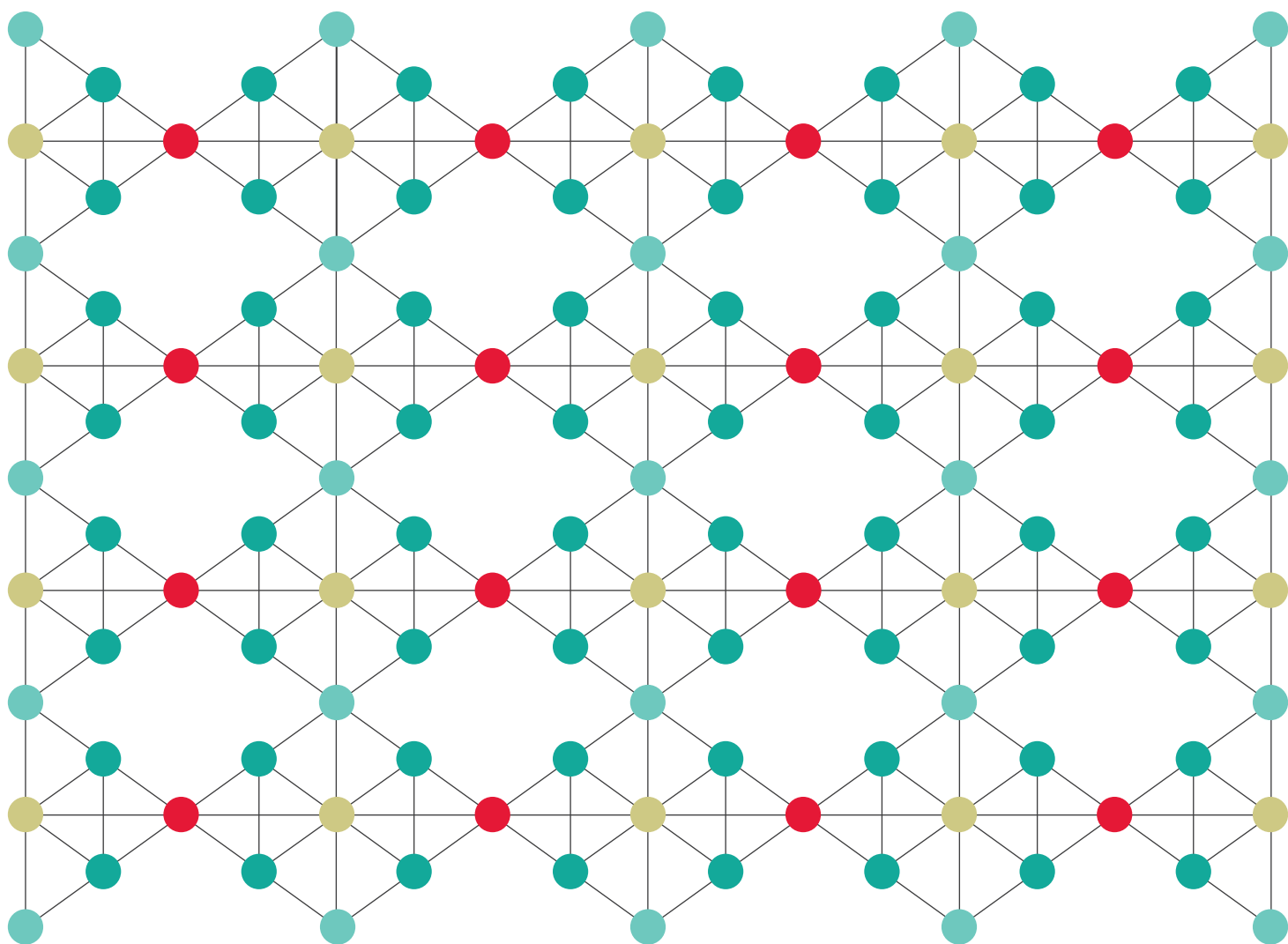


How many people living with HIV access treatment?

A triangulation of data to verify the UNAIDS global estimate of people accessing antiretroviral therapy at the end of 2015



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Introduction

Among the most closely watched indicators of the global AIDS response is the number of people on antiretroviral therapy. Antiretroviral medicines allow people living with HIV to live long and healthy lives. The medicines can also reduce the amount of HIV in the bloodstream to undetectable levels. Having such a low viral load greatly reduces the chance that a person living with HIV will transmit the virus to someone else.

The current global target, agreed by the United Nations General Assembly in June 2016, is for 30 million people living with HIV to access treatment by 2020. UNAIDS is mandated by the United Nations General Assembly to track global progress against this and other global targets. A majority of countries regularly report treatment numbers and other data against a standard set of indicators to UNAIDS through the Global AIDS Response Progress Reporting (GARPR) system. UNAIDS works in collaboration with the World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and other partners to validate these reports ahead of publication. For the minority of countries that do not provide reports, UNAIDS estimates their treatment numbers using a variety of data sources.

During the most recent reporting round, the total reported and estimated numbers of people on treatment for June 2016 were combined to obtain a global estimate of 18.2 million [16.1 million–19.0 million] people, including 910 000 [801 000–947 000] children aged under 15 years. This global estimate was reported by UNAIDS in the November 2016 publication *Get on the Fast-Track: the life-cycle approach to HIV*.¹

In an effort to verify the accuracy of the global treatment estimates, UNAIDS triangulated data from a wide range of sources. This exercise concluded that sufficient amounts of generic antiretroviral medicines were produced by manufacturers and then procured by 11 generic-accessible low- and middle-income countries² to treat the number of people reported to be on treatment in those countries in 2015. National population-based surveys and data quality assessments conducted in several of these countries provide further confidence in UNAIDS estimates of the treatment numbers and coverage of treatment among people living with HIV.

¹ http://www.unaids.org/sites/default/files/media_asset/Get-on-the-Fast-Track_en.pdf.

² World Bank income level classification of countries, 2015.

Validation of the global treatment estimate for end-2015

In the Prevention gap report,³ published in July 2016, UNAIDS reported that 17.0 million people were accessing antiretroviral therapy at the end of 2015. In addition to the regular validation activities conducted with WHO, UNICEF, the United States President's Emergency Plan for AIDS Relief (PEPFAR), the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and others ahead of publication, UNAIDS undertook a post-publication data triangulation to verify the accuracy of the global treatment estimates. This triangulation used both top-down and bottom-up approaches.

The first three of the analyses sought to answer a simple question: Are enough antiretroviral medicines produced and procured to treat the number of people reported to be on antiretroviral therapy? UNAIDS focused on the sale and procurement of generic medicines used by the vast majority of people living with HIV globally. According to the Clinton Health Access Initiative (CHAI), generic medicines are used by 94% of patients in low- and middle-income countries (1).

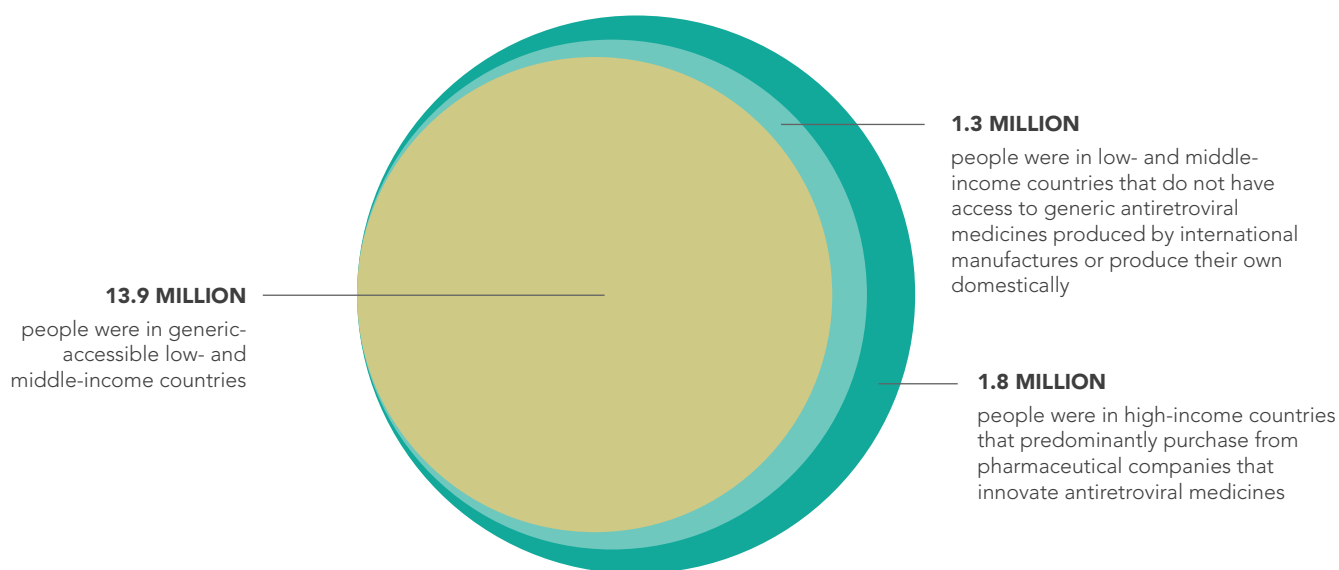
Figure 1. Top-down and bottom-up approaches used to validate the end-2015 global treatment estimate



³ http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf.

Figure 2. Estimated number of people accessing antiretroviral therapy, by country income level and generic accessibility, 2015

Of the **17.0 MILLION** people globally accessing antiretroviral therapy at the end of 2015:



Sources: Global AIDS Response Progress Reporting, 2016; UNAIDS 2016 estimates; ARV market report: the state of the antiretroviral drug market in low- and middle-income countries, 2014–2019. Boston, MA: Clinton Health Access Initiative; 2015.

Of the 17.0 million people that UNAIDS estimated to be accessing treatment at the end of 2015, an estimated 1.8 million people were in high-income countries that predominantly purchase from pharmaceutical companies that innovate antiretroviral medicines, and another 1.3 million people were in low- and middle-income countries that either do not have access to generic antiretroviral medicines from international manufacturers or produce their own domestically—Brazil, China, Mexico and Thailand.⁴ The remaining 13.9 million people on treatment were in 109 low- and middle-income countries that source the vast majority of their antiretroviral medicines from international manufacturers of generics.⁵

⁴ Not including India because the analyses centre on antiretroviral medicines produced in India.

⁵ Afghanistan, Albania, Algeria, Angola, Armenia, Azerbaijan, Bangladesh, Belarus, Belize, Benin, Bhutan, Bolivia (Plurinational State of), Bosnia and Herzegovina, Botswana, Bulgaria, Burkina Faso, Burundi, Cabo Verde, Cambodia, Cameroon, Chad, Central African Republic, Colombia, Democratic Republic of the Congo, Congo, Costa Rica, Côte d'Ivoire, Cuba, Djibouti, Dominican Republic, Ecuador, Egypt, El Salvador, Eritrea, Ethiopia, Fiji, Gabon, Gambia, Georgia, Guatemala, Guyana, Ghana, Guinea, Guinea-Bissau, Kenya, Haiti, Honduras, Hungary, India, Indonesia, Iran (Islamic Republic of), Jamaica, Kazakhstan, Kyrgyzstan, Democratic People's Republic of Korea, Liberia, Lao People's Democratic Republic, Lebanon, Lesotho, the former Yugoslav Republic of Macedonia, Madagascar, Malawi, Malaysia, Mali, Maldives, Mauritania, Mauritius, Republic of Moldova, Mongolia, Montenegro, Morocco, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Niger, Nigeria, Pakistan, Panama, Paraguay, Papua New Guinea, Peru, Philippines, Romania, Rwanda, Senegal, Serbia, Sierra Leone, Somalia, South Africa, South Sudan, Suriname, Sri Lanka, Sudan, Swaziland, Tajikistan, Timor-Leste, Togo, Tunisia, Turkey, Uganda, Ukraine, United Republic of Tanzania, Uzbekistan, Viet Nam, Yemen, Zimbabwe and Zambia.

Analysis of the reported sales of generic medicine producers

UNAIDS reviewed the reported sales figures of the largest generic medicine manufacturers: Mylan, Hetero, Aurobindo, Cipla and Aspen Pharmacare. Mylan reports that its supply of first- and second-line antiretroviral formulations is used to treat an estimated 6.4 million adults and children living with HIV (2). Hetero states that its antiretroviral formulations treat about 4.5 million people (3). The most recently available annual reports from Aurobindo and Cipla state that these two manufacturers produced antiretroviral products sufficient to treat 2.2 million and nearly 2.0 million people, respectively (4, 5). Aspen Pharmacare is reported to produce antiretroviral medicines used by approximately 1.2 million people living with HIV in South Africa (6). These five sources add up to a total of 16.3 million people on treatment, well over the 13.9 million reported to be on treatment in the countries that are purchasing the medicines.

The larger number is likely due to overlaps in the individual claims by manufacturers. For example, double counting could occur when two manufacturers are each producing part of the same daily regimen. Similarly, one manufacturer could be counting production of active pharmaceutical ingredients (APIs) that are then used within another manufacturer's final product. Although some of the reports above explicitly excluded APIs, the wording in others suggested that APIs were included in their calculations. Wastage may also be a factor.

Table 1. Five generic manufacturers' claims of the number of people living with HIV accessing their antiretroviral medicines

Company	Number of people reported to be on treatment
Mylan	6.4 million
Hetero	4.5 million
Aurobindo	2.2 million
Cipla	2.0 million
Aspen Pharmacare	1.2 million
TOTAL	16.3 million

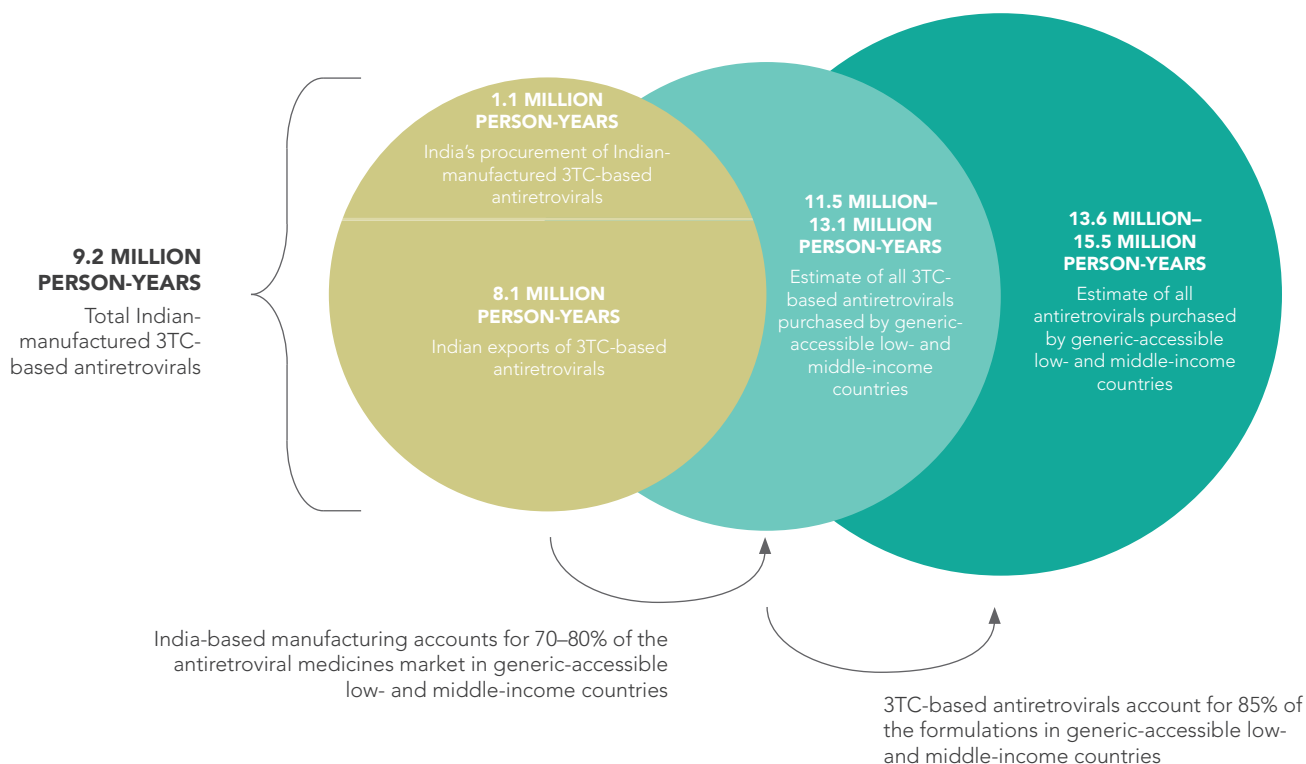
Sources: Antiretrovirals. Mylan [website] (<http://www.mylan.in/en/antiretrovirals>; accessed 2 December 2016); ARV Story. Hetero [website] (<http://www.heteroworld.com/pages/arv>; accessed 2 December 2016); Driving sustainable growth. Annual Report 2014-15. Aurobindo Pharma Limited (http://www.aurobindo.com/docs/annual-reports/Aurobindo_Annual_Report_2014_15.pdf; accessed 2 December 2016); Seventy-ninth annual report 2014-15. Cipla (http://www.cipla.com/uploads/investor/1442817668_Cipla-Annual-Report-2014-15.pdf; accessed 2 December 2016); The world's biggest generic pharmaceutical companies; analysis on 5 April 2016. pharmaceutical-technology.com [website] (<http://www.pharmaceutical-technology.com/features/featurethe-worlds-biggest-generic-pharmaceutical-companies-4853429>; accessed 2 December 2016).

Exports of antiretroviral formulations containing lamivudine produced in India

The quantity of antiretroviral medicines being produced for generic-accessible low- and middle-income countries can also be measured by reviewing export data. For this analysis, UNAIDS focused on the most common component of first- and second-line regimens, lamivudine (3TC), and the country where the vast majority of generic antiretroviral medicines are produced, India.

Lamivudine was the secondary nucleoside reverse-transcriptase inhibitor used in 85% of the antiretroviral regimens for adults living with HIV and 99.9% of the regimens for children living with HIV in low- and middle-income countries in 2015, according to market share projections produced by WHO (7).

Figure 3. Estimate of antiretroviral medicines procured by generic-accessible low- and middle-income countries using Indian export and procurement data for 3TC formulations, 2015

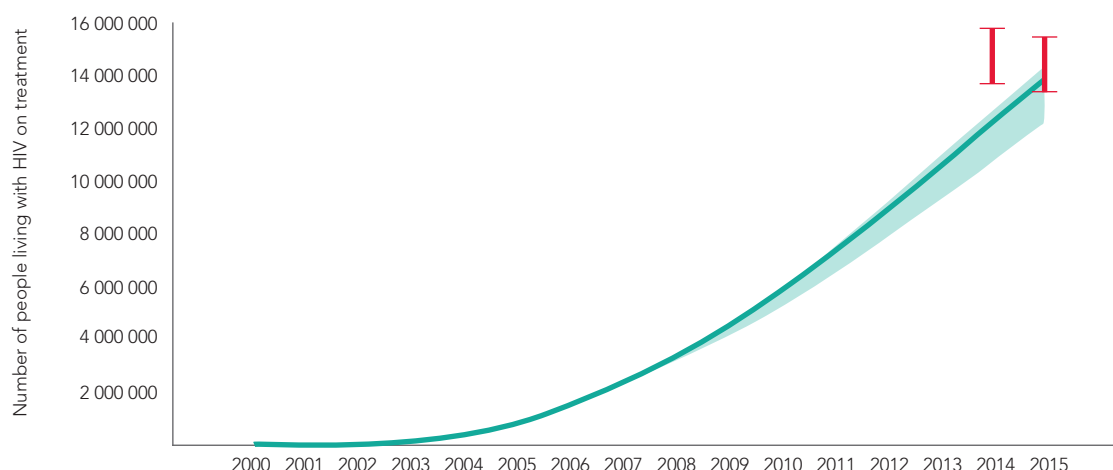


Sources: Data from Government of India customs database, obtained from Seair Exim Solutions (<https://www.seair.co.in>); Ministry of Health, India; ARV market report: the state of the antiretroviral drug market in low- and middle-income countries, 2014–2019. Boston, MA: Clinton Health Access Initiative; 2015; Combined global demand forecasts for antiretroviral medicines and HIV diagnostics in low- and middle-income countries from 2015 to 2020. Geneva: World Health Organization; 2016 (<http://apps.who.int/iris/bitstream/10665/250088/1/9789241511322-eng.pdf?ua=1>; accessed 2 December 2016).

According to CHAI’s procurement database, four Indian generic manufacturers—Mylan, Hetero, Aurobindo and Cipla—supplied about 70% of the antiretroviral medicines market in generic-accessible low- and middle-income countries by both revenue and volume. Other Indian manufacturers accounted for an additional 6% of volume and revenue. Non-Indian generic manufacturers and distributors accounted for about 17% of the revenue and about 21% of the volume. The largest of these non-Indian manufacturers was South Africa-based Aspen Pharmacare. Non-generic producers account for less than 7% of sales revenue and volume (1).

Data showing the amount of Indian-manufactured 3TC-based antiretroviral medicines exported from India and purchased within India were obtained by UNAIDS. To calculate the number of people who could be treated for one year with these medicines, each export and procurement quantity was converted into the total number of smallest possible units (TNU)—usually tablets or millilitres of liquid. The potential number of person-years on treatment was calculated as: $TNU / (\text{strength} \times \text{recommended daily dose} \times 365)$. “Person-years on treatment” assumes that all procured quantities were consumed by patients and that all women accessing antiretroviral medicines to prevent mother-to-child transmission of HIV were on Option B+ (i.e. antiretroviral therapy for life), as currently recommended by WHO. In all countries, some wastage will occur, and in a few countries significant numbers of pregnant women living with HIV are still receiving Option A or B to prevent mother-to-child transmission of HIV.

Figure 4. Reported number of people accessing antiretroviral therapy in 109 generic-accessible low- and middle-income countries, 2000–2015, and the number of people who could be treated annually with the estimated amount of medicines procured by these countries, 2014 and 2015



— Number of people living with HIV on treatment, reported to UNAIDS

I Annual number of people living with HIV that can be on treatment (range), based on report/supply by India-based generic pharmaceutical firms

Sources: Global AIDS Response Progress Reporting; UNAIDS analysis of data from Government of India customs database and National AIDS Control Organization, Ministry of Health, India.

Indian customs data show that 3200 consignments of antiretroviral formulations (excluding APIs) containing 3TC were exported in 2015 (8), an amount sufficient to treat 8.1 million people for one year. In addition, India's Ministry of Health informed UNAIDS that it had procured enough antiretroviral formulations containing 3TC in 2015 to treat 1.1 million people (9).

If formulations containing 3TC are conservatively estimated to account for 85% of the total amount of antiretroviral medicines procured by generic-accessible low- and middle-income countries in 2015, and Indian manufacturers are estimated to account for 70–80% of the market in generic-accessible low- and middle-income countries, the 9.2 million treated by India-produced 3TC formulations can be extrapolated to an estimated total quantity of generic antiretroviral medicines procured by these countries sufficient to treat 13.6 million to 15.5 million people for one year—greater than the 13.9 million people reported to be on treatment in these countries in 2015.

To account for the likelihood that much of the medicines used by people accessing treatment in 2015 were produced and procured in 2014, UNAIDS also obtained 2014 Indian export and procurement data for 3TC. The total amount for 2014 was slightly higher than in 2015, producing an estimated total quantity of generic antiretroviral medicines procured that is sufficient to treat 13.8 million to 15.7 million people for one year.

For either year, the export totals should not be directly compared to the number of people accessing treatment because the export totals do not include an unknown percentage of medicines lost to wastage, and the variable amount of time that will elapse between procurement and use of the medicines.

Table 2. Eleven generic-accessible countries with the largest number of people on antiretroviral therapy

Country	Number of people on treatment	Percentage of total number of people on treatment in generic-accessible countries
South Africa	3 384 160	24%
India	919 141	7%
Kenya	897 644	6%
Zimbabwe	878 461	6%
Uganda	834 931	6%
Nigeria	828 867	6%
Mozambique	802 659	6%
Zambia	758 646	5%
United Republic of Tanzania	740 078	5%
Malawi	595 186	4%
Ethiopia	386 123	3%
Total	11 025 896	78%

Sources: UNAIDS 2016 estimates; ARV market report: the state of the antiretroviral drug market in low- and middle-income countries, 2014–2019. Boston, MA: Clinton Health Access Initiative; 2015.

Procurement data from 11 high-burden countries

Procurement data from generic-accessible low- and middle-income countries provided further evidence to corroborate global treatment numbers. Just 11 high-burden countries are home to nearly 80% of all people on treatment in the 109 countries that rely primarily on international generic medicine manufacturers for their antiretroviral medicines. Procurement data from these 11 countries were obtained from the WHO Global Drug Price Reporting Mechanism, national procurement reports and reports from the two major donors that purchase antiretroviral medicines, PEPFAR and the Global Fund.

Data for Ethiopia, South Africa, the United Republic of Tanzania, Zambia and Zimbabwe available within the WHO Global Drug Price Reporting Mechanism clearly show that

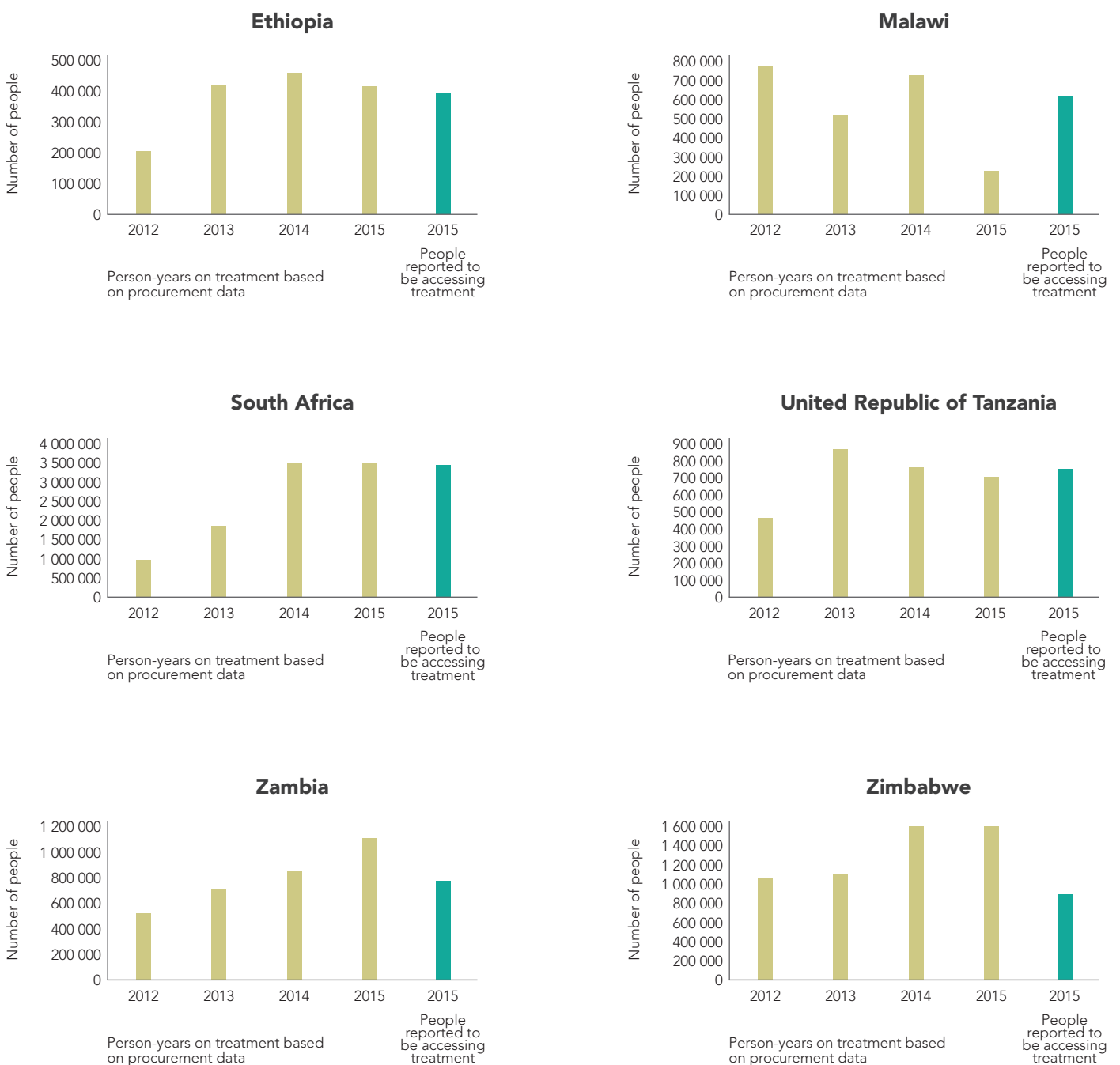
sufficient quantities of antiretroviral medicines were procured in recent years to treat the number of people reported to be accessing these medicines in 2015.⁶ In the case of Malawi, antiretroviral procurement for 2015 is less than half than the amount required for the 595 186 people reported to be on treatment in 2015. A similar gap is seen for 2013. However, these shortfalls appear to be mostly accounted for by much larger volumes procured in 2012 and 2014.

National procurement data were obtained by UNAIDS from India and Kenya. The previously mentioned data from India's Ministry of Health shows procurement in 2015 of sufficient quantities of antiretroviral formulations containing 3TC to treat 1.1 million people for one year (9)—an amount that is greater than the 919 141 people living with HIV reported to be accessing treatment in 2015. Data from the Kenya Medical Supply Authority shows that antiretroviral medicines procured in 2015 were sufficient to treat more than 870 000 people for one year—comparable to the 897 644 people reported to be accessing antiretroviral therapy in 2015.

Data from the Global Fund's online database, Price & Quality Reporting, and PEPFAR's Supply Chain Management System (SCMS) were used to review procurement for Mozambique, Nigeria and Uganda. In Nigeria, the Global Fund and PEPFAR procured sufficient quantities of antiretroviral medicines in 2015 to treat more than 790 000 people for one year, and domestic procurement was sufficient to treat more than 40 000 people—a total amount that is comparable to the 828 867 people reported to be on treatment in 2015.

⁶ The database of the WHO Global Drug Price Reporting Mechanism can be accessed at <http://apps.who.int/hiv/amds/price/hdd/>.

Figure 5. Amount of antiretroviral medicines procured (expressed in person-years on treatment), 2012–2015, compared to the number of people reported to be accessing antiretroviral therapy, 2015, six countries



Sources: Global AIDS Response Progress Reporting, 2016; WHO Global Drug Price Reporting Mechanism.

In Uganda, Global Fund procurement in 2015 was sufficient to treat more than 567 000 people for one year, and PEPFAR and national procurement in 2015 were sufficient to treat about 228 000 and 103 000, respectively—a total comparable to the 834 941 people reported to be on treatment in 2015. Global Fund Price & Quality Reporting and PEPFAR SCMS data also show that their procurement amounts for Mozambique in 2015 were sufficient to treat the number of people reported to be accessing antiretroviral therapy.

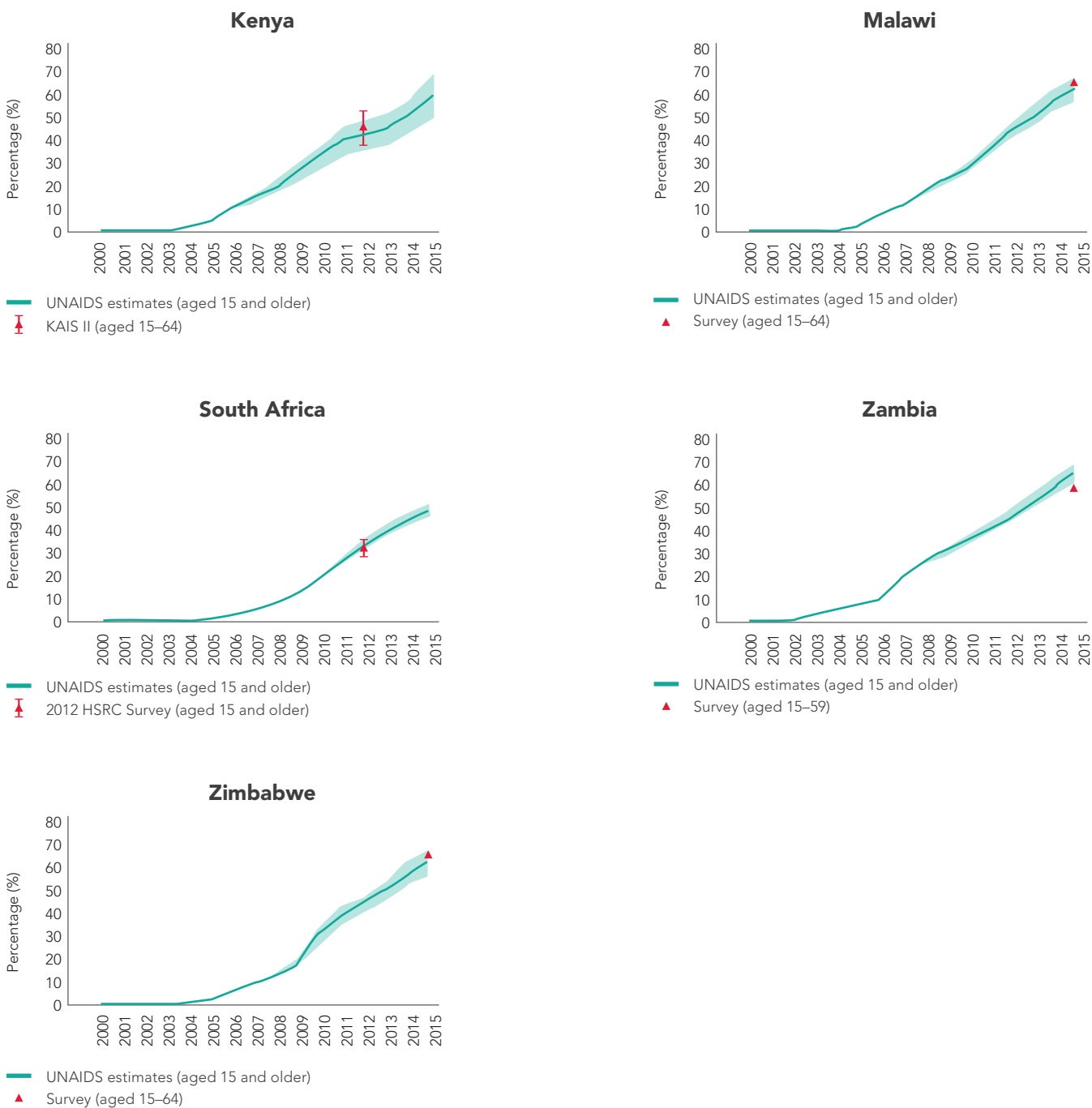
In total, the procurement data available to UNAIDS was comparable to the reported numbers of people on treatment in all 11 generic-accessible low- and middle-income countries reviewed.

National population-based surveys

Data on antiretroviral therapy coverage from national population-based surveys conducted in five high-burden countries were also compared to the treatment numbers reported by national health systems. In Kenya and South Africa, population-based surveys were conducted in 2012 that measured the presence of antiretroviral medicines in blood samples of HIV-positive participants. Comparison of the treatment coverage among people living with HIV estimated by these two surveys and those based on reported numbers show that the figures for each were well within the confidence intervals of each method.

PEPFAR-supported Population-Based HIV Impact Assessment (PHIA) surveys conducted in 2015 and 2016 in Malawi, Zambia and Zimbabwe analysed blood samples from participants and asked them whether they were accessing antiretroviral therapy. Among respondents who tested positive for HIV in each survey, the percentage who self-reported that they were living with HIV and on treatment is generally in line with UNAIDS-reported estimates of antiretroviral therapy coverage among people living with HIV for people aged 15 years and over in 2015 (10).

Figure 6. Percentage of adults living with HIV accessing antiretroviral therapy, 2000–2015, five countries



Sources: Global AIDS Response Progress Reporting, 2016; Kim AA, Mukui I, N’gan’ga L, Katana A, Koros D, Wamicwe J, et al. (2016) Progress in Reversing the HIV Epidemic through Intensified Access to Antiretroviral Therapy: Results from a Nationally Representative Population-Based Survey in Kenya, 2012. PLoS ONE 11(3): e0148068. doi:10.1371/journal.pone.0148068; Malawi population-based HIV impact assessment. MPHIA 2015-2016. Columbia University, ICAP. December 2016; Moyo S, Gouws E, Jooste S, Rehle T. Equity in Utilization of ART among adults in South Africa. 18th ICASA Conference, Zimbabwe 2015; Zambia population-based HIV impact assessment. ZAMPHIA 2015-2016. Columbia University, ICAP. December 2016; Zimbabwe population-based HIV impact assessment. ZIMPHIA 2015-2016. Columbia University, ICAP. December 2016.

Data quality assessments

Data quality assessments have been conducted in recent years in several countries supported by PEPFAR and/or the Global Fund. The assessments aimed to improve the quality of data being reported from health facilities to subnational and national health system managers. In most countries where these assessments were conducted, the data were determined to be of sufficient quality. However, problems were identified in some countries that led to underreporting and overreporting. The primary reason for underreporting was missing or delayed reporting of facility data to the national level. Overreporting was due primarily to not removing people from registries who stopped treatment, died or transferred facilities. Other errors, such as incorrectly abstracting data from facility-based registries or completing reporting forms, led to over- and underreporting to varying degrees of magnitude.

In countries where multiple data quality assessments had been conducted, the accuracy of efforts to report the number of people on treatment appeared to be improving over time, but that further progress was required. Similar assessments will be conducted in a larger number of countries in the coming years and countries with specific data quality issues will be supported in order to improve quality.

Conclusion

This triangulation exercise concluded that sufficient amounts of generic antiretroviral medicines were produced by manufacturers and then procured by generic-accessible low- and middle-income countries in 2015 to treat the number of people reported to be on treatment in these countries. National population-based surveys and data quality assessments conducted in several of these countries provide further confidence in UNAIDS estimates of the treatment numbers and coverage of treatment among people living with HIV.

Moving forward, UNAIDS, WHO and other partners will continue to support countries to improve the accuracy of the numbers of people reported to be on treatment. These efforts aim to strengthen and expand HIV programme monitoring and surveillance systems and to build the capacity of national, regional and clinical staff to collect, report and analyse data from these systems. UNAIDS and WHO are also working with medicine producers and countries to triangulate facility-reported numbers of people on antiretroviral therapy with data from medicine exports, in-country medicine distribution systems surveys and any other relevant data.

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