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HIV TREATMENT

GLOBAL UPDATE ON HIV TREATMENT 2013:

RESULTS, IMPACT AND OPPORTUNITIES

WHO report

in partnership with UNICEF and UNAIDS

JUNE 2013

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ACRONYMS AND ABBREVIATIONS

3TC	lamivudine
AIDS	acquired immune deficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
AZT	zidovudine
d4T	stavudine
EFV	efavirenz
eMTCT	elimination of mother-to-child transmission (of HIV)
FTC	emtricitabine
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
LPV/r	lopinavir/ritonavir
NNRTI	non-nucleoside reverse-transcriptase inhibitor
NVP	nevirapine
PMTCT	prevention of the mother-to-child transmission of HIV
QALY	quality-adjusted life year
TB	tuberculosis
TDF	tenofovir disproxil fumarate
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
WHO	World Health Organization

EXECUTIVE SUMMARY

The massive global expansion of access to HIV treatment has transformed not only the HIV epidemic but the entire public health landscape, demonstrating that the right to health can be realized even in the most trying of circumstances.

This publication reports on the progress being made in the global scale-up in the use of antiretroviral (ARV) medicines in low- and middle-income countries, the challenges that are being overcome or that await solutions and the opportunities for building on the achievements of the past decade.[1]

Chapter 1 provides new data on the latest developments in the global treatment effort, highlighting positive trends as well as aspects that require improvement. It also discusses the key recommendations of the 2013 WHO *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection*, which are designed to take advantage of the multiple benefits of antiretroviral therapy (ART) for treating and preventing HIV infection. Chapter 2 summarizes the impact of the scale-up in reducing AIDS-related mortality and new HIV infections. Chapter 3 examines the sequence of steps in the continuum of care from HIV diagnosis to successful provision of ART services and outlines key supportive innovations. Finally, Chapter 4 discusses the implications and anticipated impact of the new 2013 WHO ARV guidelines.

Promising results

The remarkable increase in access to life-saving ART continued in 2012. Fully 1.6 million more people were receiving ART in low- and middle-income countries at the end of 2012, compared with a year earlier – the largest annual increase ever – with the greatest contribution coming from the WHO African Region. The 300 000 people who were receiving ART in low- and middle-income countries in 2002 increased to 9.7 million in 2012.

In the WHO African Region, which continues to bear the brunt of the HIV epidemic, more than 7.5 million people were receiving treatment at the end of 2012 compared to 50 000 people a decade earlier. There has been progress in every region, including in ones that had been lagging behind. The pace of this global scale-up of treatment is being maintained even in the midst of economic crisis.

These accomplishments reflect the political commitment, community mobilization, technical innovation, domestic and international funding and other forms of support that have catalysed the global scaling up of ART.

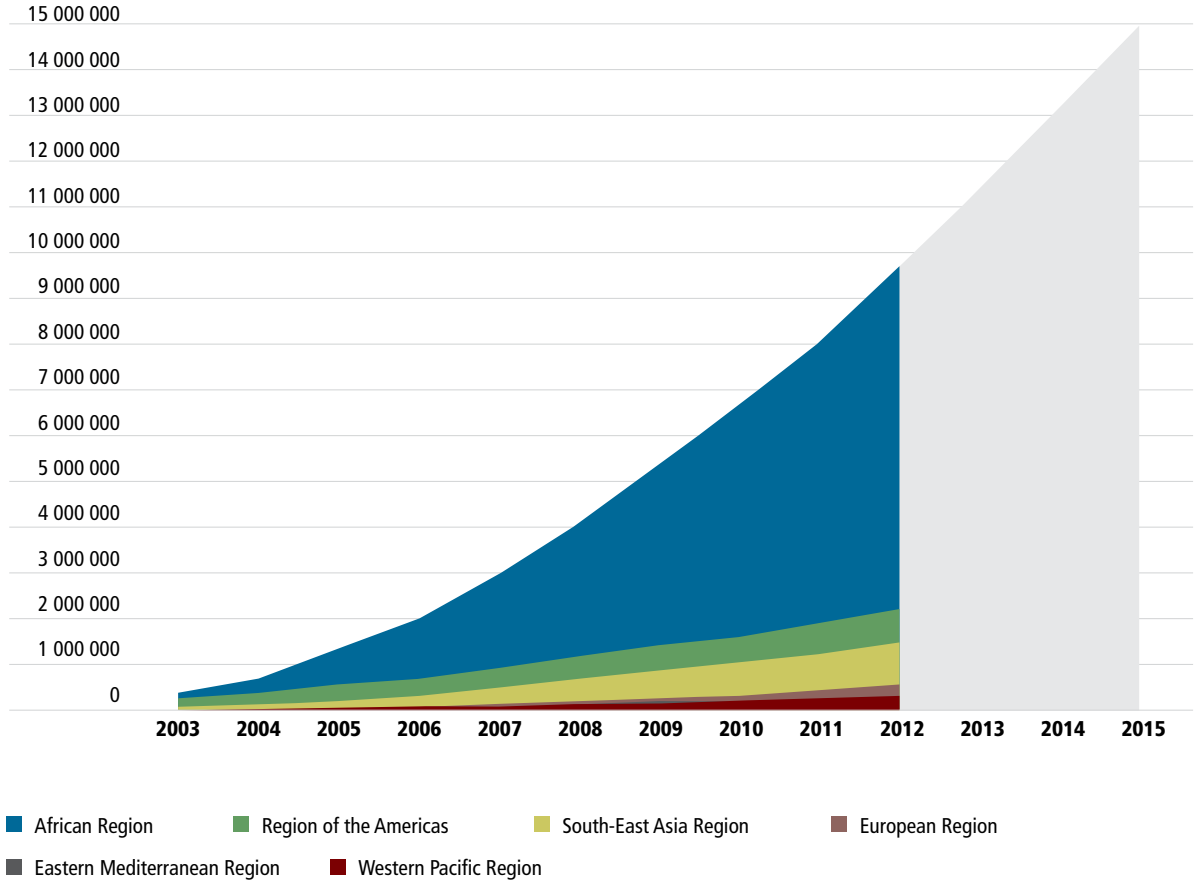
Nevertheless, substantial additional effort is needed to enable 15 million people to access ART in 2015, the target agreed to by United Nations Member States in June 2011 at the General Assembly High-Level Meeting on AIDS in New York. The 9.7 million people receiving ART in 2012 represented 65% of that 15 million target, up from 54% at the end of 2011 (Fig. 1).

The overall progress, however, masks some important disparities in access to ART. In most regions, including the WHO African Region, men eligible for ART appear to be less likely to be receiving it than women. Further, the treatment gains are not reaching enough children, adolescents and key populations who face high risk of HIV infection (including sex workers, people who inject drugs, men who have sex with men and transgender people).

The number of children younger than 15 years receiving ART in low- and middle-income countries increased from 566 000 in 2011 to 630 000 in 2012, but the increase was substantially less than for adults. In 2012, over 900 000 pregnant women living with HIV received ARV prophylaxis or treatment for PMTCT

1. At the time this report was prepared (June 2013), country-level HIV programme data for 2012 were available for most but not all countries, and estimates of the number of people eligible for ART were available only for the 22 countries prioritized in the Global Plan. The report therefore focuses on presenting and analysing data on expanding services that are based on programme reports from countries that have submitted data and limits the discussion of service coverage at the end of 2012 to the 22 priority countries in the *Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive*. References to global and regional coverage estimates are limited to 2011, using 2011 eligibility estimates generated by 2012 country models.

Fig. 1. Actual and projected numbers of people receiving antiretroviral therapy in low-and middle-income countries, and by WHO Region, 2003–2015



Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

(excluding single-dose nevirapine which WHO no longer recommends) – one third more than in 2009. However, many women living with HIV who need ART are missing opportunities to start treatment during pregnancy, including in some countries that have a high burden of HIV infection.

Based on current trends in the scaling up of ART programmes, countries can be grouped into three broad categories.[1] In the first group are countries – including some with a high burden of HIV infection – that already are providing treatment to at least 80% of the people who are eligible for it[2] along with several other countries that are poised to emulate them. A second group includes countries that have made considerable progress in scaling up treatment but that need to boost the pace and scope of their efforts significantly if they are to reach the 80% coverage target in 2015. Finally, a third group of countries is far short of the global target and is struggling with serious structural weaknesses in health and governance systems. These countries need major support to boost their treatment efforts.

Regardless of the current status of countries in scaling up ART, renewed efforts are needed everywhere in order to achieve the maximum treatment and prevention benefits.

1. The categorization is based on a linear projection of changes in the number of people receiving and eligible for ART until the end of 2015, based on the most recent year with available data for both ART provision and eligibility, i.e. the year 2012 for the 22 countries included in the Global Plan.

2. Based on the 2010 WHO treatment eligibility criteria: CD4 count ≤350 cells/mm^3.

An increasingly powerful impact

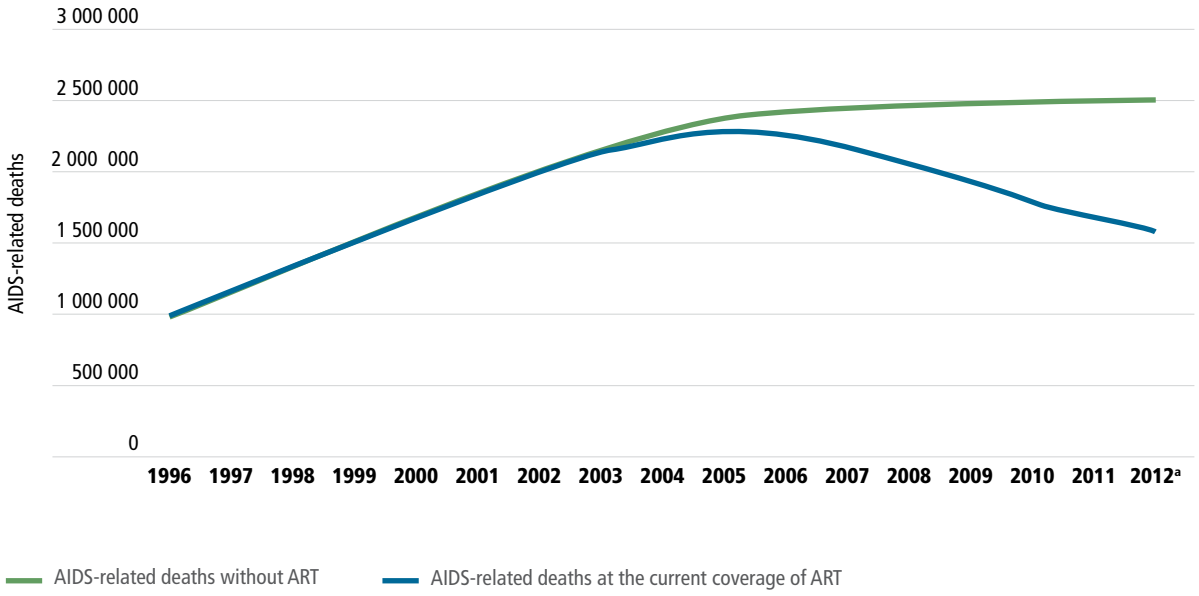
Expanding access to ART is changing the global HIV epidemic in momentous ways. AIDS-related mortality rates are declining rapidly. The scaling up of ART averted an estimated 4.2 million deaths in low- and middle-income countries in 2002–2012 (Fig. 2). Joint TB and HIV interventions saved the lives of more than 400 000 people in 2011 alone (eight times more than in 2005).

Improved access to ART is resulting in major increases in life expectancy. In South Africa, for example, data from ART programmes in three provinces show that the life expectancy of adults receiving ART is about 80% of the normal life expectancy, provided they do not start treatment late.

The preventive impact of ART is increasingly evident, including in concentrated HIV epidemics and especially when ART is combined with classical prevention efforts. A recent study in rural South Africa, for example, found that the incidence of HIV infection fell by 17% for every 10% increase in the number of people receiving ART.

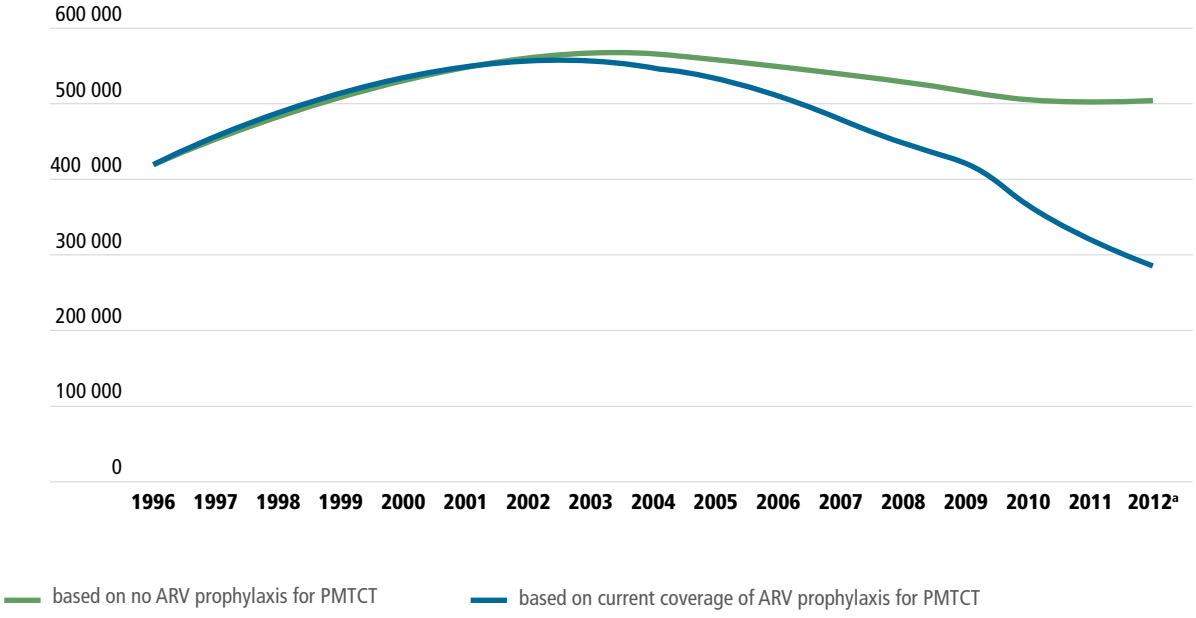
The scaling up of ART is also contributing significantly to the ongoing drop in annual new HIV infections around the world, including among children. Expanding programmes for PMTCT and the use of more effective ARV regimens helped prevent more than 800 000 children from becoming newly infected between 2005 and the end of 2012. In the 21 African priority countries in the Global Plan, which account for about 90% of all pregnant women living with HIV and new infections among children globally, mother-to-child transmission rates declined overall from an estimated 26% [23-28%] in 2009 to 17% [15-18%] in 2012.

Fig. 2. Annual number of people dying from AIDS-related causes in low- and middle-income countries globally compared with a scenario of no antiretroviral therapy, 1996–2012



[a] The data points for 2012 are projected based on the scaling up of programmes in 2009–2011 and do not represent official estimates of the number of annual AIDS-related deaths.

Fig. 3. Number of children acquiring HIV infection in low- and middle-income countries, 1996–2012



[a] The data points for 2012 are projected based on the scaling up of programmes in 2009–2011 and do not represent official estimates of the number of annual child infections.

Maximizing the benefits of ART

Programme coverage is improving in all regions, but significant numbers of adults and children still drop out of care at various points along the treatment cascade, from HIV diagnosis to long-term retention in care. Maximizing the multiple benefits of ART requires improving the uptake of HIV testing and counselling, linking people to care, enabling them to initiate ART early and supporting adherence and retention in care.

In many countries surveyed in sub-Saharan Africa more than half the people estimated to be living with HIV are not aware of their HIV status. In some countries, significant proportions of pregnant women living with HIV either remain undiagnosed or, if diagnosed, do not start on ARV medicines for their own health and to prevent the mother-to-child transmission of HIV. Other studies in sub-Saharan Africa show that close to half the people who test HIV-positive are lost between testing and being assessed for eligibility, and 32% of the people considered eligible for ART are lost between being assessed for eligibility and initiating ART. Numerous efforts are underway to reduce such attrition.

Expanding HIV testing and counselling

HIV testing is the critical first step in linking people living with HIV to the treatment cascade, and it also provides an important opportunity to reinforce HIV prevention. Testing uptake increased impressively in every region, with 118 million people in 124 low-and middle-income countries receiving HIV testing and counselling in 2012.

High coverage of provider-initiated testing and counselling has been achieved in antenatal care and TB clinics (but not in other clinical services), especially in countries with a high burden of HIV infection. Community-based HIV testing and counselling services, including for key populations, and integrating HIV testing with other disease campaigns are proving effective as strategies for effective increasing testing uptake.

However, large proportions of people remain unaware of their serostatus. In all regions, men are less likely than women to take an HIV test, and coverage of HIV testing and counselling is especially low among adolescents and key populations. Structural, operational, logistical

and social barriers – including stigma, discrimination, and punitive laws and policies – continue to hinder access to testing for key populations. Although the early diagnosis of HIV in infants is improving in many countries, in 2011 only 35% [29–41%] of infants born to mothers living with HIV received an HIV test within the first two months of life.

As a consequence, in all regions, large numbers of people test and present late for HIV treatment, usually once their health is failing, which diminishes the benefits of ART.

Linking patients from testing to care

Too many patients are being "lost" between taking an HIV test and starting ART. Several approaches for overcoming this challenge are showing promise, including supportive counselling, providing co-trimoxazole prophylaxis free of charge, ensuring shorter waiting times at clinics and using point-of-care CD4 testing.

Antiretroviral therapy initiation, retention and adherence

Initiating ART early is vital for successful treatment. The median CD4 count when ART is initiated is rising in all regions but is still too low, and about 1 in 4 people in low-income settings initiate ART late, with CD4 counts <100 cells/mm^3.

Once people start ART, the retention rates are initially high and then gradually decline. Data reported in 2013 for 18 countries with cohorts of at least 2000 people on ART indicate that the average retention rates decreased from about 86% at 12 months to 82% at 24 months and 72% at 60 months. Studies confirm that decentralizing ART services improves retention in care, including for children, and various forms of adherence support are also proving effective, including treatment support networks and community adherence clubs, using mobile-phone text reminders, diary cards and food rations.

The goal of ART is to achieve and sustain viral suppression among the people receiving ART. Recent studies show that very good outcomes can be achieved, even in poorly resourced settings. In a large study in Rwanda, for example, 86% of the people receiving ART had viral suppression 18 months after starting ART; in Senegal, about 80% of the people receiving ART were achieving viral suppression after five years. Sustaining such achievements will take special efforts, particularly as there are indications that as ART continues to be scaled up the rates of drug resistance may increase. Systems for monitoring early warning indicators and conducting surveillance of HIV drug resistance must be in place to detect these patterns in a timely manner.

Implications of the 2013 WHO antiretroviral guidelines

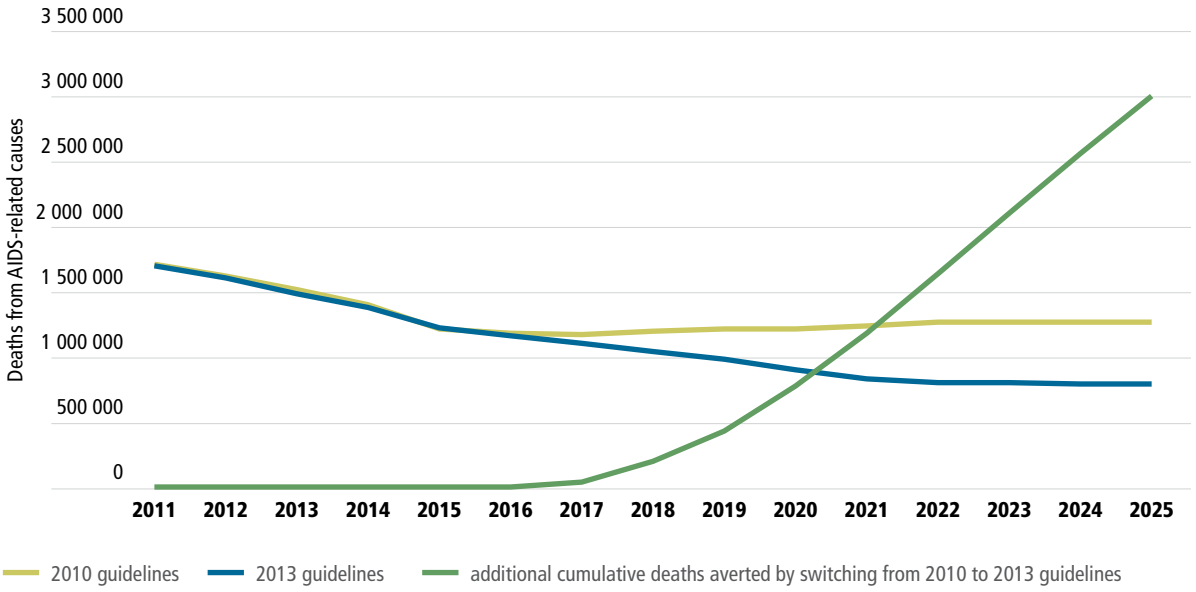
Current trends in the global scaling up of ART give great cause for optimism. Nevertheless, further improvements are both necessary and possible. To take full advantage of the enormous impact of providing ART for preventing people from dying and from becoming newly infected with HIV, WHO has revised its ARV guidelines to recommend earlier initiation of ART and immediate ART in certain circumstances. The 2013 ARV guidelines recommend initiating ART earlier – at CD4 count ≤500 cells/mm^3 – and immediately initiating ART for serodiscordant couples, pregnant women living with HIV, people with TB and HIV, people with HIV and hepatitis B, and children living with HIV who are younger than five years, irrespective of CD cell count.

If fully implemented, the 2013 WHO ARV guidelines could avert at least an additional 3.0 million deaths and prevent close to an additional 3.5 million new infections between 2012 and 2025 in low- and middle-income countries, compared with continuing with the 2010 treatment guidelines (Fig. 4 and 5).

Realizing these benefits could require a 10% increase in total annual investment in the global HIV response in the coming years, which is "very cost effective" according to global criteria. These resource needs are projected to level off over time before declining after 2025, a trend that reflects the accumulated prevention benefits of expanding the provision of ART. Greater access to ART will reduce new HIV infections and thereby eventually reduce the number of people eligible for ART.

The demonstrated benefits of ART in terms of averted deaths and prevented infections exceed many of the expectations that helped launch the global scaling up of ART a decade ago. The 2013 WHO ARV guidelines are designed to extend these benefits more widely and will increase the potential number of people eligible for ART to an estimated 25.9 million (9.2 million more people than were eligible under the previous 2010 WHO treatment guidelines). These changes underscore the need to intensify efforts globally to expand access to ART.

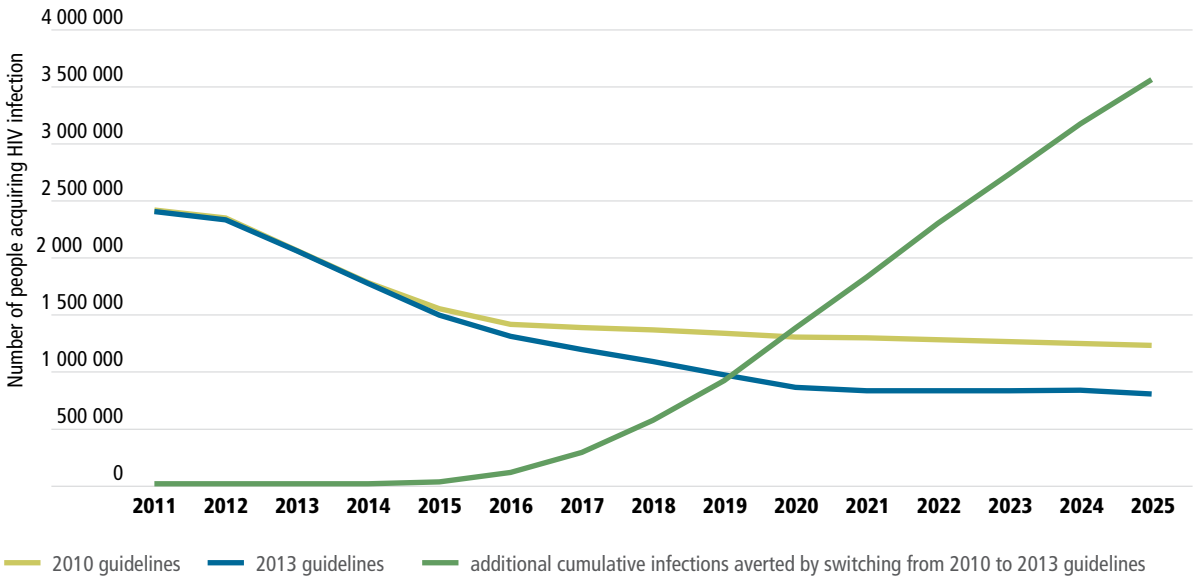
Fig. 4. Projected annual number of people dying from AIDS-related causes in low- and middle-income countries based on the 2010 WHO treatment guidelines and the 2013 WHO ARV guidelines and cumulative deaths averted by switching from 2010 to 2013 guidelines, 2011–2025



Source: special analysis conducted by Futures Institute, 2013.

Maintaining 80% coverage under the WHO 2010 treatment guidelines involves initiating ART at CD4 ≤350 cells/mm³ or clinical stages III or IV; maintaining 80% coverage under the WHO 2013 ARV guidelines involves initiating ART at CD4 ≤500 cells/mm³, and for serodiscordant couples, pregnant women living with HIV and children living with HIV younger than five years, irrespective of CD4 count.

Fig. 5. Projected annual number of people acquiring HIV infection in low- and middle-income countries based on the 2010 WHO treatment guidelines and on the 2013 WHO ARV guidelines and cumulative number of people avoiding HIV infection by switching from 2010 to 2013 guidelines, 2011–2025



Source: special analysis conducted by Futures Institute, 2013.

1. PROGRESS TOWARDS GLOBAL TARGETS

KEY POINTS

More people than ever received life-saving antiretroviral medicines in 2012

The number of people accessing antiretroviral therapy (ART) globally continues to climb rapidly, and the target of reaching 15 million people with this life-saving treatment is within grasp.

- The number of people receiving HIV treatment has tripled in five years – and reached 9.7 million in low- and middle-income countries in 2012. That total represents 65% of the global target of 15 million people set for 2015, up from 54% at the end of 2011.
- There were about 1.6 million more people on ART at the end of 2012 compared to end-2011, the largest-ever increase in a single year. The remarkable pace of scaling up ART is continuing despite the ongoing global economic crisis.
- If this substantial effort is sustained, the world can reach the global target of 15 million people receiving ART by the end of 2015.
- Most countries with a high burden of HIV infection are potentially on track to achieve universal access (defined as 80% ART coverage, based on the 2010 WHO criteria for treatment eligibility). However, some countries urgently need major support to boost their scaling up of treatment.
- Access to ART has increased in every region. The WHO African Region is leading the scale-up effort and is home to 4 of 5 people who started ART in 2012. The WHO European Region and Eastern Mediterranean Region have seen substantial rates of increase but remain the regions with the lowest estimated treatment coverage among low- and middle-income countries.

The scaling up of antiretroviral (ARV) medicines provided to prevent the mother-to-child transmission (PMTCT) of HIV is progressing well.

- In 2012, over 900 000 women globally were receiving ARV medicines for PMTCT, a third more that the number in 2009, the baseline year for the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive.
- In the 21 African priority countries named in the *Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive*, 64% [58-70%] of pregnant women living with HIV received ARV medicines for PMTCT in 2012, compared with 59% in 2011 and 49% in 2009.
- Based on current trends, one of the core targets of the Global Plan – providing ARV medicines to 90% of pregnant women living with HIV globally by the end of 2015 – appears to be within reach.

HIV treatment is still not reaching enough children and key populations.

- The number of children younger than 15 years receiving ART rose from 566 000 in 2011 to 630 000 in 2012, but the percentage increase was smaller than for adults (11% versus 21%).
- A huge effort is needed to reach the goal of providing ART to all children eligible for treatment by the end of 2015.

- Certain populations at higher risk of HIV infection are not benefiting equitably from ART, including people who inject drugs, men who have sex with men, transgender people and sex workers.
- Stigma, discrimination and punitive laws are denying these key populations the multiple benefits of ART.
- In some regions, including the WHO African Region, men eligible for ART are less likely than women to receive it.

The 2013 WHO *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection* aim to boost the impact of ART by broadening the criteria for eligibility for ART.

- The new guidelines reflect evidence indicating the multiple treatment and preventive benefits of initiating ART earlier.
- The CD4 threshold for treatment of adults living with HIV is being raised to 500 cells/mm^3, and treatment regardless of CD4 count is recommended for all children living with HIV younger than 5 years, all pregnant women living with HIV, people living with HIV and coinfected with TB or hepatitis B and HIV-positive partners in serodiscordant relationships.
- Applied to the current reality, the new 2013 guidelines would increase the total current number of people eligible for ART in low- and middle-income countries globally from 16.7 million to 25.9 million people. However, the additional prevention benefit of ART means that the total number of people eligible for ART will peak in 2021 and will then decline significantly.

Scaling up antiretroviral therapy: moving to 15 million people receiving antiretroviral therapy – and beyond

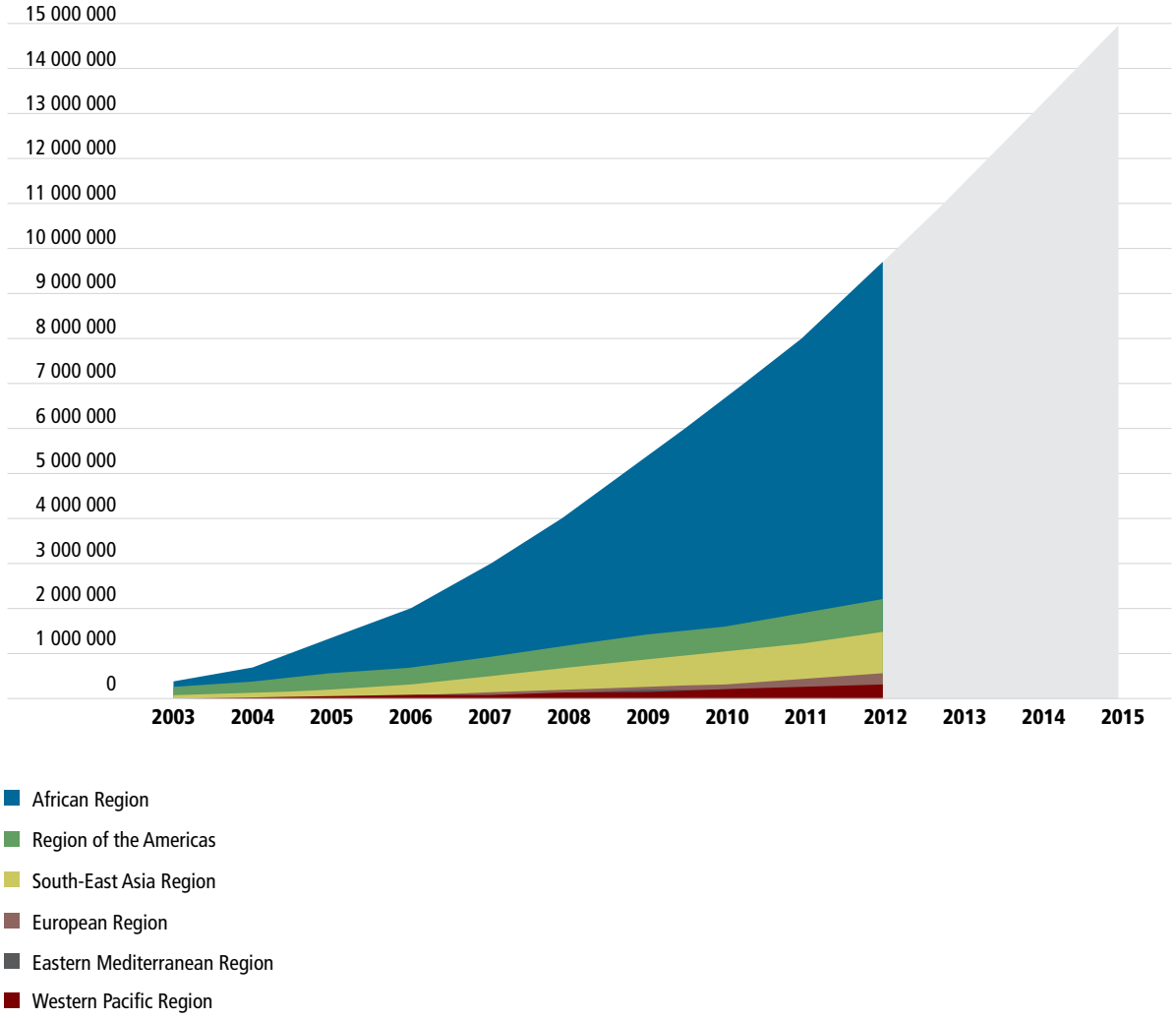
The scaling up of life-saving and infection-preventing HIV treatment across the world during the past decade constitutes one of the great public health achievements in recent decades. Its starting-point has been the fundamental principle that everyone has the right to health. The progress thus far demonstrates that this right can be realized, even in settings with extremely limited resources.

When WHO issued its first ART guidelines for resource-limited countries in 2002 *(1)*, about 300 000 people in such settings were receiving HIV treatment, half of them in Brazil. Ten years later, at the end of 2012, about 9.7 million people were receiving ART in low- and middle-income countries (Fig. 1.1).

This rapid expansion of access to ART testifies to the impact of strong political commitment, the mobilization of substantial resources, the tailoring of health systems and service delivery models and the dedication of people around the world, including people living with HIV.

The 9.7 million people receiving ART at the end of 2012 represented 65% of the 15 million target adopted by 189 United Nations Member States in June 2011 at the General Assembly High-Level Meeting on AIDS in New York *(2)*, up from 54% in 2011.

Fig. 1.1. Actual and projected numbers of people receiving antiretroviral therapy in low- and middle-income countries, and by WHO Region, 2003–2015



Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

Globally, 1.6 million more people were receiving ART in 2012 compared with 2011, the largest increase ever in one year. If the pace at which ART provision is expanding continues to increase in the coming years, the target of reaching 15 million with ART by the end of 2015 will be within reach (Fig. 1.1).[1]

Importantly, the recent pace of scaling up ART has been sustained in the 22 countries with a high HIV burden that have also been prioritized in the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive *(3)* (Table 1.1). Together, this enabled almost 1.4 million more people to be on ART by the end of 2012. In those countries, 63% [59–66%] of the people eligible for ART were receiving it in 2012, up from 54% [51–57%] in 2011.

1. Original data on progress in the AIDS response presented in this document are drawn from the "Global AIDS Response Progress Reporting (GARPR)" mechanism, which is described in detail in the methodological annex. Source data are provided by countries, and are jointly collected and validated by WHO, UNICEF and UNAIDS. Some limitations apply; these are highlighted in the annex.

Table 1.1. Antiretroviral therapy among adults and children in 22 selected countries with a high burden of HIV infection, 2011 and 2012

	Reported number of people receiving ART, 2011	Estimated number of people eligible for ART, 2011 [range]	Estimated ART coverage, 2011 [range][a]	Reported number of people receiving ART, 2012	Estimated number of people eligible for ART, 2012 [range]	Estimated ART coverage, 2012 [range][a]
Angola	35 529	96 000 [80 000–120 000]	37% [31–44%]	42 607	100 000 [87 000–120 000]	42% [35–50%][b]
Botswana	178 684	200 000 [190 000–210 000]	89% [87–93%]	212 083	210 000 [200 000–220 000]	>95% [>95–>95%]
Burundi	26 402	49 000 [43 000–57 000]	54% [47–62%]	29 121	50 000 [44 000–58 000]	58% [50–66%]
Cameroon	105 653	270 000 [250 000–290 000]	40% [37–43%]	122 783	280 000 [260 000–300 000]	45% [41–48%]
Chad	32 832	100 000 [87 000–120 000]	33% [27–38%]	40 856	100 000 [89 000–120 000]	40% [33–46%]
Côte d'Ivoire	82 721	230 000 [200 000–250 000]	37% [33–41%]	110 370	230 000 [200 000–260 000]	49% [43–54%]
Democratic Republic of the Congo	53 554	220 000 [200 000–240 000]	25% [23–27%]	64 219	220 000 [200 000–240 000]	31% [29–34%][b]
Ethiopia	265 174	480 000 [440 000–530 000]	55% [50–60%]	288 137	470 000 [440 000–510 000]	61% [56–66%]
Ghana	54 589	120 000 [100 000–130 000]	47% [42–53%]	69 870	120 000 [110 000–140 000]	58% [51–65%]
India	543 000	1 100 000 [930 000–1 200 000]	50% [45–59%]	604 987	1 100 000 [950 000–1 300 000]	50% [44–58%][b]
Kenya	538 983	780 000 [740 000–830 000]	69% [65–73%]	604 027	830 000 [790 000–880 000]	73% [69–77%]
Lesotho	83 626	160 000 [150 000–170 000]	51% [49–54%]	92 747	170 000 [160 000–180 000]	54% [52–57%]
Malawi	322 209	550 000 [530 000–590 000]	58% [55–61%]	405 131	580 000 [550 000–620 000]	69% [66–73%]
Mozambique	273 561	650 000 [600 000–730 000]	42% [37–46%]	309 851	690 000 [630 000–770 000]	45% [40–49%]
Namibia	104 531	120 000 [110 000–130 000]	86% [79–95%]	116 687	130 000 [120 000–140 000]	90% [82–>95%]
Nigeria	432 285	1 500 000 [1 400 000–1 700 000]	29% [26–32%]	491 021	1 500 000 [1 400 000–1 700 000]	32% [29–35%]
South Africa	1 702 060	2 500 000 [2 400 000–2 600 000]	69% [65–72%]	2 150 881	2 700 000 [2 600 000–2 900 000]	80% [75–83%]
Swaziland	72 402	98 000 [94 000–100 000]	74% [70–77%]	87 534	110 000 [100 000–110 000]	82% [78–86%]
Uganda	313 117	640 000 [580 000–720 000]	49% [43–54%]	438 542	680 000 [620 000–770 000]	64% [57–71%]
United Republic of Tanzania	277 070	690 000 [630 000–760 000]	40% [36–44%]	432 293	710 000 [650 000–780 000]	61% [55–66%]
Zambia	415 685	570 000 [540 000–600 000]	73% [69–77%]	480 925	610 000 [580 000–640 000]	79% [75–83%]
Zimbabwe	476 321	660 000 [630 000–700 000]	72% [68–76%]	565 675	720 000 [680 000–750 000]	79% [75–83%]
TOTAL	6 390 000	11 700 000 [11 200 000–12 500 000]	54% [51–57%]	7 760 000	12 300 000 [11 800 000–13 100 000]	63% [59–66%]

Note: some numbers do not add up because of rounding.

[a] The coverage estimate is based on the estimated unrounded number of people receiving and eligible for ART.
[b] Based on a numerator from the national Spectrum file which differs in the following countries from the value from the Global AIDS Response Reporting tool printed in the table above: Angola (43,903), Democratic Republic of the Congo (68,970) and India (549,402).

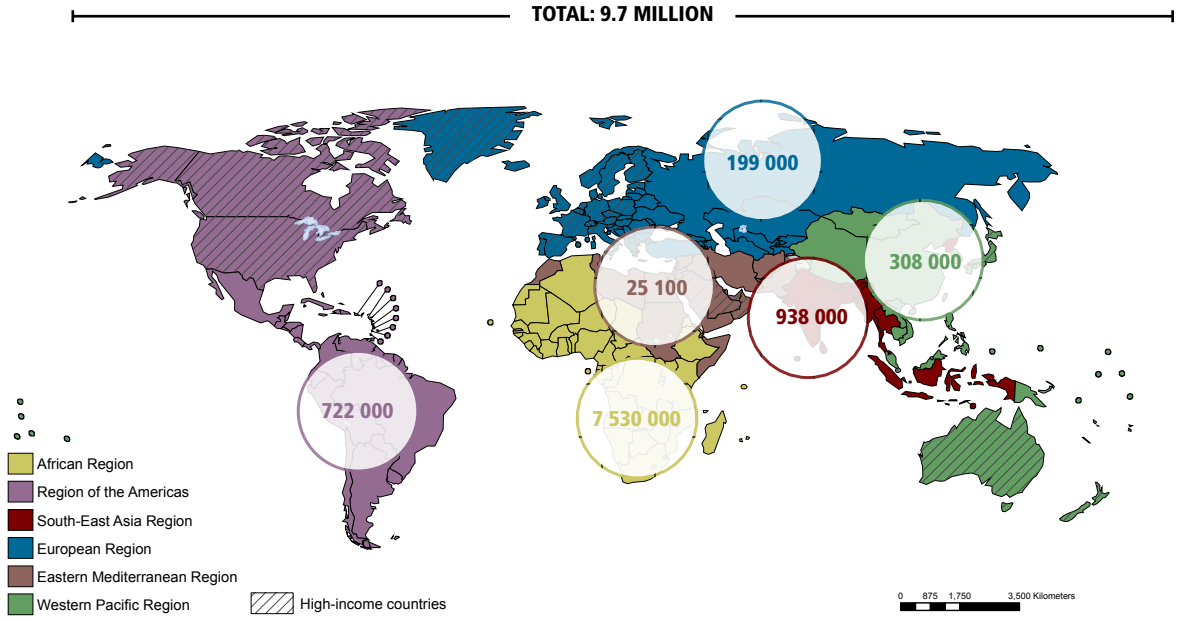
Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2013 UNAIDS/WHO estimates.

Achieving the full impact of ART requires reaching the 2015 target and continuing further scale-up beyond 2015 (Chapters 2 and 4). The preventive effect of ART on onward HIV transmission has been confirmed in both clinical trials *(4)* and routine programme settings *(5)*, highlighting the prospect that rapidly scaling up effective combination HIV prevention,[1] including ART, could enable the world eventually to achieve an AIDS-free generation *(6)*.

Confirmation of the major, broader treatment and prevention benefits of ART has led to important revisions in the new 2013 WHO ARV guidelines *(7)*. The changes include recommending earlier initiation of ART for people diagnosed with HIV (at CD4 ≤500 cells/mm^3) and immediate ART for serodiscordant couples, pregnant women living with HIV and children living with HIV younger than five years. These recommendations increase the potential number of people eligible for ART to an estimated 25.9 million in 2013 – which amounts to 9.2 million more people than were eligible under the previous 2010 WHO ARV guidelines. These changes underscore the need to intensify efforts globally to expand access to ART.

Expanding effective treatment and prevention interventions would enable countries eventually to reach a "tipping point" beyond which the number of people starting HIV treatment exceeds the number of people acquiring HIV infection. This represents an important milestone in countries' HIV responses *(6)*. Several countries with high HIV prevalence appear to have passed such a "tipping point" already (for example, Botswana, Ghana, Haiti, Malawi, Namibia, Rwanda, South Africa, Swaziland, United Republic of Tanzania, Zambia and Zimbabwe), and several others are poised to follow their example (Burundi, Ethiopia, Gabon and Uganda).[2]

Fig. 1.2. Number of people receiving antiretroviral therapy in low- and middle-income countries, by WHO region, 2012



Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

1. Combination prevention simultaneously uses complementary behavioural, biomedical and structural prevention interventions. They include ART, voluntary medical male circumcision, consistent and correct use of male and female condoms, along with other proven behavioural and structural interventions.

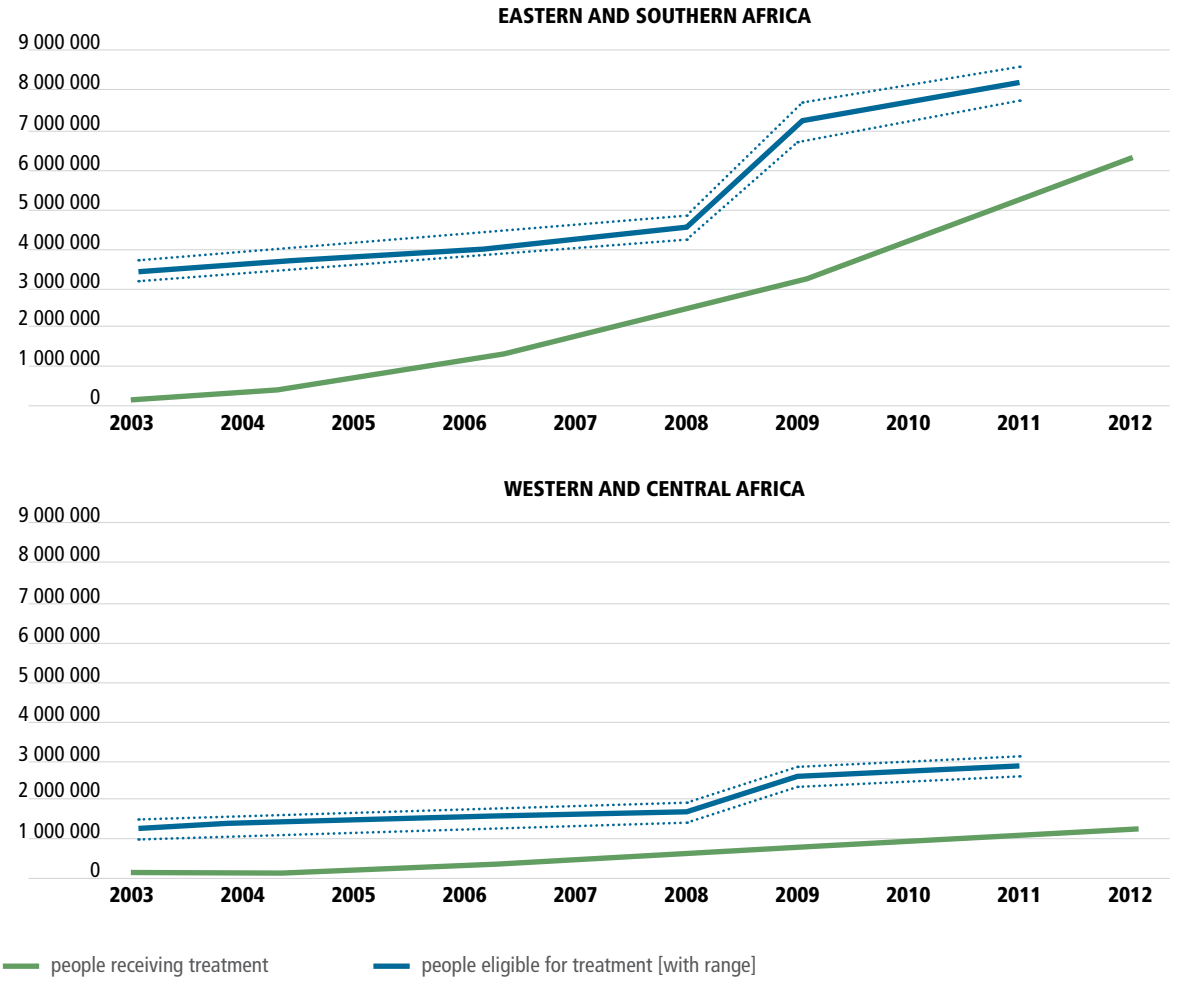
2. Based on the number of new infections, using the 2011 Spectrum estimates, and the number of people on ART, according to the 2012 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

The extent of ART provision differs considerably between regions, as Fig. 1.2 shows. In 2012, ART continued to be rolled out at a remarkable pace in the African Region[1], which bears a disproportionately large share of the global HIV burden. Home to only 12% of the world's population, the region accounts for 69% [65–73%] (23.4 million, range 22.0 – 24.7 million) of all people living with HIV. In 2011, an estimated 10.9 million [10.3 – 11.6 million] people in this region needed ART (according to the 2010 WHO treatment guidelines *(8)*), of whom 6.2 million were receiving it. The number of people on ART increased by one fifth to more than 7.5 million at the end of 2012.

As Fig. 1.3 shows, the expansion of access to ART has been particularly impressive in Eastern and Southern Africa, a region that accounts for about 50% of all people living with HIV and where almost 6.4 million people were receiving ART in 2012. South Africa's ART programme is the largest in the world, with about 2.2 million people on HIV treatment in 2012 – almost 450 000 more than in 2011. An additional 90 000 people in Zimbabwe and 65 000 in Kenya were receiving ART in 2012 compared with 2011.

Access to ART increased also in Western and Central Africa, where the number of people receiving ART increased by more than one fifth in Algeria, Benin, Cape Verde, Chad, Congo, Côte d'Ivoire, Gambia and Ghana. Nevertheless, in most countries in this part of Africa, less than half the people eligible for ART (according to the 2010 WHO treatment guidelines *(8)*) were receiving it in 2012 (see Fig. 1.3).

Fig. 1.3. Adults and children eligible for and receiving antiretroviral therapy, in low- and middle-income countries in eastern and southern Africa and in western and central Africa, 2003–2012[2]



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012 UNAIDS/WHO estimates.

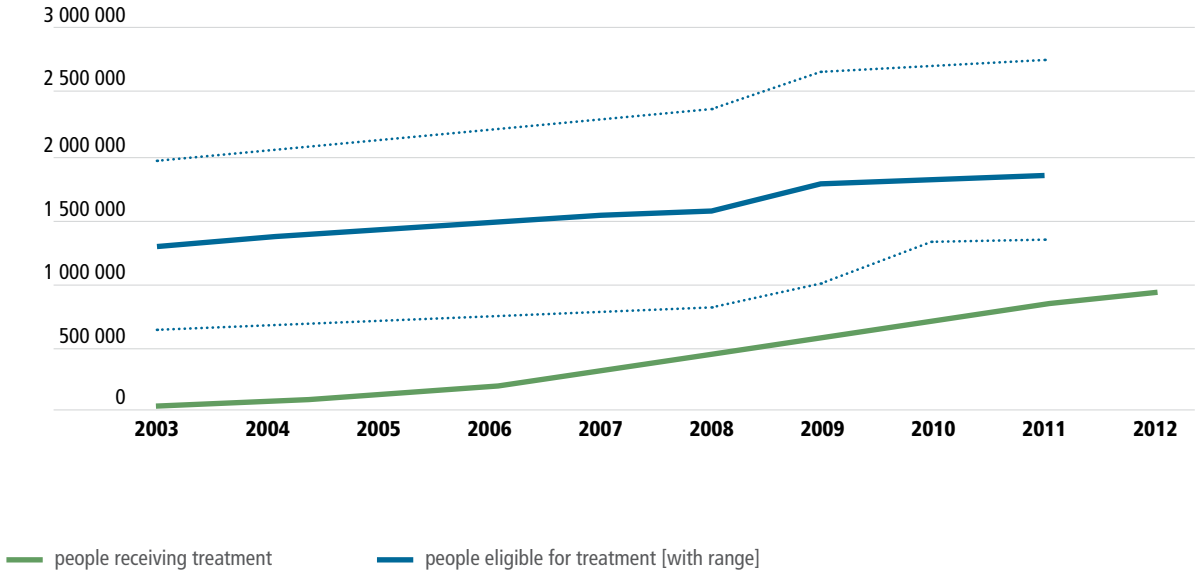
1. The WHO African Region includes Algeria but does not include Somalia, Sudan or South Sudan.

2. In Fig. 1.3 to 1.11, the number of people receiving ART is available up to end of 2012, while the number of people eligible for ART in 2012 has not yet been established and therefore is shown up to the end of 2011.

The scaling up of treatment has also expanded significantly in other regions. In the WHO South-East Asia Region[1], 938 000 people were receiving ART at the end of 2012, about 100 000 more than in 2011 (Fig. 1.4). This increase was largely driven by rapid programme expansion in India and by the consolidation of high ART coverage in Thailand.

Together, those two countries account for about 87% of the estimated number of people eligible for ART in this region. India and Thailand were the only countries in this region in which more than half the people eligible for ART in accordance with the 2010 WHO treatment criteria were receiving it in 2012.

Fig. 1.4. Adults and children eligible for and receiving antiretroviral therapy, in low- and middle-income income countries in the WHO South-East Asia Region, 2003–2012



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012 UNAIDS/WHO estimates.

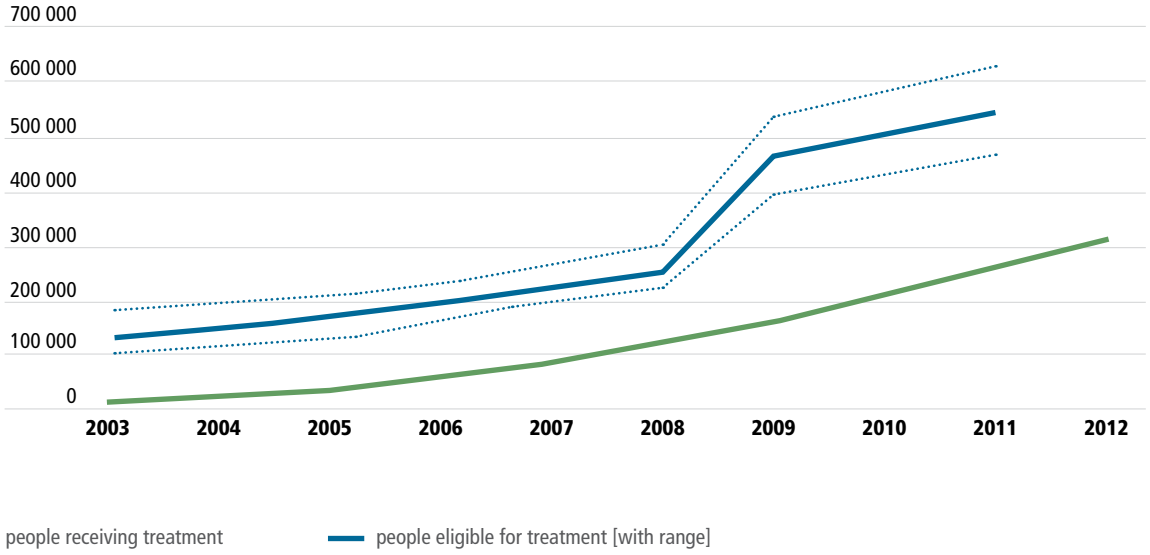
In the Western Pacific Region[2], the number of people receiving ART reached 308 000 at the end of 2012 (Fig. 1.5). The scaling up of ART is proceeding at a fast pace, largely because of increases in China, where the number of people receiving ART rose from 126 000 to 154 000 between 2011 and 2012. In Cambodia, which had already exceeded 80% ART coverage in 2011, almost 50 000 people were receiving ART by the end of 2012. Other countries in this region, including Papua New Guinea and Viet Nam, also stepped up the provision of ART in 2012.

In the WHO Region of the Americas, 722 000 people were receiving ART in 2012, about 65 000 more than the 657 000 in 2011 (Fig. 1.6). Five countries (Brazil, Cuba, the Dominican Republic, Guyana and Mexico) had already reached the 80% coverage target in 2011, and Argentina and the Bolivarian Republic of Venezuela were very close to reaching that target.

1. The low- and middle-income countries in this region are Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste.

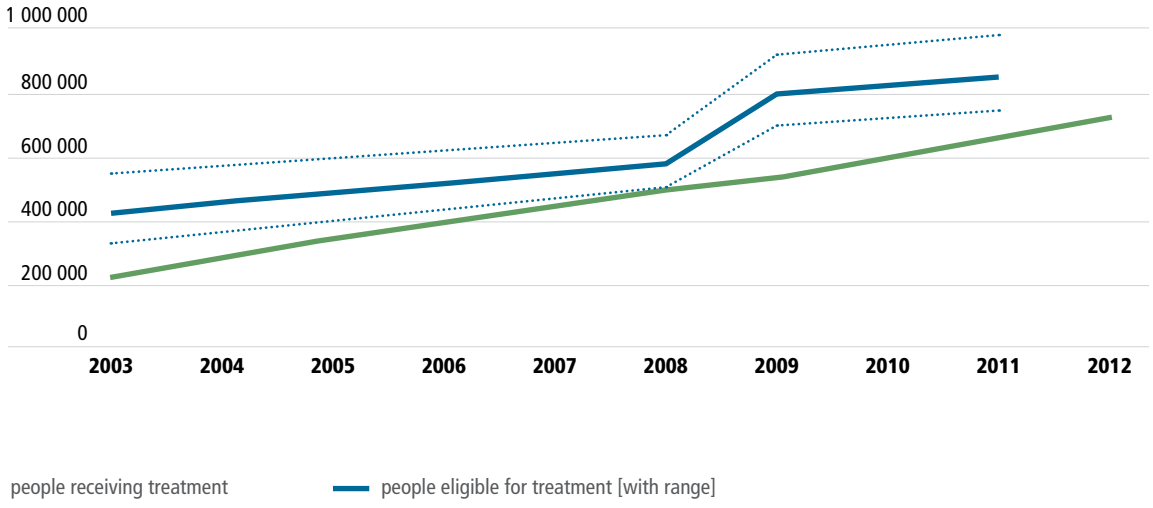
2. The low- and middle-income countries in this region are Cambodia, China, Cook Islands, Fiji, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, Niue, Palau, Papua New Guinea, Philippines, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu and Viet Nam.

Fig. 1.5. Adults and children eligible for and receiving antiretroviral therapy in low- and middle-income countries in the WHO Western Pacific Region, 2003–2012



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012 UNAIDS/WHO estimates.

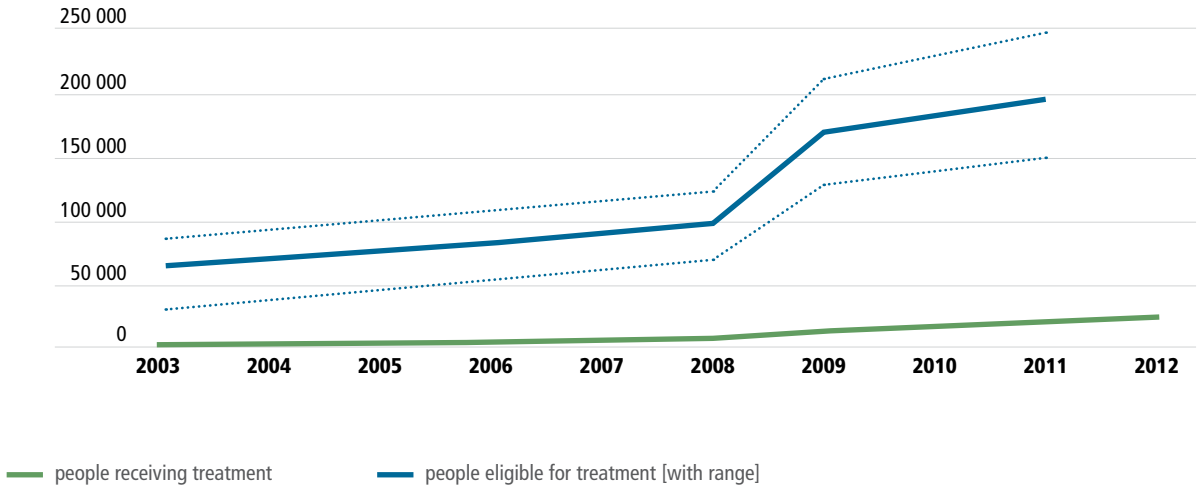
Fig. 1.6. Adults and children eligible for and receiving antiretroviral therapy in low- and middle-income countries in the WHO Region of the Americas, 2003–2012



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012 UNAIDS/WHO estimates.

The number of people receiving ART in the countries of the WHO Eastern Mediterranean Region[1] also continued to rise (Fig. 1.7) and reached 25 100 in 2012, up from 20 300 in 2011. ART coverage, however, has remained very low, with less than one in eight people eligible for ART receiving it, including in the four countries that account for about 80% of the people needing ART in the region (Iran (Islamic Republic of), Pakistan, South Sudan and Sudan).

Fig. 1.7. Adults and children eligible for and receiving antiretroviral therapy in low- and middle-income countries in the WHO Eastern Mediterranean Region, 2003–2012



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012 UNAIDS/WHO estimates.

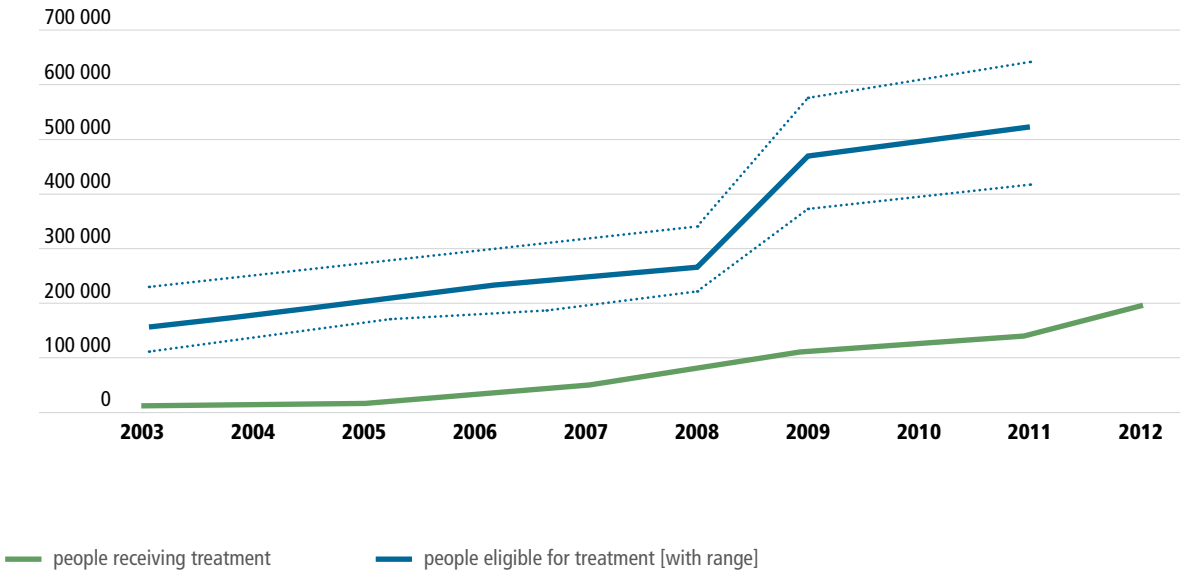
In the European Region, 199 000 people were receiving ART in 2012, 45% more than the 137 000 people in 2011 (Fig. 1.8). Access to ART expanded substantially in Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Lithuania, the Republic of Moldova, the Russian Federation, Tajikistan, Turkey, Ukraine and Uzbekistan. However, the region's scale-up efforts are not keeping pace with the annual increases in the number of people acquiring HIV infection. The HIV burden in this region is large among people who inject drugs, sex workers and men who have sex with men, but access to ART for these key populations appears to be lower than for the wider population.[2]

In the 50 high-income countries globally, an estimated 875 000 people were receiving ART in 2012.

1. The low- and middle-income countries in this region are Afghanistan, Djibouti, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Lebanon, Libya, Morocco, Pakistan, Somalia, South Sudan, Sudan, Syrian Arab Republic, Tunisia and Yemen.

2. Gauging progress towards achieving 80% coverage of ART depends on the accuracy of estimations of how many people are eligible for ART. Such estimations can be challenging, especially in countries with epidemics that are concentrated among key populations and in which HIV surveillance is based on case reporting (as in most of the European Region) rather than on sentinel surveillance in key populations. In addition, HIV data and ART are limited for the Russian Federation, which is estimated to be home to more than half the people eligible for ART in Eastern Europe and Central Asia.

Fig. 1.8. Adults and children eligible for and receiving antiretroviral therapy in low- and middle-income countries in the WHO European Region, 2003–2012



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012 UNAIDS/WHO estimates.

Increasing numbers of antiretroviral therapy sites and greater decentralization of services

A key factor associated with the increase in access to ART in recent years is the steep rise in the number of facilities providing ART services in low- and middle-income countries. The latest available data indicate that almost 30 000 facilities were offering ART in the 132 countries that reported these data. The number of sites providing ART services increased by 14% between 2010-2011 and 2012 in the 108 countries that reported data for both periods, and by 21% in the WHO African Region.

The increase in the number of facilities that provide ART in the WHO African Region has resulted mainly from extensive efforts to improve access to ART beyond cities and referral hospitals by decentralizing ART services to primary health care facilities.[1] Each of the facilities providing ART in this region serves large numbers of ART patients – an average of 498 people per facility compared with 388 in the WHO South-East Region and about 151 in the WHO Americas Region, for example.

HIV care and treatment for children is also being decentralized to primary health care facilities in several countries in the WHO African Region. One recent study reported a three-fold increase between 2008 and 2010 in the number of primary health care facilities providing HIV care and treatment for children in Kenya, Lesotho, Mozambique, Rwanda and the United Republic of Tanzania. However, the comparatively small numbers of people being treated at these facilities mean that this did not translate into large gains in the numbers of children receiving treatment *(9)*.

1. This approach, which is supported by the 2013 WHO ARV guidelines *(6)*, is also becoming more widely adopted in other regions.

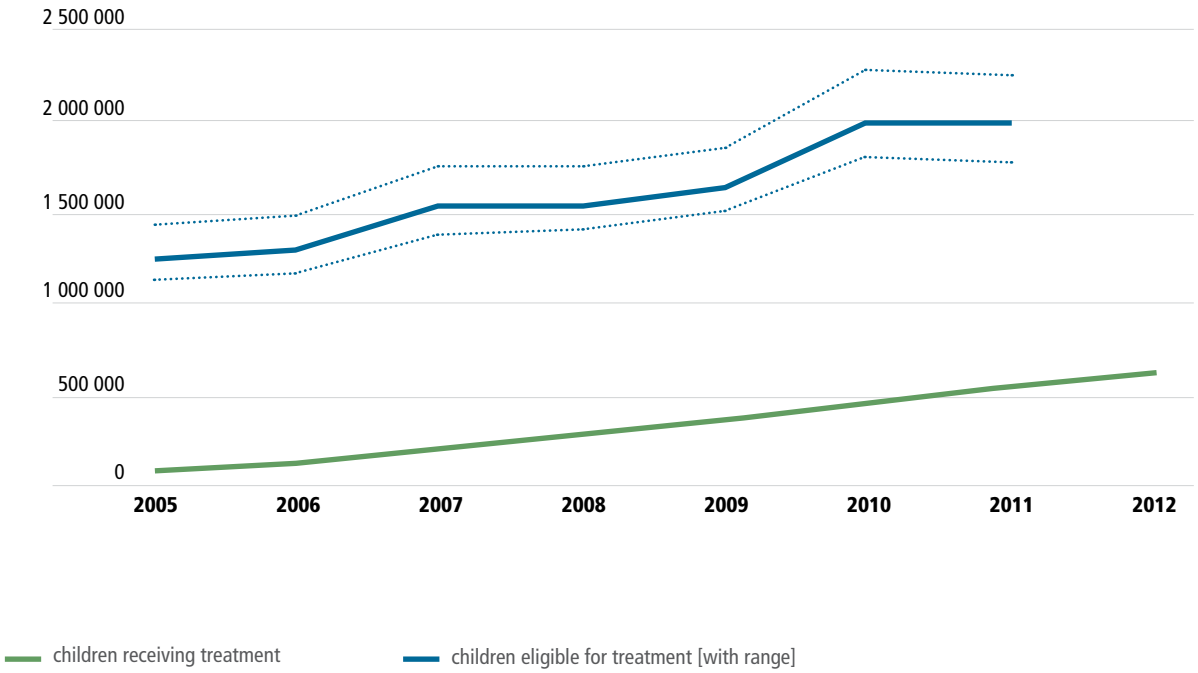
Providing antiretroviral therapy for children

Most HIV infections in children occur during the perinatal period, and result from mother-to-child transmission of HIV. Effective, established approaches to prevent mother-to-child transmission have the potential to prevent many children from acquiring HIV infections and dying from AIDS-related causes, and early HIV diagnosis and timely care and treatment can prevent many AIDS-related deaths among children living with HIV. The 2013 WHO ARV guidelines *(7)* now recommend initiating ART immediately for all children younger than five years of age who are diagnosed with HIV, irrespective of CD4 count.

More children receiving antiretroviral therapy

The number of children younger than 15 years receiving ART in low- and middle-income countries rose to 630 000 at the end of 2012, up from 566 000 in 2011. However, the percentage increase was lower than for adults: 11% versus 21% between 2011 and 2012 (Fig. 1.9 and 1.10).

Fig. 1.9. Number of children eligible for and receiving antiretroviral therapy in low- and middle-income countries, 2005–2012



Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

A global estimate of the number of children eligible for ART in 2012 is not yet available. However, the 22 priority countries[1] identified in the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive *(3)*[2] account for nearly 90% of the pregnant women living with HIV and for a similar percentage of the children living with HIV. In these 22 countries, the number of children eligible for ART (based on the 2010 WHO treatment guidelines) fell by 60 000, from 1.72 million [1.59 – 2.03 million] in 2011 to 1.66 million [1.53 – 1.95 million] in 2012.

1. The Global Plan has 22 priority countries, all but one of which (India) are in the African region. The Global Plan priority countries are: Angola, Botswana, Burundi, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, India, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.

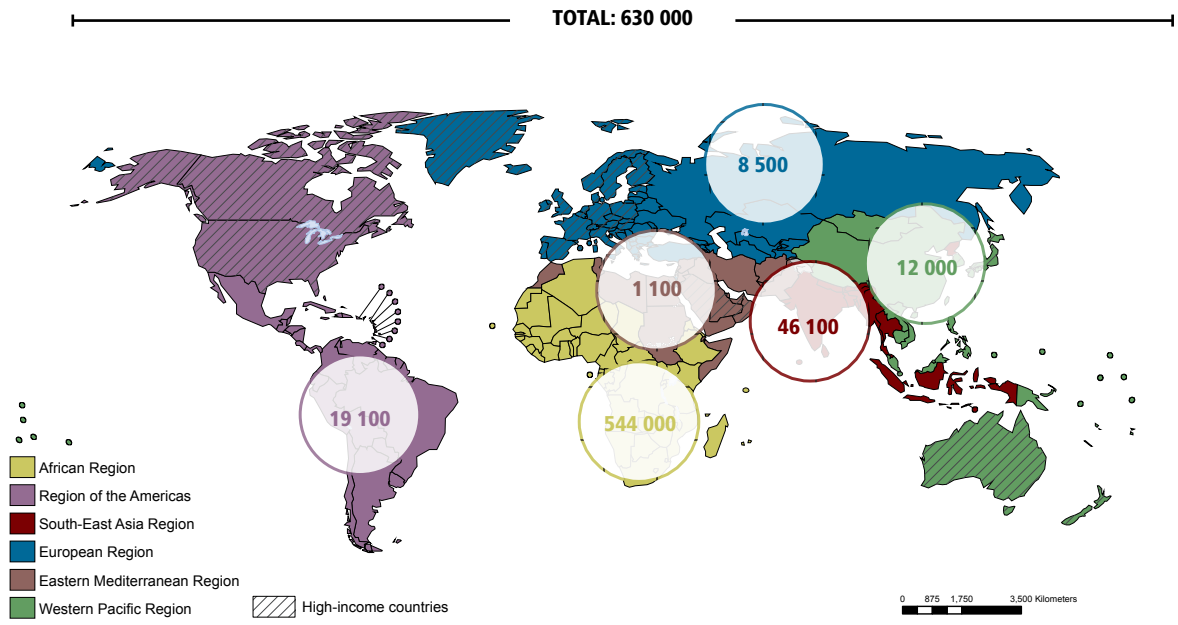
2. Launched in mid-2011, the Global Plan features two high-level targets: reduce the number of children newly infected with HIV by 90% and reduce the number of mothers dying from AIDS-related causes by 50%.

Some countries (such as Ethiopia, Malawi, Mozambique, Uganda and Zimbabwe) achieved a strong increase in PMTCT provision in 2012 that lead to a considerable impact in reducing the number of children acquiring HIV infection (and therefore also the number of children eligible for ART). Other countries (such as Namibia, South Africa and Zambia) already had high coverage of services for PMTCT in 2011 and therefore experienced a more moderate decrease in the number of children acquiring HIV infection. Only in India did the population of children eligible for ART increase significantly between 2011 and 2012 (Table 1.2).

Antiretroviral therapy for children is lagging behind

A stronger focus on expanding ART for children remains essential, especially in the 22 priority countries. As Table 1.2 shows, ART coverage in these countries increased from 29% [26–31%] in 2011 to 33% [27–33%] in 2012 – much lower than the Global Plan 2015 target of providing ART to all children in need.

Fig. 1.10. Number of children (0-14 years old) receiving antiretroviral therapy in low- and middle-income countries, by WHO region, 2012



Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

Table 1.2. Children (0–14 years old) eligible for and receiving antiretroviral therapy, and antiretroviral therapy coverage in the 22 priority countries in the Global Plan, 2011 and 2012

	Number of children receiving ART, December 2011	Estimated number of children eligible for ART, 2011 [range]	ART coverage among children, December 2011 [range][a]	Number of children receiving ART, December 2012	Estimated number of children eligible for ART, 2012 [range]	ART coverage among children, December 2012 [range][a]
Angola	2 397	19 000 [15 000–24 000]	13% [10–16%]	2 903	19 000 [15 000–24 000]	15% [12–19%]
Botswana	9 702	10 000 [9 900–10 000]	>95% [93–>95%]	10 261	10 000 [9 900-10 400]	>95% [>95–>95%]
Burundi	1 927	10 000 [8 500–13 000]	18% [15–23%]	2 023	9 700 [7 800–12 000]	21% [17–26%]
Cameroon	4 440	34 000 [30 000–39 000]	13% [11–15%]	4 992	33 000 [29 000–38 000]	15% [13–17%]
Chad	1 531	20 000 [17 000–26 000]	8% [6–9%]	5 842	20 000 [17 000–25 000]	29% [23–35%]
Côte d'Ivoire	5 190	37 000 [31 000–44 000]	14% [12–17%]	5 620	35 000 [29 000–41 000]	16% [14–19%]
Democratic Republic of the Congo	6 238	54 000 [48 000–61 000]	12% [10–13%]	4 751	53 000 [47 000–61 000]	9% [8–10%]
Ethiopia	16 000	86 000 [74 000–100 000]	19% [16–22%]	17 677	73 000 [63 000–84 000]	24% [21–28%]
Ghana	2 480	16 000 [13 000–19 000]	16% [13–19%]	3 504	14 000 [12 000–17 000]	25% [20–29%]
India	22 896	81 000 [65 000–100 000]	28% [23–35%]	34 367	86 000 [70 000–110 000]	37% [30–46%][b]
Kenya	48 546	160 000 [140 000–180 000]	31% [27–36%]	55 439	150 000 [130 000–170 000]	38% [33–44%]
Lesotho	6 095	22 000 [20 000–25 000]	27% [25–31%]	5 395	22 000 [19 000–24 000]	25% [22–28%]
Malawi	28 722	110 000 [94 000–120 000]	27% [24–30%]	36 441	100 000 [90 000–110 000]	36% [33–41%]
Mozambique	23 053	110 000 [91 000–130 000]	22% [18–25%]	27 164	100 000 [88 000–120 000]	27% [22-31%]
Namibia	10 284	13 000 [12 000–15 000]	80% [69–89%]	11 340	13 000 [12 000–15 000]	88% [77–>95%]
Nigeria	36 716	260 000 [220 000–300 000]	14% [12–16%]	31 556	260 000 [220 000–290 000]	12% [11–14%]
South Africa	151 860	230 000 [210 000–250 000]	67% [60–74%]	140 541	220 000 [210 000–250 000]	63% [57–69%]
Swaziland	6 567	14 000 [12 000–15 000]	48% [44–53%]	7 431	14 000 [12 000–15 000]	54% [49–60%]
Uganda	24 735	120 000 [99 000–140 000]	21% [18–25%]	35 453	110 000 [88 000–130 000]	33% [27–40%]
United Republic of Tanzania	18 298	130 000 [110 000–160 000]	14% [12–16%]	32 407	130 000 [110 000–150 000]	26% [22–30%]
Zambia	30 187	94 000 [85 000–100 000]	32% [29–36%]	34 084	89 000 [80 000–99 000]	38% [34–42%]
Zimbabwe	40 140	110 000 [100 000–120 000]	36% [32–40%]	46 874	100 000 [94 000–120 000]	45% [40–50%]
TOTAL	498 000	1 730 000 [1 590 000–1 930 000]	29% [26–31%]	553 000	1 550 000 [1 530 000–1 860 000]	33% [27–33%]

Note: some numbers do not add up because of rounding.

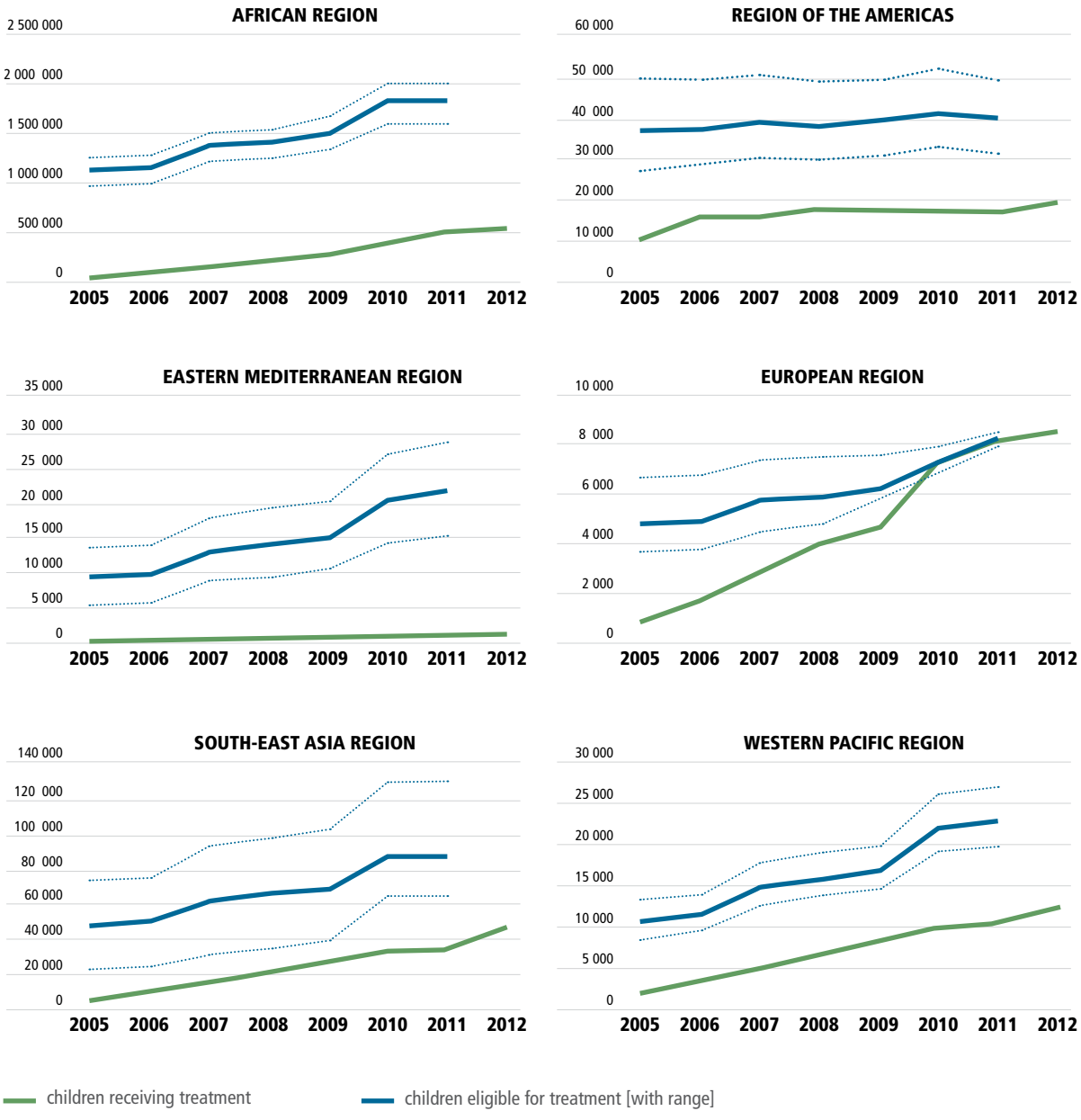
[a] The coverage estimate is based on the estimated unrounded number of children receiving and eligible for ART.
[b] Based on a numerator from the national Spectrum file which differs from the value from the Global AIDS Response Reporting tool printed in the table above: India (32,243).

Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2013 UNAIDS/WHO estimates.

Two of the Global Plan priority countries (Botswana and Namibia) have already achieved universal access (with at least 80% of the children eligible for ART receiving it), and several others have shown encouraging increases in coverage. However, the very low coverage in Angola, Cameroon, Côte d'Ivoire, the Democratic Republic of the Congo and Nigeria is a serious concern.

Fig. 1.11 depicts the regional trends in the numbers of children eligible for ART and receiving it. In the WHO African Region overall, 544 000 children were receiving ART in 2012, a 10% increase since 2011. Besides the priority countries in the region (see above), ART access for children increased encouragingly in Gambia, Guinea, Guinea Bissau, Niger and Senegal in that same period.

Fig. 1.11. Children (0–14 years old) eligible for antiretroviral therapy in low- and middle-income countries (2005–2011) and receiving it (2005–2012), by WHO region[1]



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012 UNAIDS/WHO estimates.

1. Estimating the number of children eligible for ART is particularly challenging in low-level and concentrated HIV epidemics, and yields wider ranges of uncertainty.

Access to ART also increased in the WHO South-East Asia Region. In India, the country with the largest burden of HIV infection among children in this region, the number of children receiving ART rose from 22 896 in 2011 to 34 367 in 2012.

In the WHO Region of the Americas, overall ART coverage for children remains below 50%. However, Chile, El Salvador, Guyana, Jamaica, Mexico and Paraguay all exceeded the universal access target. In the WHO Western Pacific Region, where the number of children eligible for ART is comparatively small (an estimated 23 000 children, range 20 000 – 27 000 in 2011), the number of children receiving ART also increased. Even smaller numbers of children are eligible for ART in the WHO European Region, where the number of children receiving ART increased from 8200 in 2011 to 8500 in 2012. Integrating HIV testing and ART provision into maternal and child health programmes has been an important factor in that progress. In the WHO Eastern Mediterranean Region, ART access for children increased marginally between 2011 and 2012 but remains very low.

Several improvements are needed to scale up ART for children more rapidly. Approaches to identify greater numbers of children who have acquired HIV need to be improved – for example, during routine immunization visits and during delivery by mothers who did not receive antenatal care. Stronger links between antenatal care, child health services, immunization clinics and HIV testing, care and treatment services are needed for both mothers and their children. Family-focused HIV care services should expand, while task shifting can be applied more widely. Approaches for providing HIV services (including ART) in adolescent-friendly ways are also becoming increasingly important.

Expanding the provision of antiretroviral medicines to prevent mother-to-child transmission

The Global Plan *(3)* includes three targets for ARV prophylaxis and therapy: 90% of pregnant women living with HIV receive perinatal ART or prophylaxis; 90% of pregnant women living with HIV eligible for ART for their own health receive lifelong ART; and 90% of breastfeeding mother–infant pairs (either mother or baby) receive ART or prophylaxis *(10)*.

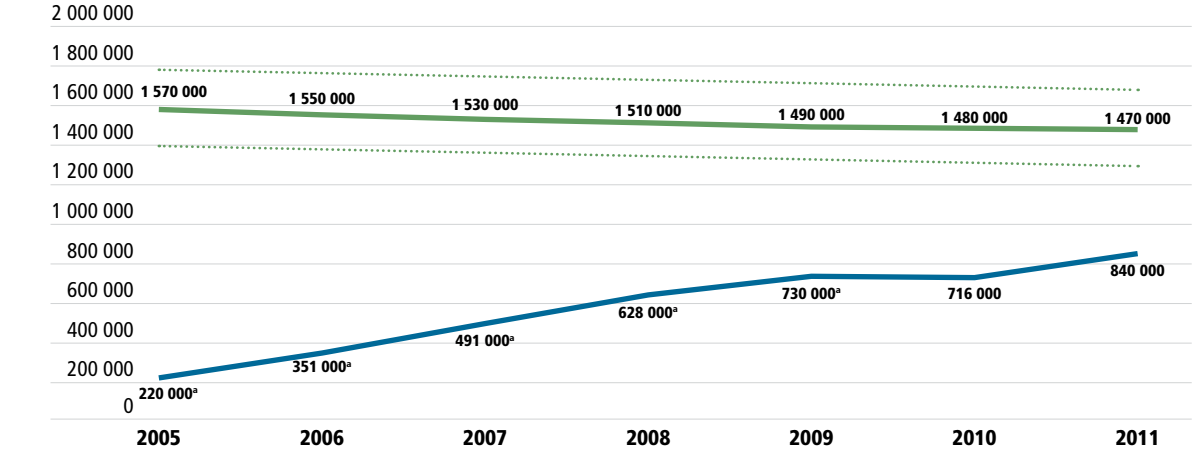
The scaling up of services for PMTCT progressed well in 2012, with over 900 000 women in low- and middle-income countries receiving ARV medicines (either ART or prophylaxis, but excluding single-dose nevirapine prophylaxis regimen no longer recommended by WHO). This was a third more than the number in 2009, the baseline year for the Global Plan. While the total need for PMTCT in low- and middle-income countries at the end of 2012 was not yet determined at the time of compiling this report, a comparison of trends among women needing for and receiving ARVs for PMTCT during 2005-2011 indicates that encouraging progress is being made towards meeting one of the core targets of the Global Plan – providing ARV medicines to 90% of the pregnant women living with HIV by the end of 2015 (Figure 1.12).

Regional differences in scaling up services for preventing mother-to-child transmission

The number of pregnant women living with HIV and who receive ART or ARV prophylaxis has expanded enormously in all regions since the early 2000s, when programmes for PMTCT were still beginning and comprised mainly pilot projects in a few facilities (Fig. 1.13).

The WHO European Region, for example, has achieved and maintained very high estimated coverage of 95% through 2011. Nevertheless, there are still pregnant women living with HIV in the Region who do not access antenatal care or who present late – especially women who inject drugs, trafficked women, sex workers, ethnic minorities, migrant women, refugees and prisoners. In some countries in the Region, substantial proportions of pregnant women living with HIV report that their sexual partners are at high risk of HIV infection. Up to 60% have partners who inject drugs and about 40% have partners with a history of imprisonment (11). In central Asia, an emerging risk factor for women acquiring HIV is having a sexual partner who is a migrant labourer *(11,12)*.

Fig. 1.12. Number of pregnant women living with HIV needing and receiving antiretrovirals for preventing mother-to-child transmission of HIV (2005–2011)



number of pregnant women living with HIV receiving any ARV medicine for PMTCT

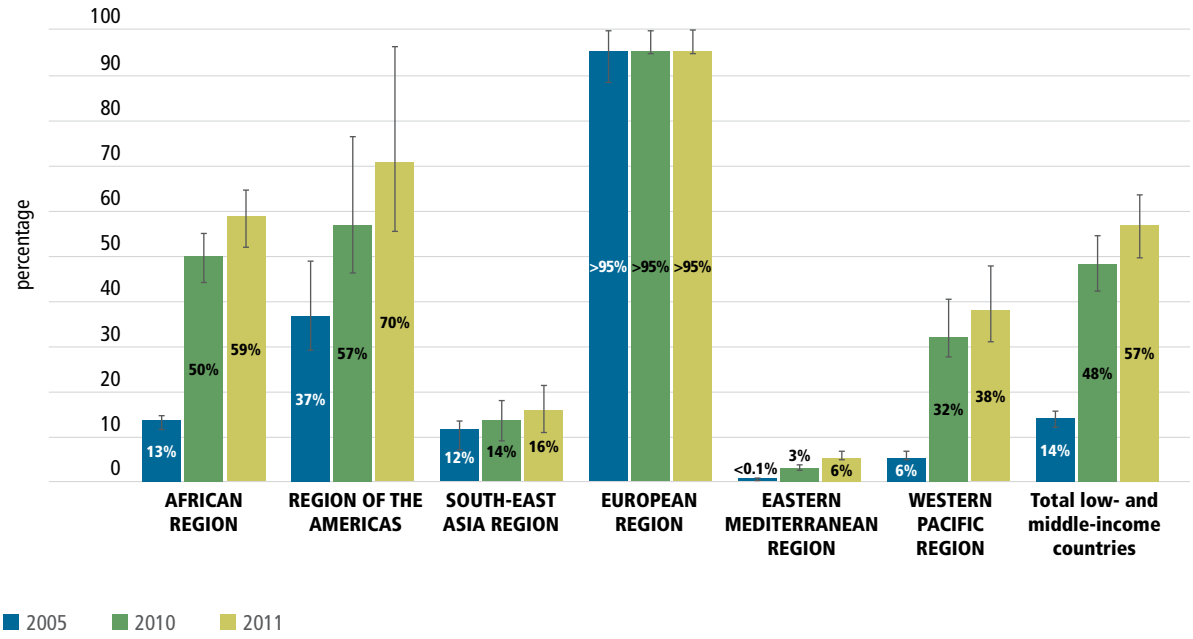
number of pregnant women living with HIV needing ARV medicines for PMTCT

[range]

[a] Single-dose nevirapine is still included in the data for the number of pregnant women living with HIV receiving ARV medicine from 2005-2009

Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

Fig. 1.13. Percentage of pregnant women living with HIV receiving antiretroviral medicines for preventing the mother-to-child transmission of HIV in low- and middle-income countries by region[a], 2005[b], 2010 and 2011



[a] Coverage is based on need estimates generated by the 2012 version of country Spectrum models

[b] The data for 2005 include single-dose nevirapine, no longer recommended

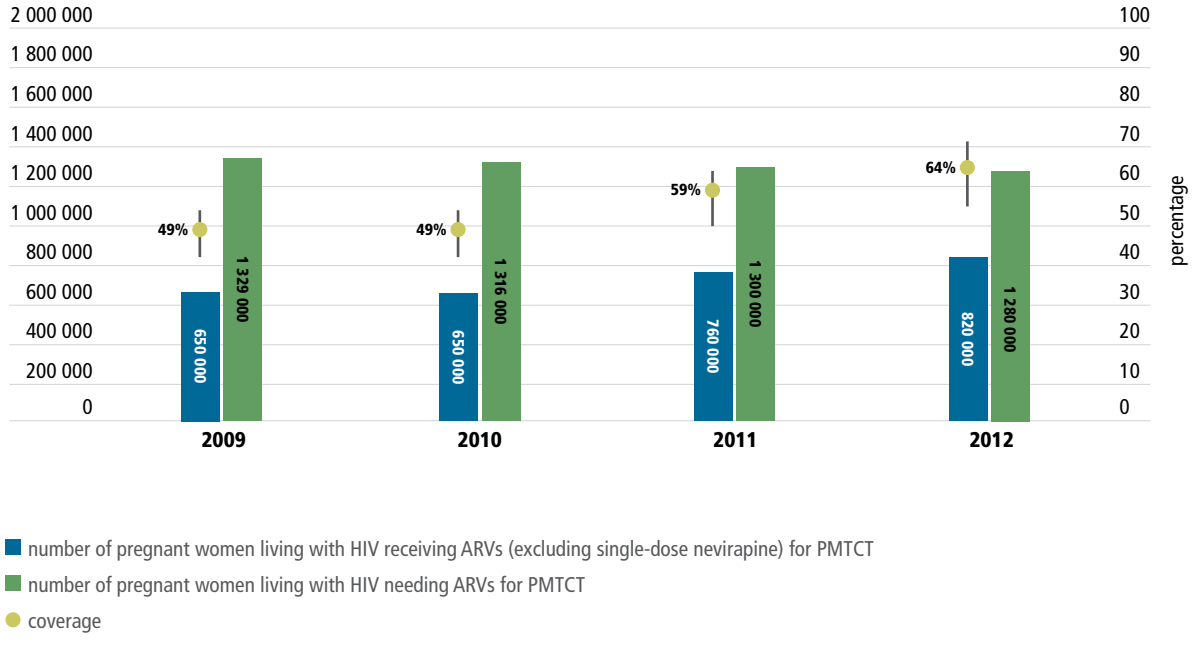
Coverage of the most effective ARV regimens for PMTCT reached 70% in the WHO Region of the Americas in 2011, up from 57% in 2010. In the WHO Western Pacific Region, coverage also improved, from 6% in 2005 to 38% in 2011. Coverage has remained fairly stagnant in the South-East Asia Region, where it was 16% in 2011 *(13)*. Nevertheless, some countries in that region (Malaysia and Thailand, for example) have achieved high coverage. In the WHO Eastern Mediterranean Region, coverage was lower, at only 6% in 2011. The WHO African Region has shown tremendous progress, with coverage increasing from 13% in 2005 to 59% in 2011. There are sub-regional differences between eastern and southern Africa (71%) and western and central Africa (26%). Overall progress in low- and middle-income countries overall mirrors the progress observed in the WHO African Region, which accounts for most of the PMTCT burden globally.

Progress in the 21 African priority countries of the Global Plan

Global progress in expanding access to services for PMTCT is being determined mainly by the scale-up of services in the 22 priority countries in the Global Plan, which are home to about 90% of pregnant women with HIV globally. Steady progress has been made with PMTCT ARV coverage increasing to 64% in 2012, compared to 59% in 2011 (Fig. 1.14). In the 21 Global Plan countries in Africa, six countries (the Democratic Republic of the Congo, Ethiopia, Kenya, Malawi, Nigeria and Uganda) account for 80% of the remaining gap in reaching 90% ARV coverage for PMTCT in 2012.

Four of the priority countries (Botswana, Ghana, Namibia and Zambia) are estimated to have achieved the Global Plan target of very high coverage of ARV medicines for PMTCT – over 90% in 2012. However, the estimated national ARV coverage for PMTCT was less than 20% in four other priority countries: Angola, Chad, the Democratic Republic of the Congo and Nigeria (Fig. 1.15; Table 1.3). Overall, 16 of the priority countries are potentially on track to reach the Global Plan target of 90% coverage in 2015.

Fig. 1.14. Pregnant women needing and receiving antiretroviral medicines for the prevention of mother-to-child transmission in 21 African priority countries of the Global Plan, 2009-2012



Note: Numbers from 2009 include single-dose nevirapine. Numbers from 2010-2012 exclude single-dose nevirapine.

Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS) and Spectrum estimates.

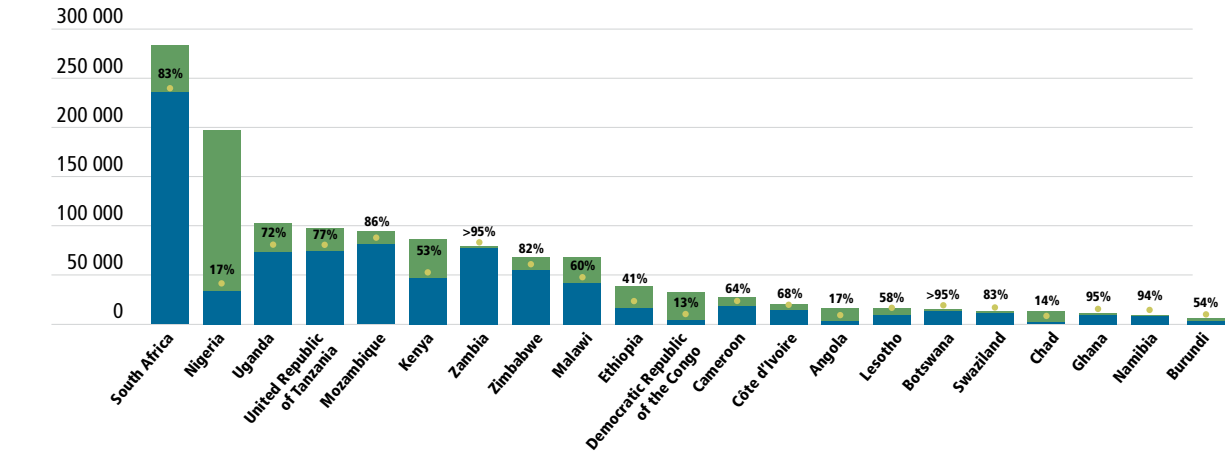
Table 1.3. Pregnant women living with HIV needing and receiving antiretroviral medicines for PMTCT and PMTCT antiretroviral coverage[a] among eligible pregnant women in the 21 African priority countries in the Global Plan, 2011 and 2012.

	Number of pregnant women living with HIV receiving antiretroviral medicines[b] for PMTCT, 2011	Estimated number of pregnant women living with HIV needing antiretroviral medicines for PMTCT, 2011	Antiretroviral coverage among pregnant women living with HIV, 2011	Number of pregnant women living with HIV receiving antiretroviral medicines[b] for PMTCT, 2012	Estimated number of pregnant women living with HIV needing antiretroviral medicines for PMTCT, 2012	Antiretroviral coverage among pregnant women living with HIV, 2012
Angola	2 584	15 000 [12 000–19 000]	17% [14–22%]	2 656	15 000 [12 000- 19 000]	17% [14–22%]
Botswana	12 738	13 000 [12 000–14 000]	>95% [88–>95%]	12 207	13 000 [11 000–14 000]	>95% [87–>95%]
Burundi	2 670	5 200 [4 100–6 600]	51% [41–65%]	2 742	5 100 [3 900- 6 500]	54% [42–70%]
Cameroon	15 190	28 000 [24 000–31 000]	55% [48–63%]	17 362	27 000 [23 000–31 000]	64% [56–74%]
Chad	1 611	13 000 [10 000–17 000]	13% [10–15%]	1 680	12 000 [10 000–16 000]	14% [10–17%]
Côte d'Ivoire	10 875	20 000 [17 000–25 000]	53% [44–65%]	13 294	20 000 [16 000–24 000]	68% [55–84%]
Democratic Republic of the Congo	2 098	33 000 [29 000–38 000]	6% [6–7%]	4 176	32 000 [28 000- 37 000]	13% [11–15%]
Ethiopia	10 103	43 000 [36 000–51 000]	24% [20–28%]	15 828	38 000 [32 000–46 000]	41% [35–49%]
Ghana	8 057	10 000 [8 300–12 000]	80% [67–>95%]	8 957	9 500 [7 800- 11 000]	95% [79–>95%]
Kenya	57 644	87 000 [77 000–98 000]	66% [59–75%]	45 397	86 000 [76 000–97 000]	53% [47–59%]
Lesotho	10 105	16 000 [14 000–17 000]	64% [58–71%]	9 153	16 000 [14 000–17 000]	58% [53–65%]
Malawi	33 557	68 000 [61 000–76 000]	49% [44–55%]	40 770	68 000 [61 000- 75 000]	60% [54–67%]
Mozambique	50 554	95 000 [83 000–113 000]	53% [45–61%]	80 779	94 000 [81 000–110 000]	86% [72–>95%]
Namibia	7 868	8 400 [7 000–9 900]	94% [79–>95%]	7 619	8 100 [6 700- 9 700]	94% [79–>95%]
Nigeria	40 517	202 000 [174 000–232 000]	20% [17–23%]	33 323	200 000 [170 000- 230 000]	17% [15–20%]
South Africa	260 073	287 000 [261 000–310 000]	91% [84–>95%]	234 952	280 000 [260 000- 310 000]	83% [77–91%]
Swaziland	10 641	12 000 [11 000–13 000]	87% [79–>95%]	10 167	12 000 [11 000–13 000]	83% [75–93%]
Uganda	47 965	99 000 [85 000–117 000]	49% [41–56%]	73 870	100 000 [88 000- 120 000]	72% [61–84%]
United Republic of Tanzania	71 041	97 000 [83 000–112 000]	73% [64–85%]	73 955	97 000 [83 000–110 000]	77% [66–89%]
Zambia	71 429	80 000 [72 000–89 000]	90% [81–>95%]	76 963	79 000 [71 000- 88 000]	> 95% [87–>95%]
Zimbabwe	35 948	68 000 [61 000–76 000]	53% [47–59%]	55 849	68 000 [60 000- 76 000]	82% [73–92%]
Total	760 000	1 300 000 [1 200 000–1 430 000]	59% [53-64%]	820 000	1 280 000 [1 180 000-1 410 000]	64% [58-70%]

[a] The coverage estimate is based on the estimated unrounded number of pregnant women needing and receiving ARVs.
[b] Excluding single-dose nevirapine regimen, which is no longer recommended

Note: some numbers do not add up because of rounding.

Fig. 1.15. Coverage of antiretroviral medicines for preventing mother-to-child transmission in 21 priority countries in the Global Plan, 2012



number of pregnant women living with HIV receiving ARV medicines (excluding single-dose nevirapine) for PMTCT

number of pregnant women living with HIV needing ARV medicines for PMTCT

PMTCT ARV Coverage

Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS) and 2013 UNAIDS estimates.

Antiretroviral prophylaxis and treatment for women's own health

In 2012, 19 of the 21 Global Plan priority countries in WHO African region reported disaggregated data for both ARV prophylaxis for PMTCT and lifelong ART for women's own health. Reporting accurate data on pregnant women receiving lifelong ART is still challenging in some countries but data has become increasingly available. On average 59% [53-64%] of the pregnant women living with HIV estimated to be eligible for ART based on CD4<350 received lifelong ART in 2012 – a marked improvement over recent years and a level of coverage approaching the overall ART coverage in the general population.

However, many pregnant women living with HIV who are eligible for ART are still missing opportunities to start treatment during pregnancy: ART coverage among eligible pregnant women was estimated to be below 40% in Chad, Côte d'Ivoire, the Democratic Republic of the Congo, Ethiopia, Mozambique and Nigeria in 2012. Among the difficulties encountered are a lack of programme support and trained personnel to initiate ART in maternal and child health clinics, incomplete links and referrals to ART sites and limited access to prompt CD4 testing to determine eligibility for ART. Given these challenges, the 2013 WHO ARV guidelines *(7)* streamline and simplify the delivery of ARV medicines to pregnant women living with HIV.

Adequate coverage of services for PMTCT requires improving health systems and addressing community-level factors so that more pregnant women living with HIV are identified and access to lifelong ART is enhanced. As overall ARV coverage increases, further analysis is needed to assess the impact of that coverage, as reflected in the estimated rates of mother-to-child transmission and the estimated numbers of children acquiring HIV infection (see Chapter 2).

Access to antiretroviral therapy for adolescents

The enormous success in preventing the vertical transmission of HIV has resulted in a decline in new HIV infections among infants. However, there remains a significant burden of HIV among older children and adolescents. This diverse cohort comprises infants who have newly acquired HIV from their mothers, surviving children who acquired HIV in that manner, as well as surviving adolescents and adolescents who acquired HIV through sexual intercourse, injecting drug use or nosocomial (hospital-acquired) transmission. All of them need treatment.

There are insufficient data currently to accurately determine the numbers of adolescents who need and receive ART.[1] The best available estimate is that about 2.2 million (6.5%) of the estimated 34 million

1. The United Nations defines adolescents as people aged 10–19 years. However, most countries with high burdens of HIV lack programmatic data on the size and characteristics of the HIV epidemic in this age group. The HIV data for adolescents are often reported in other age ranges (such as 0–14 and 15–19 years).

people living with HIV globally in 2011 were 10–19 years old. Adolescents in some countries with a high burden of HIV infection have been reported to have a very high HIV prevalence. A study in urban South Africa, for example, found an HIV prevalence of 16% among adolescents 12–17 years old *(15)*.

Inequities in access to antiretroviral therapy for key populations

Improving epidemiological surveillance has demonstrated that the HIV epidemic disproportionately affects certain populations, especially sex workers, men who have sex with men, transgender people and people who inject drugs. In some regions and countries, prison populations, refugee populations, migrants and mobile workers are also at higher risk of HIV infection. However, data detailing the access to ART of these populations remain extremely limited. One reason is that classifying people receiving ART as members of key populations can have serious human rights and legal complications in countries in which the behaviour associated with a key population is stigmatized and/or criminalized.

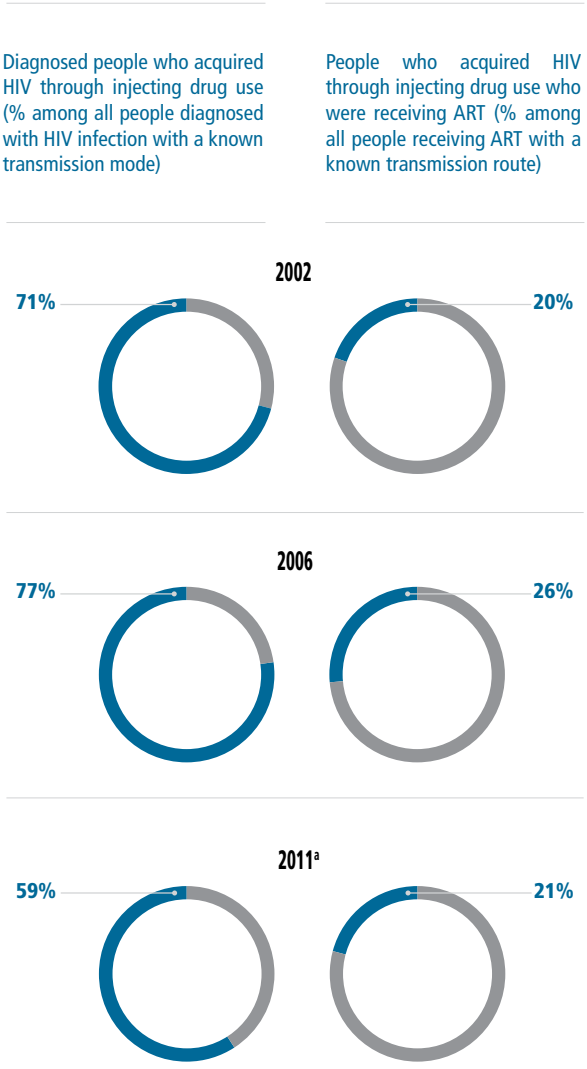
These key populations are known to encounter many barriers to accessing health services generally and HIV services specifically. In many parts of the world, they are likely to face systematic exclusion along with both social and institutionalized stigma, discrimination and harassment. In addition, sex work, injecting drug use and sex between men are criminalized in many countries, which introduces additional barriers to accessing HIV prevention and treatment services, as country-based studies have confirmed *(16,17)*.

People who inject drugs

The prevalence of HIV infection among people who inject drugs is at least 22 times higher than for the population as a whole, according to data from 49 countries *(18)*. Nevertheless, the limited available data indicate significant inequities in access to ART for people who inject drugs and who are living with HIV. For example, only an estimated 4% [2–18%] of the people living with HIV who inject drugs worldwide were receiving ART in 2009, when overall ART coverage among people living with HIV globally was estimated at 18% [17–20%] *(19)*.

More recent global data are not available. However, among the 19 countries in the WHO European Region that reported data for 2011, an average 21% of people receiving ART reported that they acquired HIV through injecting drug use (Fig. 1.16). Although this figure is prone to underreporting, it is strikingly smaller than the estimated 59% of people who were eligible for ART and who had reported injecting drug use.

Fig. 1.16. People who inject drugs as a proportion of all people living with HIV with a known transmission route and the proportion of people who inject drugs who received antiretroviral therapy in reporting countries, WHO European Region, 2002–2011



[a] Preliminary 2011 ART data and 2010 HIV surveillance (case reporting) data.

Sources: European Centre for Disease Prevention and Control and WHO Regional Office for Europe (21,22); HIV/AIDS surveillance in Europe. End-year report 2006 (23); HIV/AIDS in Europe: moving from death sentence to chronic disease management (24); Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

Such disproportionately poor access to ART is likely to be even more pronounced in specific subgroups, such as people living with HIV who inject drugs and who are pregnant. For example, a prospective cohort study in Ukraine among pregnant women with HIV showed that the mother-to-child transmission rates of HIV were almost twice as high among women who injected drugs than among women who did not. Women who injected drugs and were eligible for treatment were less likely to receive ART compared with their counterparts who did not inject drugs *(20)*.

Access to ART among people who inject drugs has been improving in some countries in Asia. In Viet Nam, for example, substantial proportions of people receiving ART report a history of injecting drug use – as many as 73% in a study in Ho Chi Minh City *(25)*. Evidence indicates that their treatment outcomes match those of non-drug-injecting populations. At two clinics in Ho Chi Minh City, the increase in median CD4 count over 24 months after initiating ART was the same for both treatment populations *(25)*.

Generally, however, many obstacles still prevent people who inject drugs from accessing and maintaining HIV care and treatment – including stigma, discrimination and punitive policies in both health care settings and wider communities. Even in countries in which large proportions of the people acquiring HIV infection are people who inject drugs, few HIV counselling and testing services are tailored for them. The people who may need ART are often unaware that they have acquired HIV. As a consequence, late HIV diagnoses are common *(26)*, and many people who inject drugs and test HIV-positive start ART with very low CD4 counts *(27,28)*. In addition, some countries resist providing ART before people have undergone drug detoxification, thus delaying access to treatment *(29)*.

A recent meta-analysis of studies done in North America, Europe and Asia found that providing opioid substitution therapy to people who inject opioids is a critical facilitator for adherence to ART – and was also associated with a 54% reduction in the risk of acquiring HIV infection among people who inject drugs *(30)*.

However, global coverage of opioid substitution therapy among people who inject opioids appears to be very low, and was estimated at 8% in 2010 *(19)*, far below the recommended target of 40% of opioid-dependent people receiving such therapy *(31)*. As many as half the countries worldwide that report HIV cases among people who inject drugs are not providing opioid substitution services. Some countries are expanding access to opioid substitution therapy, but the programmes remain small in size and limited in scope in many others, and weak links between opioid substitution therapy services and HIV testing, care and treatment services hinder progress *(32)*.

Sex workers

Globally, female sex workers are on average 14 times more likely to be living with HIV than women overall *(33)*. A recent systematic review *(33)* has shown that the average HIV prevalence among female sex workers was 37% in sub-Saharan Africa, 11% in Eastern Europe, 6% in Latin America and the Caribbean, 5% in Asia and 2% in the Middle East and North Africa. Exceptionally high HIV prevalence has been found among female sex workers in urban settings in some countries: 57% in Kisumu, Kenya *(34)*, 32% in Mauritius (according to UNGASS country reports) and 20% in Bangkok, Thailand *(35)*, for example. Migrant sex workers in low-income settings appear to be at especially high risk for acquiring HIV infection *(36)*. Transgender sex workers also have an especially high HIV prevalence, especially in low-income settings *(37)*.

Male, female and transgender sex workers face many challenges in accessing HIV care and treatment, including a fear of adverse consequences if their HIV status is disclosed, along with negative experiences in health care settings (38). The few studies that have examined AIDS-related mortality rates among female sex workers with HIV indicate that they tend to be less likely than other women with HIV to receive timely and adequate HIV treatment and care. In a study in a rural part of southern India, the AIDS-related mortality rate for sex workers with HIV was 10 times higher than the national mortality rate among women of a similar age *(39)*. Nevertheless, when sex workers are able to access ART, their treatment outcomes are generally good, and the available evidence disproves concerns about possible increases in high-risk sexual behaviour *(40)*.

Given the pervasiveness of sex work globally and the very high HIV prevalence among sex workers in many countries, the scaling up of ART has to include

much stronger efforts to support access to treatment and care for sex workers. ART services specifically designed for sex workers continue to be an exception, including in regions with very high HIV prevalence in this population group. A recent literature review of interventions for sex workers in sub-Saharan Africa *(41)*, for example, failed to identify any published studies specifically aimed at improving sex workers' access to ART. Major opportunities are being missed – not only for preventing morbidity and mortality but also for averting onward HIV transmission. For example, expanding ART access to female sex workers in Kenya could reduce the number of female sex workers acquiring HIV infection by an estimated 25% *(42)*.

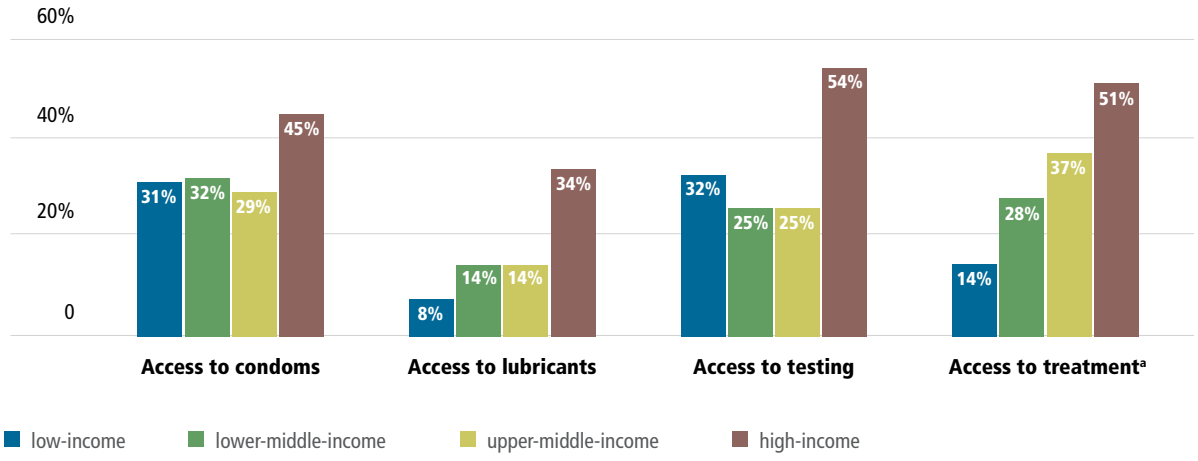
Men who have sex with men

Men who have sex with men continue to be at considerably higher risk of acquiring HIV infection worldwide than men overall. A variety of studies have found the HIV prevalence among men who have sex with men in capital cities to be an average 13 times higher than in the country's general population *(43)*.

However, there is limited information about the access of men who have sex with men to HIV prevention and treatment services. A biennial online survey conducted by the Global Forum on MSM and HIV is filling some of these data gaps. About 1000 men living with HIV around the world participated in the most recent self-administered survey, which indicated that access to HIV treatment is limited for men who have sex with men in low- and middle-income countries (Fig. 1.17).[1]

The availability of more general HIV prevention interventions that engage men who have sex with men varies widely from region to region and may mirror trends in access to ART. Despite evidence indicating high HIV prevalence among men who have sex with men in sub-Saharan Africa *(45)*, focused interventions are rare in that region. Moreover, the legal and policy environment remains hostile for this key population in many countries across the world.

Fig. 1.17. Percentage of men who have sex with men reporting that condoms, lubricants, HIV testing and HIV treatment are easily accessible, by income level, 2012



[a] Access to HIV treatment was measured only among respondents who reported living with HIV.

Source: Access to HIV prevention and treatment for men who have sex with men: findings from the 2012 Global Men's Health and Rights Study (GMHR) (44).

1. While this study provides useful insights, it was not designed to be representative of men who have sex with men in the many countries that do not have extensive access to the Internet, or who are not reached by networks of men who have sex with men.

Transgender people

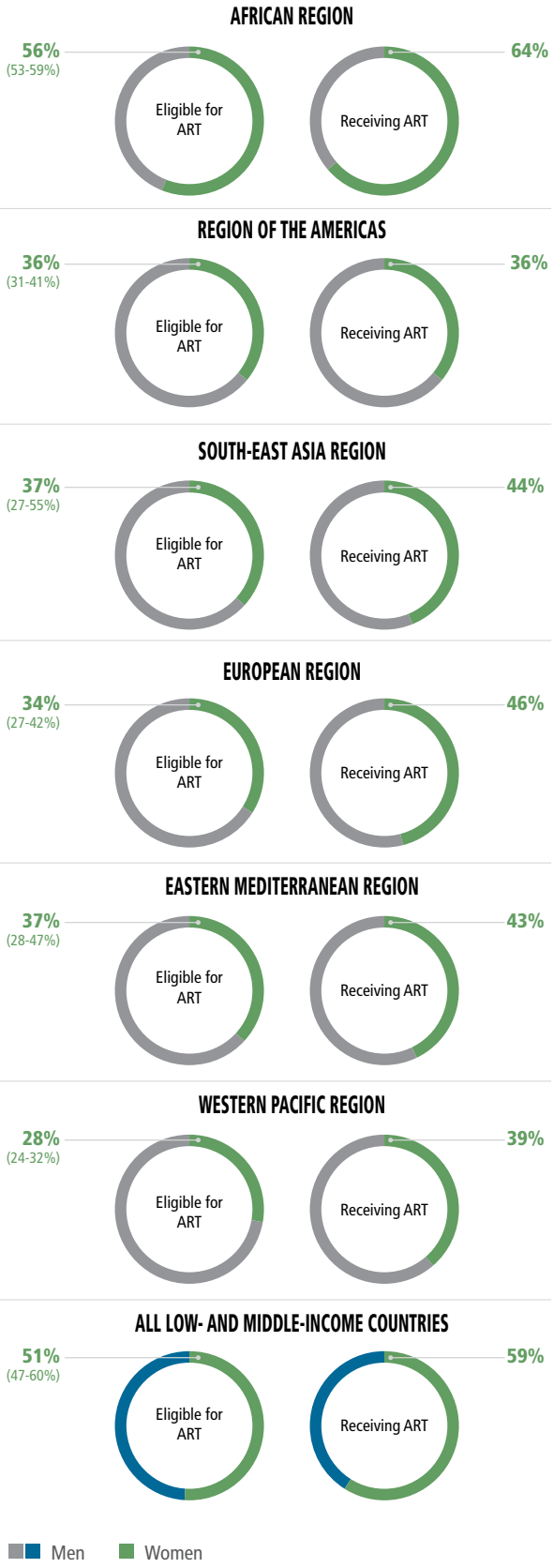
Gender disaggregation in routine ART reporting currently does not take account of transgender people,[1] but evidence indicates that this key population experiences an exceptionally high prevalence of HIV infection and need for ART. A recent meta-analysis of 39 studies performed between 2000 and 2011 in 15 countries found that transgender women were 49 times more likely to be living with HIV than the overall adult population. The aggregate HIV prevalence among transgender women was 18% in low- and middle-income countries and 22% in high-income countries *(37)*. HIV prevention services for transgender people are inadequate, and the available evidence indicates that they have poor access to ART – as shown in a recent study from India *(46)*. Research also suggests that transgender women who do start ART are less likely to have positive interactions with health care providers than other women, with lower treatment adherence rates and poorer outcomes *(47)*.

The gender gap in access to antiretroviral therapy

In most regions of the world, and especially in settings with a high burden of HIV infection, women are more likely than men to be accessing ART. This pattern has been noted especially in the WHO African Region. By end-2011, 109 countries had reported sex-disaggregated data for people receiving ART, with the data showing a total female-male ratio of 59% to 41% (Fig. 1.18).

As Fig. 1.18 shows, in the WHO African Region, men comprised only 36% of the people receiving ART but accounted for 44% of the people eligible for ART. Similar disparities have been documented at the country level in Kenya *(48)*, Malawi *(49)*, South Africa *(50,51)* and Zambia *(52)*. HIV testing rates are also consistently lower among men than women, and men tend to have lower CD4 cell counts when accessing treatment. AIDS-related mortality rates also appear to be higher among men than women in the WHO African Region, a pattern that is partly explained by the fact that they often present late for care *(49,53–56)*. All other regions have a similar pattern except the Americas, which has achieved gender parity in access to ART, although this is largely because of high ART coverage among men in a few countries with comparatively large HIV burdens, notably Brazil, the Dominican Republic and the Bolivarian Republic of Venezuela.

Fig. 1.18. Disparities in antiretroviral therapy access: women and men as percentages of all people eligible for and receiving antiretroviral therapy, by WHO Region, 2011



1. Routine ART reporting also does not specify whether people initiating ART are sex workers or men who have sex with men.

There are several possible explanations for men being underrepresented among people receiving ART *(50)*. High rates of HIV testing within antenatal care facilities may partly explain the greater access of women to ART. Men generally also tend to have poorer health-seeking behaviour than women *(57,58)*, and in settings where men are more likely than women to have paid work, the opportunity costs of visiting treatment facilities may discourage some men from starting or continuing on ART *(59)*.

Providing care for people living with HIV who have TB

Tuberculosis (TB) remains a leading cause of HIV-related morbidity and mortality worldwide. Recent autopsy studies confirm that, even in a setting with significant scaling up of ART, TB is responsible for the single-largest share of deaths among people living with HIV: 21–52%, depending on the study *(60–62)*. WHO has developed guidelines to promote collaborative TB and HIV activities along with a framework for recommended actions *(63)*. The latest full data for the scaling up of these activities will be available in the 2013 *Global tuberculosis report*.

Preventing TB among people living with HIV

WHO recommends that everyone living with HIV be screened for symptoms of TB, using a simple algorithm at each clinical encounter. The available data suggest that many countries are routinely screening increasing numbers of people living with HIV for TB, and these data are being reported through national systems. Provisional data from 62 countries showed that more than 3.5 million people attending HIV care services were screened for TB in 2012. However, additional efforts are needed to scale up these valuable interventions nationally and to improve the accuracy and completeness of reporting. Persons without signs of TB are eligible for isoniazid preventive therapy to prevent TB disease. Isoniazid preventive therapy is recommended for at least 6 months. In addition, ART has been shown to reduce the incidence of TB. According to preliminary data, more than 40 countries provided isoniazid preventive therapy to over half a million people living with HIV in 2012. Fourteen of these countries have high TB/HIV burdens, and 11 of them reported providing isoniazid preventive therapy for the first time. However, data on the overall coverage of isoniazid preventive therapy globally are not yet available, and progress towards achieving the target of 100% coverage among those in need by 2015 is difficult to assess.

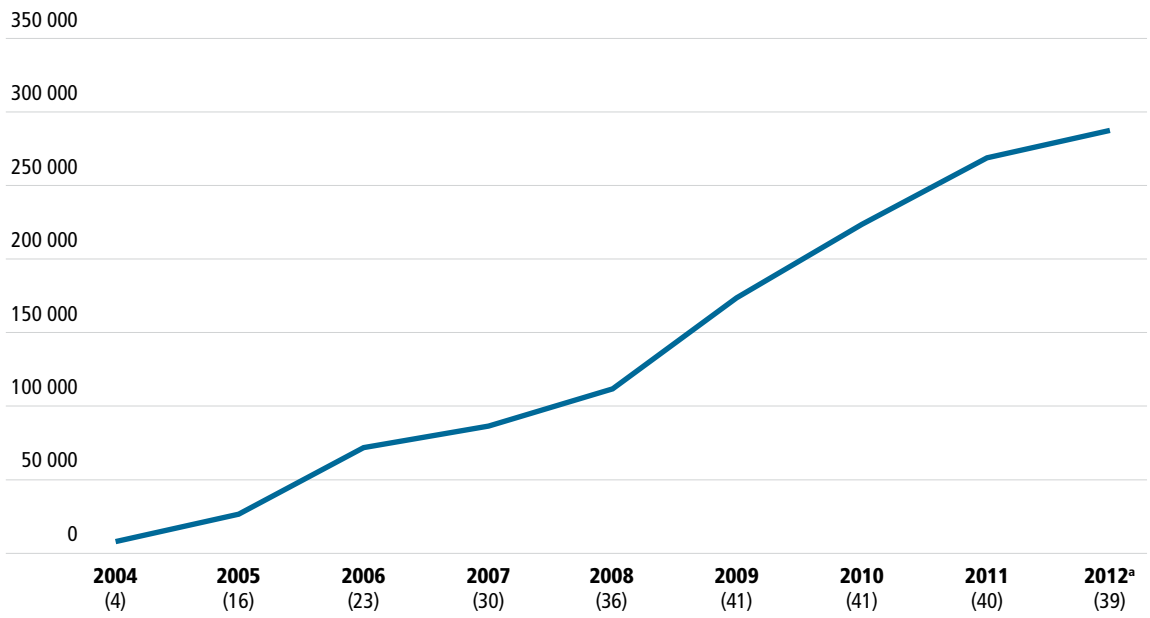
Reducing deaths from TB among people living with HIV

Everyone with TB should be routinely offered HIV testing to identify those who need HIV-related services. WHO recommends that everyone with TB and HIV receive co-trimoxazole preventive therapy and immediately initiate ART, regardless of CD4 count. Early initiation of ART among people living with HIV who have active TB reduces mortality by up to 56% compared with deferring ART until after TB treatment has been completed *(64)*.

Globally, HIV testing for people with TB has improved and is particularly high in the WHO African Region. Initial data reported for 2012 suggest that HIV testing rates continued to rise in that region and elsewhere. Among the countries with a high burden of HIV infection reporting these data, Myanmar quadrupled the number of people with TB tested for HIV (compared with 2011), while the number doubled in Angola and increased by almost 50% in China and Ethiopia and by 20% in India.

To date, coverage of ART among people with TB has remained significantly below the overall ART coverage rate among people who need ART, although more than 80% of reporting countries said they had a policy of providing ART to people with TB irrespective of CD4 count (Fig. 1.19). Urgent efforts are needed to ensure universal access to ART among all people with TB to reduce preventable deaths from TB.

Fig. 1.19. Number of people with TB and HIV receiving antiretroviral therapy in 41 countries with a high burden of TB and HIV, 2004–2012



[a] The data for 2012 are provisional, as reported by 17 June 2013.

Note: The numbers in parentheses refer to the number of countries reporting data.

Three scenarios for scaling up towards 2015 and beyond

As the 2015 deadline approaches, countries still urgently need to strengthen and safeguard their efforts to scale up treatment. An extrapolation of future ART coverage based on the assumption of continued linear growth in the number of people on ART reveals differences in countries' progress towards reaching the 2015 universal access target.[1] Based on this analysis, it possible to discern the following scale-up patterns and to highlight noteworthy successes and challenges.

Strong progress: universal access reached or within grasp

By the end of 2011, 13 countries were providing ART to at least 80% of the people estimated to be eligible for HIV treatment, based on the 2010 WHO eligibility criteria *(8)*:[2] Botswana, Brazil, Cambodia, Cuba, Dominican Republic, Fiji, Guyana, Mexico, Namibia, Rwanda, Sao Tome and Principe, Swaziland and Zambia.

Strikingly, that list includes four countries with very high HIV prevalence (although comparatively small total population sizes), and the others have lower overall HIV prevalence and epidemics that are largely concentrated among certain key populations.

Many other countries with a high burden of HIV infection[3] achieved universal access to ART in 2012 or are on track to do so (based on the 2010

1. The categorization is based on a linear projection of changes in the number of people eligible for and receiving ART until the end of 2015, based on the most recent year with available data for both ART provision and eligibility, i.e. the year 2012 for the 22 countries included in the *Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive*, and the year 2011 for other countries.

2. This threshold became equated with universal access to ART: 80% of people eligible for ART based on the 2010 WHO treatment guidelines *(8)*.

3. Countries that ranked among the 50 countries with the largest numbers of people eligible for ART at the end of 2011.

WHO guidelines *(8)*) by 2015 if they sustain the recent pace of scaling up ART. Some have large, generalized or mixed HIV epidemics (for example, Benin, Burundi, Congo, Côte d'Ivoire, Haiti, Ghana, Kenya, Malawi, South Africa, Uganda and Zimbabwe), whereas others have concentrated epidemics (for example, Argentina, Brazil, Peru, Thailand, the Bolivarian Republic of Venezuela and Viet Nam).

Although scaling up treatment involves distinct challenges in different settings, these achievements have shared certain features. Strong political support, robust funding from both domestic and external sources, solid planning and technical guidance, adapting service delivery systems (especially decentralized delivery) and meaningfully involving community structures and networks have all been central elements in rolling out treatment in these countries.

In South Africa, for example, strong political commitment in the past few years has been backed by major domestic funding for the HIV response: US$ 1.9 billion from public resources in 2011 alone *(65)*. All the African countries in the list are successfully decentralizing their ART services, and some are targeting specific groups of people who need ART with new policies. For example, Malawi's policy of initiating ART among all pregnant women living with HIV and maintaining this led to a seven-fold increase in ART uptake in that group in one year (see Chapter 3) *(66)*.

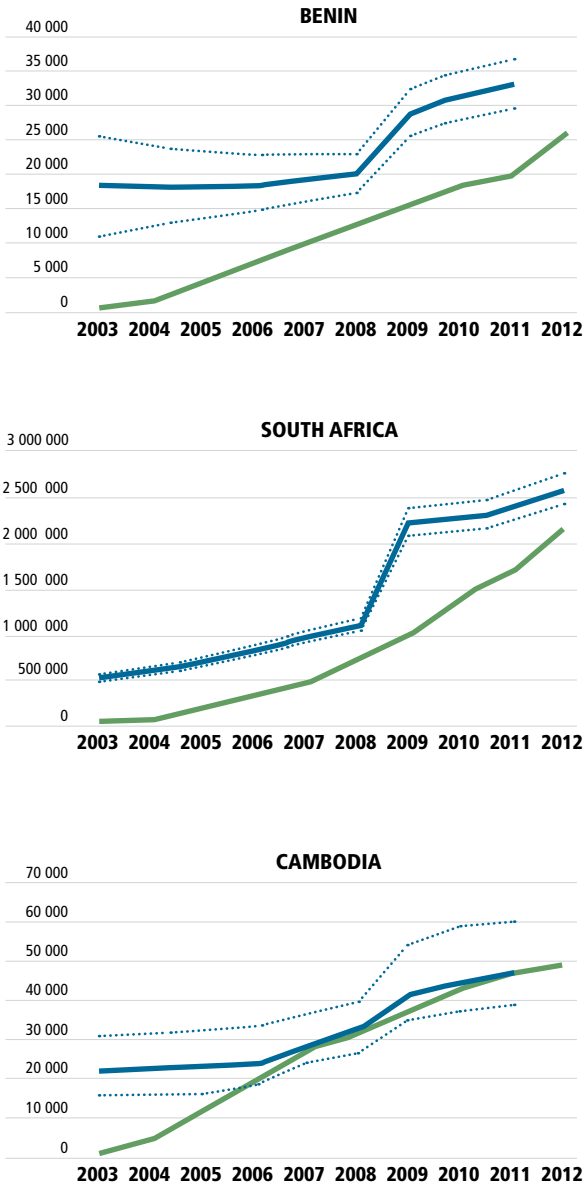
Many countries in this group have initiated a policy dialogue on expanding access to ART beyond the groups defined in the 2010 WHO treatment guidelines *(8)* to take greater advantage of the therapeutic and prevention benefits of ART. Hence, several have anticipated some of the changes to the eligibility criteria for ART detailed in the 2013 WHO ARV guidelines *(7)*.

Boost needed: universal access is in reach, but only with stronger efforts

Several other countries also significantly expanded ART access in recent years. However, they will need to step up the pace of expanding treatment if they are to reach the 80% coverage target in 2015. Countries with a high burden of HIV infection in this group include some with generalized or mixed epidemics (such as Angola, Burkina Faso, Chad, Ethiopia, Mali, Mozambique, Niger and Togo) and many countries with concentrated HIV epidemics (including China, Colombia, India, Indonesia, Myanmar, and Ukraine).

Critical factors holding back the scaling up of ART in many countries include insufficient funding from domestic and international sources, limited numbers of health workers, limitations of their current service delivery models, and difficulties in identifying,

Fig. 1.20. Number of people eligible for and receiving antiretroviral therapy in selected countries[1], 2003–2012

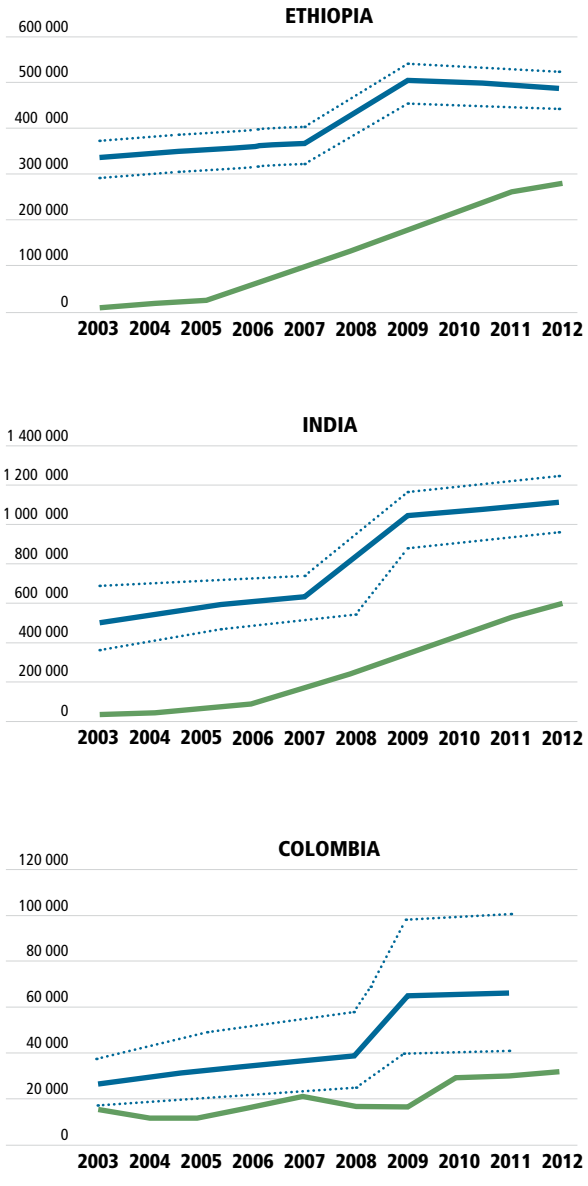


Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012/2013 UNAIDS/WHO estimates.

1. In Fig. 1.20 to 1.22, the number of people eligible for ART in 2012 in some countries has not yet been established and therefore is shown up to the end of 2011.

enrolling and maintaining people eligible for ART in ART programmes. In some countries, progress in expanding ART has been limited despite good enrolment rates because of high levels of attrition and loss to follow-up among people who have been diagnosed and enrolled (see Chapter 3).

Fig. 1.21. Number of people eligible for and receiving antiretroviral therapy in selected countries, 2003–2012



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012/2013 UNAIDS/WHO estimates.

Many of the countries in this group are taking special steps to enhance their efforts to scale up treatment. India, for example, is strengthening community support for retaining people on ART and is introducing reminder calls for CD4 testing, as well as a smart card system. In the WHO European Region, the Russian Federation and Kazakhstan have assumed complete responsibility for funding their ART programmes after grants from the Global Fund to Fight AIDS, Tuberculosis and Malaria ended. In Ukraine, the Government has assumed strong leadership in ART provision, a programme initially driven by civil society with Global Fund support. Indonesia has launched a major effort to boost ART access, with a particular focus on key populations.

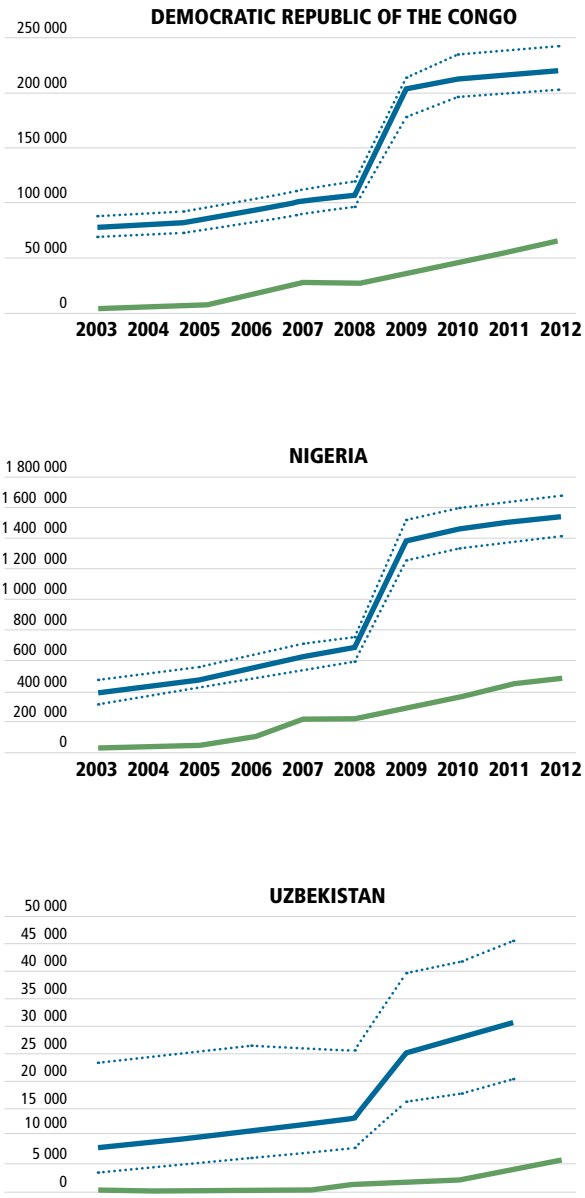
Behind schedule: major support needed to reach the universal access goal

Finally, several countries have managed to increase the number of people receiving ART by small margins in the past few years but are struggling to achieve high ART coverage. This group includes countries with generalized or mixed HIV epidemics (such as the Central African Republic, the Democratic Republic of the Congo, Nigeria and South Sudan) and countries with comparatively small concentrated epidemics (including Bolivia (Plurinational State of), Iran (Islamic Republic of), Uzbekistan and Yemen). The group also includes several countries in the WHO Eastern Mediterranean Region (including Afghanistan, Djibouti, Egypt, Pakistan, Somalia and Sudan).

Based on the current pace of their ART scale-ups, none of these countries is likely to reach 80% ART coverage in 2015 (using the 2010 WHO treatment eligibility criteria) *(7)*. Diverse factors are holding them back, including political instability and conflict, a lack of resources and weak and poorly functioning health systems (for example, weak infrastructure, supply chains and diagnostic capacity) and inadequate numbers of trained health workers.

Other reasons for their faltering progress include inadequate methods of identifying and enrolling people who need ART and retaining them on treatment, as well as persistent stigma and discrimination (including in health facilities). In Sudan, for example, it is estimated that less than one fifth of the people living with HIV are aware of their HIV status. Some of these countries are investing special efforts to enhance access more quickly.

Fig. 1.22. Number of people eligible for and receiving antiretroviral therapy in selected countries, 2003–2012



Source: 2013 Global AIDS Response Reporting (WHO/UNICEF/UNAIDS) and 2012/2013 UNAIDS/WHO estimates.

How will the new WHO guidelines affect eligibility for antiretroviral therapy?

In recent years, most countries' ART programmes have followed the treatment eligibility guidelines issued by WHO in 2010 *(8)* that recommend treatment for everyone who tests HIV-positive and has CD4 cell counts ≤350 cells/mm^3 or who is coinfected with active TB or hepatitis B.

A series of recent breakthrough scientific findings has prompted WHO to revise these guidelines in 2013. WHO's new HIV ARV guidelines *(7)* recommend earlier initiation of ART – at CD4 ≤500 cells/mm^3. In addition, they recommend immediately initiating ART for serodiscordant couples, pregnant women living with HIV, people with both HIV and TB, people with both HIV and hepatitis B and children living with HIV younger than 5 years – irrespective of CD cell count. Table 1.4 summarizes the new recommendations.

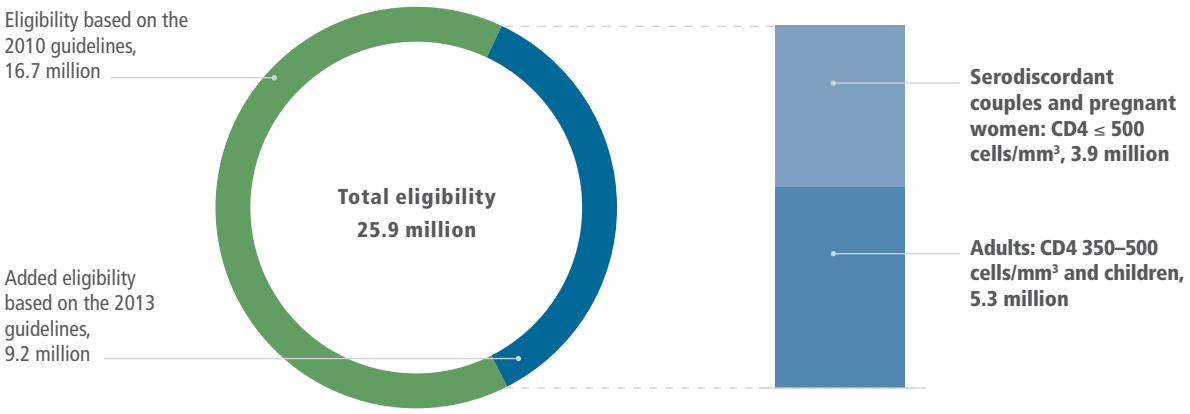
Table 1.4. Summary comparison of WHO antiretroviral guidelines: immunological criteria for initiating antiretroviral therapy, 2010 and 2013

	2010 guidelines *(8)*	2013 guidelines *(7)*
Adults and adolescents living with HIV	≤350 CD4 cells/mm^3	≤500 CD4 cells/mm^3
Children living with HIV	<24 months old: all 2–5 years old: ≤750 CD4 cells/mm^3 or 25%	<5 years old: all
Pregnant women living with HIV[a]	No specific provision	All
People coinfected with TB and HIV	All	All
People coinfected with HIV and hepatitis B	All with chronic active hepatitis	All with chronic severe liver disease
Serodiscordant couples	No specific provision	All

[a] For their own health, excluding other options with the primary purpose of preventing the mother-to-child transmission of HIV.

If applied globally, the new ARV guidelines would increase the total number of people living with HIV who are eligible for treatment in low- and middle-income countries from 16.7 million to 25.8 million, based on end-of-2012 epidemic estimates (Fig. 1.23).[1]

Fig. 1.23. Numbers of people eligible for antiretroviral therapy in low- and middle-income countries under WHO 2010 and WHO 2013 antiretroviral guidelines, based on the epidemic and response status at the end of 2012



The change in eligibility criteria will affect adults and children, people with coinfections, pregnant women and people with HIV who live in partnerships with people who are not HIV-positive. The changes will increase the numbers of people eligible for ART as follows.

- Currently, an estimated 5.1 million adults with CD4 counts ≤350 cells/mm³ have no access to ART. By moving the CD4 threshold to ≤500 cells/mm³, that number will increase to 9.3 million.
- The current number of children younger than 15 years eligible for ART who are not receiving ART, based on the 2010 ARV guidelines *(8)*, is estimated to be 1.2 million. That number will increase to 2.6 million once the expanded criteria apply to all children living with HIV younger than five years, regardless of CD4 count.
- The 2013 guidelines recommend providing ART to all pregnant women living with HIV regardless of CD4 count, which will add 0.7 million women to the current pool of people requiring ART (in addition to the women who would be eligible for ART because they have CD counts ≤500 cells/mm³).
- The 2013 guidelines also recommend ART for all HIV-positive partners in serodiscordant couples. This means an estimated 3.2 million additional people become eligible for ART: those living in serodiscordant relationships who are HIV-positive but have CD4 counts >500 cells/mm³.
- The 2010 ARV guidelines *(8)* recommend providing ART to people with HIV and active coinfection with TB or hepatitis B, regardless of CD4 count. The 2013 guidelines again include this category of people living with HIV. A large percentage of them will be eligible for ART, also because of the elevated adult CD4 threshold of ≤500 CD4 cells/mm³.

1. This is based on modelling undertaken by Futures Institute, using Spectrum (a standard tool developed by UNAIDS/WHO for national, regional and global HIV estimates) and the "Goals" model (used to model the impact of specific interventions). The end-of-2012 estimate is based on an extrapolation of previous global trends, and does not represent the official 2012 epidemic estimate, which will become available later in 2013.

The increased number of people receiving ART will have an important effect in preventing HIV transmission, which in turn will contribute to reducing the number of people eligible for ART in the long term.

Thus, modelling of future ART provision under the 2013 WHO ARV guidelines indicates that scaling up ART to 80% coverage will result in a peak of close to 24.5 million people receiving ART in 2021. This number would then gradually decrease due to a decline in the number of people eligible for ART. Such an outlook contrasts with the constant increase in the absolute numbers of people receiving ART in a scenario in which coverage rates are maintained at current levels, resulting in a similar or even higher number of people on ART in the long term.

The impact of these changes in the eligibility criteria will differ from country to country. Specific tools have been developed to help countries in modelling the effects and how increasing ART access is likely to affect AIDS-related mortality and HIV incidence, along with the associated costs and benefits.[1]

1. The tools used to model these various scenarios can be found at http://www.futuresinstitute.org/software.aspx

2. MAKING AN IMPACT: THE STRATEGIC USE OF ANTIRETROVIRAL DRUGS TO TREAT AND PREVENT HIV

KEY POINTS

Expanding access to antiretroviral therapy is changing the global HIV epidemic in momentous ways

AIDS-related mortality rates are declining rapidly, including in countries with a very high burden of HIV infection.

- The annual number of people dying from AIDS-related causes globally fell from a peak of 2.3 million in 2005 to 1.7 million in 2011.
- In Eastern and Southern Africa, AIDS claimed 38% fewer lives in 2011 than in 2005, when ART began to be scaled up in that region.
- The life expectancy for people receiving ART now approaches normal life expectancy, including in countries with a high burden of HIV infection.
- The global scale-up of treatment has saved 4.2 million lives in 2002–2012 in low- and middle-income countries.

Scaling up ART is a major factor in recent HIV prevention successes and is driving down the incidence and mortality of TB.

- The number of people acquiring HIV infection globally declined by 20% between 2001 and 2011.
- The scaling up of PMTCT services prevented more than 800 000 children from acquiring HIV infection between 2005 and the end of 2012.
- Joint TB and HIV interventions saved more than 400 000 lives in 2011 alone (8 times more than in 2005).

Widening access to ART is bringing momentous changes to the global HIV epidemic. AIDS-related mortality rates are declining rapidly, including in countries with a very high burden of HIV infection. The average life expectancy of people living with HIV who adhere to effective treatment now approaches the life expectancy in the general population *(1)*.

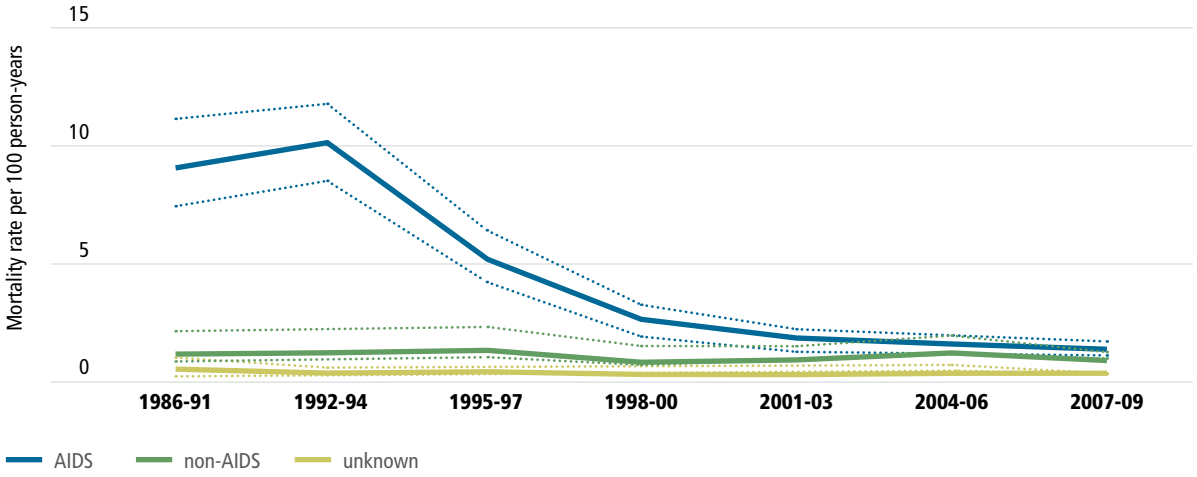
The preventive benefits of ART are also firmly established and widely recognized, following the results of the nine-country HPTN 052 study in 2011 and recent findings from programme settings *(2,3)*. The evidence has focused greater attention on the long-standing concept of treatment as prevention.[1] These developments have informed the 2013 WHO *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection (4)* (see Chapter 1). As eligibility for ART expands, the distinction between ART for treatment and ART for prevention is becoming less relevant.

1. Treatment as prevention is a term used to describe HIV prevention methods in which people living with HIV use ART, independent of CD4 cell count, to decrease the chance of onward HIV transmission.

Clinical benefits of antiretroviral therapy

The life-saving benefits of ART are vividly evident. Before ART, about 80% of the people presenting at clinics with AIDS-defining illnesses died within two years *(5)*, but even the most severely ill people living with HIV today have at least an 80% chance of survival after two years of ART *(6)*. In Brazil, for example, mortality rates from AIDS-related causes have declined dramatically – from 9.2 deaths per 100 person-years in 1986–1991 to 1.4 deaths per 100 person–years in 2007–2009;[1] in contrast, mortality rates from non-AIDS-related causes showed no change over time (Fig. 2.1) *(7)*. Meanwhile in China, mortality rates fell from 45.7 per 100 person-years in 2002 to 9.2 per 100 person-years in 2011 – a 78% decrease – as treatment coverage increased from almost zero to 63% (Fig. 2.2) *(8)*.

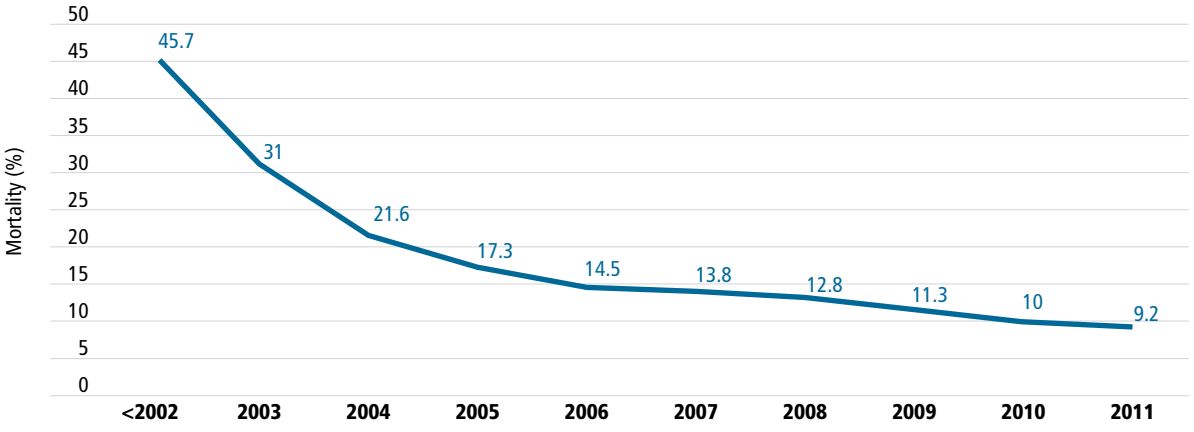
Fig. 2.1. Mortality rates in Brazil for AIDS-related, non-AIDS-related and unknown causes of death, 1986–2009



Note: the dotted lines indicate confidence intervals.

Source: Grinsztejn et al. *(7).Changing mortality profile among HIV-Infected patients in Rio de Janeiro, Brazil: Shifting from AIDS to non-AIDS related conditions in the HAART era. PLoS One, 2013, 8:e59768 doi:10.1371/journal.pone.0059768. Licensed under the Creative Commons Attribution license (CC-BY 2.5) http://creativecommons.org/licenses/by/2.5/legalcode*

Fig. 2.2. Mortality declines in China among people living with HIV meeting the eligibility criteria for antiretroviral therapy based on the 2010 WHO guidelines *(9)*, 2002–2011

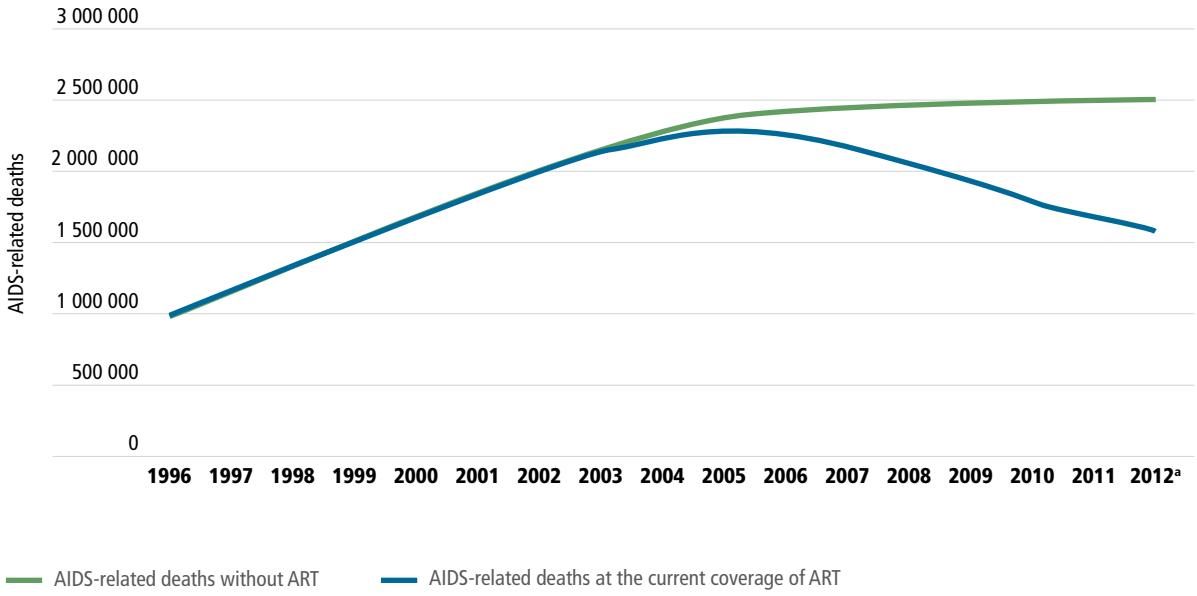


Source: National Center for AIDS Control and Prevention (NCAIDS), China: updated from a presentation at the National HIV and STI Programme Managers Meeting of Asian Countries in the Western Pacific Region, Kunming, February 2013.

1. AIDS-related deaths are defined in this report as all deaths related to HIV infection, including those among people with HIV who do not meet the clinical definition of having "AIDS".

Much wider access to ART and the steady decline in the incidence of HIV infection during the past 15 years have led to significant decreases in the number of people dying from AIDS-related causes globally. The number of annual AIDS-related deaths around the world declined from a peak of 2.3 million [2.1-2.6 million] in 2005 to less than 1.7 million [1.5-1.9 million] in 2011 *(10)*. By the end of 2012, the scaling up of ART had averted an estimated 4.2 million deaths in low- and middle-income countries in the previous decade (Fig. 2.3) *(10)*.

Fig. 2.3. Annual number of people dying from AIDS-related causes in low- and middle-income countries globally compared with a scenario of no antiretroviral therapy, 1996–2012



[a] The data points for 2012 are projected based on the scaling up of programmes in 2009–2011 and do not represent official estimates of the number of annual AIDS-related deaths.

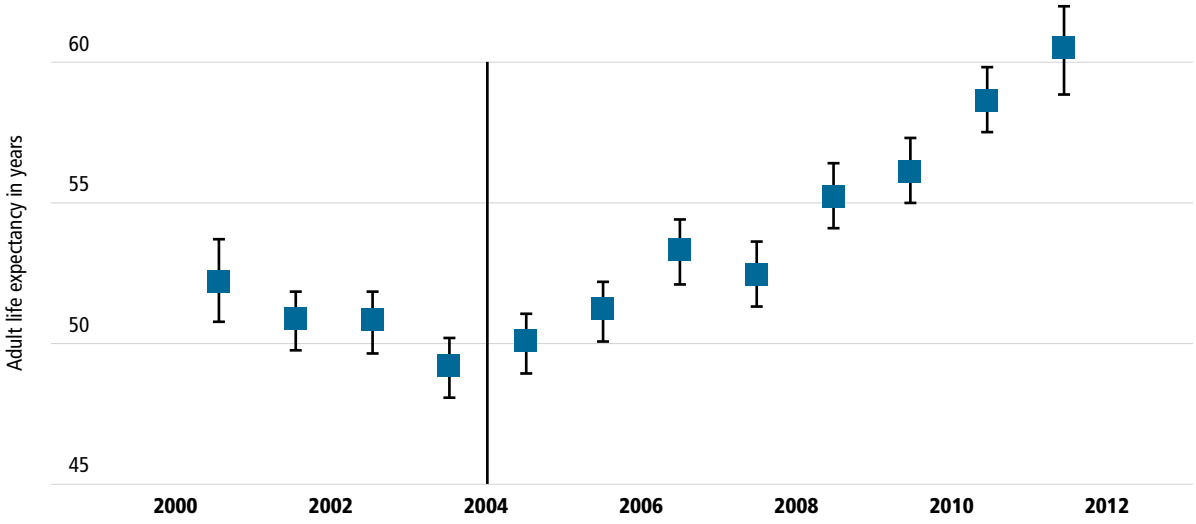
The drop in AIDS-related mortality is especially apparent in the regions with the greatest burden of HIV infection. In 2011, an estimated 800 000 [730 000–890 000] people died from AIDS-related causes in Eastern and Southern Africa, 38% fewer than the 1.3 million [1.2 million–1.4 million] dying in 2005. Several other regions have had significant declines, including in the Caribbean, where the number of people dying from AIDS-related causes decreased by 48% between 2005 and 2011. During the same period, more modest declines occurred in Latin America (10%) and Asia (4%). Two other regions, however, experienced significant increases in mortality from AIDS: Eastern Europe and Central Asia (21%) and the Middle East and North Africa (17%) *(11)*.

Antiretroviral therapy increases life expectancy

Once people living with HIV are stable on ART, they have considerably increased life expectancy. Recent studies confirm that gains in life expectancy among people living with HIV receiving ART in low- and middle-income countries are as impressive as those previously documented in the high-income countries of Europe and North America *(12,13)*. In South Africa, for example, data from six HIV treatment programmes in three provinces show that adults starting ART have a life expectancy of about 80% of normal if they start treatment before their CD4 count drops below 200 cells/mm^3 *(14)*. In Uganda, a 20-year-old person living with HIV and receiving ART can expect to live an additional 27 years: about two thirds as long as a 20-year-old in the overall population could expect to live *(15,16)*.

Between 2005 and 2011 in South Africa as a whole, the average life expectancy at birth increased from 54 to 60 years, a gain largely attributed to the rollout of ART and programmes for preventing the mother-to-child transmission of HIV (17). In one rural South African setting, overall adult life expectancy rose by more than 11 years between 2003 (the year before ART became widely available in the public health system) and 2011 – from 49.2 years to 60.5 years (Fig. 2.4) *(18)*.

Fig. 2.4. Average adult life expectancy, rural South Africa, 2000–2011



Source: Bor et al. *(18). Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. Science, 2013, 339:961–965. Reprinted with permission from AAAS.*

Box 2.1. TB remains a leading cause of death among people living with HIV

Although AIDS-related mortality is declining, it is still unacceptably high. Large numbers of people do not yet know that they are living with HIV, and many of them are eligible for ART. Among those who do seek care, many present for treatment only once their health has seriously deteriorated, often after having acquired opportunistic infections. Opportunistic infections therefore continue to be the major driver of HIV-associated morbidity and mortality *(20,21)*. In sub-Saharan Africa, for example, TB remains the leading cause of death among people with HIV. A review of autopsy studies done between 1993 and 2010 in 12 African countries *(22)* identified TB as the cause of death in 32–45% of cases. In more recent studies, TB has remained the dominant cause of death in sub-Saharan Africa *(23)* and in certain countries in other regions, such as the Russian Federation *(24)*. Globally, an estimated 400 000 people died from HIV-associated TB in 2011 *(25)*.

In high-income settings many of the recent deaths appear not to be related to AIDS *(26)*, while among the infectious cause of death viral hepatitis is a leading cause of mortality *(27)*.

Generally, life expectancy studies have found that the risk of mortality is greater and that life expectancy is correspondingly lower among people who initiate ART late in disease progression (CD4 ≤200 cells/mm^3). Similar to the general population, among people receiving ART, life expectancy is lower for men than for women (see Chapter 1) *(19)*.

An important contributing factor in the reduction of the number of people dying from AIDS-related causes has been co-trimoxazole use among people living with HIV who receive ART. A recent systematic review *(28)* estimated that co-trimoxazole prophylaxis can reduce mortality by 40–70% in the first year of ART, although the benefits over longer periods are not yet clear.

Several studies show that scaling up treatment is also yielding increases in labour productivity. Studies in South Africa, for example, show that people were almost as likely to be employed four years after initiating treatment as they had been 3–5 years before starting ART and began to fall ill *(29)*. In Cambodia, the proportion of patients with full-time employment doubled in less than 3 years after starting on ART *(30)*. There is mounting evidence of improved work performance associated with ART access *(31)*: in Kenya, for example, people were

found to be working at least 30% more after starting ART *(32)*. In Uganda, a decrease in food insecurity in households was also observed once people living with HIV began receiving ART *(33)*. These positive results were underscored in a systematic review of economic and quality of life outcomes of ART in low- and middle-income countries which found evidence of improved physical, emotional and mental health and daily function, increased work performance and decreased absenteeism *(34)*.

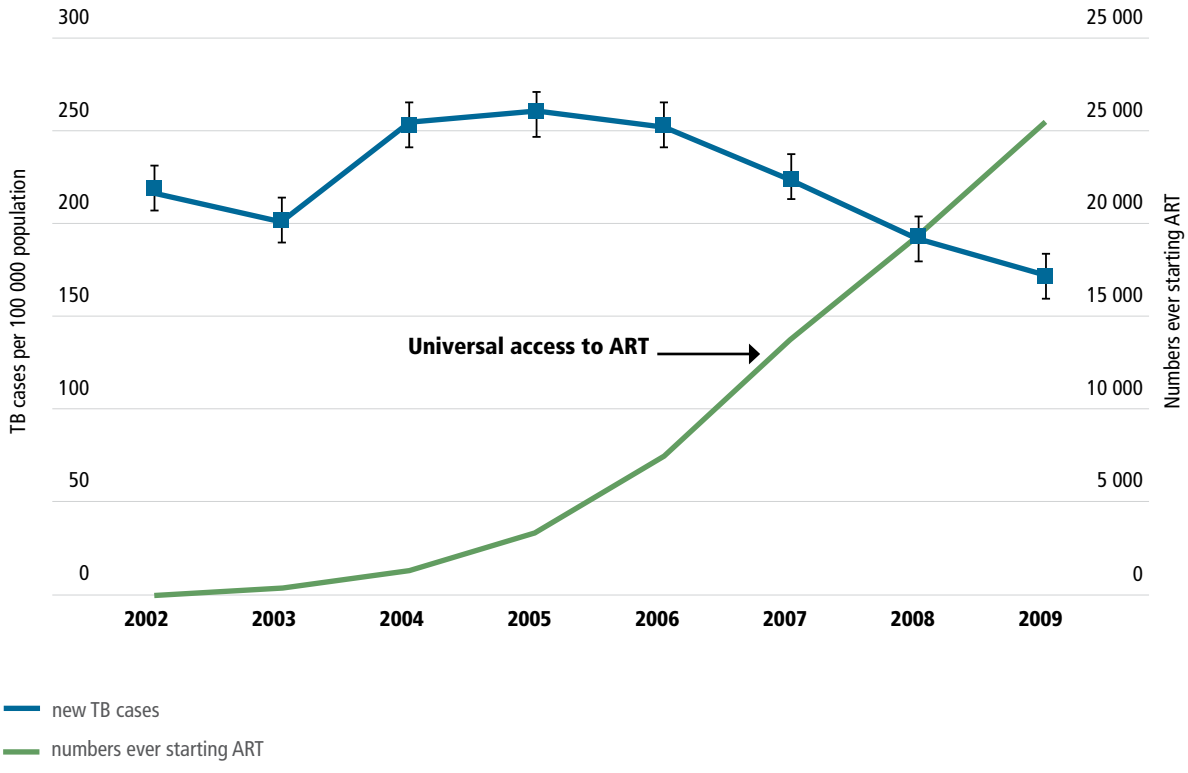
Antiretroviral drugs reduce TB and other infections

ART is also associated with significant declines in the incidence of many opportunistic infections. A recent systematic review of how ART affects 15 major HIV-related opportunistic infections and conditions among adults in low- and middle-income countries *(35)* found that the rates of most opportunistic infections fell to levels comparable to those observed in many high-income countries. During the first year of ART, the reduction in risk ranged from 61% to 98% and was greatest for oral candidiasis, toxoplasmosis, shingles, Kaposi's sarcoma and *Pneumocystis jirovecii* pneumonia and for both pulmonary and extrapulmonary TB. Some of the reduction in incident risk probably resulted from the concomitant increased use of chemoprophylaxis for protozoal and fungal infections *(35)*.

TB control is especially challenging in countries with a high prevalence of HIV infection, since HIV increases the risk of progression to active TB. However, studies from resource-limited settings have confirmed that ART is strongly associated with a reduction in the incidence of TB.

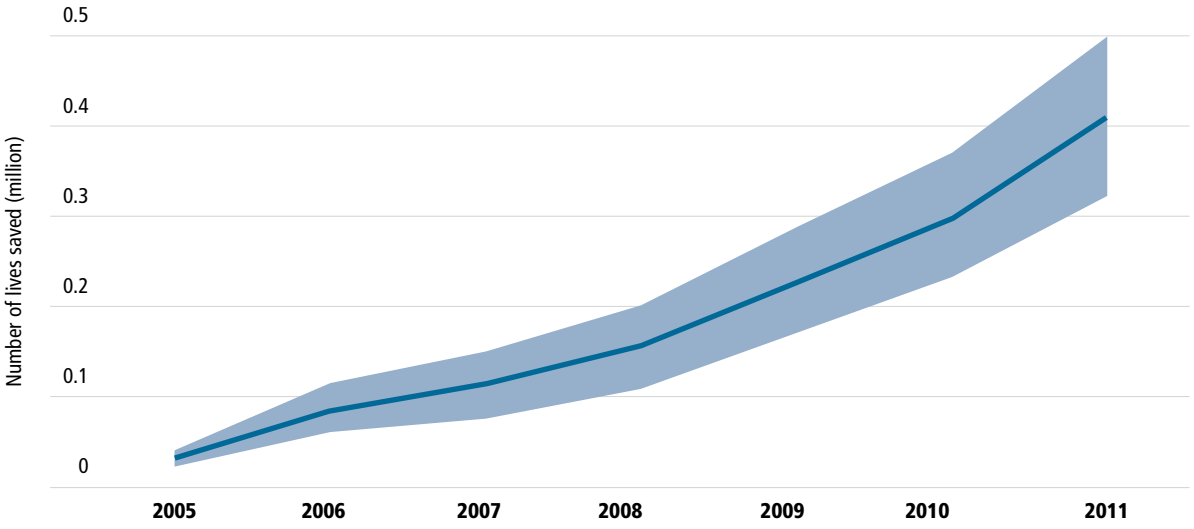
A recent meta-analysis *(36)* reviewed observational studies from low- and middle-income countries and found that ART reduced the risk of TB by up to 65%. The preventive benefit occurred even among people with high CD4 cell counts, which suggests that earlier initiation of ART may be a key strategy for reducing HIV-associated TB. At the national level, studies from Malawi *(37)* and South Africa *(38)* indicate that, when ART coverage in a population reaches a high level of coverage, TB notification rates decrease (Fig. 2.5).

Fig. 2.5. Notification of new cases of TB in relation to the scaling up of antiretroviral therapy in Thyolo District, Malawi, 2002–2009



Source: Zachariah et al. *(37). Reduced tuberculosis case notification associated with scaling up antiretroviral treatment in rural Malawi. International Journal of Tuberculosis and Lung Diseases, 2011, 15:933–937. Reprinted with permission of the International Union Against Tuberculosis and Lung Disease. Copyright © The Union.*

Fig. 2.6. Number of lives saved globally by scaling up collaborative TB and HIV activities, 2005–2011



Source: *Global tuberculosis report 2012 (25).*

The estimated number of lives saved annually with collaborative TB and HIV activities rose from fewer than 50 000 in 2005 to more than 400 000 globally in 2011 (Fig. 2.6) *(25)*. Overall, scaling up of TB and HIV collaborative activities, as recommended by WHO, saved an estimated 1.3 million [1.2 million–1.5 million] lives between 2005 and 2011 *(25,39,40)*. These activities include providing ART during TB treatment, co-trimoxazole prophylaxis during TB treatment, isoniazid preventive therapy for people living with HIV and diagnosing TB early by systematically screening people living with HIV. Studies have demonstrated that a six-month (or longer) course of isoniazid preventive therapy can reduce the risk of active TB. Isoniazid preventive therapy is therefore recommended as a key intervention in HIV care settings *(41)*.

In Eastern and Southern Africa, which has an exceptionally large burden of both TB and HIV, deaths from TB among people living with HIV declined by about 30% between 2004–2006 (when they peaked at an estimated 330 000 deaths per year) and 2011 *(42)*. Nevertheless, TB remains the leading cause of AIDS-related deaths in many resource-limited settings (Box 2.1).

Except for TB, however, the incidence of opportunistic infections and the impact of ART on these infections among adults and children in resource-limited settings are not well documented. The reasons include the absence of national reporting systems for AIDS diagnoses and the fact that standard country-level monitoring does not include opportunistic infections. Nevertheless, a recent modelling study suggests that ART might have averted as many as 900 000 cases of opportunistic infections globally in 2012, with annual cost savings of US$ 32.7 million *(35)*.

The changing epidemiology of opportunistic infections since ART was introduced has been well documented in high-income countries, where dramatic reductions in the occurrence of AIDS-defining illnesses among adults living with HIV have been reported *(43,44)*. At the same time, high-income countries are witnessing a progressive shift in the pattern of comorbid conditions, with an increasing contribution of chronic liver disease caused by hepatitis C and B (Box 2.2), cardiovascular disease and non-AIDS cancer *(45,46)*. A similar impact of ART on the incidence and prevalence of opportunistic infections has been reported among children living with HIV in high-income countries *(47)*.

Box 2.2. HIV and viral hepatitis: challenges and opportunities

Globally, about 400 million people are infected with hepatitis B virus (HBV), and 180 million are infected with hepatitis C virus (HCV). These two infections account for 60% of cirrhosis and 80% of hepatocellular carcinoma and cause 1 million deaths worldwide each year, mostly in low- and middle-income countries *(48)*.

Because of common routes of transmission, people are frequently coinfected with viral hepatitis and HIV: an estimated 5–25% of people living with HIV are also infected with either HBV (2–4 million) and/or HCV (4–5 million). Low- and middle-income countries have the greatest burden of coinfection. A recent study from Rwanda found that 5.2% of people living with HIV were antibody-positive for HBV, as were 5.7% for HCV. An estimated 3–11% of the people living with HIV in South-East Asia are coinfected with either or both HBV and HCV *(49)*. Ongoing surveys suggest that the rates of HCV coinfection among people living with HIV who inject drugs may exceed 70% in all regions.

HIV infection has been shown to significantly affect the progression of chronic HBV and HCV, with a higher risk of cirrhosis and hepatocellular carcinoma. In high-income countries, coinfection has emerged as a major cause of morbidity and mortality in recent years, and the incidence of cirrhosis and its complications, including hepatocellular carcinoma, has increased considerably.

Treatment of HBV among people living with HIV is simplified by the fact that the WHO-recommended first-line ARV drugs for treating HIV (TDF, 3TC and FTC) are also active against HBV. Treatment for HCV is more challenging. Pegylated interferon and ribavirin still constitute the standard of care for most people infected with HCV worldwide. People coinfected with HIV and HCV genotypes 2 or 3 can achieve satisfactory treatment success using these drugs; genotypes 1 or 4, however, have very low rates of treatment success *(50)*.

Important innovations are anticipated. New treatments for HCV are being developed, including directly acting antiviral agents that show very high rates of treatment success over a shorter time period compared with existing treatment and with minimal side effects. These drugs are likely to become the standard of care in most high-income countries in the near future. The simplicity and efficacy of these new drugs makes them especially suited for use in resource-limited settings, and assuring access to the preferred treatments for people infected with HCV living in those settings should be a priority.

The first set of WHO global guidelines for managing viral hepatitis is scheduled for release in early 2014.

Antiretroviral drugs prevent HIV transmission and reduce incidence

Since the potential benefit of ART for preventing the transmission of HIV was first modelled two decades ago *(51)*, numerous studies have confirmed the preventive impact of ART *(2,52,53)*, including in concentrated epidemics *(54)* and especially when ART is combined with classical prevention efforts. The estimated 2.5 million people acquiring HIV infection around the world in 2011 were 700 000 fewer than the 3.2 million in 2001. The rate of people acquiring HIV infection fell by 50% or more in 25 low- and middle-income countries – more than half of them in the WHO African Region – during that same period *(10)*.

A 2011 modeling study estimated that a combination of classical HIV prevention interventions and ART coverage of 80% (based on the 2010 WHO ARV guidelines *(9)*) could reduce the number of people acquiring HIV infection globally from more than 3 million per year to 1.2 million by 2025 *(55)*. Such a combination prevention approach would involve the simultaneous use of complementary behavioural, biomedical and structural prevention interventions, including promoting voluntary medical male circumcision, encouraging people to use male and female condoms consistently and correctly, along with other proven behavioural and structural interventions.

Large randomized trials and studies in programme settings have confirmed the modelled effects of scaling up ART on the incidence of HIV infection.

- The HPTN 052 trial among serodiscordant couples showed a 96% reduction in transmission among couples who initiated ART early compared with those who waited until the CD4 count of the HIV-positive partner dropped *(2)*.
- A prospective cohort analysis among African couples documented a 92% reduction in HIV transmission among couples who initiated ART at CD4 counts >250 cells/mm^3 compared with those who did not initiate ART with CD4 counts in the region of 250 cells/mm^3 *(56)*.
- Data from a cohort in China of almost 39 000 serodiscordant couples showed that the incidence of HIV infection was 1.3 per 100 person-years among individuals whose HIV-positive partners had initiated ART for their own health (and had done so late, with median CD4 <200 cells/mm^3) versus 2.6 per 100 person-years among individuals whose partners were not receiving ART *(57)*.

The findings of such studies are supported by ecological associations between increased coverage of ART, reduced community viral load (an indicator that is being considered as an aggregate measure of viral load in a particular geographical location or community *(58)*)[1] and lower risk of acquiring HIV.

A recent assessment of a large population-based cohort in rural South Africa found that the incidence of HIV infection was significantly lower in areas with high ART coverage (>30% of people living with HIV were receiving ART) than in areas with low coverage (<10%). For every 10% increase in the number of people receiving ART, the incidence of HIV infection fell by 17% *(59)*. Another study, also from South Africa, reported a substantial decline in community viral load as ART was scaled up. Analysis of data from all viral loads assessed in two cities between 2004 and 2011 found that the proportion of people with suppressed viral load (defined as <1000 copies/mm^3) had doubled from less than 40% to about 80% during that period *(60)*.

Impact of scaling up programmes to prevent the mother-to-child transmission of HIV

Because of rapidly expanding PMTCT programmes and more efficacious ARV regimens, the number of children acquiring HIV infection globally has been declining rapidly (Fig. 2.7). Between 2005 and the end of 2012, an estimated 890 000 children were prevented from acquiring HIV infection. The number of children acquiring HIV infection globally declined by 35% between 2009 – the baseline year of the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive *(61)* – and the end of 2012. This positive trend appeared to continue in 2012, with the number of children acquiring HIV infection decreasing by a further 37% in the 21 African priority countries defined in the Global Plan.

The Global Plan includes the target of reducing mother-to-child transmission of HIV to less than 5% in breastfeeding populations and to less than 2% in non-breastfeeding populations. Without any interventions, between 15% and 45% of infants born to mothers living with HIV will acquire HIV infection: 5–10% during pregnancy, 10–20% during labour and delivery and 5–20% through breastfeeding *(62)*.

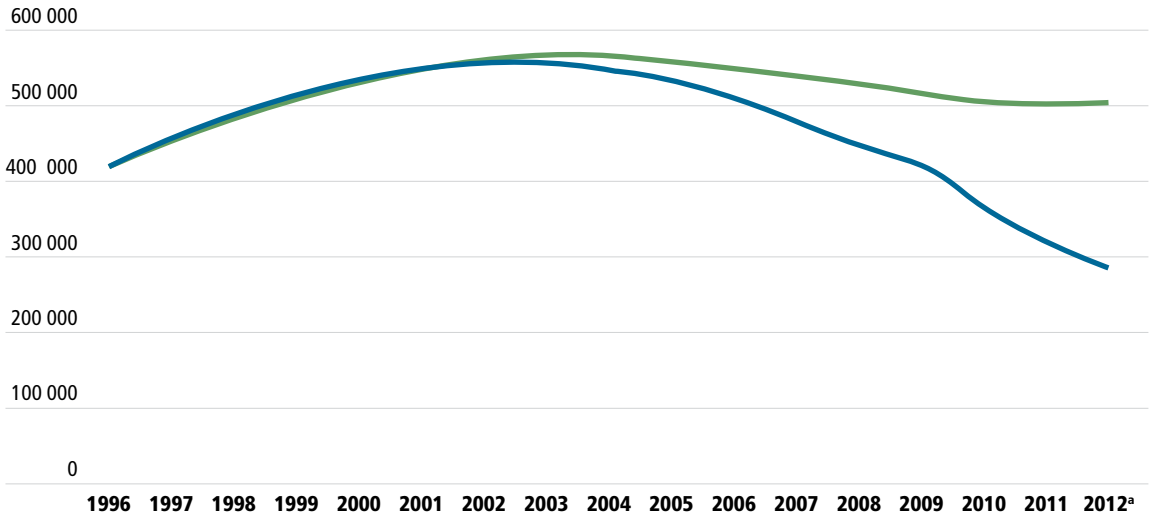
In the 21 African priority countries of the Global Plan, which account for about 90% of all pregnant women living with HIV and new HIV infections in children in low- and middle-income countries, mother-to-child transmission rates declined overall from an estimated 33% [30–36%] in 2005 to 26% [23-28%] in 2009 and 17% [15-18%] in 2012.

In addition to preventing children from acquiring HIV infection, providing lifelong ART to pregnant and breastfeeding women living with HIV improves the mother's health and prevents onward transmission to sexual partners who do not have HIV.

The impact on the number of sexual partners who can avoid acquiring HIV infection and the impact on the population-level HIV incidence will vary depending on several factors, including population size, HIV prevalence (and specifically the prevalence among pregnant women), the percentage of partnerships that are serodiscordant and the percentage of serodiscordant partnerships in which women are the infected partner (and are receiving ART) *(63)*.

1. The mean community viral load for a period of time (such as a year) is defined as the average of the most recent viral load values reported for all people living with HIV in a specific population during that period of time.

Fig. 2.7. Number of children acquiring HIV infection in low- and middle-income countries, 1996–2012



[a] The data points for 2012 are projected based on the scaling up of programmes in 2009–2011 and do not represent official estimates of the number of annual child HIV infections..

Table 2.1. Overview of the impact of services to prevent the mother-to-child transmission of HIV in the 21 African priority countries of the Global Plan

Year	Estimated number of pregnant women living with HIV needing PMTCT ARVs [range]	Estimated mother-to-child transmission rate [range]	Estimated number of children acquiring HIV infection [range]	Estimated cumulative number of infections averted by PMTCT [range] [a, b]
2005	1 390 000 [1 280 000–1 520 000]	33% [30-36%]	460 000 [420 000–510 000]	32 000 [29 000–35 000]
2006	1 370 000 [1 270 000–1 500 000]	32% [29-35%]	440 000 [410 000–490 000]	58 000 [54 000–65 000]
2007	1 360 000 [1 250 000–1 480 000]	30% [28-33%]	410 000 [380 000–460 000]	110 000 [100 000–120 000]
2008	1 340 000 [1 240 000–1 470 000]	29% [26-31%]	390 000 [350 000–440 000]	170 000 [160 000–190 000]
2009[c]	1 330 000 [1 230 000–1 460 000]	26% [23-28%]	340 000 [310 000–390 000]	280 000 [250 000–310 000]
2010	1 320 000 [1 220 000–1 440 000]	23% [21-25%]	310 000 [280 000–350 000]	410 000 [370 000–470 000]
2011	1 300 000 [1 200 000–1 430 000]	20% [18-22%]	260 000 [240 000–310 000]	580 000 [520 000–670 000]
2012	1 280 000 [1 180 000–1 410 000]	17% [15-18%]	210 000 [190 000–260 000]	770 000 [670 000–930 000]

Rounded to the nearest 10 000

[a] Compared with the background rate, assuming no ARV interventions.
[b] Includes infections averted in the 21 African priority Global Plan countries in all previous years.
[c] Baseline year for the Global Plan.

Estimates of the percentage of pregnant and breastfeeding women living with HIV who have serodiscordant partners globally range from 10% to 40% *(64,65)*. According to a 2010 meta-analysis of data from sub-Saharan Africa *(66)*, women were the HIV-positive partners in almost half (47%) of all discordant partnerships. This highlights the important opportunities that exist to reduce HIV transmission by providing lifelong ART to all pregnant and breastfeeding women living with HIV, as recommended in the 2013 WHO ARV guidelines *(4)*.

Many analyses of the national impact of PMTCT programmes are based on modelled data. They therefore are influenced by various assumptions (such as high adherence and retention) and are based on extrapolating available data from specific research settings to larger and sometimes different populations. However, data for measuring the impact of PMTCT programmes are increasingly available at the district or national levels. For example, a national study of the effectiveness of PMTCT services in South Africa estimated that population-level early transmission at 4–8 weeks was less than 4% *(67)*.[1] Similar studies are either planned or in progress in several other countries, including Malawi, Namibia, Swaziland, Zambia and Zimbabwe.

A recent prospective study in one province in Viet Nam (Thai Nguyen) *(68)* found that the rate of mother-to-child transmission of HIV had declined from 27% in 2009 to 8% in 2012. HIV-free survival at 12 months was estimated to be 77% for infants with unknown HIV status or HIV-positive status. In a study in Kazakhstan's five most severely affected regions *(69)*, the rate of mother-to-child transmission of HIV declined from 11% to 4% between 2007 and 2010.

Routinely measuring the rates of mother-to-child transmission of HIV (including final transmission rates) and the number of children acquiring HIV infection would help to improve the empirical data that are needed to support the evaluation of the impact of PMTCT services *(70)*.

Pre-exposure prophylaxis for HIV infection

The efficacy of pre-exposure prophylaxis has been assessed in four randomized controlled trials among men who have sex with men (iPrEx *(71)*), serodiscordant couples (Partners PrEP *(72)*), sexually active young adults (TDF2 *(73)* and injecting drug users *(the Bangkok Tenofovir Study (74)*). In each of these trials, the efficacy was closely linked to adherence. When adherence was high, the reduction in HIV incidence exceeded 90% *(75)*. Pre-exposure prophylaxis works best when the regimen is followed as indicated. However, some trials have failed to attract participants who are willing or able to use the drugs as directed. The FemPrEP trial, for example, was halted for "futility" *(76)*, and the VOICE trial completed only one arm after two others had been stopped *(77)*. In both these trials, adherence was very poor and little or no protective benefit was observed. A major issue is how best to implement pre-exposure prophylaxis to reach the levels of adherence that are needed to realize its full potential benefit.

Moving from an intervention with some proven level of efficacy, as demonstrated in carefully controlled trials, to an intervention that can be scaled up safely and effectively is always a challenge. Pre-exposure prophylaxis involves the challenge of identifying the populations that most need additional prevention support and that have sufficient familiarity with pre-exposure prophylaxis and are willing and able to use it. WHO is encouraging countries that have both the need and the capacity to undertake demonstration projects to explore these key implementation questions *(78)*. In July 2012, the United States Federal Drug Administration endorsed the use of daily oral TDF + FTC for preventing the sexual transmission of HIV. The United States Centers for Disease Control and Prevention developed guidance to assist clinicians in prescribing daily oral pre-exposure prophylaxis. Outside the United States of America, as of June 2013, no country has included pre-exposure prophylaxis in its HIV prevention portfolio, although there is growing interest in undertaking demonstration projects. If the implementation challenges can be overcome and sufficient levels of adherence can be attained, pre-exposure prophylaxis may slot in alongside other prevention methods as part of the combination prevention approach.

1. The study used the almost universally attended six-week immunization visits for infants as an entry point. A follow-up study is in progress to determine the final mother-to-child transmission rate, including during the breastfeeding period.

3. CHALLENGES AND OPPORTUNITIES IN STRENGTHENING THE TREATMENT CASCADE

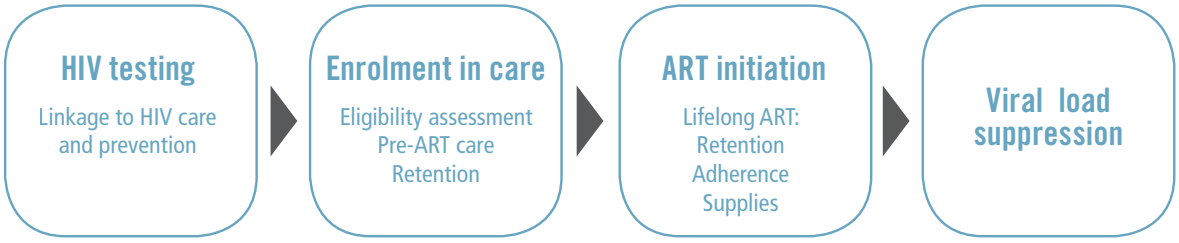
KEY POINTS

The main steps in the treatment cascade involve diagnosing HIV infection, linking people who take an HIV test to treatment and prevention services, enrolling and retaining people in pre-antiretroviral therapy (ART) care, initiating ART, ensuring long-term adherence and ultimately achieving and maintaining viral load suppression.

- Programme coverage is improving in all regions, but significant proportions of people still drop out of care at each step of the treatment cascade.
- Programmes are identifying new opportunities to improve uptake of testing, reduce the time elapsing before eligibility is assessed and treatment is initiated, and support adherence and retention in care.
- The Treatment 2.0 framework provides a lens for identifying opportunities for improvement at every step, with a focus on adapting service delivery, optimizing treatment regimens and diagnostics, reducing costs and mobilizing communities.

To maximize the multiple benefits of ART, people living with HIV should be diagnosed as early as possible after acquiring HIV infection *(1,2)*, and they should be offered appropriate prevention and care services as well as being assessed for ART eligibility. Once they start HIV treatment, support is needed to ensure long-term adherence to ART and viral suppression. Together, these elements comprise what has become known as the treatment cascade (Fig. 3.1).

Fig. 3.1. The treatment cascade



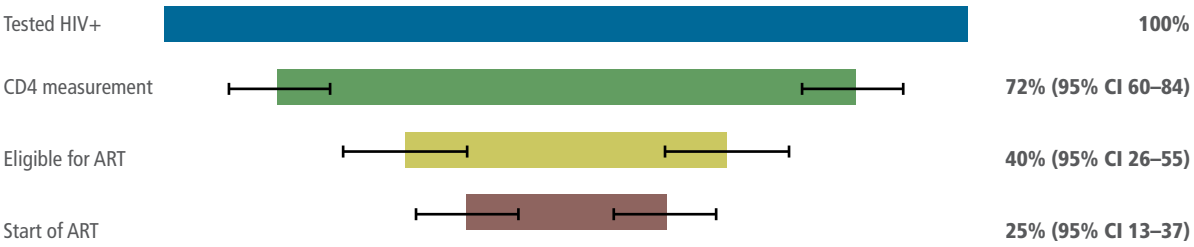
The treatment cascade provides a framework for assessing programme implementation and improving programme management so that the optimum outcomes can be achieved at each step, from HIV testing to achieving and maintaining viral load suppression, as shown in Fig. 3.1. Attrition at each step undermines the success of the overall treatment programme. It is therefore critically important to understand whether and why people are not progressing from one step to the next in

the cascade and how ART programmes can minimize losses by strengthening the weak links.

The available evidence points to high rates of attrition at each step of the treatment cascade. In most countries surveyed in Demographic and Health Surveys in the WHO African Region, for example, more than 50% of people living with HIV are not aware of their HIV status *(3)*. A systematic review of treatment cohorts in sub-Saharan Africa *(2)* shows that 41–54% of people are lost between testing and the assessment of eligibility for treatment, and 32% of those considered eligible for ART are lost between the assessment of eligibility and initiating ART. Once they start ART, about one quarter of the people temporarily interrupt treatment *(4)* and another quarter are lost within three years *(5)*. Among those lost, up to half (46%) may have died *(6)*.

Note that these estimates are not cumulative, because the treatment cascade is not a simple, linear process. People who do not complete one step in the pathway may re-enter it later and may ultimately receive successful long-term ART *(7)*. Nevertheless, cohort studies in the WHO African Region indicate that only about one quarter of the people who test HIV-positive actually initiate ART (Fig. 3.2).

Fig. 3.2. Percentage of people testing positive for HIV infection in the WHO African Region completing different stages between testing positive and starting ART

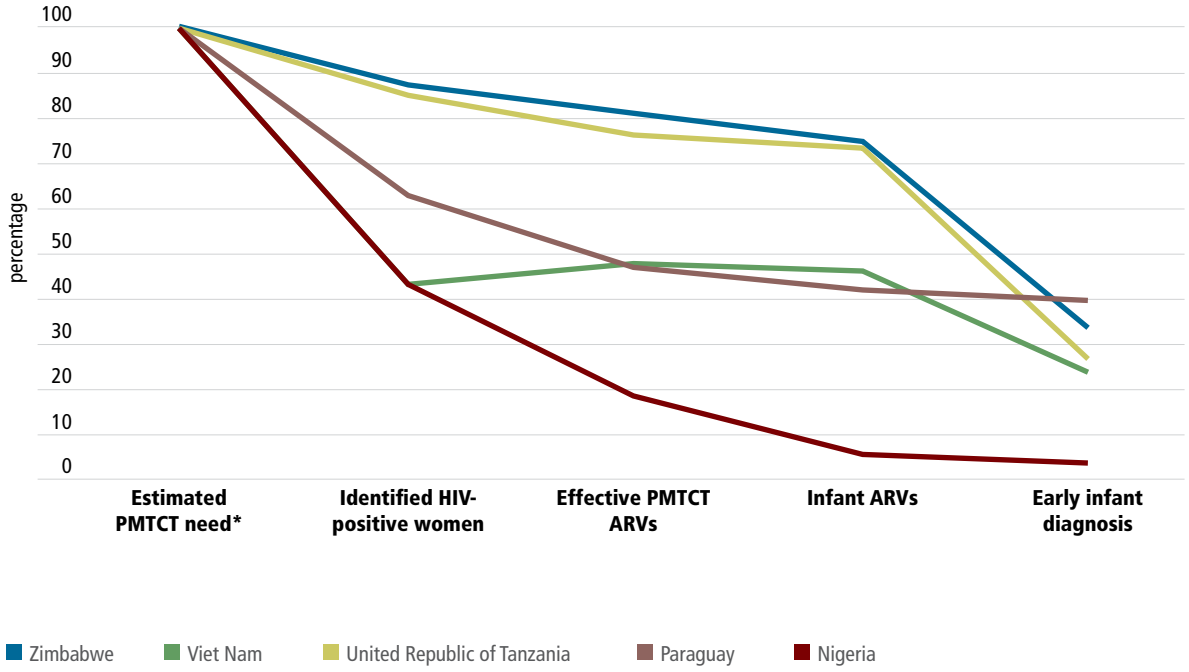


Source: Mugglin *(8)*. Loss to programme between HIV diagnosis and initiation of antiretroviral therapy in sub-Saharan Africa: systematic review and meta-analysis. *Tropical Medicine and International Health*, 2012 doi:10.1111/j.1365-3156.2012.03089.x

Similar to adults, large numbers of children are being lost along the treatment cascade. A recent systematic review of eight studies from sub-Saharan Africa and two studies from Asia found that 3–22% of the children diagnosed HIV-positive did not have their CD4 cell count or percentage measured, and 1–60% of the children eligible for treatment did not start treatment. Two studies provided data on pre–ART mortality and found rates of 6 and 13 per 100 person-years, respectively. The fact that the large majority of children (63–91%) were eligible for ART (in accordance with WHO guidelines) at first presentation highlights the general need for health systems to improve the diagnosis HIV infection among children and enrol children in HIV care early in the course of the disease *(9)*.

Similarly, for the cascade for preventing the mother-to-child transmission of HIV (PMTCT) national-level data show that, in some countries, significant proportions of pregnant women living with HIV either remain undiagnosed or, if diagnosed, do not start on ARV medicines (including lifelong treatment for their own health). Follow-up of HIV-exposed children is also noticeably weak along the cascade of PMTCT interventions (Fig. 3.3) and there is a dearth of data on the final outcomes of all HIV-exposed children. A recent systematic review and meta-analysis of 44 studies from 15 countries found that the HIV testing coverage at antenatal care facilities was 94% when offered as an opt-out option but only 58% when offered as an opt-in option. The coverage of ARV prophylaxis was 70%, while 62% of eligible pregnant women living with HIV received ART for their own health. Among HIV-exposed infants, 64% received an early diagnosis and 55% were tested for HIV once they were 12–18 months old *(10)*.

Fig. 3.3. Selected components of the cascade of preventing mother-to-child transmission in five countries



*Based on 2013 version of Spectrum model and estimates of 2012 PMTCT need in African countries, and based on 2012 version of Spectrum model and estimates of 2011 PMTCT need in other countries.

This represents a cross-sectional cascade. The estimated PMTCT need was used as the denominator to calculate various coverage estimates along the cascade of PMTCT services.

Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS)

The Treatment 2.0 initiative for enhancing HIV treatment

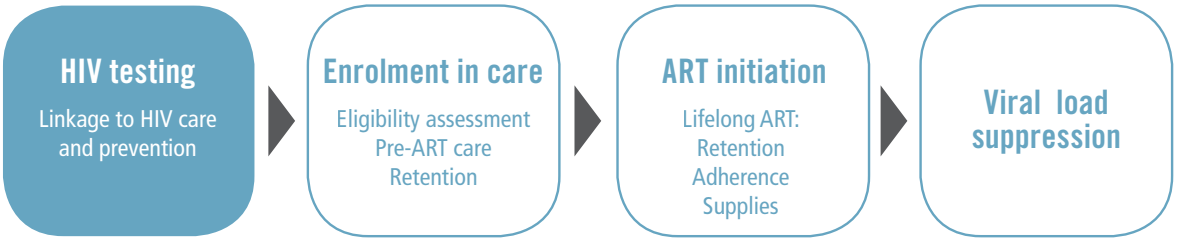
Increased concern about how to maximize retention along the treatment cascade has prompted many efforts to identify the factors that either block or facilitate linking people to ART care and that enable them to maintain treatment *(11)*. This has improved understanding of the kinds of interventions that are needed, both in health facilities and surrounding communities, to enrol and retain people in care.

Drawing on this knowledge, the WHO/UNAIDS Treatment 2.0 framework identifies the tools and strategies that can make HIV care and treatment more accessible and affordable *(12,13)*. Treatment 2.0 focuses on five dimensions in which potential improvements can be made at each step of the cascade:

- optimize drug regimens;
- provide point-of-care and other simplified diagnostic and monitoring tools;
- reduce costs;
- adapt service delivery; and
- mobilize communities.

For example, access to HIV testing can be increased through community and self-testing approaches, and identifying people who need ART can be made easier by using point-of-care CD4 tests (Box 3.8). Prescriptions for ARV medicines can be simplified, and the use of fixed-dose combinations can support treatment adherence (Box 3.10), while service delivery approaches can be improved when services are integrated and decentralized. Rationalizing the number of medicines in use can reduce costs, and communities can be involved more systematically in supporting ART services. Many countries and regions have been using the Treatment 2.0 framework to identify opportunities for resolving challenges in the treatment cascade *(14)*.

1 HIV testing and linkage to care



KEY POINTS

Early HIV testing is the first step in the pathway to successful HIV care

- Globally, about 118 million people aged 15 years and older in 124 low- and middle-income countries received HIV testing and counselling in 2012.
- In most low- and middle-income countries surveyed, most men and women living with HIV have never been tested for HIV, and therefore are not in the position to know their status.
- In all regions, women are more likely than men to have had an HIV test.
- Large numbers of people test and present late for HIV treatment, usually once their health is failing.
- Coverage of HIV testing and counselling is especially low among adolescents and key populations in most parts of the world.
- Globally, about 40% of pregnant women in low- and middle-income countries received HIV testing and counselling in 2012, up from 26% in 2009.
- Early infant diagnosis is being scaled up in many countries, but in 2011 only 35% [29–41%] of the infants born to mothers living with HIV received an HIV test within the first two months of life.
- The coverage of early infant diagnosis is less than 10% in five of the Global Plan priority countries.
- The number of people in HIV care globally who were screened for TB increased by 46% between 2010 and 2012, from 2.4 million to 3.5 million.

HIV testing is the critical first step in linking people living with HIV to the treatment cascade, and it provides an important opportunity to reinforce HIV prevention.

Globally, about 118 million people aged 15 years and older in 124 low- and middle-income countries received HIV testing and counselling in 2012. There was an 8% increase in the numbers of people taking HIV tests in a subset of 75 countries which provided data in both 2011 and 2012 (Table 3.1). All regions reported increases, with the biggest percentage increase occurring in the WHO Eastern Mediterranean Region.

Table 3.1. HIV testing and counselling in low- and middle-income countries reporting for both 2011 and 2012, by WHO region

	Number of people 15 years and older who received HIV testing and counselling[a]	
	2011	2012
African Region	**41 725 000**	**45 556 000**
Number of countries reporting	35	35
Region of the Americas	**4 256 000**	**4 304 000**
Number of countries reporting	12	12
South-East Asia Region	**19 572 000**	**20 750 000**
Number of countries reporting	9	9
European Region	**1 215 000**	**1 299 000**
Number of countries reporting	7	7
Eastern Mediterranean Region	**244 000**	**436 000**
Number of countries reporting	6	6
Western Pacific Region	**3 673 000**	**3 824 000**
Number of countries reporting	6	6
Total	**70 685 000**	**76 169 000**
Number of countries reporting	75	75

Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

[a] Rounded to nearest 1000. Based on the numbers of people tested, as reported by countries but without correcting for the fraction of people who are tested more than once.

Significant regional variation

In the WHO African Region, HIV testing and counselling services have expanded substantially, as Fig. 3.4 illustrates. This is a remarkable achievement given the human resource and other constraints in many countries in the region.

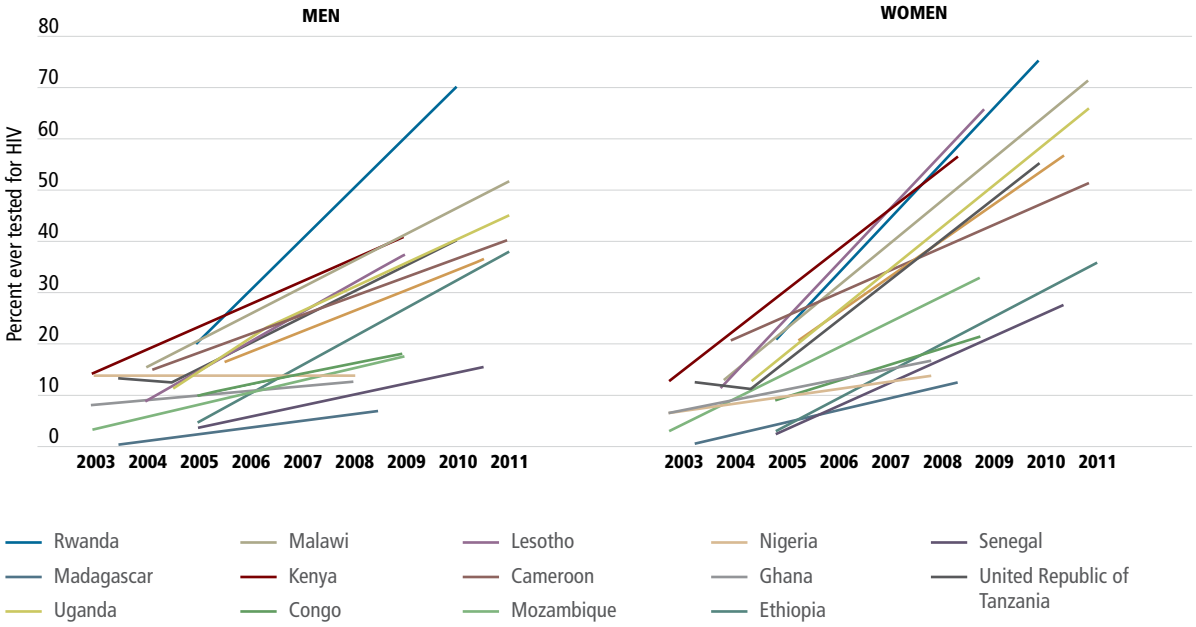
Increasing availability and access to testing, however, only addresses one of several factors that determine whether or not people take an HIV test and receive the results. A recent systematic review of studies in sub-Saharan Africa indicates that some of the main factors facilitating the uptake of HIV testing are personal and may include deteriorating physical health and/or the death of a sexual partner or child *(15)*. Other factors that appear to increase a willingness to test include decreasing stigma and discrimination, free services, the availability of ART and social network support. Barriers include people's perceptions that they have a low risk of acquiring HIV infection, concerns about confidentiality, fear of HIV-related stigma, discrimination and criminalization, the anticipated emotional burden of living with HIV and the financial costs of accessing HIV testing *(15)*.

In the WHO European Region, HIV testing services are often available routinely in clinical settings such as antenatal care services, blood donation stations, sexually transmitted infection clinics, TB clinics, drug dependence treatment facilities and prison settings. Many tests are performed annually in many countries, but this does not necessarily mean that the testing efforts focus strategically on the populations that are at highest risk for HIV, including hard-to-reach populations such as people who inject drugs.

Awareness of serostatus among people living with HIV

Expanding testing throughout clinical services and supporting the testing of partners and family members of people with HIV has increased the number of people who know their serostatus. The 25 Demographic and Health Surveys carried out in the WHO African Region since 2003 found

Fig. 3.4. Percentage of people 15–49 years old who were ever tested for HIV and received their result in selected countries in the WHO African Region, 2003–2011



Source: Staveteig S et al. (3) *Demographic patterns of HIV testing uptake in sub-Saharan Africa. Calverton, MD, ICF International, 2013* (DHS Comparative Reports No. 30).

that individuals living with HIV were more likely to have been tested for HIV than individuals who had not acquired HIV. Overall, however, coverage has remained low: in 16 of 25 countries for which data were available between 2003 and 2010, most men and women living with HIV had never been tested for HIV, and therefore were not in the position to know their status *(3)*.

Late testing

Among people who are diagnosed with HIV, significant proportions in all regions test late in their HIV infection. Many of them present for HIV treatment once they already have advanced disease, and often when they are very ill. Such late diagnosis leads to initiating ART late, which undermines its prevention and treatment benefits.

Box 3.1. Understanding the reasons for late HIV diagnosis in Georgia

A WHO study of HIV diagnoses in Georgia in 2009–2011 found that 64% of new HIV diagnoses could be considered "late", i.e. eligible for ART, and 47% had an AIDS-defining illness at the time of diagnosis. Late presenters were more likely to have a history of injecting drug use, to be male and to be older. The study concluded that the reasons for the high rates of late diagnosis included a lack of access to acceptable HIV testing and counselling services. The actions taken by the National HIV/AIDS Programme to overcome these challenges include increasing HIV testing uptake among key populations at higher risk, expanding provider-initiated HIV testing and counselling, introducing guided testing for people considered clinically to potentially have HIV and introducing continual surveillance of late HIV diagnoses to monitor progress and inform further public health actions.

Sex differences in HIV testing and counselling

In all countries, women are more likely than men to take an HIV test. This probably reflects women's more frequent contact with health services, especially with reproductive and child and maternal health services, at which HIV testing and counselling is often routinely available. Recent data from Kenya, for example, show that HIV testing rates were significantly higher among women of reproductive age (15–49 years) (49%) than among men in the same age group (29%) *(16)*. This highlights the need to develop strategies that can increase men's uptake of HIV testing and counselling, including providing testing in settings that are more accessible and acceptable to men *(17)* and devising ways to encourage more men to test with their partners in clinical settings *(18)*.

Testing for adolescents

In countries with a high burden of HIV infection, adolescents have less access to HIV testing and counselling than adults do. Restrictions related to the age of consent for testing can hinder adolescents' access to HIV and other health services. Depending on the country, the age of consent for HIV testing ranges from 12 years to 18 years. New WHO guidelines on HIV testing and counselling for adolescents (*19)* recommend that health ministries revisit those provisions given the need to uphold adolescents' rights to make decisions about their own health and well-being. Survey data from 2005 to 2010 in the WHO African Region indicate that, on average, fewer than 1 in 5 women and men 15–24 years old were aware of their HIV status. Access and coverage, however, varied considerably between countries *(20)*. Although data are scarce, ART coverage among adolescents also appears to be low *(21)*.

Low testing coverage for key populations

HIV testing and counselling services are not accessible enough to key populations that are at high risk of HIV infection. Structural, operational, logistical and social barriers – including stigma, discrimination, punitive laws and policies and vulnerable socioeconomic status – continue to hinder access to existing testing and counselling services for key populations in many countries (including in the African Region) and need to be addressed.

Mandatory and coerced testing of key populations (including prisoners *(22)*, migrants *(23,24)* and ethnic minorities) occurs in some settings, including in clinical settings *(25)*. Some countries acknowledge that substantial proportions of the HIV tests are performed either before employment or travel, or are done in another non-voluntary manner. In November 2012, WHO reiterated its opposition to mandatory testing (26) and emphasized that all forms of HIV testing and counselling should be voluntary and should adhere to the "five C's": consent, confidentiality, counselling, correct test results and connections to care, treatment and prevention

Box 3.2. Increasing testing uptake in Viet Nam

Injecting drug use is the main driver of Viet Nam's HIV epidemic. Testing uptake among people who inject drugs, however, is low. Many people living with HIV, especially people who inject drugs, initiate ART late, with most starting ART with CD4 counts <100 cells/mm^3. In 2012, the Ministry of Health started a pilot Treatment 2.0 programme in Dien Bien and Can Tho provinces in which HIV testing, counselling and treatment follow-up services were decentralized to commune health stations. This enabled the communes to reach people who inject drugs but who previously had been unable or reluctant to use district-level services. The new decentralized model, combined with outreach services, appears to be effective in some geographical areas in promoting HIV testing and counselling and in increasing ART uptake in key populations such as people who inject drugs. However, people who inject drugs still face stigma, discrimination and various structural barriers when seeking to use HIV services.

services *(27)*. Because of social vulnerabilities and the need for confidentiality, peer-led testing approaches are more likely to be suitable for some populations.

Testing for preventing the mother-to-child transmission of HIV

HIV testing and counselling for pregnant women is the first step toward enrolling mothers living with HIV in the cascade of PMTCT interventions. Globally, around 40% of pregnant women in low- and middle-income countries received HIV testing and counselling in 2012, up from 26% in 2009. As Fig. 3.5 and Table 3.2 show, however, the global coverage estimate masks differences between countries and regions. Some countries with large populations and low national HIV prevalence have low HIV testing rates. Countries with higher HIV prevalence tend to have much higher coverage of HIV testing among pregnant women, although this could be improved further.

Among the priority countries in the Global Plan *(28)*, four countries (Botswana, Mozambique, South Africa and Zambia) exceeded 95% testing coverage in 2012, but the coverage was less than 25% in three others (Chad, the Democratic Republic of the Congo and Nigeria) (Table 3.2). In the WHO African Region, 45% of pregnant women were tested for HIV, but coverage varies at 70% in eastern and southern Africa and 32% in western and central Africa.

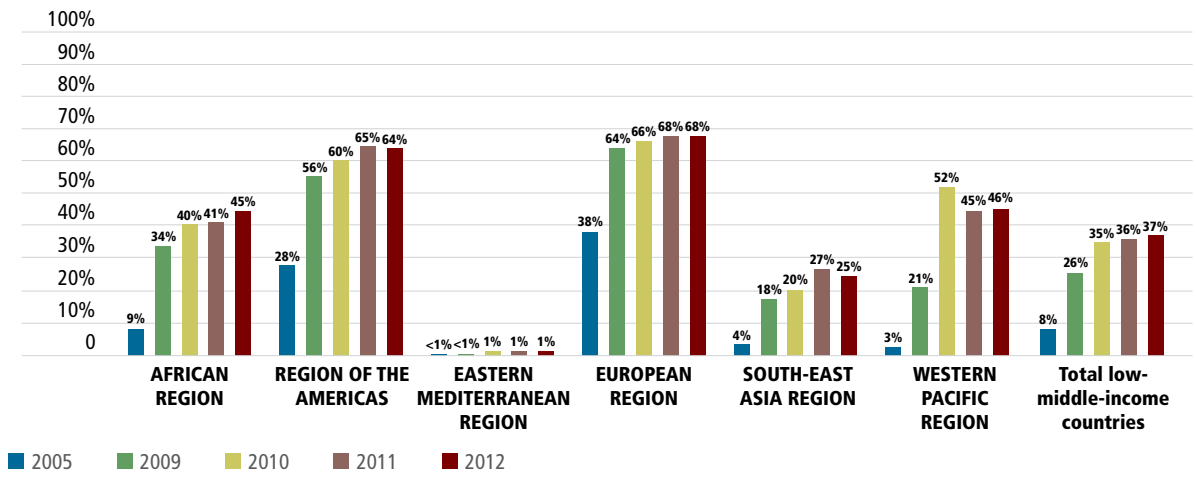
Table 3.2. HIV testing and counselling coverage among pregnant women in the Global Plan priority countries, 2012

Country	Testing coverage among pregnant women
Angola	34%
Botswana	>95%
Burundi	51%
Cameroon	42%
Chad	7%
Côte d'Ivoire	75%
Democratic Republic of the Congo	9%
Ethiopia	39%
Ghana	66%
India	31%
Kenya	85%
Lesotho	48%
Malawi	72%
Mozambique	>95%
Namibia	91%
Nigeria	19%
South Africa	>95%
Swaziland	81%
Uganda	65%
United Republic of Tanzania	68%
Zambia	>95%
Zimbabwe	90%

Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

The number of pregnant women was proxied using the estimated live births from the United Nations Department of Economic and Social Affairs, Population Division (2013). *World Population Prospects: The 2012 Revision.*

Fig. 3.5. Estimated HIV testing and counselling coverage among pregnant women, low- and middle-income countries overall and by WHO region, 2005 and 2009–2012



Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS), United Nations Department of Economic and Social Affairs, Population Division (2013). *World Population Prospects: The 2012 Revision.*

Infant diagnosis

Early testing of infants who have been exposed to HIV is essential for identifying infants who may be living with HIV and for starting them on early, life-saving treatment. In the absence of these interventions, one third of infants living with HIV die before their first birthday. Early testing can also provide important information on early HIV transmission rates and on the effectiveness of perinatal PMTCT interventions.

WHO recommends that infants exposed to HIV be tested at 4–6 weeks of age, using a virological test *(29)*. Dried blood spot to polymerase chain reaction testing or point-of-care technologies are highly suitable for decentralizing and expanding testing, and ART should be started as soon as the infants are found to be HIV-positive, regardless of clinical and immune status. Some countries are considering earlier testing, at birth, especially for children born to mothers who have not received PMTCT services.

Testing rates for infants are low, however. Globally in 2011, only 35% [29–41%] of the infants born to mothers living with HIV received an HIV test within their first two months of life. Among the Global Plan priority countries in the WHO Africa Region 2012, only South Africa and Swaziland were providing early infant diagnosis for more than 80% of infants in need, while only Namibia and Zambia had achieved early infant diagnosis coverage of 50–80% for HIV-exposed infants (Table 3.3).

Such generally low coverage of early infant diagnosis is mirrored by low HIV care coverage for infants. Currently, only about 30% of infants who are diagnosed through virological testing are promptly referred to treatment facilities to initiate ART. The coverage of early infant diagnosis is less than 10% in five of the priority countries in the Global Plan: Angola, Chad, the Democratic Republic of the Congo, Malawi and Nigeria.

Based on countries that reported data, the WHO European Region had the highest early infant diagnosis coverage of any region in 2011 (>95%, ranging from 69% to >95%), followed by the WHO Region of the Americas (46%, range 25–76%), the WHO South-East Asia Region (40%, range 30-59%), the WHO African Region (34%, range 29–40%), the WHO Western Pacific Region (23%, range 16-34%) and the WHO Eastern Mediterranean Region (2%, range 1-3%). However, within sub-saharan Africa, the average coverage of early infant diagnosis was extremely low, at 7% [6–9%] in west and central Africa, compared with 46% [40–53%] in eastern and southern Africa.

When systems exist to improve the turn-around time of test results, the numbers of children initiating ART tend to increase and mortality rates decrease. This was shown, for example, in a study in Lesotho, in which the use of mobile phone messages to communicate results reduced the waiting time for results to less than two weeks *(30)*. A study in Zambia found that a similar method shortened the average time between collecting samples and notifying the relevant health facilities and caregivers of the results from 44 days to 28 days *(31)*.

Table 3.3. Proportion of infants receiving a timely virological test in the 21 African priority Global Plan countries in 2012, as reported by countries[a]

Country	Early infant diagnosis coverage [range]
South Africa	85% [78–94%]
Swaziland	81% [73–90%]
Namibia	74% [62–89%]
Lesotho[b]	69% [63–76%]
Zambia	61% [54–68%]
Kenya	39% [35–44%]
Botswana	38% [35–42%]
Mozambique	37% [31–42%]
Cameroon	35% [31–41%]
Zimbabwe	34% [30–38%]
Uganda[b]	30% [26–35%]
United Republic of Tanzania	28% [24–32%]
Côte d'Ivoire	27% [22–34%]
Ethiopia	19% [16–22%]
Ghana	18% [15–22%]
Burundi	11% [8–14%]
Angola	7% [5–8%]
Democratic Republic of the Congo	6% [5–7%]
Malawi	4% [4–5%]
Nigeria	4% [4–5%]
Chad	4% [3–4%]

[a] In some countries, the estimated coverage for early infant diagnosis may be significantly affected by underreporting of performed diagnosis.
[b] Lesotho and Uganda did not report 2012 data, thus 2011 estimates are presented.

Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS) and UNAIDS/WHO estimates.

Box 3.3. Expanding access to early infant diagnosis in Kenya

Kenya's national ART guidelines recommend the use of molecular testing for early infant diagnosis. Before 2007, however, funding, laboratory testing infrastructure and challenges in transporting samples limited the provision of early infant diagnosis in Kenya. Testing was performed on whole blood samples, which required cold-chain processing that was only available in central locations. Consequently, fewer than 10 000 tests (less than 10% of those needed) were conducted per year. To address these issues, the Ministry of Health collaborated with partners and other stakeholders to strengthen and standardize the scaling up of early infant diagnosis. The best practices from other countries were adopted, including establishing high-throughput laboratories and an efficient system for transporting samples. This resulted in adopting dried blood spots as the preferred sample type for early infant diagnosis, increasing testing capacity (four molecular laboratories were established) and reorganizing the national system for transporting samples. Restructuring early infant diagnosis in Kenya led to rapid scale-up, with coverage increasing from less than 10% in 2007 to about 40% by the end of 2012.

Combination testing approaches

Most countries have widely accepted provider-initiated testing and counselling in health settings (Table 3.4) *(32)*. High coverage has been achieved in antenatal care and TB clinics, especially in countries with a great burden of HIV infection. A recent review of HIV testing in antenatal care reported testing uptake exceeding 80% in Botswana, Ethiopia, Malawi, Uganda and Zimbabwe *(33)*. High rates of testing can also be achieved in other clinical settings: data from 36 outpatient departments in South Africa, Uganda and the United Republic of Tanzania showed that more than 90% of the people who were referred to on-site testing and counselling services took an HIV test *(34)*.

Table 3.4. Policies and practices related to HIV testing and counselling

	Does the national policy promote provider-initiated testing and counselling?	Does the policy require health providers to offer testing and counselling in all patient encounters? (countries with generalized epidemics)	Does the country use community-based testing approaches?	Does the country have policies that support HIV point-of-care rapid testing by lay health workers?
Yes	80	26	70	42
No	3	15	15	42
Countries reporting	83	41	85	84

Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

By the end of 2012, 95% of 102 countries surveyed in the Global AIDS Response Progress Reporting process reported that they had explicit policies for provider-initiated testing and counselling in their health facilities. Among them, 49 countries with generalized HIV epidemics reported that they had policies to offer HIV testing in all patient encounters, regardless of presenting symptoms or facility type. Other countries were targeting HIV testing at specific facilities or in relation to specific symptoms. Overall, 90% of the surveyed countries confirmed that their policies note the non-mandatory nature of HIV testing and counselling.

WHO recommends that facility-based testing be complemented with a range of community-based testing approaches. Depending on the country context, multiple testing approaches are needed to increase people's awareness of HIV serostatus. They may combine various forms of stand-alone sites, home-based testing, mobile outreach (including index partner testing, testing in workplaces, schools and universities and accessible and safe venues for key populations), special testing events and testing campaigns. These approaches should include effective methods for linking people who are diagnosed with HIV to care and treatment services.

Box 3.4. South Africa's massive HIV testing and counselling campaign *(35)*

South Africa staged an intensive HIV testing and counselling campaign between April 2010 and June 2011, which urged everyone 12–60 years old to take a test. All sites providing HIV testing and counselling services were linked to referral facilities that provide CD4 testing, ART, care and support. Testing and counselling was carried out at health facilities, workplaces and community outreach sites. By the end of the campaign, it was reported that:

- more than 13 million HIV tests had been performed, with approximately 2.2 million people testing HIV-positive (of whom 52% had CD4 counts <350 cells/mm^3);
- more than 400 000 people initiated ART, including 57 000 pregnant women;
- more than 8 million people were screened for TB;
- 185 million male condoms and 524 000 female condoms were distributed;
- 237 000 males were medically circumcised, exceeding the campaign target of 100 000; and
- 3686 health facilities (80% of the total) were delivering ART, supported by task shifting and training 10 542 nurses.

Box 3.5. National testing days in El Salvador

Every June, El Salvador stages a National HIV Testing Day. Featuring parades and other entertainment, this health sector-wide campaign offers HIV testing and counselling countrywide using mobile units, health clinics, nongovernmental organization centres and various public venues. In June 2012, 117 000 people were tested in one day, of whom 0.2% were diagnosed with HIV. The campaign accounted for 28% of all HIV tests performed and yielded 20% of all HIV-positive diagnoses in 2012. The national testing day has helped to normalize HIV testing, increase knowledge and reduce stigma towards HIV.

Partner and couples testing (including in antenatal care settings) *(36)*

Data from Demographic and Health Surveys suggest that in at least two thirds of couples in which one partner is HIV-positive, the other partner is HIV-negative *(37)*. Evidence from eastern and southern Africa, for example, indicates that 50–65% of the people who acquire HIV infection in Swaziland, 35–62% in Lesotho and 44% in Kenya are within marital or cohabiting relationships *(38)*. WHO has recommended couples testing and counselling in antenatal care settings since 2006 and, in 2012, WHO recommended that all HIV-positive partners in serodiscordant relationships be offered ART regardless of their CD4 count *(39)*.

By the end of 2012, at least 14 countries had already adopted policies for couples testing and treatment of the HIV-positive partners (Table 3.5). Encouragingly, a recent randomized trial in Cameroon, the Dominican Republic, Georgia and India showed that providing couples-oriented, post-test HIV counselling increased partner testing rates in all sites – and by as much as 30-fold in one site in Georgia – compared with standard counselling *(40)*.

Country experiences in scaling up HIV testing and counselling for couples have shown that the approach can be acceptable, feasible and effective. In Uganda, peer sensitization and establishing male-friendly spaces in antenatal care facilities increased male partner testing in antenatal care from 5.9% in 2002 to 76% in 2011 *(41)*. In Rwanda, more than 80% of pregnant women now undergo HIV tests with their partners *(42)*. In South Africa, couples-based HIV testing has also been found to be highly acceptable among men who have sex with men.

Nevertheless, these are exceptions. Available data indicate that few countries have achieved couple HIV testing and counselling rates exceeding 20% in antenatal care settings. Hindrances include male partners' perception that antenatal clinics are not male-friendly, a sense that services focus too narrowly on HIV testing and counselling rather than on general health *(43)* and strong beliefs about gender roles and hierarchies *(44)*. Couples HIV testing and counselling can bring enormous benefits, including disclosure of HIV status to partners, stronger uptake of and adherence to ART and PMTCT interventions; however, couples HIV testing and counselling should be non-coercive, and health care workers should be sensitive to supporting women to test alone without their partners if they fear gender-based violence *(45)*.

Expanding HIV testing and counselling into communities

Community-level HIV testing and counselling may help to improve access and reduce the stigma and discrimination that is often associated with clinic-based testing *(46)*. According to the Global AIDS Response Progress Reporting system, 73 of 82 countries are using community-based (outside clinics) testing approaches, and 53 of 73 countries allow lay workers to perform HIV rapid testing.

A recent systematic review of 21 studies conducted in Kenya, Malawi, South Africa, Uganda and Zambia *(47)* found that home-based HIV testing and counselling was highly acceptable, with 83% of people accepting testing when offered. People living with HIV were linked to care in slightly more than half the studies included in the review. As with all HIV testing and counselling, home-based HIV testing and counselling needs to include effective procedures for referral and linkage to care and other HIV and health services *(48)*.

In some settings, community-based testing for key populations is proving to be highly acceptable and effective in reaching large populations of first-time testers and in diagnosing people living with HIV soon after seroconversion *(49)*. For these reasons, the 2013 WHO ARV guidelines *(50)* recommend that community-based testing approaches complement provider-initiated testing.

Self-testing – a potentially useful new approach to increase access to HIV screening

HIV self-testing offers an additional possible approach for enhancing testing access. Rapid diagnostic testing has been approved for self-testing in the United States of America *(51)*, and other countries are investigating the feasibility of including self-testing in their national AIDS strategies. While experience remains limited, self-testing appears to be highly acceptable. In a formal programme of self-testing for health workers in Kenya, where self-testing is included in the national HIV testing and counselling guidelines, 85% of the people who attended an information session used a self-test kit, and 64% of those with partners reported that their partners also used the kits *(52)*. Similarly high uptake and acceptability of this emerging approach has been reported recently in Malawi (Box 3.6).

Box 3.6. Supervised self-testing in Malawi *(53)*

A supervised self-testing programme in Malawi is using trained resident volunteers to offer HIV self-testing with counselling to their neighbours in neighbourhoods in the city of Blantyre. The initial results of the programme, which started in February 2012, show strong uptake but indicate a need for proactive interventions to link people testing HIV-positive to care.

- Of the 16 660 adults older than 15 years who participated in the programme, 81% took self-tests and 89% returned the kits after use to their counsellors.
- Among the self-testers, 42% were men, and 21% were younger than 20 years.
- 98% of the participants said they would recommend a self-test to friends and family.
- More than three times as many adults who were eligible for ART in the home-based arm of the programme started ART compared with those in the facility-care arm (46% versus 15%).

Further studies will assess cost–effectiveness, adherence to ART and retention in care.

WHO is examining the legal, ethical, gender, human rights and public health implications of scaling up HIV self-testing. A forthcoming WHO and UNAIDS policy brief *(54)* will outline the possible application of supervised and non-supervised HIV self-testing, associated concerns and the recommended conditions and requirements for self-testing.

Testing people with TB for HIV infection

Worldwide, the number of people with TB tested for HIV has increased consistently each year. The WHO African Region, which accounts for almost 80% of the people with TB who are HIV-positive globally *(55)*, has made particularly strong progress. Provisional data from 43 countries in the African Region show that an average 75% of people notified as having TB had a documented HIV test result in 2012 compared to only 11% in 2005; more than 40% of the people tested were HIV-positive. The final data will be available in the WHO *Global tuberculosis report 2013*.

Some countries (such as Kenya) are implementing national policies to offer HIV testing to everyone with presumptive TB. Available data indicate that a large proportion of people with presumptive TB test HIV-positive in settings with a high burden of HIV *(56)*. Data from Zimbabwe *(57)* and India *(58)* show that the prevalence of HIV among people with presumptive TB is as high as among people with diagnosed TB, with the prevalence varying according to the epidemiological context. In a study in Zimbabwe, 63% of the people with presumptive TB were diagnosed with HIV *(57)*. WHO recommends HIV testing among people with presumptive TB, but the practice is not yet routine *(59)*.

Linking people from testing to care

It is vital that people diagnosed with HIV be linked promptly to care. The reasons for poor linkage to care after testing HIV-positive are diverse and include clinical, structural and personal barriers *(60,61)*. A recent survey in sub-Saharan Africa *(62)* suggests that stigma, poor referral systems and poor post-test counselling are important deterrents. Transport and opportunity costs such as loss of income or threat of losing a job for taking time off work to seek care also act as disincentives, especially when health facilities are located far from patients' homes or workplaces *(63)*. Decentralizing treatment and care services is therefore crucial for strengthening the treatment cascade.

Linking key populations to care

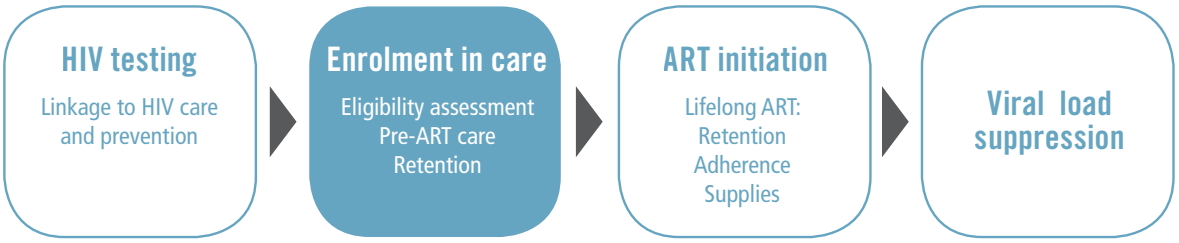
Linking key affected populations to HIV care poses particular challenges, especially for people who inject drugs. The criminalization of injecting drug use and the requirement in some countries that drug users formally register with government services act as major deterrents to seeking care. In the WHO European Region, for example, low coverage of opioid substitution therapy and a lack of integration of HIV, TB and opioid substitution therapy services are barriers to HIV care (Box 3.7).

Box 3.7. Integrating TB, HIV and opioid substitution in Belarus

TB, HIV and drug dependence services in Belarus used to be delivered via separate programmes, each with its own administration, financing and staff. This hindered uptake of ART by people who were diagnosed in TB settings, many of whom injected drugs. Belarus responded by allowing ART to be initiated in TB clinics; however, people were still not able to start opioid substitution therapy while in TB hospitals. That changed when a national consultative process in early 2012 recommended that opioid substitution therapy be able to be initiated in TB clinics, with financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria and the Belarus Ministry of Health.

Some TB clinics have created positions for narcologists or made arrangements for consultancy services. One TB hospital plans to operate a permanent distribution site for opioid substitution therapy, which would facilitate stronger integration of services. The new approach is spurring the expansion of the opioid substitution therapy programme in Belarus, which currently reaches 920 people, of whom 35% are living with HIV and 20% are receiving ART.

2 Enrolment in care and pre-antiretroviral therapy



KEY POINTS

Substantial numbers of people are being "lost" between taking an HIV test and starting antiretroviral therapy

- Linking to treatment after diagnosis and eligibility assessment for children ranges between 40% and 99% in countries.
- 68% of the pregnant women with HIV-positive test results were subsequently assessed for eligibility for ART in 2012, up from 57% in 2011.
- Access to CD4 testing remains limited, with less than 20% of the people who test HIV-positive getting a timely CD4 count in some settings.
- Point-of-care CD4 testing can significantly speed up the initiation of ART and improve retention among people who are eligible for ART.
- Interventions that are improving outcomes for people receiving pre-ART HIV care include counselling, providing co-trimoxazole prophylaxis free of charge, regular assessment for eligibility for ART, shorter waiting times at clinics and methods that encourage regular clinic visits.

Historically, whereas efforts have been made to expand testing and the initiation of ART, providing routine pre-ART HIV care for people not yet eligible for treatment has been neglected *(64)*. A 2010 audit of 122 public primary-care facilities offering HIV testing and counselling in Cape Town, South Africa, found that 78% of people who tested HIV-positive received a CD4 count and only 47% were clinically staged. Overall, less than half (47%) of the people found to be eligible for ART were referred to an ART facility.

Data on the outcomes among people waiting for ART are limited but suggest that outcomes are poor. A study from the Free State Province in South Africa analysing data from 2004–2007 *(65)* found that 23% of the people eligible for ART had died before starting ART and that men were less likely to start ART and more likely to die than women.

Several interventions have been shown to improve outcomes for people receiving pre-ART HIV care, including high-quality counselling, providing co-trimoxazole prophylaxis, various methods to encourage regular visits (such as transport allowances) and approaches that shorten the pre-ART period such as using point-of-care CD4 testing (Box 3.8) *(1)*.

Box 3.8. Point-of-care CD4 testing

Several recent studies have highlighted the benefits of point-of-care CD4 testing as a way to improve linkage between HIV testing and HIV care and to reduce the time before eligible people initiate ART. In South Africa, receipt of a CD4 count at the time of HIV testing was found to increase ART initiation rates *(72)*. In neighbouring Mozambique, using the technology in primary care clinics almost halved the loss to follow-up before initiating ART, from 64% to 33% *(73)*.

A recent systematic review of data from 18 studies *(74)* found that people using point-of-care testing were more likely to both receive a CD4 result and start ART compared to those relying on laboratory-based methods. Point-of-care CD4 testing significantly reduced both the median time between HIV diagnosis and having a CD4 test and between HIV diagnosis and receiving the test result. The use of this technology was predicted to be cost-effective and to result in more life-years saved than current methods *(74)*.

The uptake of point-of-care CD4 testing has been rapid: more than 2500 machines were in use in 41 low- and middle-income countries at the end of 2012.

CD4 testing

CD4 testing can be a key method for assessing whether people are eligible for ART. In order to avoid that lack of CD4 testing becomes a barrier to treatment initiation, WHO guidelines do not insist on a CD4 test before initiating ART, but for clinical reasons it is considered desirable at the start of treatment. However, access to CD4 testing remains limited. Indeed, some countries with a high burden of HIV infection (such as Malawi) have successfully scaled up ART without making CD4 testing mandatory *(66)*. Nevertheless, even in settings in which CD4 testing is routinely available, it is not routinely performed.

- A recent study from China reporting on data from 83 000 people in the Yunnan and Guangxi provinces found that only 37% of those who tested HIV-positive received a CD4 count within six months *(67)*.
- A study from Kenya, Uganda and the United Republic of Tanzania reported that even in a research setting in which efforts were made to reduce missing data, pre-ART CD4 counts were missing for 15% of the people living with HIV *(68)*.
- In Johannesburg, South Africa, among 437 people who had recently been diagnosed with HIV, only 19% had a CD4 test within 6 weeks, and 29% had one within 6–12 weeks of testing HIV-positive *(69)*.
- A report from a nationally representative sample of 100 clinics in the United Republic of Tanzania showed that the proportion of people with missing CD4 counts did not improve between 2004 and 2009, with one in five people lacking a CD4 count throughout that period. Mortality rates were significantly higher among the people lacking a CD4 count than among those with a recorded CD4 count *(10)*.

According to the WHO 2012 diagnostics survey *(71)*, 3781 CD4 count machines were operating in 69 low- and middle-income countries in 2011. However, even where tests are available, access may be limited because of user charges for laboratory tests, malfunctioning machines or a lack of reagents. Data from 47 countries included in the WHO 2012 diagnostics survey *(71)* found that the average CD4 count machine was used to perform about four tests per day, whereas cost-effective deployment requires testing between 20 and 100 samples per day.

One encouraging development that can increase access to CD4 is the recent and rapid deployment of point-of-care CD4 testing technology (Box 3.8). This technology can speed up the assessment of eligibility for ART and reduce losses to care before initiating ART. However, effectively using point-of-care CD4 technology requires solving several challenges, according to the WHO survey *(71)*, including shortages of reagents, non-installation, inadequate training and – especially – poor or no maintenance. These issues highlight the need for a national strategic plan for purchasing and deploying laboratory technologies.

Retention in pre-antiretroviral therapy

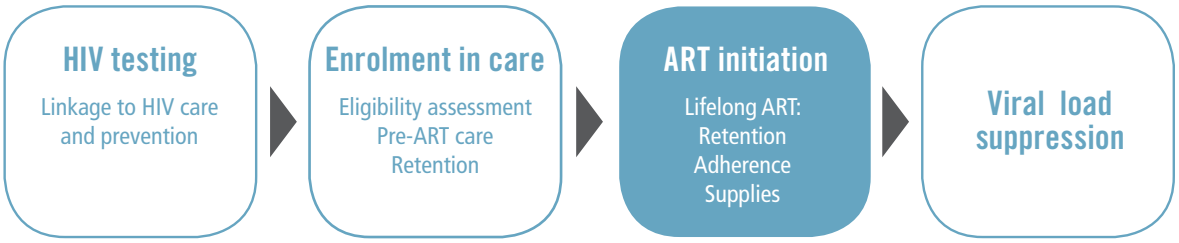
A systematic review of 28 studies in sub-Saharan Africa showed that 32% of the people considered eligible for ART are lost between their eligibility being assessed and ART being initiated *(2)*. Retaining people in pre-ART over extended periods of time poses significant challenges, many of them distinct from the factors that affect whether people are retained in ART.

Losses between HIV diagnosis and initiating ART also pose challenges for care for children, although a recent meta-analysis of studies involving more than 10 000 children living with HIV *(9)* found that linkage to care after diagnosis was better than for adults: depending on the specific study, between 40% and 99% of children diagnosed with HIV and deemed eligible for ART actually started ART.

Lack of CD4 testing or delays in receiving CD4 results (see above), long waiting times at clinics, concerns about possible drug side effects, a lack of confidence in the effectiveness of the treatment and drug stock-outs[1] can all contribute to attrition before initiating ART *(62)*. Many of the reasons are similar to those that cause people to be lost to care after initiating ART; these are discussed in the next section.

1. A stock-out occurs when the demand or need for an item cannot be met from the current inventory.

3 Antiretroviral therapy: initiation, retention and adherence



KEY POINTS

Initiating treatment early is vital for success

- As of 2012, most countries globally allowed ART to be initiated at CD4 ≤350 cells/mm^3, and a few have already moved to a higher initiation threshold of CD4 ≤500 cells/mm^3.
- Median CD4 when initiating ART is rising in all regions but is still too low: about 1 in 4 people in low-income settings initiate ART late, with CD4 counts <100 cells/mm^3.
- Option B+ for preventing the mother-to-child transmission of HIV is being rapidly adopted as a way to increase the coverage of ART for pregnant women living with HIV.
- Decentralizing HIV care improves access and retention, and an increasing number of countries have piloted or are rolling out ART delivery at the community level.

Improving retention in ART care is a key challenge for programmes

- The latest data from 23 countries indicate that the average retention rates for people on ART decreases over time, from about 86% at 12 months to 82% at 24 months and 72% at 60 months, with considerable variation between countries.

Most countries in 2012 allowed for initiation of ART at CD4 ≤350 cells/mm^3, in accordance with the 2010 WHO treatment guidelines *(75)*. A few countries (including in low-income settings in the WHO Region of the Americas and in the WHO African Region) have already moved to the higher initiation threshold for ART now recommended by WHO: CD4 ≤500 cells/mm^3 *(76)*.

An increasing number of countries are also implementing or considering policies of initiating lifelong ART earlier for specific groups. At least 14 countries have adopted a policy of providing ART to the HIV-positive partners in serodiscordant relationships, regardless of their immune status, and at least five countries are providing ART to people with a CD4 count ≤500 cells/mm^3. As of early 2013, at least 28 countries had a policy for implementing lifelong ART for pregnant women living with HIV (Option B+) *(77)*.

Timing of initiation

Increased HIV testing, policy shifts towards initiating ART earlier and expanded ART coverage have led to steady increases in all regions in the average CD4 count at which people initiate ART. As shown in Fig. 3.6, the increases have been most notable among women, especially in low- and middle-income countries. The fact that people on average are starting ART in better health, along with the massive increases in the coverage of ART in recent years, is reducing AIDS-related mortality and increasing the life expectancy of people living with HIV (see Chapter 2).

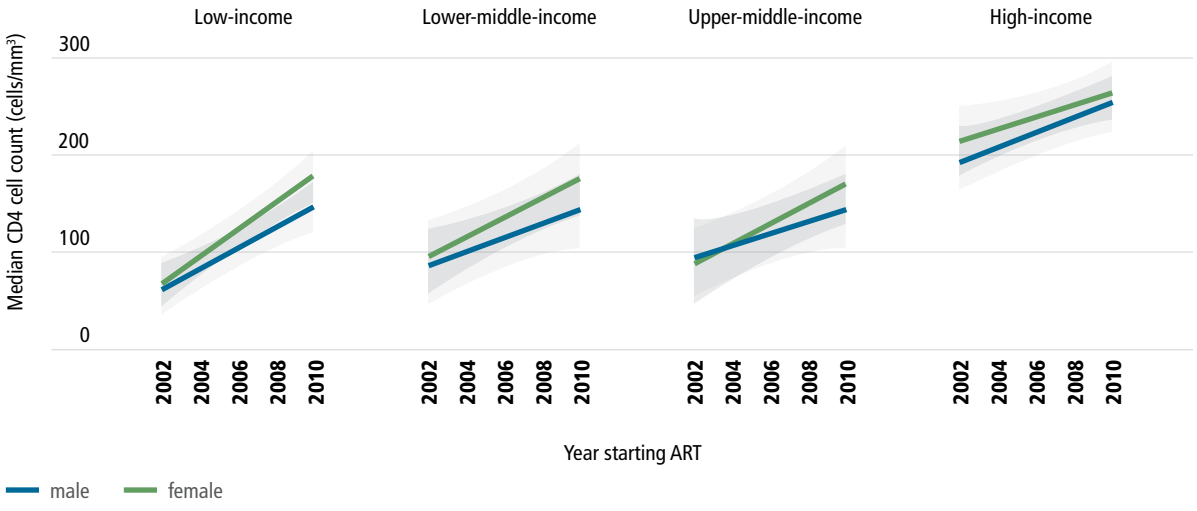
Table 3.5. Policies on initiating antiretroviral therapy in low- and middle-income countries, by WHO region

WHO region	Based on CD4 count			TB and HIV coinfection		Serodiscordant couples
	≤200	≤350	≤500	≤350	Any	
African Region	4[a]	37	2	6	23	6
Region of the Americas	1	20	2	0	17	4
South-East Asia Region	1	7	0	3[b]	7	2
European Region	0	11	1	2[c]	10[d]	5
Eastern Mediterranean Region	1	9	0	3	4	0
Western Pacific Region	1	5	0	1	4	2
Total	8	89	5	18	65	19

[a] One country <250
[b] One country at CD4 (<500)
[c] One country at CD4 (<500); one country (<350) for WHO stage I and II, otherwise at any CD4
[d] One country at any CD4 (in case of the following forms of TB: extra pulmonary; generalized; miliary; disseminated pulmonary) and WHO clinical stage IV

Sources: WHO survey on antiretroviral use, 2012; Gupta et al. *(76)*; Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

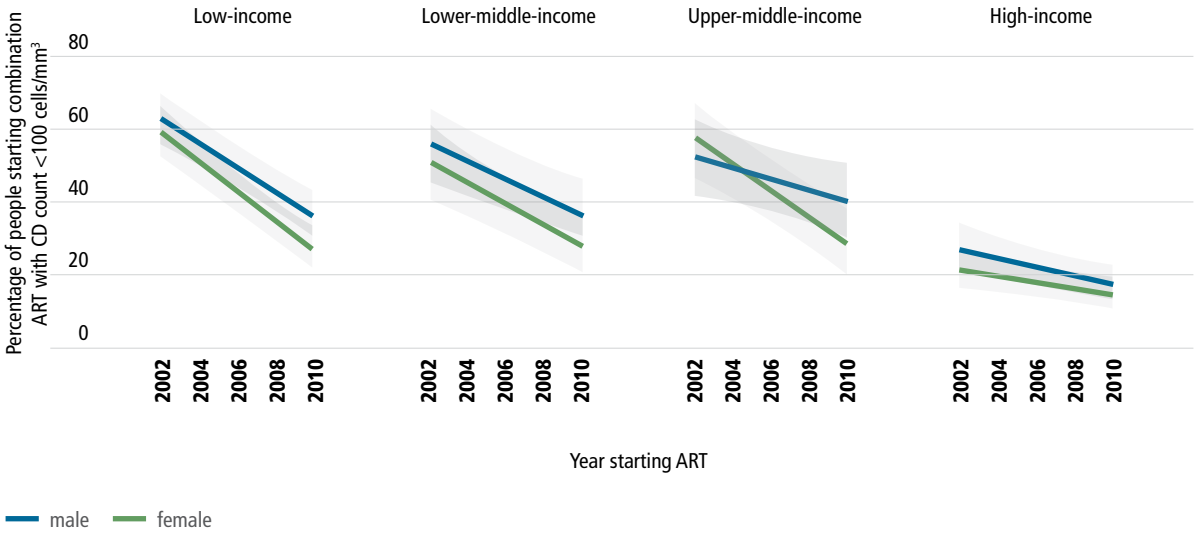
Fig. 3.6. Median CD4 count when initiating antiretroviral therapy, by sex in low-, middle- and high-income countries, 2002–2010



Source: Mugglin et al. *(78)*.

However, in all regions the average CD4 cell count when initiating ART remains far lower than the recommended threshold currently used in most countries and considerably lower in low- and middle-income countries. Significant proportions of people still present with advanced immunosuppression (CD4 cell counts ≤100 cells/mm³). According to cohort data, about one quarter of the people in low- and middle-income settings start ART with a CD4 count <100 cells/mm³. This is a major reason for the high mortality rates observed during the first months of ART *(6,79)*. Generally, men are more likely than women to begin treatment late (Fig. 3.7) *(78)*. A solid understanding of such persistent late presentation is urgently needed. Although the policy evolution towards initiating ART earlier is important for reducing HIV incidence and mortality, these data highlight the need to remain focused on identifying the people who most urgently need ART.

Fig. 3.7. Proportions of men and women starting antiretroviral therapy with CD4 <100 cells/mm³ in low- and middle-income countries, 2002–2010



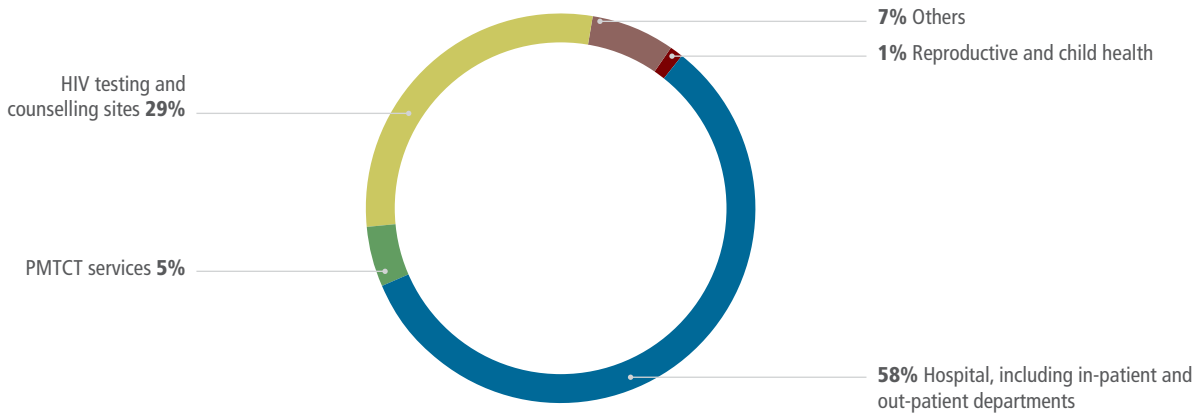
Source: Mugglin et al. *(78)* with additional data provided by the authors.

Initiating treatment among children living with HIV

Country data on the ages at which children initiate ART remain limited. In 2012, UNICEF and WHO supported rapid assessments of care for children in Swaziland, the United Republic of Tanzania and Zimbabwe. In Zimbabwe, the median age when initiating ART was 7 years; most children were referred from hospitals, which indicates that they had already presented with AIDS-related conditions or they "progressed slowly". In the United Republic of Tanzania, the median age at initiation was 4.3 years, and only 15% of children initiating ART were referred from the PMTCT programme. In Swaziland, the median age when initiating ART was 4.9 years in 2010 and 3.4 years in 2011 *(80)*. Fig. 3.8 depicts the main entry points through which children initiate ART.

The late initiation of treatment reflects several weaknesses in the treatment cascade, ranging from inadequate identification of children living with HIV to weak linkage to care *(9)*.

Fig. 3.8. Entry points for initiating antiretroviral therapy among children 0–14 years old, 2010



Source: *A rapid assessment of paediatric care and treatment in four countries: Swaziland, Tanzania, Uganda and Zimbabwe (80).*

Initiating treatment among pregnant women living with HIV

Providing ART to treatment-eligible women in PMTCT programmes has been a longstanding challenge, since it involves accessing CD4 testing and ART at decentralized maternal and child health clinics. According to the 2010 WHO treatment guidelines *(75)*, all pregnant women living with HIV should be assessed for eligibility for ART and should receive ART if they are eligible (CD4 ≤350 cells/mm^3 or Stage 3 or 4 clinical disease). Using these criteria, an estimated 40% of the pregnant women living with HIV would be eligible for treatment.

Among low- and middle-income countries, 64% of pregnant women with HIV-positive test results were subsequently assessed for eligibility for ART in 2012, up from 57% in 2011. Despite this improvement, the fact that one third of the pregnant women diagnosed with HIV had not been assessed for eligibility for ART constitutes a major missed opportunity for initiating ART and ensuring that appropriate ARV regimens for PMTCT are provided. Among women who were assessed in 2012, around 75% were assessed by CD4 count and the rest were assessed by clinical staging only. Regions and countries vary widely, however. The largest increases in ART eligibility assessment were reported in the WHO African Region and the WHO European Region.

WHO issued a technical update in 2012 detailing the advantages of Option B and Option B+ (which involve starting all pregnant women living with HIV on triple ARV medicines) *(81,82)*. Since then, many of the Global Plan priority countries have begun or are planning to provide ART to all pregnant women diagnosed with HIV, regardless of their immune status (Table 3.6) *(81,82)*.[1]

The 2013 WHO ARV guidelines *(50)* recommend that all pregnant women living with HIV initiate ART and that, in most settings, women should continue with lifelong treatment. For the women who are not eligible for ART for their own health, countries will decide their own national policies on the need to continue treatment versus stopping ART after the labour, delivery and breastfeeding risk periods for HIV transmission have ended.

Table 3.6. Regimen policy for preventing the mother-to-child transmission of HIV among pregnant women living with HIV in the 22 priority countries of the Global Plan, as of May 2013

Country	PMTCT regimen policy after WHO 2010 ARV guidelines	Current PMTCT regimen policy as of May 2013	Implementation status of ART for all pregnant and breastfeeding women living with HIV (Option B or B+)
Angola	B	B+	Select regions
Botswana	B	B	National
Burundi	B	B	National
Cameroon	A	B+	Planned
Chad	B	B	National
Cote d'Ivoire	B	B	National
Democratic Republic of the Congo	A	B+	Planned
Ethiopia	A	B+	Select regions
Ghana	A	B	National
India	A	B	Select regions
Kenya	A	A/B	Select regions, planning to move to B+
Lesotho	A	B+	National
Malawi	B+	B+	National
Mozambique	A	B+	Select regions
Namibia	A	B+	Planned
Nigeria	A/B	A/B	Select regions
South Africa	A	B	National
Swaziland	A	A	Piloting B+ in select regions
United Republic of Tanzania	A	B+	Planned
Uganda	A	B+	National
Zambia	A	B+	Planned
Zimbabwe	A	B+	Planned

Option A (maternal AZT); Option B (initiation of ART to all pregnant women living with HIV, lifelong if treatment-eligible, or through end of the mother-to-child transmission risk period if not eligible for treatment); Option B+ (initiation of lifelong ART for all HIV-positive pregnant and breast-feeding women).

Implementation of new regimen (either Option B or B+) in select regions or nationally where implementation is defined as: 1) sites selected; 2) staff training completed; 3) ART regimens available at site and supply chain management system in place.

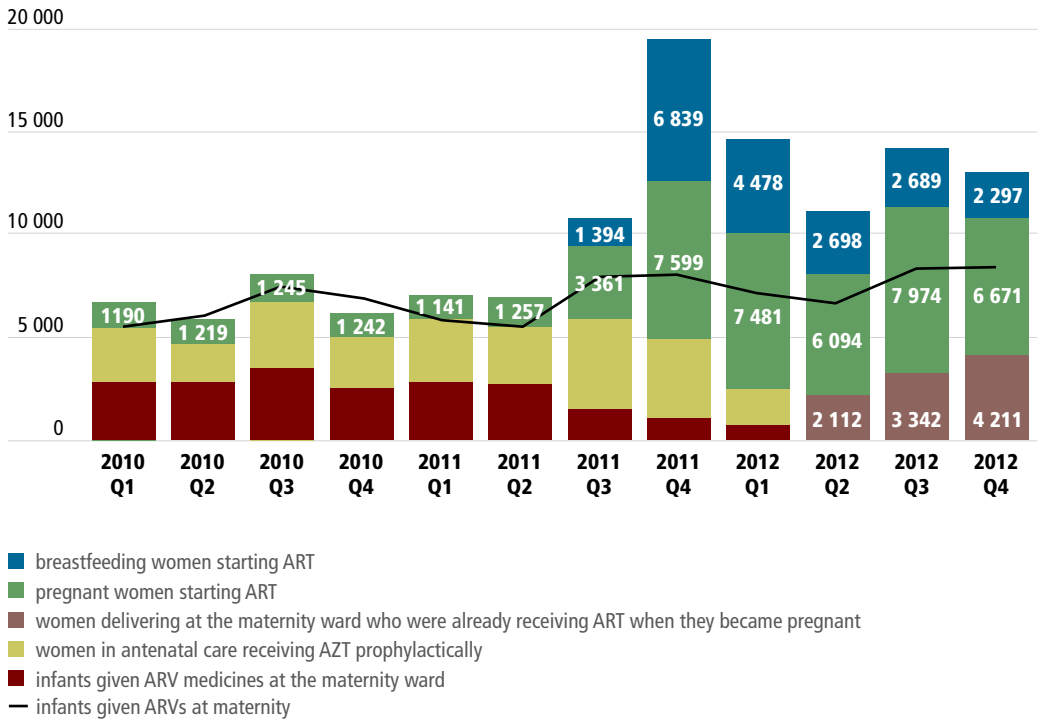
Source: unpublished reports from IATT Country Focal Points, IATT Secretariat (www.emtct-iatt.org), WHO

1. For Option B, this entails discontinuing treatment after the delivery and breastfeeding mother-to-child transmission risk period, whereas for Option B+ it involves lifelong ART.

Box 3.9. Implementing Option B+ in Malawi

In mid-2011, Malawi began implementing a policy of universal lifelong ART for all pregnant and breastfeeding women living with HIV, regardless of their CD4 count or WHO clinical stage. This approach has become known as Option B+.

Fig. 3.9. Transition from prophylactic antiretroviral regimens for preventing mother-to-child transmission to Option B+ in Malawi



Women who moved to Option B+ from single-dose NVP or AZT were counted twice between the third quarter of 2011 and the first quarter of 2012. A total of 12 000 women were probably receiving ARV medicines during these quarters. The data for women who were already receiving ART when they became pregnant are only available from the second quarter of 2012.

Source: Department of HIV/AIDS, Ministry of Health, Malawi.

Monitoring and evaluation had revealed significant difficulties affecting access to the previous ARV regimens for PMTCT and to ART for pregnant women. Most pregnant women living with HIV access care at peripheral health centres in Malawi, and delivering uninterrupted, quality-controlled CD4 count testing at more than 570 antenatal clinic sites was considered unrealistic. In addition, stopping ART after breastfeeding ended for a subset of women would have confused the public health messages about the need to continue ART for life. It also would have led to a start-stop-start approach to treatment, because of the lengthy average duration of breastfeeding (24 months), high fertility (six births per woman) and short birth intervals *(83)*.

Malawi selected TDF + 3TC + EFV for Option B+ because of the low risk of side effects and because this regimen is available as a daily fixed-dose combination tablet. The rollout of Option B+ was completed within nine months and involved retraining more than 4500 health workers and decentralizing ART services from 303 to more than 650 facilities.

Option B+ has effectively merged Malawi's PMTCT and ART programmes; all maternal and child health sites have become ART sites. This had led to simplified protocols and integrated clinical HIV guidelines for pregnant women, children and adults. Other improvements include an

integrated supply chain for all HIV commodities and one monitoring and evaluation and reporting system. Centrally coordinated, quarterly supervision visits to all sites has been a key feature of Malawi's ART programme, and this system has been expanded to include all new sites for PMTCT and ART services.

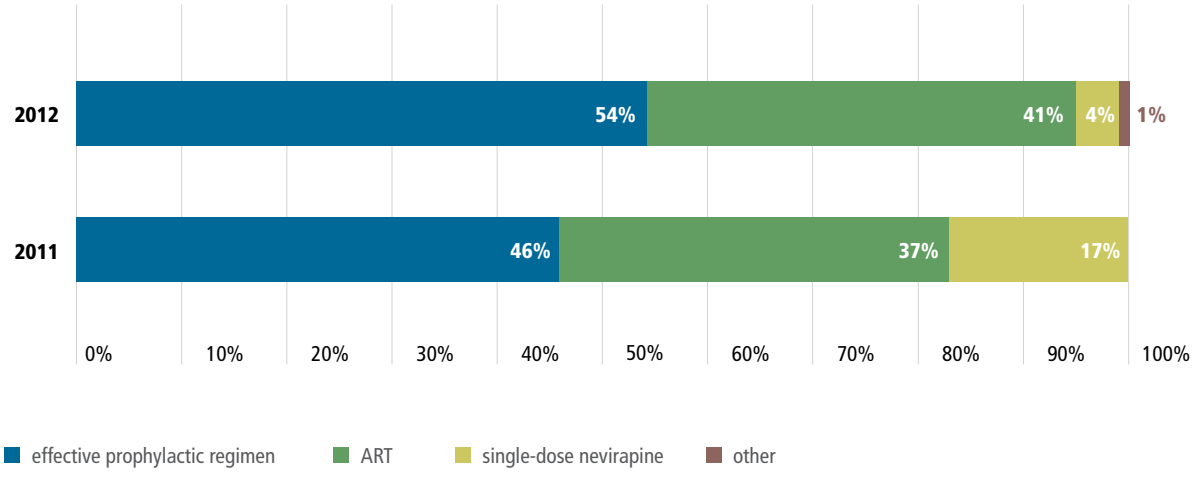
During an 18-month period in 2011–2012, almost 57 000 women started ART under Option B+, of whom 64% started in pregnancy and 36% while breastfeeding. Option B+ is expected to result in a rapid increase of coverage of ART among women of reproductive age living with HIV, offering optimal protection for subsequent pregnancies regardless of the timing of the first antenatal care visit. Data on the number of women who were already receiving ART when they became pregnant have been collected since July 2012. Between October and December 2012, 39% of the almost 11 000 women who were receiving ART during pregnancy had initiated ART before becoming pregnant.

The early data on retention rates are encouraging. In the first 18 months of implementing Option B+, 83% of women were retained on ART 6 months after ART initiation and 78% after 12 months. This is similar to the retention rates in the general ART cohort. Retention on Option B+ is expected to increase as sites gain experience with optimal patient education, preparation and follow-up.[1]

Phasing out single-dose nevirapine prophylaxis for preventing mother-to-child transmission

Significant progress has been made in phasing out single-dose nevirapine (NVP) prophylaxis for PMTCT (which WHO has not recommended for use since 2006). In the Global Plan priority countries, the percentage of women receiving only a single-dose of NVP decreased from 17% to 4% between 2011 and 2012.

Fig. 3.10. Percentage distribution of various antiretroviral regimens provided to pregnant women in 21 African priority Global Plan countries



Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

1. More details on Malawi's ART programmes and PMTCT programmes for are available at www.hivunitmohmw.org/Main/AntiretroviralTherapy, including a current set of data on access and retention on Option B+.

Choosing optimal regimens

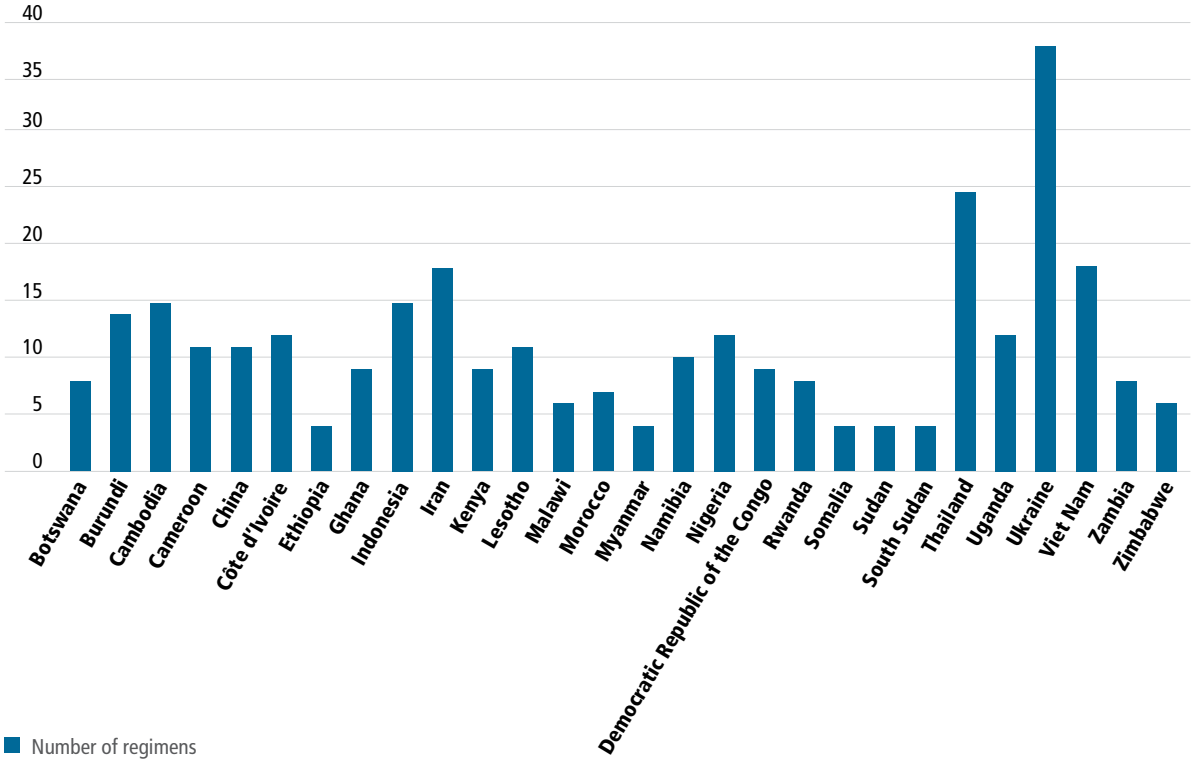
Successive WHO guidelines for ART during the past decade have sought to simplify treatment by reducing the number of recommended drugs, harmonizing regimens across different populations and age groups and promoting once-daily, fixed-dose combinations to simplify drug management and improve adherence *(84)*.

Fixed-dose combinations have been shown to provide significant benefits compared with separate tablets, including improved adherence and treatment outcomes *(85)* and reduced risk of treatment interruptions during stock-outs *(86)*. There are also indications that they are more cost-effective than separate tablets *(87)*. In line with the Treatment 2.0 framework, the 2013 WHO ARV guidelines recommend a single, preferred regimen of TDF + 3TC or FTC + EFV *(50)*, which is available as a once-daily fixed-dose combination and can be used for most people. As countries shift toward TDF-based regimens, the use of fixed-dose combinations should continue to be given priority.

Recent surveys show that many countries still have room for improvement. According to data from 80 countries that responded to WHO's 2012 annual survey on the use of ARV medicines, the number of first-line ART regimens per country ranged from a minimum of 4 to a maximum of 38 with a median of 10 (Fig. 3.11) *(77)*. A 2011 Pan-American Health Organization study found that countries in the Americas were using an average of 12 first-line regimens and 15 second-line regimens for adults, including several drugs that were no longer recommended for use because of high toxicity (such as d4T) or low efficacy (such as nelfinavir) *(14)*. Countries are advised to reduce the number of first-line regimens they use to reduce market segmentation, simplify prescribing and make procurement more efficient.

In the next 2–5 years, there is potential for further improving the alignment and sequencing of first- and second-line regimens for adults living with HIV, pregnant women living with HIV, people with TB and HIV and children older than three years living with HIV. Dolutegravir and darunavir are among the drugs considered to have the potential to improve treatment outcomes in the short term. In the longer term, current first- and second-line ART regimens are expected to be improved further as new drugs and innovative strategies (such as induction maintenance, long-acting formulations, anti-latency drugs and gene therapy) become available *(88)*.

Fig. 3.11. Number of first-line antiretroviral regimens used in selected countries, 2012



Source: *Use of ARV medicines by December 2011 based on the WHO survey in low- and middle-income countries (77).*

Box 3.10. South Africa adopts fixed-dose combinations

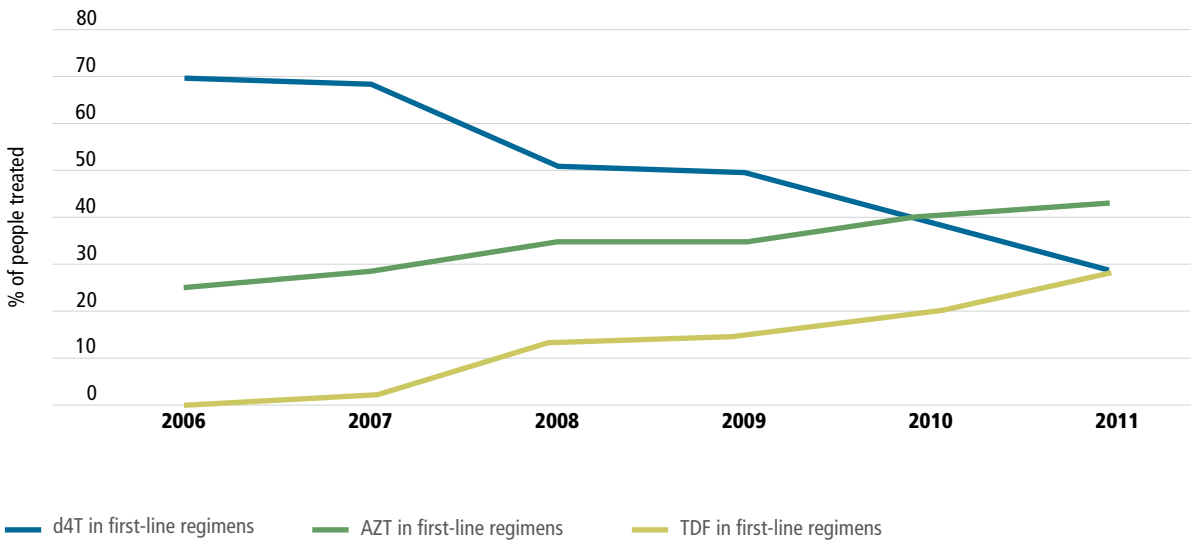
South Africa adopted a fixed-dose combination formulation of TDF + FTC + EFV as preferred first-line ART in April 2013 after successfully negotiating a price of about US$ 113 per person per year. Health workers and civil society groups have applauded the decision as an important step towards simplifying treatment from the perspective of both the people receiving ART and providers. Fixed-dose combinations are promoted in other infectious disease areas, notably malaria and TB, to limit the emergence of drug resistance. In HIV, fixed-dose combinations have been shown to offer multiple advantages over separate pills, including reduced risk of stock-outs *(86)*, improved user-reported quality of life *(89)* and improved adherence, notably among groups considered at to be at higher risk of non-adherence *(85)*. For these reasons, the WHO 2013 ARV guidelines *(50)* give preference to fixed-dose combinations.

Phasing out d4T

In 2010, WHO recommended that countries shift away from using d4T because of commonly reported toxicity issues and instead opt for AZT and TDF. In Lesotho, for example, people receiving d4T were almost six times more likely to experience a toxicity-driven regimen switch compared with people receiving TDF *(90)*, while in Cambodia, more than 90% of the people receiving ART had switched from d4T within six years of initiation because of toxicity *(91)*. These concerns have led to a progressive decline in the use of d4T globally over the past five years (Fig. 3.12).

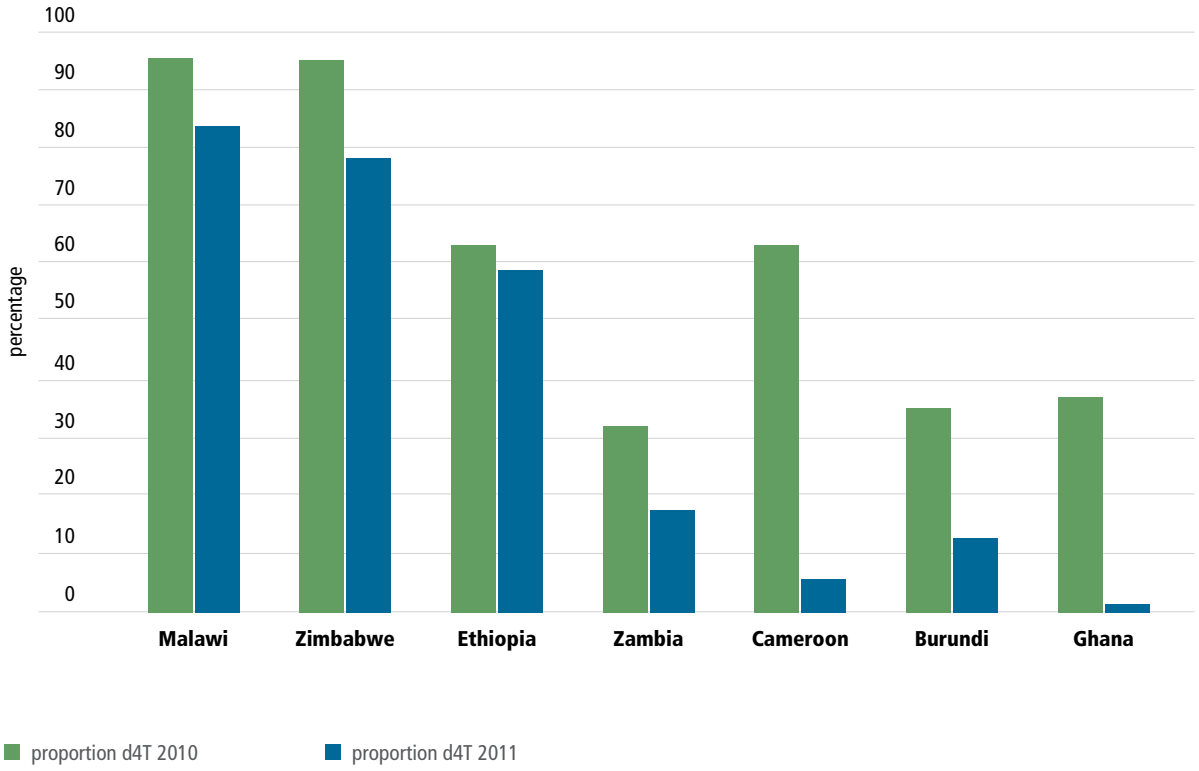
However, as Fig. 3.13 shows, the shift has been uneven, since some countries with a high burden of HIV infection have not yet phased out d4T. In 2011, about 1.1 million people were still being newly initiated on d4T-based first-line regimens, the vast majority in resource-limited settings with a high burden of HIV infection in the WHO African Region. Elsewhere, a few countries with significant HIV epidemics have been slow to phase out d4T. The latest WHO ARV survey *(77)* shows that, at the end of 2011, 31% of the people receiving ART globally were taking d4T-based regimens, and only 7% were taking the preferred first-line regimen of TDF + 3TC (or FTC) + EFV. Renewed efforts are needed to replace d4T, preferably with a TDF-based regimen in line with the 2013 WHO ARV guidelines (Box 3.11.) *(50)*.

Fig. 3.12. Trends in d4T, AZT and TDF use in first-line antiretroviral therapy regimens for adults in low- and middle-income countries, 2006–2011



Source: *Use of antiretroviral medicines by December 2011 based on the WHO survey in low- and middle-income countries (77).*

Fig. 3.13. Varied progress in phasing out d4T in selected countries in the WHO African Region at the end of 2011



Source: *Use of ARV medicines by December 2011 based on the WHO survey in low- and middle-income countries (77).*

Box 3.11. Funding support for phasing out d4T

At the end of 2012, the Global Fund to Fight AIDS, Tuberculosis and Malaria was supporting the provision of ART to 4.2 million people, up from 1.4 million five years earlier. A review to assess countries' progress in implementing the 2010 WHO treatment guidelines found that the majority of 85 countries receiving Global Fund support to deliver ART had made a policy shift away from regimens containing d4T by the end of 2012. Progress had initially been slow in some countries, but the Global Fund, working with technical partners and countries, accelerated the transition by supporting reprogramming within current grants and by providing new funding as part of a shift to a new funding model. The Global Fund continues to work with technical partners, especially WHO, to complete the shift away from d4T-based regimens.

In June 2013, UNITAID announced a proposal for a strategic collaboration with the Global Fund and WHO to accelerate phase out of d4T in favour of the preferred TDF-based first line. The collaboration, which will be confirmed in the third quarter of 2013, would support accelerated phase out by providing up to US$ 77 million to subsidize the cost of switching, negotiate lower prices with manufacturers and ensure timely supplies.

Optimizing antiretroviral therapy for children

Treatment recommendations for children should be relatively straightforward to implement at all levels of the health system, including the primary care level. However, this has not always been the case. Child-friendly drug formulations such as liquids, sprinkles, scored tablets and palatable tastes, co-formulations and fixed-dose combinations are often unavailable, creating difficulty in optimizing drugs and simplifying regimens.

Many infants who have acquired HIV infection perinatally and who have been exposed to NVP via maternal treatment, prophylaxis or treatment after prophylaxis for PMTCT have acquired viral resistance. Surveillance data have shown a prevalence of NVP resistance of up to 60% among children younger than 18 months who underwent virological testing *(92)*. The scaling up of ART in children therefore should promote the regimens that are most likely to be effective. For infants and children younger than three years of age, the preferred treatment regimen is an LPV/r-based regimen. However, the current lack of availability of appropriate formulations remains a challenge. New formulations and fixed-dose combinations are needed.

The WHO 2013 ARV guidelines *(50)* aim to further reduce barriers to children initiating treatment and to simplify programme management by recommending ART for all children living with HIV younger than five years, irrespective of immune status.

Co-trimoxazole prophylaxis for children

Co-trimoxazole is critically important for increasing survival among HIV-exposed and HIV-infected children *(93)*. It has also been shown to reduce overall infection rates (especially malaria and sepsis episodes), including among children living with HIV who are clinically stable on ART and who have achieved successful immune recovery *(94)*.

Although co-trimoxazole has been recommended since 2006 *(95)* as an essential component of the HIV care package, only 31% [26–37%] of HIV-exposed infants in the low- and middle-income countries (based on 2011 estimates) that reported those data received co-trimoxazole in 2011. Nevertheless, this did mark an increase from the 26% [22–30%] coverage reported in 2010. The increase largely resulted from progress made in countries in eastern and southern Africa, where coverage improved from 31% [29–35%] in 2010 to 42% [37–49%] in 2011. Preliminary data from 2012 show that coverage continued to expand, with 6 of the 22 priority countries in the Global Plan achieving at least 50% coverage. Overall access to co-trimoxazole remains too low, however.

Expanding access to co-trimoxazole prophylaxis requires a set of interrelated interventions, including strengthening links between HIV testing and treatment and establishing mechanisms to identify and follow up HIV-exposed infants at and after birth. Integrating co-trimoxazole provision with immunization services that are provided as part of routine maternal and child health clinic activities may help to improve co-trimoxazole coverage.

Box 3.12. Policy changes towards the rational use of co-trimoxazole in resource-limited settings *(96)*

Co-trimoxazole is a broad-spectrum antimicrobial agent that targets a range of bacteria, fungi and protozoa. Co-trimoxazole is on the essential medicines list of most countries. Providing co-trimoxazole has been part of the standard of care for preventing *Pneumocystis jirovecii* pneumonia and toxoplasmosis since the early 1990s. A survey of 81 guidelines from 50 resource-limited settings has shown a significant increase in the number of countries that have issued policy directives for using co-trimoxazole since WHO issued its 2006 guidelines recommending such an approach.

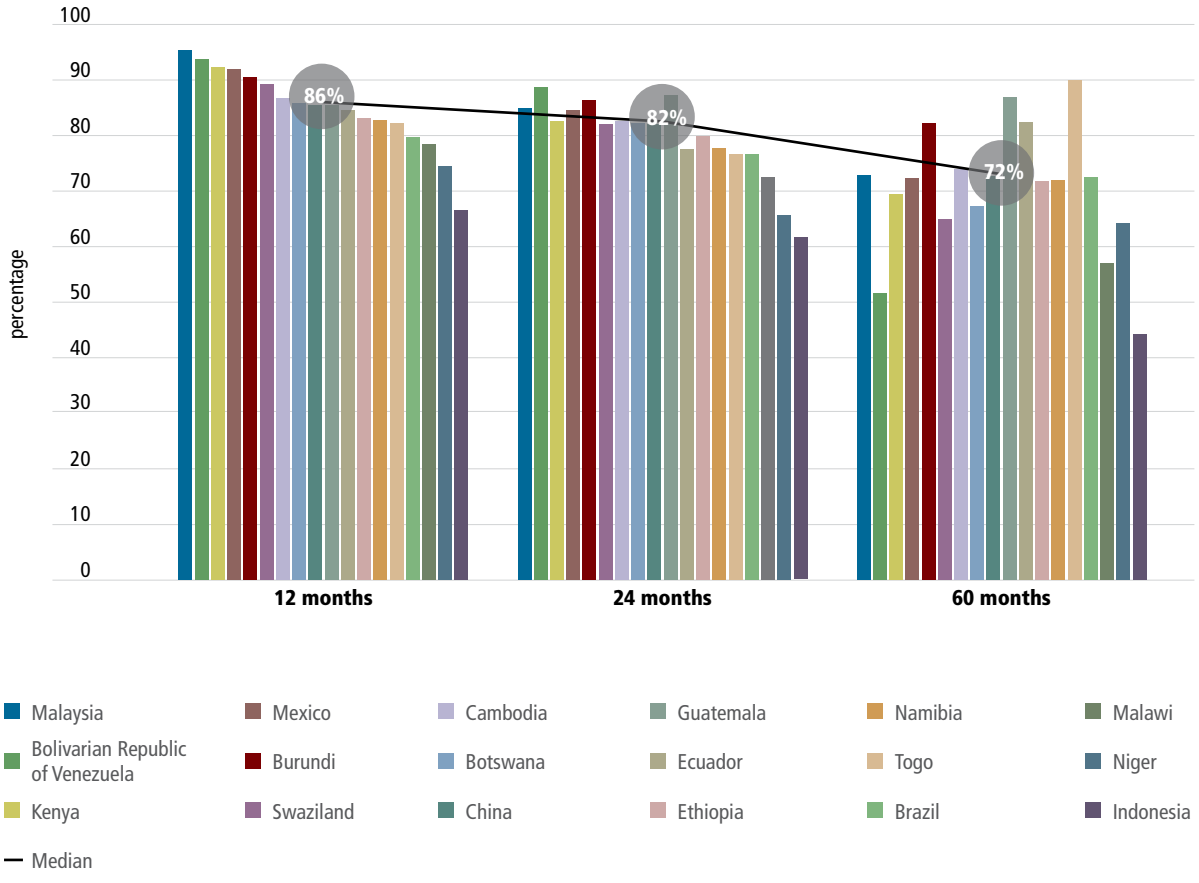
Antiretroviral therapy for older populations

HIV infection among people older than 50 years has attracted attention in high-income countries but less so in resource-limited settings, in which it has previously been assumed that people living with HIV do not live long enough for this to be a major concern. However, as life expectancy among people receiving ART improves, there is growing realization that HIV among older people is an important issue. A recent report from ART programmes in 9 countries in the WHO African Region indicated that more than 1 in 10 people initiating ART were aged 50 years and older and that the mortality of those receiving ART was higher compared with the rest of the adult cohort *(97)*. Cardiovascular disease, diseases of the nervous system, mental disorders, cancer and musculoskeletal disorders appear to be more pronounced in older individuals living with HIV *(98)*.

Supporting adherence and retention in care

Retaining people receiving ART in care and ensuring good treatment adherence are critical determinants of successful ART outcomes. Data reported in 2013 for 23 countries with cohorts of at least 2000 people on ART indicate that the average retention rates tend to decrease over time, from about 86% at 12 months to 82% at 24 months and 72% at 60 months. However, as Fig. 3.14 shows, retention rates at 60 months appear to vary considerably between countries.

Fig. 3.14. Antiretroviral therapy retention rates (%) at 12, 24 and 60 months reported by selected low- and middle-income countries, 2012



Source: 2013 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

Estimates for retention in care are often based on health facility reports, which do not always describe the outcomes of the people who are not retained in care. One systematic review has indicated that 33–48% of the people who are lost to follow-up after initiating ART had in fact died, and a further 12–54% of those lost to follow-up were "self-transfers" and were accessing care elsewhere *(6)*; more recent data from South Africa show that 13% of the people initiating ART transferred out within 2.5 years *(99)*. These findings highlight the complexity of ascribing treatment outcomes to people who appear to be lost to care and underline the need for information systems that can ascertain the vital status of people who move in and out of the health care system.

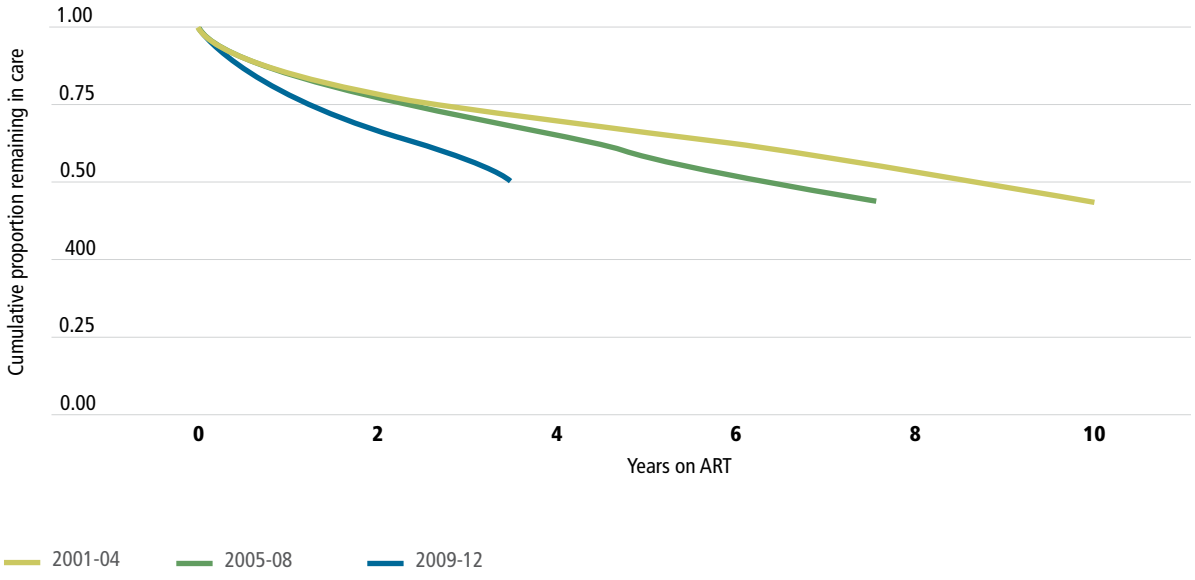
As ART programmes mature in resource-limited settings, more positive long-term outcomes are being observed. For example, programme data from South Africa showed that over 50% of the people initiating ART in 2001 were still in care at the end of 2011 (Fig. 3.15). However, the rates of loss to follow-up appear to be higher in the most recent years, possibly reflecting mounting health system challenges in managing larger cohorts of people *(100)*.

Comparable retention rates have been reported in generalized epidemics and among key populations in some concentrated HIV epidemics. A recent evaluation of the first five years of ART provision among people who inject drugs in Viet Nam found high retention at 12 months among both the people who injected drugs (82%) and those who did not inject drugs (84%) *(101)*. An earlier study in Guangxi, China reported an 87% retention rate at 12 months among people who inject drugs *(102)*.

People may disengage from care because of conflicting priorities, such as unexpected family obligations or ccompeting work schedules. Some research indicates that intentional reasons for disengagement from care also include dissatisfaction with the quality of services and care received at HIV clinics *(103)*.

On the other hand, several studies in the WHO African Region have shown that decentralizing ART services improves retention in care. In a study from South Africa comparing outcomes from 47 primary health care facilities, 9 district hospitals and 3 regional hospitals, 80% were retained on

Fig. 3.15. Proportion of people remaining in care in Khayelitsha, South Africa, according to the duration of antiretroviral therapy



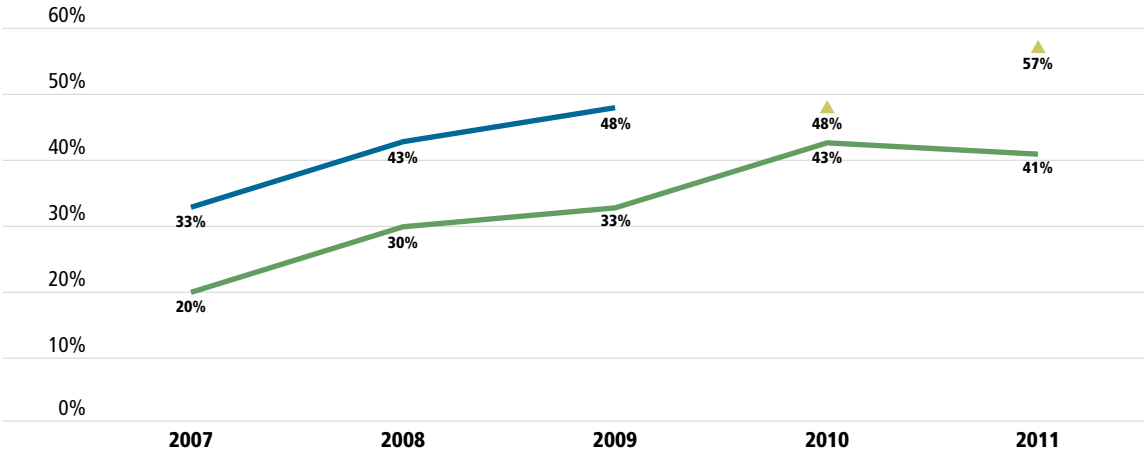
Source: Data courtesy of the Western Cape Provincial Department of Health, South Africa.

ART at primary health clinics compared with 69% at the regional hospitals *(104)*. Data from more than 4000 ART recipients in Thyolo, Malawi, showed that those accessing ART at the hospital were more likely to be lost to follow-up than those using the "lower-level" health centres *(105)*. Positive outcomes were also observed for nurse-managed treatment at the primary health care level in Lesotho *(106)*. The findings have informed the recommendation in the WHO 2013 ARV guidelines *(50)* for decentralizing ART to primary health care services. Although interventions to improve linkage to care require more rigorous evaluation, these and other studies indicate several potential ways to reduce attrition *(11,107,108)*. Table 3.7 summarizes some of the main issues related to health systems, providers and recipients that influence retention and adherence to ART along with potential remedies.

Table 3.7. Barriers to and solutions for improving access and retention in care

Factors related to the health system	Interventions
High direct and indirect cost of care to users	Antiretroviral therapy free of charge at the point of care Decentralizing and integrating ART Facility visits modified according to clinical need Reduce waiting time at the facility level: • patient appointment system; • separate clinical consultation visits from drug refill appointments; • link, integrate and coordinate care; and • family-focused care (organizing services around the need of the family), as appropriate.
Limited patient and family education and counselling, and peer support in HIV care	Engage community health workers, volunteers and people living with HIV for peer support, patient education and community-level support.
Inadequate adherence support	Task shifting for involving community health workers Linkage with community-level interventions such as peer adherence support Patient reminders (including text messaging)
Lack of systems for monitoring retention in care	Systems for patient monitoring across the care cascade, including cohort analysis
Lack of systems for transitioning people across different points of care	Interlinked patient monitoring systems across HIV, TB, maternal and child health and PMTCT services; systems for transitioning from paediatric to adult services
Provider-related factors	
Patient–provider relationships	Training health workers in treatment preparedness, adherence, retention and providing adherence support Prevent stigma in the health sector
Poor patient communication	Simplified approach for patient and family education
Lack of time for patient education	Task shifting and sharing of tasks among clinic team members, team approach to care and consider patient triage
Patient-related factors	
Comorbid conditions, alcohol or drug use, mental health disorder	Co-manage HIV with mental health, substance and alcohol use disorders, social support, community support
Patient knowledge and beliefs related to HIV infection, disease progression and treatment	Integrate patient and family education and counselling, broader community literacy and education and mobilization

Fig. 3.16. Percentage of pregnant women living with HIV and their infants who received antiretroviral medicines for preventing mother-to-child transmission, low- and middle-income countries, 2007-2011[a, b]



- percentage of pregnant women living with HIV who received ARV medicines for PMTCT[c]
- percentage of HIV-exposed infants who received ARV medicines for PMTCT
- percentage of pregnant women living with HIV who received the most effective ARV medicines for PMTCT

[a] The percentages published in previous years may be slighlty different due to the reclassification of low- and middle-income countries over the years. The data above are based on 2012 classifications for all years.
[b] Coverage is based on need estimates generated by the 2012 version of the country Spectrum models.
[c] Coverage in 2010 and 2011 cannot be compared to previous years as it does not include single-dose nevirapine which is no longer recommended by WHO.

Source: *Towards the elimination of mother-to-child transmission of HIV and keeping their mothers alive: abbreviated progress report 2012 (109).*

Antiretroviral medicines for mothers and infants

The substantial disparity between the uptake of ARV medicines for infants and for mothers, respectively, highlights the urgent need to address retention along the continuum of care for PMTCT, especially for its components related to infants. Strategies to reduce the early loss to follow-up of the mother-infant pair are also needed (Fig. 3.16).

Among the estimated 1.47 million infants born to mothers living with HIV globally in 2011, 41% (range of country values 34–49%) received infant ARV prophylaxis. Coverage was similar (43%, range of country values 36–51%) in 2010. The global coverage is primarily limited because of very low coverage in western Africa (about 10%) and low coverage in the WHO South-East Asia Region (36%) and in eastern and southern Africa (53%). In contrast, coverage exceeded 95% in the WHO European Region (which has a relatively small total number of mothers and children affected) and in some countries in the WHO Region of the Americas (including Argentina, Cuba, Guyana and Suriname), while coverage was 87% in Brazil.

Retention in care among children

Improving retention in care for children on ART is critically important. A recent multi-site evaluation assessing ART outcomes among more than 13 000 children found that the risk of loss to follow-up within 18 months of starting ART was 4% in Asia, 9% in southern Africa, 14% in eastern Africa and 22% in western Africa *(110)*.

Recent studies also show that decentralizing care for children can achieve similar or better outcomes than tertiary settings. A five-country study from the WHO African Region (Kenya, Lesotho, Mozambique, Rwanda and the United Republic of Tanzania) reported that children receiving ART were 45% less likely to be lost to follow-up if they accessed it at primary care facilities rather than hospitals *(111)*. The WHO 2013 ARV guidelines *(50)* therefore propose that HIV care for children be decentralized to increase access and strengthen retention in care.

Training and mentorship for health care workers is also needed to facilitate task shifting and allow

ART coverage to be expanded to primary health facilities. In addition, alternative models for providing care, such as family-based models, could facilitate the further expansion of ART coverage and integration of services *(112)*. Increased attention should also be paid to integrating the delivery of HIV services for children with maternal and child health services.

Community-based HIV care and treatment: innovations and opportunities

The combination of decentralizing services and task shifting has accompanied the rapid scaling up of treatment in settings with a high burden of HIV infection including Malawi (113), South Africa (114), Kenya, Mozambique and Swaziland *(115)*. Evidence suggests that task shifting can save time, can increase access to ART and can be cost-effective. Studies in South Africa *(115,116)* have shown that the quality of care generally matches that provided at hospital-based ART clinics and treatment costs are lower in some cases.

Several pilot programmes have reported that involving community-based groups in providing ART has dramatically improved retention (Box 3.13). In addition, a recent systematic review of two randomized trials from Uganda and Kenya and a prospective cohort study in Uganda found than community-based delivery of ART produced good outcomes *(117)*. Dispensing ARV medicines in communities, rather than only at clinics and hospitals, also appears to improve treatment adherence and seems especially effective in keeping men in treatment according to a study conducted in Uganda, the United Republic of Tanzania and Zambia (118). The 2013 WHO ARV guidelines (50) therefore recommend community-supported ART delivery as a strategy to expand care for people receiving ART who are clinically stable.

Community-based interventions that involve peers can address multiple barriers simultaneously and can be used effectively in a wide range of settings. In a cluster-randomized trial in rural Uganda, 15 clinics were randomized to host community-based, peer worker support interventions in which peer health workers received brief HIV training and basic remuneration. The intervention reduced viral failure by 50% at 96 weeks (119).

Some studies suggest that such models, by engaging community workers and peer supporters in the delivery of HIV services, may also contribute to reducing stigma *(120,121)* and to enhancing coverage and access to HIV care and treatment services *(122,123)*.

Box 3.13. Community groups strengthen the delivery of and retention on antiretroviral therapy in Mozambique *(124)*

In partnership with Médecins Sans Frontières, Mozambique's Ministry of Health in 2008 launched an out-of-clinic model for distributing ART, monitoring adherence and promoting support by community ART groups *(125)*. Groups of people receiving ART were formed, with individuals taking turns to collect and deliver ART for their groups, while each group member attended the clinic at least once every six months. Other roles included providing community-based adherence support, monitoring treatment outcomes and establishing a community-based treatment social support network. At the end of 2012, fully 97% of the more than 4000 people enrolled in the community ART groups remained in care. Staff at health facilities reported that the community ART groups facilitated an almost four-fold reduction in formal consultations among people who received community group-based ART care. Mozambique's experience with this approach suggests that it can also reduce the transport and opportunity costs associated with the uptake of ART.

Studies from Uganda *(126)* and Kenya *(127)* provide further evidence of the feasibility of the out-of-clinic approach to providing care and managing ART for people receiving ART who are clinically stable. The approach is also being piloted in several other countries, including the Democratic Republic of the Congo, Malawi and South Africa *(125)* as well as in countries with concentrated epidemics, such as Cambodia. Longer-term evaluation is needed to confirm the effectiveness and sustainability of this approach as a large-scale model for delivering services.

Box 3.14. Community-based scaling up of treatment in Cambodia

Cambodia, which already has achieved "universal access" to ART, has been using a community-based model for scaling up the coverage of ART. The approach involves establishing community linkage so that home-based care teams or self-help groups encourage the people who are at high risk of HIV infection to access HIV testing and counselling. Those who test HIV-positive are then linked to early care and treatment at district-level hospitals. Once these people are enrolled in pre-ART care (with the help of peer volunteers at the hospitals), they are referred back to home-based care teams or self-help groups to be supported in their own communities.

Integrating services for HIV and TB

TB remains a leading cause of death among people living with HIV *(128)*. Reducing the number of people dying from AIDS-related causes therefore requires timely case-finding for both HIV and TB, prompt treatment of both diseases and improved efforts to estimate and monitor progress. The 2013 WHO ARV guidelines *(50)* recommend integrating the delivery of ART into maternal and child health, antenatal care, TB and opioid substitution services.

Efforts to integrate services for people with TB and HIV are underway in many countries. In 2012, 41 of 86 reporting countries indicated that TB clinics provide ART, and 55 of 83 reporting countries indicated that ART clinics provide TB medication. In many cases, different personnel in the same facilities attend to patients, or people with TB are required to attend separate facilities for their HIV care and medicine refills. Effective integration involves overcoming challenges such as these, but the benefits can be huge.

Although the treatment of TB has been decentralized to the community level in most settings, people still have difficulty in accessing HIV treatment in some places with a high burden of HIV infection. Data from the *Global tuberculosis report 2012 (55)* indicate that TB facilities still tend to outnumber ART facilities, even in countries with a very high burden of both diseases. In addition, services for HIV and TB treatment are still sometimes offered at geographically separated sites.

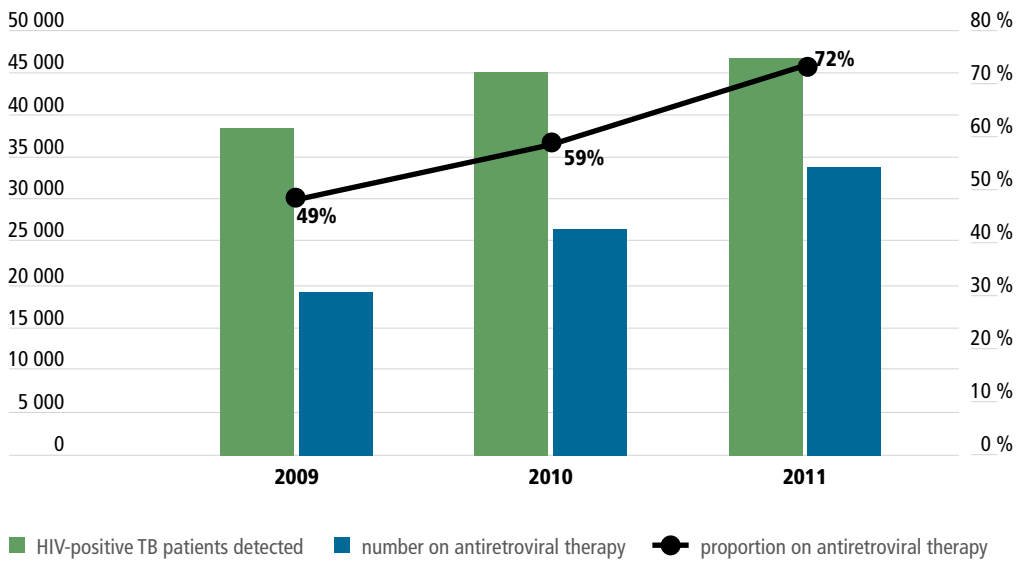
WHO's policy guidance on collaborative TB/HIV activities was updated in 2012 *(129)* and includes initiating ART earlier along with the "three I's" for HIV and TB (isoniazid preventive treatment, infection control for TB and intensified case finding for TB) as key interventions to prevent TB among people living with HIV. ART is recommended for all people with TB and HIV, irrespective of their CD4 count. These recommendations are supported by systematic reviews that show evidence of increased ART uptake and timeliness of initiating ART when it is delivered in TB treatment settings *(130–133)*. Evidence also indicates decreased mortality at sites that deliver ART in TB treatment settings *(131,134,135)*.

Box 3.15. Decentralizing and integrating antiretroviral therapy services for people with TB in India

India has the greatest TB burden and the second-greatest burdens of HIV and of TB and HIV co-infection globally. Although TB is endemic across India, the HIV epidemic is concentrated mainly in six states (Andhra Pradesh, Karnataka, Maharashtra, Manipur, Nagaland and Tamil Nadu). More than 75% of all HIV-infected TB cases notified in 2012 occurred in those states.

India began TB and HIV collaborative activities in 2003. Its 2007 joint national TB and HIV policy framework has guided the establishment of coordinating mechanisms at various levels. Under the current policy, people with TB who are living with HIV receive ART at the same facility as other individuals living with HIV. In accordance with WHO policy, all people living with HIV who have active TB initiate ART irrespective of their immune status. The number of people with TB who are diagnosed with HIV and initiate ART has increased steadily recently; by the end of 2011, about three quarters of the people with both TB and HIV were receiving ART (Fig. 3.17).

Fig. 3.17. Detection of HIV infection among people with TB and linking them to ART in India, 2009–2011



Source: quarterly reports of the National TB Control Programme.

Despite this progress, the case fatality among people with both HIV infection and TB cases in India is four times higher than that among people with TB who are HIV-negative. Timely ART is the most critical intervention for reducing that rate; currently, the median duration for initiating ART after starting TB treatment is more than 40 days, and about 15% initiate ART late (after eight weeks). Recognizing the importance of initiating ART early, India's National AIDS Control Programme is now requiring treatment sites to report on the number of people who have initiated ART within two weeks after starting TB treatment. Linking to ART facilities early and promptly initiating ART will be an important focus of the programme in the years ahead.

Integrating services can increase access to antiretroviral therapy for key populations

Lack of integration of services for people who inject drugs is recognized as a challenge in many parts of the world. Qualitative research in the Russian Federation, for example, has identified the need to integrate HIV, TB and drug treatment services to improve access to ART *(136)*. Some countries are making progress on this front. Viet Nam began expanding the provision of methadone maintenance therapy for people who inject drugs in 2008. Four years later, it was providing methadone maintenance therapy to more 12 000 people at 60 sites in 14 provinces. Increasingly, methadone maintenance therapy is being provided at integrated facilities that also deliver HIV testing and counselling and ART services. People who inject drugs are offered on-site voluntary HIV testing and counselling, and those who test HIV-positive are then linked to HIV treatment and care services. The preliminary results show that men receiving methadone maintenance therapy tend to start ART at significantly higher CD4 counts compared with the overall population of men receiving ART.

Box 3.16. Reaching men who have sex with men, sex workers and transgender populations in Peru

Peru has a concentrated HIV epidemic with a national adult HIV prevalence of 0.4% but much higher prevalence among men who have sex with men (10%) and transgender women (29%). These populations experience severe stigma, discrimination and even violence. Many men who have sex with men and transgender women are highly reluctant to access the HIV and sexually and reproductive health services they need for their health. With support from the International AIDS Alliance, the local nongovernmental organization *Via Libre* runs clinics that provide ART to men who have sex with men and to transgender sex workers as well as screening for and treatment of sexually transmitted infections, family planning counselling and HIV testing. People enrolled in this programme represent 5–6% of the people receiving ART in Peru.

To create an environment that respects the rights of men who have sex with men and of transgender sex workers, the Alliance has developed a model focused on small working groups in various localities. The groups include Ministry of Health service providers and community-based educators, some of who are former sex workers. The groups strive to sensitize communities and reduce homophobia, stigma and discrimination. They also gather high-quality data on access to health and other services for men who have sex with men and transgender women and on rights violations. In 2012, less than 10 of the 1008 people receiving ART were lost to follow-up or transferred to other treatment centres – indicating the strength of this approach.

Support for adherence

A recent review of 26 studies of adherence interventions in sub-Saharan Africa *(137)* indicates that treatment supporters, diary cards, food rations and mobile-phone text messages are potentially effective ways to improve adherence. Access to communication technology has increased exponentially in low- and middle-income countries, with more than 600 million new mobile phone subscriptions in 2011, totalling 78 subscriptions per 100 inhabitants *(138)*. The potential of mobile phone technology to serve as an adherence support tool is gaining attention, especially after positive trial results from Kenya that showed that adherence to ART improved significantly among people who received text-message reminders *(139)*. Supporting adherence through adherence clubs led by people receiving ART is another approach that is being adopted in countries with a high burden of HIV infection (Box 3.17).

Box 3.17. Scaling up antiretroviral therapy in Morocco

In Morocco a considerable number of people needing ART belong to hard-to-reach key populations, including people who inject drugs, sex workers and men who have sex with men. Nevertheless, within less than a decade, the country increased the number of people receiving ART 20-fold, and coverage is one of the highest in the Eastern Mediterranean region.

- In 2012, Morocco conducted 222 000 HIV tests, which led to a 30% increase in the number of people receiving ART. Through public and nongovernmental organization involvement, numerous HIV testing and counselling approaches are used, including fixed-site voluntary counselling and testing, provider-initiated testing across various secondary and tertiary health services, mobile testing services and HIV testing campaigns.
- HIV care and treatment services are decentralized, bringing ART closer to people who are eligible. The country's 15 ART sites cover most of its regions.
- The costs of ARVs have been lowered due to tax exemptions, price negotiations with pharmaceutical companies, the use of generic products, and improved forecasting, procurement and supply systems.
- Domestic funding for ARV and related commodities has increased.
- A national psychosocial support programme was set up with the involvement of a nongovernmental organization to support ART patients with therapeutic education and various forms of social assistance. A medical assistance scheme that fully subsidizes health care services for people living with HIV is being set up.
- Community-support groups provide adherence support, and treatment retention at 12 months is high, at 90%.

Supply of antiretroviral medicines

Stock-outs of ARV medicines are a concern in many low- and middle-income countries. According to a WHO survey *(71)*, the proportion of low- and middle-income countries reporting stock-outs declined from 35% in 2011 (38 of 108 countries) to 30% in 2012 (30 of 98 countries). Several ways of avoiding or overcoming stock-outs have proved successful in recent years. In some countries, people switched temporarily to a different ART regimen (for example, Cameroon, Guatemala and Thailand). In other cases, neighbouring health facilities or regions transferred ARV medicines to enable people to remain on the same ART combinations (for example, in Malawi, Mexico and Nigeria). Other remedial strategies included providing people a three-month supply of ARV medicines (for example, in the Maldives) or purchasing emergency supplies from neighbouring countries (for example, in Benin).

Countries considered to be at high risk of stock-outs may face financial constraints that lead to interrupted supplies of ARV medicines and other health commodities. In 2012, supported by the Clinton Health Access Initiative, UNITAID provided funds for children's and second-line ARV medicines to 21 countries in 2012.[1] The HIV/AIDS Emergency Commodity Fund of the United States President's Emergency Plan for AIDS Relief has also helped preventing stock-outs. In 2012, the Fund supported four countries in averting stock-outs of ARV and opportunistic infection medicines by funding the supply of 1.2 million ARV tablets, 97 000 test kits and 2500 opportunistic infection tablets.

More work is needed to improve drug forecasting, planning several years ahead, ensuring adequate funding and ensuring sufficient buffer stocks at the health facility and central levels.

1. Benin, Botswana, Burkina Faso, Burundi, Cameroon, China, Côte d'Ivoire, Democratic Republic of the Congo, Haiti, India, Malawi, Mali, Mozambique, Nigeria, Senegal, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.

Box 3.18. Treatment adherence clubs in South Africa

In Khayelitsha township, in South Africa's Western Cape Province, more than 25 000 people had started ART by early 2012. As the number of people receiving ART increased, the proportion of those lost to follow-up also began to rise, as clinics became overburdened. In response, Médecins Sans Frontières and the provincial health authorities set up out-of-clinic adherence clubs to support treatment adherence. The clubs meet every two months, either at the facility or at a community venue. Participation is voluntary and open to all adults who have been receiving ART for at least 12 months and who are considered clinically stable (CD4 count >200 cells/mm^3 and with two consecutive undetectable viral load tests).

Lay health workers support the groups by performing essential tasks such as measuring their weight and conducting basic symptom check-ups. The facilitator prepackages medicines for each participant, brings them to the group and refers anyone with symptoms, ill health or weight loss for further health care attention. A nurse at the facility supports the club and is available after each group session to attend to referred club members. All club members receive annual blood tests and annual clinical consultations. They also get repeat prescriptions of ART.

An evaluation of the pilot project involving the first 20 clubs found that retention in clinic care after 40 months was 97% for club members versus 85% for people who qualified for the clubs but were managed at the clinic without participating in the clubs. Participants in the clubs were 67% less likely to experience viral rebound, which indicates better adherence in clubs than in mainstream care *(140)*.

The adherence clubs began as a local solution to a local problem, but the approach is being scaled up. In early 2011, the Western Cape health department adopted the ART club model for a phased roll out starting in the greater Cape Town area. By December 2012, more than 600 adherence clubs were operating in and around the city.

Box 3.19. Antiretroviral toxicity and the need for surveillance

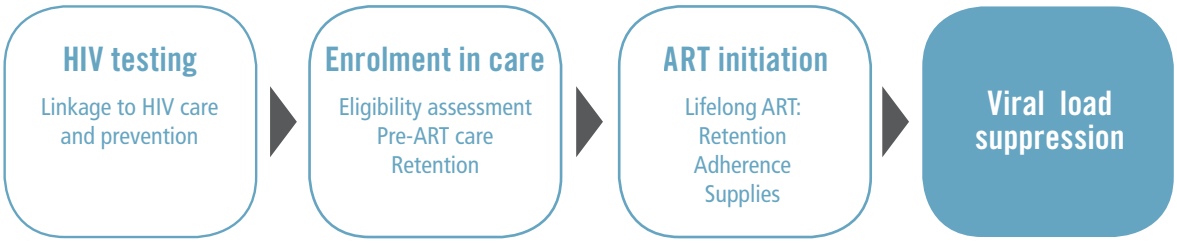
In 2012, WHO commissioned several reviews of ARV toxicity. For TDF, data on the risk of clinical events such as mortality, renal failure and bone fractures were limited and showed no difference between TDF and comparison drugs. In one clinical trial, less than 1% of the people taking TDF had severe renal disease that could be ascribed to TDF among the nearly 2500 adults taking this drug. The trial also showed a very low rate of chronic kidney disease (<6% five years after initiating ART) *(141)*.

A review of NVP and EFV found that patients on NVP were more than twice as likely as those receiving EFV to discontinue treatment because of adverse events. Among pregnant women, adverse events associated with NVP are no more frequent than observed in the general adult population, and although pregnant women with a high CD4 count may be at increased risk of adverse events, the evidence supporting this association is weak *(142)*.

Finally, a review of the safety of EFV in the first trimester of pregnancy found no evidence of increased risk of birth defects, in line with the findings of previous systematic reviews and technical guidance *(143,144)*.

WHO, the United States President's Emergency Plan for AIDS Relief, the United States Centers for Disease Control and Prevention and the United States National Institutes of Health are supporting the establishment of ARV pregnancy registries and birth defect surveillance programmes in Malawi, South Africa and Uganda. Other surveillance programmes have been established in Côte d'Ivoire (to monitor TDF use), Kenya (to monitor overall drug toxicities in adults and children living with HIV), Viet Nam (to monitor EFV and TDF toxicity among people who use ARV medicines mainly to prevent HIV infection, such as in serodiscordant couples) and the Lao People's Democratic Republic (focusing on AZT and NVP). Data from these and other initiatives will help to support improvements in the quality of care and help guide future drug regimen choices.

4 Suppressing viral load



KEY POINTS

Retaining people receiving antiretroviral therapy in care and ensuring good treatment adherence are critical determinants of successful long-term viral load suppression.

- Data from Rwanda showed that 86% of the people receiving ART had viral suppression 18 months after starting treatment. In Senegal, about 80% of the people receiving first-line therapy were achieving viral success after five years on treatment.
- Access to viral load testing remains limited but is increasing rapidly in some countries. For example, Kenya has increased its viral load testing capacity 40-fold, from fewer than 10 000 tests in 2011 to a projected 400 000 tests in 2013.

The goal of ART is to achieve and sustain viral suppression, which has both clinical and public health benefits. Recent studies show that as long as people living with HIV are virologically suppressed they are very likely to remain clinically stable with no change in CD4 count *(145)* and the risk of onward transmission of HIV is significantly reduced *(146)*. Reports from Guinea, Malawi and Mozambique showed that 85% of the people receiving ART had viral suppression within six months of starting *(147)*. Data from a nationally representative multi-site study in Rwanda showed that 86% of the people receiving ART had viral suppression 18 months after starting treatment *(148)*. As for the longer term, data from Senegal showed that about 80% of the people receiving first-line therapy were achieving viral suppression after five years on ART *(149)*.

Viral load testing

In 2010, WHO recommended that countries begin to phase in viral load testing as the preferred approach to treatment monitoring. Few countries with a high burden of HIV infection have the capacity to offer viral load testing routinely to everyone receiving ART, although the ability to test viral load is becoming increasingly available. The 2012 WHO diagnostics survey *(71)*, carried out in 83 low- and middle-income countries, found that about 576 viral load platforms (for either viral load or early infant diagnosis or both) were available in country at the end of 2011. Various approaches have been taken to increase access, including viral load pooling, using dried blood spots and reducing the frequency of testing (Box 3.20) *(150)*. Access to viral load testing is expected to improve significantly in the next few years as point-of-care viral load technologies become available; several such tests are in the final stages of development and are expected to become available in 2013 *(151)*.

Viral suppression among adolescents

Data from both high-income *(152)* and low- and middle-income settings *(153,154)* suggest that ART outcomes for adolescents tend to be worse than for adults. Disclosure of HIV status appears to be one key factor affecting ART outcomes for adolescents, according to recent data from western Africa *(155)*. Other factors include the ease with which the transition from child to adult services is managed and access to appropriate adherence counselling and support.

Box 3.20. Increasing access to viral load testing in Kenya, Malawi and the United Republic of Tanzania

Kenya's national ART guidelines have recommended the use of targeted viral load testing for monitoring treatment failure since 2005. However, funding and sample stability concerns have limited the expansion of viral load testing nationwide. To address these issues, the Ministry of Health convened partners and stakeholders to adopt best practices from the early infant diagnosis programme and to leverage existing national systems. The changes included standardizing viral load testing platforms, introducing national pricing for test reagents and using dried blood spots as the primary sample type which allowed viral load testing to be carried out in remote areas. By standardizing testing platforms, Kenya consolidated test volumes and funding and negotiated favourable reagent pricing. Consequently, Kenya is increasing its viral load testing capacity 40-fold, from fewer than 10 000 tests in 2011 to a projected 400 000 tests in 2013.

Malawi's Ministry of Health established a national programme for viral load testing in 2011, which it has funded with the support of the Global Fund and the United States President's Emergency Plan for AIDS Relief. The Ministry also coordinates the provision of technical assistance from partners. This coordinated effort has leveraged existing molecular laboratory testing capacity from the early infant diagnosis programme, enabling the Ministry to perform 100 000 viral load tests per year. Viral load testing volume is expected to grow from less than 1000 tests in 2012 to a projected 10 000 tests in 2013.

The United Republic of Tanzania has been providing early infant diagnosis services for several years. Four high-throughput automated instruments were deployed in public facilities, with a combined output of close to 160 000 tests per year. However, the early infant diagnosis programme was using only 25% of that capacity. This prompted the Ministry of Health and Social Welfare to roll out viral load testing by using the excess early infant diagnosis capacity. This has led to some equipment being upgraded for both early infant diagnosis services and viral load testing platforms, or relocated, making a total of six viral load testing sites, to improve access and ease the transport of samples. The move enabled the United Republic of Tanzania to perform many more viral load tests than would have been possible if the dedicated budget had been used solely for early infant diagnosis services.

Second-line treatment

The proportions of people receiving first- and second-line regimens vary substantially between regions, according to the latest WHO survey data *(77)*. The variation can be explained by differences in the maturity of the ART cohorts, the availability of viral load testing to diagnose treatment failure and the availability of second-line ART.

In low- and middle-income countries in Latin America and the Caribbean in 2011, 77% of adults on ART were receiving first-line regimens and 21% second-line regimens. In the other regions overall, however, 96% of the adults were receiving first-line drugs and 4% second-line regimens. Notably, in the WHO African Region viral load testing capacity for detecting treatment failure early is not commonly in place, leading to delays in the diagnosis of treatment failure.

Market segmentation remains an important factor affecting the availability of second-line ARVs. While LPV/r remains the predominant protease inhibitor (and is used globally by 86% of those receiving a second-line regimen), 12% of people receiving second-line ART used regimens that are not recommended by WHO, including regimens containing non–protease inhibitors *(77)*. Cost is another limiting factor, as second-line regimens tend to be more widely patented than first-line regimens, and standard second-line regimens tend to cost considerably more than first-line regimens in low- and middle-income countries, and third-line treatment is even more expensive (see Chapter 4).

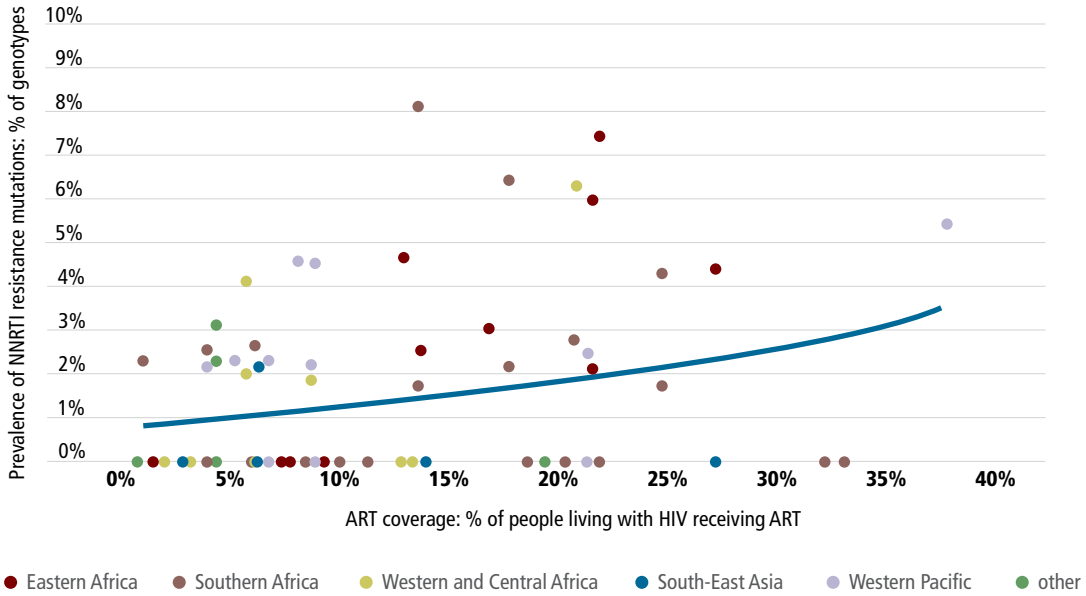
Drug resistance

WHO and partners have been monitoring the emergence of HIV drug resistance since 2004 using standardized protocols to support the identification of optimal first- and second-line treatment regimen choices and to select the most effective approaches for PMTCT and for pre- and post-exposure prophylaxis. The 2012 WHO HIV drug resistance report *(156)* recently published the data collected between 2004 and 2010.

Data from 82 surveys found evidence of increasing levels of transmitted drug resistance to NNRTIs,

particularly in the areas surveyed in the WHO African Region, where the prevalence of resistance to non-nucleoside reverse-transcriptase inhibitors (NNRTI) reached 3.4% (range of country values 1.8–5.2%) in 2009. Greater coverage of ART was associated with a higher prevalence of resistance to NNRTIs (Fig. 3.18), although this association remained modest in most of the areas surveyed.

Fig. 3.18. Relationship between transmitted resistance to non-nucleoside reverse-transcriptase inhibitor drugs and coverage of antiretroviral therapy



Note: p-value adjusted for region: 0.039. Odds-ratio = 1.4 (95% CI 1.07-1.73)

Source: *WHO HIV drug resistance report 2012 (156).*

Further data from 36 WHO surveys of acquired HIV drug resistance in low- and middle-income countries show that the prevalence of resistance to any drug among people starting ART increased from 4.8% [range of country values 3.8–6.0%] in 2007 to 6.8% [range of country values 4.8–9.0%] in 2010 *(156)*. Among people failing first-line therapy after 12 months in 40 WHO surveys, almost 30% failed with no resistance detected and potentially could have been switched unnecessarily to costlier second-line regimens. Among those with detected HIV drug resistance, the resistance patterns observed suggest that, if they were switched to second-line regimens soon after viral suppression fails, standard second-line therapies consisting of two nucleoside analogues and a boosted protease inhibitor would still be effective in achieving viral load suppression in most cases.

Monitoring HIV drug resistance early warning indicators is an important component of global and national strategies to minimize the emergence of preventable HIV drug resistance. Such clinic-level indicators can identify weaknesses in ART programmes, which may result in suboptimal treatment or treatment interruption, and potentially can lead to the emergence of HIV drug resistance. Monitoring of early warning indicators in 50 countries has highlighted the existence of important gaps in service delivery and programme performance, especially in procurement and supply systems, adherence and clinical retention.

As ART continues to be scaled up, the rates of drug resistance may increase, and robust systems for monitoring early warning indicators and surveillance of HIV drug resistance, integrated into national monitoring and evaluation frameworks, must be in place to detect these patterns in a timely manner. National programmes are encouraged to perform routine surveillance of HIV drug resistance to enhance programme planning and management and to inform ART policies.

WHO, through its partner network of collaborating institutions, is committed to monitoring HIV drug resistance globally and to advocate for expanded routine surveillance, using standardized methods and increased mobilization of national and international funds to support HIV drug resistance surveillance.

4. LOOKING FORWARD: EARLIER ANTIRETROVIRAL TREATMENT TOWARDS CONTROLLING THE EPIDEMIC

KEY POINTS

Implementing the 2013 WHO guidelines on the use of antiretroviral medicines for HIV treatment and prevention can prevent considerably more people from dying from AIDS-related causes and acquiring HIV infection

- Fully implementing the 2013 WHO ARV guidelines could reduce the number of people dying annually from AIDS-related causes from 1.7 million in 2011 to about 800 000 in 2025, compared to an anticipated reduction to 1.3 million if the 2010 treatment guidelines were fully implemented.
- Between 2013 and 2025, the total number of AIDS-related deaths averted could increase from 9 to 12 million if the 2013 WHO ARV guidelines are fully implemented.
- Fully implementing the 2013 ARV guidelines could reduce the annual number of people newly acquiring HIV infection in low- and middle-income countries from 2.4 million in 2011 to 800 000 in 2025, compared to an anticipated decrease to 1.25 million if the 2010 treatment guidelines were fully implemented.
- Between 2013 and 2025, the total number of HIV infections averted could increase from 15.5 to 19 million if the 2013 ARV guidelines are fully implemented.
- Achieving this additional impact would require increasing the total annual investment in the HIV response in low- and middle-income countries over the coming years by approximately 10% above the US$ 22-24 billion target included in the *Political Declaration on HIV and AIDS* in 2011. This additional investment can be deemed "very cost effective" according to global criteria.

Current trends in the global scaling up of ART give great cause for optimism. HIV testing and ART delivery for treatment and for PMTCT are increasing in most countries and regions with a high burden of HIV infection. The global target of reaching 15 million people with ART by 2015 appears to be attainable.

Significant improvement is still needed, however, in some regions and countries and for some key populations that are at high risk of HIV infection. As the analysis of the treatment cascade in the previous chapter shows, certain critical steps in the care pathway need to be reinforced to ensure that the maximum number of people benefit from timely HIV treatment and care interventions.

Nevertheless, the past decade has shown that enormous progress can be achieved with sufficient political commitment, funding, technical innovation and community mobilization. Clinical and implementation science continues to devise new tools and methods to support the further scaling up of testing and treatment.

These achievements and the powerful evidence of the life-saving and preventive effects of ART

have informed the 2013 WHO ARV guidelines *(1)*. If implemented, these guidelines are expected to have a major positive impact on the HIV epidemic in the coming years.

Projected impact of the 2013 WHO antiretroviral guidelines on AIDS-related mortality

It is estimated that expanding ART access to more then 80% of people eligible for treatment under the 2010 WHO treatment guidelines could avert 9 million deaths between 2013 and 2025. Initiating ART earlier, as recommended in the 2013 WHO ARV guidelines *(1)*, could increase the number of averted deaths between 2013 and 2025 to more than 12 million, thus preventing an additional 3 million people from dying (Fig. 4.1).

If the 2013 WHO ARV guidelines are implemented, the annual number of people dying from AIDS-related causes in low- and middle-income countries could fall from 1.7 million in 2011 to 800 000 in 2025, compared with a projected 1.3 million if the 2010 eligibility criteria continued to be applied.

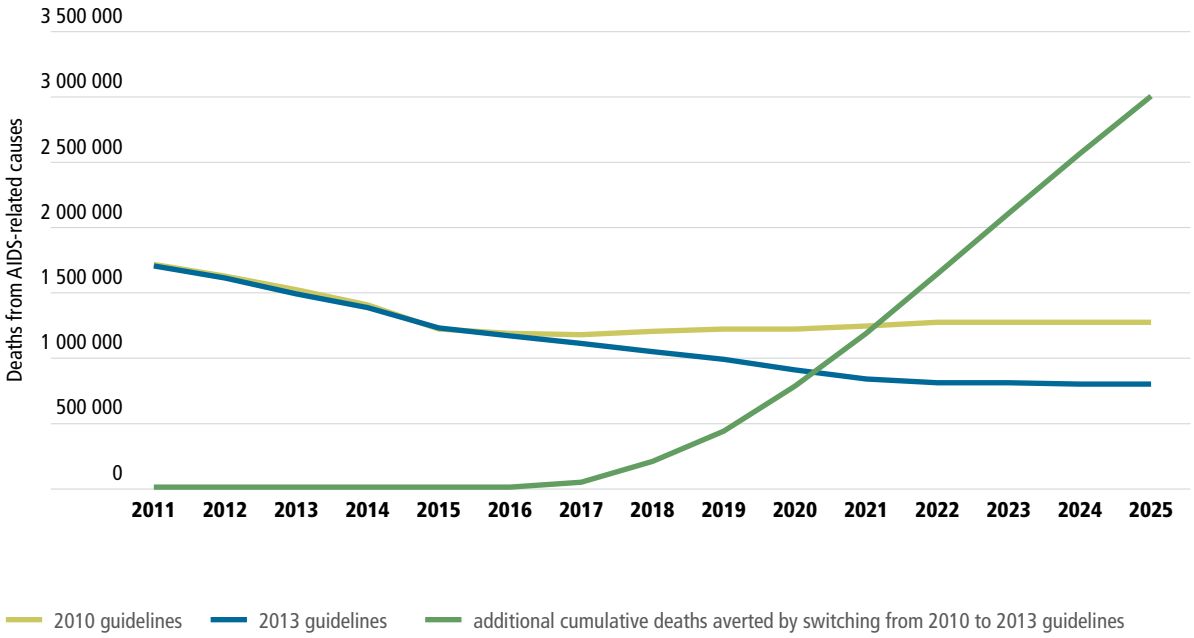
Impact of the 2013 WHO antiretroviral guidelines on HIV incidence

Full implementation of the 2010 treatment guidelines could help avert 15.5 million HIV infections between 2013 and 2025, compared with maintaining current ART coverage levels. Full implementation of the 2013 WHO ARV guidelines could help avert 19 million HIV infections between 2013 and 2025 (Fig. 4.2).

The annual number of people acquiring HIV infection could decline from 2.4 million in 2011 to close to 800 000 globally by 2025, compared with a projected 1.25 million per year if the 2010 eligibility criteria continued to be applied.

Further reductions in the number of people acquiring HIV infection depend on the scale and effectiveness of the existing array of prevention interventions, the use of new interventions such as pre-exposure prophylaxis of HIV and the potential development of effective microbicides and/or an HIV vaccine.

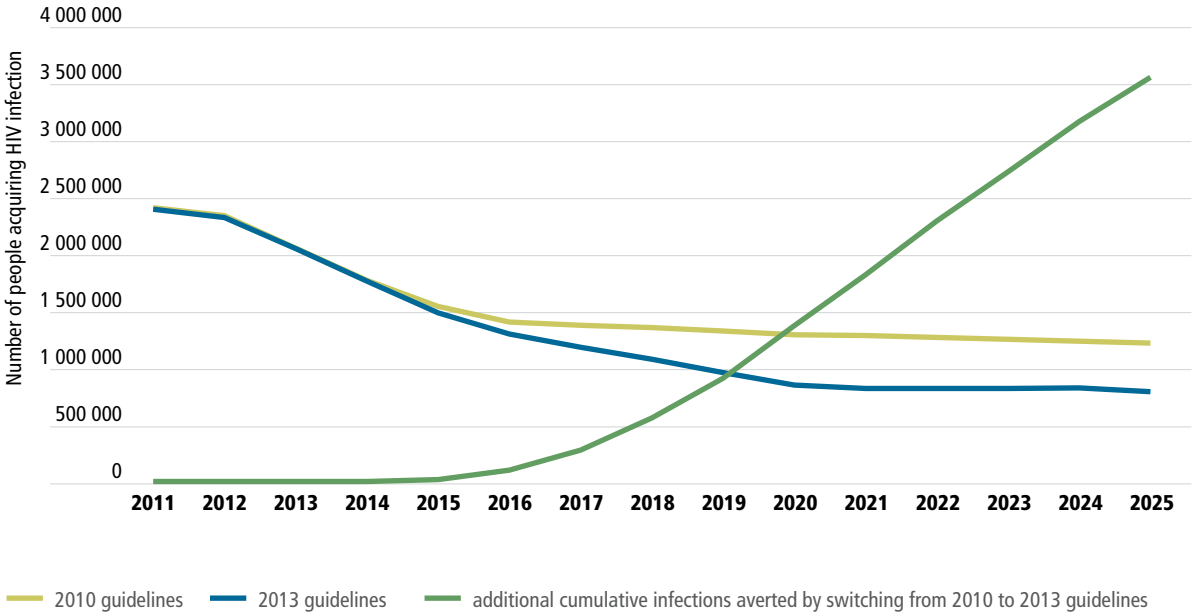
Fig. 4.1. Projected annual number of people dying from AIDS-related causes in low- and middle-income countries based on the 2010 WHO treatment guidelines and the 2013 WHO ARV guidelines and cumulative deaths averted by switching from 2010 to 2013 guidelines, 2011–2025



Source: special analysis conducted by Futures Institute, 2013.

Achieving 80% coverage under the WHO 2010 treatment guidelines implies initiating ART at CD4 ≤350 cells/mm^3 or clinical stages III or IV; achieving 80% coverage under the WHO 2013 ARV guidelines implies initiating ART at CD4 ≤500 cells/mm^3, and for serodiscordant couples, pregnant women living with HIV and children living with HIV younger than five years, initiating ART irrespective of CD4 count.

Fig. 4.2. Projected annual number of adults acquiring HIV infection in low- and middle-income countries based on the 2010 WHO treatment guidelines and on the 2013 WHO ARV guidelines and cumulative number of people avoiding HIV infection by switching from 2010 to 2013 guidelines, 2011–2025



Source: special analysis conducted by Futures Institute, 2013.

Achieving 80% coverage under the WHO 2010 treatment guidelines implies initiating ART at CD4 ≤350 cells/mm³ or clinical stages III or IV; achieving 80% coverage under the WHO 2013 ARV guidelines implies initiating ART at CD4 ≤500 cells/mm³, and for serodiscordant couples, pregnant women living with HIV and children living with HIV younger than five years, initiating ART irrespective of CD4 count.

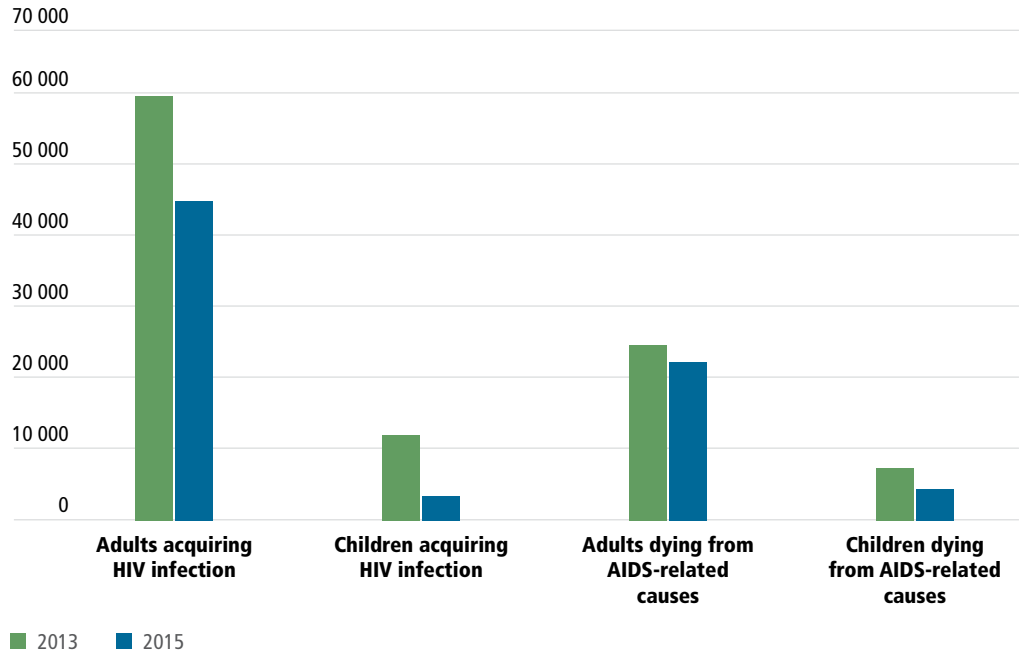
Box 4.1. Impact of the new antiretroviral therapy guidelines on Zambia's epidemic

Zambia is currently assessing the impact of implementing new policies on initiating ART. Preliminary analysis suggests that shifting towards initiating ART at CD4 ≤500 cells/mm³ in Zambia would lead to a small (5%) increase in the number of people eligible for ART – from about 733 000 in 2013 to 763 000 in 2015, with the number then levelling off until 2020. Implementing the 2013 WHO ARV guidelines would yield rapid gains, according to modelling studies.

Adopting the new eligibility criteria would reduce the projected prevalence of HIV infection among adults from 12.4% in 2013 to 11.8% in 2015 and to 10% in 2020. That decrease implies significantly fewer people acquiring HIV infection. Projections indicate that the total annual number of people acquiring HIV infection would drop from 59 600 in 2013 to 45 000 in 2015. The number of children (0–14 years old) acquiring HIV infection would decrease from 11 500 in 2013 to 3130 in 2015 (Fig. 4.3). In contrast, maintaining the current policy of initiating treatment at CD4 ≤350 cells/mm³ would reduce the total number of people acquiring HIV infection from a projected 73 700 in 2013 to 61 900 in 2015.

Overall, estimates indicate that implementing the new eligibility threshold would slightly reduce the number of adults dying from AIDS-related causes: from 24 400 in 2013 to 22 400 by 2015. However, the number of children (0–14 years old) dying from AIDS-related causes would almost halve from 7230 deaths in 2013 to 4260 deaths in 2015.

Fig. 4.3. Projected numbers of adults and children acquiring HIV infection and dying from AIDS-related causes in 2013 and 2015 in Zambia based on the 2013 WHO ARV guidelines



Costs and cost-effectiveness

Estimates from 2011 indicated that an effective global HIV response (including providing treatment based on the 2010 WHO treatment guidelines *(2)* would cost US$ 22 billion to US$ 24 billion annually in 2015 *(3)*.

Countries' abilities to fund their ART programmes vary enormously and depend on the size of their overall budgets, the proportions of those budgets that are allocated to the health sector in general and to HIV programmes in particular, the structure of countries' health systems and the extent of external aid and other forms of assistance that are available. Low- and middle-income countries have increased their own investment in HIV responses in recent years – by an estimated 15% between 2010 and 2011 alone *(4)*. Nevertheless, many low-income countries will only be able to increase their domestic contributions to a limited extent, and many countries will continue to require additional external support. Countries and their external partners have a joint responsibility to fill the treatment investment gap together, by investing their respective fair shares.

Fully implementing the 2013 WHO ARV guidelines *(1)* would expand the pool of people eligible for ART globally to a potential 25.9 million people, compared with close to 16.7 million under the 2010 guidelines. Progressively scaling up of ART to achieve high coverage for this larger group of eligible people will require increased funding but will also generate substantially greater returns.

Assuming that ART coverage increases gradually to about 80% of the total number of people eligible for treatment, total annual investment in the HIV response in low- and middle-income countries would increase by approximately 10% above the target of US$ 22-24 billion included in the *Political Declaration on HIV and AIDS* by the United Nations General Assembly in 2011 *(5)*. This increase is based on the assumption that the basic approach in the HIV response and costs for delivering services would not change significantly over the next few years. This assumption may be affected by various factors that could offset the additional investments for treatment, such as efficiency savings in some aspects of the response. Over time, these additional resource needs are projected to level off and then decline, reflecting the accumulated prevention benefits of expanding ART provision. Greater access to ART will reduce the number of people acquiring HIV infection and thereby eventually reduce the number of people eligible for ART.

The modelling estimates are based on constant costs for HIV treatment. However, future unit costs may decrease. For example, further efficiency gains can be achieved if facilities serve more people, visits and check-ups become less frequent and task shifting and the decentralization of ART activities to community-based services expand. These adjustments would save costs and provide simpler, improved and more accessible services. In addition, improving access to durable and affordable point-of-care diagnostics, along with less expensive and quicker laboratory tests, might save costs in both diagnosis and monitoring. There are also potential cost savings on commodities, including medicines (Box 4.2), as intellectual property hindrances are removed or overcome, as economies of scale increase and as treatment optimization reduces the doses of active pharmaceutical ingredients used in ARV medicines.

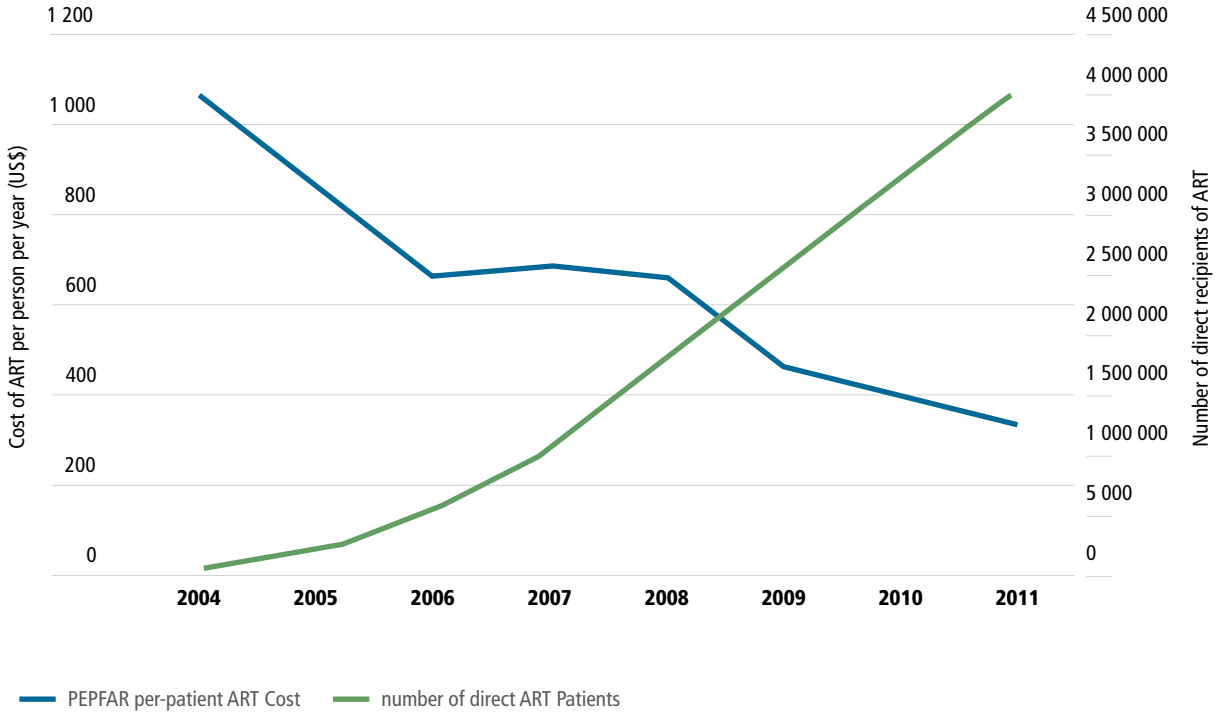
Efficiencies in the HIV response may also be achieved by more closely focusing all relevant HIV services. With significant decreases in new infections following the strategic scale-up of basic programme components, the pool of people living with HIV will start to shrink over the coming decade and the majority of those living with HIV will be receiving effective ART. These factors may well offset additional treatment investments, including those based on the new guidelines and eligibility criteria.

Recent experiences confirm the potential for further gains. Exploiting existing opportunities for cost efficiency has more than halved the average cost per person receiving ART in programmes supported by the United States President's Emergency Plan for AIDS Relief, from more than US$ 1000 to less than US$ 400 per year between 2004 and 2011 (Fig. 4.4). Whether such drastic efficiency savings can be achieved in programmes at their current levels of maturity is uncertain.

However, significant cost drivers must also be acknowledged. Reaching rural and marginalized populations who currently do not access ART may be more difficult and expensive. Testing and retesting services will have to be greatly expanded, additional investment in strengthening health infrastructure might be needed, and the ratio of first- to second- and third-line treatment might shift towards more costly regimens. Instead of commodity prices falling, prices might increase because of patent restrictions and if there is a weakening in the generic competition that has helped to drive down the prices of first-generation ARV medicines.

In all scenarios, the substantial return in people averting HIV infection and life-years saved will justify investment in expanding ART. Compared with maintaining current levels of ART provision, each additional quality-adjusted life-year (QALY) gained globally by implementing the 2013 WHO ARV guidelines would cost approximately US$ 630, and each additional person avoiding acquiring infection would cost less than US$ 6000 – assuming that the unit costs remain stable. Since the cost per QALY gained is substantially lower than the annual per capita gross domestic product in all regions, providing ART in accordance with the 2013 ARV guidelines *(1)* is regarded as being very cost-effective *(7)*. Similarly, recent comparative modelling of the cost-efficiency of shifting from Option A for preventing mother-to-child transmission (ART only for pregnant women with CD4 counts ≤350 cells/mm^3) to Option B (ART for all pregnant women regardless of CD4 count) and Option B+ (continuing ART for life after delivery) in Kenya, South Africa, Viet Nam and Zambia indicated that Option B+ is the most cost-efficient scenario in all four countries *(8)*.

Fig. 4.4. Annual ART costs per person in US dollars and numbers of direct ART recipients in the programme supported by the United States President's Emergency Plan for AIDS Relief, 2004–2011



Source: United States Department of State, PEPFAR blueprint: creating an AIDS-free generation. 2012. *(6)*

The allocation per person was estimated as the total treatment allocation of the United States President's Emergency Plan for AIDS Relief divided by the overall number of directly supported people receiving ART, not including potential financial contributions by others than the United States President's Emergency Plan for AIDS Relief.

The implications of applying the 2013 WHO ARV guidelines *(1)* will vary between countries (Boxes 4.2 and 4.3). Countries will have to adopt a strategic approach in scaling up their ART programmes by combining increased HIV testing of appropriate populations, broadened treatment eligibility criteria and stronger systems for linking people diagnosed with HIV infection into care.

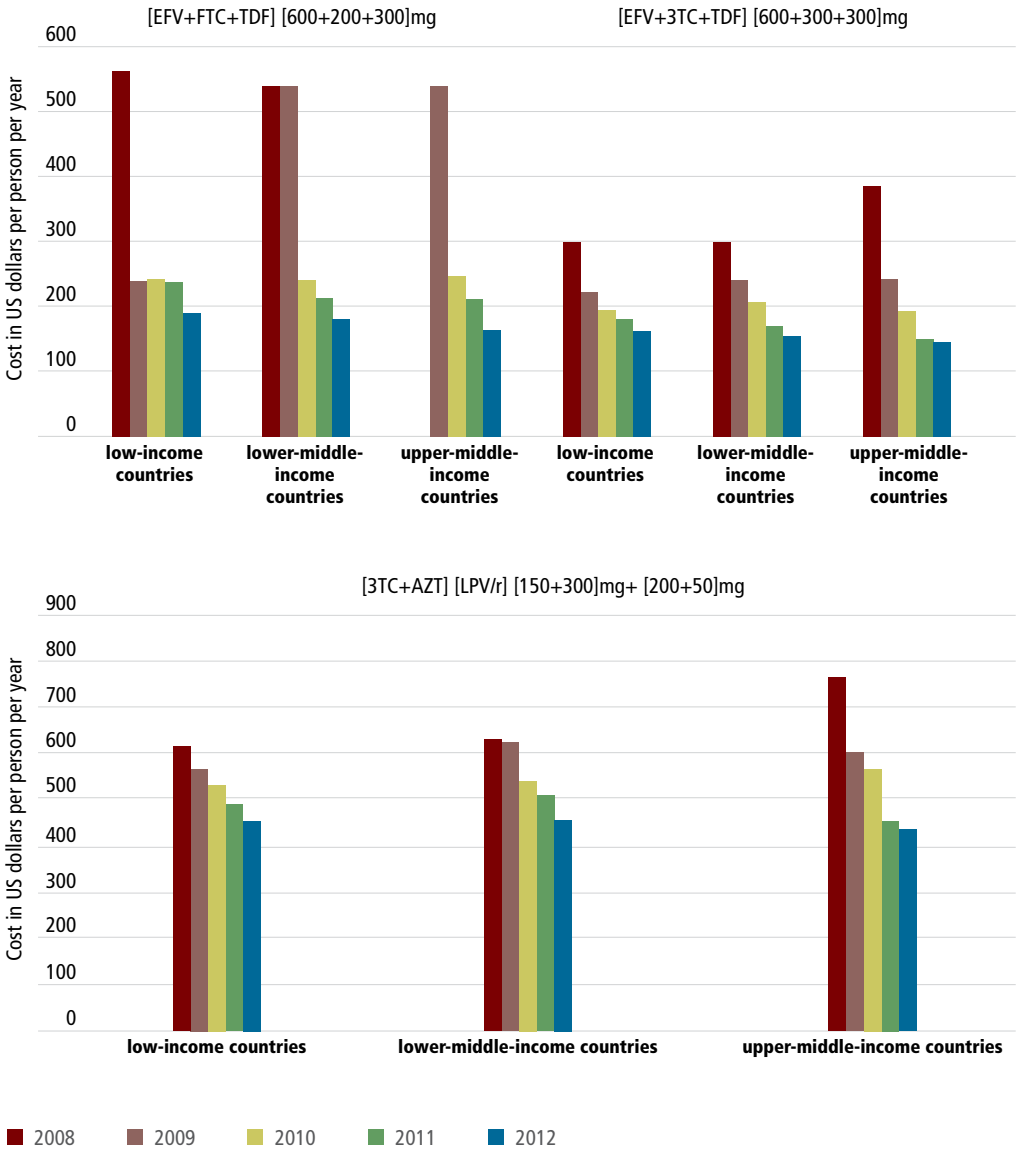
Countries' strategic choices will depend largely on country-specific costs and their capacity for diagnosing more people living with HIV, enrolling these individuals in ART programmes and providing eligible individuals with life-long ART (see Chapter 3). These factors can significantly influence the overall cost-effectiveness of an ART programme *(11)*. However, the return in investment for specific approaches will always remain one among the many factors that are appraised in building a national consensus for expanding HIV treatment.

The demonstrated benefits of ART in terms of preventing people from dying and from acquiring HIV infection exceed many of the expectations that helped launch the global scale-up of ART a decade ago. Current evidence also confirms the enormous potential for further progress. The 2013 WHO ARV guidelines *(1)* reflect this evidence and aim to extend the multiple benefits of initiating ART earlier for both prevention and treatment and boosting the overall impact of ART in all regions. The past decade has shown that combining firm political commitment, adequate funding and resourcing, strong community mobilization, and technical and logistical innovation can save millions of lives. The new ARV guidelines hold the potential for expanding these achievements much further.

Box 4.2. Antiretroviral drug prices in low- and middle-income countries

Declining prices for ARV medicines in recent years have made expanding treatment programmes more affordable. Prices have declined despite the wider adoption of more expensive TDF-based regimens, which can be attributed to the continued scaling up of treatment programmes (leading to larger transaction volumes), greater predictability of demand and increased competition among manufacturers. Prices can be reduced further. For example, the cost of the fixed-dose combination of the WHO-recommended first-line regimen of TDF + FTC + EFV was US$ 186 per person per year in 2012, whereas a two-pill regimen using the same drugs costs only US$ 112 (Fig. 4.5).

Fig. 4.5. Median prices per person per year in US dollars for first- and second-line antiretroviral therapy regimens in low-, lower-middle- and upper-middle-income countries, 2008–2012



Source: Global Price Reporting Mechanism of the AIDS Medicines and Diagnostics Service.
The median prices might obscure price outliers; the Global Price Reporting Mechanism has limited coverage.

However, the costs can be much higher in middle-income countries: Brazil and the Russian Federation, for example, pay more than US$ 1000 per person per year for the WHO-recommended first-line TDF + [3TC or FTC] + EFV.

The prices of second-line regimens also declined substantially between 2010 and 2012, but the median prices remained higher than for first-line regimens. In 2012, the median reported cost of the most commonly used second-line regimen (3TC + AZT + LPV/r) was US$ 453 per person per year in low-income countries, US$ 451 per person per year in lower-middle-income countries and US$ 442 in upper-middle-income countries. These prices vary widely from country to country, however *(9)*. Several factors have contributed to the price trend for second-line regimens since the mid-2000s. They include decreases in the prices of abacavir, LPV/r and TDF and the prequalification of generic versions of LPV/r. Greater economies of scale, new pricing policies by research-based pharmaceutical companies and efforts to expand the market for second-line regimens also contributed. Although these developments are encouraging, addressing the relatively higher cost of second-line regimens is an important priority.

Options beyond second-line treatment remain extremely costly. There are no WHO-prequalified generic versions of raltegravir, etravirine or darunavir, and prices remain extremely high. The lowest possible price for a third-line regimen containing raltegravir, etravirine or boosted darunavir is around US$ 2000 in low-income countries, almost 18 times more than the lowest price for first-line regimens. Some middle-income countries are paying much higher prices. In 2012, Georgia paid US$ 13 225 per person per year for raltegravir, Paraguay paid US$ 7782 per person per year for etravirine, while Armenia paid US$ 8468 and Thailand paid US$ 4760 per person per year for darunavir *(10)*.

ANNEX: METHODS OF DATA COLLECTION AND VALIDATION

Methods of data collection and validation

Most of the health sector response data presented in this report were collected by WHO, UNICEF and UNAIDS through the joint Global AIDS Response Progress Reporting and Health Sector Reporting processes *(1)*, unless stated otherwise. Country data were submitted based on guidance to national AIDS programmes and partners on the use of core indicators for measuring and reporting on national HIV responses. Countries submitted data between March and April 2013, using the joint online reporting system. A data validation process followed the country submission.

The country offices of WHO, UNICEF and UNAIDS worked jointly with national counterparts and partner agencies to validate data in a single collaborative consultation process. When discrepancies or inconsistencies were identified in the reported data, national authorities were asked to clarify or resolve them.

Number of people 15 years and older who received HIV testing and counselling and know the results

The number of adults who received HIV testing and counselling in the past 12 months and know the results in a given country is collected from routine reports from all service points, including voluntary counselling and testing sites, clinics, hospitals and nongovernmental organization outreach points. The data are compiled at the district or local level and then finally at the national level. A total of 97 low- and middle-income countries reported data for 2012 while data from 27 countries were imputed from the latest available year in the period 2009 to 2011. If countries did not have a system to remove double-counting, these data are not corrected for the fraction of people who have been tested more than once in the year.

Regional data are presented on the availability of HIV testing and counselling services at the national level for adults in 75 low- and middle-income countries for 2011 and 2012.

Number of people receiving and eligible for antiretroviral therapy

For December 2012, 107 of the 144 low- and middle-income countries had provided data on access to ART. These 107 countries accounted for 94% of the people receiving treatment at the end of 2012. An additional three countries (Botswana, Islamic Republic of Iran and Thailand) submitted data for cut-off points between September and November 2012. Together, these 110 countries represent more than 98% of the total estimated number of people receiving ART at the end of 2012 in low- and middle-income countries. Fourteen countries submitted data for cut-off points between January and March 2012. Only 20 countries, all with relatively small HIV epidemics, did not report these data for 2012.

Estimating the number of people receiving ART involves some uncertainty for countries that have not yet established regular reporting systems for capturing accurate data on people who initiate treatment for the first time, people who discontinue treatment, and people who are lost to follow-up which may include people who have self-transferred (i.e. still in care), died or have been truly lost to follow up.

Uncertainty may also arise because of difficulties in measuring the extent of ART provided in the for-profit and not-for-profit private sectors. Some people receive treatment through nongovernmental organizations and/or private clinics that do not report through official channels in some countries. Private companies may have programmes to support the provision of ART to workers with advanced HIV disease, but do not necessarily report those data to the public health

authorities. When available, data from the private sector have been included.

In addition, the report presents the most recent available data from high-income countries.

Estimating treatment eligibility and coverage

Standard methods were used for estimating the size and course of the HIV epidemic, number of people living with HIV, number of people newly infected, mortality attributable to AIDS and eligibility for treatment *(2,3)*. Eligibility for treatment is estimated using statistical modelling methods that include all people who meet the criteria for initiating ART, whether or not these people know their HIV status and their eligibility for ART. At the time this report was prepared, the eligibility for 2012 had been estimated for 22 priority countries only.[1] Estimates of ART coverage were calculated by dividing the number of people receiving ART at the end of 2012 by the estimated number of people who were eligible for treatment in 2012. The ranges around the levels of coverage are based on the uncertainty ranges around the estimates of eligibility *(4)*. Some countries have developed their own methods for estimating treatment eligibility, which could differ from the estimates derived using WHO/UNICEF/UNAIDS methods and tools. The report uses standardized estimates of treatment eligibility calculated using WHO/UNAIDS methods.

Chapter 1 provides data on access to ART disaggregated by sex and by age (adults – 15 years and older; children – younger than 15 years) for low- and middle-income countries. Disaggregated data on the number of children and adults receiving ART are available for 139 low-and middle-income countries of which 124 countries reported breakdowns for 2012. Data disaggregated by sex that were used in this report were available for 109 countries by end of 2011.

The 2010 WHO treatment guidelines *(3)* recommend that all children younger than 24 months living with HIV be provided with ART regardless of CD4 counts.

The estimates of ART coverage for children in the 22 priority countries were calculated by dividing the number of children receiving ART at the end of 2012 by the estimated number of children who were eligible for treatment in 2012 (based on WHO/UNAIDS methods). The ranges around the levels of coverage are based on the uncertainty ranges around the estimates of eligibility *(4)*.

As changes in recommendations for ART eligibility came into effect in 2009, (8) i.e. initiation of ART for adults living with HIV at or below CD4 350 cells/mm3 instead of CD4 200 cells/mm3, all ART line-charts in this report depicting trends in ART eligibility for adults and children (combined) will show increases as of 2009.

Similarly, changes in age-specific eligibility criteria for children living with HIV – from younger than 12 months of age to younger than 24 months of age -- took effect in 2010 in accordance with the revised WHO treatment guidelines for infants and children (2010). Hence, all ART line-charts in this report depicting trends in ART eligibility for children will show increases as of 2010.

Prevention of mother-to-child transmission

Number of pregnant women living with HIV receiving antiretroviral medicine for preventing mother-to-child transmission

The number of pregnant women living with HIV and who are receiving antiretroviral (ARV) medicine for preventing mother-to-child transmission (PMTCT) is based on national programme data that are aggregated from facilities or other service delivery sites, as reported by countries.

A total of 129 countries reported these data for 2012; together, they account for nearly all of the estimated pregnant women living with HIV in low- and middle-income countries. This report focuses on the 21 African priority countries of the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive *(5)*. Among these countries, 19 submitted disaggregated data indicating whether ARV regimens were provided as prophylaxis or as lifelong treatment in 2012.

The estimated coverage of ARV medicine for PMTCT includes only the most effective regimens (ART and combination regimens) and excludes single-dose nevirapine, which WHO no longer recommends.

Estimating the number of pregnant women living with HIV who are eligible for antiretroviral medicine for preventing mother-to-child transmission

The number of pregnant women living with HIV who are eligible for ARV medicine for PMTCT is estimated using standardized statistical modelling. This is based on UNAIDS/WHO methods that consider various epidemic and demographic parameters, such as the

1. The 22 priority countries are Angola, Botswana, Burundi, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, India, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.

HIV prevalence among women of reproductive age and the effect of HIV on fertility *(2)*. Regular scientific updates have been provided on these tools *(6)*.

Coverage of pregnant women living with HIV receiving antiretroviral medicine for preventing mother-to-child transmission

The coverage of ARV medicine for PMTCT is calculated for the 22 priority countries by dividing the number of pregnant women living with HIV who received ARV medicine for PMTCT in 2012 by the estimated number of pregnant women living with HIV needing ARV medicine for PMTCT in a given country (PMTCT need).

The ranges around the levels of coverage are based on the uncertainty ranges around the estimates of PMTCT need.

Classification of countries

Classification by income

Unless stated otherwise, all data analysis in this report is based on data from the 144 countries the World Bank classifies as low- and middle-income countries as of July 2012 *(7)*. The economies are classified as low, middle or high income according to the gross national income per capita, calculated using the World Bank Atlas method (to reduce the effect of exchange-rate fluctuation). The groups are:

- low-income, US$ 1025 or less;
- lower-middle-income, US$ 1026 to US$ 4035, and upper-middle-income, US$ 4036 to US$ 12 475; and
- high-income, US$ 12 476 or more.

Classification by HIV epidemic level

HIV epidemics are categorized as low-level, concentrated and generalized based on the following principles.

Low-level epidemic

Although HIV infection may have existed for many years, it has never spread to significant levels in any subpopulation. Recorded infection is largely confined to individuals with high-risk behaviour, such as sex workers, people who inject drugs and men who have sex with men. This epidemic state suggests that networks of risk are rather diffuse (with low levels of partner exchange or sharing of drug-injecting equipment) or that the virus has been introduced very recently.

Concentrated epidemic

In concentrated epidemics, HIV has spread rapidly in a defined subpopulation but is not well established in the general population. This epidemic state suggests active networks of risk within the subpopulation. The frequency and nature of links between highly infected subpopulations and the general population determines the future course of the epidemic.

Generalized epidemic

In generalized epidemics, HIV is firmly established in the general population. Although populations at higher risk may continue to contribute disproportionately to the transmission of HIV, sexual networking in the general population is sufficient to sustain an epidemic independent of populations at higher risk of infection and transmission.

Classification of Member States by WHO region

This report presents data on low- and middle-income countries classified by WHO region. WHO has 194 Member States grouped in six regions, and 144 of these are low-and middle-income countries: WHO African Region (n = 45); WHO Region of the Americas (n = 29); WHO Eastern Mediterranean Region (n = 16); WHO European Region (n = 22); WHO South-East Asia Region (n = 11); and WHO Western Pacific Region (n = 21). There are 50 high-income countries.

Explanatory notes on the analysis performed by Futures Institute

The special analysis conducted by Futures Institute to model the implications of switching from the 2010 WHO treatment guidelines *(8)* to the 2013 WHO ARV guidelines *(9)* is based on applying the Goals model *(10)*, which is part of the Spectrum software package, to model the potential impact of various interventions in 24 countries that together account for 85% of the people newly infected with HIV in low- and middle-income countries.

The model estimates the annual number of adults newly infected with HIV by sex and risk group (sex workers and clients, men who have sex with men, people who inject drugs, heterosexual couples in stable relationships and men and women with casual partners), as a function of behaviour (number of sexual partners, acts per partner, condom use, age at first sex, rates of behaviour change and needle-sharing) and according to the characteristics of partners (stage of infection, presence of other

sexually transmitted infections, male circumcision and use of ART).

The population living with HIV is tracked by CD4 count, and mortality is determined by CD4 count category and ART status. The number of children newly infected with HIV by mother-to-child transmission is estimated, and the children are tracked as they progress to eligibility for treatment and death. The parameter values for progression and mortality rates have been published previously *(6,11)*. The data inputs for each country were drawn from national surveys (Demographic and Health Surveys and AIDS Indicator Surveys) and national progress reports (available on the UNAIDS web site) and were adjusted to match the prevalence trends from national estimates as reported to UNAIDS *(12)*. The results were adjusted for countries that were not explicitly modelled to represent the totals for all low- and middle-income countries.

Futures Institute used the model to estimate eligibility for ART and the cost and impact of providing ART between 2013 and 2025 under the 2010 WHO treatment guidelines *(8)* and the 2013 WHO ARV guidelines *(9)*. The work builds on previous modelling on costs and the impact of the overall HIV response, which was published as the Investment Framework for HIV in 2011 *(13)*. For both the 2010 and 2013 WHO guideline scenarios, the same pattern for scaling up and costing for a basic package of prevention and structural interventions was assumed. These included scaling up to universal access for all "basic programmes" (PMTCT, voluntary male medical circumcision, outreach to most-at-risk populations, condom promotion and behaviour change) as well as a package of "critical enablers" (including counselling and testing, community mobilization and mass media).

The differences between the two scenarios were limited to assumptions about the scaling up of ART. The 2010 guidelines scenario assumed reaching at least 80% coverage of ART for adults (that is, CD count <350 cells/mm^3), 100% coverage of ART for children and 90% coverage for PMTCT in 2015, with the coverage subsequently maintained over time. For the 2013 guidelines scenario, it was assumed that treatment coverage would be 80% for adults (CD4 count <500 cells/mm^3 plus all serodiscordant couples, all people living with HIV who have active TB and all people with HIV and hepatitis B virus with active liver disease) and 100% coverage for children in 2020. Table 1 provides details.

For the impact analysis, it was assumed that ART reduces the rate of transmission from virally suppressed people living with HIV by 80% for all levels of CD4 counts and in all scenarios if ART is provided through high-quality programmes.

Futures Institute used a cost per person per year of treatment of US$ 515 based on a weighted average median price in 2011 of US$ 145 for first- and second-line ARV medicines *(14)*, US$ 222 for average costs of service delivery and monitoring *(15)* plus an additional 40% for costs above the facility level for administration, logistics, training, planning etc. Sensitivity analysis was performed for a 20% cost increase or decrease by 2025.

Table 1. Assumptions about antiretroviral coverage

	2010 WHO guidelines			2013 WHO guidelines		
Population	**2015**	**2020**	**2050**	**2015**	**2020**	**2050**
People living with HIV by CD4 count (cells/mm^3)						
<200	80%	80%	80%	80%	90%	90%
200–250	70%	70%	70%	70%	80%	80%
250–350	50%	60%	60%	50%	80%	80%
350–500	5%	5%	5%	5%	60%	60%
>500	0%	0%	0%	0%	0%	0%
Total adults	50%	65%	65%	50%	85%	85%
Total children in need	75%	90%	90%	75%	90%	90%
Special populations						
Pregnant women living with HIV	0%	0%	0%	0%	80%	80%
Serodiscordant couples	0%	0%	0%	0%	80%	80%
People with HIV and TB	0%	80%	80%	0%	80%	80%
People with HIV and HBV	0%	80%	80%	0%	80%	80%

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