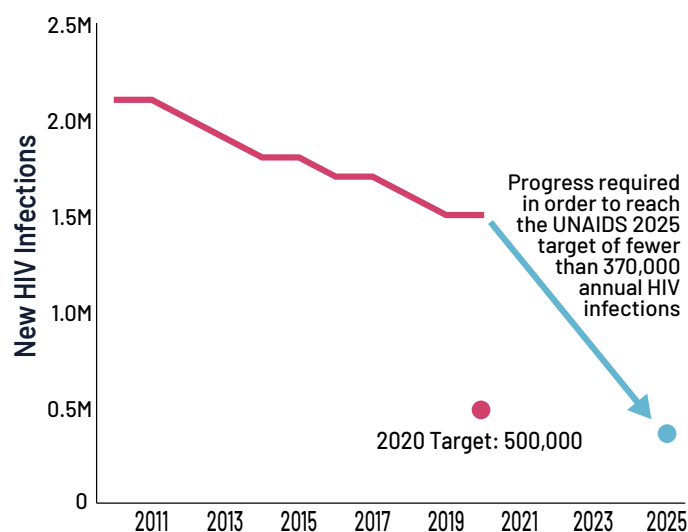
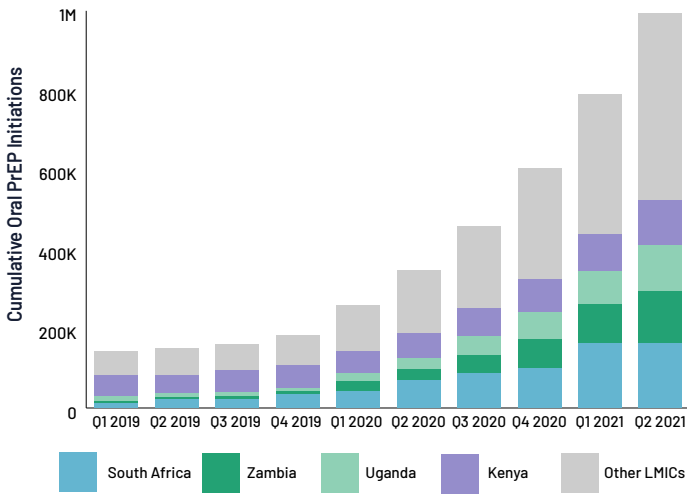


Figure 38: Cumulative Oral PrEP Initiations in LMICs and Four Largest Programs, as of Q2 2021<sup>lxxxiii</sup>



### Despite service interruptions, oral PrEP uptake has remained resilient throughout the COVID-19 pandemic

Oral pre-exposure prophylaxis (PrEP) is a highly effective prevention option, and available data indicate marked increases in oral PrEP initiations throughout 2020 despite the COVID-19 pandemic. As of Q2 2021, nearly one million people in LMICs have (re-)initiated oral PrEP—82 percent of these initiations occurred in 2020 and 2021 [Figure 38].<sup>lxxxiii</sup>

The WHO declared oral PrEP an essential health service that should be maintained during COVID-19, and suggested adaptations such as MMD, telemedicine, and community-based services to mitigate disruptions to oral PrEP delivery.<sup>lxxxiv</sup> Similarly, CHAI found that differentiated service delivery methods, such as telephone screenings and a transition to virtual demand generation, were crucial for increasing oral PrEP initiations in LMICs during COVID-19.<sup>lxxxviii</sup> These adaptations have the potential to simplify the delivery of prevention services to reach more people with PrEP beyond COVID-19.

### New research reinforces the benefits of oral PrEP, even with some seroconversions and drug resistance

Results from the ongoing Global Evaluation of Microbicide Sensitivity (GEMS) project, the first study to investigate the seroconversion and resistance rates

among oral PrEP users under real-world conditions in sub-Saharan Africa, showed only 229 seroconversions among an estimated 104,000 oral PrEP users in programs in Eswatini, Kenya, South Africa, and Zimbabwe. 23 percent of those who received resistance testing demonstrated resistance to oral PrEP drugs TDF and/or FTC. While this resistance rate exceeds background levels of transmitted resistance in the region, the very low seroconversion rate suggests that, overall, the benefits of preventing new HIV infections with oral PrEP are likely to outweigh the risks of drug resistance.<sup>lxxxv</sup>

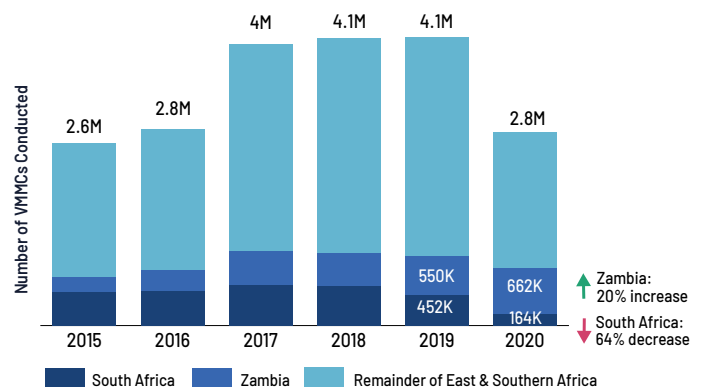
Researchers also sought to fill an important knowledge gap to better understand oral PrEP adherence and acceptability among adolescent girls and young women (AGYW), a population at high risk of HIV acquisition. Preliminary results from the REACH study indicate AGYW not only found oral PrEP acceptable, but nearly 60 percent of participants were considered highly adherent users, as indicated by drug levels suggesting they took oral PrEP at least four times a week.<sup>lxxxvi</sup>

### Innovations in service delivery drive rebounds in VMMC procedures in some countries

In areas with high HIV prevalence and low rates of male circumcision, voluntary medical male circumcision (VMMC) is a cost-effective, one-time intervention that can greatly contribute to HIV prevention goals.<sup>lxxxvii, lxxxviii</sup>

Despite the benefits, country programs performed significantly fewer VMMCs in UNAIDS priority countries in 2020 due to service disruptions caused by COVID-19.

Figure 39: VMMCs conducted in East and Southern Africa, 2015 to 2020<sup>xvii</sup>



Approximately 2.8 million procedures were performed in 2020, compared with 4.1 million in 2019 [Figure 39].<sup>xvii</sup>

In South Africa, strict lockdowns in 2020 contributed to a 64 percent decrease in VMMC procedures compared to 2019. However, in the same period, programs in some countries recovered quickly and even expanded during the rest of 2020—notably in Zambia, where VMMCs increased by 20 percent in 2020. In these countries, virtual demand generation and integration into broader service delivery within health facilities enabled VMMC services to continue safely despite the disruptions caused by COVID-19.<sup>i</sup>

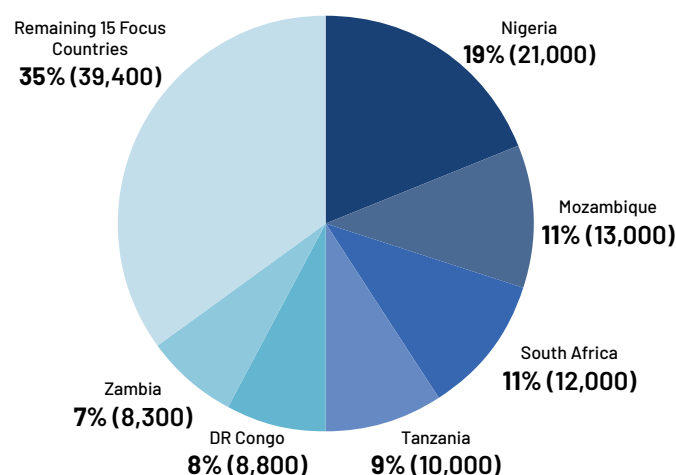
### Despite PMTCT gains, six countries accounted for two-thirds of vertical transmissions in UNAIDS focus countries in 2020

Country programs dramatically reduced the number of vertical HIV infections between mothers and children from over 520,000 in 2000 to 150,000 in 2020.<sup>xvii</sup> Despite these gains, further progress in the prevention of mother-to-child transmission (PMTCT) remains stubborn in many countries. Among 21 UNAIDS focus countries, which account for 80 percent of all pediatric infections, six are home to nearly two thirds of children who acquired HIV in 2020, with Nigeria accounting for almost one in five cases among focal countries [Figure 40].<sup>lxxxix</sup>

ART coverage among pregnant women in UNAIDS focus countries has remained steady at nearly 90 percent since 2015. In the same period, countries globally have experienced a slowdown on the path to elimination of vertical transmission.<sup>lxxxix</sup> Regional differences in ART coverage among pregnant women may play a significant role. In 2020, 60 percent of all pregnant women living with HIV who were not on ART were in West and Central Africa. Nigeria alone represents 23 percent of the global gap in ART coverage among pregnant women living with HIV.<sup>xvii</sup>

A recent Ugandan study also found that while uptake of ART among pregnant women living with HIV was above 90 percent, only three-quarters were adhering to ART two months after (re-)initiating treatment—suggesting an ART adherence gap may also contribute to sustained vertical transmission after childbirth and throughout breast feeding.<sup>xc</sup>

Figure 40: Share of New HIV Infections in Children Aged 0–14 Years in UNAIDS Focus Countries, 2020<sup>lxxxix</sup>



### Long-acting pipeline products poised to shift the HIV prevention paradigm

Persistently high HIV incidence, despite oral PrEP rollout, universal test and treat, and increasing ART coverage, suggests that more options are needed to effectively curb the HIV epidemic. The product pipeline for HIV prevention is robust and diverse, with novel long-acting products holding the potential to expand user choice with more acceptable options, while also reducing user barriers associated with daily use [Figure 41].<sup>xcii</sup> Recent findings on several near-term products, including long-acting injectable cabotegravir (CAB-LA), islatravir, lenacapavir, the dapivirine vaginal ring (DVR), and the dual prevention pill (DPP), are highlighted below.

Figure 41: HIV Prevention Pipeline Products<sup>xcii</sup>

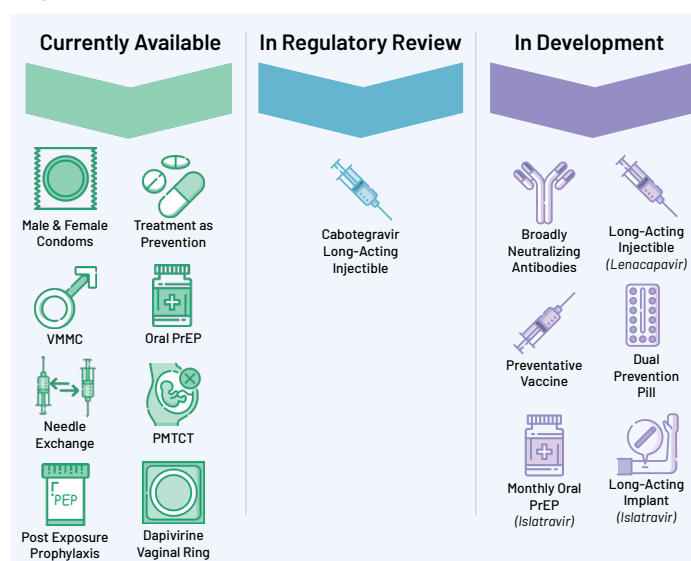
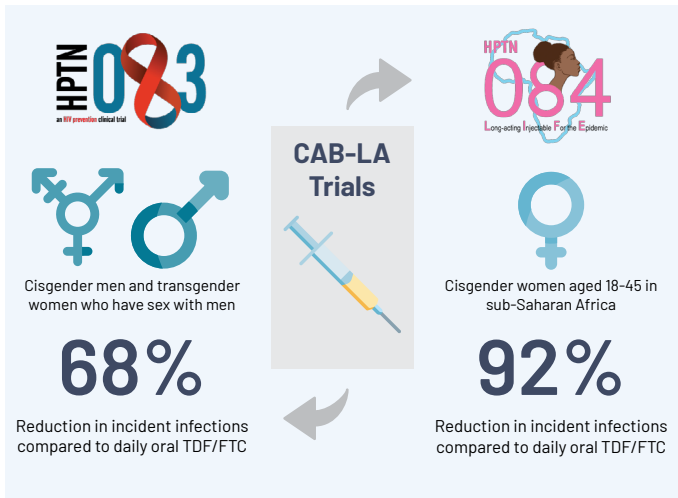


Figure 42: Summary of CAB-LA Efficacy Trials



**Long-acting Cabotegravir**

User acceptability studies and discrete choice experiments demonstrate that injectables are a highly preferred formulation among many populations at elevated risk of HIV, including MSM, transgender people, AGYW, and women.<sup>xcii, xciii, xciv</sup>

ViiV’s CAB-LA is an injectable form of PrEP administered every eight weeks. Two efficacy trials demonstrated that CAB-LA is safe and highly effective at preventing HIV and is superior to daily oral TDF/FTC [Figure 42].<sup>xcv, xcvi, xcvi</sup> Ancillary studies are also underway to understand the safety and acceptability of CAB-LA in adolescents.<sup>xcviii</sup> Further research is needed to explore use of CAB-LA in pregnant and breast feeding women.

ViiV submitted a rolling application to the US FDA for approval of CAB-LA in May 2021 and was granted priority review. A final US FDA decision is anticipated in January 2022; if approved CAB-LA would be the first long-acting injectable for HIV PrEP.<sup>xcix</sup>

**Islatravir**

Merck is beginning phase III efficacy trials for islatravir, an investigational NRTTI for once-monthly oral PrEP. Safety and efficacy studies IMPOWER 22 and IMPOWER 24 will compare monthly oral ISL to daily oral TDF/FTC among cis gender women aged 16 to 45, MSM, and transgender women.<sup>c</sup> Positive 24-week results from a prior phase IIa pharmacokinetic

study of ISL—conducted among a diverse population of adult men and women at low risk of HIV infection in Israel, South Africa, and the United States—showed drug levels above the pre-specified threshold for HIV prevention eight weeks after the last dose.<sup>ci</sup>

Additionally, Merck is planning further studies for a new formulation of ISL in the form of a small removable implant. Phase I study results showed that the ISL implant could provide over a year of sufficient drug levels to act as PrEP or form part of combination antiretroviral therapy for well over a year [Figure 43].<sup>cii</sup>

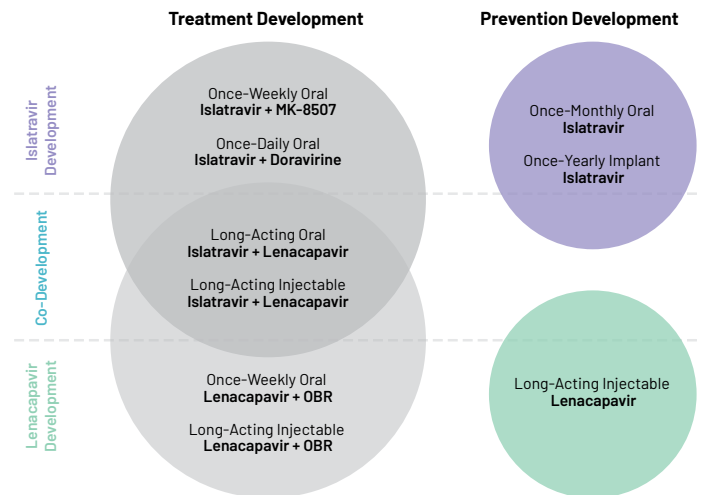
**Lenacapavir**

In August 2021, Gilead began the PURPOSE 1 trial to investigate both the six-month subcutaneous injectable form of LEN and oral TAF/FTC for PrEP among cis gender adolescent girls and young women in Uganda and South Africa.<sup>ciii</sup> Gilead will conduct a parallel companion study, PURPOSE 2, to study six-month injectable LEN among men and people of trans experience [Figure 43].<sup>civ, cv</sup>

**Dapivirine Vaginal Ring**

The DVR is a self-inserted, flexible silicone ring that women can wear continuously for one month to reduce the risk of HIV transmission during vaginal sex.<sup>cvi</sup> Two phase III efficacy trials demonstrated that the DVR could reduce risk of HIV acquisition by 27%<sup>cvi</sup> and

Figure 43: Islatravir and Lenacapavir Development for HIV Treatment and Prevention



31<sup>cviii</sup> percent—additional data provided during the European Medicines Agency review of the DVR led to an upward revision of this latter result to a 35 percent reduced risk for HIV infection.<sup>cix</sup> Open-label extensions of these trials estimated a risk reduction of approximately 39<sup>cx</sup> and 63 percent<sup>cvi</sup> compared to simulated controls. In 2021, the WHO prequalified the DVR and released a conditional recommendation that it may be offered as an additional prevention choice for women at substantial risk of HIV infection as part of combination prevention approaches—though only when oral PrEP is not available or cannot be used.<sup>xxx</sup> The DVR is also currently under review by the US FDA.<sup>cxii</sup>

At IAS 2021, interim results from the REACH study indicate 88.5 percent of AGYW found the DVR acceptable, with just over half showing full adherence based on residual drug levels in returned rings, filling an important research gap.<sup>lxxxvi</sup> Implementation considerations and key research on cost and cost effectiveness of the DVR are forthcoming. Notably, reference pricing for the DVR at nearly US \$13 per ring is significantly higher than the monthly cost of oral PrEP.<sup>cxii</sup>

## Women-centered products offer tailored approaches to dual HIV prevention and contraception

Many women worldwide are confronted with two significant, overlapping health risks: unintended pregnancy and HIV, in addition to other sexually transmitted infections. More than 218 million women in LMICs have an unmet need for contraception.<sup>cxiii</sup> Additionally, despite significant advances in HIV treatment and prevention, over 650,000 women aged 15 and above were newly infected with HIV in 2020. In sub-Saharan Africa, women and girls accounted for 63 percent of all new HIV infections.<sup>xvii</sup> There is continued recognition of the need for women-controlled combination prevention products that provide women with more choice and greater agency to simultaneously control their reproductive health and susceptibility to HIV.<sup>lxxxix</sup>

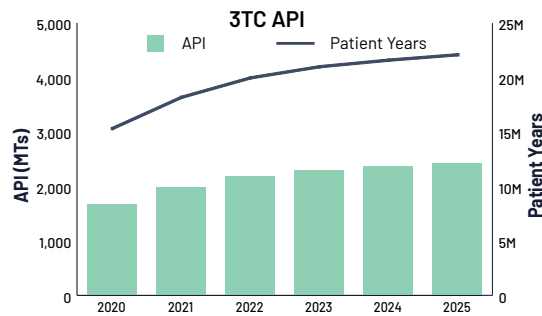
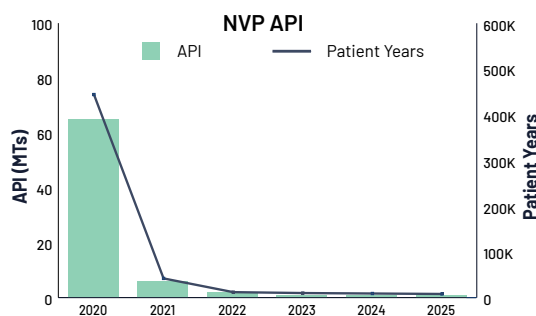
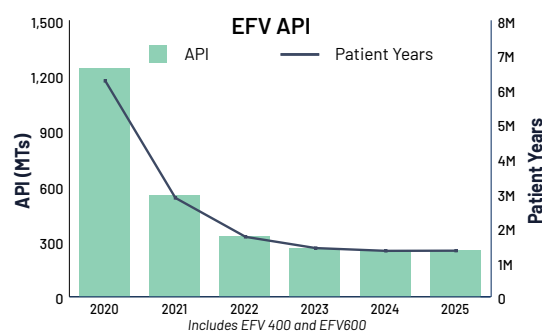
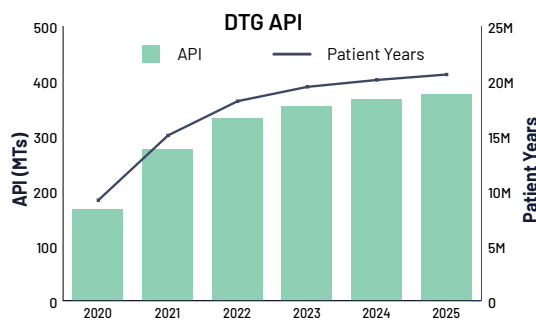
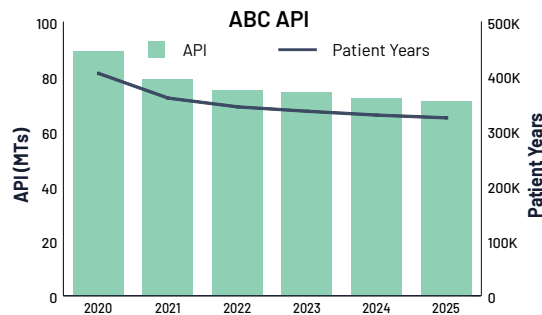
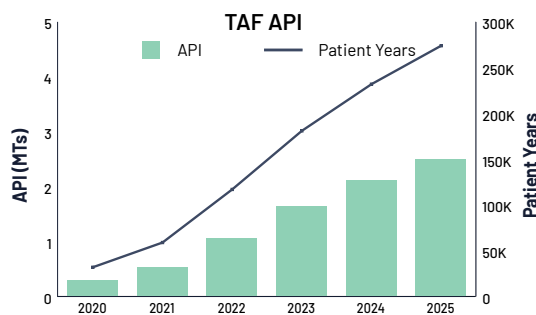
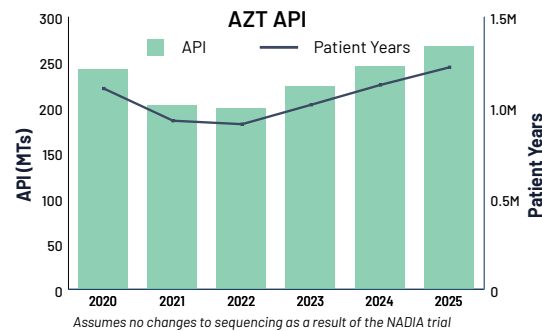
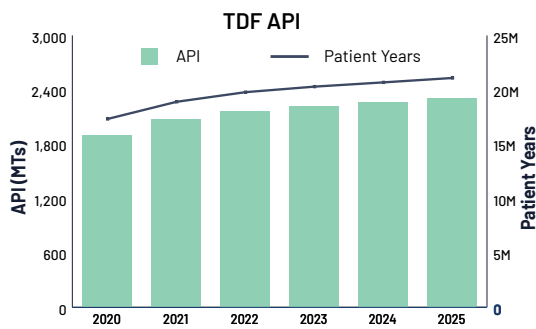
Multipurpose prevention technologies (MPTs) that combine contraception with PrEP have the potential to help address adherence and uptake challenges seen with oral PrEP and stigma associated with HIV service delivery. Currently, condoms are the only available MPT, however male condoms are not within the control of a woman and the use of female condoms has been limited by low acceptability and high costs.<sup>cxiv</sup>

CHAI is part of a coalition of partners supporting the development and introduction of a DPP, a novel MPT for prevention of pregnancy and HIV, via support from the Children's Investment Fund Foundation. The DPP is a co-formulated tablet, combining TDF/FTC for PrEP and levonorgestrel/ethinyl estradiol for hormonal contraception. As a single product, the DPP offers the opportunity to integrate HIV prevention and family planning services and further empower women to space their pregnancies and protect themselves from HIV. The DPP is also seen as an opportunity to lay the groundwork for the introduction of other MPTs currently in the research pipeline, such as vaginal rings, injectables, implants, and films.<sup>cxv</sup>

## Appendix A:

# FORECASTED ADULT API DEMAND IN GA LMICs

The graphs below show the estimated generic-accessible patient demand and active pharmaceutical ingredient (API) volume (in metric tons) forecast for key adult ARVs. Patient years represent the effective number of patients on treatment for a full year and are used to calculate yearly API demand. Patient years are calculated by assuming newly-initiated patients are on treatment for six months on average in the year of initiation, and a 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 (US \$) for key adult and pediatric ARVs. Prices are Ex-Works (EXW).

PRODUCT	PACK SIZE	GLOBAL FUND PPM PRICE MAR. 2021 <sup>1</sup>	GHSC-PSM E-CATALOG PRICE SEP. 2021 <sup>2</sup>	RSA WEIGHTED AVE TENDER PRICE 2019-2022 <sup>3</sup>
<b>Adult Products</b>				
ABC/3TC (600/300 mg)	30 tablets	\$8.78	\$8.90	\$7.60
ATV/r (300/100 mg)	30 tablets	\$13.45	\$13.47	
AZT/3TC (300/150 mg)	60 tablets	\$5.55	\$6.05	\$4.85
DTG (50 mg)	30 tablets	\$2.60	\$2.48	\$2.38
DTG (50 mg)	90 tablets		\$8.08	
EFV (600 mg)	30 tablets	\$2.50		\$2.32
LPV/r (200/50 mg)	120 tablets	\$18.65	\$18.65	\$11.69
NVP (200 mg)	60 tablets			\$1.85
RTV (100 mg) heat-stable	60 tablets	\$7.00	\$7.00	\$3.25
TDF (300 mg)	30 tablets	\$2.40	\$2.40	\$2.07
TDF/3TC (300/300 mg)	30 tablets	\$3.40	\$3.20	
TDF/FTC (300/200 mg)	30 tablets	\$4.35	\$4.65	\$3.08
TDF/3TC/DTG (300/300/50 mg) No Carton	30 tablets	\$5.15*		\$4.82**
TDF/3TC/DTG (300/300/50 mg) No Carton	90 tablets	\$15.25	\$15.25	
TDF/3TC/DTG (300/300/50 mg) No Carton	180 tablets	\$30.50	\$30.29	
TDF/3TC/EFV (300/300/400 mg) No Carton	30 tablets	\$5.25*		
TDF/3TC/EFV (300/300/400 mg) No Carton	90 tablets	\$16.60	\$15.85	
TDF/3TC/EFV (300/300/600 mg) No Carton	30 tablets	\$5.65*		
TDF/FTC/EFV (300/200/600 mg) No Carton	30 tablets	\$6.10*		\$5.11
<b>Pediatric Products</b>				
<b>Optimal Formulary</b>				
ABC/3TC (120/60 mg) disp. scored	30 tablets	\$3.10	\$3.10	
ABC/3TC (120/60 mg) disp. scored	60 tablets		\$6.05	
AZT (50/5 mg/ml) oral solution	240 mL bottle			
AZT/3TC (60/30 mg) disp. scored	60 tablets	\$1.90	\$1.80	
DTG (10 mg) disp. scored	90 tablets	\$4.50	\$4.50	
LPV/r (100/25 mg) heat-stable	60 tablets	\$6.50	\$6.50	\$3.71
LPV/r (40/10 mg) oral granules	120 sachets	\$17.25	\$18.25	
NVP (50/5 mg/ml) oral solution (with syringe)	100 mL bottle	\$2.00	\$2.00	\$0.73
<b>Limited-Use List</b>				
3TC (50/5 mg/ml) oral solution	240 mL		\$3.02	\$1.06
DRV (75 mg)	480 tablets		\$54.00	\$43.35
DRV (150 mg)	240 tablets			\$37.86
LPV/r (40/10 mg) oral pellets	120 capsules	\$17.25	\$16.45	
NVP (50 mg) disp. scored	60 tablets	\$1.45	\$1.45	
RAL (100 mg) granules	60 sachets		\$57.00	
RTV (25 mg) heat-stable	30 tablets		\$3.25	

1) Global Fund Pooled Procurement Mechanism Reference Pricing: ARVs, Mar. 22, 2021. [Link](#).

2) Global Health Supply Chain – Procurement and Supply Management (GHSC-PSM) E-Catalog: ARVs, September 2021. [Link](#).

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\*PPM lists have slightly higher prices with cartons, please refer to latest price list for more information.

\*\*Price shown for packaging with carton.

## Appendix C:

## 2021 OPTIMAL FORMULARY AND LIMITED-USE LIST FOR PEDIATRIC ARVs

## Optimal Formulary

DRUG	DOSAGE FORM	STRENGTH	RATIONALE FOR USE	PACK SIZE
DTG <sup>1</sup>	Tablet (dispersible, scored)	10 mg	For first-line or second-line ART for infants and children who are $\geq 4$ weeks of age and weighing 3 to $<20$ kg	90-count pack
ABC + 3TC	Tablet (dispersible, scored)	120 mg/60 mg	For preferred first-line or second-line ART for infants and children weighing 3-25 kg	30- and 60-count packs
AZT <sup>2</sup>	Oral Solution	50 mg/5 mL	For postnatal prophylaxis and neonatal treatment only	240 mL bottle
NVP	Oral Solution	50 mg/5 mL	For postnatal prophylaxis and neonatal treatment only	100 mL bottle
LPV/r	Tablet (heat stable)	100 mg/25 mg	For alternative first-line or second-line ART for children weighing $\geq 10$ kg and who are able to swallow tablets whole	60-count pack
LPV/r	Oral granules	40 mg/10 mg	For alternative first-line or second-line ART for children weighing $\leq 10$ kg and who are unable to swallow 100 mg/25 mg tablets whole	120-count pack
AZT + 3TC	Tablet (dispersible, scored)	60 mg/30 mg	For second-line ART for infants and children weighing 3-25 kg	60-count pack

1) DTG 50 mg film-coated tablets are the preferred formulation for children weighing  $\geq 20$  kg (and co-formulated DTG 50 mg + TDF 300 mg + 3TC 300 mg, also known as TLD, for those weighing  $\geq 30$  kg) to reduce the pill burden, simplify supply chain processes and reduce programme costs. Programs should ensure that the  $\geq 20$  kg population is accounted for during quantification for DTG 50 mg tablets.

2) As of March 2021, AZT oral solution is only available in a 240 mL bottle. This formulation is only anticipated to be used for neonatal treatment or enhanced infant prophylaxis. AZT oral solution has a four-week shelf life after opening, and if infants use AZT oral solution for longer than this period, a new bottle should be issued after four weeks.

## Limited-Use List

DRUG	DOSAGE FORM	STRENGTH	RATIONALE FOR USE	PACK SIZE
NVP	Tablet (dispersible, scored)	50 mg	Only for postnatal prophylaxis when NVP oral solution is not available	60-count pack
3TC	Oral Solution	50 mg/5 mL	Only for treating neonates	240-mL bottle
RAL	Granules for suspension	100 mg	Only for treating neonates	60-count pack
LPV/r	Oral pellets	40 mg/10 mg	For specific circumstances in which DTG 10 mg dispersible, scored tablets or LPV/r oral granules are not available or clinically indicated	120-count pack
DRV	Tablet	75 mg, 150 mg	For third-line ART regimens for children 3 years and older	480- and 240-count packs
RTV	Tablet	25 mg	For superboosting of LPV/r during TB treatment and required for use when administering DRV	60-count pack

## Appendix D:

# NOTES ON METHODOLOGY

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

**ART Patient Forecast:** Each year, CHAI develops a forecast for the total number of patients 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. The largest *generic-inaccessible* countries are Argentina, Brazil, China, Mexico, and Russia.

CHAI compiles historic data on the number of patients on ART from the UNAIDS AIDSinfo Database. For each country, CHAI assumes that the number of people receiving treatment will increase linearly 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 September 2021. 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 patient 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 patient forecast to project ARV demand in GA LMICs over the next five years on a country-by-country level that is then aggregated at the global level. CHAI’s 2021 ARV demand forecast for current drugs includes data from: Benin, Burkina Faso, Cambodia, Cameroon, DRC, Eswatini, Ethiopia, India, Kenya, Laos, Malawi, Nigeria, Senegal, South Africa, Tanzania, Togo, Uganda, Zambia, and Zimbabwe. These countries represent approximately 78 percent of adult patients on ART in GA LMICs in 2020.

**ARV Market Sizing Analysis:** Each year, CHAI combines known regimen and formulation splits by country with pricing data to calculate the size of the ARV market in dollar terms, and to calculate the weighted average cost of treatment for 1L and 2L adult and pediatric patients. The market size is an estimate of the cost of 1L and 2L treatment (drug costs only) in GA LMICs for all of 2020, and assumes that the countries CHAI has data for are representative of the remaining 22 percent of the market in GA LMICs. It is not an estimate of the cost of ARV procurement in 2020. The assumed price paid for ARVs comes from two sources: 1) South Africa procurement informs the weighted average price paid for each respective formulation within a given year for South Africa’s regimens and formulations; 2) For all other countries, the average Global Fund Pooled Procurement Mechanism (PPM) pricing across 2020 is used.

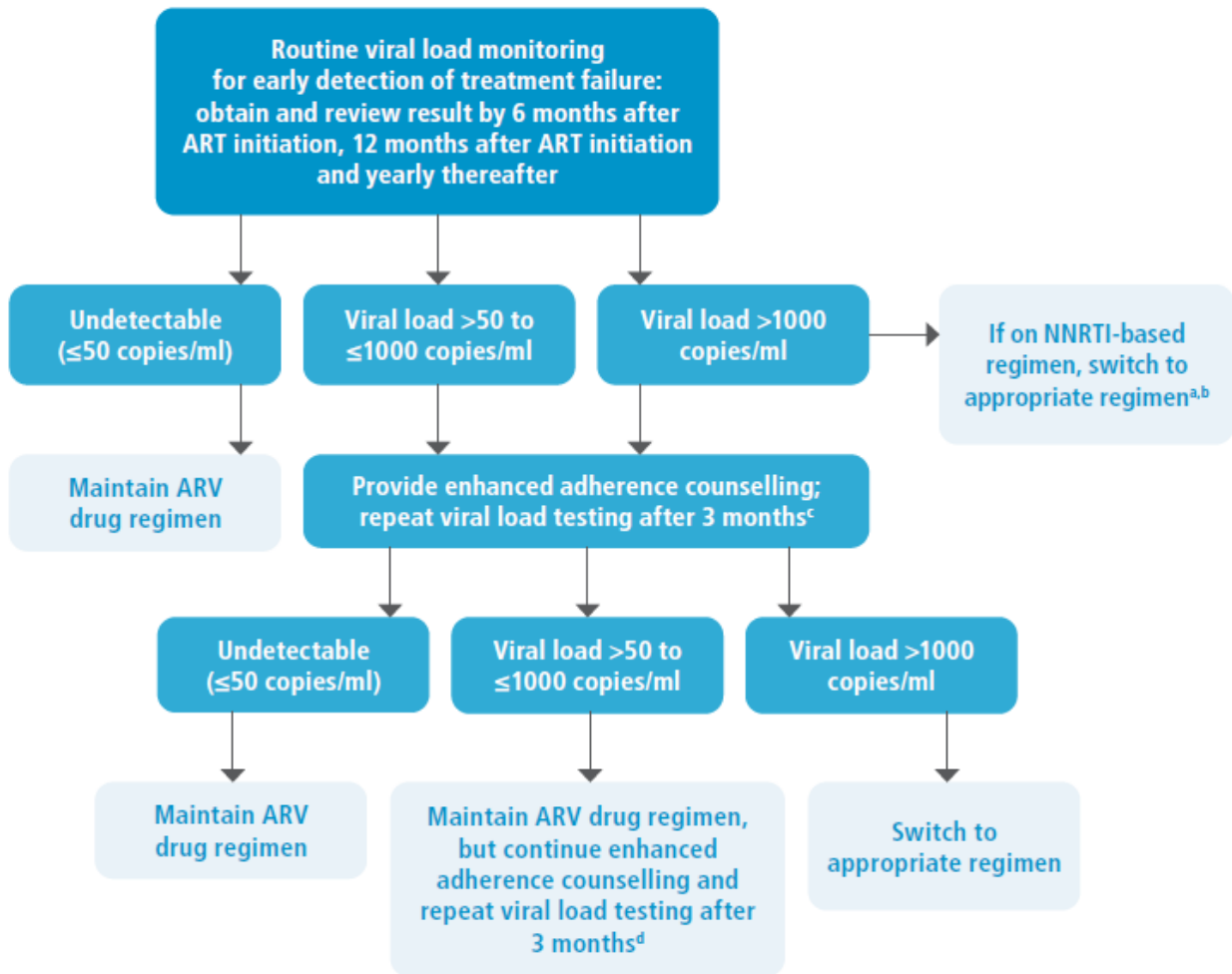
**Diagnostics Forecasts:** CHAI’s VL, EID, and CD4 diagnostics forecasts have two primary components: 1) diagnostic testing *demand*, and 2) diagnostic testing *need*. While the exact methodology differs slightly between VL, EID, and CD4 tests, the general approach is as follows.

For *demand*, CHAI collects baseline (2020) testing volumes from CHAI country teams, publicly available dashboards, or other sources. 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 patients each year and country-level testing guidelines for each type of test. For all test types, CHAI forecasts at the country level and then aggregates globally across all LMICs in this report.

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

Appendix E:

# 2021 WHO TREATMENT MONITORING ALGORITHM



**Adherence counselling** should be provided at all visits to ensure that viral suppression is maintained or given priority throughout care

<sup>a</sup> Switch after a single elevated viral load should be considered.

<sup>b</sup> A second viral load may be considered before regimen switch if DTG-based regimens are unavailable and the results of a viral load test can be returned and acted on rapidly.

<sup>c</sup> Conduct same-day testing using point-of-care viral load testing for a repeat viral load test, where available, to expedite the return of results. If not available, viral load specimens and results for a repeat viral load test should be given priority across the laboratory referral process (including specimen collection, testing and return of results). See subsection 4.7.2 on point-of-care viral load testing.

<sup>d</sup> Consider switching ART for those receiving NNRTI-based regimens based on clinical considerations and address any adherence concerns.

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