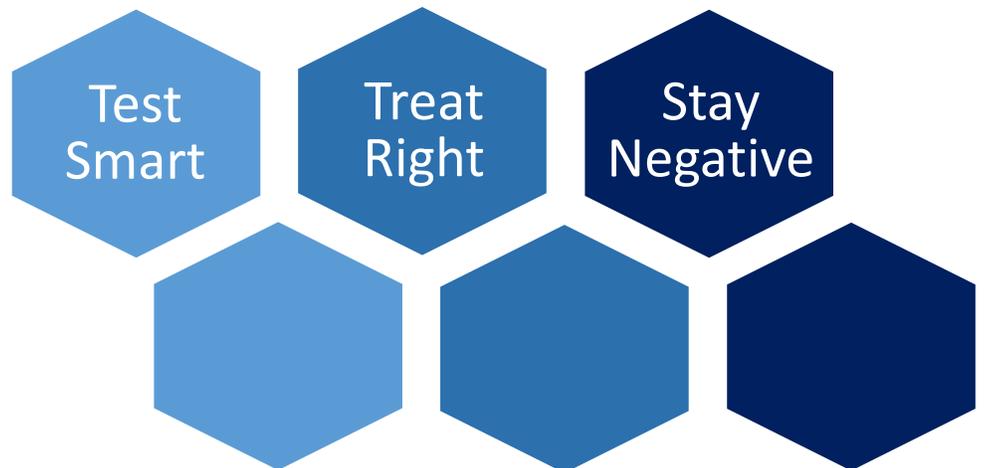




HIV MARKET REPORT

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

Issue 10, September 2019



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Acronyms Used

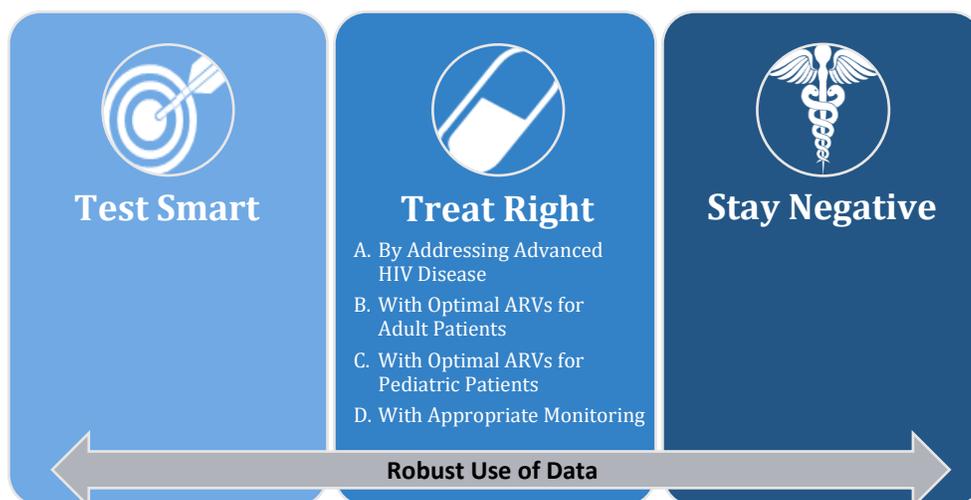
1L	First-line	LNG	Levonorgestrel
2L	Second-line	LPV/r	Lopinavir/ritonavir
3TC	Lamivudine	LTFU	Lost to follow up
ABC	Abacavir	MMS	Multi-month scripting
AGYW	Adolescent girls and young women	MOH	Ministry of Health
AHD	Advanced HIV disease	MSF	Médecins sans Frontières
AIDS	Acquired Immune Deficiency Syndrome	MSM	Men who have sex with men
ALD	ABC/3TC/DTG	NAIHS	Nigeria HIV/AIDS Indicator and Impact Survey
API	Active pharmaceutical ingredient	NAT	Nucleic acid testing
APWG	ARV Procurement Working Group	NNRTI	Non-nucleoside reverse transcriptase inhibitor
ART	Antiretroviral therapy	NRTI	Nucleoside reverse transcriptase inhibitor
ARV	Antiretroviral	NTD	Neural tube defect
ATV/r	Atazanavir/ritonavir	NVP	Nevirapine
AZT	Zidovudine	OI	Opportunistic infection
BioPIC	Biomedical Prevention Implementation Collaborative	OPD	Outpatient department
BMGF	Bill & Melinda Gates Foundation	PADO	Pediatric ARV Drug Optimization
CAB-LA	Cabotegravir long-acting	PDR	Pre-treatment drug resistance
CADO	Conference on Antiretroviral Drug Optimization	PEPFAR	President's Emergency Plan for AIDS Relief
CAGR	Compound annual growth rate	PI	Protease inhibitor
CHAI	Clinton Health Access Initiative	PITC	Provider-initiated testing and counseling
CLHIV	Children living with HIV	PLHIV	People living with HIV
CM	Cryptococcal meningitis	POC	Point-of-care
COP	Country operating plan	PPM	Pooled Procurement Mechanism
CrAg	Cryptococcal antigen	PPPY	Per patient per year
CTX	Co-trimoxazole	PQ	Prequalification
DRV/r	Darunavir/ritonavir	PrEP	Pre-exposure prophylaxis
DT	Dispersible tablet	RAL	Raltegravir
DTG	Dolutegravir	RDT	Rapid diagnostic test
ED-PrEP	Event-driven PrEP	RFP	Request for proposal
EFV	Efavirenz	RPV	Rilpivirine
EID	Early infant diagnosis	RRI	Rapid Responsive Initiative
ERP(D)	Expert Review Panel (Diagnostics)	TAF	Tenofovir alafenamide fumarate
FDC	Fixed-dose combination	TB	Tuberculosis
FTC	Emtricitabine	TDF	Tenofovir disoproxil fumarate
GA	Generic-accessible	TLD	TDF/3TC/DTG
GAP-f	Global Accelerator for Pediatric Formulations	TLE400	TDF/3TC/EFV400
GF	Global Fund to Fight AIDS, Tuberculosis, and Malaria	TLE600	TDF/3TC/EFV600
GHSC-PSM	Global Health Supply Chain Program-Procurement and Supply Management	TPT	TB preventive therapy
HCW	Healthcare worker	US FDA	United States Food and Drug Administration
HIC	High-income country	USAID	United States Agency for International Development
HIV	Human Immunodeficiency Virus	VL	Viral load
HIVST	HIV self-test	VMMC	Voluntary medical male circumcision
IAS	International AIDS Society	WHO	World Health Organization
INSTI	Integrase strand transfer inhibitor	XTC	Emtricitabine or lamivudine
IUD	Intrauterine device	ZLN	AZT/3TC/NVP
LFA	Lateral flow assay		
LMIC	Low- and middle-income country		

Foreword

The first edition of CHAI's HIV Market Report (then called the ARV Market Report) came out in 2010. When it was published, under 8 million patients were on antiretroviral therapy (ART) globally, a CD4 count below 350 cells/ μ L was the threshold for treatment initiation, stavudine (d4T) made up over 50 percent of the first-line (1L) nucleoside reverse transcriptase inhibitor (NRTI) market in generic-accessible low- and middle-income countries, and dolutegravir (DTG) was yet to start the pivotal phase III SINGLE trial.

This is the 10th edition of the CHAI HIV Market Report. Much has changed since the first report. Over 23 million patients accessed ART globally in 2018, with nearly 2 million added between 2017 and 2018 alone. Almost all countries have implemented Treat All policies, and most country programs have entirely phased out d4T. DTG, an investigational drug in 2010, has changed the treatment landscape across the globe as national programs move to transition both first- and second-line (2L) patients to DTG-based regimens.

As we began writing, we decided to break with the historical report structure in the spirit of changes to the HIV landscape over the past 10 years. Instead of distinct sections for adult and pediatric market trends, prevention, and diagnostics, we have structured this version to reflect a more integrated approach to eliminating HIV/AIDS as a public health threat. The framework for this edition also reflects CHAI's approach to improving access to HIV diagnostic, prevention, and treatment commodities.



Countries must be smart and targeted about the way they test for HIV, provide the right treatment in the right way to those identified as positive, and provide cost-effective prevention options to those who are negative. All of this must be informed by robust use of data and a focus on individual, community, and country context.

To realize the 90-90-90 targets, with the deadline now just a year away, the global HIV community will need to continue to break down siloes that exist within donors, implementing partners, and ministries of health. For example, screening and treatment for advanced HIV disease (AHD) and related co-infections is critical to reduce mortality and cannot be considered in isolation from CD4 testing systems that are essential to diagnosing patients with AHD in the first place. Better integration of HIV and sexual and reproductive health services will ensure that women are able to access essential health services during the same visit. The list of potential opportunities for integration goes on.

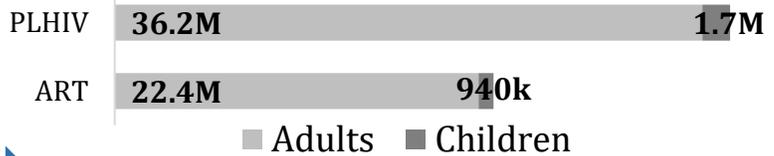
Much work remains to end the HIV/AIDS epidemic as a public health threat. CHAI is focused on meeting this goal by working with ministries of health, communities, suppliers, and partners to ensure that all people in need have access to the best HIV commodities at affordable and sustainable prices, no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

2019 Market Report At-a-Glance

HIV Data Overview, 2018

37.9M people living with HIV globally

23.3M people on treatment globally



62% Global ART Coverage Rate

Test Smart

8 Million people globally did not know their HIV status in 2018

As testing volumes increase, positivity rates are decreasing



Targeted testing strategies can increase **testing yield** and more effectively allocate resources

Now 3 HIVSTs with WHO PQ

OraQuick
INSTI
Mylan

Treat Right

DTG is now recommended by the WHO as the **preferred 1L treatment** for all adults (including women of childbearing potential) and children >4 weeks

- Risk of NTDs much lower than previously thought

Pediatric DTG 5 mg dispersible expected to be filed with the US FDA in Q4 2019, with **generic 10 mg scored dispersible** filing shortly after

DTG-based regimens included in the national **treatment guidelines of > 75 LMICs** with **procurement initiated in > 35 LMICs**

Ped LPV/r (40/10 mg) pellets and granules expected to have expanded production capacity and supply by Q1 2020

NVP is being phased out for children and adults by PEPFAR and the Global Fund

TAF is listed as a 1L drug for use in *special circumstances* among adults in updated WHO guidelines



Advanced HIV Disease (AHD)

30-40%

of (re-)initiates starting ART have AHD

(<200 cells/ μ L, WHO stage 3 or 4, all children under 5)

AHD Package of Care

- Screening, treatment, and prophylaxis for opportunistic infections
- Rapid ART initiation
- Intensified adherence support

Stay Negative

>300k cumulative global **oral PrEP** initiations

The WHO now recommends **Event Driven-PrEP** (the use of PrEP only when an individual expects to engage in risky sexual activity) for MSM

TAF/FTC found to be **non-inferior** to **TDF/FTC** as oral PrEP



ECHO Trial

No difference in rate of HIV acquisition between 3 commonly used forms of long-acting contraception

GENERAL TRENDS

The cost of HIV-related commodities has continued to decrease

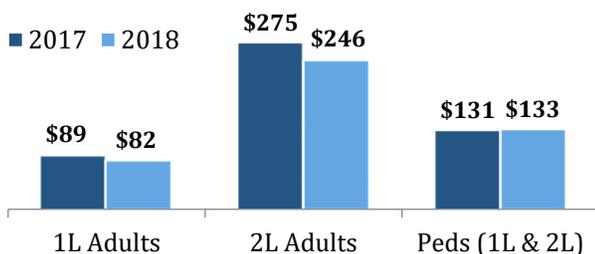
Pricing for HIV-related treatment and prevention commodities continues to decrease, while pricing and procurement for diagnostic commodities is becoming more transparent and streamlined [Figure 1].

Figure 1: Major HIV Pricing Updates as of Sep. 2019

	<ul style="list-style-type: none"> • 1L treatment with TLD, TLE400, and TLE600 all cost below US \$70 PPPY (using cartonless 90-packs)ⁱ • Optimal 2L drug ATV/r has dropped below US \$13/pack for the first time (US \$12.90/pack)ⁱ
	<ul style="list-style-type: none"> • TDF/FTC, a key product for oral PrEP, now costs less than US \$5 per month (US \$4.75)ⁱ
	<ul style="list-style-type: none"> • GHSC-PSM launched a global VL & EID RFP requiring suppliers to bid “all-inclusive” prices inclusive of service, maintenance, and device placementⁱⁱ

Treatment costs, in particular, have continued to decrease between 2017 and 2018 for adult 1L and 2L, while the cost of pediatric treatment regimens has increased slightly with the introduction of more optimal products such as LPV/r (40/10 mg) pellets and granules [Figure 2].

Figure 2: Generic-accessible (GA) LMIC Weighted Average Regimen Price (USD, PPPY)ⁱⁱⁱ

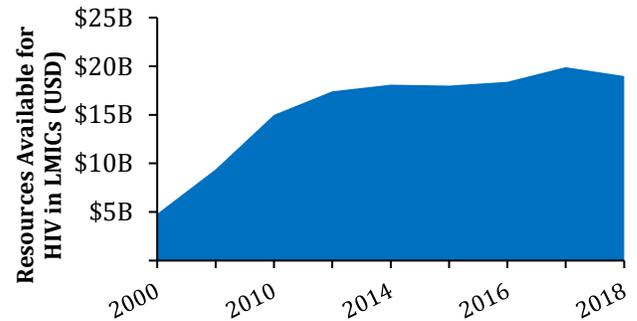


Overall, the antiretroviral (ARV) market size in generic-accessible¹ low- and middle-income countries (GA LMICs) remained relatively flat in 2018 compared to 2017 at around US \$1.7B for adult and pediatric treatment combined.ⁱⁱⁱ

Global funding discrepancies across countries tied to differences in progress against epidemic

Funding for HIV programs in LMICs has been relatively flat over the past few years, with only a 4 percent increase in international funding since 2010. However, total investment decreased by US \$900 million between 2017 and 2018 [Figure 3].^{iv}

Figure 3: HIV Resources in LMICs, 2000-2018^v



Funding distribution has been unequal. In regions where expenditure per person living with HIV has reached resource needs estimates, such as eastern and southern Africa, there is more progress toward the 2020 Fast Track targets. In regions such as western and central Africa, the total HIV resources available are only 48 percent of the estimated need, and progress has occurred at a more gradual rate.^{iv}

In light of these funding challenges, countries are finding unique ways to increase domestic financing

In an environment with stagnating international HIV funding, many donors are also increasingly expecting countries to contribute more national funds to HIV programs. In order to do this, countries will have to devise new and innovative ways of generating funds.

Uganda has levied a 2 percent tax on alcohol and soft drinks in an effort to increase domestic funding. The estimated US \$2.5 million tax is expected to generate per year will be used to help fund the country’s HIV treatment programs.^{vi}

As the community gets closer to the 90-90-90² targets, collecting and using reliable data is becoming increasingly important

Data informs much of the HIV response, from country level decision making to donor priorities. As such, having and utilizing accurate data is critical to eradicating HIV as a public health threat. Below are two country examples highlighting the importance of data to the HIV response.

¹ See Appendix D for definition of generic-accessible.

² 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 effective treatment, and 90 percent of those treated being virally suppressed by 2020.



The Government of India, with the support of CHAI, developed a machine learning-based model to predict the likelihood of a patient becoming lost-to-follow-up (LTFU). The model uses over 400 demographic, immunological, and behavioral factors including age, gender, education level, past adherence, CD4 count, regimen, and others to predict potential LTFU. In early tests, the model was able to identify 72 percent of LTFU patients in the top 20 percent of patients categorized as “at-risk” by the model. This implied a LTFU rate of 24 percent for the “at-risk” cohort, compared to a 6.6 percent LTFU rate nationally.ⁱⁱⁱ

CHAI is currently assisting the Ministry of Health (MOH) in designing a pilot to assess implementation modality and measure impact of subsequent interventions to prevent LTFU. If validated, the MOH plans to integrate the model in the existing patient management tool to provide proactive instead of reactive care and reduce the cost of linking back patients who are LTFU.



As another example of the importance of data, in 2018 the Government of Nigeria, the President’s Emergency Plan for AIDS Relief (PEPFAR), the Global Fund (GF), and other partners conducted the Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS) to better understand the HIV epidemic in the country. The NAIIS found that the HIV epidemic in Nigeria was overestimated, with the survey showing a decrease from previous estimates in total people living with HIV (PLHIV) and a concomitant increase in ART coverage.^{vii} While large decreases in PLHIV estimates, such as those seen in Nigeria, are uncommon, the survey underscores the importance of ensuring that accurate data is collected and used.

Ministries of health, partners, and donors are looking beyond new drugs for treatment optimization

While the introduction of optimal ARVs, such as dolutegravir (DTG), is the cornerstone of any treatment optimization program, there are a number of other interventions that can improve outcomes for PLHIV.

➔ Multi-Month Scripting

Multi-month scripting (MMS), a form of differentiated service delivery where stable patients receive more than one month’s worth of medicine at a time, has been a topic of interest for years. Benefits of MMS include reduced patient travel burden to clinics, as well as decongestion of clinics, allowing healthcare workers (HCWs) more time to focus on unstable patients.

One challenge with MMS for patients is the unwieldiness of carrying several bottles from the clinic. PEPFAR has indicated broad interest in moving to larger pack sizes, both 90- and 180-count bottles, for the transition to TDF/3TC/DTG (TLD) as a way to further support and implement MMS. At the 2019 International AIDS Society conference (IAS), PEPFAR presented data showing their

fiscal year 2020 demand, with nearly 20 percent of TLD orders being for 90- or 180-count bottles.^{viii}

To assist country programs with the transition to MMS, PEPFAR has developed the “Multi-month prescribing and treat all calculator” hosted on www.differentiatedcare.org.

➔ User-Centered Design

Uptake of and adherence to daily oral pre-exposure prophylaxis (PrEP) is a considerable challenge, especially among adolescent girls and young women (AGYW) who are at high risk of HIV acquisition. The “medicalization” of PrEP can be a barrier to uptake and adherence among an otherwise healthy population group.

To address these issues, the United States Agency for International Development (USAID) funded a human-centered design project to redesign the oral PrEP experience, culminating in the launch of V™ for oral PrEP. V™



Photo Credit: Project EMOTION

reframes oral PrEP from a medicine to an empowering experience that fits into a young woman’s day-to-day lifestyle, by aligning with her favorite fashion and

beauty products. USAID is continuing its support for V™ in 2019 by partnering with a range of stakeholders to introduce V™ in Zimbabwe.^{ix}

V™ includes implementation resources to enhance oral PrEP branding and the client experience. All V™ materials are open source and available online for programs to adapt and use in their own settings. Learn more at www.conrad.org/launchingv and by contacting LaunchingV@USAID.gov.

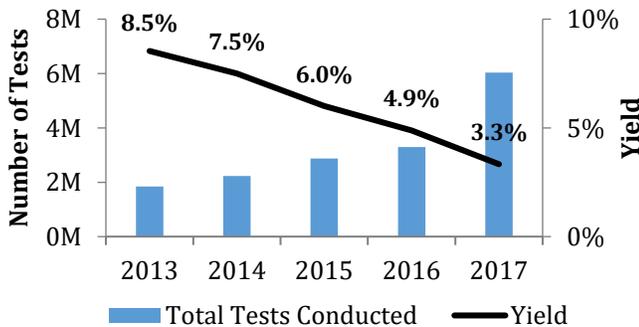


TEST SMART

As testing yields decrease and resources flatline, increasingly targeted testing is required to find undiagnosed PLHIV

Outside of China and India, approximately 150 million professional-use HIV rapid diagnostic tests (RDTs) were procured in LMICs in 2018.^x Despite this high volume of tests, yields are decreasing globally as the world gets closer to reaching the “First 90” target and global incidence decreases [Figure 4]. Given the declining budget for testing programs, the global testing strategy must change in order to find the remaining undiagnosed PLHIV and link them to care more efficiently.

Figure 4: Testing Volumes and Yield in Zambia (2013-2017)ⁱⁱⁱ



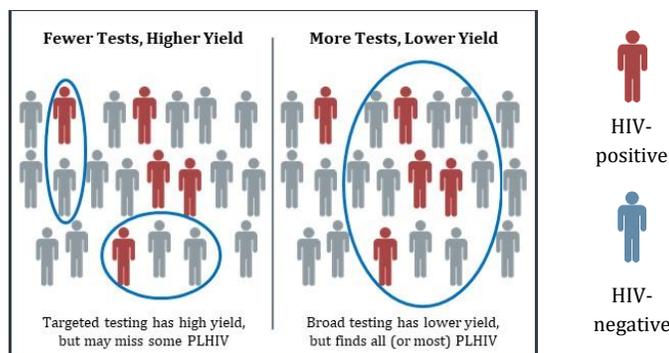
PEPFAR is encouraging a cessation of over-testing the general population. Instead, country programs have been advised to focus on targeted testing strategies such as differentiated testing based on ART coverage, index testing, and self-testing.^{xi}

“[COP19] HIV testing volume targets should be less than COP18 targets with this focused testing strategy...”

- PEPFAR COP19 Guidance^{xii}

With limited resources, national programs must balance testing efficiency with finding as many unidentified PLHIV as possible to link them to care [Figure 5].

Figure 5: Balancing Yield and Testing Volumes



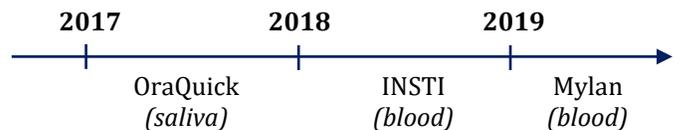
Abbott’s Determine HIV-1/2 is the World Health Organization (WHO) prequalified (PQ) professional-use RDT with the largest market share.ⁱⁱⁱ It is currently priced at US \$0.72 per test (without accessories), while many other test brands have slightly higher prices.^{xiii} Global HIV RDT pricing has been relatively flat in recent years, but lower pricing for malaria RDTs (some as low as US \$0.22 per test) suggests the potential for price reductions for HIV RDTs.^{xiv}

HIV self-testing (HIVST) is currently a niche product with a premium price

Seventy-seven countries have reported that they have HIVST policies, although not all have reached the implementation and rollout stages.^{xv} However, despite increasing country and donor interest in HIVST, it currently remains a niche product used to test hard-to-reach populations. Compared to ~150M professional-use RDTs procured outside India and China in 2018, there were only ~4.9M HIVSTs procured.^{xv}

Since the announcement of the US \$2.00 public sector price for the OraQuick HIVST^{xvi}, two additional HIVSTs have received WHO PQ [Figure 6]. Whereas increased market entrants will hopefully lead to a reduction in prices, there is a risk of HIVST falling into a low-volume, high-price trap if it continues to be used as a niche product.

Figure 6: Timeline of HIVST WHO PQ^{xvii}

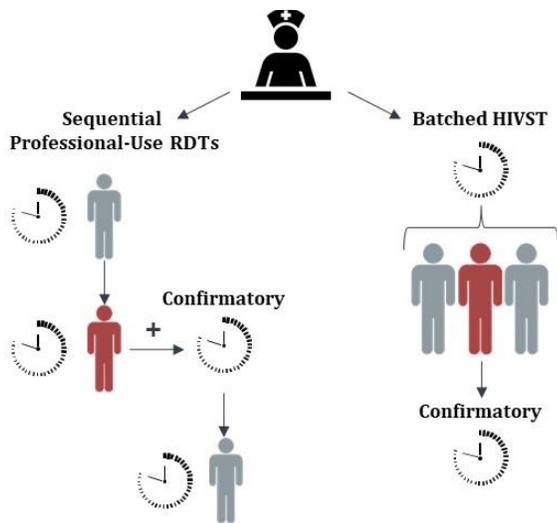


Facility-based HIVST has great potential to close the “First 90” gap, while freeing up HCW time to focus on quality of care

Testing yield drops as countries get closer to the “First 90” target and fewer unidentified PLHIV remain to be found. As such, a HCW in a facility may spend a significant amount of time administering tests on negative clients. Even under “high-yield” scenarios, over 80 percent of HCW time could be spent on negative tests.ⁱⁱⁱ

HIVST can enable batched testing within a health facility, where a HCW oversees the testing of multiple clients at once (with appropriate privacy accommodations), thus allowing HCWs to focus primarily on patients with a reactive test (and thus need a confirmatory professional-use RDT) [Figure 7]. In certain settings, human resource cost savings may well offset the current price premium for HIVST commodities over professional-use RDTs, while in other settings only a smaller premium may be offset. In all settings however, the significant time savings could allow HCWs to spend more time improving quality of care and improving indicators such as linkage and retention.

Figure 7: Sequential Professional RDT vs. Batched Use of Facility-Based HIVST



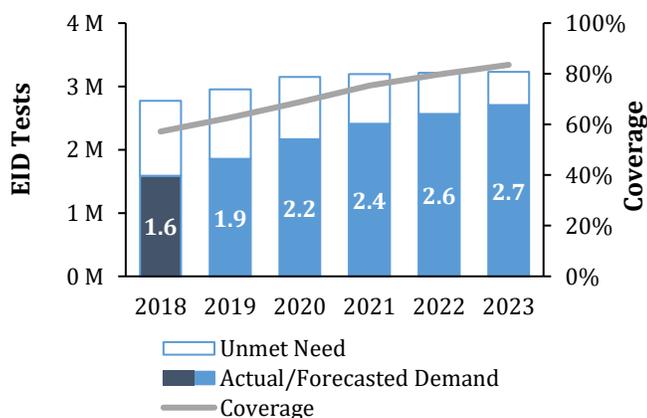
The feasibility of such an approach was demonstrated by a study in Malawi, which not only showed that the use of HIVST within facilities was acceptable, but that it even increased testing uptake within the context of provider-initiated testing and counselling (PITC) among target populations, such as men.^{xviii} This increased case finding without compromising yield.

Thus, it is conceivable that the use of HIVST in facilities could support the dual goals of improving efficiency of HIV testing service delivery and closing the PLHIV identification gap, while at the same time moving HIVST from a niche to a high-volume product, breaking the low-volume high-price trap.

EID testing continues scale up as countries adopt normative recommendations

Nearly 1.6 million early infant diagnosis (EID) tests were conducted globally in 2018, with the market forecasted to surpass 2 million tests by 2020 [Figure 8].^{xix}

Figure 8: LMIC EID Demand Forecast^{xix}



While EID testing volumes have scaled up relatively slowly, a number of factors are expected to drive an increase in the EID market in the next few years [Figure 9].

Figure 9: Anticipated Drivers of Increased EID Uptake

- Increasing adoption of POC testing
- Updated WHO algorithm with NAT at 9 months (instead of an RDT)
- Adoption of birth testing
- Testing at alternative entry points outside of PMTCT settings

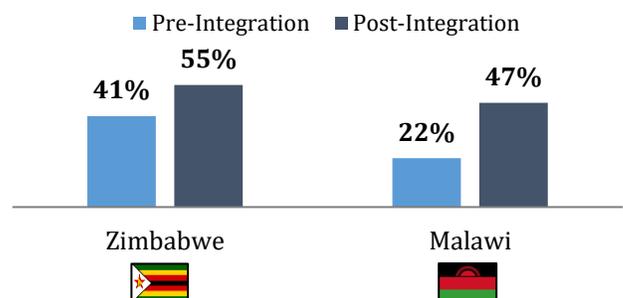
Growing support for integrated testing may help POC EID (and VL) growth

As global interest in point-of-care (POC) EID grows, country programs must decide how they will accommodate demand for these new testing volumes. Programs can either purchase a new near-POC or POC platform (such as the GeneXpert or m-PIMA), or utilize existing spare capacity on platforms already placed in labs and health centers.

There has been a global trend toward integration of testing multiple disease types on the same platform instead of purchasing different platforms for different diseases. Integration has primarily been piloted on the GeneXpert, which can run a number of different assays across diseases and has a large footprint across LMICs. While many GeneXpert devices were initially purchased for use by tuberculosis (TB) programs in decentralized labs, global aggregate GeneXpert utilization remains low, and in many cases spare capacity at a site could be used to run EID or targeted viral load (VL) tests without the need to purchase additional instruments.

A concern that has remained for non-HIV programs is that their own testing needs would be overwhelmed or sidelined if HIV testing were integrated on their platforms. Pilot studies conducted by CHAI in conjunction with the ministries of health in Malawi and Zimbabwe found that integrated TB and EID/targeted HIV VL testing on the GeneXpert platform was feasible, enabling increased device utilization without compromising TB testing services [Figure 10]. In fact, TB testing volumes increased slightly in both countries; thus, integration may be a way to scale up POC EID (and targeted VL) testing without additional spending on new platforms.

Figure 10: GeneXpert Capacity Utilization in TB/HIV Testing Integration Pilots (all test types)^{xx}



However, integration on existing GeneXpert devices may not be optimal in all settings. Some lower-level sites may require availability of a true POC platform, such as the m-PIMA, due to either accessibility issues or a lack of infrastructure required for larger machines. In other cases, a “hub-and-spoke” model with a network of spoke sites referring samples to a larger hub site (with an m-PIMA, GeneXpert, or conventional platform depending on volumes and patient needs) may be more appropriate for a given context.

The Vatican High-Level Dialogue on Paediatric HIV included diagnostics for the first time

Since 2016, the Vatican has hosted four high-level dialogues on ending pediatric HIV where stakeholders meet and make commitments to reduce pediatric HIV morbidity and mortality. These commitments make up the *Rome Action Plan*. The most recent meeting was in December 2018 where, for the first time, commitments were made related to pediatric HIV diagnostics.^{xxi} Stakeholders including ministries of health, donors, implementing partners, faith-based organizations, and diagnostics manufacturers made public commitments as to how their individual organizations would “accelerate research, development, registration, introduction and uptake of HIV diagnostics...” to end pediatric HIV [Figure 11].^{xxi}

Figure 11: Major Diagnostic Announcements at the 2018 Vatican High-Level Dialogue on Paediatric HIV^{xxi}

- 
- 1 Abbott announced a **volume-dependent “all-in” pricing structure** for POC EID and VL testing on their POC **m-PIMA device**
 - 2 Diagnostic **manufacturers** committed to “make every effort” to **stay in the EID market to meet the Fast Track targets**
 - 3 **Donors** committed to **further support scaling up POC EID technologies**

Targeted testing and use of screening tools can help close the undiagnosed CLHIV gap

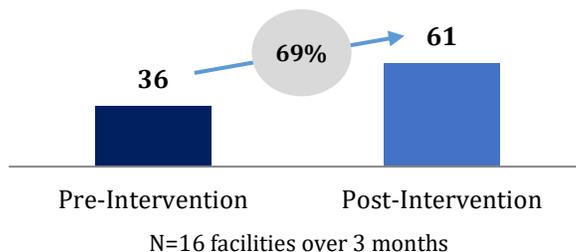
As the number of children living with HIV (CLHIV) *not* on ART declines through sustained efforts to link children to care, more targeted testing strategies are needed in alternative settings to find the remaining children living with undiagnosed HIV, many of whom may not be identified through traditional testing channels. Through work funded by The ELMA Philanthropies, CHAI is supporting countries in developing a smart, targeted, and comprehensive approach to pediatric case finding.



There is an opportunity to expand targeted testing in higher-volume entry points such as outpatient departments (OPD), where pediatric volumes are significantly higher than those in inpatient or nutrition wards. Testing coverage is often low in OPDs due to high patient volumes and resource constraints. The use of screening tools offers a method to increase efficiency of testing large volumes of both sick and well at-risk children.

Zimbabwe has piloted symptomatic screening tools to identify at-risk children and adolescents [Figure 12]. CHAI analysis based on program pilot data in Zimbabwe estimated that OPD screening (compared to general PITC) is less costly per child identified with HIV. In addition, OPD screening has the potential to identify more children and require fewer tests than general PITC.

Figure 12: Children Identified via HIV Risk Screening Tool – Zimbabwe OPD Pilot (children 5-14 years)^{xxii}



Strengthening and scaling up index testing is also a proven means of accelerating identifications of children. Tracing biological children of newly identified HIV-positive adults through index testing has shown substantial gains in pediatric identifications and high yields. CHAI modeling, based on program pilot data in Malawi, estimated that passive index testing may be slightly more expensive (approximately US \$5 more) per child identified with HIV than general facility PITC. However, the strategy has the potential to increase the number of CLHIV identifications while driving a substantial reduction in the number of tests per facility.ⁱⁱⁱ

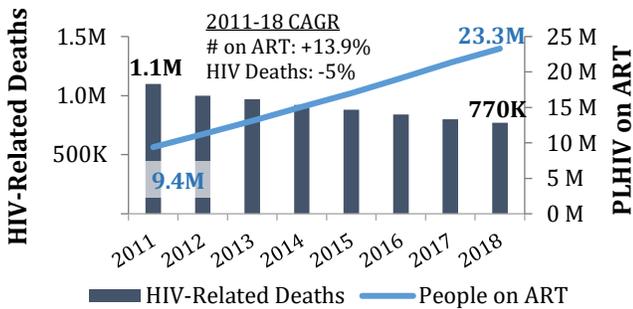
TREAT RIGHT

A) TREAT RIGHT BY ADDRESSING ADVANCED HIV DISEASE (AHD)

Reduction of HIV-related deaths in recent years has been relatively stagnant

Although there has been a remarkable decline in HIV-related mortality over the last two decades from its peak of 1.7M estimated deaths in 2004, there are still over 750K AIDS-related deaths each year, a number that has remained relatively stagnant despite ongoing improvements in ART coverage [Figure 13].^{xxiii}

Figure 13: Global HIV-Related Deaths and PLHIV on ART (all ages)^{xxiii}



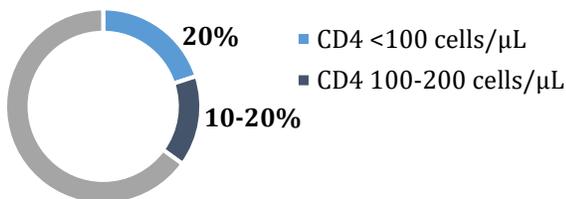
This stubbornly high mortality figure is due in large part to patients developing opportunistic infections (OIs) as a result of AHD and the lack of appropriate treatment.

Figure 14: WHO Definition of AHD^{xxiv}

WHO Definition of AHD	
Adults and Children (Ages 5+)	Children (Ages <5)
CD4 < 200 cells/ μ L or WHO stage 3 or 4	All children under 5 living with HIV

Patients with AHD are more susceptible to OIs, with TB and Cryptococcal meningitis as the leading causes of HIV-related mortality.^{xxiv} It is estimated that 30-40 percent of patients initiating treatment (or re-initiating after a gap) have AHD [Figure 15].^{xxiv} Approximately 10 percent of those starting ART with CD4 counts below 100 cells/ μ L die within three months.^{xxv}

Figure 15: Percent of (Re-)Initiating PLHIV Starting ART with Various CD4 Cell Counts^{xxiv}

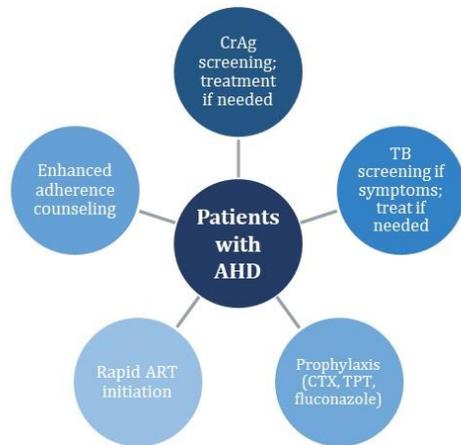


Normative guidance to treat AHD patients exists, and donors are supportive

The WHO released general AHD guidelines in 2017 and Cryptococcal meningitis-specific guidelines in 2018.^{xxiv,xxvi} The general AHD guidelines include a specific package of care that all patients presenting with AHD should be offered [Figure 16]. Major HIV funders such as PEPFAR and the Global Fund have indicated support of this package of care.

Figure 16: WHO AHD Package of Care^{xxiv}

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."



Commodities to address AHD are often unavailable or underutilized in LMICs; new Unitaid AHD initiative to address access barriers

Despite normative guidance released in light of the high proportion of patients (re-)initiating care with AHD, the diagnostic tools, treatments, and preventive services required to address AHD are virtually non-existent in most LMICs. The access barrier is due to a number of both supply and demand-side challenges [Figure 17].

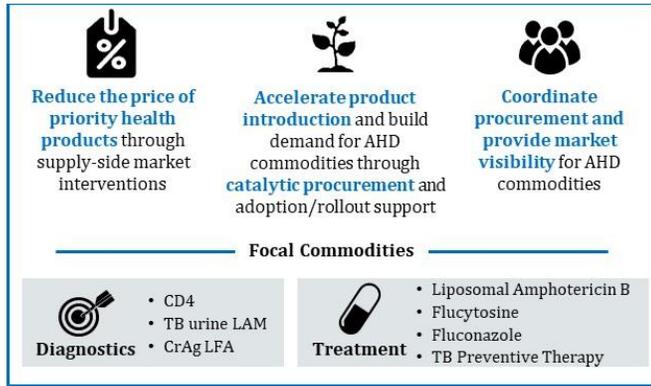
Figure 17: Supply and Demand Challenges for AHD Commodities

Supply Challenges	Demand Challenges
<ul style="list-style-type: none"> High prices stemming from low and sporadic demand Limited supplier base servicing generic market Lack of registration and availability of optimal products in-country 	<ul style="list-style-type: none"> Lack of AHD-specific country guidelines Low provider awareness of AHD services when available Siloed treatment programs across disease types



To address these challenges and access barriers, Unitaid has partnered with CHAI on an AHD initiative in seven countries that aims to reduce morbidity and mortality and improve cost efficiencies by accelerating access to affordable, optimal products for preventing, testing, and treating key OIs [Figure 18].^{xxvii}

Figure 18: Key Unitaid-CHAI Interventions to Improve Access to AHD Commodities



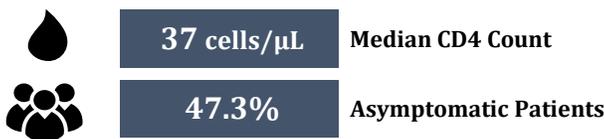
At IAS 2019, Unitaid and CHAI hosted a satellite session on accelerating access to diagnostics and drugs for AHD. The session brought together ministries of health, donors, implementing partners, and community advocates to share best practices and highlight what’s necessary to implement the WHO AHD package of care.^{xxviii}

Finally, the ARV Procurement Working Group (APWG) has expanded its scope beyond ARVs for the first time in the group’s seven year history to include a number of AHD commodities. This will bring some of the proven benefits of the group’s coordinated procurement and market intelligence sharing to these commodities.^{xxix}

Successfully treating AHD requires access to CD4 to identify AHD patients in the first place

In the context of diagnosing AHD, country programs cannot rely on clinical staging alone as studies have shown that large percentages of patients with AHD may be asymptomatic despite very low CD4 counts [Figure 19].

Figure 19: Median CD4 Count and Symptom Status of Patients in REALITY Trial^{xxx}



In order to implement the WHO package of care and stop needless deaths, countries will need to prioritize the identification of patients with AHD through a renewed focus on CD4 testing at treatment initiation.

An unfortunate byproduct of the WHO recommendation of “Treat All” in 2016 was that programs no longer saw CD4 testing as having any importance for ART initiation. Along with an increased focus on VL scale-up for treatment

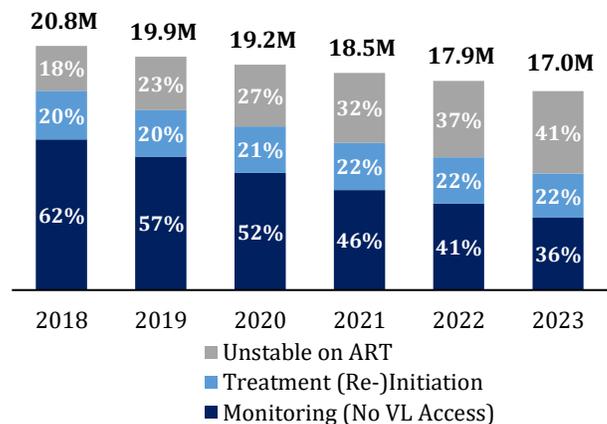
monitoring, this meant that CD4 testing was relegated to being low priority or non-existent in programs, even as a significant device footprint remained in many countries.

“HIV positivity is only a partial diagnosis of HIV status. It is critical for patients to know their AHD status as well.”

- Dr. Stephen Watiti, MD
Watiti Foundation; AHD survivor

As VL scales up, CHAI expects that the need for CD4 testing for treatment monitoring will decrease. Additionally, the superior efficacy of TLD should result in fewer CD4 tests needed for unstable patients. However, while the absolute volume of need for CD4 may decrease, it remains significant and is critical to address in order to save lives [Figure 20].

Figure 20: Estimated LMIC CD4 Need by Testing Categoryⁱⁱⁱ



Note: Based on WHO CD4 testing guidelines. “Unstable on ART” category assumes status quo viral suppression rates, which could potentially improve with TLD rollout.

CHAI analysis suggests that although there is sufficient aggregate CD4 testing capacity in many countries to meet all of the AHD screening need, access to onsite POC CD4 testing varies by country and a lack of funding for reagents and programmatic support remain the key barriers to meeting this need. A focus on CD4 network optimization is likely required to right size the CD4 fleet to ensure optimal access.

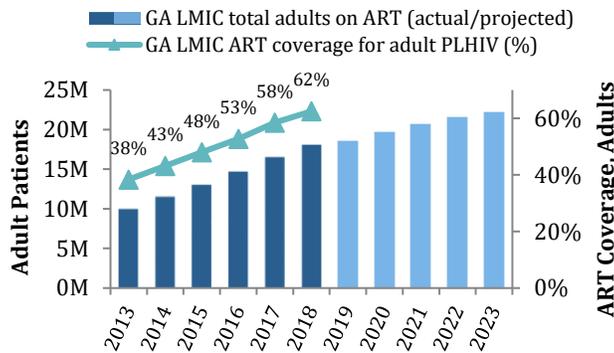
One product that may improve rates of AHD identification is the Visitect CD4 Advanced Disease test from Omega Diagnostics. This is a semi-quantitative device-free assay that can detect if a patient’s CD4 levels are below 200 cells/μL (WHO threshold for AHD). In mid-September, the Global Fund Expert Review Panel for Diagnostics (ERPD) announced that the product will be eligible for procurement following a review of the procurement request and the issue of a no-objection letter from the Global Fund.^{xxxi} Funds from both UN bodies and the Global Fund may be used to procure this product. The product has also been submitted for WHO prequalification. Médecins sans Frontières (MSF) is currently conducting field evaluations to assess both product performance and usability.

B) TREAT RIGHT WITH OPTIMAL ARVs FOR ADULT PATIENTS

Over 22 million adults on treatment globally in 2018, with nearly 19 million in GA LMICs

Nearly 2 million adults initiated on ART globally between 2017 and 2018. While this is a large number of patients, adult ART coverage in GA LMICs is still only approximately 62 percent.^{xxxiii}

Figure 21: Adults on ART and Adult ART Coverage in GA LMICs^{xxxiii}



New WHO guidelines list TLD as preferred for all PLHIV >30 kg, including women of childbearing potential

At IAS 2019, the WHO released updated guidelines recommending TLD for all patient populations (over 30 kg), including women of childbearing potential not on effective contraception [Figure 22]. The strength of this recommendation was elevated from “conditional” to “strong” in this new guidelines release.^{xxxiii}

Figure 22: WHO Adult Preferred and Alternative First-Line (1L) ART Regimens, July 2019^{xxxiii}

Population	Preferred 1L	Alternative 1L
Adults and adolescents >30 kg	TDF + XTC + DTG	TDF + 3TC + EFV400mg

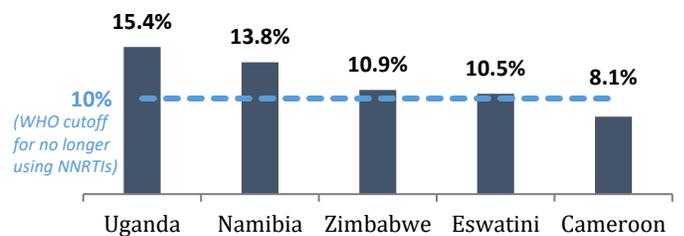
These updated guidelines were partially informed by new data from the Botswana Tsepamo study, which found the risk of neural tube defects (NTDs) among children born to mothers taking DTG at the time of conception to be significantly lower than what was initially reported in May 2018.^{xxxiv} Additionally, out of 382 DTG-exposed pregnancies monitored in Brazil, there were no reported NTDs.^{xxxv} Given the rarity of NTDs, it may be impossible to ever fully refute the safety signal, but current data with over 2,000 preconception exposures in Botswana and Brazil suggests that any elevation in risk with DTG is very small: 0.20-0.27 percent higher.^{xxxiv} Health economics and impact modelling also suggested a strong positive impact of widespread use of DTG over EFV.^{xxxvi, xxxvii}

“The risk-benefit models suggest that the benefits of DTG for women of childbearing potential newly initiating ART... are likely to outweigh the risks...”

- Updated 2019 WHO Guidelines^{xxxiii}

In addition to DTG’s superior efficacy over non-nucleoside reverse transcriptase inhibitors (NNRTIs), high rates of pre-treatment drug resistance (PDR) have further underscored the need for a non-NNRTI in 1L treatment. Out of 18 countries surveyed by the WHO between 2014 and 2018, 12 had NNRTI PDR rates of over 10 percent [Figure 23], which is the WHO threshold for switching from an EFV-based regimen to an alternate 1L regimen.^{xxxviii} The rate of NNRTI PDR in women is nearly twice that of men, further highlighting the importance of access to DTG for all women.

Figure 23: Reported Rates of NNRTI PDR in LMICs in Sub-Saharan Africa^{xxxviii}



Since the initial advisories in May 2018, tireless work from the community of women living with HIV reinforced the importance of informed access to DTG in a manner that does not create unnecessary barriers. As with the update in 2018, the WHO’s July 2019 update recommends a woman-centered approach to health care delivery and ART, which includes a woman’s right to be given all available information pertaining to medication and the right to choose what is best for them.

The WHO also reaffirmed its previous recommendations on the use of DTG in second-line (2L) for patients failing an NNRTI-based 1L regimen [Figure 24].

Figure 24: WHO Adult Preferred and Alternative 2L ART Regimens, July 2019^{xxxiii}

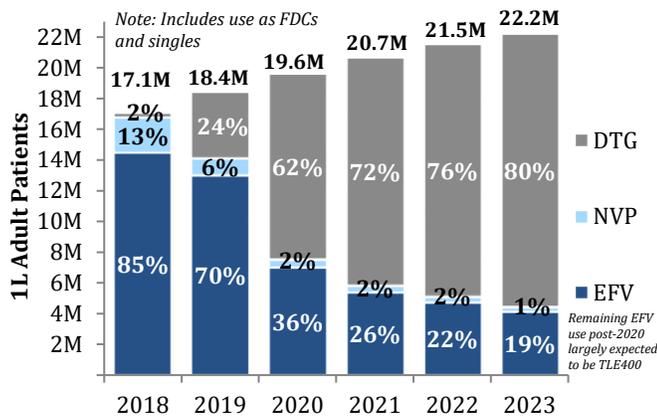
Failing 1L	Preferred 2L	Alternative 2L
TDF + XTC + DTG	AZT + 3TC + ATV/r (or LPV/r)	AZT + 3TC + DRV/r
TDF + XTC + EFV/NVP	AZT + 3TC + DTG	AZT + 3TC + boosted PI
AZT + 3TC + EFV/NVP	TDF + XTC + DTG	TDF + XTC + boosted PI

Finally, in addressing high rates of TB-HIV coinfection in many LMICs, there have been a number of studies that have showed that DTG and TB medication can be taken together safely and effectively – a double dose of DTG 50 mg with rifampicin and no dose adjustment needed with rifampentine and isoniazid.^{xxxix, xl}

Global TLD rollout continues in earnest, and will likely speed up with latest WHO confirmation of DTG use for all PLHIV

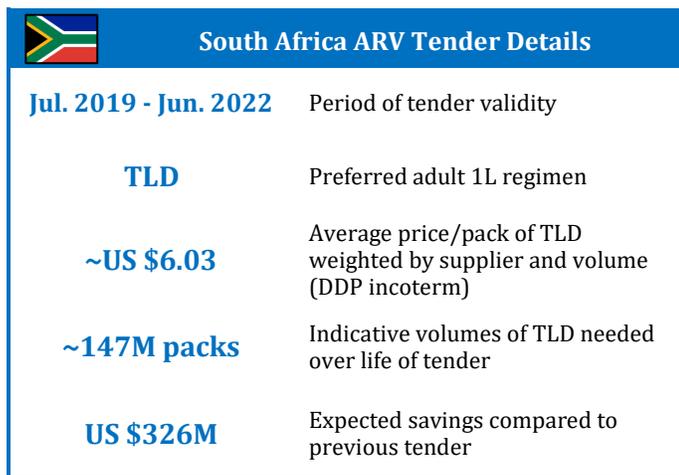
By early 2019, over 75 LMICs had included DTG-based regimens in their national treatment guidelines and over 35 had initiated procurement of DTG.^{xxxiii} At IAS 2019, PEPFAR indicated that most PEPFAR-supported countries in sub-Saharan Africa are expected to complete their 1L TLD transitions by Q1 2020.^{xli}

Figure 25: 1L Adult INSTI/NNRTI Use in GA LMICs, Patient Growth and Share^{xxxii}



South Africa, the single largest national procurer of ARVs in the world, adjudicated their ARV tender in February 2019 [Figure 26], which signaled a broad and aggressive switch to TLD. Given their market power, South Africa’s tender results have broad implications in terms of pricing and market competition.

Figure 26: South Africa’s ARV Tender Details^{xlii, xliii}



Kenya is another LMIC rapidly expanding access to TLD. At the time of publication, Kenya had put over 400,000 patients on TLD.^{lxix} Kenya’s National AIDS and STI Control Programme (NASCO) achieved this via an intensive transition plan called the *Rapid Response Initiative (RRI)* [Figure 27]. Other countries with over 200K patients already on TLD include Malawi, Uganda, and Zambia.^{lxx}

Figure 27: Kenya’s RRI to Transition to TLD^{xliv}

Kenya’s Rapid Response Initiative

Purpose

- Initial TLD uptake in Kenya was slow due to Tsepamo study safety signal
- RRI designed to rapidly transition eligible patients to TLD (or TLE400 per eligibility criteria)

Process

- Timeline and Reach
 - Three rounds over three months in Q1 2019
 - Reached all 47 counties, all county referral hospitals, and many high-volume ART clinics
- Key Activities
 - Virtual and in-person site and HCW trainings
 - Transition monitoring and staff mentorship
 - Patient education

Impact

- Over 300,000 patients on TLD** by end of RRI (Mar. 2019), paving the way to scale to over 400K patients by Sep. 2019

At the time of publication, seven suppliers of TLD were eligible for Global Fund procurement, of which five are also eligible for PEPFAR procurement, thus providing reassurance of supply security [Figure 28].

Figure 28: TLD Approvals/WHO PQ (as of Sep. 2019)^{xlv, xlvi, xlvii}

Tentative US FDA	WHO PQ	GF ERP
Aurobindo*	Cipla*,#	Emcure
Hetero#	Mylan*,#	
Laurus*		
Macleods		
Mylan*,#		

* Also has tentative US FDA approval for DTG 50 mg single tablets
 # Also has WHO PQ for DTG 50 mg single tablets

TLE400 now preferred alternative over TLE600

Whereas previously the WHO guidelines listed both TLE600 and TLE400 as alternative regimens to TLD, TLE400 is now listed as the single alternative regimen due to lower rates of treatment discontinuation and severe treatment-related adverse events compared to TLE600.^{xxxiii} Further promoting the use of TLE400 over TLE600, PEPFAR is no longer procuring TLE600 (or TDF/FTC/EFV600).^{xlvi}

Despite listing TLE400 as an alternative 1L regimen, the WHO recommends that country programs use boosted PIs as alternative regimens (in place of EFV) in settings with EFV PDR above 10 percent.^{xxxiii}

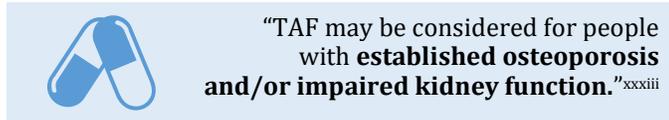
A number of countries, most notably Kenya, Zambia, and Zimbabwe, have moved large numbers of patients from TLE600 to TLE400. With the updated guidance from the WHO on the use of TLD, it is expected that these countries will shift many patients on TLE400 to TLD.

As of this writing, only Mylan and Macleods have tentative US Food and Drug Administration (US FDA) approval and/or WHO PQ for TLE400, compared to 5 TLE600 suppliers.^{xlv, xlvii}

TAF makes first appearance in WHO treatment guidelines; clinical questions remain

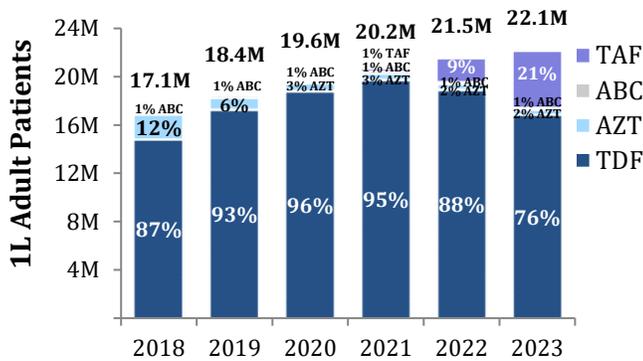
Tenofovir alafenamide fumarate (TAF) is a tenofovir pro-drug that could replace TDF in formulations such as TLD. Interest in TAF is primarily based on potential cost savings relative to TDF-based regimens and smaller pill size given a lower required dose (25 mg TAF compared to 300 mg TDF).

The WHO listed TAF, in the form of TAF + XTC + DTG in their July 2019 guidelines update as a regimen for use in special circumstances in adults and adolescents, and an alternative 1L in children with approved TAF dosing.^{xxxiii}



Key studies to inform broader TAF use, including use in important populations such as pregnant women, are ongoing. Full data to inform a potential broader inclusion of TAF in WHO guidelines is not expected until 2020, with broader uptake likely starting in 2021 [Figure 29].

Figure 29: 1L Adult NRTI Market in GA LMICs, Patient Growth and Share^{xxxii}



Zambia is one of the first LMICs in sub-Saharan Africa to plan to introduce TAF-based regimens in their national treatment program for special circumstances.

Data from the ADVANCE study presented at IAS 2019 [Figure 30] showed significant weight gain associated with patients on both TAF/FTC + DTG as well as TDF/FTC + DTG (compared to patients on TDF/FTC/EFV600).^{xlx} However, weight gain was highest in patients on the TAF/FTC + DTG regimen. Further work is needed to understand this effect, its extent, and any potential programmatic impacts.

Figure 30: ADVANCE Study Weight Gain^{xlx}

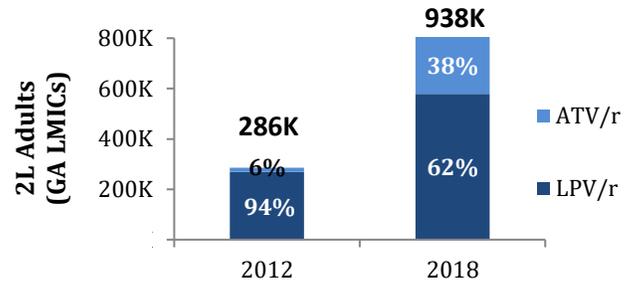
Mean Change in Weight (kg) at Week 96			
	TAF/FTC+DTG	TDF/FTC+DTG	TDF/FTC/EFV
Men	+5 kg	+4 kg	+1 kg
Women	+10 kg	+5 kg	+3 kg

At the time of publication, Mylan is the only generic supplier with tentative US FDA approval for TAF-based products: both TAF/FTC/DTG and TAF/3TC/DTG.^{xlv}

Improved options for 2L will create some flux in ARV choice over the next few years

In terms of current adult protease inhibitor (PI) use in 2L, ATV/r continues to increase its market share [Figure 31].

Figure 31: ATV/r's Market Share Increase in GA LMICs since 2012ⁱⁱⁱ



Although many country programs are focusing on their 1L TLD transitions, a number are planning to use DTG in 2L regimens as well, including South Africa, Kenya, Cambodia, and Laos. As noted in last year's HIV Market Report, there are ~80 percent cost savings with DTG over LPV/r.^l

DRV has superior clinical efficacy, a favorable tolerability profile, and high genetic barrier to resistance relative to other PIs on the market. However, the updated 2019 WHO guidelines continue to list DRV/r as an alternative 2L regimen, in part due to lack of availability of a generic FDC.

Affordability is another key barrier to uptake of DRV in LMICs. CHAI and Unitaid have been working to address the affordability barrier pending regulatory approval of a generic DRV (400/50 mg) FDC.^{li} DRV can also be used in third-line (with dose adjustment) after use of PIs in 2L.^{xxxiii}



Major funders stop procurement of NVP and review other non-optimal products



Given high rates of PDR and lower efficacy compared to other ARVs, PEPFAR and the Global Fund are moving away from the procurement of nevirapine (NVP)-based regimens. As previously shown in Figure 25, NVP accounted for approximately 14 percent of the adult 1L market in 2018.

“Nevirapine-based ART regimens should no longer be utilized for adult and pediatric patients... No country should be using NVP-based regimens and PEPFAR will not fund procurement of NVP-based regimens”

- PEPFAR COP19 Guidance^{xlii}

In the latest large buyer forecast (aggregating future orders from PEPFAR, the Global Fund, South Africa, and Kenya), PEPFAR and the Global Fund reported no planned procurement of NVP 200 mg tablets or adult AZT/3TC/NVP (ZLN) tablets.^{xlviii} In addition, both products have been removed from the GHSC-PSM e-Catalog and Global Fund pooled procurement mechanism (PPM) price list.

USAID has also implemented a new “ARV order review” process for orders fulfilled via GHSC-PSM to ensure that programs procure the most clinically appropriate drugs – each product is assigned to a tier with an associated approval process [Figure 32]. This will also help simplify supply chains and consolidate orders around key products.

Figure 32: USAID ARV Order Review Tiers^{lii}

Tier	Description
1	Preferred product list; most clinically appropriate; formulated in packaging to simplify supply chain
2	Orders require USAID pharmacist review
3	Orders require additional review process
4	Products are not eligible for procurement

Pipeline ART products are moving closer to potential use

The current paradigm of three-drug oral ART may potentially change in the coming years as a number of new products get closer to being available [Figure 33]. More details on pipeline products can be found in the HIV i-Base Pipeline report at www.i-base.info/htb/36278.

Figure 33: Pipeline ART Products

Two-Drug ART

- Data from Ph. III GEMINI I & II and TANGO has shown oral DTG+3TC to be non-inferior to three-drug ART in both treatment-naïve and experienced patients^{liii,liiv}
- Based on these data, ViiV received US FDA approval for *Dovato* (DTG/3TC) in April 2019 for treatment-naïve adult patients.^{xliv} Another oral two-drug regimen *Juluca* (DTG/RPV) from Janssen and ViiV had been approved in November 2017 for treatment-experienced adults.^{xlv}
- CADO3 workshop in Dec. 2017 **did not support use of two-drug regimens in LMICs** as studies to date have not considered the LMIC context (e.g., no data on TB or pregnant women, as well as programmatic challenges)^{lv}

Injectable ART

- Ph. III ATLAS and FLAIR studies showed **monthly injectable CAB/RPV to be non-inferior to three-drug oral ART** among treatment-experienced and naïve patients^{lvi,lvii}
- ViiV submitted a New Drug Application (NDA) to the US FDA in April 2019. If approved, this would be the first injectable ART product on the market^{lviii}
- However, likely **pricing for LMICs is unknown and RPV requires cold chain**, so it remains to be seen how this product may impact the LMIC market

New Drug Classes

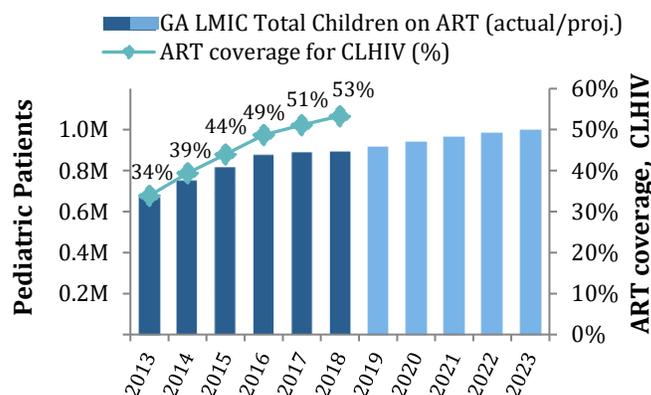
- Ph. III trial data on ViiV’s *fostemsavir*, a first-in-class attachment inhibitor, was presented at IAS 2019
- Data showed **improvements in viral suppression among heavily treatment-experienced patients** from previous week 48 data (54% to 60% viral suppression at weeks 48 and 96 respectively)^{lix}
- ViiV to submit a dossier for US FDA review in late 2019^{lx}

C) TREAT RIGHT WITH OPTIMAL ARVs FOR PEDIATRIC PATIENTS

890K pediatric patients on ART in GA LMICs in 2018, but coverage low at 53 percent

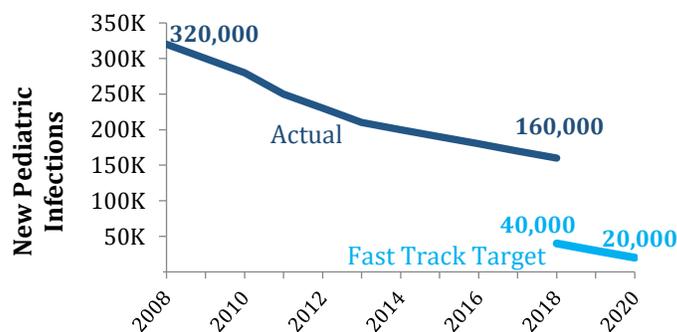
In 2018, there were 1.7 million children under the age of 15 living with HIV globally, according to UNAIDS estimates.^{xxiii} While an estimated 890,000 CLHIV were on treatment in 2018 in GA LMICs, the rate of pediatric treatment scale-up is still slow [Figure 34].^{xxiii}

Figure 34: Number of Pediatric Patients on ART and Pediatric ART Coverage in GA LMICs^{xxxii}



While the number of new pediatric HIV infections has been cut in half since 2008, this still falls short of progress needed to reach the Super-Fast-Track goal of less than 20,000 new pediatric infections by 2020 [Figure 35].

Figure 35: Global Number of New Pediatric Infections, 2008-2018^{xxxii}



Geographic discrepancies in pediatric ART coverage are still significant. West and central Africa continue to lag behind with only 28 percent of children on ART, far below the global average of 54 percent.^{xxiii} At the same time, east and southern Africa pediatric ART coverage is above the global average at 62 percent, but progress has slowed with only a 2 percentage point increase from 2017.^{xxiii}

Updated WHO guidance continues to prioritize DTG and demote NNRTIs to “use in special circumstances”

Given its superior efficacy, fewer side effects, and higher barrier to resistance, the WHO has maintained its July 2018 recommendation of DTG as the preferred 1L option for all children above 4 weeks, and raltegravir (RAL) for neonates [Figure 36]. Given high levels of PDR and the availability of more efficacious drugs, such as DTG, NNRTIs continue to be recommended only in special circumstances.

Figure 36: Updated 1L Pediatric Treatment Regimens, WHO, July 2019^{xxxiii}

	Preferred 1L	Alternate 1L	Special Circumstances
Children < 30 kg	ABC + 3TC + DTG*	ABC + 3TC + LPV/r	ABC + 3TC + EFV (or NVP)
		ABC + 3TC + RAL	AZT + 3TC + EFV (or NVP)
		TAF* + XTC + DTG	AZT + 3TC + LPV/r (or RAL)
Neonates	AZT + 3TC + RAL	AZT + 3TC + NVP	AZT + 3TC + LPV/r

*Only where dosing available

DTG 50 mg tablets provide an immediate access option for children ≥20 kg

Based on preliminary data from the ODYSSEY trial, the WHO updated its treatment guidelines in early 2019 to recommended DTG 50 mg tablets for use by children down to 20 kg.^{xxxiii}

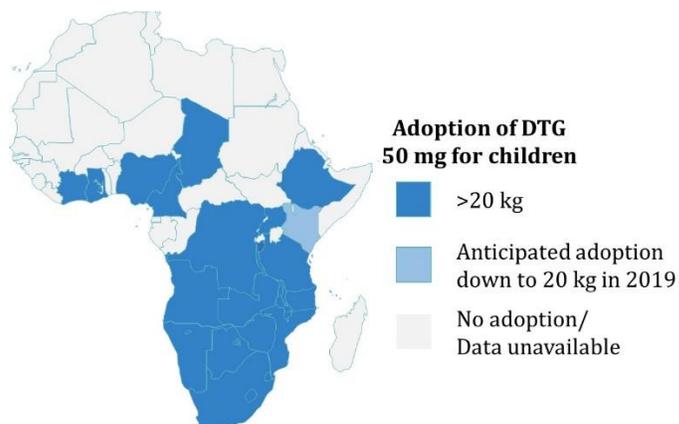
Figure 37: DTG and NRTI Backbone Formulations for Children ≥ 20 kg

20-24.9 kg	ABC/3TC (120/60 mg) dispersible dual + DTG 50 mg single
25-29.9 kg	ABC/3TC (600/300 mg) dual + DTG 50 mg single
≥ 30kg	TDF/3TC/DTG (300/300/50 mg) FDC

Note: Table represents formulations. Dosing will vary by weight band.

Both the DTG 50 mg single and TLD FDC are readily available in many country supply chains. Extending access to existing formulations of DTG will allow an estimated additional 500,000 children to start or transition to a more durable DTG-based ART regimen.^{lxi} Numerous countries have begun adopting the recommendation to prescribe DTG 50 mg down to 20 kg [Figure 38].

Figure 38: Adoption of DTG 50 mg for Children Living with HIV down to 20 kg in Sub-Saharan Africa^{lxi}



Accelerated development of a generic DTG 10 mg dispersible scored tablet underway for children < 20 kg

Despite inclusion in WHO guidelines, pediatric dosing guidance for DTG in children < 20 kg is still in development and no generic formulation is yet available.

Data from the ODYSSEY trial presented at IAS 2019 provided pharmacokinetic data for children 6-20 kg to help inform weight-based dosing.^{lxii} WHO guidance is expected in late 2019 following analysis of this and other data.



Additionally, Mylan and Macleods, who won a competitive RFP from CHAI including a financial incentive

from Unitaid and technical assistance from ViiV, are working to develop a generic DTG 10 mg dispersible scored tablet for pediatric patients.

Through this innovative public-private partnership, a novel filing strategy has been developed and discussed with the US FDA via official pre-IND correspondence. This strategy could significantly decrease the time between approval of innovator drug and generic drug, a process that can typically take several years.

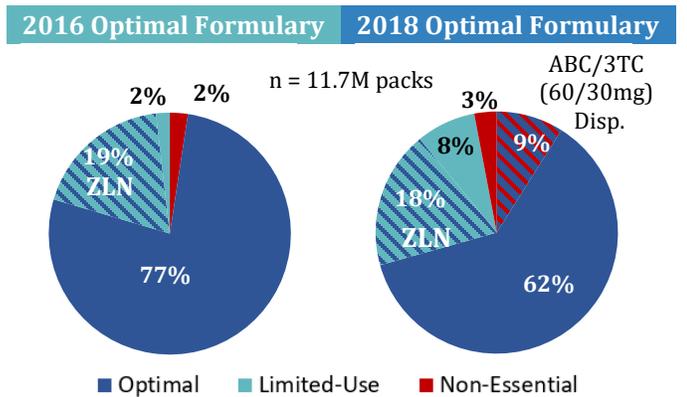
Per the commitments made at the Vatican High-Level Dialogue on Paediatric HIV in December 2018, ViiV is expected to file their 5 mg dispersible (disp.) tablet with the US FDA by December 2019, and Mylan and Macleods will file their 10 mg scored dispersible tablets in Q1/Q2 2020 per the collaboration between the companies.^{lxiii}

A pediatric triple FDC of ABC/3TC/DTG (ALD) is also being developed, but is likely at least 2-3 years away from being on the market. Such a product would greatly simplify pediatric treatment by providing the WHO-recommended regimen in a single formulation. National programs should plan to take rapid advantage of innovations in pediatric formulations as they come to market, while not delaying optimization to await a FDC formulation.

Although pediatric regimen splits in 2018 reflect a continued focus on optimization, NVP use is still high

Over the past few years, there have been significant gains towards optimizing pediatric treatment in LMICs. In 2018, procurements reflected a high level of optimization even when compared against the new 2018 Optimal Formulary that was released only in the middle of that year [Figure 39].

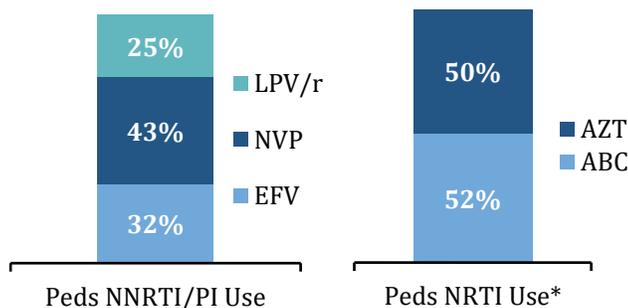
Figure 39: Product Status of Pediatric Procurements Monitored by the APWG in 2018^{lxiv}



Hatched sections represent product status transitions between formulary editions (e.g., optimal to limited-use)

However, ZLN continues to be a relatively high-volume product despite being demoted to Limited-Use status in 2016 by the IATT. At the end of 2018, 43 percent of children on pediatric formulations continued to be on NVP-containing regimens [Figure 40]. Convenience (availability of a triple FDC) and familiarity continue to be main drivers of use, despite poor treatment outcomes compared to other products.

Figure 40: 2018 Pediatric Regimen and Formulation Splits for GA LMICs (pediatric formulations only)^{xxxii}



*Total is >100% due to some regimens including both ABC and AZT

The continued use of NVP is concerning given the WHO estimates that one in two children has pre-treatment drug resistance to NVP or EFV (although rates vary greatly across countries).^{lxv} A 2018 study from Malawi similarly found that 44 percent of children in the study had drug resistance mutations to NVP or EFV.^{lxvi}

The Global Fund and PEPFAR have ceased procurement of pediatric NVP

Given the high levels of pre-treatment NVP resistance in children, and the availability of more optimal drugs, the Global Fund and PEPFAR have ceased NVP procurement for use in treatment. NVP oral solution for post-natal prophylaxis will still be permitted. Countries will no longer be able to procure NVP through these channels except in special circumstances. As countries begin to develop new pediatric treatment plans, the Global Fund and PEPFAR have encouraged swift transitions to more optimal regimens even if some NVP stock wastage will occur.^{lxvii,xii}

Short-term heavy reliance on LPV/r-based formulations for CLHIV until pediatric DTG is available

Although DTG is the preferred treatment option for all children above 4 weeks, countries phasing out NVP will need to transition to LPV/r in the short- to medium-term future until a generic formulation and dosing recommendations for DTG have been developed for patients under 20 kg. For children under 20 kg who are able to swallow pills, countries can transition to LPV/r (100/25 mg) tablets. However, for children unable to swallow pills, several products are currently available and in development [Figure 41].

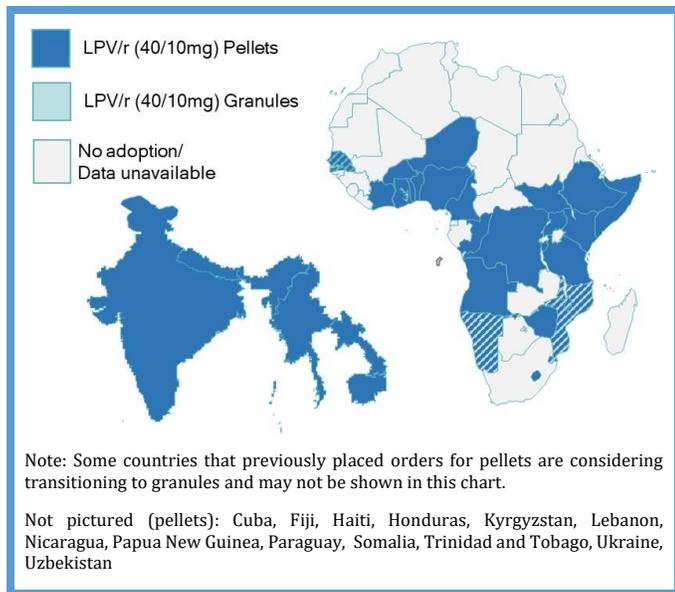
Figure 41: Pediatric LPV/r Options

LPV/r Formulations for Children 3 – 20 kg (who are unable to swallow tablets whole)	
LPV/r (80 mg + 20 mg/ml) Oral Solution	<ul style="list-style-type: none"> • Unpleasant taste often resulting in adherence issues • Cold chain requirements
LPV/r (40/10 mg) 2-in-1 Pellets and Granules	<ul style="list-style-type: none"> • Currently being implemented in countries • Supply constraints easing after extended period of challenge
ABC/3TC/LPV/r (30/15/40/10 mg) 4-in-1 Granules	<ul style="list-style-type: none"> • Similar to 2-in-1 granules but complete regimen provided • In development but will share production capacity with LPV/r pellets and granules

Both Cipla (pellets) and Mylan (granules) have committed to significantly expand capacity for their respective 2-in-1 LPV/r products by January 2020.^{xxxix} Given increased supply security and renewed motivation to move away from NVP-based regimens, a number of countries have adopted and are scaling up pellets or granules [Figure 42].

The APWG is closely monitoring the volumes of orders placed, and engaging suppliers in monthly calls to ensure demand does not outstrip supply. Latest guidance and information can be found on the group’s website (www.arvprocurementworkinggroup.org).

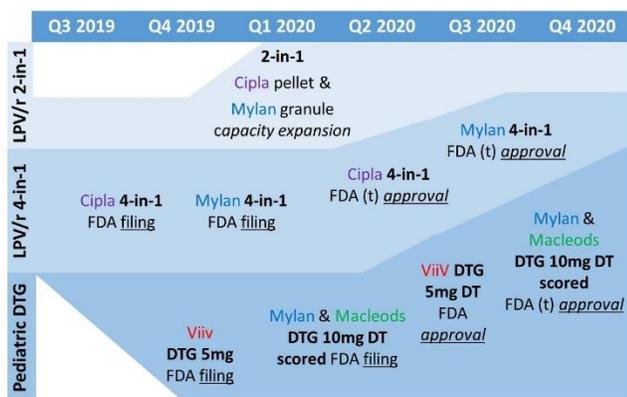
Figure 42: Map of Countries that have Procured LPV/r Pellets/ Granules^{lxviii}



Development of the 4-in-1 FDC of ABC/3TC/LPV/r (30/15/40/10 mg) is also underway. Cipla is planning on filing in September 2019, and Mylan plans to file with the US FDA by Q1 2020 [Figure 43].^{lxix} Assuming timely submission and a priority (6 mo.) review, the first of these products could be tentatively approved as early as Q2 2020.

With DTG 10 mg dispersible and scored tablets expected to be available relatively soon after the 4-in-1 products, it remains to be seen how uptake of the 4-in-1 will unfold since national programs would be advised to use the best available option and accelerate access to DTG as soon as dosing and formulations are available. However, there will continue to be a need for a PI FDC option, such as the 4-in-1, for 2L or children who cannot tolerate DTG, particularly in the absence of a pediatric DRV/r FDC.

Figure 43: Estimated Timeline for Key Pediatric Product Development^{lxix}



Regulatory and normative timelines are target dates assuming priority (6 mo.) review, and are subject to change. Availability in country depends further on timing of national registration or import waivers.

PADO4 convened to update development priorities for pediatric ART

The fourth Pediatric ARV Drug Optimization (PADO4) meeting was held in December 2018, bringing together key stakeholders and experts to determine priorities in pediatric product development.

Key outputs from this meeting were the PADO4 medium- and long-term priority lists that identify key products where development should be accelerated [Figure 44]. Several products were removed from previous versions of both lists either as a result of limited interest from countries, feasibility issues, or limitations of the product.

Figure 44: Updated PADO4 Medium- and Long-Term Priority Lists^{lxx}

Medium-term Priorities (3–5 years)	Long-term Priorities (5–10 years)
DRV/r (120/20 mg)	MK 8591
DTG (10 mg) Dispersible Scored Tablets	Doravirine
ABC/3TC/DTG (60/30/5 mg) Tablets	Long acting oral/ injectable
TAF/XTC Dispersible Tablets	Neutralizing antibodies (bNAb)
TAF/XTC/DTG Dispersible Tablets	New delivery technologies

The PADO4 medium-term priority list reflects the move to DTG-based regimens for all in the latest WHO guidance.

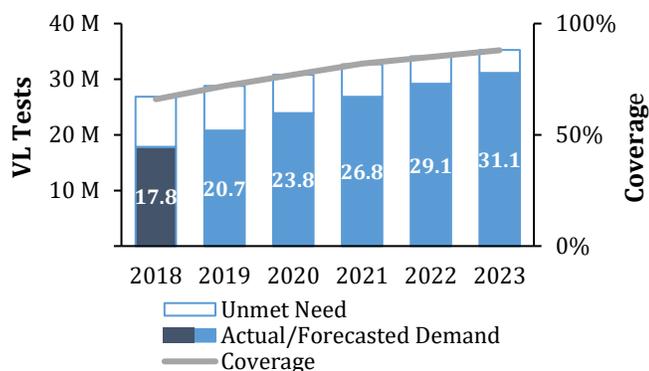
As discussed earlier, there are a number of exciting developments in treatment innovation for adults. It will be important to ensure that children are able to access these new products as quickly as possible after adult approval. To this end, the Global Accelerator for Pediatric Formulations (GAP-f) is a new mechanism working to support and formalize collaboration across sectors to ensure that new optimal pediatric ARVs are available as soon as possible.^{lxxi}

D) TREAT RIGHT WITH APPROPRIATE MONITORING

Routine VL testing continues to grow amid a push for pricing transparency

As with EID testing, country programs continue to scale up their VL programs with nearly 18 million tests run in 2018 in LMICs. CHAI projects that the number of VL tests run could double by 2023, reaching 31 million tests [Figure 45].

Figure 45: LMIC VL Demand Forecast^{lxxii}



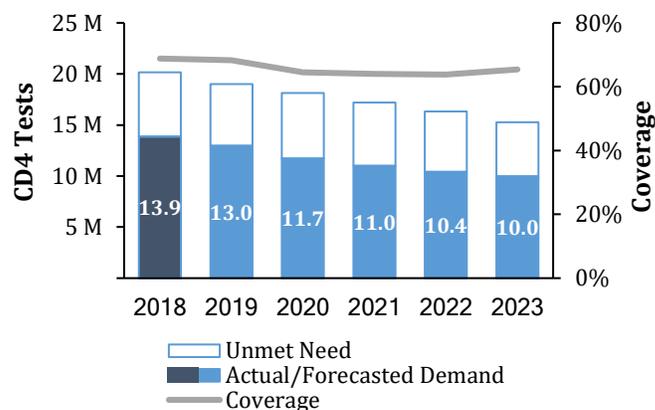
In the three years since the WHO recommended the use of routine VL testing (in lieu of CD4) for treatment monitoring, most LMICs have implemented this in some fashion.^{lxxiii}

In early 2019, GHSC-PSM (which manages PEPFAR commodity procurement) launched a global RFP for VL (and EID) tests over the next three years, with awards expected to be announced in Q4 2019.ⁱⁱ The ultimate goal of the RFP is to move all PEPFAR testing procurement to an “all inclusive” pricing model that will standardize and streamline pricing and procurement in LMICs. This builds upon last year’s announcement of the market’s first all-inclusive price deal – a US \$12 per patient test price for HIV, Hepatitis B & C, and Human Papilloma Virus assays run on the Hologic Panther.^{lxxiv}

CD4 monitoring remains critical for monitoring where there is no access to VL

CD4 testing was previously discussed in the context of AHD. As discussed earlier, CHAI expects that the need for CD4 testing for treatment monitoring will decrease as VL access improves. Additionally, the superior efficacy of TLD should result in fewer CD4 tests required due to treatment failure. [Figure 20, page 13]. However, while the absolute volume of need for CD4 may decrease, the need remains significant and is critical to address in order to save lives, particularly among patients with AHD. CHAI projects that although demand will continue to fall in the short term, 10 million CD4 tests are likely to still be run in 2023 with renewed commitments to address AHD [Figure 46].

Figure 46: LMIC CD4 Demand Forecast^{lxxv}



Patient access to timely VL results is critical to ensuring a prompt, appropriate response to viral failure

While slower than the uptake of POC EID, POC VL continues to be an important testing strategy for patients requiring a fast result turnaround time and/or those who may live in remote areas without access to centralized VL testing. A number of developments have occurred in the past year supporting the case for POC VL [Figure 47].

Figure 47: Developments Supporting POC VL



Abbott’s **m-PIMA device received WHO PQ for POC VL** testing in April 2019, making this the first true POC VL offering in the market^{xvii}



Abbott released an **all-in price for POC VL/EID on the m-PIMA** at the Vatican High-Level Dialogue on Paediatric HIV in December 2018^{xviii}

This is the first **all-in price for a POC test**, showing further movement toward this pricing structure in the market



PEPFAR COP19 guidance supports the use of **POC VL** testing for **pregnant women** and **breastfeeding mothers**^{xix}

Use of POC VL for these populations will help **quickly identify mothers at high-risk of vertical transmission** and allow rapid action to re-suppress their viral loads

As with EID, there is similar global interest in integration of VL on existing platforms (such as the GeneXperts for TB). See page 10 for more information on testing integration.

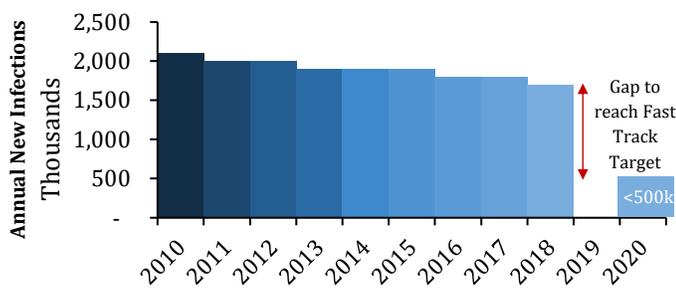


STAY NEGATIVE

New HIV infections decreased to 1.7 million in 2018, but transmission rates are still high

Annual new HIV infections have declined globally by ~16 percent since 2010, but this decline falls far short of the rate needed to reach the Fast Track target of less than 500,000 new infections by 2020 [Figure 48].^{xxiii} In 2018, key populations and their partners accounted for over 50% of new infections.^{iv} Access to a comprehensive package of prevention methods and approaches targeted to key populations will be necessary to reach this Fast Track target.

Figure 48: Estimated Annual New HIV Infections Globally between 2010 and 2018^{xxiii}



Oral PrEP scales up in some LMICs, but further adoption and expansion of PrEP programs is still needed

The use of oral PrEP, a daily dual ARV preventive therapy, can greatly reduce the chance of HIV acquisition by about 99 percent when taken consistently.^{lxxvi} As of July 2019, there were over 300,000 cumulative oral PrEP initiations globally.^{lxxvii} While a large percentage of oral PrEP users are based in high-income countries (HICs), several LMICs have introduced and begun scaling up oral PrEP. It is important to note that even within HICs, access to oral PrEP is highly variable and evolving.

Figure 49: US Preventive Services Task Force Recommendation for Oral PrEP

US Preventive Services Task Force recommends oral PrEP for all high-risk groups

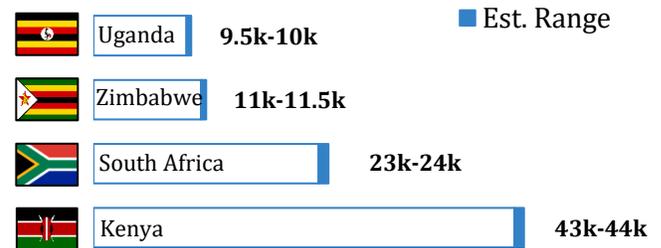
Under the Affordable Care Act, this means that **US insurers are required to offer PrEP at no cost to clients by 2021.**^{lxxviii}



In contrast, only after several legal challenges did the National Health Service in England begin to offer limited access to oral PrEP through the PrEP Impact Trial.^{lxxix} Otherwise, individuals must resort to online pharmacies to access PrEP.^{lxxx}

Kenya has become a leader in the oral PrEP space in LMICs with an impressive scale-up of PrEP enrollment since national launch in May 2017.^{lxxxi} South Africa's oral PrEP program has also initiated a substantial number of individuals since rollout began in June 2016.^{lxxxii} While there are several other LMICs beginning to scale up oral PrEP programs, the number of people initiated remains modest.

Figure 50: Top 4 LMICs by Cumulative Oral PrEP Initiations per PrEPWatch as of July 2019^{lxxvii}

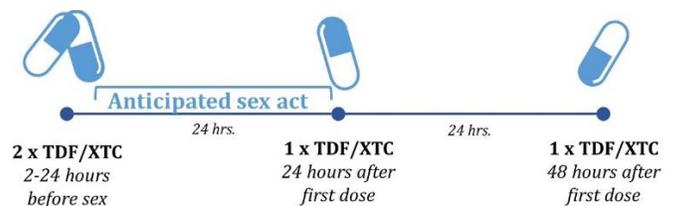


A significant challenge in monitoring oral PrEP scale-up is that the cumulative number of client initiations does not demonstrate current or continuous usage. It can be challenging to quantify the number of current PrEP users given variable continuation rates.

WHO has endorsed event-driven PrEP for men who have sex with men

While oral PrEP has been proven to be an effective prevention tool, clients sometimes struggle with or prefer not to take medication daily. Event-driven (ED)-PrEP, the use of PrEP immediately preceding and following when an individual expects to engage in risky sexual activity, could ease the burden of daily adherence [Figure 51].

Figure 51: ED-PrEP Dosing Schedule^{lxxxiii}



The IPERGAY trial results from 2015 and 2017 suggested efficacy of ED-PrEP in high-risk men who have sex with men (MSM).^{lxxxiii} A more recent demonstration project in France, where ED-PrEP is included in national guidelines, reported no breakthrough HIV-infections with either daily or ED-PrEP.^{lxxxiv}

Given this further evidence, the WHO now recommends that event-driven dosing be offered to MSM as an additional option to daily dosing.^{lxxxiii} Further studies are needed to determine the eligibility of other groups for this dosing strategy.

Promising results for TAF/FTC in DISCOVER trial but questions remain for LMIC context

Results from the phase III DISCOVER trial have shown that TAF/FTC, brand name Descovy, is non-inferior to Truvada (TDF/FTC) for use as oral PrEP for cisgender men and transgender women who have sex with men.^{lxxxv} There was also suggestion of an improved bone and renal side effect profile.^{lxxxv}

Following these promising results, Gilead submitted a supplemental New Drug Application with the US FDA using a Priority Review voucher in April 2019.^{lxxxvi} In August 2019, a US FDA advisory panel recommended that Descovy be approved for MSM and transgender women, but not for cisgender women in the absence of clinical trials data confirming safety and effectiveness in that population.^{lxxxvii} A final decision by the US FDA is expected by the end of 2019.

The lower dose required for TAF over TDF leads to a smaller pill size and the potential for price reduction. However, any price reduction will likely be dependent on widespread use of generic TAF for HIV *treatment* in order to drive economies of scale. As discussed in the Treat Right section, there are several open questions about the role of TAF for HIV treatment in LMICs. Finally, AGYW are a major focus of prevention efforts in LMICs. Thus, should the US FDA follow the advisory panel recommendation on a more limited indication for Descovy, this may mean that TAF plays a limited role in oral PrEP in these settings.

Biomedical Prevention Implementation Collaborative will facilitate the coordinated development and introduction of future biomedical prevention products

A major learning from oral PrEP introduction in LMICs was that key components of product introduction were not well timed. For example, large-scale demonstration projects were not planned in parallel to clinical trials and were not coordinated to comprehensively answer critical implementation questions, leading to delays in scale-up.

To avoid these issues in the future, the Biomedical Prevention Implementation Collaborative (BioPIC) was launched in Q3 2018 by the Bill & Melinda Gates Foundation (BMGF), ViiV Healthcare, and the Prevention Market Manager. This first-of-its-kind collaborative between over 80 organizations and over 100 experts aims to develop a comprehensive, coordinated product introduction agenda and access strategy for pipeline prevention products. Strategic planning for the introduction of the BioPIC's first focal product, the cabotegravir long-acting injectable (CAB-LA) for prevention, is presently underway as the product is concurrently evaluated in clinical trials (HPTN 083 and HPTN 084).

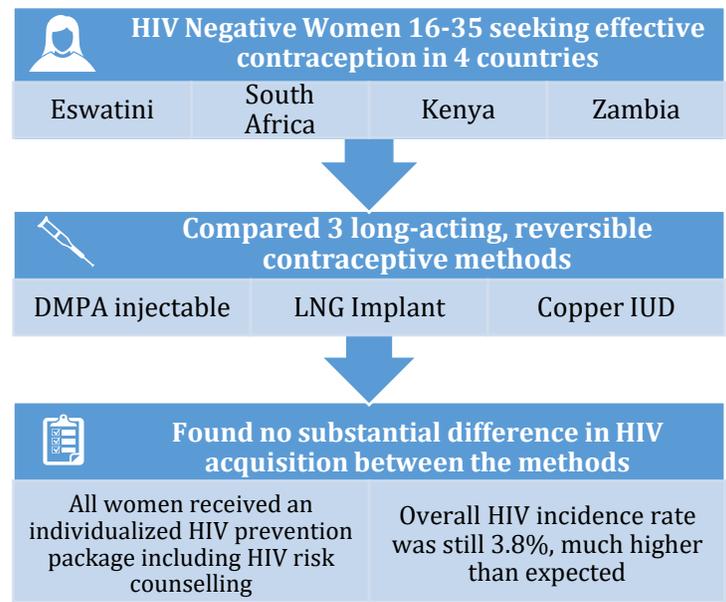
CAB-LA is anticipated to be one of the first long-acting preventive methods to come to market. Should CAB-LA receive regulatory approval, the BioPIC aims to shorten the time between clinical trial results and public health impact, by ensuring activities are well-designed, well-timed, and well-funded to meet the needs of global and country decision-makers. This approach will be distilled into a new

product introduction framework that is adaptable to any future biomedical prevention product.

ECHO trial found no difference in HIV acquisition across long-acting contraceptive methods, but high rates of HIV acquisition across all groups

Prior to the results of the ECHO trial [Figure 52], the impact of various contraceptive methods on HIV acquisition was unknown.

Figure 52: Summary of ECHO Trial and Results^{lxxxviii}



Women were not recruited based on characteristics of HIV risk; therefore the trial results emphasize “the need for more aggressive HIV and sexually transmitted infection prevention and management efforts for African women, including PrEP and HIV prevention integrated with contraceptive services.”^{lxxxix}

Sustaining high VMMC coverage is critical to reduce future burden of HIV

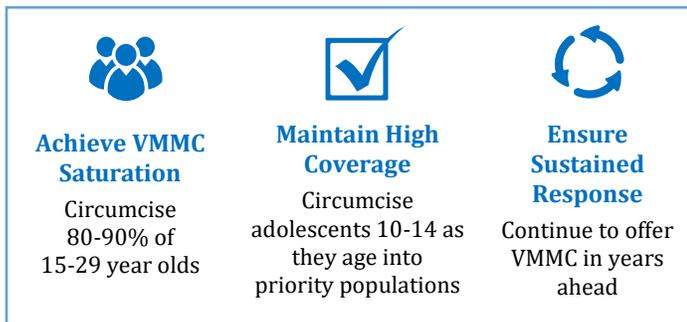
Voluntary medical male circumcision (VMMC) remains a highly cost effective once-off HIV prevention method appropriate for settings with high HIV incidence rates. Achieving a high VMMC coverage rate, especially among men aged 15-29 years has a more immediate effect on HIV acquisition risk whereas VMMC among adolescent boys aged 10-14 years is mainly an investment in the future.^{xc}

Sustained support from the global level down to the facility level is a key factor for successful VMMC scale-up. In addition, VMMC implementation requires coordinated partnerships that are effective and efficient in meeting scale-up needs.

In 2018, approximately 4.1 million VMMCs were conducted in 14 priority countries.^{xxiii} Countries with mature VMMC programs, such as Zambia and Zimbabwe, are transitioning from rapid scale up to long-term, routine service delivery.

However, given the different rates of *subnational* coverage within countries, there are three core principles that can help direct national strategy from transition to sustainability [Figure 53].

Figure 53: Principles for VMMC Sustainability



Vaccine trial launched in southern Africa aims to provide proof-of-concept efficacy

The Imbokodo (HVTN 705/HPX2008) phase II clinical trial of an HIV prevention mosaic vaccine is currently underway in Malawi, Mozambique, South Africa, Zambia, and Zimbabwe and recently achieved full enrollment.^{xci} During the trial, the experimental vaccine developed by the Janssen unit of Johnson & Johnson will be given to 2,600 sexually active HIV-negative women between the ages of 18 and 35 years.^{xci} Results are expected by 2021 and will help provide essential data for the potential development of the first universal HIV vaccine. Another trial of the vaccine is also set to begin in Europe and the US by the end of the year.^{xcii}

There are a number of other vaccines in various stages of development. See <https://www.avac.org/prevention-option/hiv-vaccine> for more information.

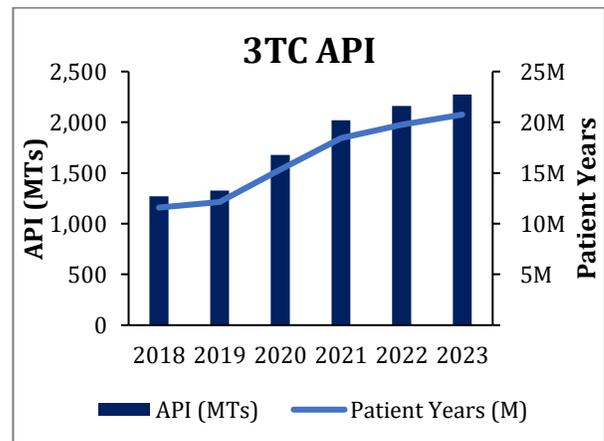
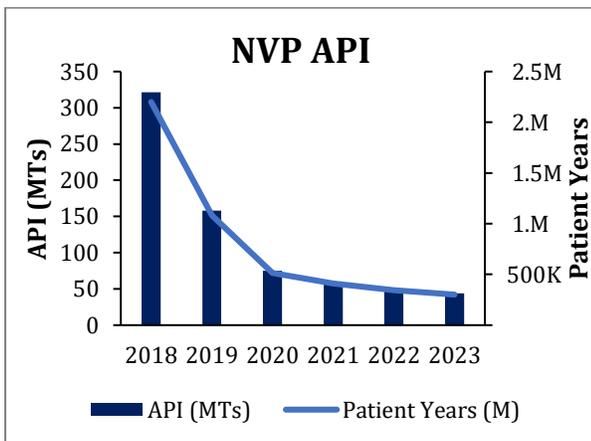
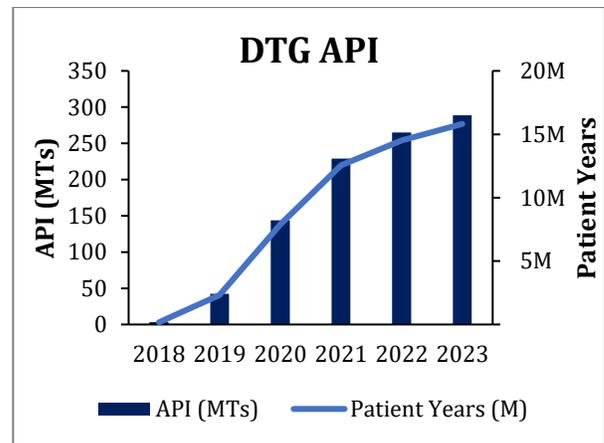
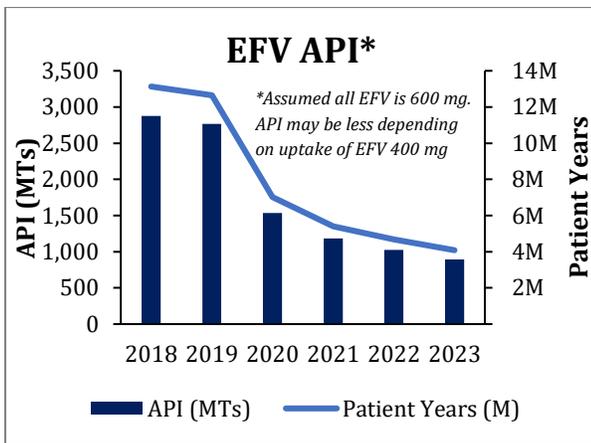
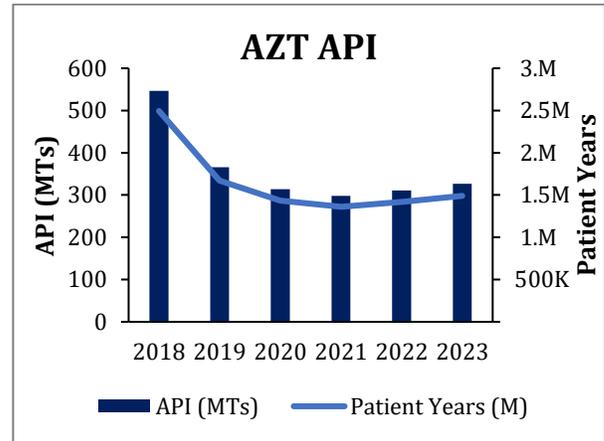
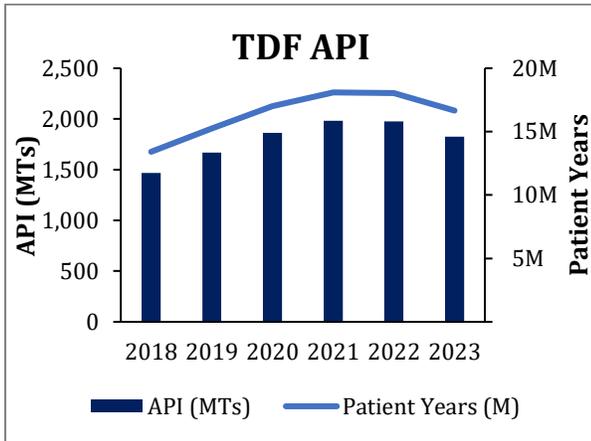
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Appendix A: Forecasted Adult API Demand in GA LMICs

The graphs below show the estimated generic-accessible patient demand and active pharmaceutical ingredient (API) volume 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 adults and pediatric ARVs. Prices are Ex-Works (EXW) unless otherwise noted.

Product	Pack Size*	Global Fund PPM Price Aug. 2019 ^[1]	GHSC-PSM E-Catalog Price Aug. 2019 ^[2]	MSF Price Jul. 2018 ^[3]	RSA Weighted Av. Tender Price 2019-2022 ^[4]
Adult Products					
ABC/3TC (600/300 mg)	30 tablets	\$9.20	\$9.20	\$9.96	-
ATV/r (300/100 mg)	30 tablets	\$12.90	\$13.49	\$15.00	-
AZT/3TC (300/150 mg)	60 tablets	\$5.25	\$5.70	\$5.28	\$6.06
AZT/3TC/NVP (300/150/200 mg)	60 tablets	-	-	\$6.48	-
DTG (50 mg)	30 tablets	\$3.50	\$3.60	\$5.01	-
EFV (600 mg)	30 tablets	\$2.55	-	\$2.70	\$2.90
LPV/r (200/50 mg)	120 tablets	\$17.00	\$18.95	\$18.00	\$14.61
NVP (200 mg)	60 tablets	-	-	\$1.98	\$2.31
RTV (100 mg) heat-stable	60 tablets	\$6.85	\$6.85	\$6.84	\$4.06
TDF (300 mg)	30 tablets	\$2.40	\$2.80	\$2.34	\$2.59
TDF/3TC (300/300 mg)	30 tablets	\$3.55	\$3.20	\$3.24	-
TDF/FTC (300/200 mg)	30 tablets	\$4.75	\$4.60	\$3.99	\$3.84
TDF/3TC/DTG (300/300/50 mg)	30 tablets	\$5.85**	\$6.25	\$6.21	\$6.03
TDF/3TC/EFV (300/300/400 mg)	30 tablets	\$6.00**	\$5.75	\$6.15	-
TDF/3TC/EFV (300/300/600 mg)	30 tablets	\$6.00**	-	\$6.00	-
TDF/FTC/EFV (300/200/600 mg)	30 tablets	\$6.40**	-	\$6.24	\$6.39
Pediatric Products					
Optimal Formulary					
ABC/3TC (120/60 mg) disp. scored	30 tablets	\$3.49	\$3.30	\$3.30	-
ABC/3TC (120/60 mg) disp. scored	60 tablets	-	\$7.50	\$7.74	-
AZT (50/5 mg/ml) oral solution	100 mL bottle	-	-	\$1.00	-
AZT/3TC (60/30 mg) disp. scored	60 tablets	\$1.90	\$1.80	\$1.92	-
LPV/r (100/25 mg) heat-stable	60 tablets	\$6.00	\$7.00	\$4.98	\$4.64
LPV/r (40/10 mg) oral pellets	120 capsules	\$19.20	\$19.20	\$19.20	-
LPV/r (40/10mg) oral granules	120 sachets	\$19.20	\$18.25	\$18.48	-
NVP (50 mg) disp. scored	60 tablets	\$1.45	\$1.25	\$1.26	-
NVP (50/5 mg/ml) oral solution	100 mL bottle	\$1.45	-	\$1.30	-
RAL (25 mg) chewable scored	60 tablets	\$3.49	\$212.00	\$18.00	\$15.87
Limited Use List					
3TC (50/5 mg/ml) oral solution	100 mL	\$1.25	-	\$1.30	-
ABC (60 mg) disp. scored	60 tablets	\$4.72	\$3.80	\$4.02	\$3.37
ATV (200 mg)	60 capsules	\$20.00	\$26.00	\$25.02	-
AZT/3TC/NVP (60/30/50 mg) disp. scored	60 tablets	\$3.00	-	\$3.00	-
DRV (75 mg)	480 tablets	-	\$729.8***	\$54.72	-
EFV (200 mg) single scored	90 tablets	\$6.40	\$9.30	\$6.39	-
EFV (200 mg) double scored	90 tablets	\$9.30	-	\$9.27	-
LPV/r (80/20 mg/ml) oral solution	5 x 60ml bottles	\$30.82	-	\$30.90	-
RAL (100mg) granules	60 sachets	-	\$212.00	\$57.00	-
RTV (100 mg) powder	30 packets	-	-	-	-
RTV (25 mg)	60 tablets	\$1.25	-	\$7.50	-

*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 discounted prices for products with a "no carton" presentation, please refer to latest price list for more information.

***Reflects ceiling pricing for product since no orders have been placed yet.

[1] Global Fund Pooled Procurement Mechanism Reference Pricing: ARVs, Aug 30, 2019. [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, Aug 2019. [Link](#)

Prices represent the latest blended average pricing of actual procurement.

[3] Médecins Sans Frontières (MSF), Stopping Senseless Deaths: Overcoming access barriers to affordable, lifesaving diagnostics and treatments for HIV and opportunistic infections, July 2018. [Link](#)

Prices shown converted to pack prices from unit prices; generally, the lowest stringent regulatory authority (SRA) approved supplier reference price shown.

[4] 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; prices are on a delivered basis and inclusive of 15% VAT; prices subject to forex-based adjustments.

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 the majority of 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. ‘Generic-accessible’ denotes countries where global generic manufacturers can register and supply a large proportion of that country’s ARV needs. For this purpose, GA countries are defined 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 2019. 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 the data, an internally developed forecasting model, and the ART patient forecast (above) to project ARV demand in GA LMICs over the next five years. CHAI’s ARV demand forecast for current drugs includes data from: Benin, Burkina Faso, Cambodia, Cameroon, DRC, Eswatini, Ethiopia, India, Kenya, Laos, Lesotho, Malawi, Myanmar, Nigeria, Senegal, South Africa, Tanzania, Togo, Uganda, Vietnam, Zambia, and Zimbabwe. The countries included represent 79 percent of adult patients on ART in GA LMICs in 2018.

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 focal countries based on CHAI’s country intelligence, as well as for GA RoW as a 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 regimen/drug in a given year in GA LMICs.

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 average cost of treatment for first- and second-line adult and pediatric patients. The assumed price paid for ARVs is informed by 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 2018 is used.



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