CLINTON HEALTH ACCESS INITIATIVE

HIV MARKET REPORT

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

Issue 11, September 2020

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Acronyms Used

1HP	One month daily rifapentine + isoniazid for TPT
1L	First-line
2L	Second-line
3L	Third-line
3HP	Three months weekly rifapentine + isoniazid for TPT
3TC	Lamivudine
5FC	Flucytosine
ABC	Abacavir
AHD	Advanced HIV disease
AIDS	Acquired immunodeficiency syndrome
ALD	ABC+3TC+DTG
ANC	Antenatal care
API	Active pharmaceutical ingredient
APWG	ARV Procurement Working Group
ART	Antiretroviral therapy
ARV	Antiretroviral
ATV/r	Atazanavir/ritonavir
AZT	Zidovudine
BioPIC	Biomedical Prevention Implementation Collaborative
CAB-LA	Cabotegravir long-acting
CAGR	Compound annual growth rate
CHAI	Clinton Health Access Initiative
CHW	Community health worker
CIFF	Children's Investment Fund Foundation
CLHIV	Children living with HIV
CM	Cryptococcal meningitis
COP	Country operating plan
CrAg	Cryptococcal antigen
Disp.	Dispersible
DPV	Dapivirine
DRV/r	Darunavir/ritonavir
DTG	Dolutegravir
EFV	Efavirenz
EID	Early infant diagnosis
EIMC	Early infant male circumcision
EMA	European Medicines Agency
EMAV	Early market access vehicle
ERP	Expert review panel
EXW	Ex-Works
FDC	Fixed-dose combination
FTC	Emtricitabine
GA	Generic-accessible
GF	Global Fund to Fight AIDS, Tuberculosis, and Malaria
GHSC-PSM	Global Health Supply Chain Program-Procurement and Supply Management
HCW	Healthcare worker
HEI	HIV-exposed infant
HIV	Human immunodeficiency virus
HIVST	HIV self-test
HPTN	HIV Prevention Trials Network
HTS	HIV testing services
IAS	International AIDS Society
INH	Isoniazid
INSTI	Integrase strand transfer inhibitor
L-AmB	Liposomal amphotericin B
LDL	Lower detection limit
LFA	Lateral flow assay
LMIC	Low- and middle-income country
LPV/r	Lopinavir/ritonavir
MMD	Multi-month dispensing
MoH	Ministry of Health
MPT	Multipurpose technology
MTCT	Mother-to-child transmission
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NRTTI	Nucleoside reverse transcriptase translocation inhibitor
NTD	Neural tube defect
NVP	Nevirapine
PADO	Pediatric ARV Drug Optimization
PEPFAR	President's Emergency Plan for AIDS Relief
PI	Protease inhibitor
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PPM	Pooled Procurement Mechanism
PPPY	Per patient per year
PQ	Prequalification
PrEP	Pre-exposure prophylaxis
RDT	Rapid diagnostic test
RPT	Rifapentine
RTV	Ritonavir
SSA	Sub-Saharan Africa
STI	Sexually transmitted infection
TAF	Tenofovir alafenamide fumarate
TB	Tuberculosis
TDF	Tenofovir disoproxil fumarate
TLD	TDF+3TC+DTG
TLE400	TDF+3TC+EFV400
TLE600	TDF+3TC+EFV600
TPT	TB preventive therapy
US FDA	United States Food and Drug Administration
VL	Viral load
VMMC	Voluntary medical male circumcision
WHO	World Health Organization
XTC	Emtricitabine or lamivudine
YOY	Year-over-year
ZLN	AZT+3TC+NVP

Foreword

2020 was already a consequential year in the HIV space before the COVID-19 pandemic swept across the globe. This was the last year for countries to make progress toward the 90-90-90 targets set by UNAIDS in 2014 with the goal that by 2020: 90 percent of people living with HIV would know their status, 90 percent of those who know their status would be on treatment, and 90 percent of those on treatment would be virally suppressed.

Even prior to COVID-19, it was almost certain the world would not achieve these targets on time as only 14 countries met them by the end of 2019. However, COVID-19 impacted the entire HIV cascade with disruptions to services critical to meeting each target. From causing drops in HIV testing and viral load volumes as clients avoided clinics, to disrupting ARV supply chains and HIV prevention outreach due to lockdowns across the globe, COVID-19 is threatening the progress the global community has made against HIV.

Despite the challenges the community is facing in 2020, there are bright spots reflecting the resilience of people living with HIV (PLHIV) and those involved in the global response. The transition to TLD continues in earnest, with over six million PLHIV on this optimal regimen by the time of publication. Widespread rollout of multi-month dispensing, long championed as a way to deliver differentiated care, scaled up to reduce the potential for patient and healthcare worker exposure to COVID-19. Despite some COVID-19-related delays, provision of the advanced HIV disease package of care, jumpstarted in many countries in 2019, continues with initial procurement of optimal products such as flucytosine (5FC) arriving in countries and virtual healthcare worker trainings ongoing.

While there is no doubt that COVID-19 has disrupted HIV services and stalled progress toward the 90-90-90 targets, the global HIV community has experienced challenges before. CHAI is hopeful that programs will build back stronger than ever with increased program resiliency.

Much work remains to end the HIV/AIDS epidemic as a public health threat. CHAI is focused on meeting this goal by working with ministries of health, communities, suppliers, and partners to ensure that all people in need have access to the best HIV commodities at affordable and sustainable prices, no matter where they live.

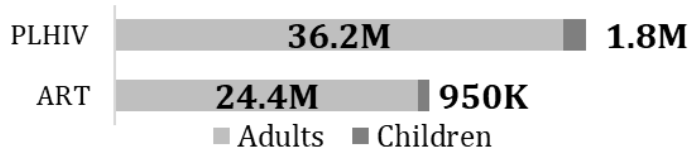
2020 Market Report At-a-Glance

HIV Data Overview, 2019

38M People living with HIV globally

25.4M People on treatment globally

67% Global ART Coverage Rate



The COVID-19 pandemic has disrupted services across the HIV continuum, threatening progress toward the 2020 Fast-Track targets

Fast Track Target Progress

1st 90: **81%** PLHIV globally know their status

2nd 90: **82%** of those who know their status are on ART

3rd 90: **88%** of those on ART are virally suppressed

Test Smart

HIV testing volumes decreased due to the COVID-19 pandemic, but are beginning to rebound

HIV self-tests (HIVSTs) helped to ensure continued access to testing during lockdown

4 HIVSTs have WHO PQ

OraQuick	INSTI
Mylan	Sure Check

with several additional ongoing PQ applications

Updated WHO Guidelines on HIV Testing Services

- ✓ Recommend a 3-test algorithm where HTS positivity is < 5%
- ✓ Recommend syphilis testing in antenatal care

Treat Right

AHD

US $3.98 per test price deal reached for VISITECT CD4 AHD, a groundbreaking, device-free, same-day CD4 test

Adult ARVs

TLD has been adopted by over 120 countries

>6M patients were on DTG as of publication (Sep. 2020)

MMD access was accelerated due to COVID-19

LPV/r shortages accelerated ongoing 2L optimization to DTG and ATV/r

Pediatric ARVs

DTG 10 mg (disp. & scored) tablets are expected to **receive US FDA approval** by the end of 2020, following the approval of DTG 5 mg (disp.) tablets in June 2020

NVP continues to be phased out (except for infant prophylaxis) as children switch to more optimal regimens

Stay Negative

1.7M

new annual HIV infections in 2019

> 60% driven by key populations and their partners

***Descovy:* TAF/FTC (25/200 mg)** was **approved by the US FDA** in Oct. 2019 for use as oral PrEP excluding cisgender women and other individuals at risk from receptive vaginal sex

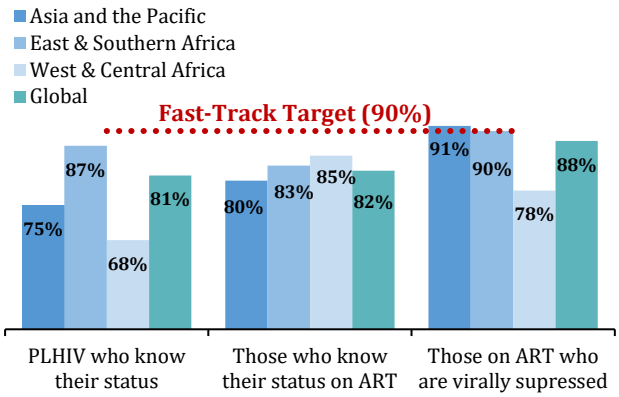
Cabotegravir Long-Acting (CAB-LA) injectable PrEP found to be ***superior* to daily oral TDF/FTC** for cisgender men and transgender women who have sex with men

GENERAL TRENDS

Despite progress, the world was off track to reach the 90s targets by 2020, and the COVID-19 pandemic has created additional challenges

Over the last five years, countries across the globe achieved considerable progress toward the 90-90-90 Fast-Track targets[1]. However, even before the COVID-19 pandemic, it was very likely that the world would fall short of achieving these goals by 2020 [Figure 1].[ii]

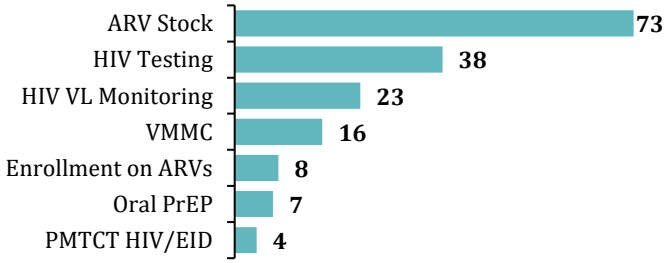
Figure 1: Regional Progress toward the 2020 Fast-Track Targets (2019, All Ages)[i]



By the end of 2019, only 14 countries achieved all three of the 90s targets; nine of these were low- and middle-income countries (LMICs) (Botswana, Cambodia, Eswatini, Namibia, Rwanda, Thailand, Uganda, Zambia, and Zimbabwe).[ii] Eswatini also achieved the 2030 95-95-95 targets more than ten years ahead of the deadline, making it the first country in Africa to accomplish this goal.[ii]

The COVID-19 pandemic has affected progress toward the Fast-Track targets across the entire HIV cascade. HIV services are being impacted by disruptions to supply chains, increased burdens on already strained health systems, and restriction of movement due to lockdowns [Figure 2].[iii]

Figure 2: Number of Countries Reporting HIV Service Disruptions due to COVID-19 (as of Jun. 2020)[iii]



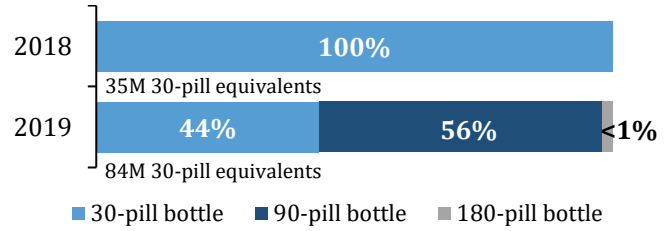
In light of these setbacks, it is more critical than ever that countries maintain and expand HIV services to ensure the COVID-19 pandemic does not further stall progress toward the Fast-Track targets.

COVID-19 expedited an ongoing shift toward multi-month dispensing to ensure continued access to ARVs

Multi-month dispensing (MMD), where patients receive several months of antiretrovirals (ARVs) at one time, allows for less frequent facility visits resulting in reduced travel for patients and less congestion in clinics. These benefits have additional importance during this pandemic when MMD could decrease the risk of exposure to COVID-19 and reduce the burden on healthcare facilities.

Even before the COVID-19 pandemic, PEPFAR prioritized MMD, requiring that it be included in annual quantifications and ceasing procurement of 30-pill bottles beginning in 2020.[iv] In 2019, many countries began to procure larger pack sizes as they moved to implement MMD [Figure 3].

Figure 3: TLD Orders by Pack Size (of those monitored by the APWG)[v]



The pandemic accelerated this ongoing shift with increased implementation of MMD by countries and expanded access across patient populations. As of July 2020, 90 percent of countries surveyed by the WHO had adopted MMD.[iii] Additionally, in many countries, access to MMD was expanded in 2020 to include children, TB/HIV co-infected individuals, and pregnant and breastfeeding women who were often previously ineligible.[vi]

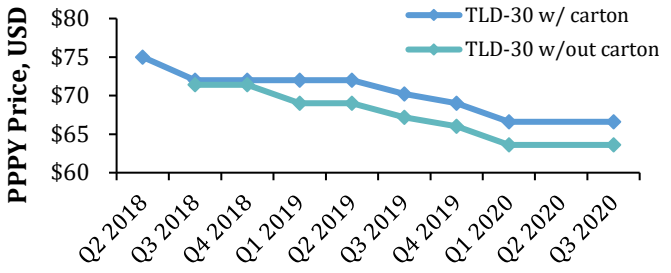
Data presented by the WHO at the AIDS 2020 virtual conference confirms MMD has intensified in countries where there is sufficient ARV stock. However, in places where there is stock insecurity, countries have curtailed MMD to avoid risk of national-level stockouts.[iii]

While the cost of HIV commodities continues to decrease, COVID-19 may cause pricing upticks

Recent years have seen decreasing costs for a number of HIV commodities. One of the most relevant examples of this is the cost of TLD, the WHO-preferred first-line (1L) adult treatment regimen, which has decreased by more than US $11 per patient per year (PPPY) over the past three years [Figure 4].[vii]

[1] The UNAIDS Fast-Track 90-90-90 treatment targets aim for 90 percent of people infected with HIV knowing their status, 90 percent of those diagnosed with HIV receiving treatment, and 90 percent of those being treated being virally suppressed.

Figure 4: Global Fund PPM Reference Price for TLD 30-pill bottle (USD, PPPY)[vii]

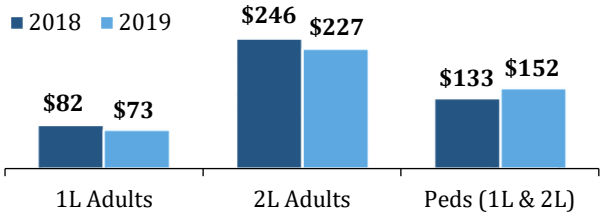


Note: Larger pack sizes may be available at lower costs.

CHAI estimates that the approximate ARV market size in generic-accessible[2] (GA) LMICs in 2019 was US $1.7B (based on weighted average treatment costs and formulations in-use in 2019).[viii] Since 2017, the ARV market size has stayed relatively stable at ~US $1.7B as ARV prices continue to drop while more PLHIV initiate treatment.[viii]

Between 2018 and 2019, adult 1L treatment costs in GA LMICs declined by nearly US $10 PPPY, reflecting a continued drop in the price of TLD and optimization away from more expensive regimens. Adult second-line (2L) treatment costs also continue to decline as patients transition to optimal, less expensive ATV/r- or DTG-based regimens. At the same time, pediatric treatment costs rose as patients move from sub-optimal but inexpensive NVP-based regimens to LPV/r-based regimens in the interim before generic pediatric DTG becomes available [Figure 5].

Figure 5: GA LMIC Weighted Average Regimen Prices[viii]



However, impacts to the production and distribution of medicines as a result of COVID-19 could potentially lead to increased costs.[ix] Due to COVID-19, ARV manufacturers are experiencing increased overhead and transportation costs, difficulty sourcing active pharmaceutical ingredients (API), and currency fluctuations, which could result in increased final product costs.[ix] For manufacturers in India alone, UNAIDS estimates that a 10–25 percent cost increase among suppliers as a result of these factors could result in an annual increase of final ARV costs between US $100M and US $225M, which would likely be passed on to buyers.[ix]

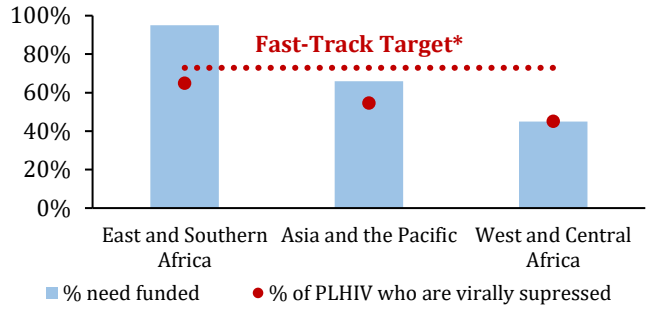
Reductions in HIV funding continue to impact progress against the epidemic

Amidst these potential COVID-related cost increases, funding for HIV programs continues to decrease, creating funding gaps in many countries and regions. Between 2018 and 2019, HIV funding in LMICs decreased from US $19B to US $18.6B.[ii] The level of funding received in 2019 only represents about 70 percent of the total UNAIDS-estimated need for the HIV response in LMICs.[ii]

There are further concerns that funding of the COVID-19 response could affect the funds allocated to HIV programs. For example, in March 2020, the Global Fund released guidance that countries could reallocate up to 5 percent of HIV funds for COVID-19 responses.[x] While this reallocation allowed countries to quickly access funds needed for COVID-19, continued long-term diversion of HIV funds could pose a threat to the success of HIV programs.

The amount of funding received often relates directly to progress, with improved viral suppression in regions where HIV funding met or came closer to the estimated need [Figure 6].

Figure 6: Regional Funding Need Met vs Progress on the 90-90-90 Targets[i,ii,xi]



**Achievement of all three Fast-Track targets results in a minimum of 73% of people living with HIV having suppressed viral loads.*

Community input continues to play an essential role in decision-making and product rollout

Communities of PLHIV and their advocacy continue to be critical in developing equitable treatment policies. For example, the 2018 Kigali women's meeting played a pivotal role in ensuring continued access to DTG for women of childbearing potential in the context of uncertainty about the (now resolved) neural tube defect safety signal.

Similarly, in February 2020, CHAI and AfroCAB, supported by Unitaid and BMGF, hosted a community meeting in Kigali, Rwanda to discuss the implications of weight gain and hyperglycemia associated with certain ARVs. The unanimous consensus of the meeting was that PLHIV should be allowed to make informed decisions regarding their treatment options.[xii]

> "We believe that people should be fully informed about the benefits and possible side effects of DTG. As the beneficiaries, **we believe in our ability to make informed decisions and we demand a choice in our treatment options**."
>
> *– 2020 Community Forum on DTG and Weight Gain[xii]*

This advocacy has helped to safeguard DTG access and ensure HIV programs can best serve the needs of PLHIV.

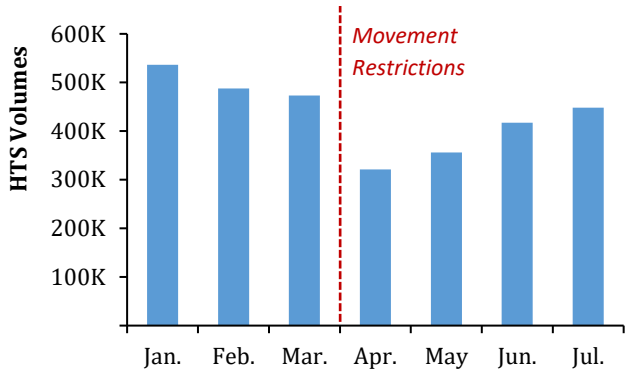
[2] See Appendix D (p. 28) for a definition of generic-accessible.

TEST SMART

HIV testing volumes initially impacted by the COVID-19 pandemic are beginning to rebound

The COVID-19 pandemic greatly impacted HIV testing services (HTS) across the globe, with 38 countries reporting disruptions in a WHO survey conducted in June 2020.[iii] These disruptions further exacerbated pre-COVID-19 concerns around reaching the First 90 target. Movement restrictions as a result of lockdowns hampered access to clinics and fear of exposure to COVID-19 made many people reluctant to visit health facilities.[xiii] Between March and April 2020, HTS volumes decreased between 30 percent and 63 percent across Malawi, Kenya, Zambia, and Zimbabwe.[xiv] There is some evidence that testing rates are beginning to bounce back, although not yet to pre-pandemic levels and the rate of rebound varies by country. For example, in Kenya, while HTS volumes initially decreased over 30 percent following COVID-19 related movement restrictions, they have rebounded significantly in recent months [Figure 7].[xiv]

Figure 7: HIV Testing Volumes in Kenya (Jan. – Jul. 2020)[xiv]

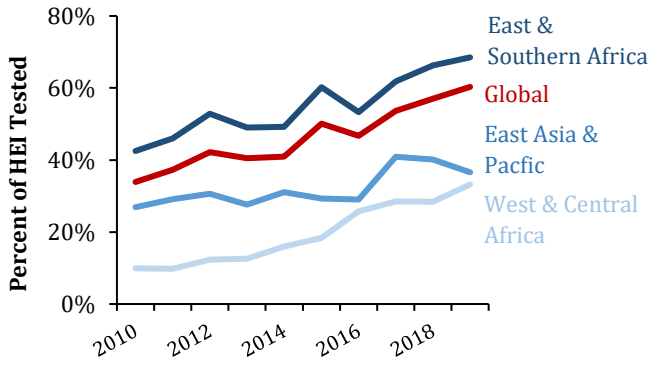


As lockdowns lift and countries continue to work to control the pandemic, increasing HTS volumes and improving linkage to care in the COVID-19 era (and after) will remain a priority for national programs.

Early infant diagnosis continues to scale up, albeit slowly

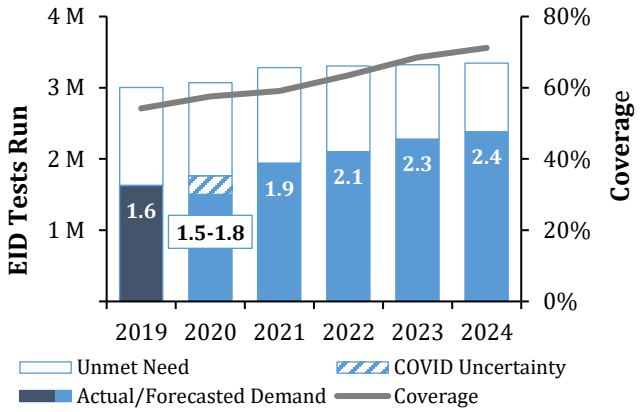
Scale-up of early infant diagnosis (EID) continues, although progress has been relatively slow. In 2019, 60 percent of HIV-exposed infants (HEI) globally received an HIV test within two months of birth, compared to only 26 percent in 2010 [Figure 8].[i] However, given the WHO recommends nucleic acid testing until nine months of age and risk of HIV-acquisition continues during breastfeeding, this two-month metric does not give a complete picture of the EID landscape.

Figure 8: HEIs Tested for HIV within 2 Months of Birth by UNAIDS Region (2010 – 2019)[i]



In 2019, programs conducted approximately 1.63M EID tests globally in LMICs, a slight increase from the 1.59M conducted in 2018 [Figure 9].[xv] Unlike viral load testing, which is experiencing significant disruptions during COVID-19 (see *Monitoring* section for further details, p. 20), EID testing volumes have fluctuated less but have still been impacted by the COVID-19 pandemic.

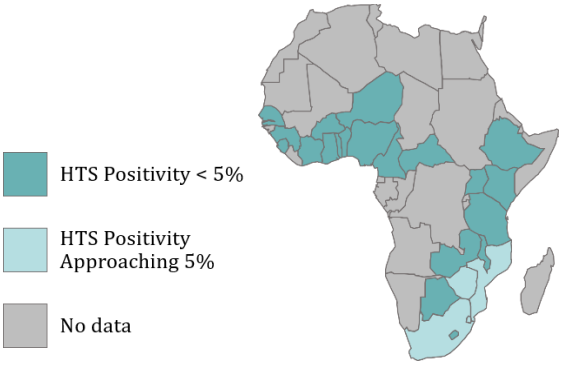
Figure 9: LMIC EID Demand Forecast[xv]



Updated WHO guidelines on HIV testing recommend a three-test algorithm in nearly all settings, and syphilis testing in antenatal care

The WHO continues to emphasize that countries should transition to three consecutive reactive tests to establish an HIV-positive diagnosis in countries where national HTS positivity (percent of tests run that are positive) is less than five percent.[xvi] Over recent years, successful scale-up of HTS resulted in increased identification of PLHIV and fewer undiagnosed PLHIV. As a result of these factors, when HTS positivity falls below five percent, the positive predictive value of two consecutive tests is less than the WHO recommendation. The WHO encourages adding a third consecutive test to limit false positive diagnoses. The majority of countries in sub-Saharan Africa (SSA) have now reached HIV positivity rates below five percent [Figure 10].[xvi]

Figure 10: HTS Positivity Rates in Sub-Saharan Africa (as of 2018)[xvi]



In countries that have not yet reached this threshold, national programs should continue to monitor HTS positivity and transition to a three-test algorithm when HTS positivity falls below five percent.

Additionally, there is now a strong WHO recommendation that pregnant women receive testing for HIV, syphilis, and Hepatitis B at least once during pregnancy, preferably in the first trimester.[xvi] The WHO confirmed that the dual HIV/syphilis rapid diagnostic test (RDT) is an option as the first HIV test for pregnant women in antenatal care (ANC), and that countries should review and consider the use of an HIV/syphilis dual test to simplify administration.[xvi] There are currently three HIV/syphilis dual tests with WHO prequalification (PQ): the Alere HIV/Syphilis Duo, the STANDARD Q HIV/Syphilis Combo Test, and the First Response HIV 1+2/Syphilis Combo Card Test, which cost between US $1.50 and US $3.40 per test.[xvii]

New strategies and insights on HIV testing for men could result in increased uptake

A number of studies have shown that men are less likely than women to test for HIV.[xviii] However, recent data provides new insights around the testing barriers men face, and highlights key opportunities to overcome them.

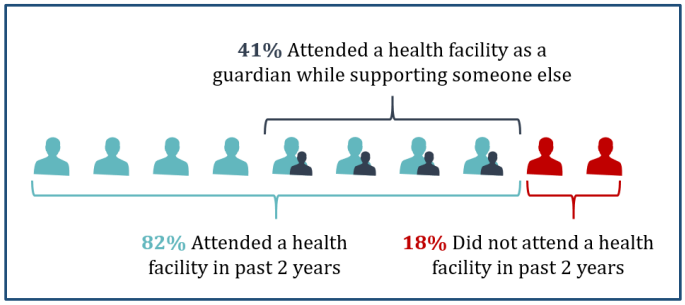
Data focused on testing in Zambia from the PopART Study suggests that the behavior of other members of the household plays an important role in a man's decision to get tested [Figure 11].[xix]

Figure 11: Previously Untested Men's Likelihood to Accept an HIV Test from a CHW[xix]

Additionally, the study found that certain characteristics of the community health worker (CHW) offering the test influenced the likelihood of testing acceptance. Men were more likely to accept a test offered by an older CHW compared to a CHW of a similar age.[xix]

Another study in Malawi challenged the narrative that men do not attend health clinics and therefore must be reached in the community. The data showed that 82 percent of men in need of testing attended a health facility in the past two years, and 41 percent of men's most recent visits were as a guardian supporting another individual [Figure 12].[xx]

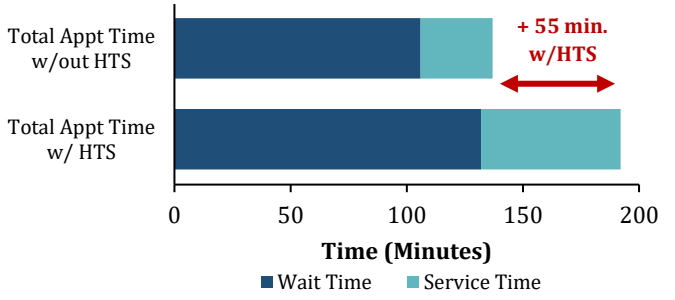
Figure 12: Health Facility Attendance of Adolescent Boys and Young Men (15 – 24) in Malawi[xx]



Despite the fact that men were presenting at clinics more often than previously thought, only seven percent of men reported that a healthcare worker (HCW) offered them an HIV test in the past year.[xx] This indicates a number of missed opportunities to test men for HIV while at clinics for other reasons.

Researchers found similar trends in South Africa in a study that also identified time burden as a barrier to uptake for HIV testing across both men and women. An analysis of duration of wait and service times found that receiving an HIV test increased patient wait time by 26 minutes and service time by 29 minutes [Figure 13].[xxi] This addition of almost an hour to a baseline visit time of more than two hours can be a prohibitive barrier for testing uptake.

Figure 13: Wait and Service Times in Health Clinics in South Africa[xxi]



This could also represent an opportunity for facility-based HIV self-testing (HIVST), which could decrease both service and wait times for test recipients.

The HIV self-testing market continues to grow, as new suppliers and increased donor support prime market for expansion

As of COP FY20, PEPFAR will now support facility-based HIV self-testing when prices are below US $1 per test.[iv] At this price, evidence suggests that HIVST could be a cost-effective method of increasing testing uptake for priority populations while simultaneously decreasing burden on

healthcare workers.[iv] While there are currently no HIVSTs available at this price, this policy is an important signal to the HIVST market that lower prices will likely result in increased product demand.

Additionally, in October 2019, the Children's Investment Fund Foundation (CIFF) pledged US $25M to support scale-up of HIVST during the Global Fund's 2020-2022 funding cycle.[xxii] The CIFF funding will be available in five countries (Cameroon, Mozambique, Nigeria, Tanzania, and Uganda) and aims to rapidly scale up HIVST implementation and significantly expand procurement.[xxii]

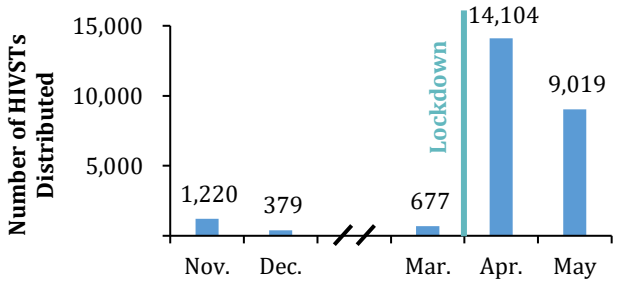
As these signals indicate potential growth in the HIVST market, the number of suppliers of HIVSTs with WHO PQ is also growing. In November 2019, Chembio Diagnostics became the fourth HIVST supplier with WHO PQ [Figure 14].[xxiii] There are also a number of additional HIVSTs in development with several already submitted to the WHO for prequalification.[xxiv] On the demand side, nearly all countries in sub-Saharan Africa have developed or are in the process of developing HIVST policies.[xxv]

Figure 14: HIVSTs with WHO PQ (as of publication)[xxiii]

Product Name	Manufacturer	Test Type
OraQuick	OraSure	Saliva
INSTI	bioLytical Labs	Blood
Mylan	Atomo Diagnostics	Blood
Sure Check	Chembio Diagnostics	Blood

Facility-based HIVST, both for primary use by the individual and through secondary distribution to sexual partners, also represents an opportunity to reduce patient/HCW contact during the COVID-19 pandemic. For example, distribution of HIVST kits in Eswatini by the Ministry of Health with support from Population Services International (PSI) increased rapidly during lockdown, allowing critical access to HIV testing when movement was restricted [Figure 15].

Figure 15: HIVST Kits Distributed in Eswatini (Nov. 2019 – May 2020)[xxvi]



Of the kits distributed in Eswatini, 49 percent were given to men and 17 percent to individuals who had never been tested for HIV in the past.[xxvi] Furthermore, of clients successfully reached for follow-up, the HIVSTs had high usage rates (89 percent) and of those newly diagnosed as HIV–positive, 59 percent ultimately initiated on ART.[xxvi] This example demonstrates the importance of HIVST in the COVID-19 era in particular, but also shows the benefits of HIVST for reaching priority populations.

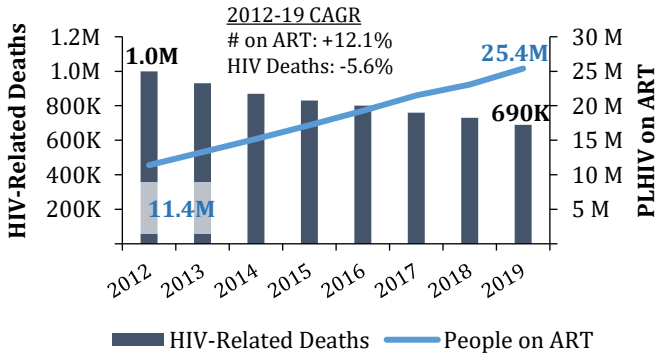
TREAT RIGHT

A) TREAT RIGHT BY ADDRESSING ADVANCED HIV DISEASE

HIV-related deaths slightly decreased in 2019, but remain high relative to ART scale-up

In 2019, HIV-related deaths fell below 700,000 [Figure 16].[i] Despite decreasing from one million deaths in 2012, this is still far too many given HIV is now a manageable chronic condition with 1L treatment available for under US $70 PPPY in LMICs.[vii] While improving access to antiretroviral therapy (ART) is a critical step in reducing HIV-related deaths, country programs must also improve access to commodities for the management of advanced HIV disease (AHD). This is especially salient with the COVID-19 pandemic disrupting service delivery and threatening to reverse previous gains in reducing HIV-related deaths.

Figure 16: All-Age Global HIV-Related Deaths and PLHIV on ART[i]



Underscoring the urgency of expanding access to AHD care beyond just ART coverage, 80.2 percent of hospitalized HIV/TB patients in a study in Malawi and South Africa were on ART (median duration one year) at admission, and two-month mortality post-hospitalization was still 30.7 percent.[xxvii] Rapid access to ART is only one piece of the WHO-recommended package of care for AHD [Figure 17].

Figure 17: WHO AHD Package of Care[xxviii]

World Health Organization

"A package of interventions including **screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation, and intensified adherence support interventions** should be offered to everyone presenting with advanced HIV disease."

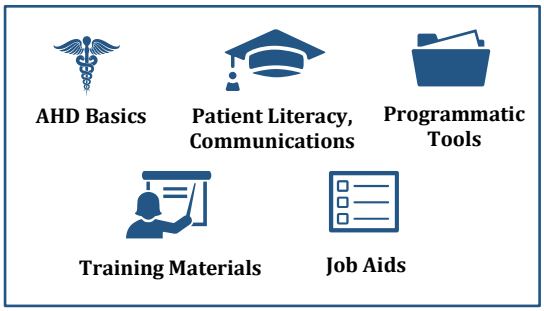
AHD services have not been spared from disruption during the COVID-19 pandemic and related lockdowns. In South Africa, TB testing decreased by 50 percent and CD4 testing decreased by 33 percent during their five-week level five lockdown.[xxix] In addition, cryptococcal antigen (CrAg)

testing decreased by approximately 25 percent during South Africa's level five lockdown.[xxx] There were similar trends in other countries in the region, which is worrisome as these diagnostic services are critical to reducing HIV-related mortality.

Robust implementation guidance from donors and partners assists countries in scaling up AHD care

In order to support countries with the rollout of the WHO AHD package of care, the Unitaid-CHAI Implementation Steering Committee and a coalition of partners[3] produced an AHD Toolkit hosted on the IAS Differentiated Service Delivery website: https://www.differentiatedcare.org/Resources/Resource-Library/Global-Advanced-HIV-DiseaseToolkit [Figure 18].

Figure 18: Key Components of the AHD Toolkit[xxxi]



Additionally, global and national stakeholders have issued new guidance to assist with AHD management [Figure 19].

Figure 19: Select Global, Regional, and National AHD Guidance

Global	• In July 2020 the WHO released **AHD guidelines focused on children and adolescents** [xxxii] • The WHO also released updated guidelines on the **prevention of TB**, including the first conditional recommendation for one-month daily rifapentine and isoniazid (1HP) [xxxiii]
Regional	• In November 2019, the **Southern African HIV Clinicians Society** released updated guidelines for the **management of cryptococcal disease among PLHIV** to reflect changes in the AHD landscape • Major updates include increasing the CrAg screening threshold from <100 to <200 CD4 cells/µL, and including 5FC for induction treatment of cryptococcal meningitis (CM) [xxxiv]
National	• **Lesotho's MoH published an AHD Implementation Manual** in June 2020 to support rollout of AHD services [xxxv] • The **MoH in Uganda incorporated key AHD provisions** in their 2020 consolidated HIV guidelines update, including the use of **5FC and liposomal amphotericin B as preferred therapy** for CM [xxxvi]

**Not exhaustive.*

In terms of funders, both PEPFAR and the Global Fund have signaled their support for AHD in recent COP guidance and the latest HIV Information Note, respectively [Figure 20].

Figure 20: Summary PEPFAR & GF AHD Guidance[iv,xxxvii]

	PEPFAR	Global Fund
CD4 Testing	Where AHD prevalence >15%	No minimum AHD prevalence rate
CrAg Screening	Under 200 CD4 cells/µL	Under 200 CD4 cells/µL
CM Treatment	According to WHO guidelines	Supportive
TPT	Required	Required where high TB/HIV co-infection

New pricing deals and regulatory approvals expand access to vital AHD commodities

In the past year, a flurry of pricing deals and new products entered the market that will allow more patients with AHD to access life-saving commodities [Figure 21].

Figure 21: AHD Product Pricing & Supply Updates[xxxviii]

	Product	Price (USD, EXW)	Suppliers
Pricing Updates	**5FC** (500 mg) – 100	$75/pack *(prev. $110)*	Mylan, Strides
	RPT (150 mg) – 24	$5/pack *(prev. $15)*	Sanofi
	RPT/INH (300/300 mg) – 36	$15/pack *(new)*	Macleods
	VISITECT AHD RDT	$3.98/test *(new)*	Omega

Flucytosine (5FC)

Through the Unitaid-CHAI AHD Initiative's partnership with the Global Fund and PEPFAR, 5FC from Mylan and Strides received favorable quality reviews from FHI 360, allowing for procurement prior to US Food and Drug Administration (US FDA) approval or WHO PQ. Since that initial quality audit, Strides attained US FDA approval and Mylan applied for WHO PQ.[xxxix,xl] 5FC can now be produced at scale to meet demand in LMICs, and early adopters include Botswana, Lesotho, Nigeria, and others.[xli]

CHAI and Unitaid also negotiated the price per pack down from US $110 to US $75 (EXW), representing an approximate reduction of 30 percent. Prior to these quality and pricing developments, 5FC was only intermittently accessible and relatively costly to procure.[xxxviii]

Rifapentine (RPT)

In Q4 2019, Unitaid and partners successfully negotiated a 70 percent reduction in the price of Sanofi's RPT, a medicine used in TB preventive therapy (TPT). The price per 3-month

[3] See AHD toolkit website for full list of partners.

course of RPT (for use in 3HP) decreased from US $45 to US $15 (EXW) as part of a volume-based discount.[xlii] Country programs taking advantage of this price reduction include Cambodia, Costa Rica, Malawi, Zimbabwe, and others.[xli]

Sanofi's RPT has both US FDA approval and WHO PQ.[xxxix,xl]

RPT/Isoniazid (RPT/INH)

Macleods has developed a generic fixed-dose combination (FDC) of RPT and isoniazid (INH) for use in 3HP as a form of TPT. Countries planning to procure this FDC include Brazil, Eswatini, Ghana, Kenya, Zambia, and others.[xli]

CHAI, with Unitaid's backing, negotiated the price of a full 3-month treatment course to be set at US $15 (EXW), and Macleods currently has received Global Fund Expert Review Panel (ERP) status and has filed for WHO PQ.[xliii]

VISITECT CD4 Advanced Disease

Unitaid and CHAI have also announced an innovative agreement with medical device manufacturer Omega Diagnostics to help deliver groundbreaking, device-free same-day CD4 testing for PLHIV in over 130 LMICs at just US $3.98 per test (EXW).[xliv]

In addition to this pricing agreement, implementing partners can apply for Unitaid funding to support the rollout of Omega's VISITECT CD4 Advanced Disease test via an Early Market Access Vehicle (EMAV), coordinated by CHAI. CHAI has received expressions of interest from multiple countries, and procurement has commenced in Nigeria and Uganda.

See Figure 22 for more information on the product, pricing agreement, and EMAV. Partners may reach out to emav@clintonhealthaccess.org for more information.

Figure 22: VISITECT CD4 AHD and EMAV[xliv,xxiii]

Product Info

- VISITECT CD4 Advanced Disease Rapid Test
- Instrument-free point-of-care CD4 test to identity patients with CD4 cell counts below 200 cells/µL (threshold for AHD)

Benefits

- Can be used in all levels of care by any cadre
- Rapid diagnosis of AHD, enabling providers to offer WHO package of care to patients in need of intervention

EMAV

- Initiative to allow implementers to gain early experience using the product with product costs covered by Unitaid
- Interested governments and implementing partners can submit expression of interest: emav@clintonhealthaccess.org

Price & Reg.

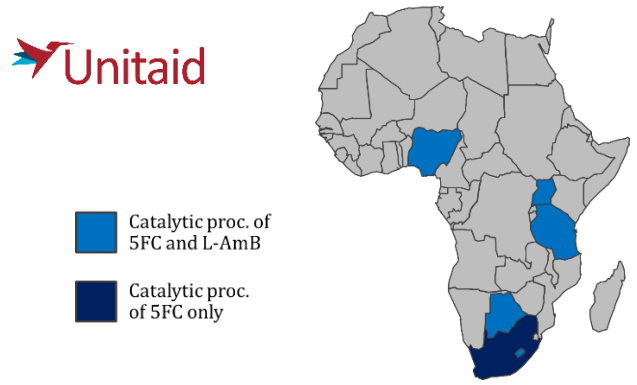
- US $3.98 per test (EXW) available in over 130 low- and middle-income countries
- Has received WHO prequalification

Technical working groups oversee catalytic procurement of optimal AHD commodities to jumpstart programs in sub-Saharan Africa

Catalytic procurement can serve as a mechanism for country programs to quickly gain experience with new products and mobilize future investment from procurers.

In late 2019 and early 2020, led by ministries of health and national technical working groups, catalytic procurement funded by Unitaid began for key AHD commodities such as 5FC and L-AmB in a number of countries in sub-Saharan Africa [Figure 23].

Figure 23: AHD Catalytic Procurement Highlights



The early experience country programs will gain with these catalytic procurements as part of a phased implementation will enable the broader rollout of the AHD package of care, while also generating evidence and lessons learned for further adoption in other high-burden countries.

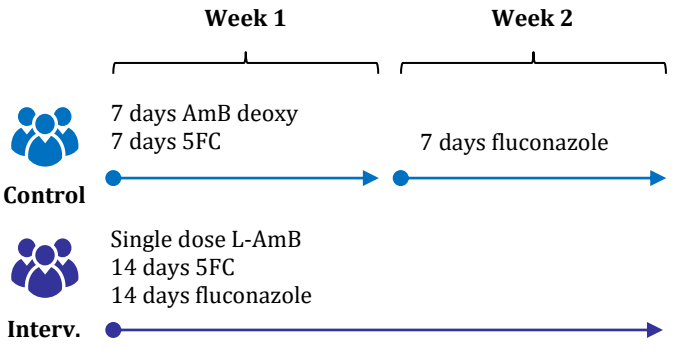
For example, Malawi's phased implementation involves the initial rollout of the AHD package of care in over 100 facilities. These sites are located in every district, and are representative of the diversity in health facilities across Malawi. The second phase will include over 250 additional facilities, and will utilize lessons learned from the initial phase of the implementation.[xlv]

Ongoing clinical trials and new products in development may further improve AHD care

While AHD partners have spent much of the last year improving access to existing products, a number of clinical trial results and pipeline products could further improve care of PLHIV with AHD.

Current WHO guidelines for the treatment of cryptococcal meningitis recommend a week of amphotericin B deoxycholate (AmB) and 5FC, followed by a week of fluconazole.[xlvi] However, AmB is poorly tolerated and requires extensive monitoring for drug toxicity. The AMBITION trial looks to assess whether a single, high- dose of *liposomal* amphotericin B (L-AmB) is non-inferior to current WHO recommendations [Figure 24]. If successful, this would drastically simplify the management of cryptococcal meningitis, reduce toxicity, and be less costly.

Figure 24: AMBITION Trial Study Design[xlvii]



On the diagnostics front, two products are in development that would improve and further decentralize the diagnosis of both tuberculosis and cryptococcal disease.

Fujifilm is developing a urine-based TB LAM test, FujiLAM, for diagnosing TB among AHD patients. The FujiLAM test has an improved sensitivity over the existing TB LAM test from Abbott.[xlviii] However, the COVID-19 pandemic led to delays in the WHO's clinical evaluation, which postponed its potential endorsement and ultimate rollout.

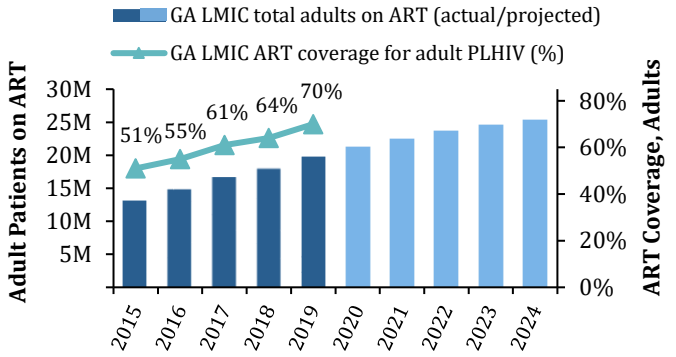
In terms of cryptococcal disease, current rapid diagnostic tests in LMICs are qualitative and require confirmatory diagnosis of cryptococcal meningitis via lumbar puncture, which is operationally challenging in many LMICs. IMMY is developing a semi-quantitative CrAg lateral flow assay that may negate the need for confirmatory lumbar puncture to determine treatment options. It will allow HCWs to stratify CrAg-positive patients according to levels of antigen, which can provide the basis for differentiated management. However, the COVID-19 pandemic has delayed CE-marking and US FDA approval.

B) TREAT RIGHT WITH OPTIMAL ARVs FOR ADULT PATIENTS

Over 24 million adults on treatment globally in 2019, with over 19 million in GA LMICs

The number of patients (re-)initiating on ART continues to increase, with over two million adult patients added between 2018 and 2019.[i] In GA LMICs, adult ART coverage increased to 70 percent in 2019 from 64 percent in 2018 [Figure 25].[xlix]

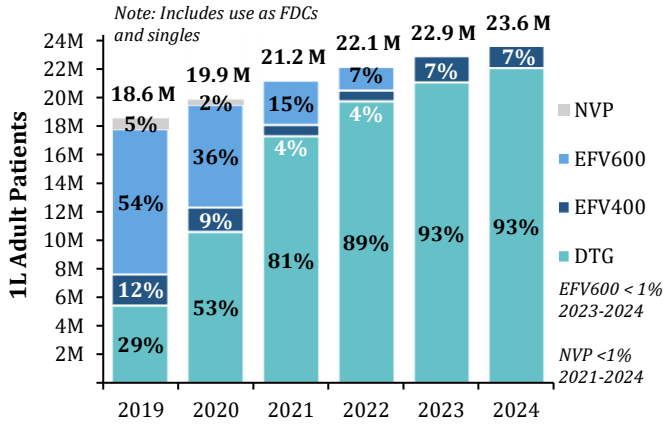
Figure 25: Adults on ART and Coverage in GA LMICs[xlix]



Ongoing rollout of DTG picks up speed in LMICs as countries phase out NVP and EFV600

The rollout of DTG-based regimens continues to scale up with large increases anticipated over the next few years. In 2019, 29 percent of 1L adults in GA LMICs were estimated to be on DTG-based regimens, with that number increasing to almost 90 percent by 2022 [Figure 26].

Figure 26: 1L Adult INSTI/NNRTI Use in GA LMICs, Patient Growth and Share[xlix]



There was an initial delay in access to DTG in 2018 for some women of childbearing potential due to concerns of neural tube defects (NTDs) among infants born to women taking DTG at conception. However, updated evidence from the Tsepamo study demonstrated that the prevalence of NTDs among infants born to women receiving DTG at conception

seems to be stabilizing at approximately 0.2 percent, which is not statistically different from women taking non-DTG regimens.[l] Consequently, DTG scale-up has now bounced back to match pre-NTD safety signal expectations of uptake and adoption. In fact, current DTG scale-up closely matches CHAI's forecast published in 2017 (pre-safety signal) which projected 30 percent DTG market share in 1L in 2019.[li]

The majority of LMICs have now adopted or have plans to adopt TLD, with inclusion or planned inclusion in over 120 national guidelines.[xxv] As of publication, there were more than six million patients estimated to be on TLD in GA LMICs, and several countries including Kenya, Nigeria, South Africa, and Tanzania have transitioned over 700K 1L patients to TLD.[lv]

The number of TLD suppliers also continues to increase, with nine suppliers with WHO prequalification and/or tentative US FDA approval as of publication [Figure 27].

Figure 27: US FDA TLD Approvals/WHO PQ (as Sep. 2020)[xl,xxxix]

Tentative US FDA	WHO PQ
Aurobindo	Cipla
Celltrion	Hetero
Hetero	Laurus
Laurus	Macleods
Macleods	Mylan
Mylan	Strides
	Sun Pharma

As countries transition to DTG-based regimens, NVP and EFV use continues to decrease. Given PEPFAR and the Global Fund no longer support the procurement of NVP for adult or pediatric treatment (only for infant prophylaxis), NVP is expected to comprise a negligible portion of future regimens. EFV use has also decreased with the minority of 1L patients who will remain on EFV transitioning from EFV600 to EFV400 as countries move to implement the WHO alternate regimen of TLE400.

Evidence of weight gain with DTG continues to mount, particularly when combined with TAF

As rollout of DTG accelerates, additional data is providing insights on its use in broader populations. New evidence of weight gain on DTG is generating conversations on potential implications for the ongoing rollout of TLD and future optimal products. The ADVANCE trial 96-week results, presented at AIDS 2020, found that weight gain continues in patients on DTG with no evidence of a plateau. The data also suggest higher weight gain in women and in DTG combinations with TAF. The ADVANCE trial is continuing until week 192, and will provide further information on long-term weight gain with DTG and TAF.[lii]

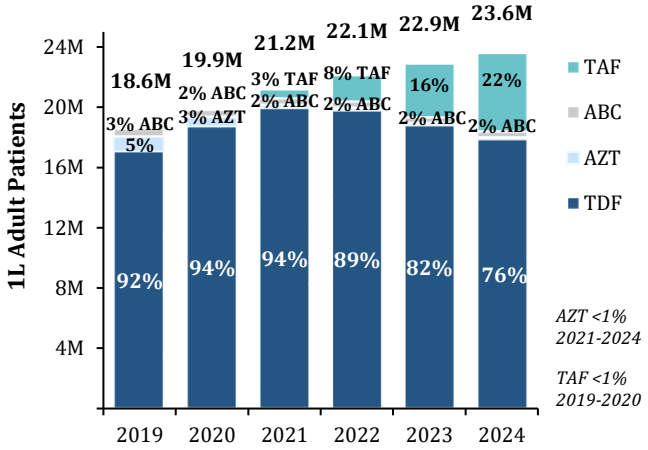
As discussed in the *General Trends* section (p. 8), CHAI and AfroCAB hosted a community forum (with support from Unitaid and BMGF) in February 2020 to discuss the evidence of weight gain with DTG and determine the community response. PLHIV representing 21 countries in Africa unanimously concluded that PLHIV should be allowed to make informed decisions regarding their treatment, and that patients should be informed of potential side effects of all treatment options.[xii]

TDF continues to comprise the majority of 1L regimens as countries consider the place of TAF

As the majority of 1L patients transition to TLD, TDF's share of 1L regimens continues to increase [Figure 28]. Introduction of TAF, a tenofovir pro-drug that could replace TDF at a reduced cost and with a smaller pill size, has been limited to date as countries focus on the transition to TLD. Given TAF is only currently recommended by the WHO for use in adults in special circumstances, TAF will likely play a secondary role to TDF in adult 1L regimens unless it is promoted to alternate or preferred status in a future guidelines update (Figure 28 below assumes TAF becomes an alternate regimen option).[liii]

Additionally, a broader implementation of TAF is dependent on outstanding data on use in HIV/TB co-infected patients and pregnant women as well as ongoing research on weight gain. Data to support rollout in these populations is expected by the end of 2020.

Figure 28: 1L Adult NRTI Use in GA LMICs, Patient Growth and Share[xlix]



**Totals may not sum to 100% due to rounding.*

Botswana, Zambia, and Zimbabwe have become early adopters of TAF with limited introductions targeting specific populations. For example, Zimbabwe has included TAF as an alternate 1L and 2L adult regimen in their treatment guidelines and has ongoing limited introduction for patients over 50, patients with creatinine clearance of 30-60 ml/min., and HIV/Hepatitis B co-infected patients.[liv] Zambia has also began limited introduction with ongoing research and extensive pharmacovigilance monitoring [Figure 29].[lv]

Figure 29: TAF Adoption in Zambia[lv]

TAF Adoption in Zambia

Implementation

- Included in national guidelines as an alternate regimen for adults and a preferred regimen for some special populations
- Current limited introduction prioritizes children >25 kg and adults with renal failure
- 125K patients on TAF as of publication

Research

- VISEND, a randomized control trial for DTG-based regimens including TAF, will provide further insights on a number of topics including weight gain

Active Pharmacovigilance

- Zambia is conducting cohort event monitoring for drug effects of DTG and TAF including weight gain, hyperglycemia, and rashes
- Nine sentinel sites are currently active with anticipated expansion to 77 sites and a target sample of 99,000 PLHIV on ART to be followed for over two years

Presenters at AIDS 2020 raised a potential benefit of TAF in women using Depo-Provera (Depo), one of the most common forms of contraception in sub-Saharan Africa. Depo use was found to be associated with a doubling of bone loss in women on TDF-containing ART in clinics around Kampala.[lvi] Given TAF has less impact on bone density loss compared to TDF, this could represent a potential use case for TAF, albeit more research is needed.[lvii]

Countries begin to eye second-line DTG use as first-line transitions wrap up

As a 2L treatment, DTG has significant clinical and cost benefits compared to LPV/r.[lviii,vii] While DTG has already been adopted as a preferred regimen for *new* 2L patients in many countries, some countries are planning to proactively switch *existing* 2L patients on protease inhibitors (PIs) to DTG. Some of this transition began earlier in 2020 due to shortages with adult LPV/r, which required programs to transition patients to more optimal regimens. While these supply shortages have since been resolved, DTG will still play an increasing role in 2L treatment moving forward.

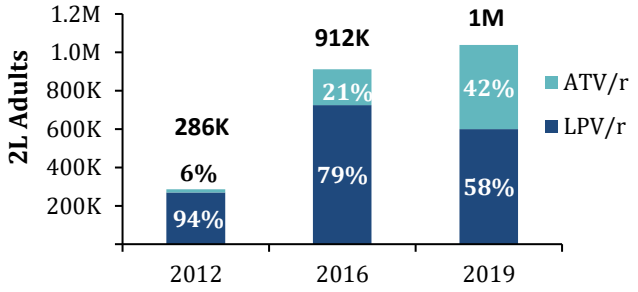
Recently generated evidence found that retaining TDF after 1L failure was associated with better outcomes compared to switching to AZT among patients in Haiti. Patients who switched to an ATV/r-based 2L regimen had improved retention, adherence, and viral load (VL) suppression if they retained TDF instead of switching to AZT. For patients switching to a LPV/r-based 2L regimen, retaining TDF was associated with improved VL suppression but not improved retention or adherence [Figure 30].[lix] Based on this new data, TLD as a FDC (vs DTG singles with AZT/3TC) could have an expanded role in 2L for patients failing TDF-containing non-DTG 1L ART.

Figure 30: Impact of Retaining TDF vs. Switching to AZT after 1L Treatment Failure in Haiti[lix]

	Retaining TDF in 2L with ATV/r	Retaining TDF in 2L with LPV/r
Improved retention	✓	X
Improved adherence	✓	X
Improved VL suppression	✓	✓

While country programs weigh decisions on DTG's use in 2L, ATV/r has continued to increase its market share compared to LPV/r [Figure 31]. Given the supply issues, LPV/r use will likely decrease even further in the coming years as programs replace it with ATV/r or DTG.

Figure 31: 2L Adult PI Market Share in GA LMICs (2012, 2016, 2019)[xlix]



In the long term, DRV/r will also likely play a role in adult 2L treatment, especially for patients who are failing a DTG-based regimen and need to move to the best available PI. However, the lack of an affordable generic FDC of DRV co-formulated with RTV has limited uptake thus far and represents an equity gap given the US FDA first approved DRV 14 years ago in 2006.[xxxix] CHAI and Unitaid continue to work to address the affordability of a generic DRV/r (400/50 mg) FDC for use in 2L.

Novel adult treatment products currently in development continue to make progress

The development of new adult treatment products continues, expanding delivery options and introducing new classes of drugs. Two adult pipeline products have recently received regulatory approval in the US [Figure 32].

Figure 32: Recently Approved Adult ART Products

DOLUTEGRAVIR/LAMIVUDINE (*DOVATO*)

- *Dovato*, a once-daily, two-drug oral regimen containing DTG and 3TC received US FDA approval for *treatment-experienced* patients in Aug. 2020 having already received approval for use in *treatment-naïve* patients in Apr. 2019 [lx]
- Questions remain concerning the use of two-drug regimens in LMIC settings due to concerns about resistance and use in special populations (e.g., TB)

FOSTEMSAVIR

- ViiV's *Rukobia* (fostemsavir) became the first US FDA-approved attachment inhibitor when it received approval for heavily treatment-experienced PLHIV in Jul. 2020 [lxi]

Additional products are in development, several of which have the potential to transform treatment delivery with injectable or other long-acting formulations [Figure 33].

Figure 33: Pipeline Adult Products

CABOTEGRAVIR/ RILPIVIRINE LONG-ACTING INJECTABLE FOR TREATMENT

- In Dec. 2019, the US FDA declined approval of ViiV's long-acting injectable cabotegravir/rilpivirine for treatment (*Cabenuva*) due to concerns regarding chemistry and manufacturing controls [lxii]
- ViiV resubmitted *Cabenuva* to the US FDA in Jul. 2020 with a decision expected in early 2021[lxiii]
- Health Canada approved *Cabenuva* in Mar. 2020 [lxiv]

ISLATRAVIR

Islatravir, a NRTTI (nucleoside reverse transcriptase translocation inhibitor) in development by Merck with high potency and a long plasma half-life, is under consideration for HIV treatment and oral pre-exposure prophylaxis (PrEP).

Treatment

- Data from a Ph. IIb study of islatravir plus doravirine and lamivudine for treatment-naïve patients showed no viral rebound >200 copies/ml in the islatravir arms at week 48 [lxv]
- Ph. III studies of a two-drug FDC of doravirine/islatravir are planned or ongoing [lxv]

Oral PrEP

- Given the high potency of islatravir, a once-monthly oral formulation (reducing pill burden and potentially increasing adherence) is in a Ph. II clinical trial [lxv]

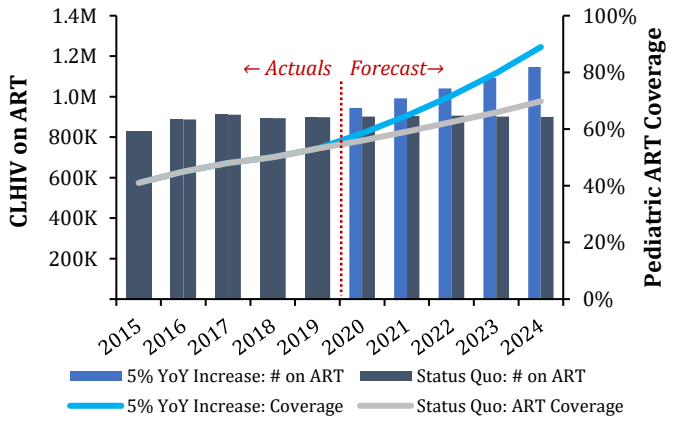
The HIV i-Base Pipeline report contains more information on pipeline products: www.i-base.info/htb/37221.

C) TREAT RIGHT WITH OPTIMAL ARVs FOR PEDIATRIC PATIENTS

Innovative ways to find and retain children on life-saving treatment needed to avoid stagnant pediatric ART numbers

Between 2016 and 2019 there has been very little change in the absolute number of children living with HIV (CLHIV) on ART in GA LMICs [Figure 34].[i] The slight, concomitant increase in coverage is due to the fact that the number of CLHIV (i.e., the denominator) is decreasing each year as children age into the adult cohort or die, and prevention of mother-to-child transmission (PMTCT) continues to succeed. Under the status quo, CHAI estimates the number of CLHIV on ART in GA LMICs to remain stable at around 900K through 2024, even though coverage is projected to increase to 70 percent.[xlix] However, this trend is not set in stone. Adopting innovative approaches to case finding and retention that increase the number of CLHIV on ART by just five percent year-over-year (YoY) will lead to an estimated 2024 coverage rate of 90 percent ["5% YoY Increase: Coverage" in Figure 34].[xlix]

Figure 34: Actual and Forecasted Pediatric Patients on ART and Pediatric ART Coverage in GA LMICs[i,xlix]



Regionally, while pediatric treatment coverage is relatively low across the board, West and Central Africa continues to fall behind with only 33 percent coverage compared to 58 percent in East and Southern Africa.[i]

Continued pediatric optimization efforts have paid off, with a sharp decrease in AZT/3TC/NVP procurement and use in 2019

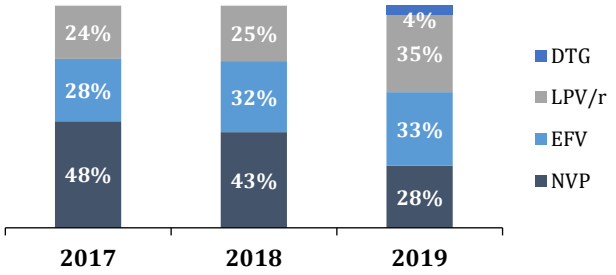
With both PEPFAR and the Global Fund's directives to stop procurement and use of NVP for treatment in 2019, there has been a dramatic decrease in procurement of these products. In 2019, pediatric dispersible AZT/3TC/NVP (ZLN) was not amongst the top five pediatric products procured by volume for the first time since 2010 as tracked by the ARV Procurement Working Group (APWG) [Figure 35].[v,lxvi] NVP oral solution is still eligible for PEPFAR and Global Fund procurement for use as infant prophylaxis.

Figure 35: Top Five Pediatric Products Procured by Number of Packs (as Monitored by the APWG)[v,lxvi]

2010		2019	
1	AZT/3TC/NVP (60/30/50 mg)	1	ABC/3TC (120/60 mg)
2	NVP Oral Solution	2	LPV/r (100/25 mg)
3	3TC Oral Solution	3	NVP Oral Solution
4	EFV (50 mg)	4	ABC/3TC (60/30 mg)
5	d4T/3TC/NVP (6/30/50 mg)	5	LPV/r (40/10 mg) oral granules

While not completely eliminated in use, NVP (primarily in the form of ZLN) accounted for only 28 percent of NNRTI/PI use in pediatric patients at end 2019 (compared to 48 percent in 2017) [Figure 36].[xlix] CHAI expects this to drop precipitously in 2020 as stocks run down (without replenishment) and country programs continue to remove NVP from national formularies in favor of optimal products.

Figure 36: Estimated Pediatric NNRTI/PI/INSTI Use in GA LMICS[xlix]



**Regimens with backbones comprised of pediatric formulations only.*

It is important to note that while programs are phasing out NVP use in *treatment*, it is still a critical product for use as infant prophylaxis (especially in the oral solution formulation). As such, suppliers must ensure they continue to produce this vital product, which saw shortages and extended lead times in 2020 due to API issues.

Generic, pediatric-friendly formulation of DTG expected by end of 2020

In 2019, the WHO recommended DTG 50 mg tablets for use by children down to 20 kg.[liii] ViiV filed their DTG 5 mg dispersible reference product with the US FDA in December 2019 and received approval in June 2020. This approval also included a label update to the DTG 50 mg label for use in children down to 20 kg (which aligns with WHO recommendations on this dosing).[lxvii]

To accelerate access to pediatric-friendly, WHO-preferred DTG formulations for CLHIV below 20 kg, CHAI and Unitaid, in cooperation with ViiV, collaborated with Mylan and Macleods to develop a generic DTG 10 mg dispersible and scored product. Mylan and Macleods filed new drug applications for their DTG 10 mg products with the US FDA in Q2 2020, with the first tentative approval expected by the end of 2020. When approved, this would represent the shortest time from innovator to generic approval for an ARV in US FDA history.

In addition to the clinical benefits of DTG, the DTG 10 mg dispersible and scored tablets will significantly reduce pill burden and simplify dosing in children [Figure 37].

Figure 37: WHO Pediatric Dosing by Weight Band[lxix]

	3-5.9 kg	6-9.9 kg	10-14.9 kg	15-19.9 kg
DTG (10 mg) Disp. and Scored Tablets	0.5	1.5	2.0	2.5
LPV/r (40/10 mg) Pellet Capsules/ Granule Sachets	4	6	8	10
ABC/3TC/LPV/r (30/15/40/10 mg) Granule Capsules	4	6	8	10

LPV/r-based products likely to play smaller role after DTG 10 mg approval

The PEPFAR and Global Fund directives to phase out NVP for treatment in 2019 have caused an increase in LPV/r use as a replacement until a pediatric formulation of DTG is generically available.

To address this increased demand, both Cipla and Mylan scaled up the production capacity of their LPV/r 2-in-1 pellets and granules, respectively, which has eased the long-standing global supply shortage.[lxviii] LPV/r (100/25 mg) tablets are another LPV/r-based option for children greater than 10 kg and able to swallow whole tablets, although there have been ongoing supply shortages since late 2019.

Cipla's ABC/3TC/LPV/r 4-in-1 granules are anticipated to receive US FDA approval in Q4 2020, almost concurrently with DTG 10 mg dispersible and scored tablets. Given the proximity of these expected approvals, the WHO and other partners recommend country programs focus on the rollout of DTG per WHO recommendations, which list it as the preferred 1L and 2L option for CLHIV.[liii] LPV/r-based formulations like the 4-in-1, while important, will likely be retained for use in the small number of CLHIV who are intolerant to DTG, at least until better a better PI option, such as DRV/r, is developed as an FDC.

> "Overall, countries should focus on rapidly implementing optimal regimens according to WHO guidelines and **accelerate transitions to DTG-based therapies."**
>
> ***- WHO Policy Brief, July 2020***
> *Considerations for Introducing New Antiretroviral Drug Formulations for Children*[lxix]

Additional optimal pediatric products further afield

With the support of Unitaid, CHAI is working to accelerate development of the next generation of optimal formulations of pediatric ARVs.

A number of generic manufacturers are working to develop a pediatric triple FDC of ABC/3TC/DTG (ALD) to simplify treatment and provide the WHO-recommended regimen for

children in a single formulation. However, national programs should plan to take rapid advantage of *current* innovations in pediatric treatment (e.g., DTG 10 mg dispersible, scored single tablets) as they come to market, while not delaying optimization to await an ALD FDC.

Darunavir, a best-in-class protease inhibitor, has long been a priority product for the Pediatric ARV Drug Optimization Group (PADO). However, generic suppliers have not yet developed a dispersible FDC with ritonavir due to high API costs and a relatively small market size. This drug is still needed for children who fail DTG-based therapies and move to 2L and third-line (3L) regimens. In partnership with Unitaid, CHAI launched an incentive program in September 2020 to catalyze the development of a pediatric DRV/r FDC and bring this product to market for CLHIV in-need. More information can be found at: https://www.clintonhealthaccess.org/rfp-for-2nd-line-hiv-treatment-for-children/.

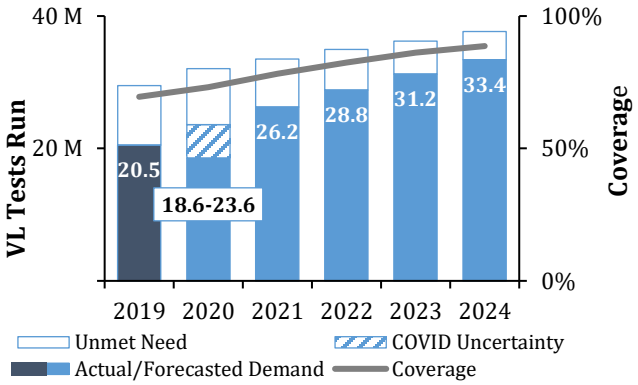
Planning for development of pediatric-friendly, dispersible TAF-containing products has started through a grant Penta received from the European & Developing Countries Clinical Trials Partnership (EDCTP), in which CHAI is listed as the formulation development partner, to investigate the dosing and other clinical data to support these products.

D) TREAT RIGHT WITH APPROPRIATE TREATMENT MONITORING

Viral load (VL) scale-up continues, with most countries adopting routine VL for monitoring

In 2019, the number of viral load tests run in LMICs passed 20 million for the first time, representing a global coverage rate of approximately 70 percent [Figure 38].

Figure 38: LMIC Viral Load Demand Forecast[lxx]



This 20-million-test milestone comes as a recent WHO survey shows that nearly all countries have adopted routine viral load testing for treatment monitoring, with fewer than ten not implementing viral load testing or using targeted viral load testing only.[xxv]

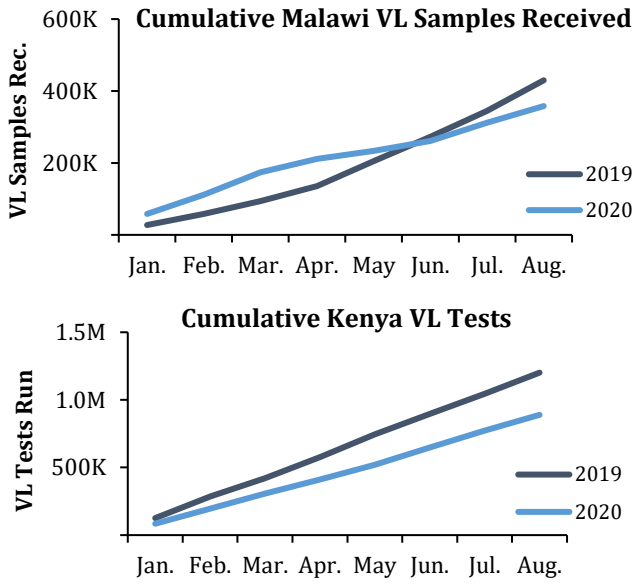
As viral load programs mature in many countries, national programs have developed more nuanced algorithms for high-risk groups, such as more frequent testing for children and adolescents. Additionally, there has been a shift to recognize the need to manage low-level viremia in patients with viral loads below 1,000 copies/mL but above the lower detection limit (LDL) of the test [Figure 39].

Figure 39: Sub-Population VL Algorithms[lxxi,lxxii,lxxiii]

	Children and Adolescents	Low-Level Viremia
Eswatini	Every 6 months *(ages 10-19)*	N/A
Kenya	Every 6 months *(ages 0-24)*	Between LDL and 1,000 copies/mL; Manage as if over 1,000 copies/mL
Namibia	Every 6 months *(ages 0-19)*	Between 40-1,000 copies/mL; Consult specialist

The COVID-19 pandemic and related lockdowns are impacting viral load testing volumes, with many countries seeing declines in testing so far in 2020 [Figure 40]. While it remains to be seen how the future of the pandemic will play out in LMICs, CHAI is hopeful that viral load testing volumes in 2021 will rebound back to their pre-COVID trajectory as countries restart critical health services.

Figure 40: COVID-19 Impact on VL Volumes[lxxiv,lxxv]

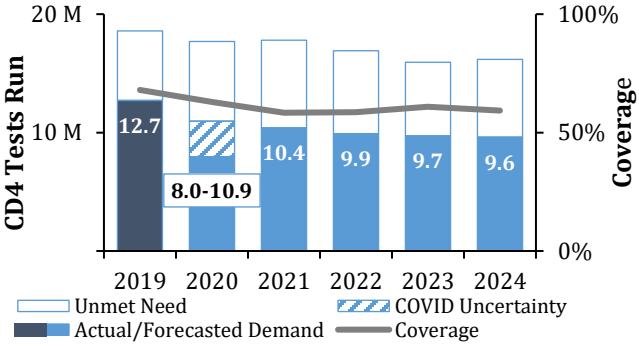


Despite increased access to VL testing, millions of device-based CD4 tests still conducted

The overall global need and demand for CD4 testing is decreasing as viral load continues to scale up and optimal regimens improve viral suppression rates. Despite this overall decrease, CHAI estimates that programs conducted nearly 13 million CD4 tests in 2019 [Figure 41].

Although the need for CD4 tests is decreasing overall, CD4 testing at treatment (re-)initiation is still required to identify patients with AHD. This need will remain even if there is universal viral load testing coverage.

Figure 41: LMIC Device-Based CD4 Demand Forecast[lxxvi]



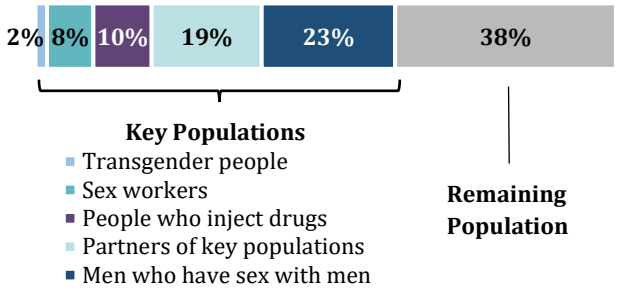
The widespread rollout of the VISITECT CD4 Advanced Disease test (discussed in the *Advanced HIV Disease* section, p. 13), may shift the market away from device-based CD4 testing to device-free CD4 testing, allowing for further decentralization and improving rates of AHD identification. The widespread use of this product may also slightly increase CD4 volumes, as countries who are not currently testing ART initiates may begin given the convenience and low cost of the VISITECT product.

STAY NEGATIVE

The number of new annual HIV infections remained stagnant at 1.7M in 2019

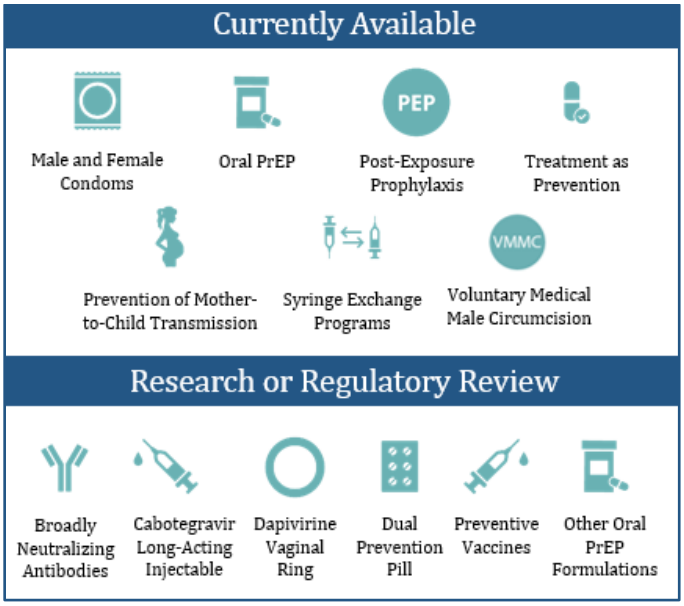
While HIV infection rates decreased modestly in recent years, the number of new infections held constant between 2018 and 2019 at 1.7M.[i] The share of key population-driven infections continues to increase, with over 60 percent of new infections occurring in key populations and their partners [Figure 42].

Figure 42: Distribution of New HIV Infections Globally by Population, 2019 (n=1.7M)[ii]



As we approach the 2020 Fast-Track target deadline, it is clear that the world will not achieve the annual target of 500K or fewer new HIV infections.[ii] COVID-19 disruptions further threaten global progress toward this goal as a number of countries report disruptions to oral PrEP, VMMC, and PMTCT programs.[iii] Ensuring and expanding access to existing interventions and advance planning for pipeline products are critical to curbing the HIV epidemic [Figure 43].

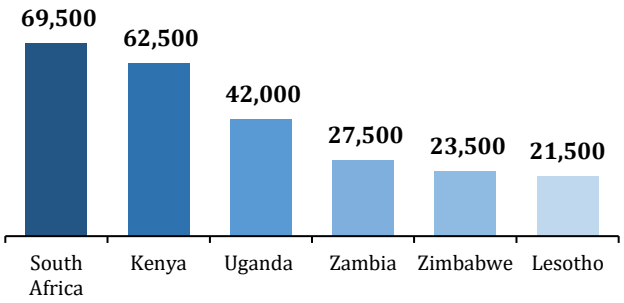
Figure 43: Existing Prevention Interventions and Product Pipeline



Oral PrEP initiations increase in LMICs as continued evidence demonstrates its efficacy

When taken correctly, oral PrEP can greatly reduce the risk of HIV acquisition.[lxxvii] As of August 2020, there were approximately 661,000 cumulative oral PrEP initiations globally, with over 50 percent of these in LMICs [Figure 44].[lxxviii] Despite scale-up within LMICs, initiations are still far from the ambitious UNAIDS Fast-Track target of 3M clients on oral PrEP by 2020.

Figure 44: Top Six LMICs by Cumulative Oral PrEP Initiations per PrEPWatch as of Aug. 2020[lxxviii]



For those at risk of HIV acquisition, oral PrEP is a key prevention method with mounting evidence of success in resource-limited settings. A large cluster-randomized study presented at AIDS 2020 found that oral PrEP prevented an estimated three-quarters of HIV infections in people within the study population at high risk of HIV in Kenya and Uganda.[lxxix] This impressive result is the largest reduction in HIV infections yet reported from an oral PrEP program in sub-Saharan Africa.

Additionally, continued analysis of data from the ECHO Study, which reported last year that Depo-Provera does not increase the risk of HIV acquisition, found that offering oral PrEP to women in South Africa cut HIV incidence by 55 percent across all participants, whether or not they themselves took oral PrEP.[lxxx]

Additional oral PrEP options arrive on market, but questions remain around access and applicability in LMICs

Until recently, the only product approved for use as oral PrEP by the US FDA was TDF/FTC (300/200 mg), manufactured by Gilead as *Truvada*. In October 2019, Gilead's *Descovy* [TAF/FTC (25/200 mg)] received US FDA approval for a limited oral PrEP indication, excluding cisgender women [Figure 45].

Figure 45: US FDA Approval of TAF/FTC for Cisgender Men and Transgender Women[lxxxi]

Descovy: TAF/FTC (25/200 mg)

Descovy [TAF/FTC (25/200 mg)], received approval from the US FDA for use as oral PrEP excluding individuals at risk from receptive vaginal sex.

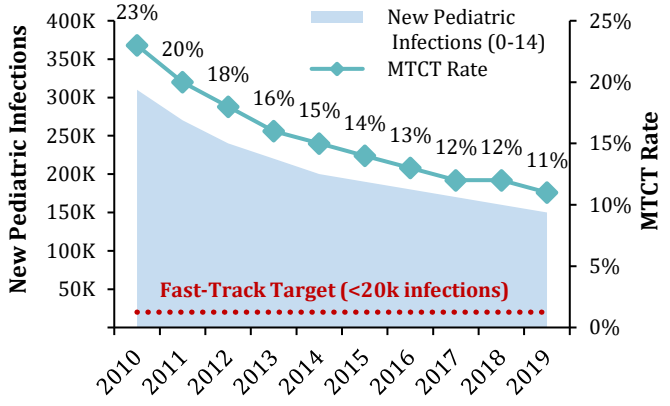
Gilead is required to complete a clinical trial for cisgender women and adolescent girls by 2024.

- Until such data are available, this product may have limited reach for LMIC settings where women are a priority population for oral PrEP
- Additionally, given there is currently no generic formulation available and TAF is not currently prioritized for treatment, cost will likely be a limiting factor in adoption of this product in LMICs. Cost could potentially decrease if TAF-based products are rolled out widely for treatment

Programs making headway toward the elimination of mother-to-child transmission of HIV, but progress has stalled

Significant reductions have occurred in mother-to-child transmission (MTCT) of HIV since 2010.[ii] However, over the past five years, MTCT rates declined more slowly (three percent decrease from 2015 to 2019) compared to previous years (eight percent decrease from 2010 to 2014) and will fall far short of the Fast-Track target of less than 20,000 new annual HIV infections in children by 2020 [Figure 46].

Figure 46: Global Mother-to-Child Transmission Rates and New Pediatric Infections (2010 – 2019)[i]



There are three main factors driving these continued transmissions: remaining unmet need for maternal ART, acute infection during pregnancy or breastfeeding, and loss of access to HIV care for HIV-positive mothers and HIV-exposed infants. According to UNAIDS, in 2019 these three factors accounted for almost 90K new infections in children and should remain a focus for programs moving forward.[lxxxii] Continued efforts to improve EID coverage are essential to addressing these key gaps. Introduction of point-of-care EID paired with demand generation for EID testing outside of PMTCT could increase uptake, and

routine monitoring of mothers and infants could improve retention in care through the breastfeeding period.

Future uptake of voluntary medical male circumcision impacted by the COVID-19 pandemic and changes in PEPFAR policy

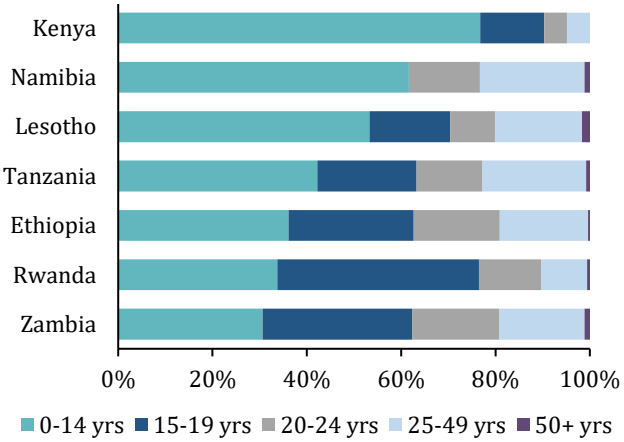
Voluntary medical male circumcision (VMMC) is a one-time, highly cost-effective intervention that reduces the risk of HIV infection. Since 2016, more than 15M men and boys have undergone VMMC in the 15 UNAIDS VMMC priority countries in East and Southern Africa.[ii]

Similar to many other HIV services, VMMC programs are experiencing ongoing disruptions due to COVID-19. Given the heavy reliance on outreach-based models, many VMMC programs are at risk of seeing a dramatic reduction in performance due to COVID-19-related restrictions.

Additionally, a recent change to PEPFAR's VMMC funding policy will greatly impact VMMC programs. Based on analysis of adverse events and impact on immediate incidence, PEPFAR will no longer fund the circumcision of males under the age of 15.[iv] This includes early infant male circumcision, although some exceptions may be considered.

This change in policy will have a significant impact as many programs have historically circumcised large numbers in the under-15 age group. Across the 12 UNAIDS VMMC priority countries that reported age-disaggregated data, up to 77 percent of all VMMCs were performed on boys between the age of 0 and 14 years old in 2019 [Figure 47].[lxxxiii]

Figure 47: Graph of Age Distribution of VMMCs in Select UNAIDS Priority Countries (2019)[lxxxiii]



**Not exhaustive.*

As countries approach VMMC saturation (defined as reaching at least 80 percent circumcision coverage in the 15–29 year age group, although this definition may vary across countries), focus will begin to shift to maintaining VMMC gains by circumcising males as they age into target groups. Given this new guidance, countries will need to re-evaluate sustainability strategies and potentially determine new focal age groups.

These changes, as well as the impact of the COVID-19 pandemic, are likely to continue to impact uptake of VMMC and could limit VMMC's impact on new infections in the coming years.

In light of these challenges, new approaches to VMMC will help to expand scale-up and ensure resiliency in national programs. With support from CHAI, the VMMC programs in Zambia and Zimbabwe have developed systems to facilitate effective program scale-up and achievement of data-driven targets. However, to maintain VMMC program gains and set more nascent programs on a similar path, HIV prevention programs will need to shift to a more institutionalized, integrated, and sustainable approach. Over the next four years through the STRIDE grant (Sustainable Transitions to Resilient, Integrated combination prevention and Dissemination of Evidence), CHAI aims to further develop resilient and integrated HIV prevention programs in Zambia and Zimbabwe that can effectively respond to the evolving needs of the programs and the dynamic HIV landscape.

Prevention products currently in development offer long-acting and discreet options for HIV prevention

There have been a number of exciting landmarks in the development of new prevention products, many of which focus on novel delivery options for HIV prevention.

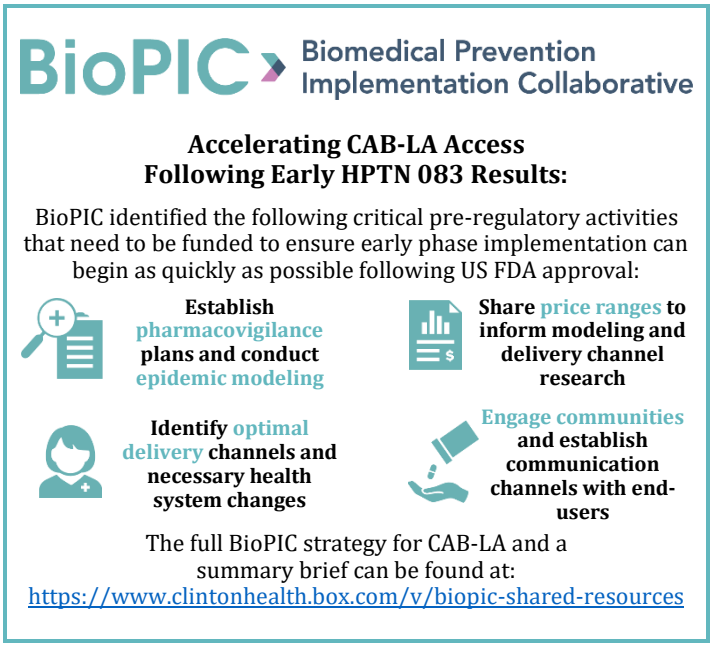
Cabotegravir Long-Acting for Prevention

Updated results from the HPTN 083 clinical trial found that cabotegravir long-acting (CAB-LA) injectable PrEP is *superior* to daily oral TDF/FTC for cisgender men and transgender women who have sex with men.[lxxxiv] Data is still being collected on use by cisgender women in the companion HPTN 084 study. This endpoint-driven study will be regularly reviewed to assess outcomes, but may continue until 2023.[lxxxv]

While these results are extremely encouraging, there are still many steps before product introduction can begin. CAB-LA will require regulatory approval in both high-income countries and LMICs, global and national normative guidance will need to be developed, and optimal delivery channels identified and capacitated.

In order to accelerate product introduction, the Biomedical Prevention Implementation Collaborative (BioPIC) has identified activities critical to rapid, high-quality product introduction of CAB-LA [Figure 48].

Figure 48: Biomedical Prevention Implementation Collaborative (BioPIC) Introduction Strategy[lxxxvi]



Dapivirine (DPV) Vaginal Ring

The DPV ring is a flexible, silicone ring that is self-inserted into the vagina to reduce the risk of HIV transmission via vaginal sex. In July 2020, the DPV ring received a "positive, conditional scientific opinion" by the European Medicines Agency (EMA) for use outside of Europe when oral PrEP is not available.[lxxxvii] EMA scientific opinion under Article 58 does not provide market authorization in any country and the ring still needs to obtain US FDA approval or WHO prequalification, and ultimately national drug regulatory authority (NDRA) approval for use in-country. Further information on price and supply security have not yet been shared. **Given clinical research demonstrated the DPV ring only reduced HIV risk by 30 to 35 percent, the EMA emphasized that it should only be used when oral PrEP cannot be used or is not available.**[lxxxvii]

Multi-Purpose Technologies (MPTs)

While still several years away from market availability, there are close to 30 MPTs currently in development that deliver varied combinations of HIV prevention, other sexually transmitted infection (STI) prevention, and contraception.[lxxxviii] These MPTs offer a more streamlined delivery of sexual and reproductive health products, which could increase uptake across forms of protection, resulting in fewer HIV infections, other STIs, and unintended pregnancies.

More details on additional pipeline MPT products are available at http://mpts101.org/.

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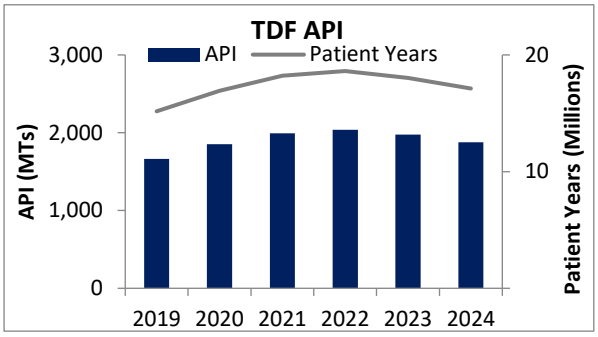
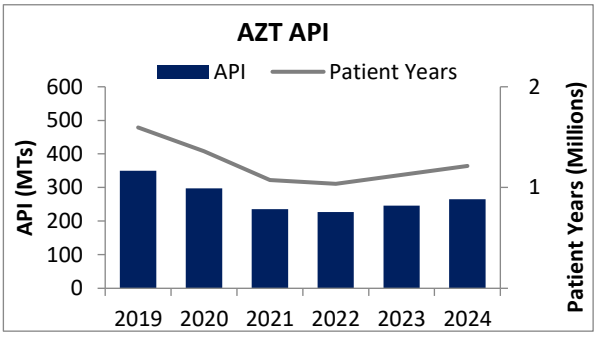
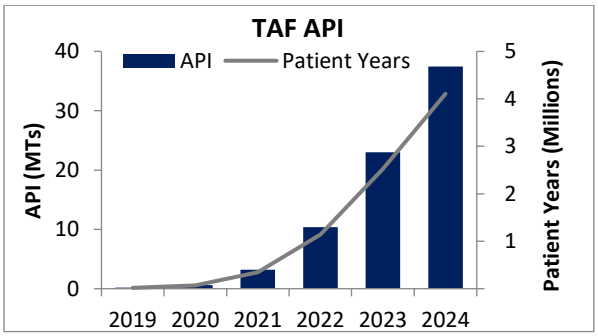
[lxxxvi] Biomedical Prevention Implementation Collaborative (May 2020) *A Shared Strategy for Cabotegravir Long-Acting Injectable*. Link
[lxxxvii] EMA press release (Jul. 24, 2020) *Vaginal ring to reduce the risk of HIV infection for women in non-EU countries with high disease burden*. Link
[lxxxviii] Initiative for Multipurpose Technologies (IMPT) MPT Product Development Database. Acc. Sep. 2020 Link

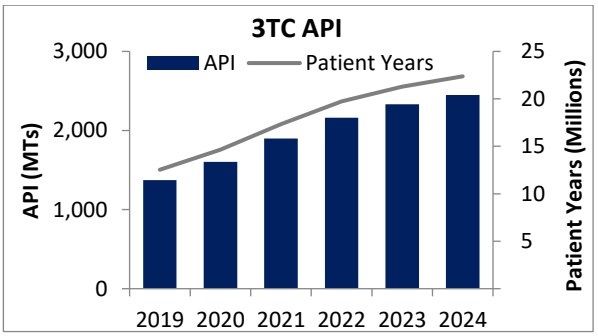
Appendix A: Forecasted Adult API Demand in GA LMICs

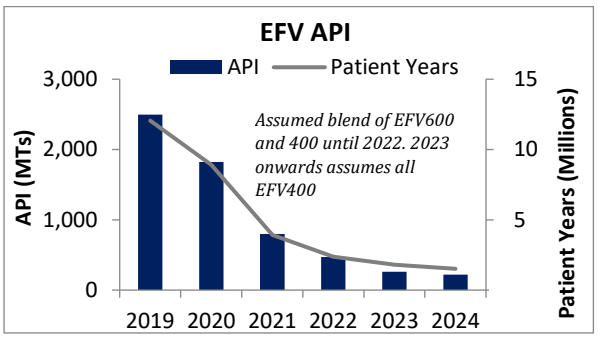
The graphs below show the estimated generic-accessible patient demand and active pharmaceutical ingredient (API) volume (in metric tons) forecast for key adult ARVs. Patient years represent the effective number of patients on treatment for a full year and are used to calculate yearly API demand. Patient 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.

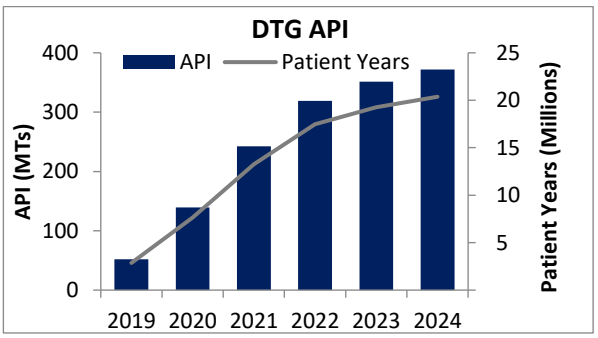


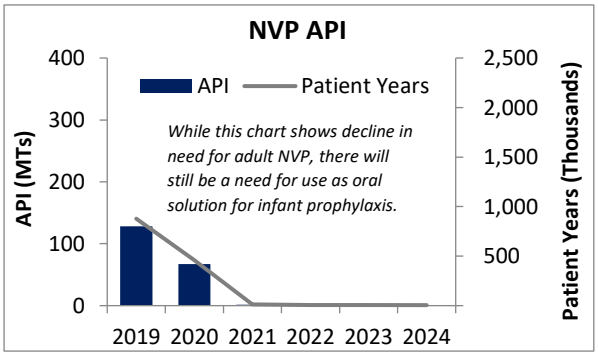












Appendix B: CHAI ARV Benchmark Price Comparison List

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

Product	Pack Size*	Global Fund PPM Price Jul. 2020[1]	GHSC-PSM E-Catalog Price Jul. 2020[2]	RSA Weighted Av. Tender Price 2019-2022[3]
Adult Products				
ABC/3TC (600/300 mg)	30 tablets	$9.20	$9.20	$7.60
ATV/r (300/100 mg)	30 tablets	$12.90	$13.50	-
AZT/3TC (300/150 mg)	60 tablets	$5.25	$6.05	$4.85
DTG (50 mg)	30 tablets	$3.20	$3.50	$2.38
EFV (600 mg)	30 tablets	$2.50	-	$2.32
LPV/r (200/50 mg)	120 tablets	$18.65	$18.95	$11.69
NVP (200 mg)	60 tablets	-	-	$1.85
RTV (100 mg) heat-stable	60 tablets	$6.85	$6.85	$3.25
TDF (300 mg)	30 tablets	$2.40	$3.50	$2.07
TDF/3TC (300/300 mg)	30 tablets	$3.40	$3.15	-
TDF/FTC (300/200 mg)	30 tablets	$4.50	$4.60	$3.08
TDF/3TC/DTG (300/300/50 mg) No Carton	30 tablets	$5.30**	$5.49	$4.82***
TDF/3TC/DTG (300/300/50 mg) No Carton	90 tablets	$15.65	$15.62	-
TDF/3TC/DTG (300/300/50 mg) No Carton	180 tablets	$31.00	$31.49	-
TDF/3TC/EFV (300/300/400 mg) No Carton	30 tablets	$5.50**	-	-
TDF/3TC/EFV (300/300/400 mg) No Carton	90 tablets	$16.40	$15.99	-
TDF/3TC/EFV (300/300/600 mg) No Carton	30 tablets	$5.75**	-	-
TDF/FTC/EFV (300/200/600 mg) No Carton	30 tablets	$6.15**	-	$5.11
Pediatric Products				
Optimal Formulary				
ABC/3TC (120/60 mg) disp. scored	30 tablets	$3.49	$3.30	-
ABC/3TC (120/60 mg) disp. scored	60 tablets	-	$6.50	-
AZT (50/5 mg/ml) oral solution	100 mL bottle	$1.36	-	-
AZT/3TC (60/30 mg) disp. scored	60 tablets	$1.90	$1.80	-
LPV/r (100/25 mg) heat-stable	60 tablets	$6.50	$7.00	$3.71
LPV/r (40/10 mg) oral pellets	120 capsules	$18.25	$15.00	-
LPV/r (40/10mg) oral granules	120 sachets	$18.25	$18.25	-
NVP (50 mg) disp. scored	60 tablets	$1.45	$1.45	-
NVP (50/5 mg/ml) oral solution (with syringe)	100 mL bottle	$1.45	$1.25	$0.73
RAL (25 mg) chewable scored	60 tablets	-	$18.00	$12.69
Limited Use List				
3TC (50/5 mg/ml) oral solution	100 mL	$1.25	-	-
ABC (60 mg) disp. scored	60 tablets	$4.72	$3.80	$2.69
ATV (200 mg)	60 capsules	$20.00	-	-
AZT/3TC/NVP (60/30/50 mg) disp. scored	60 tablets	$3.00	-	-
DRV (75 mg)	480 tablets	-	$54.00	-
EFV (200 mg) single scored	90 tablets	$6.40	$6.43	-
EFV (200 mg) double scored	90 tablets	$9.30	-	-
LPV/r (80/20 mg/ml) oral solution	5 x 60ml bottles	$30.82	$30.82	$15.53
RAL (100 mg) granules	60 sachets	-	$212.00	-
RTV (100 mg) powder	30 packets	-	-	$2.47
RTV (25 mg) heat-stable	60 tablets	-	-	-

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

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

**** Price shown for packaging with carton.*

[1] Global Fund Pooled Procurement Mechanism Reference Pricing: ARVs, Jul. 20, 2020. Link
Prices shown can be treated as ceiling prices and used for budgeting purposes; lower prices may be accessible.

[2] Global Health Supply Chain – Procurement and Supply Management (GHSC-PSM) E-Catalog: ARVs, Jul. 2020. Link
Prices represent the latest blended average pricing of actual procurement.

[3] Republic of South Africa 2019-2022 Tender, weighted average price across awarded suppliers, 1 USD = 14.35 ZAR exchange rate used per US Treasury Dept. as of Dec. 31, 2018 effective at tender adjudication; Supplementary Tender Feb. 2020, weighted average price across awarded suppliers, 1 USD = 15.57 ZAR exchange rate used per US Treasury Dept. as of Dec. 31, 2019; Ex-Works prices have been calculated by removing 15% VAT and 5% in shipping; prices subject to forex-based adjustments; some pack sizes differ slightly from those listed above, see tender for full details.

Appendix C: 2018 Optimal Formulary and Limited-Use List for Pediatric ARVs

Optimal Formulary		
Product	**Dosage**	**Formulation**
AZT	50 mg/5 mL	Oral Solution – 100 mL
NVP	50 mg	Tablet (Dispersible, Scored)
NVP	50 mg/5 mL	Oral Solution – 100 mL
LPV/r	100 mg/25 mg	Tablet (Heat Stable)
LPV/r	40 mg/10 mg	Solid Oral Dosage Form
AZT/3TC	60 mg/30 mg	Tablet (Dispersible, Scored)
ABC/3TC	120 mg/60 mg	Tablet (Dispersible, Scored)
RAL	25 mg	Tablet (Chewable, Scored)

Limited-Use List		
Product	**Dosage**	**Formulation**
LPV/r	(80 + 20 mg)/mL	Oral Solution
3TC	50 mg/5 mL	Oral Solution – 100 mL
ABC	60 mg	Tablet (Dispersible, Scored)
DRV	75 mg	Tablet
RTV	25 mg	Tablet
RTV	100 mg	Powder
ATV	200 mg	Capsule
AZT/3TC/NVP	60 mg/30 mg/50 mg	Tablet (Dispersible, Scored)
EFV	200 mg	Tablet (Scored)
RAL	100 mg	Granules for Suspension

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 2020. 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 2020 ARV demand forecast for current drugs includes data from: Benin, Burkina Faso, Cambodia, DRC, Eswatini, Ethiopia, India, Kenya, Laos, Lesotho, Malawi, Mozambique, Myanmar, Nigeria, Senegal, South Africa, Tanzania, Togo, Uganda, Zambia, and Zimbabwe. These countries represent approximately 84 percent of adult patients on ART in GA LMICs in 2019.

Pipeline (i.e., newer or not on market) ARV uptake is modeled based on 12 high-volume countries and the GA rest of world (GA RoW). Expected launch years and uptake curves are selected for each of the 12 countries based on CHAI's country intelligence, as well as for GA RoW as a collective group, separately for existing and newly initiating patients. These uptake curve choices for new products relative to current products estimate the total number of patients on each new drug in a given year in GA LMICs.

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 2019. It is not an estimate of the cost of ARV procurement in 2019. 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 2019 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 (2019) testing volumes from CHAI country teams, publically 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).

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