

PREVENTING AND RESPONDING TO HIV DRUG RESISTANCE IN THE AFRICAN REGION

REGIONAL ACTION PLAN 2019-2023



World Health
Organization

REGIONAL OFFICE FOR

Africa

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Preventing and responding to HIV drug-resistance in the African Region: regional action plan 2019-2023

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ACRONYMS

ADR	Acquired HIV drug resistance
AIDS	Acquired Immune Deficiency Syndrome
AMR	Antimicrobial resistance
ART	Antiretroviral therapy
ARV	Antiretroviral (drugs)
CDC	United States Centers for Disease Control and Prevention
EWI	Early Warning Indicators
GAP	Global Action Plan
HIV	Human Immunodeficiency Virus
HIVDR	HIV Drug Resistance
HIVResNet	WHO HIV Drug Resistance Network
M&E	Monitoring and Evaluation
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
PDR	Pre-Treatment HIV Drug Resistance
PEPFAR	United States President's Emergency Plan for AIDS Relief
PLHIV	People Living with HIV
PMTCT	Prevention of Mother -To-Child Transmission of HIV
PrEP	Pre-Exposure Prophylaxis
RAP	Regional Action Plan
TB	Tuberculosis
TDR	Transmitted HIV Drug Resistance
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
US\$	US Dollar
WHO	World Health Organization

EXECUTIVE SUMMARY

Global action to combat HIV/AIDS has had an immense impact in the African Region. By the end of 2017, 15.3 million people living with HIV (PLHIV) in the African Region were accessing life-saving antiretroviral drugs (ARVs), representing 70% of the 21.7 million people accessing antiretrovirals (ARV) globally (1).

WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS) have set the target of 90% of people living with HIV on antiretroviral therapy (ART) achieving virological suppression by 2020. However, the potential positive impact from the scale-up of ART is under threat from an increase in the prevalence of HIV drug resistance (HIVDR). As the prevalence of HIVDR in the African Region increases, the impact on society, the economy and on health could be severe (2,3). If the prevalence of pretreatment HIV drug resistance (PDR) to non-nucleoside reverse-transcriptase inhibitors (NNRTIs) in sub-Saharan Africa exceeds 10% and NNRTIs continue to be used in first-line ART regimens, over a five-year period, NNRTI PDR may be responsible for a cumulative 135 000 AIDS-related deaths, 105 000 new HIV infections and an additional US\$ 650 million will be spent on ARVs in sub-Saharan Africa (2).

The potential positive impact from the scale-up of ART is under threat from an increase in the prevalence of HIV drug resistance (HIVDR).

In response to this emerging threat, the World Health Organization (WHO) launched the Global Action Plan (GAP) on HIV Drug Resistance in 2017 (3). The GAP, developed with WHO's partners and stakeholders, outlines a framework for action to minimize the emergence and transmission of HIVDR and to ensure the most effective treatment for all PLHIV. It outlines suggested actions for Member States and other stakeholders according to five strategic objectives:

1. Prevention and response: Implement high-impact interventions to prevent and respond to HIVDR;
2. Monitoring and surveillance: Obtain quality data on HIVDR from periodic surveys; expand the coverage and quality of routine viral load and HIVDR testing; monitor quality of service delivery;

3. Research and innovation: Encourage relevant and innovative research, leading to interventions that will have the greatest public health impact on minimizing HIVDR;
4. Laboratory capacity: Strengthen laboratory capacity and quality to support and expand the use of viral load monitoring and build capacity to monitor HIVDR in low- and middle-income countries; and
5. Governance and enabling mechanisms: Ensure that governance and enabling mechanisms (advocacy, country ownership, coordinated action and sustainable funding) are in place to support action on HIVDR.

The WHO African Regional Action Plan (RAP) on HIVDR articulates the priorities of the African Member States to monitor and prevent HIVDR as well as ensure availability and effectiveness of life saving ARVs. Implementation of the strategic objectives of the GAP since 2017, although slow, has progressed in some Member States in the African Region. Hence, to ensure implementation of the recommended set of actions outlined in the the GAP, the RAP adapts the GAP's strategic objectives to an African context and prioritizes suggested actions based on feedback from WHO Member States. The five-year RAP extends beyond 2021 and is aligned with the WHO thirteenth general program of work (GPW 13) 2019 -2023.

The objectives of the five-year (2019 - 2023) Regional Action Plan on HIVDR are:

1. To raise the priority accorded to the prevention of and response to HIVDR in national and regional agendas throughout the African Region.
2. To strengthen national commitment, capacity, governance and partnerships to accelerate country responses for the prevention, monitoring, and response to HIVDR.
3. For Member States to work collectively to implement the strategic objectives.

The RAP strives to contribute to the global drive towards the 90-90-90 targets.

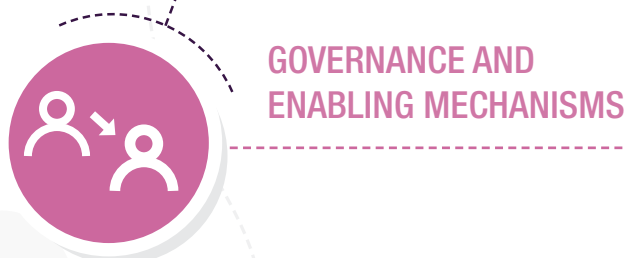
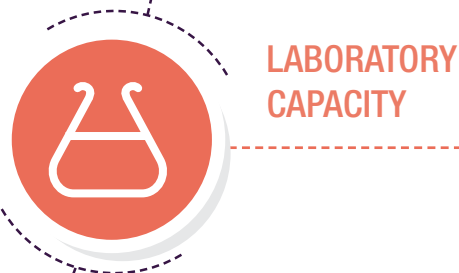
FIGURE 1: THE AFRICAN REGIONAL ACTION PLAN ON HIV DRUG RESISTANCE

STRATEGIC OBJECTIVES

1. To raise the priority accorded to the prevention of and response to HIVDR in national and regional agendas throughout the African Region.

2. To strengthen national commitment, capacity, governance and partnerships to accelerate country responses for the prevention, monitoring, and response to HIVDR.

3. For Member States to work collectively to implement the strategic objectives.



ACTION PLAN

- 1. Increase viral load monitoring
- 2. Optimize ART service delivery
- 3. Routinely monitor and respond to EWI of HIVDR at clinical and national levels
- 4. Ensure health workers are trained to prevent, monitor and respond to HIVDR

- 5. Implement routine national HIVDR surveys
- 6. Monitor Early Warning Indicators (EWI)
- 7. Integrate EWIs into routine national M&E activities
- 8. Develop Regional HIVDR reports or contribute to the global HIVDR report
- 9. Use HIVDR database to clean and link epidemiological and HIVDR sequence data

- 10. Collate all relevant HIVDR research
- 11. Identify evidence-based programmatic interventions
- 12. Assess the impact of identified interventions

- 13. Ensure that HIVDR strategies to include the training of laboratory health professionals
- 14. Expand viral load testing services
- 15. Include resistance testing to new drug classes and genotyping using dried blood spots
- 16. Convene the HIVDR laboratory network

- 17. Develop a five-year national HIVDR strategy
- 18. Create linkages with other AMR programmes
- 19. Form a national HIVDR technical working group
- 20. Identify funding mechanisms
- 21. Include cost estimates
- 22. Develop HIVDR strategy implementation plans
- 23. Develop a country-level communication strategy
- 24. Build community engagement

1

OVERVIEW

The African Regional Action Plan on HIV Drug Resistance (HIVDR) 2019-2023, is a five-year action plan aligned with the strategic objectives of the World Health Organization (WHO) Global Action Plan on HIV Drug Resistance 2017-2021 (3), WHO 2015 Global Action Plan on Antimicrobial Resistance (4), HIV/AIDS Strategy for the WHO African Region (2016) (5), the Global Health Sector Strategy on HIV 2016-2021 (6) and the the Thirteenth general program of work 2019-2023 (GPW 13) (7).

This Regional Action Plan on HIVDR provides a comprehensive framework for action by Member States, WHO's Regional Office for Africa, implementing partners, researchers, civil society and other stakeholders, and describes a package of interventions and resources to guide the response to HIVDR (Fig. 1).

VISION

The Regional Action Plan on HIV Drug Resistance envisions an African Region in which the emergence and transmission of HIV drug resistance is monitored, prevented, managed and reversed, and every person living with HIV has access to effective lifelong treatment.

GOALS

1. To enable the African Region to effectively prevent, monitor and respond to HIVDR.
2. To ensure that HIVDR does not undermine the attainment of regional targets on health, ending AIDS and the sustainable development goals.

OBJECTIVES

1. To raise the priority accorded to the prevention of and response to HIVDR in national and regional agendas in the WHO AFRO Member States.
2. To strengthen national commitment, capacity, governance and partnerships to accelerate country responses for the prevention, monitoring, and response to HIVDR.
3. For Member States to work collectively to implement the strategic objectives.

GUIDING PRINCIPLES

The following provides an overarching ethical framework under which the Regional Action Plan on HIVDR shall operate.

A human rights approach towards universal access:

Where human rights are promoted and safeguarded, the impact of HIV/AIDS is reduced. A human rights approach ensures an open and supportive environment exists for PLHIV and that they are protected from discrimination, treated with dignity, and provided with access to treatment, care and support. This approach encourages individuals to seek testing and allows those people who are HIV positive to seek and receive treatment and psychosocial support and to take measures to prevent transmission to others.

Country ownership and accountability: Strong political engagement and leadership are essential to enable countries to own and direct their national AIDS response. This ownership requires the engagement of civil society, PLHIV and the population in general to ensure the development and implementation of participatory national HIV strategies.

Comprehensive, coordinated and integrated service delivery and effective partnerships: Collaboration at global, regional and national levels and between key partners (including Member States, nongovernmental organizations, civil society organizations, United Nations programmes and agencies, and international implementing partners and donors) allows for improved service delivery, greater and more sustained impact, more efficient mobilization and use of resources, greater sharing of information, and enhanced research into innovative approaches.

Financing for sustainability: Resources should be allocated to combinations of interventions that will achieve the greatest impact, are aligned with national programmes and strategies, and that maximize the investment of major development agencies and donors in the global response to HIV.

TARGETS BY 2023

In accordance with the Global Action Plan, this Regional Action Plan shall pursue these targets under five strategic objectives:

1. Prevention and response
2. Monitoring and surveillance
3. Research and innovation
4. Laboratory capacity
5. Governance and enabling mechanisms (Fig. 2)

Through this Action Plan, the African Region has an opportunity to contribute to the 2020 global targets to:

- reduce HIV-related deaths in Africa to below 500 000;
- ensure 90% of people living with HIV in the African Region, who are on treatment, achieve viral load suppression;
- increase research into, and development of, HIV-related medicines for use in treatment and prevention especially in the African health context;
- ensure all countries integrate essential HIV services into national health financing arrangements; and
- ensure overall financial investments for the AIDS response in low-and middle-income countries reach at least US\$ 26 billion, with continued increases from the current levels of domestic public sources.

BOX 1: WHO IS THIS ACTION PLAN FOR?

The Regional Action Plan is targeted at several categories of actors, each playing an essential role. The Action Plan recognizes that many different skills, capacities, resources, and approaches are needed to respond to HIVDR and that collaborative partnerships are needed between these actors to achieve their common goals. This plan is intended for the following actors:

- **Member States**, especially their ministries of health and HIVDR technical working groups, are the main implementers of the Regional Action Plan. This plan provides a range of priority actions that Member States can tailor and prioritize for their national contexts, as well as suggestions for various enabling and supporting mechanisms to ensure Member States receive the resources they need to realize their objectives.
- **The WHO Regional Office for Africa** plays a convening role in developing collaborative networks and partnerships between different actors. The Regional Office sets regional standards, guidelines, and best practice, harmonizing the efforts of various Member States and holding them accountable for their contribution to HIVDR prevention, monitoring, and response.
- **Civil society** including PLHIV, communities affected by HIV and advocacy groups are critical to the successful implementation of the Regional Action Plan. The RAP prioritizes raising awareness within communities in order to generate the widespread support necessary for the successful attainment of its goals. Civil society representation should be integrated into decision-making, planning and implementation processes to ensure that all interventions reflect the will and interests of citizens.
- **International development agencies** are sources of technical and financial resources for national and regional HIVDR programmes. This Action Plan advocates sustained support from international partners for the African Region and outlines key areas of strategic action where their contributions will make the biggest impact.
- **Research institutions** provide the evidence necessary to build an effective HIVDR prevention programme. This action plan suggests steps toward coordinating regional research activities and disseminating findings to maximize effective application and improve accessibility in resource-constrained contexts.

FIGURE 2: TARGETS BY 2023

S01 PREVENTION AND RESPONSE

TARGETS:



- <15% of African countries with any ART medicine stock-out during a 12-month period
- >80% of African countries switching patients to second-line ART according to WHO guidelines
- >80% of African countries with <5% patients on second-line ART
- >90% of African countries reporting >85% retention on treatment
- 90% of African countries with 90% viral load suppression among people on ART with viral load test results available
- 100% of African Fast-Track countries responding to HIVDR through programme adjustments and/or ART national guidelines revision
- 50% of African countries with ≥70% people on ART having a 12-month viral load test result available in their medical record

S02 MONITORING AND SURVEILLANCE

TARGETS:



- 100% of African Fast-Track countries with up to date HIVDR prevention, monitoring and response strategy
- 100% of African Fast-Track countries implementing HIVDR surveillance
- 90% of African Fast-Track countries assessing quality-of-care indicators for HIVDR
- One midterm and one final report published by WHO Regional Office for Africa

S03 RESEARCH AND INNOVATION

TARGETS:



- Investigations initiated or planned on at least 50% of priority research questions for the African Region defined in a WHO Regional Office position paper

S04 LABORATORY CAPACITY

TARGETS:



- 70% of WHO HIV Drug Resistance Network (HIVResNet) labs designated for HIVDR testing using dried blood spots
- 70% of WHO HIV Drug Resistance Network (HIVResNet) labs having capacity for integrase inhibitor (INI) genotyping

S05 GOVERNANCE AND ENABLING MECHANISMS

TARGETS:



- 100% of African Fast-Track countries including HIVDR activities in funding proposals to Global Fund, PEPFAR, other sources, or country health budgets
- 100% of total HIVDR budget committed from countries allocations and external resources
- 100% of Member States with national HIVDR strategies

2

THE EMERGING THREAT OF HIV DRUG RESISTANCE IN AFRICA

BOX 2: KEY CONCEPTS AND DEFINITIONS

HIVDR is caused by mutations in the genetic structure of HIV that affects the ability of a particular drug or combination of drugs to block the replication of the virus. All current ARV drugs, including newer classes, are at risk of becoming partially or fully inactive due to the emergence of resistant virus strains. In general, there are three main categories of HIVDR:

1. Acquired HIVDR (ADR) develops when HIV mutations emerge due to viral replication in individuals receiving ARV drugs.
2. Transmitted HIVDR (TDR) is detected in ARV drug naïve* people with no history of ARV drug exposure. TDR occurs when previously uninfected individuals are infected with virus that has drug resistance mutations.
3. Pretreatment HIVDR (PDR) is a useful operational definition for public health planning purposes. PDR is detected in ARV drug naïve people initiating ART or people with prior ARV drug exposure initiating or reinitiating first-line ART. PDR is either transmitted or acquired drug resistance, or both. PDR may have been transmitted at the time of infection (i.e. TDR), or it may be acquired by virtue of prior ARV drug

exposure, such as in women exposed to ARV drugs for the prevention of mother-to-child transmission (PMTCT) of HIV, or in people who have received pre-exposure prophylaxis (PrEP), or in individuals reinitiating first-line ART after a period of treatment interruption.

*ARV drug naïve applies to people with no history of ARV drug exposure.

The WHO public health approach to ART is based on using three sequential ART standardized regimens constituting 2 NRTIs with an integrase inhibitor - Dolutegravir - as the first-line regimen, and, upon treatment failure, switched to a ritonavir boosted protease inhibitor (PI) + 2 new or recycled NRTIs as the second-line regimen, followed by integrase strand transfer inhibitor (INSTI) + 1 or 2 new or recycled NRTIs as third line ART.

Source: World Health Organization. 2017. Global action plan on HIV drug resistance 2017–2021

THE GLOBAL IMPACT OF HIVDR

Antimicrobial resistance (AMR) is a growing global public health threat, which urgently requires collective action to ensure effective prevention and treatment of infections. HIVDR is a type of AMR and minimizing the emergence and transmission of drug-resistant HIV is a critical aspect of the broader global response to AMR.

HIVDR is rising in every region studied, including eastern Africa, southern Africa, western and central Africa

The WHO HIVDR 2017 (1) report, which utilized survey data from 14 countries¹, revealed that HIVDR is rising in every region studied, including eastern Africa, southern Africa, western and central Africa, Latin America and Asia. According to the report, resistance to NNRTI among people retained on ART ranged from 4% to 28%, while among people with unsuppressed viral loads on first-line NNRTI regimens, it ranged from 47% to 90%. This is consistent with a previous systematic review of studies (7) which assessed PDR levels of adults across 63 low- and middle-income countries from 2001-2016 and concluded that levels of HIVDR are increasing globally.

According to the UNAIDS Global AIDS Update 2018 (1), as of 2018, 21.7 million people were receiving ART globally. The report states that larger numbers of people must initiate and successfully maintain HIV treatment for life to achieve global

targets for epidemic control. HIVDR occurs due to treatment failure, the transmission of HIV drug-resistant virus to newly infected people and quality gaps in HIV service delivery. Therefore, despite the tremendous successes of the last decade, it is likely that there will be an increase of HIVDR as the number of people on antiretroviral treatment and the average duration of therapy increases.

The increase of HIVDR will have a significant impact on the 90-90-90 initiative, an ambitious set of global targets established by UNAIDS and partners in 2014 (Fig. 3). These targets have been widely adopted by the global community and reflect its commitment to expanding access to ART for PLHIV.

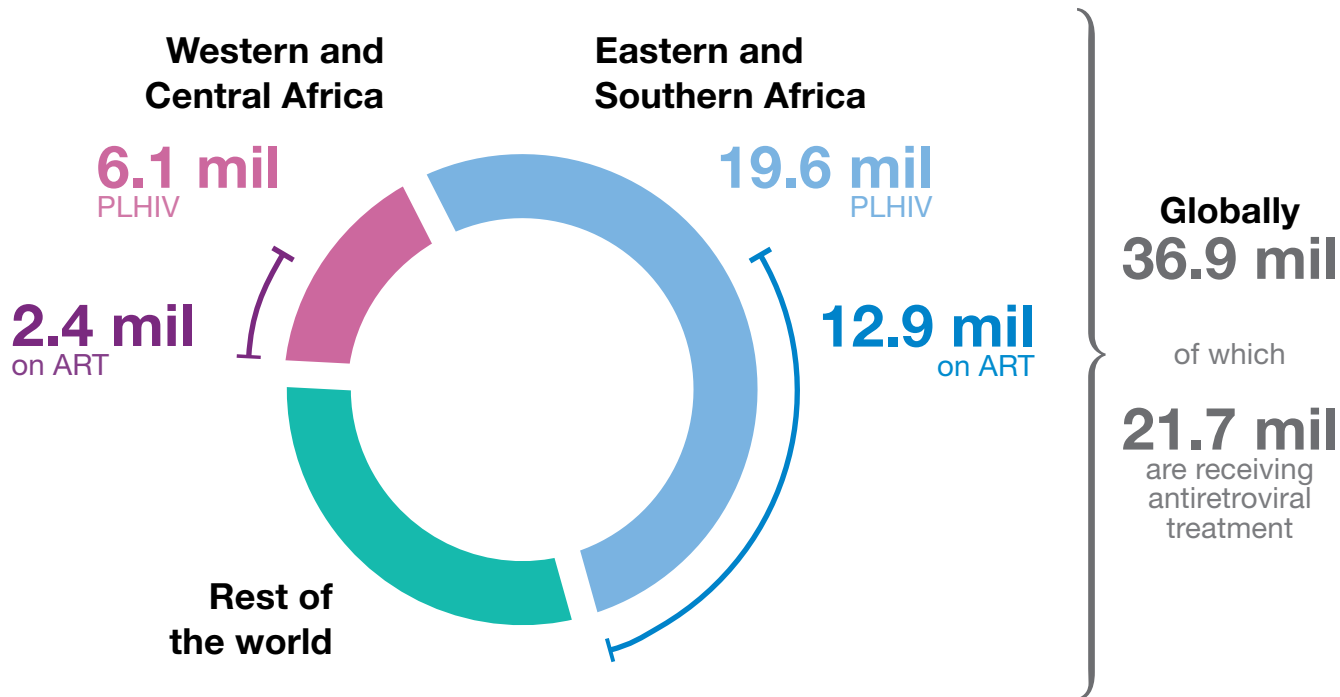
According to the UNAIDS 2018 report, as of 2017, high testing and treatment coverage in the Eastern and Southern Africa region (ESAR) have resulted in 81% of PLHIV being diagnosed, 66% of those who knew their HIV status were receiving ART, and 52% of those on treatment had viral suppression (1). On the other hand, in West Central Africa region (WCAR) 48% of PLHIV had been diagnosed, 40% of those who knew their HIV status were receiving ART, and 29% of those on treatment had achieved viral load suppression. In the African region, especially in the WCAR, ensuring optimal ART program performance to prevent, monitor and respond to HIVDR are key to achieving the global 90-90-90 targets. Achieving optimal viral load suppression, defined as 73% viral suppression, a goal which is frustrated by HIVDR, is critical to reaching the 90-90-90 fast track targets by 2020 and eliminating AIDS as a public health threat by 2030.

FIGURE 3: GLOBALLY ADOPTED HIV/AIDS TARGETS 2020



¹ Argentina, Brazil, Cameroon, Colombia, Guatemala, Mexico, Myanmar, Namibia, Nicaragua, South Africa, Uganda, Viet Nam, Zambia and Zimbabwe

FIGURE 4: PEOPLE LIVING WITH HIV (ALL AGES)



THE COST OF INACTION

An ethical approach to addressing HIVDR is essential to achieving the 90-90-90 targets, particularly “the third 90”, which relates to viral load suppression among individuals on treatment. The human cost of HIVDR cannot be underestimated. If resistance to ARV drugs remains unchecked, the viral load suppression target may not be reached due to limited therapeutic options and the higher costs of second- and third-line treatment regimens.

People who have acquired HIVDR are less likely to achieve viral suppression, more likely to experience virological failure or death, more likely to discontinue treatment, and more likely to acquire new HIVDR mutations. Preventing, monitoring and responding to HIVDR is therefore critical to maintaining current achievements, improving treatment outcomes for PLHIV, protecting donor and state investments, and guaranteeing the long-term sustainability of care and treatment programmes.

THE GROWING THREAT OF HIVDR IN AFRICA

Nowhere is the fight against HIV more critical than in Africa, which is home to 70% of the world’s PLHIV as well as 66% of all new infections occurring globally (1). With the growing threat of HIVDR, the continent is central to the global fight against HIV. Despite these statistics, the continent has made significant progress in its fight against HIV. In southern and eastern Africa, an area which holds 53% of the world’s population of PLHIV, collective action, implementation of key initiatives and an increase in domestic and international funding for research has resulted in a 30% reduction in new

HIV infections as well as a 42% reduction in AIDS-related deaths between 2010 and 2017 (1).

Successful implementation of the 2016 WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection (9) recommendation for all people to start ART regardless of CD4 cell counts has contributed to a cumulative total of 15.3 million people currently accessing ARVs in the African Region (Fig. 4). Increased access to ARVs has in turn contributed to a decline in HIV incidence and mortality in the African Region. This is especially significant in eastern and southern Africa, where increased access to ARVs has been accompanied with a decline in AIDS-related death and marked reduction in reported incidences of infection.

“Nowhere is the fight against HIV more critical than in Africa, which is home to 70% of the world’s PLHIV as well as 66% of all new infections occurring globally

Although Africa’s success so far is commendable, the increased access to ARVs for HIV treatment and prevention has resulted in a rise in levels of HIVDR. Nationally representative surveys conducted from 2014 to 2016 in four African countries showed that NNRTI PDR (defined as resistance to efavirenz or nevirapine) - Uganda, Namibia, Zimbabwe and Cameroon - show levels of NNRTI PDR of

15.4%, 13.8%, 10.9% and 8.1% respectively, on average above the alert threshold of 10% (Fig. 5). The levels of PDR to NNRTIs in women were estimated to be two-times higher than in men (2). HIVDR will diminish the effectiveness of current first-line treatment while also threatening to undo global progress in meeting the 90-90-90 targets.

Further indication of high levels of HIVDR in Africa can be seen in recent population-based HIV impact assessment surveys that were conducted in Malawi and Zimbabwe among newly diagnosed people (2). In addition, a systematic review of studies on HIVDR conducted in the African Region corroborates findings showing an increased prevalence of NNRTI PDR over time as well as a significantly high prevalence of NNRTI and NRTI PDR among individuals with prior ARV exposure, compared to ARV drug-naïve individuals (8). These revealed consistently high levels of PDR to NNRTI (21.6%) in individuals with prior ARV drug exposure either initiating or reinitiating first-line of NNRTI PDR compared to ARV drug-naïve individuals (8.3%).

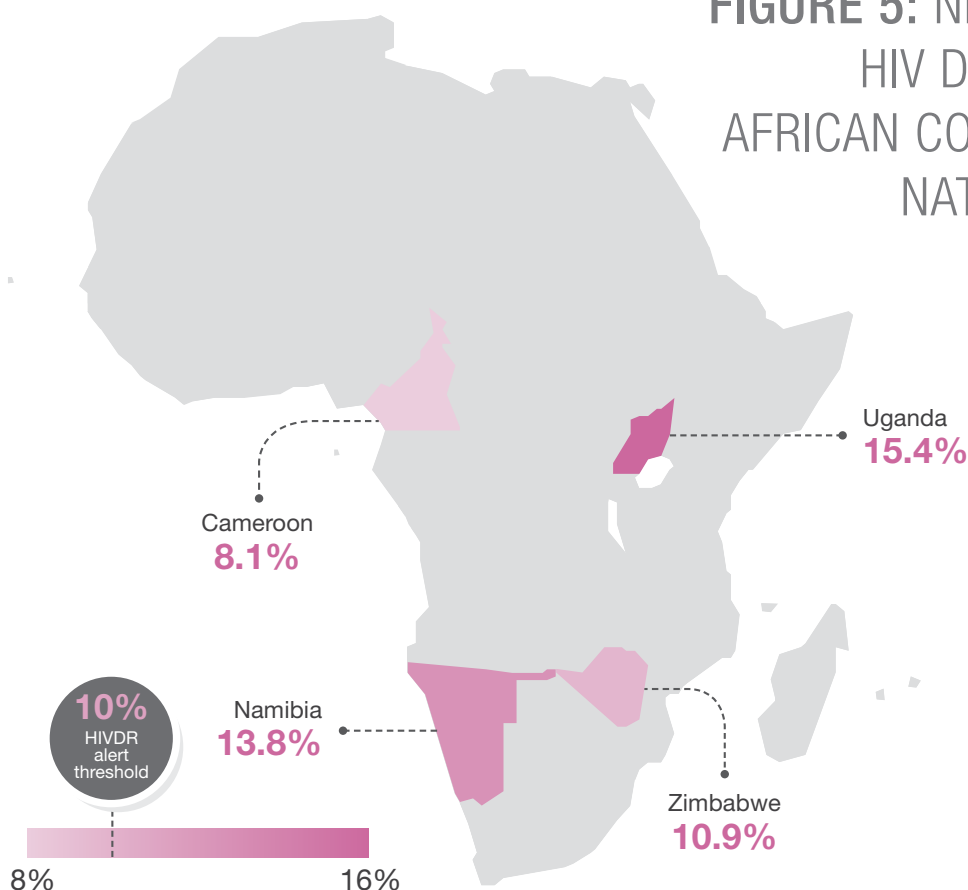
Regarding HIVDR among African infants (less than 18 months old) diagnosed with HIV through Early Infant Diagnosis (EID) between 2014 and 2016, only one nationally representative survey of HIVDR from this population was reported. This single survey was conducted in South Africa and showed levels of any HIV drug resistance of 63.7%. Data regarding

this population are limited. However, PDR levels to NNRTIs is alarmingly high in infants who become infected despite use of PMTCT. A meta-analysis of nationwide studies conducted between 2011-2014 in Mozambique, Swaziland, South Africa, Uganda and Zimbabwe showed that 1 in 2 infants are infected with virus harbouring NNRTI PDR prior to treatment initiation, and PDR to NNRTI was up to 63% in Zimbabwe (10).

Collectively, available data indicates an alarming increase of HIVDR in Africa. On the whole, increases in NNRTI resistance have been greatest in eastern and southern Africa, where the prevalence of pre-treatment NNRTI resistance is above 10%. Among patients failing treatment, 70-90% had NNRTI resistance while 53%-88% had resistance to the nucleoside backbone.

If NNRTIs continue to be included in first-line ART treatments in the context of high levels of pretreatment HIVDR, then the global target to end AIDS as a public health threat by 2030 may not be attained (3). Moreover, the potential human and economic impact will be severe. Over a five-year period, NNRTI PDR may be responsible for a cumulative total of 135 000 AIDS-related deaths, 105 000 new HIV infections and US\$ 650 million spent on ART in sub-Saharan Africa (Fig. 6). To circumvent the effects of high levels of NNRTI PDR, WHO recommends that countries with national levels of NNRTI

FIGURE 5: NNRTI PRETREATMENT HIV DRUG RESISTANCE* IN AFRICAN COUNTRIES REPORTING NATIONAL SURVEY DATA TO WHO, 2014-2016



*Resistance to efavirenz or nevirapine

Source: World Health Organization. 2017. WHO HIV Drug Resistance Report 2017

FIGURE 6: THE POTENTIAL COST OF HIVDR

In African countries with **HIVDR* $\geq 10\%$**

The predicted impact of HIVDR over 5 years could be severe



105 000 new HIV infections



135 000 AIDS-related deaths



US\$ 650 million cumulative treatment costs $\geq 10\%$

Source: WHO Global action plan on HIV drug resistance 2017-2021

*Non-nucleosidal reverse transcriptase inhibitor pretreatment drug resistance, defined as resistance to efavirenz or nevirapine

PDR above 10% transition to non-NNRTI based ART in first-line. Several countries in Africa are transitioning to Dolutegavir (DTG), an integrase based inhibitor with a high genetic resistant barrier. This represents an important step and is expected to mitigate, at least temporarily, the threat of HIVDR. As DTG is introduced in low- and middle-income countries, viral load levels and drug resistance outcomes need to be closely monitored, thus, HIV drug resistance surveillance remains critical to inform care and treatment guidelines and programme functioning.

Surveillance of pretreatment HIV drug resistance is important for establishing baseline polymorphic profiles of the integrase gene in HIV-1 non-subtype B, some of which might have an impact on DTG clinical response or non-response in various subtypes and populations. In addition, levels of viral load suppression and resistance among individuals on DTG-based ART who are not virally suppressed are not well known and require close monitoring. Therefore, surveillance of acquired HIV drug resistance and robust nationally representative measures of viral load suppression are critical to assess programme functioning with respect to DTG.

Ongoing assessment of NRTI pretreatment drug resistance will remain important and relevant for two reasons. The first is for its possible and as yet unknown impact on DTG-based ART coadministered with two NRTIs. The second is to measure the population burden of NRTI resistance caused by preexposure prophylaxis to tenofovir (TDF) and emtricitabine (FTC).

Furthermore, WHO recommends use of protease inhibitor (PI) based regimens in children younger than 6 years of age, irrespective of PMTCT exposure. However, despite these recommendations, a WHO Global ARV use survey conducted in 66 low- and middle-income countries (LMIC) reported only 14% of 748 638 children aged 0–5 years received protease inhibitor boosted by ritonavir (PI/r) based first-line ART regimens (3).

HIV drug resistance surveillance remains critical to inform care and treatment guidelines and programme functioning.

The increasing prevalence of HIVDR, coupled with Africa having the largest population of PLHIV, requires a collaborative response to the emerging threat of HIVDR in order to meet the 90-90-90 targets, to minimize the enormous cost to human life and development in Africa and to ensure that Africa continues its success in combating HIV/AIDS.

3

THE RESPONSE TO HIVDR IN THE WHO AFRO REGION

PROGRESS IN AFRICA

Generally, an increase in the availability of HIV resources in eastern and southern Africa has led to an expansion of HIV responses over the past decade (1). Funding for HIV initiatives from domestic and international sources has also increased during this time, with 42% of total resources in 2017 derived from domestic investments. Although western and central Africa have not been able to mobilize as many resources for HIV programmes, a regional HIV advancement programme was initiated in 2016 (1).

The 2016 Political Declaration on HIV/AIDS (13) recognized that Africa remains the worst affected region, especially as 22 'Fast-Track Countries' - countries in which urgent action is required - are situated in the region. The WHO Regional Office for the African Region has subsequently identified HIVDR as a priority for response.

The HIV/AIDS framework for the WHO African Region (2016) (5) aims to accelerate national HIV responses and stimulate progress in achieving country targets for universal access to HIV prevention, treatment, care and support. Additionally, the African Regional Action Plan on HIVDR is aligned with the Global Action Plan on HIVDR and the HIV/AIDS Framework for action in the WHO African Region 2016-2020 (5). The Regional Action Plan's priority actions support the WHO African Region's Africa Health Transformation Programme 2015-2021: a vision for universal health coverage (13), in addition to the WHO Global Health Sector Strategy on HIV endorsed by the Sixty-ninth World Health Assembly in 2016 (Fig. 7) (6).

The African Regional Action Plan on HIVDR is further informed by the Regional Office for Africa's regional consultations as well as by survey data provided by 36 African countries¹. This survey data determined which priority actions were needed to address the emerging threat of HIVDR in the African Region in line with the strategic objectives of the Global Action Plan on HIVDR.

CHALLENGES IN THE AFRICAN REGION

The Regional Action Plan has been developed for its Member States in Africa and will be implemented in a context that includes:

Limited resources (human and financial) in the health sector:

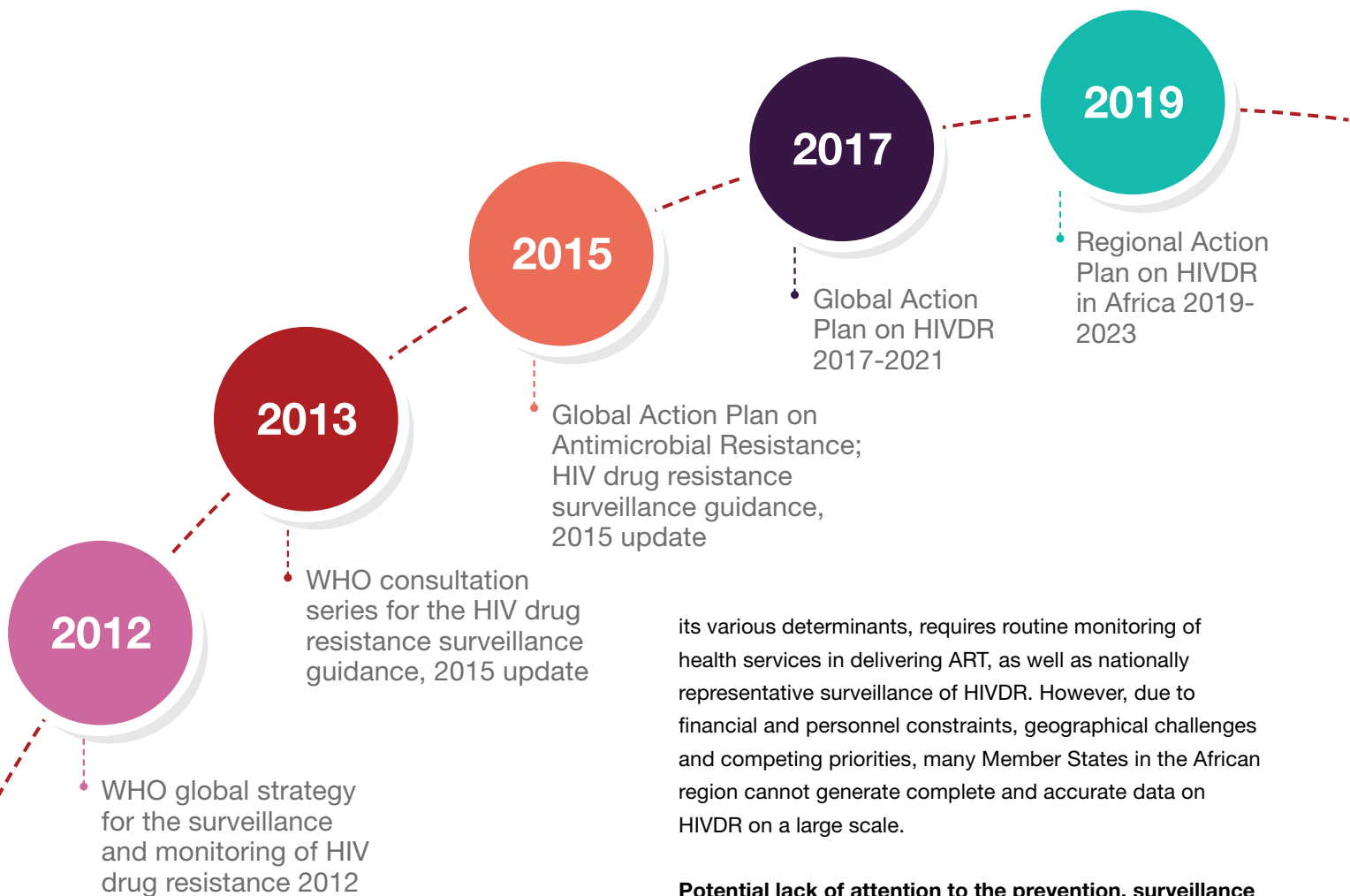
Significant financial resources and personnel are needed to guarantee adequate supplies of ART day-to-day and to ensure the human resources for screening, counselling, and follow-up over time. In sub-Saharan Africa there are far fewer than 2.28 physicians or nurses per 1 000 people, which is the minimum threshold required to deliver basic health services (15). Health systems in Africa are generally under-resourced which may undermine the roll out of the RAP. Significant constraints include a lack of expertise that is required for PDR and ADR surveys, weak laboratory capacity to support a scale up of viral load testing and HIVDR testing, and frontline health workers that must contend with heavy workloads and stockouts of ARVs (16).

Psychosocial and economic barriers to ART adherence:

Findings from various surveys suggest that although PLHIV are highly motivated to take ARVs as prescribed, constraints such as drug stock-outs, transport costs, long waiting

¹ Algeria, Angola, Benin, Botswana, Burundi, Cameroon, Central African Republic, Chad, Comoros, Congo, Cote d'Ivoire, Democratic Republic of Congo, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Gabon, Gambia, Ghana, Guinea, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Rwanda, Sao Tome et Principe, Senegal, Sierra Leone, South Sudan, the United Republic of Tanzania, Uganda, Zambia and Zimbabwe

FIGURE 7: TIMELINE OF WHO HIVDR INITIATIVES



times, hunger, stigma, side effects and lack of appropriate counselling undermine their intentions to do so (17). Patients with sub-optimal ART adherence are therefore at risk for HIVDR, which in turn compromises individual- and population-level treatment outcomes (18).

Insufficient data on HIVDR in the African region: Understanding HIVDR at the population level to support country decision-making, and the interaction between

its various determinants, requires routine monitoring of health services in delivering ART, as well as nationally representative surveillance of HIVDR. However, due to financial and personnel constraints, geographical challenges and competing priorities, many Member States in the African region cannot generate complete and accurate data on HIVDR on a large scale.

Potential lack of attention to the prevention, surveillance and response to HIVDR from decision makers: Given the environmental, economic and social challenges faced by Member States and the various demands an HIVDR response makes on national systems, it may be that activities related to the monitoring, prevention and response to HIVDR is not prioritized, especially when it comes to government resource allocation. Without awareness and understanding of the potential effects of HIVDR and the risk of reversing the many gains made over the last two decades, there is a risk that prevention, surveillance and response HIVDR will not garner the attention it requires at the national and sub-national level, especially among decision makers.

4

THE ACTION PLAN

The Regional Action Plan outlines priority actions for Member States in the African Region and supporting actions for the African Regional Office over the next five years. These priority actions were identified through a consultative process with Member States and are aligned with the five strategic objectives outlined in the HIVDR Global Action Plan:

1. Prevention and response
2. Monitoring and surveillance

3. Research and innovation
4. Laboratory capacity
5. Governance and enabling mechanisms.

Although these actions are relevant to all countries in their response to the HIV epidemic, there is a special focus on Fast-Track countries: countries in which HIV services are being rapidly scaled up, which together account for the vast majority of all new HIV infections worldwide.

STRATEGIC OBJECTIVE 1: PREVENTION AND RESPONSE

Use all available evidence in a timely manner to inform public health actions to prevent and control HIVDR.



ACTION PLAN

1. Develop a national HIVDR strategy,
2. Increase viral load monitoring,
3. Routinely monitor and respond to EWI of HIVDR at clinical and national levels
4. Ensure health workers are trained to prevent, monitor and respond to HIVDR

Preventing HIVDR is critical for the success of any HIV treatment programme and is achieved by optimizing the quality of ART services and eliminating gaps within HIV treatment programmes. The first line of action for any HIVDR programme is to **develop a national HIVDR strategy (1)** that is integrated into national health sector strategic plans and aligned with the monitoring and evaluation (M&E) frameworks. National HIVDR strategies should outline key priority actions for minimizing the emergence of HIVDR and for effectively responding to challenges in programme implementation.

National strategies should incorporate quality improvement approaches and outline preventative actions within programmatic response frameworks. Priority actions should include introducing stronger systems for drug procurement, increasing the use of viral load monitoring to inform

adherence counselling and timely and appropriate **switching to second- or third- line ART regimens (2)**, improving provision of second-line ART regimens, improving treatment retention, and strengthening community engagement and awareness.

It is critical that national strategies emphasize the **routine monitoring of programme quality indicators (3)** that are relevant for HIVDR or early warning indicators (EWIs), to ensure the timely identification of gaps in the programmatic response to HIV. Indicators should be in line with WHO's normative standards and guidelines for surveillance (19). National HIVDR strategies should use the results of this indicator monitoring to form the basis of recommendations for quick action, either at clinic level or, if many clinics do not achieve desired targets, at the national ART programme level. Action should be preceded by a period of investigation at

BOX 3: LESSONS FROM CAMEROON'S EWI MONITORING

In recognition of the need to minimize the emergence and transmission of HIVDR, Cameroon has conducted five rounds of EWI monitoring in clinics since 2008. After each round of monitoring, the national HIV programme developed and implemented national- and clinic- level recommendations based on the findings.

In 2017, an investigation was carried out by the national programme in a subset of ART clinics to assess the impact of the recommendations generated as a result of EWI monitoring. The investigation showed that messaging on adherence to ART provided by social workers substantially increased on-time medication pick-up in some clinics, with adherence improving from a range of 10–51% in year one to 91–100% by year four. 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.

Source: World Health Organization. 2017. Global action plan on HIV drug resistance 2017–2021

both national and clinic levels, to identify local and national causes for suboptimal performance and their solutions. Investigations may include qualitative interviews of patients and providers at both high functioning and low-functioning clinics, and may include case series or case control studies to assess for determinants of poor performance.

Once programme gaps are identified, it is imperative that Member States implement a systematic response for addressing those gaps and improving the quality of ART

delivery. These measures require that health professionals are **adequately trained to effectively implement strategic actions (4)** in line with WHO's Guidelines on the public health response to pretreatment HIV drug resistance (20). Support for national capacity building and training efforts are to be provided by WHO, along with other technical partners. By mid-2018, 24 African countries had requested support for technical assistance on HIVDR survey protocols and 29 for EWI monitoring from WHO.

STRATEGIC OBJECTIVE 2: MONITORING AND SURVEILLANCE

Strengthen surveillance and programme data, implement surveillance of HIVDR, monitor quality of service delivery and collect programmatic data using standardized methods, based on WHO's normative guidance and tools.



ACTION PLAN

- 5. Implement routine national HIVDR surveys
- 6. Monitor Early Warning Indicators (EWI)
- 7. Integrate EWIs into routine national M&E activities
- 8. Develop Regional HIVDR reports or contribute to the global HIVDR report
- 9. Use HIVDR database to clean and link epidemiological and HIVDR sequence data

National policy decisions on ART service delivery must be informed by reliable national data on HIVDR prevalence and trends. WHO recommends routine **nationally representative surveys of HIVDR (5)** to monitor the emergence and transmission of HIVDR, provide data to support the selection of optimal ART regimens, and measure the extent to which the emergence and transmission of HIVDR are minimized through programme practices.

Since 2004, 271 surveys have been implemented in 69 countries. In the African Region between 2017 and 2018, WHO-recommended PDR and ADR surveys have been conducted in 14 and 12 countries respectively (Fig. 8). An additional 18 African countries have surveys planned for completion in 2019. Infant surveys have been conducted between 2014-2018 in Nigeria, Malawi, Cameroon and South Africa and are planned for Angola, Ethiopia, Namibia, Uganda, Tanzania and Zimbabwe.

WHO also recommends that countries monitor programme quality indicators also known as **Early Warning Indicators (EWIs) (6)** in order to assess clinic-level data and identify programmatic gaps. Data should be used to inform decision-making regarding clinical and national-level actions to close gaps in service delivery. HIVDR **EWIs should be integrated into existing national M&E systems (7)** and regularly reported (21, 22, 23) By mid-2018, 29 African countries had integrated some or all EWI monitoring into routine national M&E activities.

To assist Member States in implementing surveys, WHO provides standardized guidance, operational toolkits and a database to support countries and WHO-designated HIVDR genotyping laboratories in the quality assurance of genotyping data. There is also a move toward the use of remnant specimens for ADR, as well as drug resistance monitoring in PrEP. Sustainable scale-up of surveillance activities will be country-specific and will vary according to the African sub-regions.

STRATEGIC OBJECTIVE 3: RESEARCH AND INNOVATION

Encourage relevant and innovative research that leads to the greatest impact; fill the gaps in knowledge on the risk of HIVDR to newer ARV drugs and the impact of service delivery interventions on viral load suppression and HIVDR.



ACTION PLAN

- 10.** Collate all relevant HIVDR research
- 11.** Identify evidence-based programmatic interventions
- 12.** Assess the impact of identified interventions

In the future, communities and civil society organizations should play an increasingly important role in documenting gaps in ART service delivery and in developing locally sustainable solutions. Advocacy activities at the local level are critical to raising awareness regarding the role of communities in monitoring the quality of ART delivery.

Innovative research, specific to African contexts, is vital to help address regional knowledge gaps and create location-specific interventions that will have the greatest impact on minimizing HIVDR. It is recommended that the Regional Office takes the lead in establishing a regional network of research institutions in order to ensure knowledge and information sharing on the continent.

Member States, in collaboration with the regional research network and the Regional Office, should **collate all relevant HIVDR-related research (10)** in repositories at the regional and national levels. Existing gaps in research should be identified and key research questions developed in order to fill those knowledge gaps. The Regional Office can support Member States in the prioritization of these research

questions and in facilitating collaboration between national, regional, and international research institutions and networks for implementation of high-priority research initiatives.

Scientific research can lead to the development of new ARV drugs, innovative service delivery models, and new approaches for adherence support and treatment retention. Using the information generated from these priority research initiatives, Member States should **identify specific evidence-based programmatic interventions (11)** within their national ART programmes. These interventions should be integrated or aligned with national HIVDR strategies and action plans.

Follow-up research and M&E activities should be utilized to **assess the impact of these interventions (12)**.

Mathematical modelling and cost-effectiveness analysis are useful for weighing the relative impact of interventions and determining pathways for future action. Member States should use these assessments in subsequent intervention design, creating a positive feedback loop.

FIGURE 8:
NATIONALLY REPRESENTATIVE WHO HIVDR SURVEYS AND EARLY WARNING INDICATOR INTEGRATION

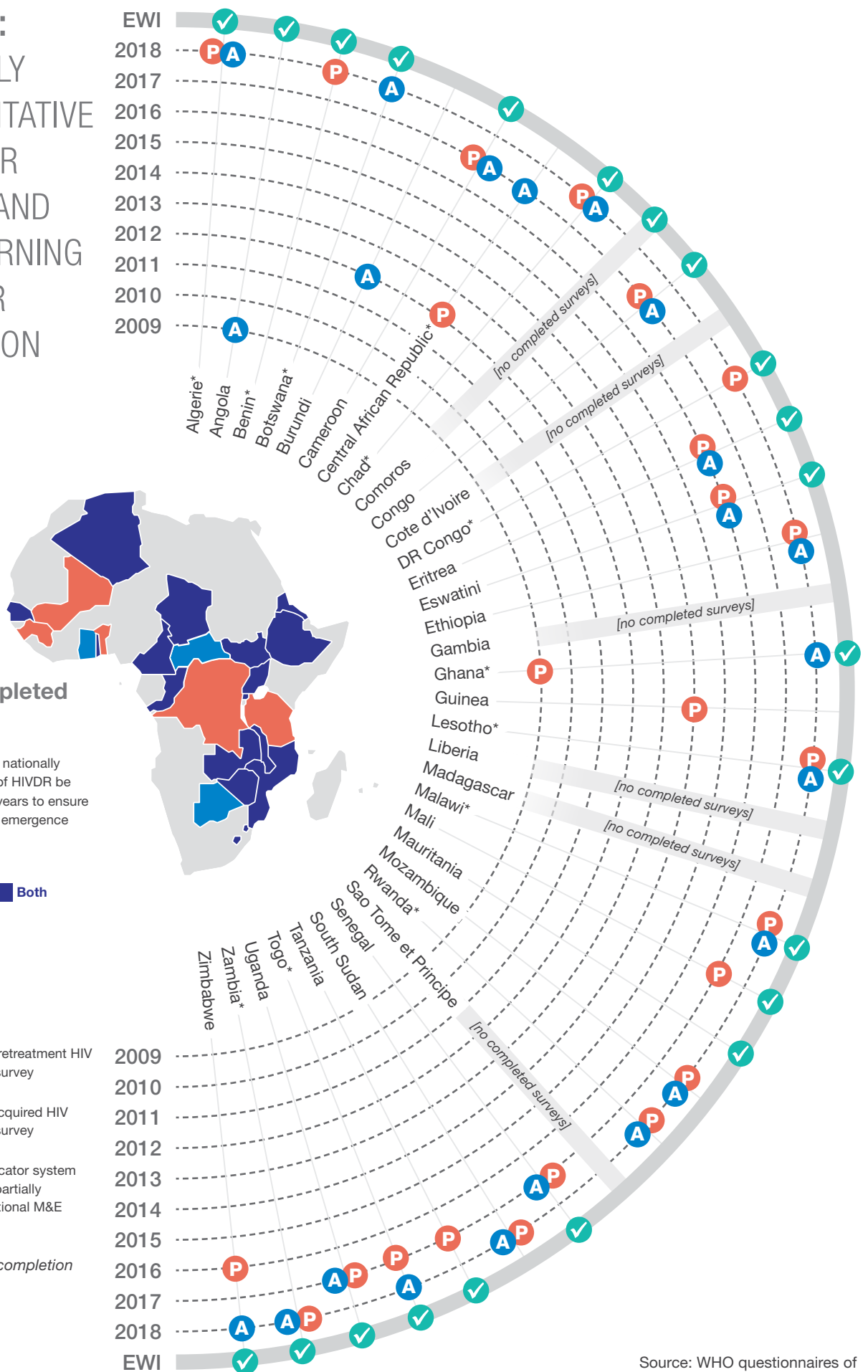
Surveys completed since 2015

WHO recommends that nationally representative surveys of HIVDR be conducted every three years to ensure adequate monitoring of emergence and transmission

PDR **ADR** **Both**

- P** Last completed Pretreatment HIV Drug Resistance survey
- A** Last completed Acquired HIV Drug Resistance survey
- ✓** Early warning indicator system has been fully or partially integrated into national M&E framework

**Survey planned for completion in 2019*



Source: WHO questionnaires of national HIVDR surveillance activities

STRATEGIC OBJECTIVE 4: LABORATORY CAPACITY

Strengthen laboratory capacity and quality to ensure the availability of a comprehensive global laboratory network that supports viral load and HIV drug resistance testing in low- and middle-income countries.



ACTION PLAN

- **13.** Amend HIVDR strategies to include the training of laboratory health professionals
- **14.** Expand viral load testing services
- **15.** Include resistance testing to new drug classes and genotyping using dried blood spots
- **16.** Convene the HIVDR laboratory network

Laboratory capacity in individual Member States should be assessed and opportunities identified for improvement. Essential laboratory services for preventing, monitoring and responding to HIVDR should be incorporated in national laboratory strategies, action plans and budgets. National strategies should be amended to include **training of laboratory health professionals (13)**, specimen management, quality assurance for HIVDR, infrastructure and laboratory information systems, and laboratory contribution to the HIVDR network in the region.

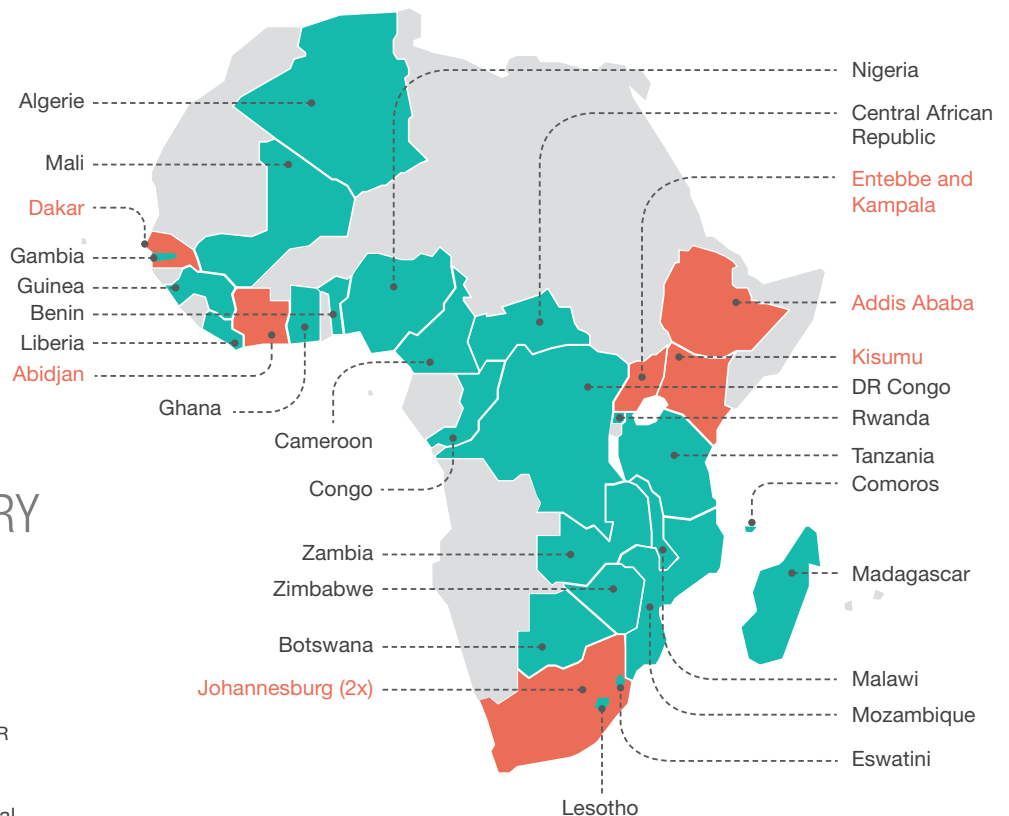
Access to high-quality and routine viral load monitoring is fundamental to ensuring sustainable population-level effectiveness of ART. Viral load testing coverage remains

below the target of 90% in most African countries. In order to meet global targets, **viral load testing services (14)** in the region must be expanded. Furthermore, national and regional laboratory capacity should be expanded to include **resistance testing to new drug classes (15)**.

Since HIVDR testing in low- and middle-income countries is limited, WHO and HIVResNet will offer support to Member States in conducting HIVDR testing and HIVDR surveillance. HIVResNet comprises 31 laboratories, of which eight are located in the African Region. By mid-2018, 24 countries in Africa had expressed interest in WHO HIVDR laboratory designation (Fig. 9).

FIGURE 9:
HIVDR LABORATORY DESIGNATION

- WHO designated laboratories for HIV drug resistance testing
- Countries expressing interest in HIVDR laboratory designation



Source: WHO questionnaires of national HIVDR surveillance activities

STRATEGIC OBJECTIVE 5: GOVERNANCE AND ENABLING MECHANISMS

Ensure that enabling mechanisms (advocacy, country ownership, coordinated action, and sustainable funding) are in place to support action on HIVDR.



ACTION PLAN

- 17. Develop a five-year national HIVDR strategy
- 18. Create linkages with other AMR programmes
- 19. HIVDR technical working group
- 20. Identify funding mechanisms
- 21. Include costed estimates
- 22. Develop HIVDR strategy implementation plans
- 23. Develop a country-level communication strategy
- 24. Build community engagement

Coordination, integration, alignment and country ownership

The first action for Member States is to **develop a costed five-year national HIVDR strategy (17)** that guides HIVDR response by assessing the national HIVDR situation, outlines key priority actions, and identifies mechanisms for implementation and funding. This national strategy should be integrated within broader national AMR strategies, plans and working groups in order to **create linkages and leverages with other AMR programmes (18)**. As of mid-2018, six African countries had national HIVDR strategies.

Member States should ensure that national HIVDR strategies include the **formation of a national HIVDR working group (19)**, chaired by the national ART programme. National working groups should be charged with the planning and execution of the HIVDR strategy, including routine HIVDR surveys, programmatic assessments of EWIs, prevention and response to HIVDR, strengthening of laboratory capacity, and the use and dissemination of HIVDR research.

Sustainable funding

Without adequate financing, implementing HIVDR strategies will not be possible. Resource mobilization is therefore a critical element of all national planning activities.

Member States will need to mobilize resources from both domestic and external sources of financing. **Identifying domestic and external funding mechanisms (20)** for HIVDR prevention and response should be included in the national HIVDR strategy, as well as the national HIV and ART strategies and action plans.

For all elements of HIVDR prevention and response in these national strategies, **cost estimates should be included (21)**. These costs should be integrated and aligned with larger HIV and AMR programmes and associated national budgetary allocations in order to identify and advocate for domestic sources of financing.

For elements that cannot be supported by domestic sources of finance, multilateral and bilateral collaborating partners with a focus on HIVDR control should be utilized as key sources of finance. A 2018 mid-term review of Global Fund grants shows that 20 African countries had requested funding for prevention and surveillance of HIVDR, with a total US\$ 14.6 million awarded to the African Region.

Advocacy and communication

Country ownership of national HIVDR priority actions is a critical element of any successful national ART programme. The development of HIVDR **working groups and implementation plans (22)** as a part of national HIVDR strategies is an important first step in fostering country ownership over HIVDR prevention and response.

The development of governance and policy mechanisms must also be paired with advocacy and awareness-raising measures, in government, civil society and with the general population, in order to garner stakeholder buy-in. The HIVDR working group should **develop a country-level communication strategy (23)** to improve understanding of HIVDR amongst target audiences such as policymakers, healthcare professionals, communities, civil society organizations, and PLHIV.

Synergies between national AMR and HIVDR programmes create opportunities for collective efforts to **build community engagement (24)** for preventing and responding to AMR and HIVDR. AMR and HIVDR working groups within Member States should adopt a collaborative approach to improving patient and health worker literacy on AMR and HIVDR in order to maximize impact and effective use of resources.

MONITORING AND EVALUATION

The Regional Action Plan Monitoring and Evaluation (M&E) framework (Annex 1) seeks to assess progress in implementing the African Region's response to HIVDR using internationally-agreed indicators that are in line with the Global Action Plan's HIVDR M&E framework. At the regional level, regular reviews by the WHO Regional Office will assess the progress on the various targets outlined in the framework. These reviews will build on data received from countries through various reporting mechanisms and procedures. Benchmarking will also be used to assess and compare performance levels between and within countries.

The Regional Action Plan is designed to be sufficiently flexible for adaptation at the national level, accounting for local needs, capacities, and limitations. Acknowledging the different forms that a national HIVDR strategy may take, the Regional Office will provide support to countries for the harmonized and standardized collection of indicators and for preparing reports for regional and global monitoring processes.

Strong North-South and South-South partnerships are essential for creating networks through which technical and financial resources reach those countries and regions most in need.

COLLABORATIVE PARTNERSHIPS

An effective HIVDR response requires a long-term, committed effort from a variety of actors working at different levels of governance across a range of sectors both regionally and internationally. Strong North-South and South-South partnerships are essential for creating networks through which technical and financial resources reach those countries and regions most in need.

The WHO African Regional Office, working closely with WHO headquarters can play an important role in facilitating and encouraging these partnerships. In bringing together different stakeholders in support of a coordinated and coherent response to HIVDR, WHO recognizes that each actor has specific roles and responsibilities:

- Member States are responsible for developing, funding, and implementing national strategies to prevent, monitor and respond to HIVDR. While governments should take the lead on implementing these strategies, they cannot do it alone - external support is needed. Collaborative partnerships with development partners, regional financial and research institutions, and other African countries are crucial for the attainment of regional and national HIVDR objectives.
- WHO headquarters and the WHO Regional Office for Africa provide strategic leadership in the development of norms and standards for HIVDR prevention, monitoring, and response. WHO also has an important convening role in developing networks through which funding opportunities, innovative research findings, best practice, technological expertise, and global policies and action plans can be exchanged and shared amongst key actors. WHO provides a platform through which national, regional, and international HIVDR programmes can be harmonized vertically, as well as horizontally with related AMR, HIV, tuberculosis, and malaria programmes.
- International development agencies are important sources of finance and technical expertise for the implementation of national HIVDR programmes. Major multilateral and bilateral donor agencies, including the Global Fund, Unitaid, PEPFAR, and CDC, can provide support to Member States in mobilizing resources; strengthening national capacity for surveillance; monitoring and evaluation; policy and strategy development; innovative research; and communication and dissemination of information.
- Communities and civil society will play an increasingly important role in local advocacy and communication and in implementing and monitoring HIVDR priority actions on the ground. HIVDR working groups should establish close partnerships with civil society organizations and incorporate representation from these organizations in decision-making processes. Civil society representatives can advise HIVDR working groups on the effectiveness and feasibility of HIVDR priority actions and facilitate the dissemination of HIVDR guidelines and best practice.

ACCOUNTABILITY FRAMEWORKS

Well-functioning, transparent accountability mechanisms are critical to the implementation of the Regional Action Plan and, more broadly, to the achievement of the 90-90-90 targets. Given the wide range of partners and stakeholders involved in the response to HIVDR, it is important to hold each actor accountable for the role that they play in the global effort to prevent and respond to HIVDR.

The development of national accountability mechanisms should be outlined in national HIVDR strategies. National HIVDR working groups should be held accountable for the establishment of these mechanisms and alignment or integration with national ART programme accountability frameworks.

Effective accountability mechanisms should incorporate the following important elements: full engagement of all relevant stakeholders; clear national targets that reflect regional and global HIVDR action plans and targets; appropriate indicators on impact of interventions to track progress; and transparent and inclusive assessment and reporting process.

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ANNEX 1: FRAMEWORK FOR THE RAP ON HIVDR

This annex defines the indicators that will be used to report on the implementation of the strategic objectives outlined in the Regional Action Plan (RAP). The monitoring and evaluation framework aims at monitoring RAP implementation at regional and country level, and outcomes resulting from its implementation.

Table A: Summary of monitoring and evaluation approach for the RAP on HIVDR

RAP strategic objectives	Areas of work	Indicator	2023 target ¹	Method of verification
S01. Prevention and Response	ARV medicine stock-outs	% of countries reporting any ARV medicine stock-out during a 12-month period	<15% of African countries with any ART medicine stock-out during a 12-month period.	Reports received from countries (source: EWI of HIVDR; Global AIDS Monitoring Survey (GAM))
	Second-line ART regimens	% of countries switching patients to second line ART according to WHO guidelines (among countries reporting data)	>80% of African countries switching patients to second-line ART according to WHO guidelines.	Reports received from countries: (source: EWI, programme data)
		% of countries reporting >5% patients on second-line ART (among countries reporting data)	>80% of African countries with >5% patients on second-line ART (among countries reporting data)	Drug procurement (AIDS medicine and diagnostic survey (AMDA) and global Price Reporting Mechanism (GPRM))
	Retention of treatment	% of countries reporting adequate (more than 85% at a defined time point) retention of treatment (among countries reporting data)	>90% of African countries reporting >85% retention on treatment	Reports received from countries: EWI; GAM; programme data
	Viral load suppression	% of countries reporting having met 90% viral load suppression target amongst people on ART with viral load test result available (among countries reporting data)	>90% of African countries with 90% viral load suppression among people on ART with viral load test results available	Reports from countries; EWI; programme data, ADR survey, GAM
	National response to HIVDR	Number of countries implementing a national response to HIVDR (among all Fast-Track countries)	100% of African Fast-Track countries responding to HIVDR through programme adjustments and/or ART national guidelines revision	Reports received from countries; WHO survey

¹ Targets established during RAP consultation process

RAP strategic objectives	Areas of work	Indicator	2023 target ¹	Method of verification
SO2. Monitoring and Surveillance	National HIVDR strategy	% of countries with national HIVDR strategy (among all Fast-Track countries)	100% of African Fast-Track countries with HIVDR strategy up to date	Reports received from countries; WHO survey
	Surveillance	% of countries conducting and reporting on HIVDR surveillance (among all Fast-Track countries)	100% of African Fast-Track countries implementing HIVDR surveillance	Reports received from countries; WHO survey; GAM
	Quality-of-care indicators relevant for HIVDR	% of countries monitoring all EWI of HIVDR (2 consecutive years)(among all Fast-Track countries)	90% of African Fast-Track countries assessing quality-of-care indicators for HIVDR	Reports received from countries; GAM
	Programmatic data	% of countries achieving >70% viral load coverage (among countries reporting data)	50% of African countries with ≥70% people on ART having a 12-month viral load test result available in their medical record	Reports received from countries (source EWI, programme data)
	Regional report on HIVDR	Timely regional report on HIVDR surveillance	2 reports published by WHO Regional Office for Africa	WHO publication
SO3. Research and Innovation	Research	Implementation of HIVDR-related research established in the RAP on HIVDR	Investigations initiated or planned on at least 50% of regional research questions defined in a WHO Regional Office position paper	WHO survey, WHO HIVResNet meeting report(s) and/or relevant peer-reviewed publications
SO4. Laboratory Capacity	Expansion of HIVDR testing capacity	% of WHO HIVResNet labs are designated to test HIVDR using dried blood spot (DBS), and % of WHO HIVResNet labs are designated to genotype in the integrase region	70% of WHO HIVResNet labs designated for HIVDR testing using DBS 70% of WHO HIVResNet labs designated for genotyping in the integrase region	Reports received through HIVResNet laboratory network, WHO publication
SO5. Governance and Enabling Mechanisms	Mobilization of resources to implement the RAP	% of Fast-Track countries including HIVDR in funding proposals to Global Fund, PEPFAR, other sources or country health budgets	100% of African Fast-Track countries including HIVDR activities in funding proposals to Global Fund, PEPFAR, other sources or country health budgets	Global Fund and PEPFAR report, country reports
	Mobilization of resources to coordinate, monitor and support the RAP's implementation	% of total budget committed from countries' allocations and external resources	100% of total HIVDR budget committed from countries' allocations and external resources	WHO survey

¹ Targets established during RAP consultation process

ANNEX 2: SCALE-UP PLAN FOR HIVDR SURVEILLANCE

Efforts to scale up the response to HIVDR in the Fast-Track countries need to be coherent and delivered with support from all relevant partners. The framework for HIVDR surveillance activities should be adapted at the regional and national levels. If the cost-effective actions outlined in the framework are implemented to scale, significant progress will be made in achieving the global targets to end the AIDS epidemic. Sustainable scale-up will be country specific and dependent on competing public health priorities, budgeting allocations and health-system strengthening.

Table B provides estimated total costs of monitoring HIVDR at a country level. It assumes that PDR and ADR surveys are monitored concomitantly every three years, that EWI are monitored annually, and that surveys in children <18 months

of age are performed every five years. The average annual cost for HIVDR surveys and EWI monitoring is US\$ 0.56 per person on ART per year in Fast-Tracked countries¹. This cost is derived from the sum of the cost of combined PDR and ADR surveys in adults (which should be implemented twice over a five-year period), the cost of annual EWI monitoring, and the cost of surveys in infants (one survey over a five-year period) – corresponding to a five-year investment of US\$ 227 100 per country. Implementation of paediatric ADR surveys will result in a limited increase in the annual budget. Estimates of survey costs are based on WHO surveys of country expenditure for survey implementation. Table C provides estimated costs for specific countries in the region based on WHO surveys of planned HIVDR surveillance activities between 2019-2023.

Table B: Estimate of costs of HIVDR surveys and EWI monitoring

		PDR & ADR combined survey ²	Early warning indicators ³	Infants <18 months survey ⁴
Budget/survey (US \$)	Protocol development and training	25 000		10 000
	Survey coordination	107 000		14 000
	Site support visits	16 000		
	Viral load	56 400		
	Genotyping	94 350		75 000
	Other laboratory costs	21 200		3 700
	Technical support	22 800		22 800
	Data analysis and interpretation, quality assurance, report production and distribution	25 000	50 000 ⁵	14 000
TOTAL (US \$)		373 000	50 000	139 500

¹ US \$227 100 (annual cost for survey implementation) x 35 (Fast-Tracked countries) / 13 957 769 people on ART in the 35 Fast-Track countries.

² ADR includes two time points: patients on ART for 12 months (460 specimens) and patients on ART for 48+ months (560 specimens). Budget based on the following assumptions: 30 ART clinics sampled; 1350 specimens tested; resistance testing at US\$ 150; viral load testing at US\$ 60.

³ EWI implementation costs should be integrated into HIV monitoring and evaluation budget as WHO advises countries to integrate the collection of these indicators routinely as part of the global monitoring and evaluation health sector plans. EWI cost reflects the fund needed for existing data verification/validation.

⁴ Based on sample size of 490 specimens.

⁵ The cost of EWI monitoring can be further reduced or be nil in countries with robust M&E systems able to capture and report the EWI routinely.

Table C: Summary of monitoring and evaluation approach for the RAP on HIVDR

Country	GF ¹	PEPFAR ²	2019				2020				2021				2022				2023			
			EWI	ADR	PDR	Infant	EWI	ADR	PDR	Infant	EWI	ADR	PDR	Infant	EWI	ADR	PDR	Infant	EWI	ADR	PDR	Infant
Angola	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Botswana	✓	✓	✓				✓	✓			✓		✓		✓		✓	✓	✓			
Cameroon	✓	✓	✓	✓	✓		✓			✓	✓	✓		✓				✓				
Chad	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Cote d'Ivoire	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
DR Congo	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Eswatini	✓	✓	✓	✓	✓		✓				✓				✓			✓				
Ethiopia	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Ghana	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Kenya	✓	✓	✓			✓	✓	✓	✓		✓				✓			✓	✓	✓		
Lesotho	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Malawi	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Mali	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Mozambique	✓	✓	✓				✓	✓	✓		✓				✓		✓		✓	✓	✓	
Namibia	✓	✓	✓		✓		✓	✓		✓		✓			✓			✓	✓	✓		
Nigeria	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
South Africa	✓	✓	✓			✓	✓	✓	✓		✓				✓			✓	✓	✓		
South Sudan	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Tanzania	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Uganda	✓	✓	✓	✓	✓		✓				✓				✓			✓				
Zambia	✓	✓	✓				✓	✓	✓		✓				✓			✓	✓	✓		
Zimbabwe	✓	✓	✓		✓		✓	✓			✓				✓			✓	✓			

PDR: Pretreatment drug resistance survey. Survey population ART initiators including those with prior PMTCT/PrEP/PEP exposure or defaulters restarting first-line ART

ADR: Acquired drug resistance survey. Survey population individuals on ART

EWI: Early warning indicators of HIVDR. Programme and clinic factors associated with HIVDR

Infant: HIVDR surveys among children <18 months based on DBS specimens from early infant diagnosis

1 Communication from the Global Fund 2016

2 PEPFAR website: <http://www.pepfar.gov/countries/bilateral/>



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