

2018 PROGRESS REPORT

JULY 2018

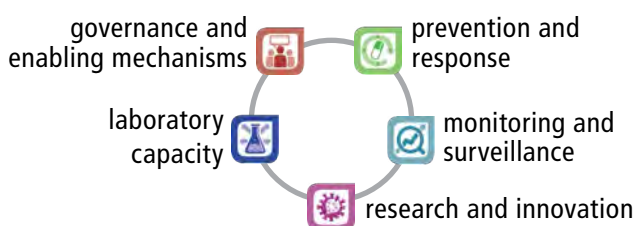
HIV DRUG RESISTANCE



EXECUTIVE SUMMARY

The rise in antimicrobial resistance is a growing global health concern that requires collective and coordinated action. Minimizing the emergence and transmission of drug-resistant HIV is a critical aspect of the global response to antimicrobial resistance. Increasing prevalence of HIV drug resistance to commonly used antiretroviral drugs poses a threat to the HIV response, with the potential to fuel an increase in HIV incidence, mortality and treatment costs if not adequately addressed.

In 2017, WHO and partners jointly developed and launched a comprehensive five-year Global Action Plan on HIV drug resistance (2017–2021), which outlines key actions for country and global stakeholders to prevent, monitor and respond to HIV drug resistance and to protect the ongoing progress towards achieving the global targets for epidemic control by 2030. The Global Action Plan has five strategic objectives:



This report summarizes the progress in implementing the Global Action Plan achieved during the first year (2017 to 2018) and the remaining challenges, with specific focus on 45 countries accounting for more than 85% of the total burden of HIV infection.

ADVANCEMENTS ON THE GLOBAL ACTION PLAN

- ✓ improved uptake of HIV drug resistance surveillance, better awareness of the relevance of HIV drug resistance and increased commitment by countries and donors to measuring HIV drug resistance;

- ✓ incorporating integrase inhibitor resistance testing in surveillance activities in anticipation of dolutegravir use in low- and middle-income countries;
- ✓ progress by the global research community in addressing critical research gaps related to HIV drug resistance; and
- ✓ positive advances in community engagement in tackling HIV drug resistance and awareness of the link between HIV drug resistance and the quality of care.

AREAS FOR FURTHER ACTION

- Need for further improvement in the quality of care to attain the set targets of the Global Action Plan for retention in treatment, viral load testing coverage, viral load suppression, antiretroviral drug stock-outs and appropriate use of second-line antiretroviral therapy;
- need for increased visibility of the reporting and use of quality-of-care indicators;
- need for timely response to documented high levels of pretreatment drug resistance; and
- need to strengthen links between HIV drug resistance and other global health policy priorities, including antimicrobial resistance and universal health coverage.

CONCLUSIONS

An effective response to HIV drug resistance requires a long-term multi-partner effort working at different levels across a range of sectors. The Global Action Plan on HIV drug resistance is a five-year plan offering the global community a framework for concerted action. One year has passed, and several examples of positive results have been achieved. Over the next four years, continued and greater engagement is required to maximize these efforts to fully achieve the goals of the Global Action Plan.

INTRODUCTION

FIG. 1.
High levels of pretreatment HIV drug resistance to efavirenz/nevirapine

In several low- and middle-income countries,

1 in 10  **adults** starting HIV treatment harbour resistant virus

3 in 10  **adults restarting first-line ART** with prior exposure to antiretroviral drugs harbour resistant virus

Women



starting first-line ART are **two times more** likely than men to harbour a resistant virus

5 in 10  **young children** newly diagnosed with HIV harbour resistant virus

The *WHO HIV drug resistance report 2017 (1)* documents that, in several low- and middle-income, more than **1 in 10 adults** starting antiretroviral therapy had HIV that was already resistant to efavirenz or nevirapine, the most commonly used first-line antiretroviral drugs¹ (**Fig. 1**).

In these settings, **women are two times more likely than men** to carry virus with pretreatment resistance, posing a significant challenge to the elimination of mother-to-child transmission of HIV (PMTCT) and to maternal and child health outcomes (1).

One in five people starting first-line treatment reports previous exposure to antiretroviral drugs (such as PMTCT-exposed women or people restarting first-line treatment after a period of treatment interruption). This group is **three times more** likely to harbor virus with pretreatment resistance to efavirenz or nevirapine than antiretroviral-naïve individuals (1).

Children represent a very vulnerable population: **one out of two children** newly diagnosed with HIV is infected with virus harbouring resistance to efavirenz and nevirapine,¹ thus at high risk of suboptimal treatment (2). HIV drug resistance among people starting or restarting antiretroviral therapy (pretreatment HIV drug resistance) has been increasing annually after the roll-out of antiretroviral therapy.

By the end of 2017, 21 million people were receiving life-saving antiretroviral therapy. A further 15.8 million are expected to start treatment in accordance with the WHO “treat all” recommendation, resulting in 36.7 million people who must be successfully maintained on lifelong treatment. Achieving high HIV testing access (at least 90% of all people living with HIV) and treatment coverage (at least 90% of the people who know their HIV-positive status) coupled with high levels of viral load suppression (at least 90% of the people receiving treatment) should lead to eliminating HIV as a public health threat by 2030.

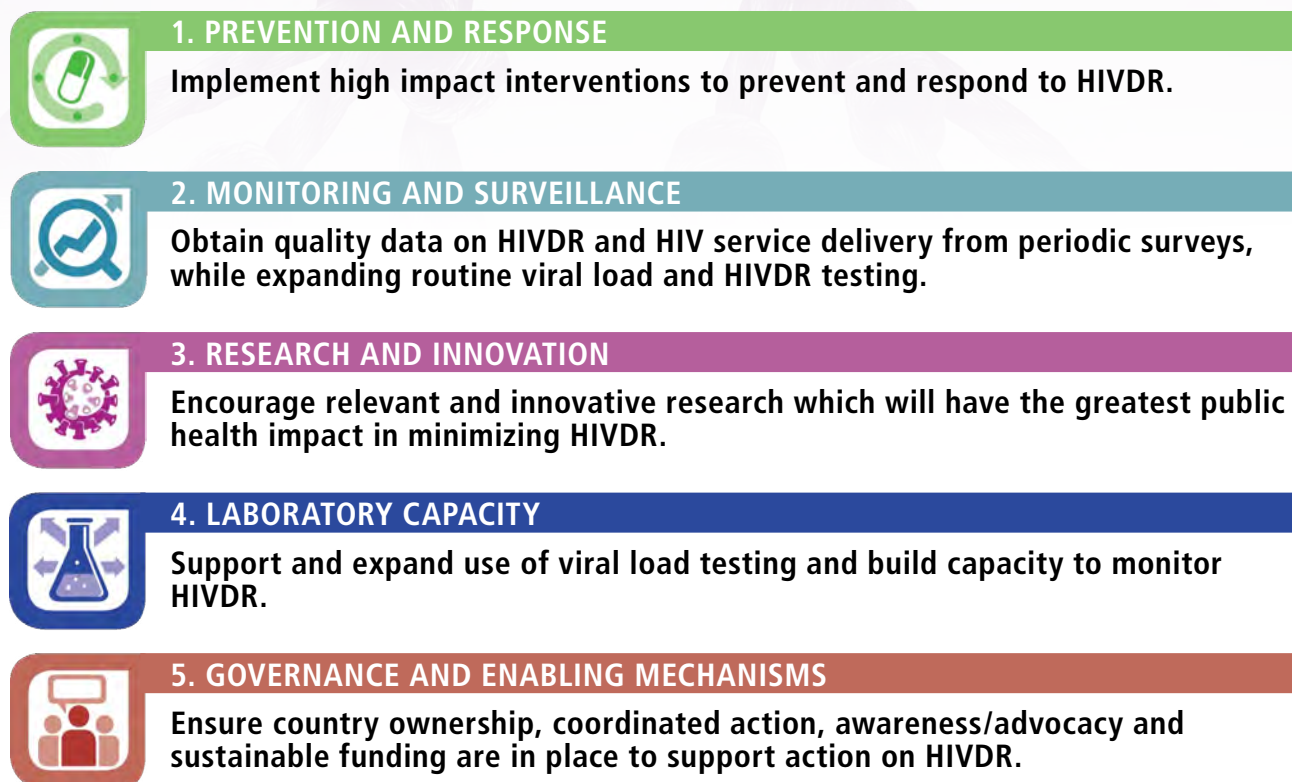
This publication was written by Silvia Bertagnolio and Seth Inzaule, Department of HIV and Global Hepatitis Programme, World Health Organization (WHO), under the overall guidance of Meg Doherty and Gottfried Hirschall (WHO). Copy editing: David Breuer, Denmark. Graphic design: Sue Hobbs, minimum graphics, New Zealand

¹ As of end of 2016, efavirenz and nevirapine were used in 86% and 14% of adults, and 29% and 47% of children on first-line HIV treatment, respectively (Clinton Health Access Initiative. ARV Market Report: The State of the Antiretroviral Drug Market in Low- and Middle-Income Countries, 2016–2021. 2017 https://clintonhealthaccess.org/content/uploads/2017/09/2017-ARV-Market-Report_Final.pdf (accessed July 07, 2018).

In 2017, WHO and partners jointly developed and launched a comprehensive five-year **Global Action Plan (3)** that articulates key synergistic actions for countries and stakeholders to prevent, monitor and respond to HIV drug resistance (Fig. 2).

This report summarizes the current progress in implementing the Global Action Plan on HIV drug resistance, one year after the initial launch, and specifically focuses on 45 WHO focus countries for HIV, which account for more than 85% of the global burden of HIV infection.²

FIG. 2. Global Action Plan on HIV drug resistance (HIVDR) and its five Strategic Objectives



² Angola, Botswana, Brazil, Cambodia, Cameroon, Chad, China, Côte d'Ivoire, Dominican Republic, Democratic Republic of the Congo, Ethiopia, Ghana, Guatemala, Haiti, India, Indonesia, Islamic Republic of Iran, Jamaica, Kenya, Lesotho, Malawi, Malaysia, Mali, Mexico, Morocco, Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, Russian Federation, Somalia, South Africa, South Sudan, Sudan, Eswatini (Swaziland), Thailand, Uganda, Ukraine, United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe.



PROGRESS ON HIV DRUG RESISTANCE PREVENTION AND RESPONSE

Preventing resistance emergence

Preventing HIV drug resistance is critical for the success of any HIV treatment programme and is achieved by optimizing the quality of antiretroviral therapy services and eliminating programmatic gaps along the cascade of HIV treatment. These gaps are identified by routinely monitoring programme quality indicators that are associated with the emergence of preventable resistance: retention on treatment, adherence to HIV treatment, viral load testing coverage, viral load suppression, timely switch to second-line antiretroviral therapy and antiretroviral drug stock-outs.

All 45 focus countries reported data in 2018 to WHO/UNAIDS³ based on 2016–2017 cohorts. Overall information was variably reported, with the percentage of missing data ranging from 16% to 40% for the various indicators.

Table 1 summarizes the proportion of countries achieving the targets for the programme quality indicators related to HIV drug resistance in 2017. These results can be considered as baseline information to evaluate and assess future trends.

TABLE 1. Programme quality indicators associated with HIV drug resistance (HIVDR) and associated targets

Programme quality indicator for HIVDR	Indicator target	Proportion of focus countries achieving indicator target as of 2017 ^a
Antiretroviral drug stock-outs	Zero antiretroviral drug stock-outs during a 12-month period	14 of 27 (52%)
Retention on antiretroviral therapy ^b	≥ 85% of people living with HIV retained on antiretroviral therapy 12 months after initiation	8 of 26 (31%)
Viral load testing coverage ^c	≥ 90% of people on antiretroviral therapy receiving at least one routine viral load test in a year	3 of 31 (10%)
Viral load suppression ^d	≥ 90% viral load suppression among people on antiretroviral therapy with a viral load test result available	4 of 14 (29%)
Use of second-line antiretroviral therapy regimens	At least 5% of people receiving second-line antiretroviral therapy	13 of 28 (46%)

^a Source: UNAIDS/WHO Global AIDS Monitoring tool 2018 (section 1.3 and 1.4) and WHO/AIDS Medicines and Diagnostics Survey on the use of ARV medicines and laboratory technologies and implementation of WHO Related Guidelines 2018. Overall, 60–84% of the 45 HIV focus countries contributed data for each indicator; countries' dataset that did not meet the minimum criteria were excluded (as described in b,c,d).

^b Countries' datasets were included if comprise ≥70% of people newly initiated on antiretroviral therapy; or <70% but reported to be nationally representative.

^c Data came from countries responding with the proportion of people on treatment who received a viral load test in the 12 months period. Countries' datasets were included if collected from all patients on ART or from a national representative data set. The results may however have been overestimated in countries where reporting did not account for multiple tests per patient

^d Countries' datasets were included if viral load testing coverage was ≥70% or <70% but reported to be nationally representative

³ Reported in 2018 through (1) UNAIDS/WHO Global AIDS Monitoring tool: online tool for monitoring the 2016 United Nations Political Declaration on Ending AIDS; and (2) WHO/AIDS Medicines and Diagnostics Survey on the use of ARV medicines and laboratory technologies implementation of WHO Related Guidelines

▶▶▶ Based on the data reported by countries to WHO/UNAIDS few countries had achieved the indicator targets in 2017 (**Table 1**). Specifically, **52%** of the countries reported zero antiretroviral drug stock-outs, **31%** reported $\geq 85\%$ retention on treatment, **10%** reported $\geq 90\%$ viral load testing coverage and **29%** reported viral load suppression $\geq 90\%$. Finally, a low rate of switching to second-line antiretroviral therapy is also a challenge in most low- and middle-income countries. Although about 10–20% of people have documented elevated viral load while receiving first-line antiretroviral therapy (4) and may need to switch to second-line regimens, only **46%** of countries had at least 5% of the people receiving antiretroviral therapy on a second-line regimen, which indicates a suboptimal use of available treatment options. These findings highlight important programmatic gaps suggesting the need for a proactive approach to improving the quality of HIV treatment and care services in order to minimize the emergence of preventable HIV drug resistance.

Some countries are already taking important steps to address programme gaps (**Box 1**). It is critical that antiretroviral therapy programmes develop national frameworks for improving quality to enable them to effectively respond to challenges in programme implementation. Such a framework should incorporate quality improvement approaches to assess clinic functioning and introduce locally sustainable solutions to complex problems, including stronger systems for drug procurement and supply chain, increased use of viral load testing and differentiated care models to maximize adherence and retention. Finally, increased community engagement is essential to monitor the quality of antiretroviral therapy delivery and prevent the emergence of HIV drug resistance.

BOX 1.

Antiretroviral therapy programme in Cameroon responds to programme quality gaps

WHO recommends that programmes routinely monitor a minimum set of quality indicators associated with the emergence of preventable HIV drug resistance (early warning indicators). Recognizing the need to minimize the emergence and transmission of HIV drug resistance, Cameroon has conducted five rounds of monitoring of the early warning indicators in 10–50 clinics since 2008. When each round was completed, national and clinic-level recommendations were developed and implemented based on the findings.

In 2017, an investigation was carried out by the national programme in a subset of antiretroviral therapy clinics⁴ to assess the impact of recommendations generated as a result of monitoring early warning indicators. Messaging on adherence to antiretroviral therapy provided by social workers substantially increased on-time pill pick-up in some clinics, with adherence improving from a range of 10–51% in year 1 to 91–100% by year 4. This improvement is especially important given the limited viral load testing coverage in the country. In addition, 100% of the people receiving treatment were given appropriate triple-drug combinations in all five rounds.

Countries' responses to high levels of pretreatment drug resistance

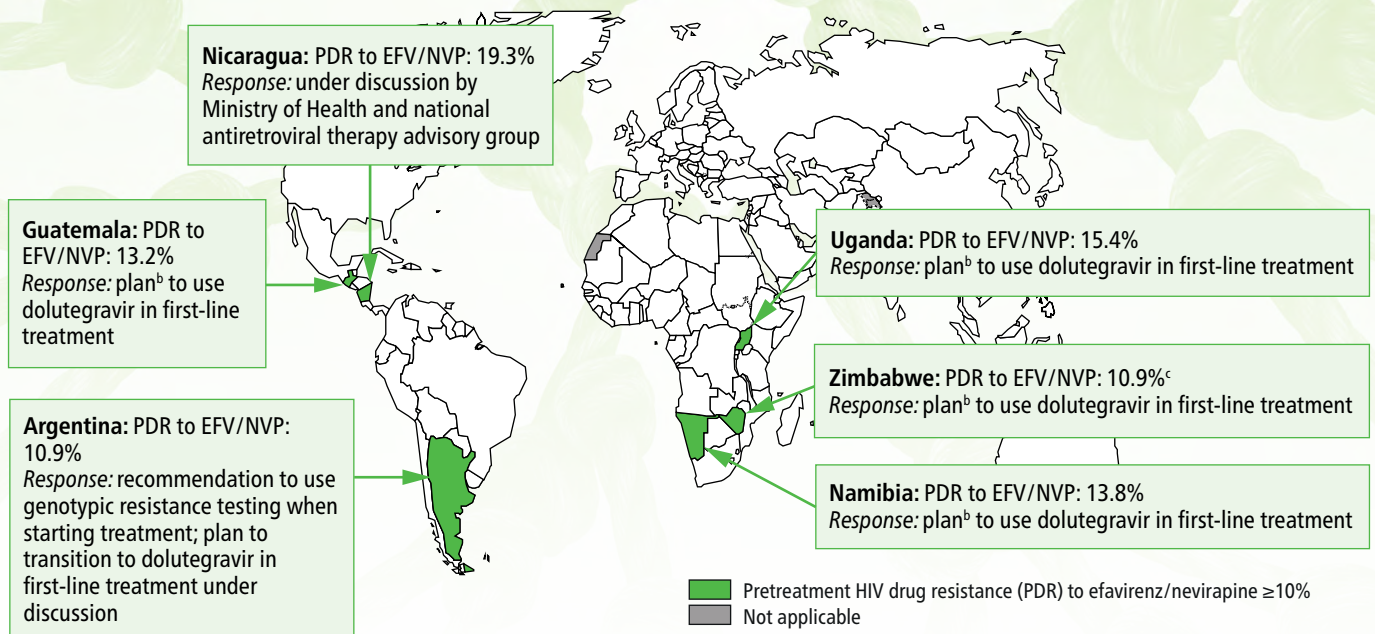
WHO 2017 guidelines (5) recommend that, in countries in which the prevalence of pretreatment HIV drug resistance to efavirenz or nevirapine is $\geq 10\%$, an alternative first-line regimen that does not contain non-nucleoside reverse-transcriptase inhibitors (NNRTI) such as efavirenz or nevirapine, should be urgently considered. If this is not feasible, using HIV drug resistance testing to guide the selection of an optimal regimen for people starting treatment can be considered (5).

In 2017, **6 of 11 countries** implementing national HIV drug resistance surveys (Argentina, Guatemala, Namibia, Nicaragua, Uganda and Zimbabwe) reported a prevalence of pretreatment HIV drug resistance to efavirenz or nevirapine exceeding 10%. **Fig. 3** shows the policy changes made by these countries in response to the high levels of pretreatment HIV drug resistance.

⁴ National report on early warning indicators of HIV drug resistance, Cameroon. 2018.

FIG. 3.

Response to levels of pretreatment HIV drug resistance (PDR) to efavirenz/nevirapine (EFV/NVP) at or above 10% among people initiating first-line antiretroviral therapy: uptake of WHO recommendations^a



^a Guidelines on the public health response to pretreatment HIV drug resistance. Geneva: World Health Organization; 2017.

^b Transition plan to use dolutegravir has been delayed or under revision due to safety concerns for infants born to women who are on dolutegravir at time of conception.

^c Only ARV drug naive starting first-line antiretroviral therapy were included.

One alternative drug in first-line for use in countries with high levels of NNRTI pretreatment HIV drug resistance is dolutegravir (DTG), an integrase inhibitor, in combination with two nucleoside reverse-transcriptase inhibitors (NRTIs). Given the advantages of DTG compared to

NNRTI, and its recent availability as a low-cost fixed-dose combination of tenofovir, lamivudine and DTG in 92 low- and middle-income countries, many countries made plans to transition to DTG in first-line antiretroviral therapy.

▶▶▶ The transition plan to use DTG in first-line HIV treatment was accelerated in countries with high levels of pretreatment HIV drug resistance. However, recent findings from an observational study in Botswana on the use of DTG among women at the time of conception signalled the potential association between DTG use and neural tube defects among children (6). As a result, the accelerated roll-out of DTG has slowed in some countries as more information on the signal of risk is obtained. Other countries implemented policy changes in response to high levels of pretreatment resistance, even if the prevalence was below the recommended 10% threshold for public health action.

In Mexico, for example, where a national prevalence of pretreatment resistance was 9.2% (14.8% in women), resistance testing was recommended for children and adolescents starting HIV treatment and in pregnant women with prior exposure to antiretroviral drugs.

Brazil had been an early adopter of DTG and had a prevalence of resistance to NNRTI measured in naive individuals of 6.8%. Following the recent safety concerns associated with DTG, the use of HIV drug resistance testing has been recommended for all individuals of child bearing potential starting HIV treatment and not using an effective contraceptive method (intrauterine device or hormone implant) to select the most suitable regimen.



PROGRESS ON HIV DRUG RESISTANCE MONITORING AND SURVEILLANCE

HIV drug resistance surveillance

WHO recommends periodic nationally representative surveys to inform the emergence and transmission of HIV drug resistance (**Box 2**), provide data to support the selection of optimal antiretroviral therapy in a country and measure the extent to which the emergence and transmission of drug-resistant virus are minimized through programme practices and antiretroviral stewardship.

HIV drug resistance has emerged to all antiretroviral drugs developed to date, including DTG, and resistance surveillance should therefore be conducted routinely regardless of the regimen used.

To assist countries in implementing surveys, standardized guidance, operational toolkits and a database to support countries and genotyping laboratories in the quality assurance of epidemiological and sequence data are available (7).

BOX 2.

WHO's guidance on nationally representative HIV drug resistance survey: purpose and public health use

Pretreatment drug resistance: assess resistance present at the time of initiating antiretroviral therapy to support a country's choice of recommended regimens for first-line antiretroviral therapy and pre- and post-exposure prophylaxis.

Acquired drug resistance: assess resistance among people receiving treatment to guide the selection of second- and third-line regimens, monitor practices in switching treatment and inform national estimates of viral load suppression.

Resistance among HIV infected, treatment-naive infants: assess resistance among infants less than 18 months old, who have not started treatment, to support the selection of first-line antiretroviral therapy and the composition of subsequent regimens.

WHO recommends to repeat pretreatment and acquired HIV drug resistance surveys every 3 years, and surveys in infants every 5 years.

Upcoming WHO's guidance on HIV drug resistance surveillance

▶▶▶ As viral load testing coverage increases in countries, the prevalence of acquired drug resistance can be estimated by genotyping remnant viral load specimens from people with viral non-suppression routinely collected at the central laboratory level. This approach offers an alternative to a standard acquired drug resistance survey in countries with optimal viral load testing coverage and data system; WHO is developing guidance for implementation.

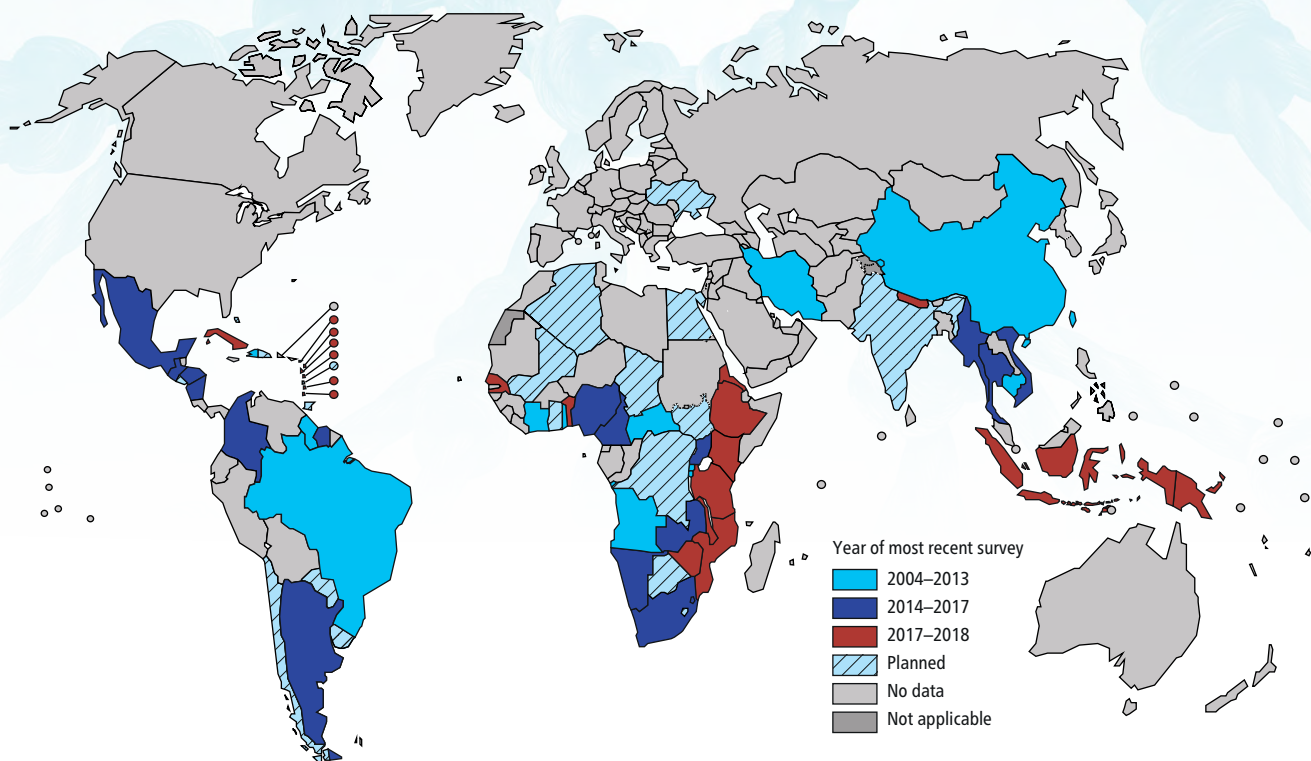
▶▶▶ Pre-exposure prophylaxis (PrEP) is an effective approach to prevent HIV infection by using antiretroviral drugs. Resistance can emerge as a result of poor adherence to PrEP without frequent repeat HIV testing. WHO is developing guidance for countries to monitor resistance emerging from PrEP.

Progress in survey implementation

Since 2004, 271 surveys have been implemented in 69 countries. Substantial progress in implementing surveys has been achieved in this period (**Fig. 4**).

Between 2017 and 2018, 20 WHO-recommended pretreatment HIV drug resistance surveys and nine acquired drug resistance surveys were initiated in 20 countries, and an additional 28 countries plan to conduct surveys in 2018 (**Fig. 5**). Of the 45 HIV focus countries, 47% have implemented at least one of the recommended HIV drug resistance surveys over the previous three years. The survey results will be reported in the next WHO HIV drug resistance report.

FIG. 4.
Implementation of WHO recommended HIV drug resistance surveys, 2004–2018



Progress in routine monitoring of program quality indicators

▶▶▶ In 2016–2017, 9 of 21 HIV focus countries reported data to WHO, indicating progress in monitoring programme quality indicators associated with prevention of HIV drug resistance.

WHO recommends that countries integrate early warning indicators of HIV drug resistance into routine monitoring and evaluation systems (8). This means assessing routinely available clinic-level data (Table 1) and taking local- or national-level actions to close gaps in service delivery.

▶▶▶ By mid-2018, 11 of 16 HIV focus countries that reported this information have integrated monitoring of EWI of HIV drug resistance into routine monitoring and evaluation activities.

In the future, the community and civil society will need to play an increasingly important role in documenting gaps in high-quality antiretroviral therapy service delivery and their causes and in developing sustainable solutions.



PROGRESS ON RESEARCH AND INNOVATION

Relevant and innovative research is vital to help to address knowledge gaps and create interventions that will have the greatest impact on minimizing HIV drug resistance.

▶▶▶ In November 2017, the WHO HIV drug resistance network (WHO HIVResNet) held a consultative meeting to discuss and review key research questions related to HIV drug resistance that need to be addressed in the short and medium term, with special focus on transition to DTG-based regimens (9) (Table 2). A rapid assessment of research question implementation among the research community and a review of the published literature as of July 2018 showed that 92% of the high-priority questions are being studied.

TABLE 2.
Summary of progress in addressing current research gaps related to HIV drug resistance

EPIDEMIOLOGY AND CLINICAL	
■ Effect of pre-existing resistance to the NRTI backbone on the efficacy of dolutegravir based antiretroviral therapy	✓
■ Levels of viral suppression and prevalence and pattern of HIV drug resistance mutations among people failing dolutegravir -based antiretroviral therapy in low- and middle-income countries	✓
■ Cost-effectiveness of individualized HIV drug resistance testing for people failing a boosted protease inhibitor or DTG-based regimen to minimize unnecessary switches to subsequent lines	✓
■ HIV drug resistance emerging in programmes scaling up PrEP	✓
■ Impact of K65R/M184V mutations on the efficacy of truvada-based PrEP	✓
■ Validated local, inexpensive and sustainable corrective actions to minimize the emergence and transmission of preventable drug resistant virus	—
■ Clinical impact of raltegravir-based antiretroviral therapy among children infected with NRTIs-resistant HIV	✓
■ Clinical impact of dolutegravir administered twice daily among children failing raltegravir-based antiretroviral therapy	✓
■ Optimal viral load switching algorithm to minimize the emergence of resistance	✓
■ Simple algorithm for interpreting HIV drug resistance for use by caregivers	✓
■ Efficacy of dolutegravir administered twice daily as a strategy to increase the potency of the regimen in individuals with partially active NRTI backbone	✓
■ Levels of viral suppression and acquired HIV drug resistance among people receiving second-line boosted protease inhibitors in low- and middle-income countries, with particular focus on atazanavir/ritonavir	✓
■ Response of tenofovir, lamivudine and dolutegravir in populations at high risk of suboptimal adherence (e.g. adolescents) and in people co-infected with TB and HIV	✓
■ Clinically significant thresholds of low-abundance NNRTI-resistant variants	✓
■ Cost-effectiveness analysis tools for use in countries for financing and advocacy of optimized treatment	✓
VIROLOGICAL ASPECTS	
■ Correlation of genotype-phenotype and clinical significance for all mutations	✓
■ List of transmitted integrase inhibitor mutations	✓
■ Minimum set of mutations for protease inhibitors, reverse-transcriptase inhibitors and integrase inhibitors for clinical purposes for point-mutation technology	—
■ Impact of novel drug delivery methods (such as long-acting drug formulations) on the selection of HIV drug resistance	✓
INNOVATIVE TECHNOLOGIES	
■ Simple and affordable point-of-care HIV drug resistance assays	✓
■ Inexpensive, simple, easy-to-interpret tests that combine viral load and HIV drug resistance testing that can be used to minimize unnecessary switches to subsequent regimens	✓
■ Simple and affordable next-generation sequencing bioinformatics algorithms	✓
■ Newer collection matrices for HIV drug resistance testing	✓
■ Affordable, simple and easy-to-use point-of-care tests to measure drug levels to distinguish patients failing treatment due to poor adherence from those failing due to resistance	✓

Methods: rapid assessment of research question implementation among research community and review of the published literature

■ Tier 1 research question; ■ Tier 2 research question

✓ Research currently undergoing; — No evidence that research is being conducted



PROGRESS ON STRENGTHENING LABORATORY CAPACITY

Viral load testing coverage

Access to high-quality and routine viral load monitoring is fundamental to ensuring sustainable population-level effectiveness of antiretroviral therapy and monitoring the global targets for HIV epidemic control.

▶▶▶ As shown in **Table 1**, viral load testing coverage remains below the target of 90% in most countries (**Fig. 5**). Overall, more than half the countries reported <50% access to viral load testing; this means that more than half the people receiving antiretroviral therapy do not receive one viral load test per year.

Laboratory network for HIV drug resistance surveillance

Since access to HIV drug resistance testing is limited in low- and middle-income countries, WHO and its HIVResNet laboratory network support countries in conducting HIV drug resistance testing for the purpose of surveillance (**Fig. 7**).

▶▶▶ HIVResNet comprises 30 laboratories, and an additional five are building capacity towards WHO designation. Ten of the 30 laboratories have capacity for genotyping from dried blood spot specimens, a field-friendly specimen type most suitable for use in many low- and middle-income countries.

WHO is encouraging and strengthening laboratory capacity for integrase resistance testing in preparation for transition to integrase inhibitor-based regimens.

▶▶▶ By mid-2018, 18 of the 30 laboratories reported having capacity for testing integrase inhibitors for resistance, while plans for developing this ability were ongoing in an additional nine laboratories.

▶▶▶ Recent important advances have been made to improve the availability of low-cost HIV drug resistance testing technologies (next-generation sequencing, point-mutation assays or inexpensive commercially available kits). In 2017–2018, two global consultations were held (Johannesburg, South Africa in 2017 and Winnipeg, Canada in 2018) to explore the future use of these technologies and to engage global partners in steering this pillar of the Global Action Plan (9).

FIG. 5. Viral load testing coverage among 45 HIV focus countries (as of December 2017)

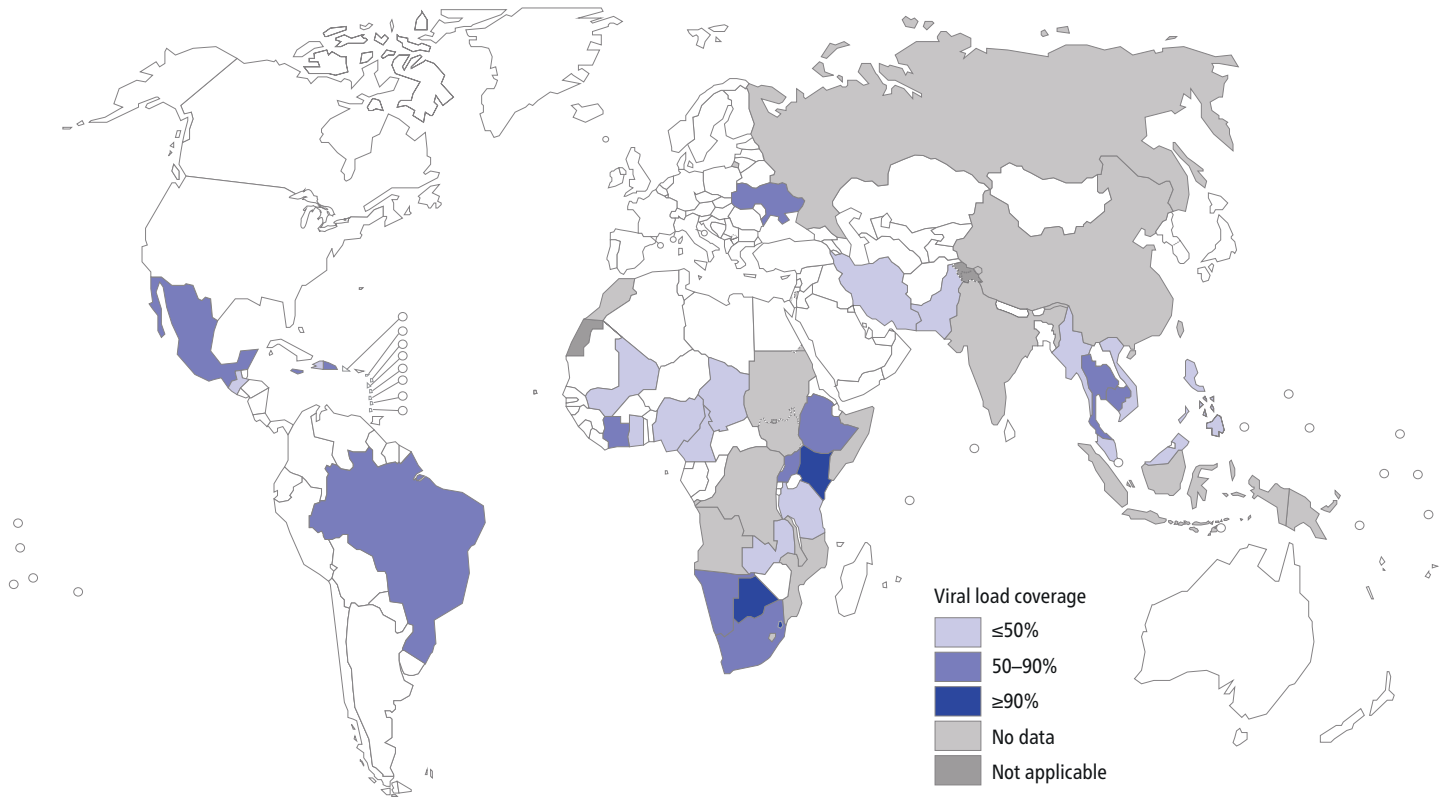
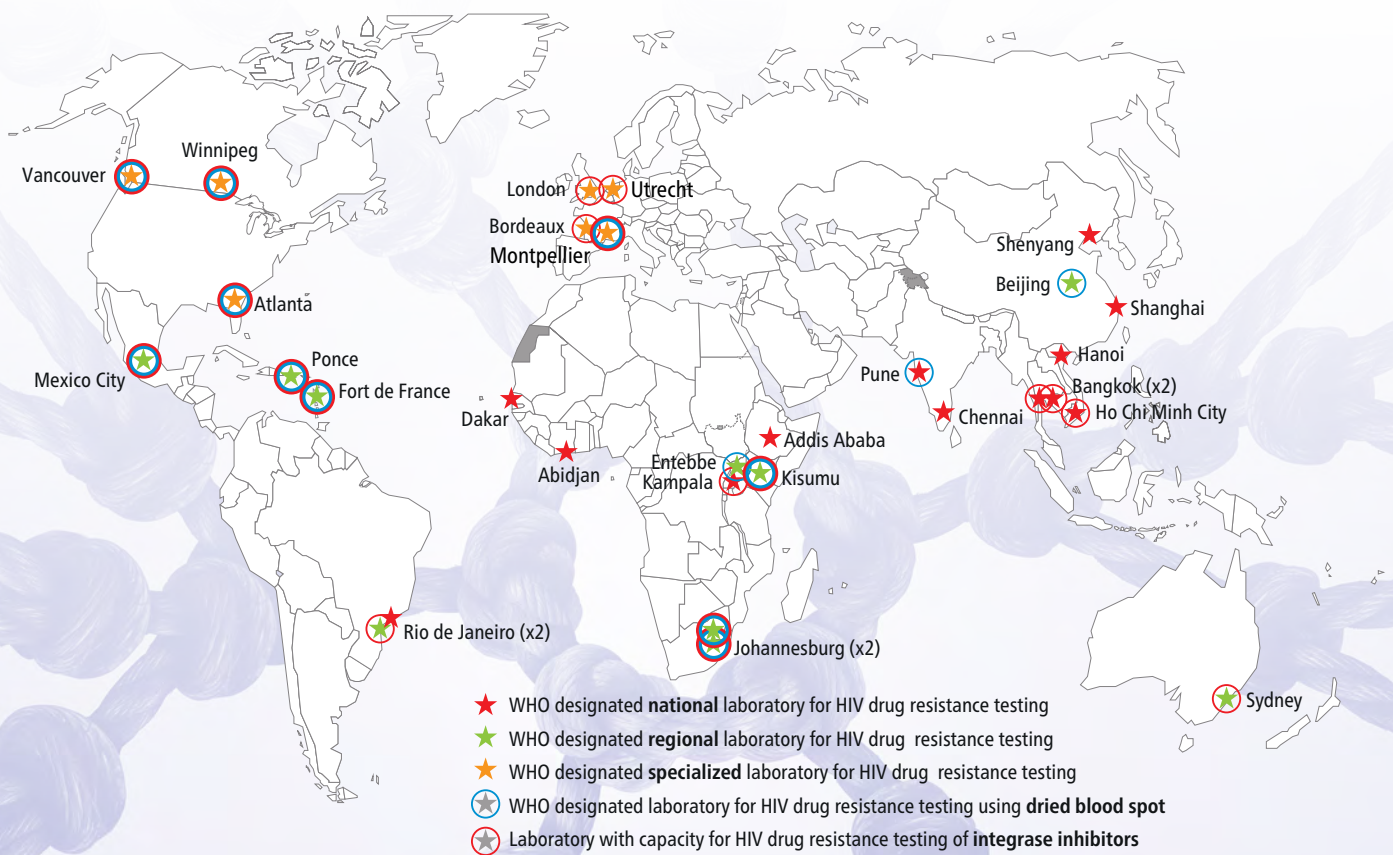


FIG. 6. WHO HIVResNet HIV drug resistance laboratory network





PROGRESS ON BUILDING SUSTAINABLE GOVERNANCE AND ENABLING MECHANISMS

Financing HIVDR activities

Countries and the global community should share responsibility for monitoring, preventing and responding to rising levels of HIV drug resistance within the wider context of health policies, strategies and resource mobilization. Global partners, such as the Global Fund and the United States President's Emergency Plan for AIDS Relief (PEPFAR) have committed to funding HIV drug resistance surveillance activities in countries, strengthening health-care systems and building laboratory capacity to achieve universal viral load testing coverage.

▶▶▶ A 2018 mid-term review of Global Fund grants shows that the number of countries requesting funding for prevention and surveillance of HIV drug resistance increased from 24 in 2015–2017 to 34 countries in 2018–2020. PEPFAR is also supporting 12 countries to implement HIV drug resistance surveys in 2018–2019.

Country ownership and antiretroviral drug stewardship

Governance and ownership of HIV drug resistance prevention, monitoring and response is a critical element of a well-functioning antiretroviral therapy programme. WHO recommends that countries develop a national HIV drug resistance plan as part of their broader HIV response strategy.

▶▶▶ By mid 2018, 46% of 28 focus countries reporting data to WHO had instituted a national strategic plan to guide the prevention and monitoring of HIV drug resistance, suggesting a broad in-country commitment. WHO and global partners also offer technical assistance to countries implementing Global Action Plan activities, including developing national HIV drug resistance plans, surveillance and response of HIV drug resistance, monitoring and response to programmatic quality indicators and strengthening laboratory quality systems for HIV drug resistance genotyping.

Advocacy and awareness

Advocacy and awareness of the burden and impact of HIV drug resistance among policy-makers, health-care workers, communities, patients and civil societies is key but generally insufficient.

▶▶▶ To galvanize the global community around the HIV drug resistance advocacy agenda, WHO, the Joep Lange Institute, AIDS Fond and the Partnership to Inspire, Transform and Connect the HIV response (PITCH) met in The Hague, Netherlands, in March 2018 with civil society advocates, community representatives, health practitioners, researchers and policy-makers to define the building blocks of a bold advocacy strategy to promote the implementation of the Global Action Plan (10). Overall, the meeting affirmed the critical role of the community and civil rights groups in preventing and monitoring HIV drug resistance and identified ways to engage them (**Box 3**).

BOX 3.

Recommendations for improving HIV drug resistance advocacy and community engagement (The Hague meeting, 2018)

- Emphasize HIV drug resistance as an HIV and quality-of-care issue that requires community engagement and innovative solutions for its monitoring and prevention.
- Develop simplified, evidence-informed messaging regarding HIV drug resistance, including using social media to raise awareness.
- Strengthen links between HIV drug resistance and other global health policy priorities, including antimicrobial resistance and universal health coverage.
- Visibly benchmark countries and regions based on their quality-of-care indicators to trigger community engagement in supporting quality improvement processes and stimulating advocacy actions.

CONCLUSIONS

The launch of the Global Action Plan in 2017 demonstrated increased commitment by the global community to prevent, monitor and respond to the threat posed by increasing levels of HIV drug resistance to ensure the long-term durability and efficacy of available and future antiretroviral drugs. Progress in implementing the Global Action Plan has been made over the first year; however, more efforts are required, as highlighted by ongoing gaps in antiretroviral therapy service delivery. Particular attention must be focused on supporting retention, maximizing adherence, preventing drug stock-outs and scaling up and using viral load testing. Frameworks for clinics and programmes to identify the causes of performance gaps are also needed to support the development of sustainable locally tailored solutions.

Suboptimal quality of care may result in resistance emergence even to drugs with a high genetic barrier such as DTG. As countries transition to this new drug, it is critical that viral load and resistance outcomes be closely monitored. Thus, HIV drug resistance surveillance will continue to play a critical role in monitoring the continuous efficacy of currently available and future antiretroviral drugs and inform changes in public health treatment policies.

Increased commitment is required from all stakeholders to guarantee successful implementation of the Global Action Plan and to attain the wider global goals for controlling the HIV epidemic. More countries must embrace ownership of preventing and monitoring HIV drug resistance and antiretroviral drug stewardship. When coupled with increased commitment from global partners, advocacy from community activists and involvement by researchers and policy-makers, the strategic objectives of the Global Action Plan will be achieved.

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For more information, contact:
World Health Organization
Department of HIV/AIDS
20, avenue Appia
1211 Geneva 27
Switzerland

E-mail: hiv-aids@who.int
www.who.int/hiv
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ACTION PLAN

HIV DRUG RESISTANCE