



TECHNICAL REPORT

ANTIRETROVIRAL MEDICINES IN LOW- AND MIDDLE-INCOME COUNTRIES: FORECASTS OF GLOBAL AND REGIONAL DEMAND FOR 2021–2025

DECEMBER 2021

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CONTENTS

LIST OF FIGURES	iv
LIST OF TABLES	v
ACKNOWLEDGEMENTS	vi
ABBREVIATIONS AND ACRONYMS	vii
EXECUTIVE SUMMARY	viii
1. INTRODUCTION	1
2. METHODS FOR DETERMINING KEY FORECAST VARIABLES	3
2.1 TOTAL NUMBER OF PEOPLE RECEIVING TREATMENT	3
2.2 NUMBER OF PEOPLE RECEIVING FIRST- AND SECOND-LINE THERAPY	4
2.3 PROPORTION OF ADULTS ON FIRST LINE RECEIVING TREATMENT BY ARV DRUG	6
2.4 PROPORTION OF ADULTS ON SECOND LINE RECEIVING TREATMENT BY ARV DRUG	10
2.5 PROPORTION OF CHILDREN ADULTS RECEIVING TREATMENT BY ARV DRUG	12
4. DISCUSSION	14
REFERENCES	15

LIST OF FIGURES

Fig. 1. Model used for forecasting ARV drug demand	2
Fig. 2. Projections of the number of adults and children receiving ART (millions)	3
Fig. 3. Proportion of adults on ART receiving second-line ART (2011–2020) projected to 2025	5
Fig. 4. Historical and projected market share of primary NRTIs for adults	7
Fig. 5. Market share for secondary NRTIs in first-line ART for adults	8
Fig. 6. NNRTI and DTG: share of first-line ART market for adults	9
Fig. 7. Second-line primary NRTIs for adults	10
Fig. 8. Second-line secondary NRTIs for adults	10
Fig. 9. NNRTIs, PIs and DTG: share of second-line ART market for adults	11
Fig. 10. Distribution of primary NRTIs for children	12
Fig. 11. Distribution of secondary NRTIs for children	13
Fig. 12. Distribution of NNRTIs, PIs and DTG for children	13

LIST OF TABLES

Table 1. The number of adults and children receiving ART by first- and second-line regimens in low- and middle-income countries	6
Table 2. Market share for AZT, ABC and TAF	8

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ABBREVIATIONS AND ACRONYMS

3TC	lamivudine
ABC	abacavir
ART	antiretroviral therapy
ARV	antiretroviral
ATV	atazanavir
ATV/r	ritonavir-boosted atazanavir
AZT	zidovudine (also known as ZDV)
CHAI	Clinton Health Access Initiative
d4T	stavudine
ddI	didanosine
DRV	darunavir
DTG	dolutegravir
EFV	efavirenz
ETV	etravirine
FTC	emtricitabine
GAM	Global AIDS Monitoring
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
IDV	indinavir
LPV	lopinavir
LPV/r	ritonavir-boosted lopinavir
NNRTI	non-nucleoside reverse-transcriptase inhibitor
NRTI	nucleoside reverse-transcriptase inhibitor
NtRTI	nucleotide reverse-transcriptase inhibitor
NVP	nevirapine
PI	protease inhibitor
RAL	raltegravir
RTV	ritonavir
SQV	saquinavir
TDF	tenofovir
TAF	tenofovir alafenamide
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund

EXECUTIVE SUMMARY

After exceeding the previous goal of getting 15 million people on treatment by 2015, the global community aimed to achieve the Fast-Track 90–90–90 targets by 2020. As of the end of 2020, over 25 million people were receiving antiretroviral therapy (ART) in low- and middle-income countries. Between 2017 and 2020, the number of people receiving treatment grew at an average of 1.9 million per year, indicating significant progress during the test and start initiative.

The goal of this report is to provide countries and suppliers with estimates of the global market for antiretroviral (ARV) medicines in low- and middle-income countries for 2021–2025. The report includes estimates of the global demand for both active pharmaceutical ingredients and ARV formulations for adults receiving first-line treatment to enable suppliers with managing their manufacturing capacity accordingly.

To be consistent with previous reports, this report uses three forecasting approaches to project the demand for ART, expressed as the number of people receiving treatment from 2021 to 2025:

- the linear regression forecast extrapolates from the historical trends of the previous three years (2018, 2019 and 2020) in the number of people receiving ARV drugs;
- the country target model reflects the reported programme goals of national programmes; and
- the 95–95–95 estimates that assume that, by 2025, 95% of people living with HIV will know their HIV status, 95% of the people who know their HIV-positive status are accessing treatment and 95% of the people receiving treatment have suppressed viral loads.

The 95–95–95 projection probably represents an upper limit on demand. It would result in 32.4 million people receiving ART in 2025. The linear projection has an even higher figure for 2025 and is therefore probably too high. The country targets approach projects 30.6 million by 2025.

The assumptions underlying the forecasts for demand for active pharmaceutical ingredients for 2021–2025 were developed through the work of the Technical Working Group Meeting on Global Antiretroviral Demand Forecast, which included staff members from the Clinton Health Access Initiative (CHAI), Avenir Health, the Global Fund to Fight AIDS, Tuberculosis and Malaria, the Joint United Nations Programme on HIV/AIDS (UNAIDS), the Medicines Patent Pool, the Office of the United States Global AIDS Coordinator, the Global Health Supply Chain Program, the United Nations Children’s Fund (UNICEF), the United States Agency for International Development and WHO. The Technical Working Group coordinated several sources of data on ARV drugs, including the WHO survey on ARV drug use, the Global Price Reporting Mechanism data on procurement, Supply Chain Management System procurement, national guidelines and CHAI data on drug recipients to consolidate key assumptions and generate the projected demand for active pharmaceutical ingredients.

To improve the accuracy of forecasting demand, this year’s report was able to build on the depth of historical data from WHO’s annual survey of ARV drug use, Global AIDS Monitoring and CHAI consolidated data for 19 countries with a high burden of HIV infection.

This report provides the estimated number of adults receiving first-line ART on individual ARV drugs by consolidating data from Global AIDS Monitoring reports for 2020 ARV drug use and CHAI projected market share data for active pharmaceutical ingredients. The active pharmaceutical ingredient market shares for adults were categorized as follows:

- primary nucleoside reverse-transcriptase inhibitors (NRTIs) and nucleotide reverse-transcriptase inhibitors (NtRTIs): stavudine (d4T), zidovudine (AZT), tenofovir disoproxil fumarate (TDF), abacavir (ABC) and tenofovir alafenamide (TAF);
- secondary NRTIs: lamivudine (3TC) and emtricitabine (FTC); and
- non-nucleoside reverse-transcriptase inhibitors (NNRTIs) and dolutegravir (DTG): nevirapine (NVP), efavirenz (EFV) and DTG.

The figures in this report are not meant to predict the definitive consumption of ARV drugs from 2021 to 2025 but provide a range of possible demand for ARV drugs if current trends continue.

Estimates and projections of ART in low- and middle-income countries (millions), 2020–2025

Indicator	2020	2021	2022	2023	2024	2025
Number of adults receiving ART	24.6	25.7–26.3	27.3–27.8	28.7–29.1	30.1–30.4	31.4–31.6
Number of children receiving ART	0.91	0.92–1.03	0.92–1.4	0.91–1.02	0.90–0.98	0.92–0.92
Percentage receiving second-line ART	6.9%	7.0%	7.2%	7.4%	7.6%	7.8%

Note: The ranges represent the 95–95–95 and country targets scenarios.

1. INTRODUCTION

The objectives of this report are to:

- to provide information on the projected number of people living with HIV who will be receiving antiretroviral therapy (ART) from 2021 to 2025;
- to update the forecasts of global demand for antiretroviral (ARV) drugs prepared in 2020; and
- to forecast the global number of adults receiving first-line ARV drugs from 2021 to 2025.

The data sources for this report are:

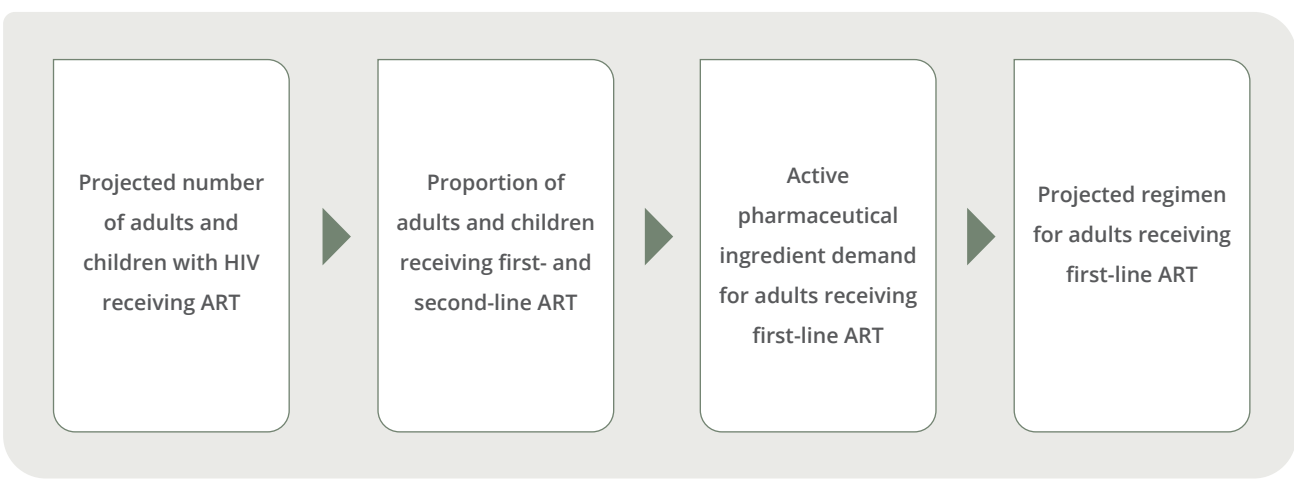
- country reports on the use of ARV drugs and the number of people receiving ART submitted to the Global AIDS Monitoring system(aidsinfo.unaids.org);
- country projections of ART coverage for 2021–2025;
- the projected regimen for adults receiving first-line treatment ART by the Clinton Health Access Initiative (CHAI) (1) and the Medicines Patent Pool; and
- the projected number of people who need ART and the number receiving ART from the UNAIDS Global AIDS Strategy 2021–2026 (2).

Forecasting the global demand for ARV drugs involves the following steps:

- project the total number of people receiving ART;
- determine the number of people receiving first-line and second-line ART based on a projection of the trend from 2008 to 2030; and
- apply the distribution of people receiving first- and second-line ART by ARV drug.

Fig. 1 illustrates the model used for forecasting ARV drug demand in this report.

Fig. 1. Model used for forecasting ARV drug demand



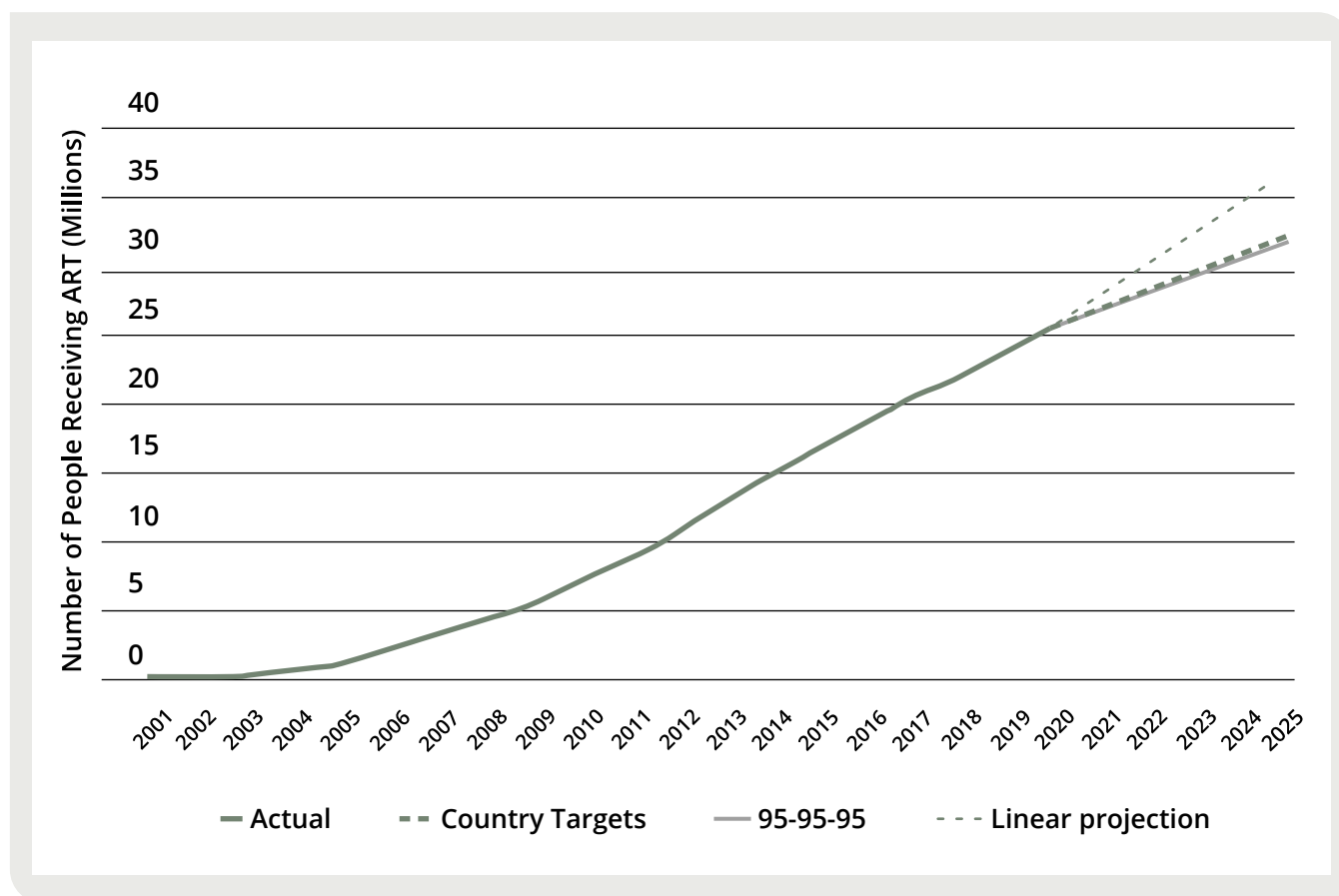
2. METHODS FOR DETERMINING KEY FORECAST VARIABLES

2.1. Total number of people receiving treatment

The total number of people receiving treatment was projected in three ways.

1. Linear projection. This is a linear projection based on the country reports to Global AIDS Monitoring. Actual data are available through 31 December 2020. A linear projection of the trend from 2018 to 2020 was extended to 2026.
2. Country forecast. Each year when country programmes prepare their HIV estimates, they are asked to provide projections of ART coverage through 2025. Some countries enter figures from detailed plans, and others might assume that global targets are achieved.
3. Global plan. The UNAIDS Global AIDS Strategy 2021–2026 sets 95–95–95 targets by 2025. This means that every country should achieve 95% of people living with HIV knowing their HIV status, 95% of the people who know their HIV-positive status are accessing treatment and 95% of the people receiving treatment have suppressed viral loads.

Fig. 2. Projections of the number of adults and children receiving ART (millions)



2.1.1 Linear projection

In the past, this report always included a linear projection of the last three years of the number of people receiving ART. This often provided a reasonable short-term projection, although in some years the actual experience exceeded the linear trend. This year we have also considered a linear projection of the last three years, which adds about 2 million people to the number receiving treatment, reaching 35.8 million by 2025. This number exceeds the 95–95–95 global targets described below. Since the global coverage of all people living with HIV (adults and children) reached 72% in 2020 and 44% of the people living with HIV lived in countries with ART coverage of 80% or higher, growth is likely to slow down as coverage plateaus. The linear projection is therefore likely too high to be realistic.

2.1.2 Country target projection

When country teams prepare their annual estimates using the Spectrum/AIM software, they enter the actual number receiving ART for 1995 to 2020 and then add a projection to 2025. The projection may be based on their treatment plan, treatment targets, global targets or past trends. These targets are therefore not consistently defined across countries. Nevertheless, they do represent some form of country expectations and are available for 134 low- and middle-income countries. The results show the total number receiving ART increasing from 25.5 million in 2020 to 32.5 million by 2025.

2.1.3 95–95–95 projection

UNAIDS released a new global strategy in 2021 (Global AIDS Strategy 2021–2026) that defined new goals for 2025. These include the 95–95–95 treatment targets: 95% of people living with HIV know their HIV status, 95% of the people who know their HIV-positive status are accessing treatment and 95% of the people receiving treatment have suppressed viral loads. These targets apply to all countries and all population groups. As such, they probably represent an upper limit on what can be expected. However, the strategy also includes aggressive primary prevention targets that lead to a sharp reduction in the number of people acquiring HIV, thus limiting the number of people newly needing ART. In the strategy, the number of people receiving ART increases to 32.4 million by 2025.

2.2 Number of people receiving first- and second-line ART

Two data sources were used to determine the trends in the proportion of adults receiving second-line ART.

- Global AIDS Monitoring includes reports from 87 of 131 low- and middle-income countries on the proportion of adults on ART receiving second-line ARV drugs. These countries represent 91% of all people receiving ART. The countries not reporting data were assigned the regional percentage. For 2020, this approach estimates that 5.7% of people receiving ART in low- and middle-income

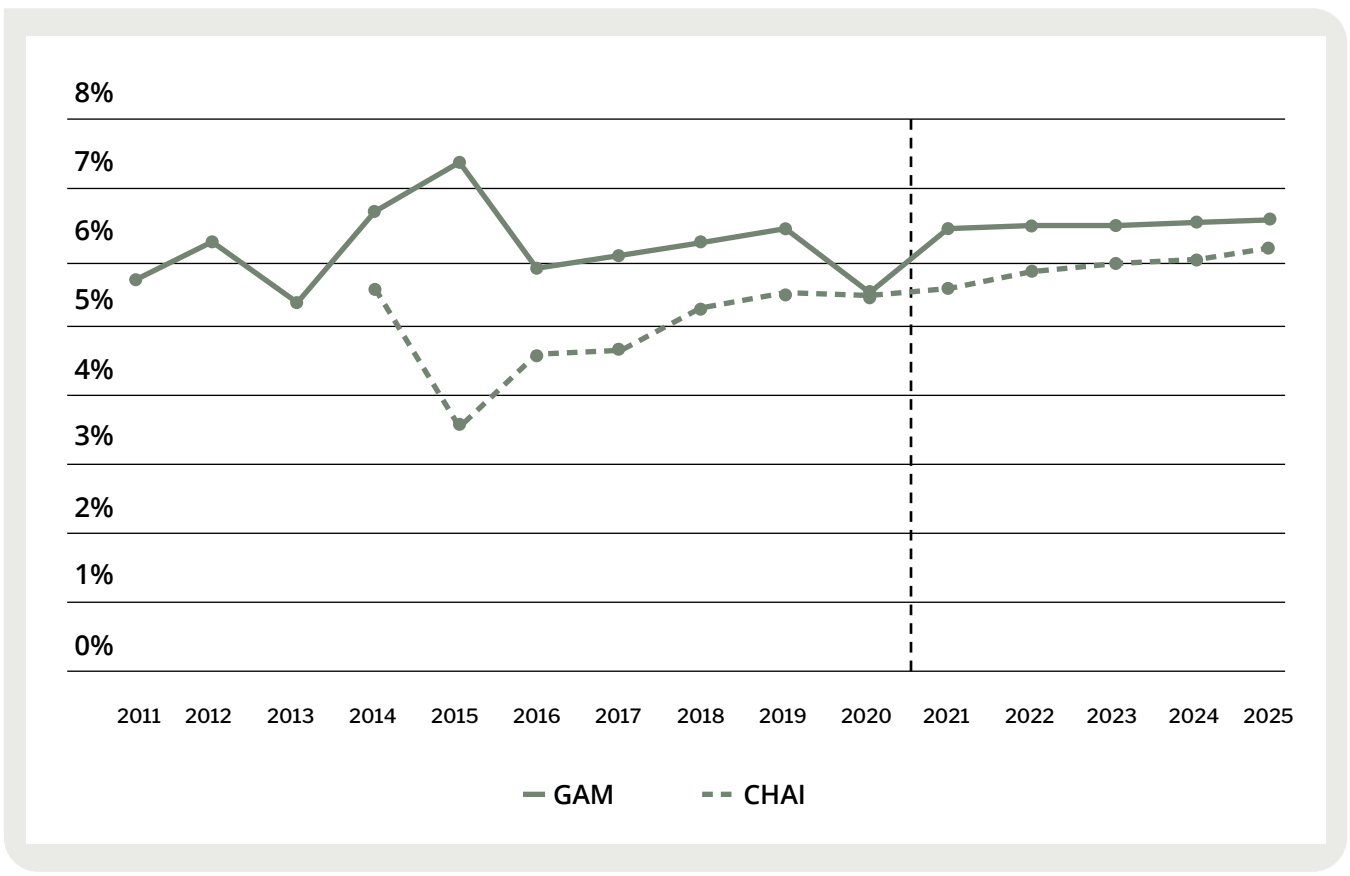
countries received second-line ARV drugs. A linear projection from 2008 to 2020 indicates a continuing but slow rise to about 6.8% in 2025.

In 2021, CHAI collected data on the number of people receiving second-line treatment in 19 countries with a high burden of HIV from country teams and published literature. CHAI then estimates the future numbers of people receiving second-line ART in each country by considering such factors as treatment failure rates and attrition rates.

CHAI then aggregates the second-line ART estimates across the 19 countries and extrapolates these results to the people in the remaining low- and middle-income countries. The proportion of people receiving second-line ART is calculated by dividing this figure by the total number of people receiving ART.

Fig. 3 illustrates the results. Both approaches show a similar trend. The Global AIDS Monitoring results show a higher percentage receiving second-line ART than the CHAI projections, mostly because of the different countries included. The CHAI results include only countries in sub-Saharan Africa, whereas the Global AIDS Monitoring results include other regions, including Latin America, which has much more second-line ART.

Fig. 3. Proportion of adults on ART receiving second-line ART (2011–2020) projected to 2025



The information for children is incomplete. Although 59 countries reported data on children receiving second-line ART, they account for only 35% of all children receiving ART in low- and middle-income countries, and more than half of the reported total is from Malawi and Uganda. The reported data indicate that 13% of children receiving ART were receiving second-line ART.

Table 2 shows the number of adults and children projected to be on first- and second-line ART according to the country forecast projection.

Because of the lack of data on children receiving second-line ART, the percentage of adults receiving second-line ART has been applied to children as well.

Note that, although COVID-19 caused disruptions in many health services, most programmes were able to adapt their services to maintain treatment coverage and increase the number of people receiving ART in 2020 compared with 2019.

Table 1. The number of adults and children receiving ART by first- and second-line regimens in low- and middle-income countries

Population	2020	2021	2022	2023	2024	2025
Adult, first line	21 300 000	22 800 000	23 900 000	25 000 000	25 900 000	26 900 000
Adult, second line	1 580 000	1 710 000	1 710 000	1 990 000	2 130 000	2 270 000
Children, first line	847 000	852 000	855 000	848 000	834 000	845 000
Children, second line	62 700	64 100	66 300	67 800	68 600	71 500
Total	23 800 000	25 400 000	26 700 000	27 900 000	28 900 000	30 100 000

2.3 Proportion of adults receiving first-line ART by ARV drug

The individual ARV drugs for first-line ART are organized by the following market categories:

- primary nucleoside reverse-transcriptase inhibitors (NRTIs) and nucleotide reverse-transcriptase inhibitors (NtRTIs): stavudine (d4T), zidovudine (AZT), tenofovir

disoproxil fumarate (TDF), abacavir (ABC) and the expected introduction of tenofovir alafenamide (TAF);

- secondary NRTIs: lamivudine (3TC) and emtricitabine (FTC); and
- non-nucleoside reverse-transcriptase inhibitors (NNRTIs) and dolutegravir (DTG): nevirapine (NVP), efavirenz (EFV) and DTG.

The estimates of adults receiving first-line ART by individual ARV drug presented below show both historical data and projections to 2025. The historical portion (2011 to 2020) is from the WHO surveys (2011–2018) and Global AIDS Monitoring data (2019–2020). The projections (2021–2025) are based on CHAI’s global ARV drug forecast. CHAI collects data from country teams and published literature on regimens, national guidelines, attrition rates, failure rates,

toxicity rates, future ARV drug trends and other key factors in countries with high ART use. CHAI then uses these data and an internally developed forecasting model to project ARV drug demand by drug and by regimen in each country over the next five years. CHAI then aggregates estimates across the countries and extrapolates these results to patients in the remaining low- and middle-income countries.

Fig. 4 shows trends and projections of the market share for the primary NRTIs for adults. TDF has clearly come to dominate this market, but there is still some demand for other drugs in this category, as shown in Table 2.

Fig. 4. Historical and projected market share of primary NRTIs for adults

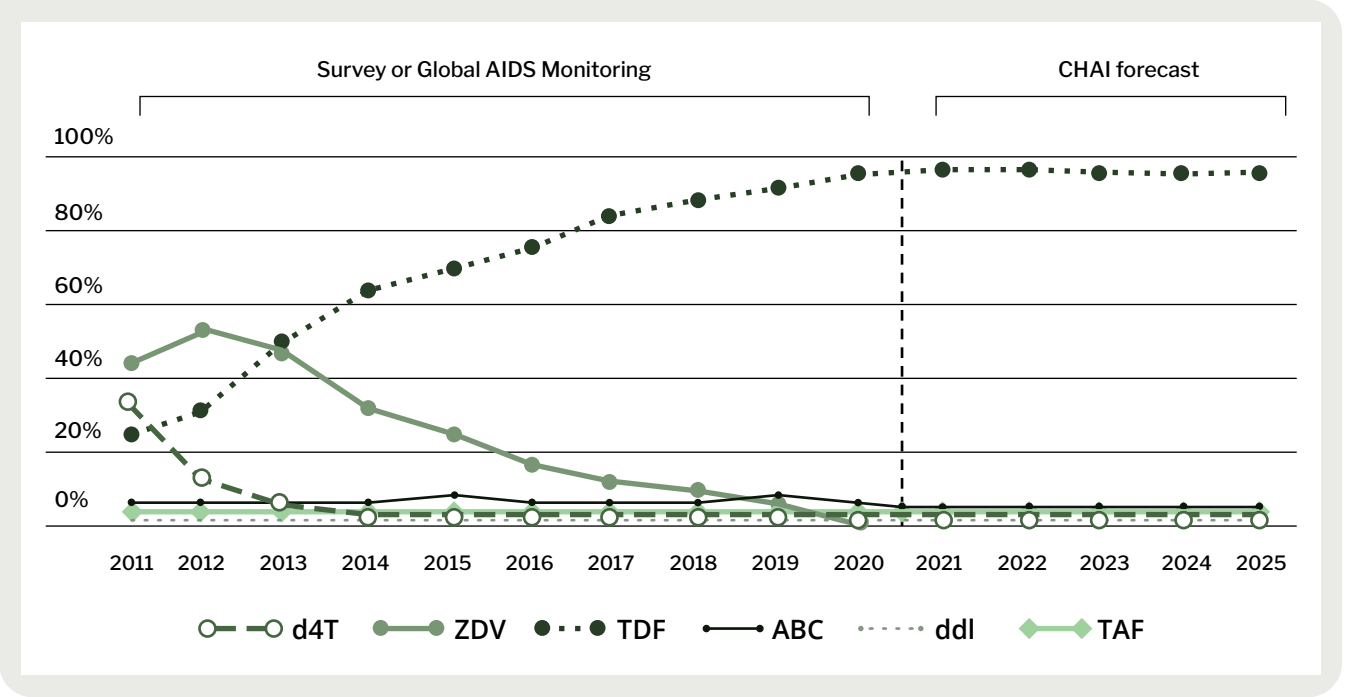


Table 2. Market share for AZT, ABC and TAF

Drug	2020	2021	2022	2023	2024	2025
AZT	2.2%	0.5%	0.3%	0.3%	0.2%	0.2%
ABC	2.0%	1.8%	1.7%	1.6%	1.6%	1.5%
TAF	0.2%	0.4%	0.7%	1.0%	1.2%	1.4%

Fig. 5 shows the market share for secondary NRTIs in adult first-line treatment. 3TC is expected to increase to about 95% of the market over the next few years.

Fig. 5. Market share for secondary NRTIs in first-line ART for adults

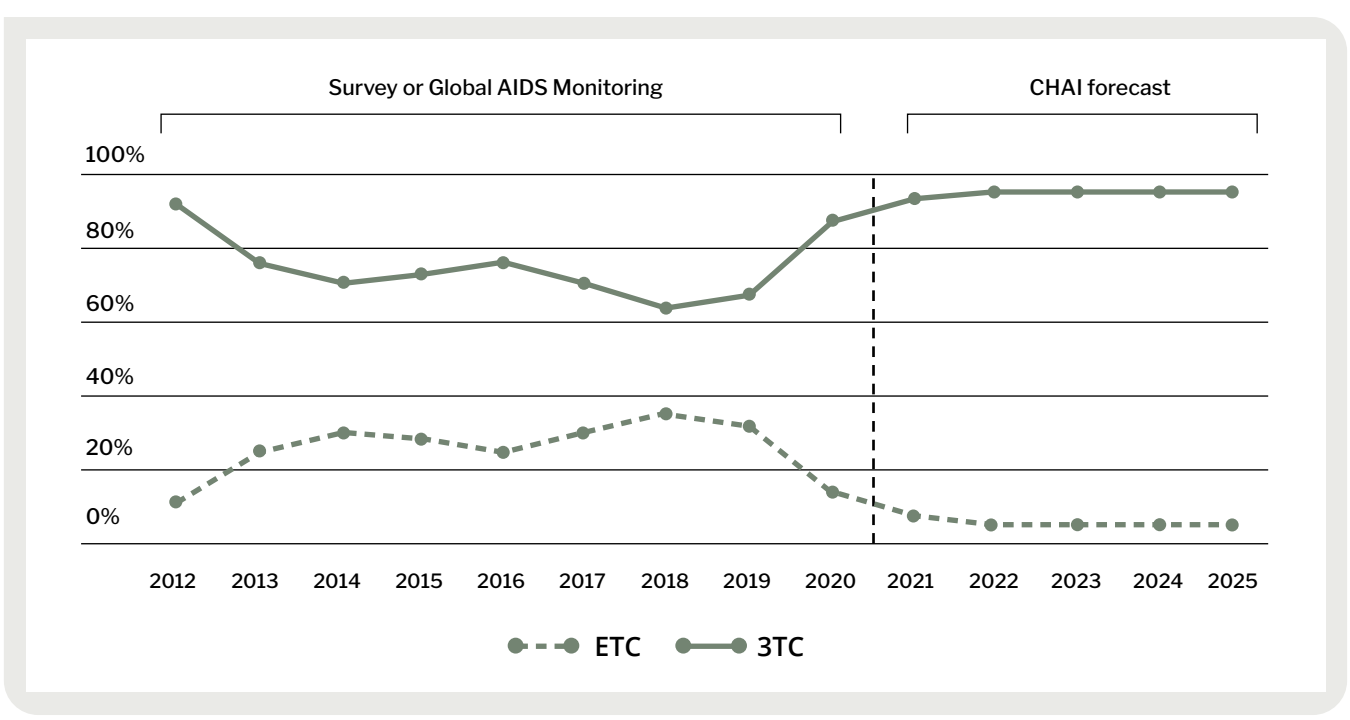
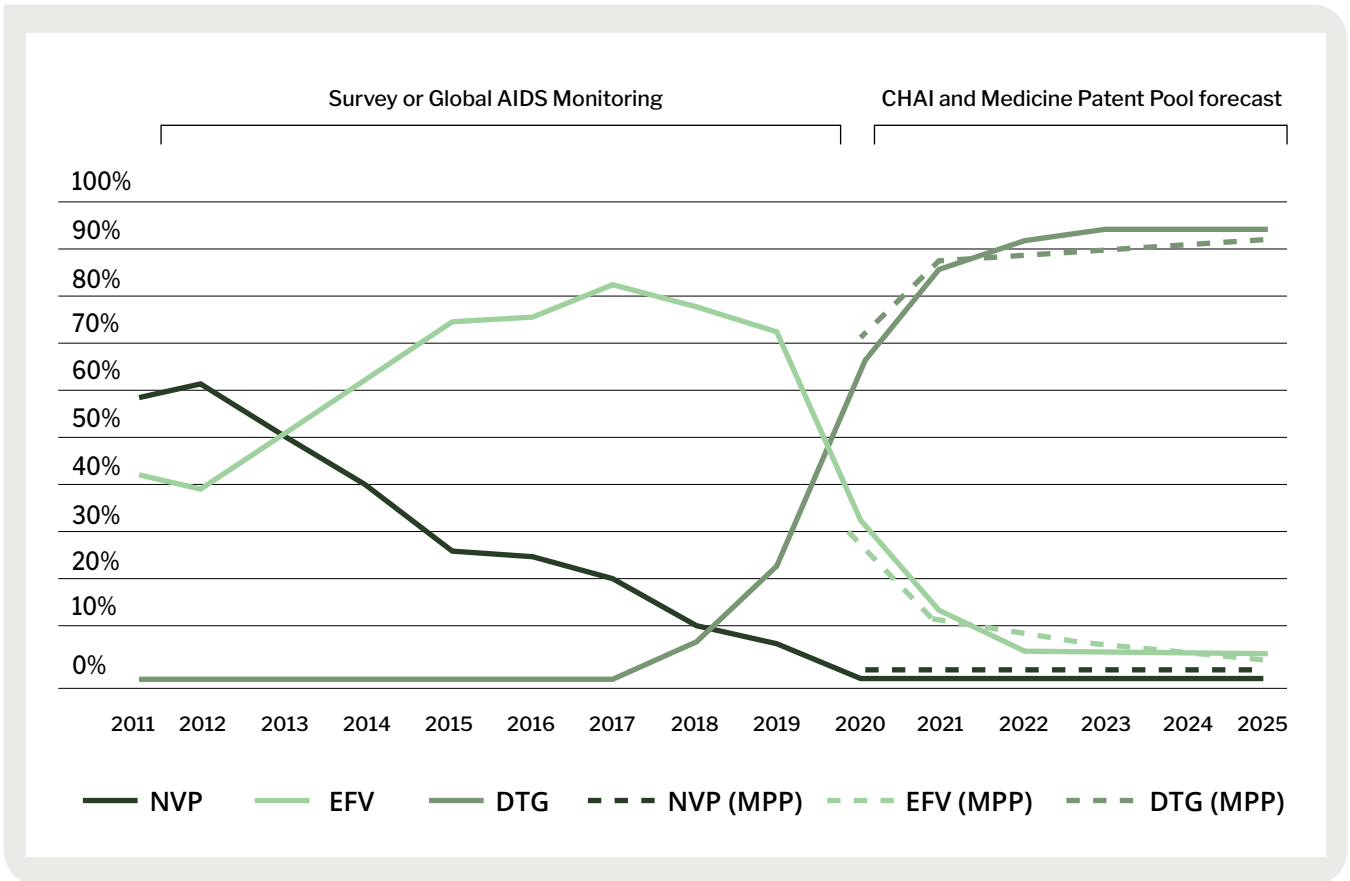


Fig. 6 shows the market share for NNRTIs and DTG for adult first line treatment. DTG has been increasing market share and increase is expected to continue until it reaches 90%-95% in the next few years. EFV is expected to drop to about 6% by 2025. NVP is expected to be phased out completely this year or next.

Fig. 6. NNRTI and DTG: share of first-line ART market for adults



2.4. Proportion of adults receiving second-line ART by ARV drug

Fig. 7-9 show the historical trends for the three categories of second-line ARV drugs for adults. CHAI has not made projections for second-line ARV drugs, so these charts just present the historical trends.

Fig. 7. Second-line primary NRTIs for adults

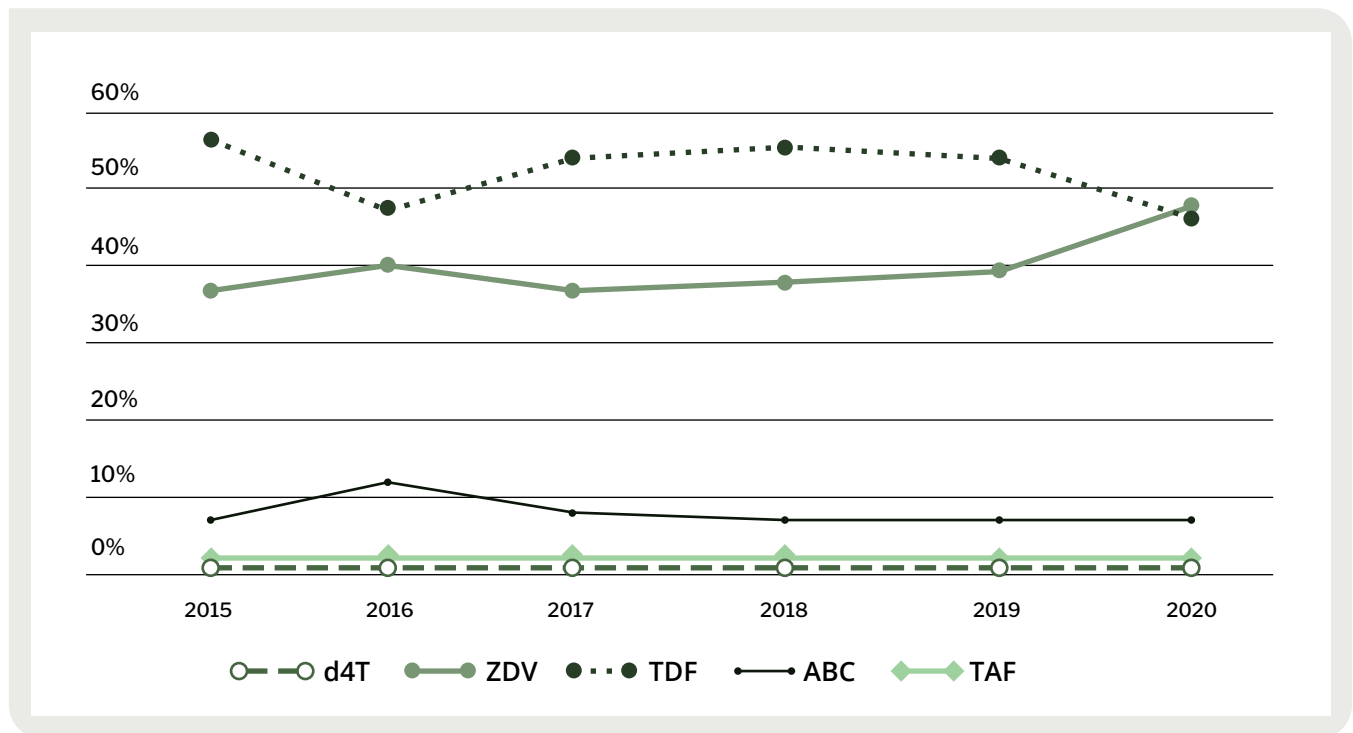


Fig. 8. Second-line secondary NRTIs for adults

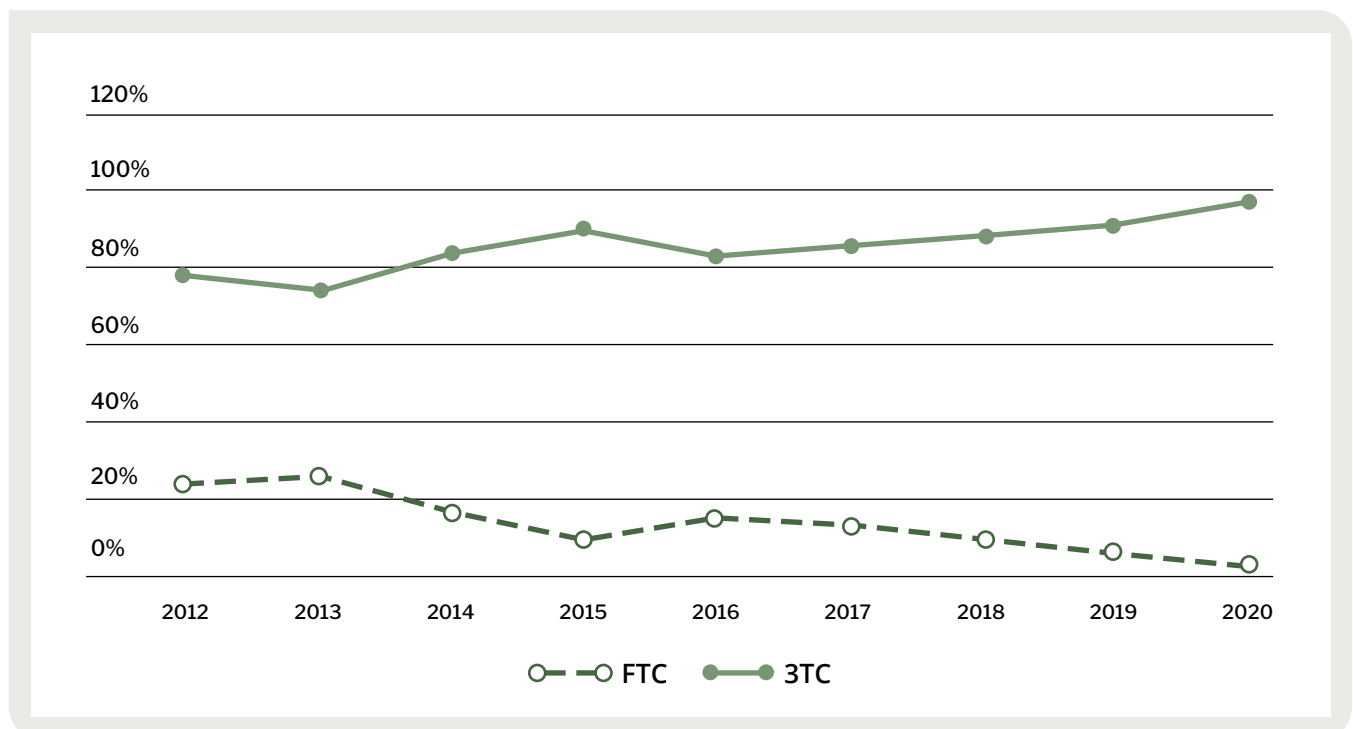
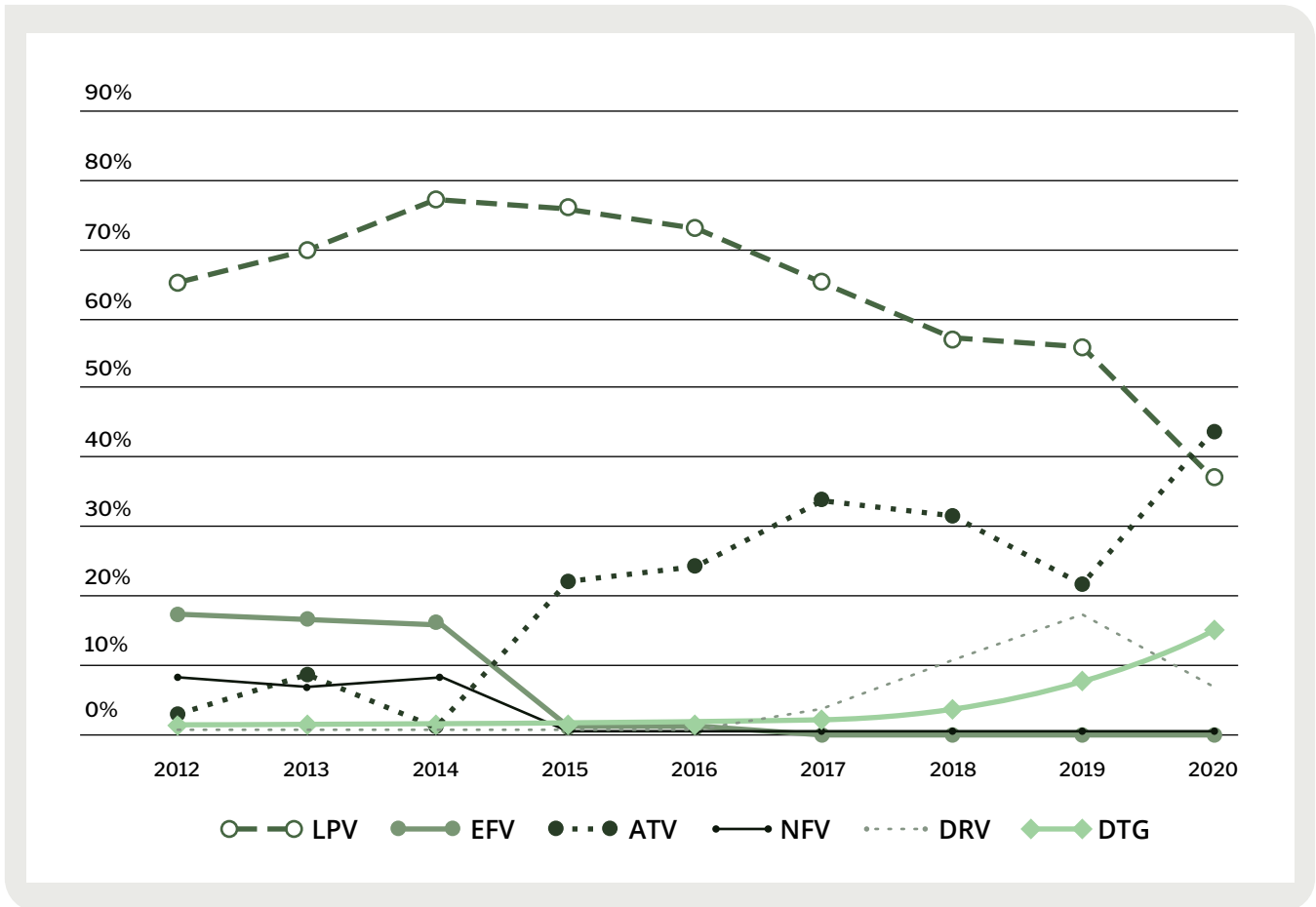


Fig. 9. NNRTIs, PIs and DTG: share of second-line ART market for adults



2.5. Proportion of children adults receiving treatment by ARV drug

Fig. 10–12 show the historical trends in the distribution of ARV drugs in the three treatment categories. In 2020, ABC increased substantially in the primary NRTI market. This was driven primarily by large increases in Kenya, Nigeria, Uganda, Zambia and Zimbabwe. 3TC continues to be the preferred secondary NRTI. DTG replaced more than half of NVP use from 2019 to 2020.

Fig. 10. Distribution of primary NRTIs for children

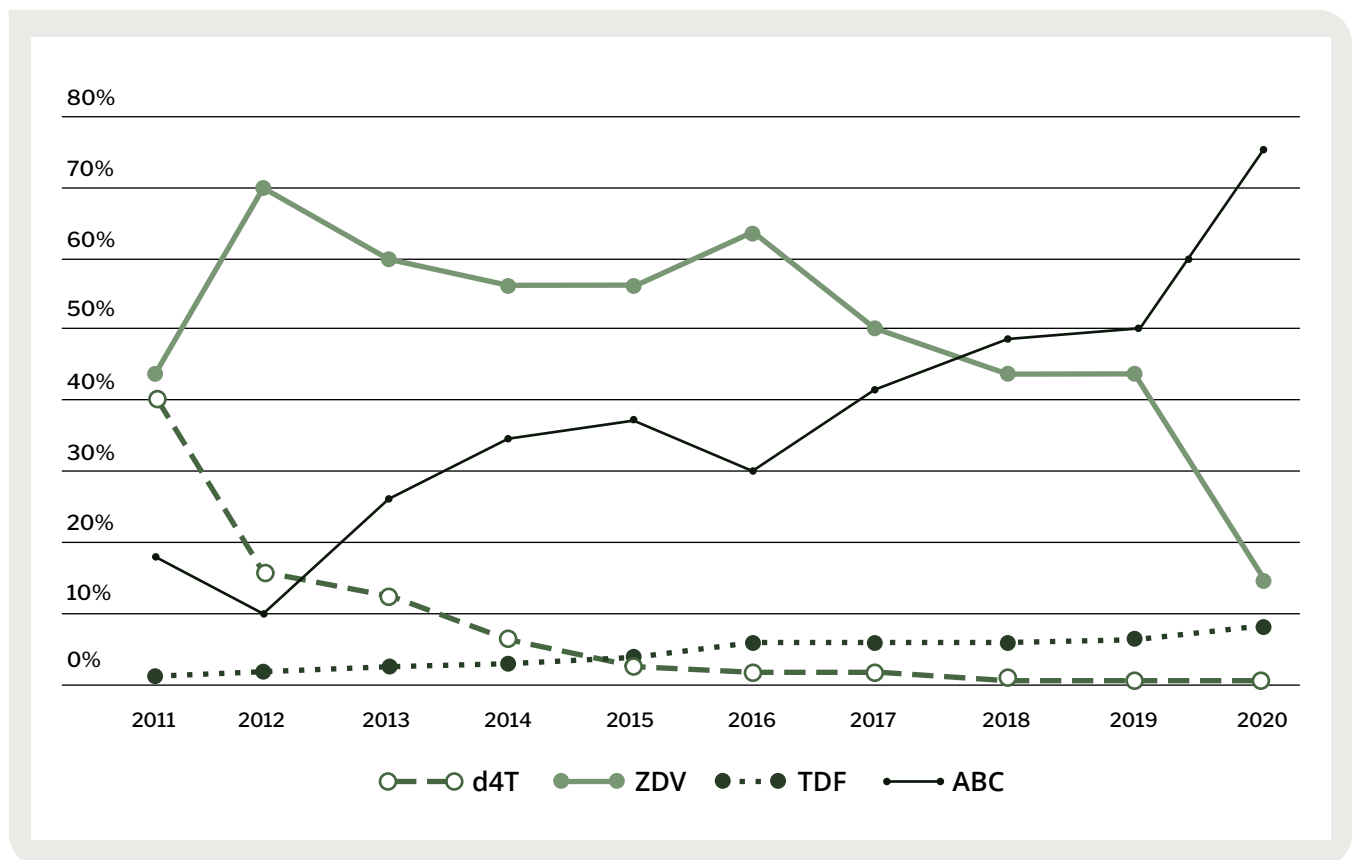


Fig. 11. Distribution of secondary NRTIs for children

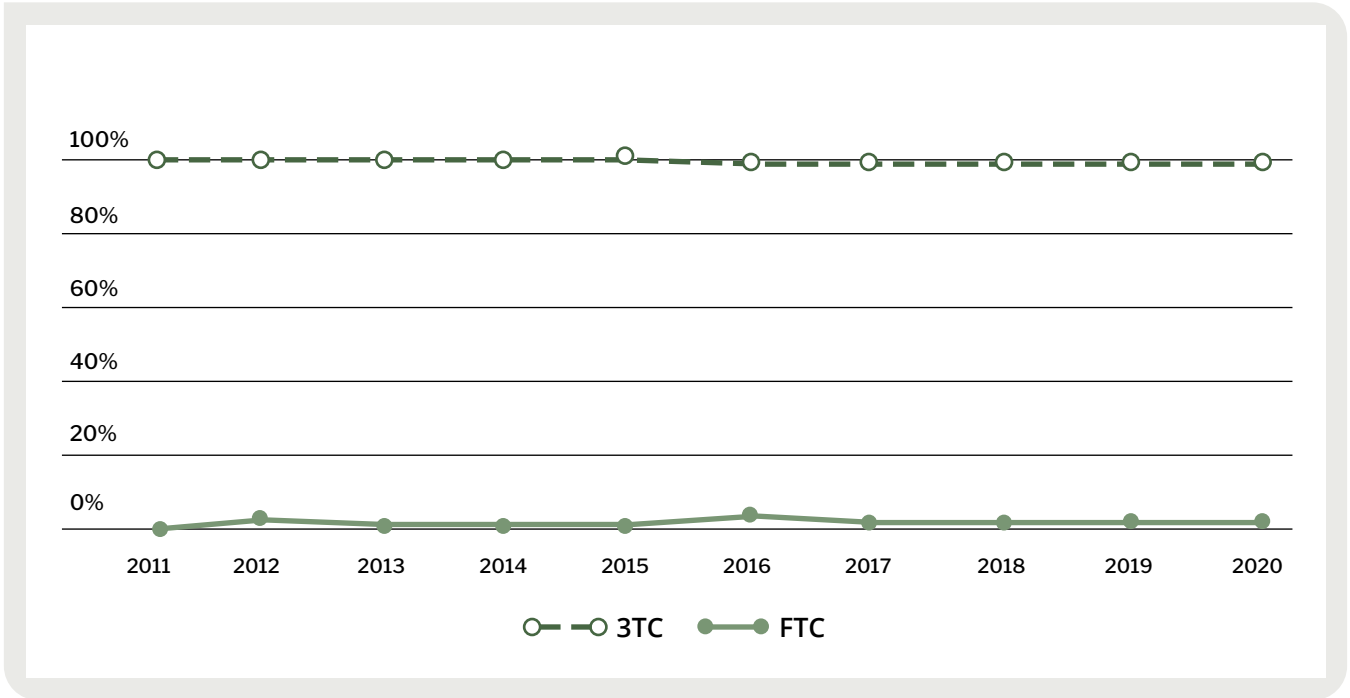
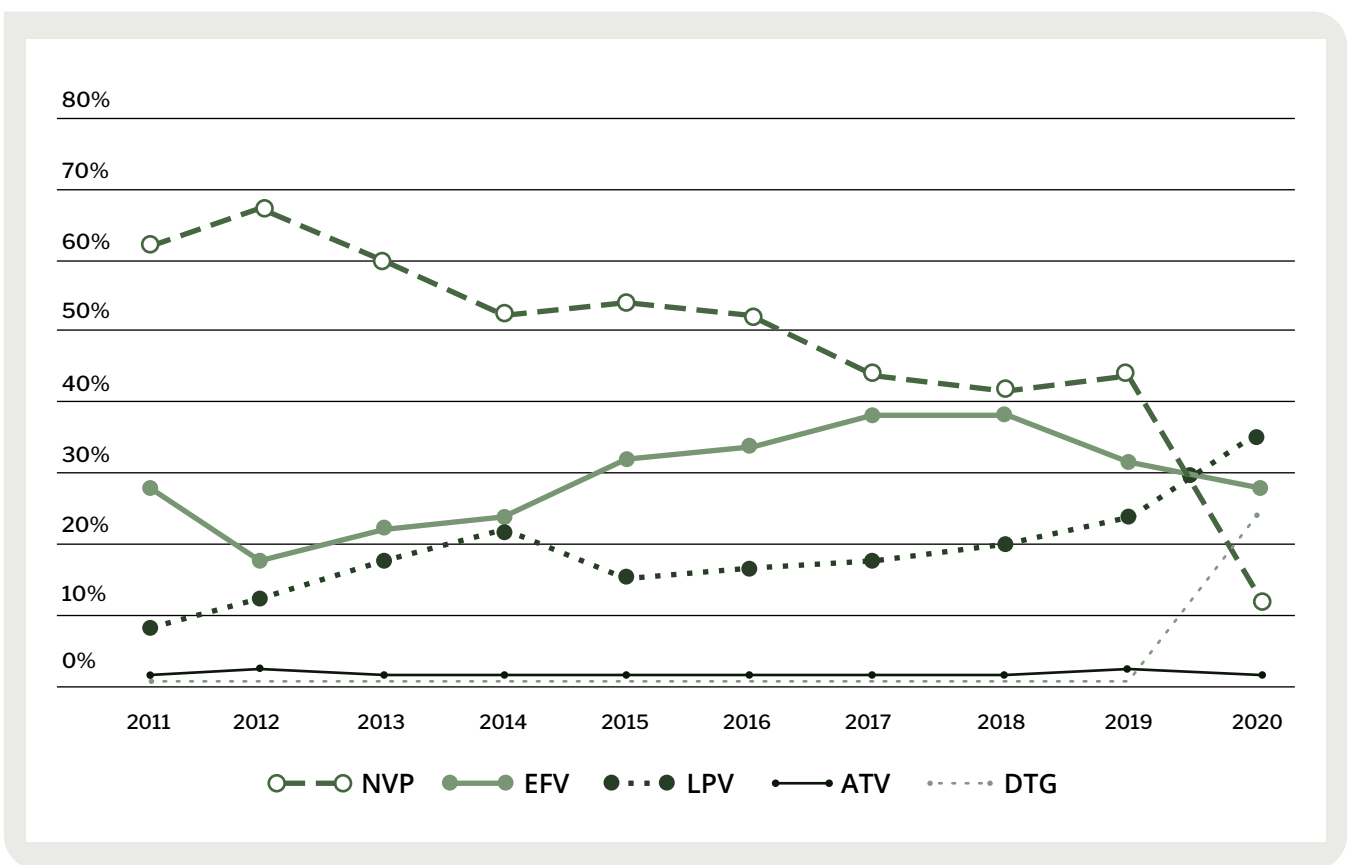


Fig. 12. Distribution of NNRTIs, PIs and DTG for children



4. DISCUSSION

The approach outlined in this report builds on previous annual forecasts by providing estimates and projections for the number of adults and children receiving ART. Historical trends in the market share of ARV drugs are shown based on the WHO annual survey up to 2018 and the country reporting to Global AIDS Monitoring in 2019 and 2020. For first-line ART for adults, CHAI has projected these trends to 2025.

Despite the disruptions caused by COVID-19, the numbers of people receiving ART continued to grow. For all low- and middle-income countries, the number receiving ART grew from 23.6 million in 2019 to 25.5 million in 2020. This number is projected to be 25% larger by 2025. By then, annual growth will be slowing from about increases of about 2 million per year now to slightly more than 1 million per year by 2025 as coverage approaches maximum levels in many countries with a high burden of HIV.

Slow increases in the proportion of adults receiving second-line ART plus growth in the numbers of people receiving ART means that the number of people receiving second-line ART will grow by 50% from 2020 to 2025.

Among the most important changes in the distribution of ARV drugs are the disappearance of d4T-based regimens and DTG replacing NVP and EFV.

The number of children receiving ART is projected to remain roughly constant as increases in coverage are balanced by reductions in the numbers of children living with HIV. For the market for children, the projections show a reduction in the growth of the number of children living with HIV as more adults are accessing treatment and more children transition to adult treatment, although increased case-finding efforts are needed to improve the treatment coverage of children, which lags behind that of adults.

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