World Health Organization

TECHNICAL REPORT

HIV DRUG RESISTANCE

GLOBAL REPORT ON EARLY WARNING INDICATORS OF HIV DRUG RESISTANCE

JULY 2016

World Health Organization

TECHNICAL REPORT

GLOBAL REPORT ON EARLY WARNING INDICATORS OF HIV DRUG RESISTANCE

JULY 2016

WHO Library Cataloguing-in-Publication Data

Global report on early warning indicators of HIV drug resistance: technical report, July 2016.

1.Drug resistance, Viral. 2.Anti-HIV Agents – therapeutic use. 3.HIV Infections. I.World Health Organization.

ISBN 978 92 4 151117 9 (NLM classification: WC 503.2)

Layout L'IV Com Sàrl, Villars-sous-Yens, Switzerland.

Printed in South Africa.

TABLE OF CONTENTS

ACRONYMS

ART	Antiretroviral therapy
ARV	Antiretroviral (drugs)
CI	Confidence interval
DRC	Democratic Republic of the Congo
EWI	Early warning indicator of HIV drug resistance
GEE	Generalized estimating equation
GAP	Global Action Plan
HIVDR	HIV drug resistance
LMIC	Low- and middle-income countries
LTFU	Loss to follow-up
NNRTI	Non-nucleoside reverse-transcriptase inhibitor
NRTI	Nucleoside reverse-transcriptase inhibitor
PI	Protease inhibitor
PrEP	Pre-exposure prophylaxis
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

ACKNOWLEDGEMENTS

This report was written by Michael R. Jordan (Consultant, HIV/AIDS Department), Natalie Dean (Consultant, HIV/AIDS Department), David Maradiaga (Consultant, HIV/AIDS Department), and Silvia Bertagnolio (HIV/AIDS Department), who coordinated the overall report development with Meg Doherty (HIV/AIDS Department). We are grateful for the contributions of Judith Van Holten (Consultant, HIV/AIDS Department), Hiwot Haile-Selassie (Consultant, HIV/AIDS Department), and Jhoney Barcarolo (Consultant, HIV/AIDS Department). This work would not have been possible without the collaboration of national HIV programme managers and staff, who supplied the data underpinning the report.

Funding to support this work came from the Bill & Melinda Gates Foundation and the United States President's Emergency Plan for AIDS Relief.

EXECUTIVE SUMMARY

With increasing global use of antiretroviral therapy (ART) to both treat and prevent HIV, and increasing global trends in HIV drug resistance (HIVDR), efforts to improve HIV programme quality and prevent the emergence and transmission of drug-resistant HIV must be strengthened. In many low- and middle-income countries (LMIC), HIVDR testing is neither routinely available nor recommended for individual patient management. However, monitoring patient and clinic factors associated with the emergence of preventable HIVDR is comparatively inexpensive, and can be used to identify gaps in the quality of ART service delivery favouring the emergence of HIVDR. Several ART programme and clinic factors are associated with the emergence of HIVDR or with successful population-level viral load suppression. These factors, or early warning indicators (EWIs) of HIVDR, include: the prescribing of ART according to national or international guidelines; loss to follow-up (LTFU) and retention on ART 12 months after treatment initiation; on-time pill pick-up; on-time appointment keeping; pharmacy stock outs; and viral load suppression. Monitoring and the site level quality improvements in response to EWIs form the foundation of HIVDR prevention, and link WHO-recommended surveillance of HIVDR to programmatic interventions designed to minimize it. EWI definitions and targets follow an international standard, and the World Health Organization (WHO) recommends that countries monitor them on an annual basis through the implementation of the *Consolidated strategic information guidelines for HIV in the health sector*.[1]

This global report is based on 59 countries that reported data from more than 12 000 clinics from cohorts of patients receiving ART between 2004 and 2014. The report includes the most recent clinic-level data reported to WHO in 2015–2016 and reflects a lag due to the 12 month cohort reporting period. Globally, amongst the clinics reporting data, high levels of appropriate antiretroviral (ARV) drug prescribing were observed, with over 99% of people prescribed regimens according to national or international HIV treatment guidelines. Global levels of LTFU at 12 months during the same period averaged 20%, exceeding the WHO-recommended target of 15%. Moreover, global levels of LTFU among clinics reporting data increased significantly over time, from 11.9% in 2004 to 24.5% in 2012 ($p<0.001$). Globally, retention on ART at 12 months averaged only 73.5% amongst clinics reporting data, falling short of the WHO-recommended target of 85% or above. Estimates of retention varied considerably across regions. Adherence, as estimated by on-time pill pick-up and on-time appointment keeping, fell below global targets. On-time pill pick-up was a strong predictor of clinic-level viral load suppression ($p<0.001$) suggesting that identifying clinics with less-than-desirable pill pick-up, then targeting their patient populations for adherence interventions, may lead to improvements in overall population-level outcomes. Amongst 1150 clinics monitoring drug stock outs, 35.7% had at least one drug stock out of routinely dispensed ARV drugs during their respective reporting year, thus failing to attain the WHO-recommended target of no ARV drug stock outs.

This report examines national and regional EWI prevalence estimates to compare performance over time within and across regions. In general, significant variability of clinic performance within countries was noted. EWI methods use colour-coded score cards (performance strata) to visualize clinic performance, which facilitate identification of gaps in service delivery. From a country perspective, understanding clinic-level variability of EWI results is critical to improving overall programme performance. Variability should be explored to characterize best practices to improve quality and facilitate their application in clinics not achieving global EWI targets.

Depending on the nature and extent of the problems identified, countries have responded to EWI results through various policy changes, both at the ART programme and clinic levels. Examples of documented actions include: strengthened record-keeping systems; training of providers in optimal ARV prescribing practices; operational research on defaulter tracing to identify suitable approaches to early identification and re-engagement to care; increased resources for patient tracing given to clinics struggling with retention; implementation of SMS reminders to improve adherence; and changes in record-keeping systems to allow for the monitoring of clinic-level ARV drug supply.

This report has several limitations and results should be viewed in this context: with few exceptions, data reported by countries were not derived using representative clinic selection, and countries collecting and reporting EWI data do not represent all LMIC. Caution is therefore warranted when interpreting global, regional and national estimates and trends and, results should not be generalized beyond the clinics monitored. When too few data elements were reported, no statistics were applied to the descriptive analysis.

WHO's 2016 *Consolidated guidelines on the use of ARV drugs for treating and preventing HIV infection* stress the importance of initiating ART in all HIV-infected individuals regardless of immunological status, and advise combination prevention of HIV, including the use of pre-exposure prophylaxis (PrEP) for those at highest risk of HIV infection.[2] Results from the clinics monitored suggest appropriate ARV drug prescribing and high levels of viral load suppression amongst those alive and receiving a viral load test after one year, speaking to the success of the treatment optimization and monitoring guidance uptake.

[1] Consolidated strategic information guidelines for HIV in the health sector. Geneva: World Health Organization; 2015. Available at: http://apps.who.int/iris/bitstream/10665/164716/1/9789241508759_eng.pdf?ua=1&ua=1.

[2] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Second edition. Geneva: World Health Organization; 2016. Available at: http://www.who.int/hiv/pub/arv/arv-2016/en/.

However, increased attention is urgently needed to decrease levels of LTFU, support retention, maximize adherence, and prevent drug stock outs. The updated *Consolidated guidelines on the use of ARV drugs for treating and preventing HIV infection*, has an expanded service delivery chapter containing new recommendations to support linkage, retention, adherence and supply chain management to address the lack of standard evidence-informed approaches and interventions found in some programmes and clinics. Closing these gaps and maximizing the quality of ART service delivery are especially important in light of the increasing levels of HIVDR recently documented in several LMIC. WHO is developing a comprehensive Global Action Plan (GAP) for HIVDR for the period 2017–2021, which will coordinate all stakeholders and encourage action at all geographic levels. This global call to action, which will outline appropriate responses to HIVDR, is planned for release in early 2017.

As of 2015, 17 million people were receiving ART globally[1], and over the next decade, ever larger numbers of people must initiate and be successfully maintained on ART. Although reporting of clinic-specific EWIs has declined in recent years, this is in part due to the transition of these indicators into a subset of recommended global and national indicators in WHO's 2015 *Consolidated strategic information guidelines for HIV in the health sector*. Therefore, reporting and a comprehensive response to documented suboptimal performance is anticipated to increase in coming years as countries fully adopt and implement the WHO indicator reporting along the cascade of treatment and care. Integration of HIVDR EWIs into routine clinic and programme monitoring and evaluation (M&E) system, followed by rapid investigation and response to suboptimal performance (data use), will allow ART clinics and programmes to improve the quality of service delivery. This EWI report reaffirms the need to develop a GAP for HIVDR to ensure HIVDR does not undermine the achievement of the global targets on health and HIV, and to secure effective high-quality treatment for all target groups, including key populations, pregnant women, children and adolescents – thereby helping to ensure a future generation free from AIDS.

[1] Global AIDS Update 2016. Geneva: UNAIDS. 2016. Available at: http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf.

INTRODUCTION

Scale-up of antiretroviral therapy (ART) for the treatment of all HIV-infected individuals is an international health-care priority. To date, the success of global ART scale-up has been largely due to a public health approach to treatment, which includes standardized and simplified treatment regimens consistent with international standards and appropriate to local circumstances. This public health approach has been the keystone of the WHO treatment and care approaches and has been well supported by the sustained commitment of national governments, international agencies and donors.

In 2015, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set ambitious global targets, including "90-90-90" by the year 2020 (i.e. 90% of all people living with HIV have been diagnosed; 90% of all people with diagnosed HIV infection are taking ART; and 90% of all people taking ART have suppressed viral load), and the elimination of AIDS as a public health threat by 2030.[1]

As of 2015, 17 million people were receiving ART globally – this means that by 2020, an additional 15 million people must initiate and be successfully maintained on ART for life. The treatment of millions of people with antiretroviral (ARV) drugs will inevitably be accompanied by the emergence and transmission of drug-resistant virus.

The 2016 World Health Organization (WHO) *Consolidated guidelines on the use of ARV drugs for treating and preventing HIV infection* recommend testing and treating all patients, regardless of CD4 cell count, and the use of pre-exposure prophylaxis (PrEP) for those at high risk of infection.[2] The "Treat All" approach combined with scale-up of PrEP will undoubtedly lead to a decrease in HIV incidence and propel the global community toward the elimination of AIDS as a public health threat. Yet paradoxically, despite these prevention and treatment recommendations, an increase in HIV drug resistance (HIVDR) amongst those infected may be observed because as the number of new infections decrease, the proportion due to transmission from people with previous exposure to ARV drugs through PMTCT or previous treatment will increase; therefore, the risk of transmitted HIVDR among the very few infected may increase.[3,4]

The human and financial consequences of HIVDR are likely to be significant. With limited access in low- and middle-income countries (LMIC) to a broad range of ARV drugs from different drug classes, HIVDR will limit treatment options and may necessitate a switch to more expensive regimens associated with greater long-term toxicity. Additionally, significant population-levels of HIVDR may lead to a reversal of hard-won gains in HIV/AIDS-related morbidity and mortality.[5]

Levels of pre-treatment HIVDR in LMIC have increased between 2004 and 2010. This increase has primarily been driven by raised levels of resistance to non-nucleoside reverse-transcriptase inhibitors (NNRTIs) in Africa.[6,7] More recently, higher levels of HIVDR have been observed amongst people naïve to ARV drugs in several LMIC settings, including Angola (16%), Argentina (10%), Botswana (10), Cuba (22%), Mexico (9%), Papua New Guinea (16%), and South Africa (14%).[8,9,10,11,12,13,14]

Faced with the need to initiate and maintain millions more people on ART, in order to eliminate AIDS as a public health threat during a time of limited global financial resources, efforts to identify gaps in ART programme functioning and to improve the quality of ART service delivery cannot be underestimated. The identification and correction of gaps in the quality of service delivery, as detected through the monitoring of early warning indicators (EWIs), will help to maximize the long-term durability and effectiveness of current and future recommended regimens, and to ensure that the WHO/UNAIDS targets to eliminate AIDS as a public health threat are achieved. Now, more than ever, to achieve the 90-90-90 global target, it is imperative that "Treat All" be accompanied by a greatly heightened focus on quality. It is only in this way that access to ART for all can achieve its greatest impact and usher in an AIDS-free generation.

---

[1] 90–90–90 : An ambitious treatment target to help end the AIDS epidemic. Geneva: UNAIDS; 2014. Available at: http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf.
[2] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Second edition. Geneva: World Health Organization; 2016. Available at: http://www.who.int/hiv/pub/arv/arv-2016/en.
[3] Nichols BE, Sigaloff KC, Kityo C, Mandaliya K, Hamers RL, Bertagnolio S et al. Averted HIV infections due to expanded antiretroviral treatment eligibility offsets risk of transmitted drug resistance: a modeling study. AIDS. 2014;28(1):73–83.
[4] Cambiano V, Bertagnolio S, Jordan MR, Pillay D, Perriëns JH, Venter F et al. Predicted levels of HIV drug resistance: potential impact of expanding diagnosis, retention, and eligibility criteria for antiretroviral therapy initiation. AIDS. 2014;28(Suppl 1):S15–S23.
[5] Cambiano V, Bertagnolio S, Jordan MR, Lundgren JD, Phillips A. Transmission of drug resistant HIV and its potential impact on mortality and treatment outcomes in resource-limited settings. J Infect Dis. 2013;207(Suppl 2):S57–62.
[6] WHO HIV drug resistance report 2012. Geneva: World Health Organization; 2012. Available at: http://www.who.int/hiv/pub/drugresistance/report2012/en/.
[7] Gupta RK, Jordan MR, Sultan BJ, Hill A, Davis DHJ, Gregson J et al. Global trends in antiretroviral resistance in treatment-naive individuals with HIV after rollout of antiretroviral treatment in resource-limited settings: a global collaborative study and meta-regression analysis. Lancet. 2012;380(9849):1250–8.
[8] Afonso JM, Bello G, Guimarães ML, Sojka M, Morgado MG. HIV-1 genetic diversity and transmitted drug resistance mutations among patients from the North, Central and South regions of Angola. PLoS ONE. 2012;7(8):e42996.
[9] Emiliano Bissio, Argentina ART Programme. Personal communication. May 2016.
[10] Rowley CF, MacLeod IJ, Maruapula D, Lekoko B, Gaseitsiwe S, Mine M et al. Sharp increase in rates of HIV transmitted drug resistance at antenatal clinics in Botswana demonstrates the need for routine surveillance. J Antimicrob Chemother. 2016;71(5):1361–6.
[11] Pérez L, Kourí V, Alemán Y, Abrahantes Y, Correa C, Aragonés C et al. Antiretroviral drug resistance in HIV-1 therapy-naive patients in Cuba. Infect Genet Evol. 2013 June;16:144–50.
[12] Avila-Rios S, Garcia-Morales C, Tapia-Trejo D, Matías-Florentino M, Quiroz-MoralesV, Casillas –Rodríguez J et al. HIV pre-treatment drug resistance in Mexico: a nationally representative WHO survey. Abstract 64. XXV International HIV Drug Resistance Workshop, Boston, USA, 2016.
[13] Lavu E, Dala N, Gurung, A, Kave E, Mosoro E, Markby J et al. Transmitted HIV drug resistance survey in two provinces in Papua New Guinea. Poster: MOPED723. IAS 2015. Vancouver, Canada.
[14] National Institute for Communicable Diseases, Division of the National Health Laboratory Service. Prospective sentinel surveillance of human immunodeficiency virus related drug resistance. Communicable Disease Communiqué. 2016 March; 15:10-11.

WHO global HIVDR surveillance and monitoring strategy

Because of the error prone nature of HIV, its high mutation rate in the presence of drug selective pressure and the need for lifelong treatment, some HIVDR will inevitably occur among patients taking ART even when optimal adherence to therapy is supported. To address this threat to the success of ART scale-up, WHO developed a global HIVDR surveillance and monitoring strategy in 2004, subsequently updating it in 2015.[1] The strategy consists of four key activities:

(1) the annual monitoring of EWIs of HIVDR at all ART clinics, or a representative sample of ART clinics within a country;

(2) surveillance of pre-treatment HIVDR in adult populations initiating first-line ART;

(3) surveillance of acquired HIVDR in adults and children on treatment; and

(4) surveillance of HIVDR in infants less than 18 months of age.

The WHO HIVDR strategy is designed to provide countries with actionable information to improve clinic and programme performance, and to support ART regimen selection. EWI monitoring forms the foundation of the WHO-recommended HIVDR strategy to improve quality. Monitoring EWIs of HIVDR provides a record of clinic and programme performance, which helps contextualize results from national surveillance of HIVDR. Additionally, clinic- and programme-level responses taken to improve suboptimal performance will support not only the minimization of preventable HIVDR, but also the optimization of population ART outcomes. More details about the WHO HIVDR strategy can be found at: http://www.who.int/hiv/topics/drugresistance/en/. The strategy is supported by the WHO HIVResNet HIVDR Laboratory Network – a network of 31 WHO-designated laboratories, which undergo an annual evaluation and provide high-quality HIVDR genotyping for countries implementing HIVDR surveys.[2]

[1] HIV drug resistance surveillance guidance: 2015 update. Geneva: The World Health Organization; 2015. Available at: http://www.who.int/hiv/pub/drugresistance/hiv-drug-resistance-2015-update/en/.

[2] Bertagnolio S, Derdelinckx I, Parker M, Fitzgibbon J, Fleury H, Peeters M et al. World Health Organization/HIVResNet drug resistance laboratory strategy. Antiviral Therapy. 2008;Vol.13;(Suppl 2):49–57.

EWIs OF HIVDR: MEASUREMENT OF PROGRAMMATIC QUALITY

Many factors are associated with the emergence of HIVDR. They include viral factors (e.g. subtype, replication capacity, and pre-existing polymorphisms); drug-related factors (e.g. drug potency, pharmacokinetics, drug-drug interactions, drug tolerability, and genetic barrier to selection of resistance); and programme factors (e.g. patient adherence to prescribed ART, drug supply continuity, and retention of patients on treatment). Although viral and drug-related factors are often beyond the control of public health or programme action, the monitoring of programme factors associated with HIVDR can alert ART programmes to situations that may favour the emergence of HIVDR or virological failure at the population level.

EWIs monitor factors related to patient care (appropriate prescribing and viral load suppression at 12 months); patient behaviour (adherence); and clinic-level and programme management (loss to follow-up, retention on ART, and procurement and supply management of ARV drugs).

Each EWI has an internationally agreed-upon standardized definition and accompanying target(s). This allows clinics to be classified into one of three performance strata: green (excellent performance, achieving the desired level); amber (fair performance, not yet at desired level); and red (poor performance, below desired level).[1] Stratified EWI targets provide clinic-specific and programme-level benchmarks against which to assess performance – thus facilitating identification of areas of greatest need and allocation of resources to close gaps in service delivery. ART clinic or programme performance below desired targets prompts investigation and implementation of programmatic and/or public health actions to improve quality of ART service delivery – thereby minimizing the emergence of preventable HIVDR (see *Examples of ART programme action taken by countries in response to EWI results*, page 40). Annual monitoring of EWIs allows for measurement of degrees of improvement or decline over time, both within and between clinics. To encourage their routine monitoring and use, EWIs have been fully integrated into WHO's 2015 *Consolidated strategic information guidelines for HIV in the health sector.*[2]

WHO-recommended EWIs of HIVDR and their respective targets are summarized in **Table 1.** Associations between EWIs and HIVDR are discussed in the following section. Additional information about EWIs may be found in the *Epidemiological methods* section of the **Annex**.

Development of EWI definitions and targets

EWIs use standardized definitions and targets grounded in medical and scientific literature. The original definitions and targets were proposed in 2008. In 2011, an advisory panel reviewed existing EWI definitions and targets; each EWI was considered separately for its association with HIVDR. After critical review of available medical literature using the GRADE methodology, the panel used a mix of **normative and criterion referencing** to set EWI targets[3]. **Normative referencing** is the establishment of targets based on mean levels of performance. When using normative referencing results above a central value are considered "good" performance, and results below a central value are considered "poor" performance. A systematic review of the literature provided the mean levels of performance for each EWI. An important limitation of normative referencing is that it may reflect poor existing practices and lack aspiration. **Criterion referencing** is the establishment of targets based on attainment of desirable levels of performance. Criterion referencing may be evidence-based but often necessitates expert opinion to set targets. To balance the strengths and limitations of normative and criterion referencing, a "mixed methods" approach to target setting was used and expert opinion was used to establish targets when available evidence was lacking. More information on how EWI targets were established, including results from the systematic review of the literature may be found online in the *Report of the early warning indicator advisory panel meeting (11–12 August 2011): Using early warning indicators to prevent HIV drug resistance*; available at: http://www.who.int/hiv/pub/meetingreports/ewi_meeting_report/en/.

[1] The EWIs "prescribing practices" and "drug stock outs" have only two strata: green (excellent) and red (poor).
[2] Consolidated strategic information guidelines for HIV in the health sector. Geneva: World Health Organization; 2015. Available at: http://www.who.int/hiv/pub/guidelines/strategic-information-guidelines/en/.
[3] Using early warning indicators to prevent HIV drug resistance. Report of the Early Advisory Indicator Panel meeting (11–12 August 2011). Geneva: World Health Organization; 2012. Available at: http://www.who.int/hiv/pub/meetingreports/ewi_meeting_report/en/.

Table 1. WHO HIVDR EWIs: definitions and associated targets

EWI	Target: ● excellent performance ● fair performance ● poor performance
Prescribing practices % of ART prescriptions congruent with national/international guidelines	●: 100% ●: <100%
LTFU at 12 months[1] % of patients LTFU 12 months after ART initiation	●: <15% ●: 15–25% ●: >25%
Retention at 12 months[2] % of patients retained in care 12 months after ART initiation	●: >85% ●: 75–85% ●: <75%
On-time pill pick-up[3] % of patients with 100% on-time drug pick-up during the first 12 months of ART or during a specified time period	●: >90% ●: 80–90% ●: <80%
On-time appointment keeping[4,5] % of patients attending all clinic appointments on time during the first 12 months of ART or during a specified time period	●: >80% ●: 70–80% ●: <70%
Drug stock out[6] % of months with any day(s) of stock out of any routinely dispensed ARV drug	●: 0% ●: >0%
Viral load suppression[7] % of patients with viral load <1000 copies/mL 12 months after ART initiation	●: >90% ●: 80–90% ●: <80%
Viral load completion[8] % of patients with a 12-month viral load test result available	●: ≥70% ●: <70%

[1] Patients not known to have died or transferred care to another clinic, and who have not returned to the clinic or pharmacy within 90 days (≤90 days) of the 12-month date, are classified as LTFU. The LTFU indicator was dropped in 2011 in favour of the retention indicator.
[2] Operationally, data may represent the percentage of patients retained on first-line ART at 12 months, or retained in care at the 12-month date.
[3] Three variations of this indicator were used during the reporting period. One assessed on-time pill pick-up amongst a cohort of ART initiators during the first 12 months of therapy, and defined "on time" as on or before the pills would run out if taken according to schedule. The second was a cross-sectional version which assessed on-time pill pick-up amongst individuals on ART regardless of treatment duration or regimen line; "on time" was defined as picking up pills on or before they would run out if taken according to schedule. The third was a cross-sectional version which assessed on-time pill pick-up amongst individuals on ART regardless of treatment duration or regimen line; "on time" was defined as picking up pills within two days of the run-out date, if taken according to schedule.
[4] Appointments were classified as "on time" if they were within seven days of the scheduled clinic appointment.
[5] On-time appointment keeping was dropped as an EWI in 2011 due to insufficient evidence for its association with HIVDR or population-level viral load suppression.
[6] The stock out indicator monitors whether ART clinics (dispensaries) maintain a continuous supply of routinely dispensed ARV drugs at all times. Specifically, this indicator measures the proportion of months in a calendar year with any ARV drug stock out; data are derived from pharmacy stock records.
[7] The denominator for the viral load suppression indictor is the number of patients alive and on ART 12 months after treatment initiation who have a viral load test result available.
[8] The denominator for the viral load completion indicator is the number of patients alive and on ART 12 months after treatment initiation, who are therefore, per policy, expected to have a viral load test result available in the primary medical record.

ASSOCIATION BETWEEN EWIs AND HIVDR

Prescribing practices

The goals of HIV treatment include a reduction in HIV-associated morbidity and mortality, restoration and preservation of immunologic function, durable suppression of plasma HIV viral load, and prevention of HIV transmission. Achieving viral suppression requires the use of three active drugs from two or more drug classes. The evidence that virological failure and HIVDR are closely associated with the prescription of suboptimal ART is supported by a large number of prospective randomized clinical trials and observational studies.

In the late 1980s and mid-1990s, studies of nucleoside reverse transcriptase inhibitor (NRTI) or protease inhibitor (PI) mono-therapy reported initial reductions in levels of circulating virus, followed by high rates of virological failure, accompanied by selection of HIVDR.[1,2,3] Randomized trials of different ARV drug combinations documented the virological and clinical superiority of double NRTI therapy over NRTI mono-therapy.[4] Subsequently, the superiority of three drugs, including either a PI or NNRTI, over double NRTI regimens was confirmed.[5,6,7,8]

Based on this evidence, as well as other data measuring levels of virological suppression,[9] the prescribing of mono- or dual-therapy for the treatment of HIV infection is never recommended by national or international treatment guidelines. Ensuring that individuals being treated for HIV infection receive appropriate triple-drug therapy is therefore an essential step towards maximizing population-level viral load suppression and minimizing HIVDR. The prescribing practices indicator evaluates ART clinic compliance with prescribing regimens congruent with national and/or international ART guidelines.

The WHO-suggested target for prescribing practices is 100% of patients being dispensed appropriate ART, where "appropriate" is defined as a regimen appearing on national or international treatment guidelines.

LTFU at 12 months

From the perspective of a clinic initiating ART, the majority of treatment initiators should be alive and on treatment at the same clinic after one year. However, some patients will have died, transferred care to a different clinic (transfer out), or stopped treatment while remaining at the same clinic. Still others will have unknown outcomes, and thus be classified as "loss to follow-up" (LTFU). The LTFU classification means that information is unavailable to classify patients as deceased, alive and in care (at the site of treatment initiation or at a different one), or having disengaged from care three months after their last scheduled appointment or drug pick-up. As ART services are increasingly decentralized, many individuals may in fact have stopped treatment at one clinic and reinitiated it at another, without documentation or transfer of records. This practice is commonly referred to as a "silent transfer". The relative frequency of each of these reasons for "loss" has been observed to vary across clinics.[10,11,12,13,14] The frequency and duration of treatment gaps experienced due to silent transfers is largely unknown; however, it is likely that many of these people experience treatment interruptions placing them at substantial risk for selection of resistant virus. For example, 24% of individuals with previous treatment interruption who experienced virological failure on an NNRTI-based regimen three months after its re-initiation had resistance to the NNRTI drug class.[15] Preliminary analysis of a 2015 study conducted by WHO and the Ministry of Health in Malawi showed that 40% of 52 individuals traced after having been classified as LTFU, who had successful HIVDR genotyping at two sites in Malawi, harboured major NNRTI dug-resistance mutations (WHO and Ministry of Health, Malawi, unpublished data, 2015).

---

1 Fischl MA, Richman DD, Grieco MH, Gottlieb MS, Volberding PA, Laskin OL et al. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial. N Engl J Med. 1987;317:185–191.

2 Ho DD, Neumann AU, Perelson AS, Chen W, Leonard JM, Markowitz M. Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection. Nature. 1995;373:123–126.

3 Larder BA, Darby G, Richman DD. HIV with reduced sensitivity to zidovudine (AZT) isolated during prolonged therapy. Science. 1989;243: 1731–1734.

4 Hammer SM, Katzenstein DA, Hughes MD, Gundacker H, Schooley RT, Haubrich RH et al. A trial comparing nucleoside monotherapy with combination therapy in HIV-infected adults with CD4 cell counts from 200 to 500 per cubic millimeter. AIDS Clinical Trials Group Study 175 Study Team. N Engl J Med. 1996; 335:1081–1090.

5 D'Aquila RT, Hughes MD, Johnson VA, Fischl MA, Sommadossi JP, Liou SH et al. Nevirapine, zidovudine, and didanosine compared with zidovudine and didanosine in patients with HIV-1 infection. A randomized, double-blind, placebo-controlled trial. National Institute of Allergy and Infectious Diseases AIDS Clinical Trials Group Protocol 241 Investigators. Ann Intern Med. 1996;124(12):1019–1030.

6 Hammer SM, Squires KE, Hughes MD, Grimes JM, Demeter LM, Currier JS et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. AIDS Clinical Trials Group 320 Study Team. N Engl J Med. 1997;337:725–733.

7 Montaner JS, Reiss P, Cooper D, Vella S, Harris M, Conway B et al. A randomized, double-blind trial comparing combinations of nevirapine, didanosine, and zidovudine for HIV-infected patients: the INCAS Trial. Italy, The Netherlands, Canada and Australia Study. JAMA. 1998;279:930–937.

8 Djomand G, Roels T, Ellerbrock T, Hanson D, Diomande F, Monga B et al. Virologic and immunologic outcomes and programmatic challenges of an antiretroviral treatment pilot project in Abidjan, Cote d'Ivoire. AIDS. 2003;17(Suppl. 3):S5–15.

9 Jordan R, Gold L, Cummins C, Hyde C. Systematic review and meta-analysis of evidence for increasing numbers of drugs in antiretroviral combination therapy. BMJ. 2002;324(7340):757.

10 McGuire M, Munyenyembe T, Szumilin E, Heinzelmann A, Le Paih M, Bouithy N et al. Vital status of pre-ART and ART patients defaulting from care in rural Malawi. Trop Med Int Health. 2010;15(Suppl 1):55–62.

11 Maskew M, MacPhail P, Menezes C, Rubel D. Lost to follow up: contributing factors and challenges in South African patients on antiretroviral therapy. S Afr Med J. 2007;97(9):853–7.

12 Amuron B, Namara G, Birungi J, Nabiryo C, Levin J, Grosskurth H et al. Mortality and loss-to-follow-up during the pre-treatment period in an antiretroviral therapy programme under normal health service conditions in Uganda. BMC Public Health. 2009;9:290. doi: 10.1186/1471-2458-9-290.

13 Geng EH, Bangsberg DR, Musinguzi N, Emenyonu N, Bwana MB, Yiannoutsos CT et al. Understanding reasons for and outcomes of patients lost to follow-up in antiretroviral therapy programs in Africa through a sampling-based approach. J Acquir Immune Defic Syndr. 2010;53(3):405–11. doi: 10.1097/QAI.0b013e3181b843f0.

14 Dalal RP, Macphail C, Mqhayi M, Wing J, Feldman C, Chersich MF et al. Characteristics and outcomes of adult patients lost to follow-up at an antiretroviral treatment clinic in Johannesburg, South Africa. J Acquir Immune Defic Syndr. 2008;47(1):101–7.

15 Luebbert J, Tweya H, Phiri S, Chaweza T, Mwafilaso J, Hosseinipour MC et al. Virological failure and drug resistance in patients on antiretroviral therapy after treatment interruption in Lilongwe, Malawi. Clin Infect Dis. 2012;55(3):441–8. doi: 10.1093/cid/cis438.

The LTFU indicator measures the proportion of patients with unknown outcomes at a single point in time: 12 months after ART initiation. Operationally, because known deaths and documented transfers of care to other clinics are censored (i.e. excluded from the denominator), the indicator estimates a clinic's performance in classifying deaths, documenting transfers of care from one facility to another, and minimizing patient disengagement from care. LTFU is therefore closely related to retention in care at 12 months. WHO's suggested target for this indicator is less than 15% LTFU at 12 months.

Retention on ART at 12 months

Maintaining high levels of engagement with patients in care and on continuous ART is fundamental to achieving global HIV treatment goals. Studies document that most attrition occurs during the first two years on ART, a time when mortality is known to be highest.[1,2] Treatment programmes with active tracing of defaulters have higher overall levels of retention (80.0% vs. 75.8%; p = 0.04) and higher retention at the original clinic of treatment initiation (80.0% vs. 72.9%; p = 0.02).[3] As with LTFU, patients not retained on ART have experienced treatment interruption and are therefore at risk for selection of drug-resistant virus, which could in turn compromise individual- and population-level treatment outcomes.

Monitoring the number of patients retained on ART is important for estimating the proportion of patients dying or experiencing disengagement from care. As with LTFU, accurately characterizing these outcomes can lead to targeted interventions to minimize treatment interruptions and decrease mortality. The retention indicator monitors a clinic's performance in maintaining patient engagement in care, effectively preventing deaths and minimizing unknown treatment outcomes. WHO's suggested target for retention at 12 months is above 85%.

On-time pill pick-up and on-time appointment keeping

Sustained long-term adherence to ART is critical to achieving the desired individual- and population-level benefits of HIV treatment. Studies document virological failure and selection of drug-resistant HIV amongst individuals receiving NNRTI-based regimens who experience treatment interruptions of more than 48 hours.[4,5] Despite the clear link between suboptimal adherence to ART and the emergence of HIVDR, the estimation of patient and population adherence to ART may pose challenges. For example, patient self-reported adherence and provider perception of patient adherence have been shown to be unreliable.[6] Despite limitations, prescription or pill-based methods do not rely on special technology (e.g. MEMS caps) or require significant human and financial resources (e.g. unannounced home-based pill counts) to estimate adherence. They are objective estimates calculated by abstraction and analysis of routinely captured pharmacy or clinic dispensing data.[7] Although simple, these methods have been demonstrated to predict virological and drug-resistance outcomes.[8,9,10,11,12]

The on-time pill pick-up indicator provides a high-level assessment of how well populations of patients at a clinic perform in picking up prescribed ART on or before the pill run-out date, if taken according to schedule. WHO's suggested target for desirable clinic-level performance for on-time pill pick-up is above 90%.

Like on-time pill pick-up, on-time clinic appointment keeping is a proxy measure of patient adherence to ART, and has been correlated with ART adherence.[13,14] The on-time appointment keeping indicator estimates clinic performance in successfully engaging patients to attend scheduled appointments. Late clinic attendance has been shown to be associated with virological failure.[15] WHO's suggested target for desirable clinic-level performance of this indicator is above 80%.

---

[1] Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. AIDS. 2008;22(15):1897–908.
[2] Hassan AS, Mwaringa SM, Ndirangu KK, Sanders EJ, Rinke TF, Berkley JA. Incidence and predictors of attrition from antiretroviral care among adults in a rural HIV clinic in Coastal Kenya: a retrospective cohort study. BMC Public Health. 2015;15:478.
[3] McMahon JH, Elliott JH, Hong SY, Bertagnolio S, Jordan MR. Effects of physical tracing on estimates of loss to follow-up, mortality and retention in low and middle income country antiretroviral therapy programs: a systematic review. PLoS ONE. 2013;8(2):e56047.
[4] Oyugi JH, Byakika-Tusiime J, Ragland K, Laeyendecker O, Mugerwa R, Kityo C et al. Treatment interruptions predict resistance in HIV-positive individuals purchasing fixed-dose combination antiretroviral therapy in Kampala, Uganda. AIDS. 2007;21(8):965–71.
[5] Parienti JJ, Massari V, Descamps D, Vabret A, Bouvet E, Larouzé B et al. Predictors of virologic failure and resistance in HIV-infected patients treated with nevirapine- or efavirenz-based antiretroviral therapy. Clin Infect Dis. 2004;38(9):1311–6.
[6] Goldman JD, Cantrell RA, Mulenga LB, Tambatamba BC, Reid SE, Levy JW et al. Simple adherence assessments to predict virologic failure among HIV-infected adults with discordant immunologic and clinical responses to antiretroviral therapy. AIDS Res Hum Retroviruses. 2008;24:1031–5.
[7] McMahon JH, Jordan MR, Kelley K, Bertagnolio S, Hong SY, Wanke CA et al. Pharmacy adherence measures to assess adherence to antiretroviral therapy: review of the literature and implications for treatment monitoring. Clin Infect Dis. 2011;52(4):493–506.
[8] Harrigan PR, Hogg RS, Dong WW, Yip B, Wynhoven B, Woodward J et al. Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. J Infect Dis. 2005;191(3):339–47.
[9] King MS, Brun SC, Kempf DJ. Relationship between adherence and the development of resistance in antiretroviral-naive, HIV-1-infected patients receiving lopinavir/ritonavir or nelfinavir. J Infect Dis. 2005;191(12):2046–52.
[10] Jonas A, Sumbi V, Mwinga S, DeKlerk M, Tjituka F, Penney S et al. HIV drug resistance early warning indicators in Namibia with updated World Health Organization guidance. PLoS ONE. 2014;9(7):e100539.
[11] Orrell C, Cohen K, Leisegang R, Bangsberg DR, Maartens G, Wood R. Comparing adherence methods: which best predicts virological and resistance outcome? Conference on Retroviruses and Opportunistic Infections. Boston. February 2016. Poster 1029.
[12] V Cambiano, Lampe FC, Rodger AJ, Smith CJ, Geretti AM, Lodwick RK et al. Use of a prescription-based measure of antiretroviral therapy adherence to predict viral rebound in HIV-infected individuals with viral suppression. HIV Medicine. 2010;11(3):216–224.
[13] Chalker JC, Andualem T, Gitau LN, Nitaganira J, Obua C, Tadeg H et al. Measuring adherence to antiretroviral treatment in resource-poor settings: the feasibility of collecting routine data for key indicators. BMC Health Serv Res. 2010;10:43. doi: 10.1186/1472-6963-10-43.
[14] White YR, Pierre RB, Steel-Duncan J, Palmer P, Evans-Gilbert T, Moore J et al. Adherence to antiretroviral drug therapy in children with HIV/AIDS in Jamaica. West Indian Med J. 2008;57(3):231–7.
[15] Blacher RJ, Muiruri P, Njobvu L, Mutsotso W, Potter D, Ong'ech J et al. How late is too late? Timeliness to scheduled visits as an antiretroviral therapy adherence measure in Nairobi, Kenya and Lusaka, Zambia. AIDS Care. 2010;22(11):1323–1331.

Drug stock outs

Procurement (the country-level process of ordering ARV drugs) and supply chain management (the systems by which they are distributed to health-care facilities) are critical processes required to move ARV drugs from manufacturers to patients. Success of ART access in a country depends not only on procurement, but also on a robust and reliable drug distribution system, which is able to account for stock down to the lowest level (often a clinic dispensary). This is because what affects patients most is drug availability at the place where it is picked up, not its availability at a district or central warehouse. Stock outs of ARV drugs are linked to the emergence of HIVDR, and may even double the risk of treatment interruptions and death.[1] To avoid treatment interruptions, clinics may resort to substitution of one ARV drug for another, or switch patients to a drug from a different class. These obligatory changes may be associated with suboptimal adherence, unanticipated toxicity or adverse events. An additional strategy in the face of limited stock is dispensing fewer days of the drug than prescribed – a strategy that may negatively impact adherence and ultimately lead to a decrease in retention.

The stock out indicator monitors whether ART clinics (dispensaries or pharmacies) maintain a continuous supply of routinely dispensed ARV drugs at all times. This indicator is particularly important given that data, not surprisingly, link stock outs to treatment interruptions.[2] Specifically, this indicator measures the proportion of months in a calendar year with any ARV drug stock out. As all routinely dispensed ARV drugs are expected to be available at clinic dispensaries at all times, WHO's suggested target for this indicator is 0% of months with a stock out.

Viral load suppression

The association between virological failure and HIVDR is strong. Three randomized controlled trials report selection of HIVDR in at least 70% of patients with virological failure,[3,4,5] with two of the three studies documenting no HIVDR at ART initiation.[3,4] Additionally, numerous studies document HIVDR in significant proportions of patients with virological failure.[6,7,8,9,10,11] Achieving high levels of viral load suppression within populations on ART minimizes morbidity and mortality and decreases HIV incidence; furthermore, the emergence of HIVDR is prevented amongst those with virological suppression. The viral load suppression indicator measures how well clinics perform in reaching virological suppression targets. WHO's suggested target for desirable performance for this indicator is over 90% viral load suppression amongst those alive and on ART 12 months after treatment initiation.

Viral load completion

Attaining high levels of viral load suppression is inextricability linked with high levels of viral load access and completion. The lack of routine viral load monitoring and appropriate action to detected virological failure is associated with the emergence of HIVDR, as patients remain on a failing regimen and accumulate resistance mutations.[12,13,14,15] The viral load completion indicator measures the proportion of patients with a 12-month viral load test result available in their medical records. WHO's 2016 ART guidelines[16] recommend early viral load testing (within six months of treatment initiation), again at 12 months, and at least annually thereafter. The viral load completion indicator measures a programme's capacity to implement viral load testing and assure that the result is returned to a patient's records, maximizing the likelihood of it being reviewed and acted upon by providers, if necessary. WHO's recommended target for this indicator is 70% or greater viral load completion at 12 months.

---

[1] Pasquet A, Messou E, Gabillard D, Minga A, Depoulosky A, Deuffic-Burban S et al. Impact of drug stock-outs on death and retention to care among HIV-infected patients on combination antiretroviral therapy in Abidjan, Côte d'Ivoire. PLoS ONE. 2010;5(10):e13414.

[2] Marcellin F, Boyer S, Protopopescu C, Dia A, Ongolo-Zogo P, Koulla-Shiro S et al. Determinants of unplanned antiretroviral treatment interruptions among people living with HIV in Yaoundé, Cameroon (EVAL survey, ANRS 12-116). Trop Med Int Health. 2008;13(12):1470–1478.

[3] Bussmann H, Wester CW, Thomas A, Novitsky V, Okezie R, Muzenda T et al. Response to zidovudine/didanosine-containing combination antiretroviral therapy among HIV-1 subtype C-infected adults in Botswana: two-year outcomes from a randomized clinical trial. J Acquir Immune Defic Syndr. 2009;51(1):37–46.

[4] Lyagoba F, Dunn DT, Pillay D, Kityo C, Robertson V, Tugume S et al. Evolution of drug resistance during 48 weeks of zidovudine/lamivudine/tenofovir in the absence of real-time viral load monitoring. J Acquir Immune Defic Syndr. 2010;55(2):277–283.

[5] Ndembi N, Goodall RL, Dunn DT, McCormick A, Burke A, Lyagoba F et al. Viral rebound and emergence of drug resistance in the absence of viral load testing: a randomized comparison between zidovudine-lamivudine plus Nevirapine and zidovudine-lamivudine plus Abacavir. J Infect Dis. 2010;201(1):106–113.

[6] Ahoua L, Guenther G, Pinoges L, Anguzu P, Chaix ML, Le Tiec C et al. Risk factors for virological failure and subtherapeutic antiretroviral drug concentrations in HIV-positive adults treated in rural northwestern Uganda. BMC Infectious Diseases. 2009; 9:81.

[7] Ferradini L, Jeannin A, Pinoges L, Izopet J, Odhiambo D, Mankhambo L et al. Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment. Lancet. 2006;367(9519):1335–1342.

[8] Garrido C, Zahonero N, Fernandes D, Serrano D, Silva AR, Ferraria N et al. Subtype variability, virological response and drug resistance assessed on dried blood spots collected from HIV patients on antiretroviral therapy in Angola. J Antimicrob Chemother. 2008;61(3):694–698.

[9] Kouanfack C, Montavon C, Laurent C, Aghokeng A, Kenfack A, Bourgeois A et al. Low levels of antiretroviral-resistant HIV infection in a routine clinic in Cameroon that uses the World Health Organization (WHO) public health approach to monitor antiretroviral treatment and adequacy with the WHO recommendation for second-line treatment. Clin Infect Dis. 2009;48(9):1318–1322

[10] Ramadhani HO, Thielman NM, Landman KZ, Ndosi EM, Gao F, Kirchherr JL et al. Predictors of incomplete adherence, virologic failure, and antiviral drug resistance among HIV-infected adults receiving antiretroviral therapy in Tanzania. Clin Infect Dis. 2007;45(11):1492–1498.

[11] WHO HIV drug resistance report 2012. Geneva: World Health Organization; 2012. Available at: http://www.who.int/hiv/pub/drugresistance/report2012/en/.

[12] van Zyl GU, van der Merwe L, Claassen M, Zeier M, Preiser W. Antiretroviral resistance patterns and factors associated with resistance in adult patients failing NNRTI-based regimens in the Western Cape, South Africa. J Med Virol. 2011;83(10):1764–9.

[13] Cozzi-Lepri A, Paredes, Phillips AN, Clotet B, Kjaer J, Von Wyl V et al. The rate of accumulation of nonnucleoside reverse transcriptase inhibitor (NNRTI) resistance in patients kept on a virologically failing regimen containing an NNRTI. HIV Med. 2012;13(1):62–72.

[14] Gupta R, Pillay D, Ranopa M et al. Rapid accumulation of thymidine-analog mutations and virologic implications in the absence of viral load monitoring. 2011. 18th Conference on Retroviruses and Opportunistic Infections. Boston, Massachusetts. Abstract 618.

[15] Hoffmann CJ, Charalambous S, Sim J, Ledwaba J, Schwikkard G, Chaisson RE et al. Viremia, resuppression, and time to resistance in human immunodeficiency virus (HIV) subtype C during first-line antiretroviral therapy in South Africa. Clin Infect Dis. 2009;49(12):1928–35.

[16] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection Recommendations for a public health approach - Second edition; Geneva: World Health Organization; 2016. Available at: http://www.who.int/hiv/pub/arv/arv-2016/en.

STATISTICAL METHODS

Data on completed EWI monitoring rounds were reported to WHO by 59 countries, primarily in the form of detailed clinic-level results, including a numerator and denominator for each EWI assessed. Fifteen countries reported aggregated data, in the form of the number of clinics meeting each EWI target out of the total number of clinics monitored.[1] As data were reported at the clinic level, disaggregation by age and gender was not feasible.

The primary analysis includes data from 55 countries providing detailed clinic-level results. National prevalence estimates were generated as the sum of the clinic numerators divided by the sum of the clinic denominators in a given round for a given EWI. Regional and global prevalence statistics were constructed in a similar fashion. To enhance the data set to allow for deeper investigations, data on countries were gathered from multiple sources including Global AIDS Response Progress Reporting, country HIVDR reports submitted to WHO, and WHO/UNAIDS global reports for the years of EWI monitoring. Variables assessed included the total number of ART clinics in the country, total number of people on ART, total number of people living with HIV, and country income classification.[2] Analyses did not consider funding from bilateral and multilateral agencies used to support ART scale-up. Country income classification was considered a proxy for health infrastructure and does not account for external support provided to HIV programmes. Additional detail about the statistical analyses is available in the *Statistical methods* section of the **Annex**.

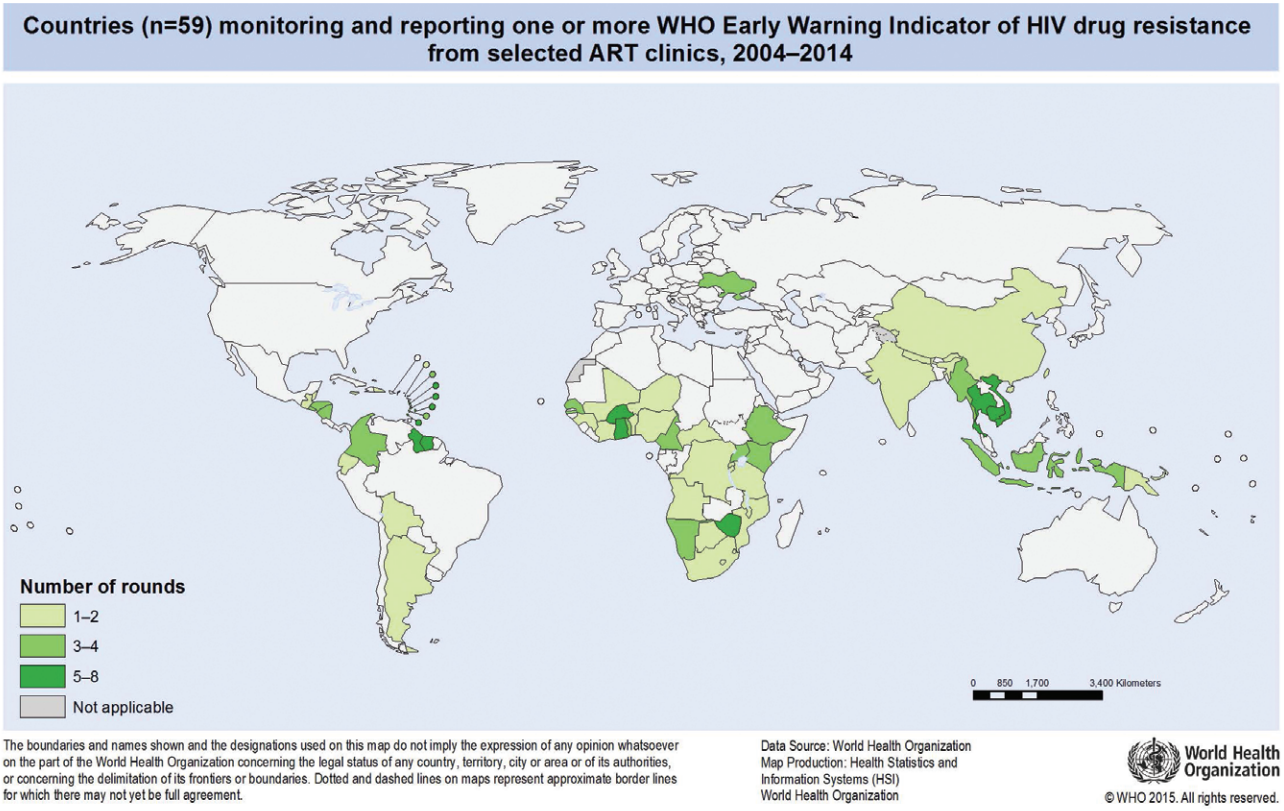
This report has limitations. With very few exceptions, data reported by countries were not derived using representative clinic selection; therefore, country-specific prevalence estimates reflect the aggregated prevalence of a given indicator derived from purposefully sampled clinics in a given round; thus limiting the generalizability beyond the clinics reporting. Additionally, not all countries implemented EWI monitoring or reported results. Caution is therefore warranted when interpreting global, regional and national estimates and trends. To mitigate this effect, time trends are analysed using a model that prioritizes data collected from repeated rounds within countries, limiting the impact of countries reporting only a single round of data.

[1] Some countries reported aggregate-level data for some rounds and clinic-level data for other rounds in different cohort years.
[2] The World Bank. What is the World Bank Atlas method? Available at: https://datahelpdesk.worldbank.org/knowledgebase/articles/378832-what-is-the-world-bank-atlas-method.

COVERAGE OF EWI MONITORING

From a total of 165 rounds between 2004 and 2014, 59 countries reported EWI data to WHO (see **Fig. 1**).

Fig. 1. Countries (n=59) monitoring and reporting one or more EWI of HIVDR from selected ART clinics, 2004–2014



Fifteen countries reported aggregate-level data from 19 rounds. Detailed clinic-level data from 146 rounds of EWI monitoring were reported from 7569 clinics[1] in 55 countries. All analyses presented in this report use the detailed clinic-level data reported from the 55 countries, with the exception of regional-level aggregate data presented in the section *Aggregate EWI results by region* (page 35).

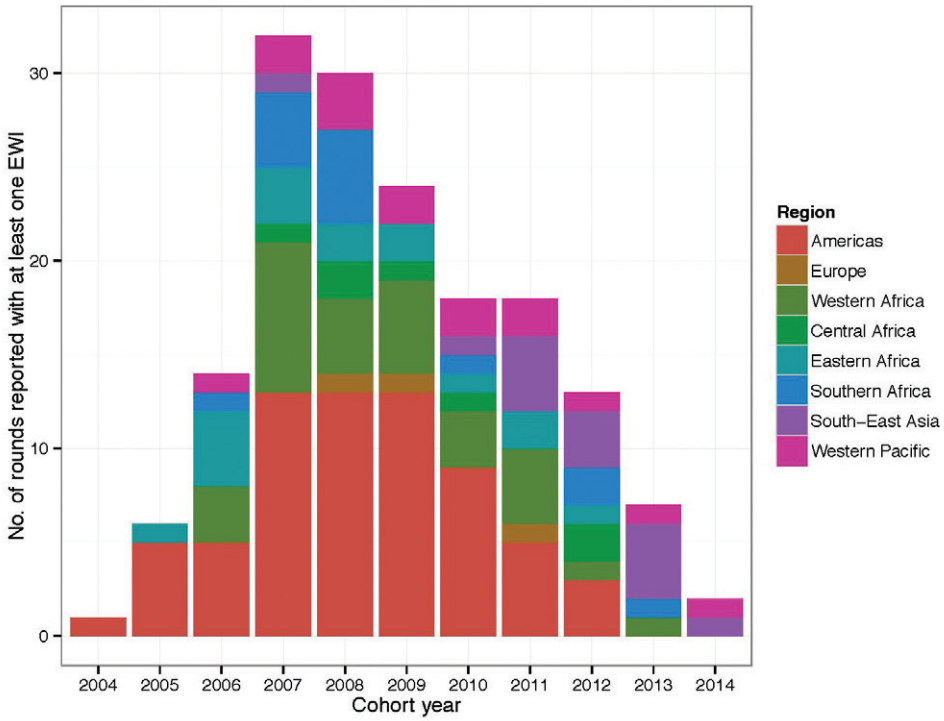
Amongst the 55 countries reporting clinic-level data, at the time of their most recent EWI monitoring round, 19 (35%) were classified as low-income countries; 21 (38%) as lower-middle-income; 13 (24%) as upper-middle-income; and 2 (4%) as upper-income. The majority of low-income countries (89%) reporting EWIs are located in Africa. Among upper-middle- and high-income countries, 80% are from the Americas.

When reporting implementation, EWI rounds are reported by "cohort year". A cohort year is defined as the year from which the majority of data contributing to an EWI reporting round were originally entered into patient medical or pharmacy records. **Fig. 2** shows the total number of rounds reporting clinic-level EWI data by cohort year and by region for the period 2004–2014.

In 2004, only one country in the Americas monitored one or more EWI. By 2007, 31 countries from seven regions were moitoring EWIs in 32 unique rounds. A steady decline in EWI monitoring occurred between 2008 and 2014, with 30 countries reporting in 2008 and only two countries (in South-East Asia and the Western Pacific) reporting in 2014.

[1] Clinics may be counted more than once if rounds of EWI monitoring are repeated at the same clinic over time.

Fig. 2. Number of rounds reported with at least one EWI by region and year, 2004–2014



A *cohort year* is defined as the year from which the majority of data contributing to an EWI reporting round were originally entered into patients' medical or pharmacy records.

In total, between 2004 and 2014, detailed clinic-level data were reported from 7569 clinics.[1] The global decline in reporting of clinic-level EWIs observed after 2011 is likely multifactorial, and may be partly related to a decrease in funding for EWI specific monitoring and partly due to transitioning of these indicators into national M&E systems. The observed decline in EWI reporting is addressed in greater detail in the section *Improving monitoring and response for EWIs of HIVDR* (page 43). Ongoing reporting of EWIs from South-East Asia was driven primarily by Thailand, which exemplifies the integration of routine EWI monitoring into a country's electronic medical record-keeping system.

Considerable variation in the number and proportion of clinics reporting EWIs within a county was observed. This variation likely reflects ART programme decisions about how to pilot and scale up EWI reporting. It may also, to some extent, reflect robustness of clinic-level record keeping.

The proportion of clinics within a country participating in EWI monitoring varied by region. Median participation was 30.5% in the Americas; 25.8% in Western Africa; 9.2% in Central Africa; 11.6% in Eastern Africa; 24.6% in Southern Africa; 19.7% in South-East Asia; and 11.0% in the Western Pacific. In general, small island nations in the Americas had very high levels of participation due to the small number of clinics. With the exception of Thailand, where up to 98.3% (2010–2011) of clinics reported, and Niger and Ghana, where up to 91.7% (2007) and 89.5% (2009–2010) of clinics reported respectively, the proportion of clinics monitoring EWIs was low (median participation of 24%).

While some countries monitored EWIs at few ART clinics, other countries conducted larger rounds with many clinics monitored. These countries included the Democratic Republic of the Congo (DRC), Ghana, South Africa, Thailand, Uganda and Viet Nam. **Table 1A** in the **Annex** summarizes the top 15 EWI rounds with the most clinics included. Of the clinics that reported to WHO in this data set, 75.2% (5742) came from the six unique countries listed in this table.

As the proportion of clinics within a country reporting EWIs varied, so too did the frequency with which individual EWIs were monitored in each round. Over 90% of rounds reported on prescribing practices and retention; 72% of rounds monitored LTFU at 12 months; 42% and 30% reported on-time pill pick-up and on-time appointment keeping, respectively; 44% of rounds monitored drug stock outs; and only 19% of rounds monitored viral load suppression at 12 months. The frequency with which countries and clinics monitored particular indicators may have been due to national ART programme preference regarding which indicators to prioritize, and was likely influenced by ease of data abstraction from existing clinic and pharmacy records. The low uptake of viral load suppression as an indicator reflects the limited availability of routine viral load monitoring in most countries during the reporting period.

[1] Clinics may not be unique: they may be counted more than once if EWI rounds were repeated at the same clinic over time.

Among countries reporting detailed clinic-level data to WHO, the total number of clinics and patient records evaluated for each EWI is summarized in **Table 2**. Although viral load suppression 12 months after ART initiation was assessed in 71 387 patients from 4461 clinics across 13 countries, data are almost exclusively from Thailand (96%); therefore, global and regional statements regarding this indicator are not made.

Table 2. Number of clinics and patient records evaluated by EWI, 2004–2014

	Prescribing practices	LTFU	Retention	On-time pill pick-up	On-time appointment keeping	Drug stock outs	Viral load suppression
No. of clinics	7 269	1 837	7 062	5 871	1 388	1 150	4 461
No. of records	1 144 058	169 233	368 364	579 998	113 957	NA	71 387

NA: not applicable

Results of each EWI are discussed in the following section. **Table 2A** in the **Annex** provides detailed EWI results by round and by country.

EWI MONITORING RESULTS

Prescribing practices

KEY FINDINGS

Countries: 52

ART clinics: 7269

Patients: 1 144 058

Period: 2005–2014

Finding: 99.1% (95% CI: 96.0–99.8%) of patients receiving ART were prescribed regimens following national or international guidelines. This result is just below the WHO-suggested target of 100%.

Global trend: On average, appropriate ART prescribing increased over time globally ($p<0.001$).

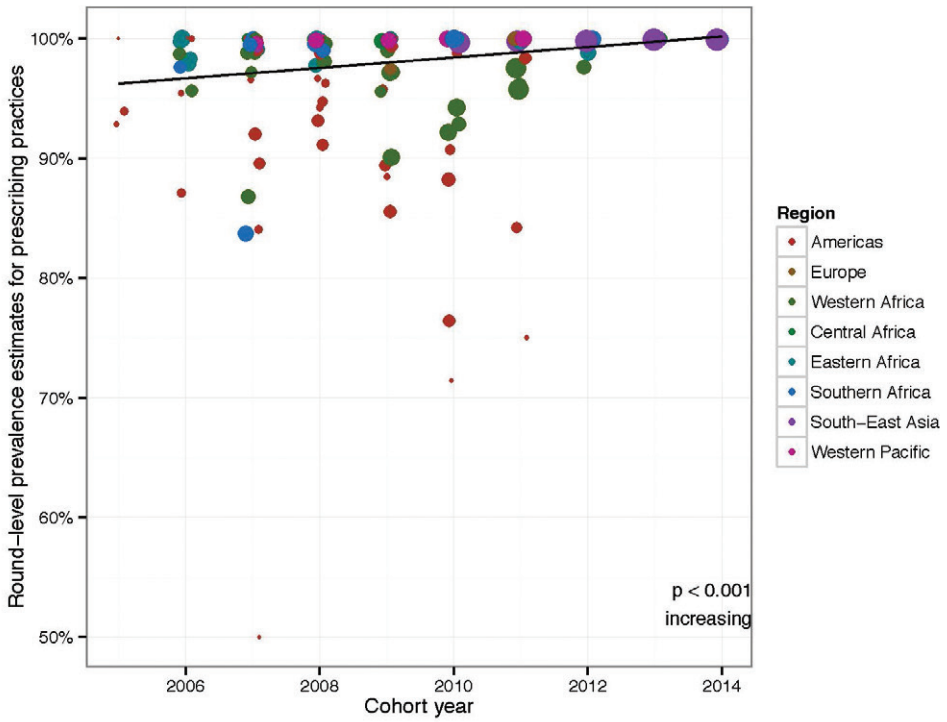
Inappropriate prescribing practices are closely associated with the emergence of HIVDR. Specifically, the prescribing of mono- or dual-therapy for the treatment of HIV infection is not recommended by national or international treatment guidelines, due to the rapid selection of drug-resistant virus when fewer than three active drugs are used. Region-specific ART prescribing practices are shown in **Table 3**.

Table 3. ART prescribing practices by region, 2005–2014

Region	No. of countries reporting data	No. of clinics	No. of records	% of patients prescribed ARVs as per national guidelines (mean)	95% confidence interval
Americas	17	147	12 833	92.7%	87.2–96.0%
Europe	1	33	2 672	99.4%	98.8–99.7%
Western Africa	10	1 047	170 544	95.9%	92.5–97.8%
Central Africa	3	223	15 644	99.8%	99.5–99.9%
Eastern Africa	7	414	44 245	99.5%	98.6–99.8%
Southern Africa	6	361	56 169	98.5%	90.4–99.8%
South-East Asia	5	4 805	817 197	99.9%	99.7–99.9%
Western Pacific	3	239	24 754	99.9%	99.9–100%
Total	**52**	**7 269**	**1 144 058**	**99.1%**	**96.0–99.8%**

Overall, very high levels of appropriate prescribing were observed. The lowest levels of appropriate prescribing were reported in the Region of the Americas (92.7% (95% CI: 87.2–96.0%)). Prescribing practices were also lower in the Western Africa subregion (95.9% (95% CI: 92.5–97.8%)). The observation in Western Africa is worrisome. It was not possible to verify the extent to which these suboptimal results were due to the inclusion of mono- or dual-drug regimens prescribed for the prevention of mother-to-child transmission, which at the time would have been considered contextually appropriate. Global trends over time are shown in **Fig. 3**.

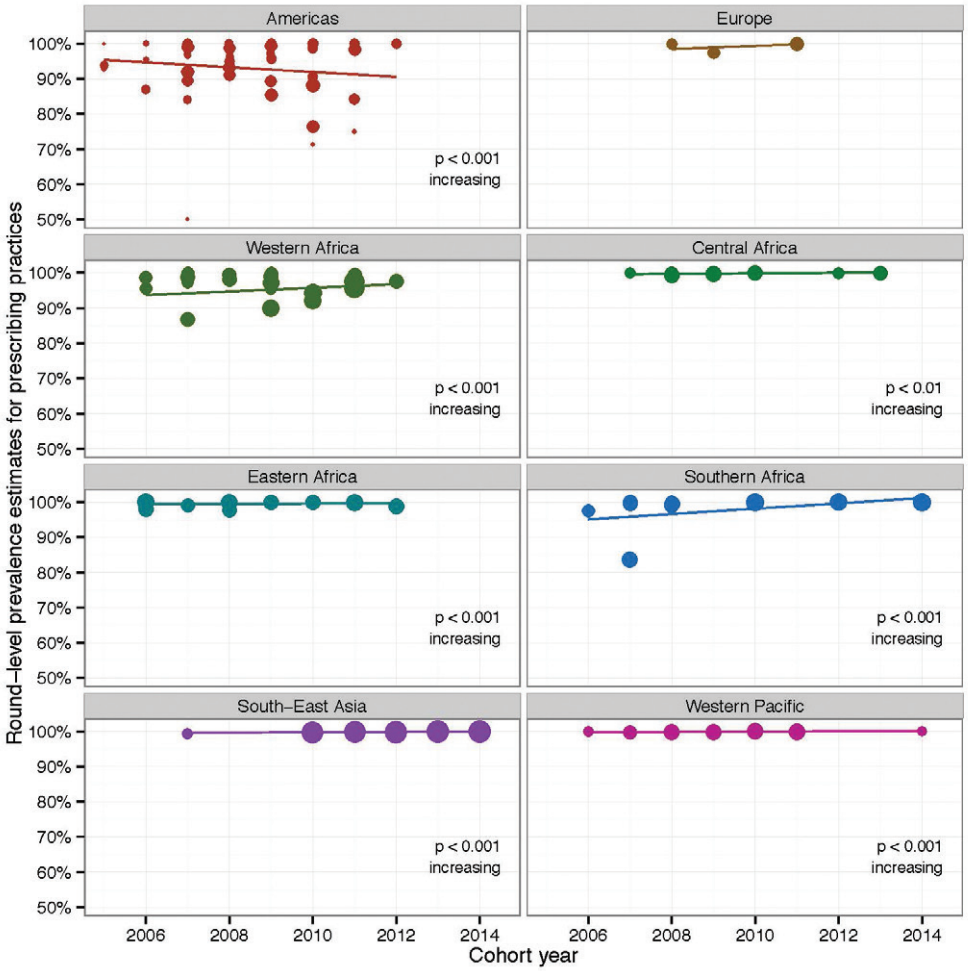
Fig. 3. ART prescribing practices – global time trends, 2005–2014



Each dot represents the round-level prevalence estimate for this EWI. The size of the dots is proportional to the log of the total number of patients monitored, and the colour reflects the region. Results from statistical testing are reported for all regions combined, including the statistical significance and the direction of the temporal trend.

Region-specific trends in ART prescribing practices over time are shown in **Fig. 4**.

Fig. 4. ART prescribing practices – regional time trends, 2005–2014



Each dot represents the round-level prevalence estimate for this EWI. The size of the dots is proportional to the log of the total number of patients monitored. Results from statistical testing are reported for each region, including the statistical significance and the direction of the temporal trend.

When assessing time trends within regions, only regions reporting data from at least three different countries, and with two or more rounds reported per country, were tested.

Time trends in most regions are of limited impact, because levels of appropriate ART prescribing are consistently high. Greater variability is observed in the Americas, Western Africa and, to a lesser extent, Southern Africa. Appropriate prescribing is either stable or increasing over time in all regions.[1] Amongst the clinics reporting in the Americas, the lower average of appropriate performance in ART prescribing is unlikely due to the prescribing of mono- or dual-therapy; rather, there are several possible explanations. In specific cases, prescribing may have been due to an individualized approach to care, whereby prescribers take into account individual patient preference, previous ARV drug exposure, and anticipated toxicities or adverse events. In many cases, PI-based regimens were prescribed at a time when national guidelines recommended the use of an NNRTI in combination with two NRTIs. Although prescription of a PI-based regimen is not a risk factor for the emergence of HIVDR, it does demonstrate suboptimal compliance of prescribers to treatment guidelines.[2]

Globally, suboptimal performance of this indicator is unlikely due to dispensing of mono- or dual-therapy. Indeed, in a sub-analysis of countries specifically monitoring the prescribing of mono- or dual-therapy for the treatment of HIV infection, data from 11 countries (5176 clinics and 946 275 patients) revealed very high levels (99.5% (95% CI: 97.3–99.9%)) of appropriate triple-drug prescribing (two NRTIs in combination with either a boosted PI or an NNRTI).

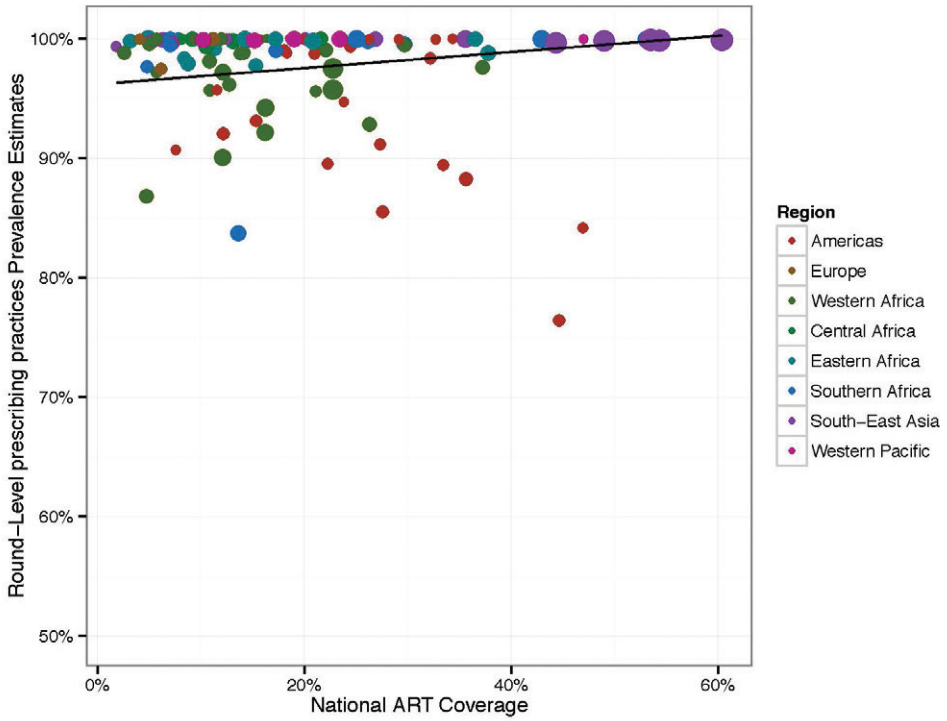
[1] Data from Europe were excluded in trend analyses, because only one European country (Ukraine) reported results for this indicator.
[2] Jack N, Ravasi G, Schrooten W, Sutherland D, Ghidinelli M, Del Riego A. Implementing early-warning indicators of HIV drug resistance in the Caribbean. Clin Infect Dis. 2012;54(Suppl 4):S290–S293.

Programme and economic factors assessed for association with prescribing practices

Clinic size. A comparison of prescribing practices and clinic size demonstrated high levels of appropriate prescribing at large clinics. This is not surprising, as larger clinics may be more likely to be urban and up to date on ART guidelines. The average performance at clinics with more than 1000 ART patients was 99.8%.

ART coverage. When the relationship between national ART coverage and prescribing practices was investigated, a significant positive correlation was observed: countries with higher ART coverage reported higher levels of appropriate prescribing ($p<0.05$) (see **Fig. 5**). However, no association was observed between prescribing practices and rate of expansion of ART coverage ($p>0.1$), suggesting that countries undergoing rapid increases in ART coverage between consecutive EWI monitoring rounds did not experience significantly different outcomes from countries with little or no change in ART coverage over the same period of time.

Fig. 5. ART prescribing practices compared to levels of ART coverage



Each dot represents the round-level prevalence estimate for this EWI. The size of the dots is proportional to the log of the total number of patients monitored, and the colour reflects the region.

Gross national income. Finally, when compared to gross national income in current United States dollars, no statistically significant relationship between prescribing practices and income ($p>0.1$) was observed. This suggests that countries at the lowest income levels are able to maintain high levels of appropriate prescribing.

In summary, appropriate prescribing to minimize the unnecessary emergence of HIVDR is the basis of successful ART treatment outcomes. Global results demonstrate that ART programmes in even the most resource-limited countries can achieve and maintain very high levels of appropriate prescribing – **a finding that is likely due to the use of some of the key principles of the public health approach: standardized treatment protocols and simplified fixed-dose combinations**.

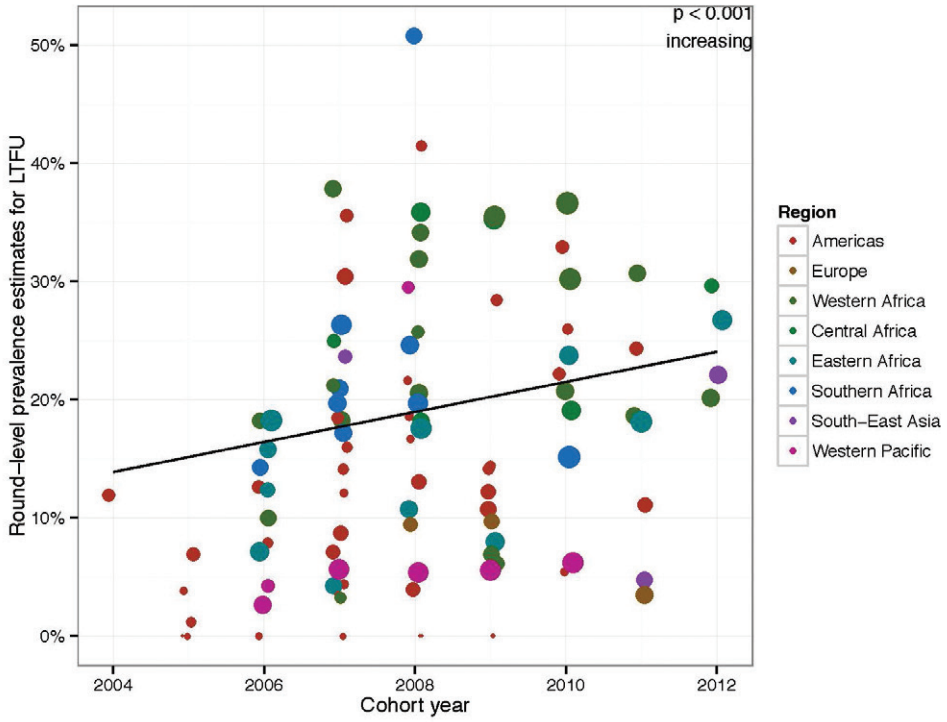
LTFU at 12 months

KEY FINDINGS

Countries:	48
ART clinics:	1837
Patients:	169 233
Period:	2004–2012
Finding:	20% (95% CI: 14.1%–27.5%) of patients were LTFU from care 12 months after treatment initiation, a result exceeding the WHO-recommended target of 15%.
Global trend:	LTFU increased over time globally; p<0.001.

Estimating clinic LTFU, understanding its local determinants and taking steps to accurately classify unknown outcomes maximizes retention on ART, and minimizes treatment interruptions and the emergence of preventable HIVDR. Moreover, accurate classification of unknown treatment outcomes minimizes generation of potentially biased retention estimates, which could misdirect resources at the clinic and national levels if not properly accounted for. Global trends in LTFU amongst the clinics reporting are shown in **Fig. 6**.

Fig. 6. LTFU – global time trends, 2004–2012



Each dot represents the round-level prevalence estimate for this EWI. The size of the dots is proportional to the log of the total number of patients monitored, and the colour reflects the region. Results from statistical testing are reported for all regions combined, including the statistical significance and the direction of the temporal trend.

When assessing time trends within regions, only regions reporting data from at least three different countries, and with two or more rounds reported per country, were tested.

The prevalence of LTFU amongst the countries reporting by region is shown in **Table 4**. The Western Pacific had the lowest reported level at 5.7% (95% CI: 3.9–8.3%), followed by Europe at 5.9% (95% CI: 4.1–8.6%). LTFU in the Region of the Americas was 15.7% overall (95% CI: 11.1–21.6%), while in South-East Asia it was 16.3% (95% CI: 7.4–32.4%), although only two countries reported from this region. Overall levels of LTFU in EWI surveys were high in Africa, with estimates of 29.9% (95% CI: 20.6–41.3%), 29.6% (95% CI: 18.6–43.7%), 16.8% (95% CI: 11.5–24.0%), and 20.1% (95% CI: 13.0–29.8%) for Western Africa, Central Africa, Eastern Africa and Southern Africa, respectively.

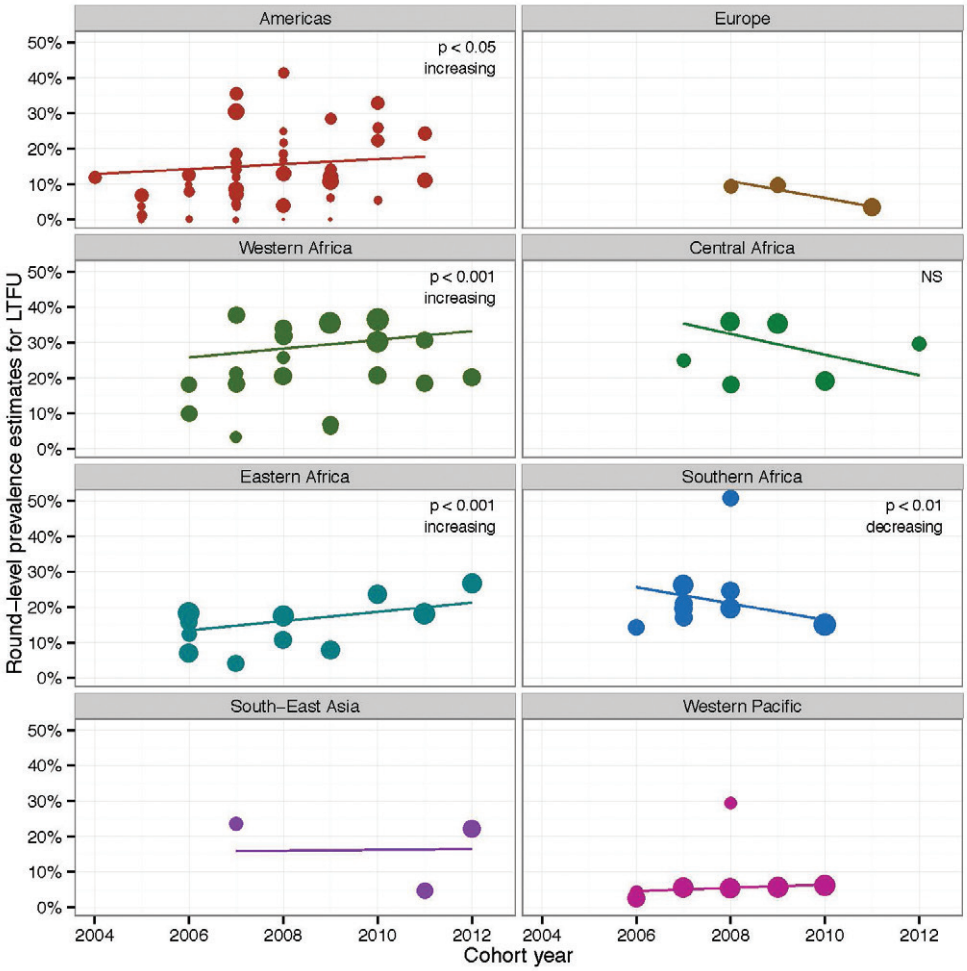
Table 4. Percentage of patients LTFU 12 months after ART initiation by region, 2004–2012[1]

Region	No. of countries reporting data	No. of clinics	No. of records	% of patients LTFU (mean)	95% confidence interval
Americas	18	108	8 742	15.7%	11.1–21.6%
Europe	1	33	2 651	5.9%	4.1–8.6%
Western Africa	9	574	45 811	29.9%	20.6–41.3%
Central Africa	3	208	12 853	29.6%	18.6–43.7%
Eastern Africa	7	411	41 444	16.8%	11.5–24.0%
Southern Africa	5	215	29 295	20.1%	13.0–29.8%
South-East Asia	2	51	3 002	16.3%	7.4–32.4%
Western Pacific	3	237	25 435	5.7%	3.9–8.3%
Total	**48**	**1 837**	**169 233**	**20.0%**	**14.1–27.5%**

[1] LTFU was dropped as an EWI of HIVDR in 2011 in favour of assessing retention at 12 months.

Regional trends of LTFU over time are presented in **Fig. 7**.

Fig. 7. LTFU – regional time trends, 2004–2012



Each dot represents the round-level prevalence estimate for this EWI. The size of the dots is proportional to the log of the total number of patients monitored. Results from statistical testing are reported for each region, including the statistical significance and the direction of the temporal trend. NS – not significant; p >0.05.

When assessing time trends within regions, only regions reporting data from at least three different countries, and with two or more rounds reported per country, were tested.

Between 2004 and 2012, LTFU increased in the Americas amongst the clinics reporting, although there was considerable between-country heterogeneity. Amongst clinics reporting EWIs in Western Africa, LTFU increased between 2006 and 2012 ($p<0.001$). Over the same period, LTFU also increased amongst clinics reporting in Eastern Africa ($p<0.001$). Levels in Central Africa remained stable between 2007 and 2012, while in Southern Africa LTFU decreased between 2006 and 2010 ($p<0.01$). Testing for regional trends was not performed in Europe, South-East Asia and the Western Pacific due to limited data. A sub-analysis assessing regional time trends, which was restricted to countries reporting data from at least three rounds, corroborates the general finding that LTFU increased over time amongst countries reporting EWI data ($p<0.001$).

Reasons for increasing levels of LTFU at 12 months over time are variable and may include: deterioration of programme capacity to retain increasing numbers of patients on ART; weak record-keeping systems; inadequate or inaccessible death registries; and insufficient or underfunded staff to manage data or trace patients to correctly differentiate between deaths, true defaults from care, and transfers of care to other clinics (with or without records). It is not believed that the increase in LTFU observed in this analysis is attributable to statistical bias, a phenomenon described in a recent simulation study.[1] This is because outcomes are measured cross-sectionally, and patients with transient gaps in treatment do not re-enter the cohort. The observation could also be due to different countries and clinics reporting data over time.

[1] Johnson LF, Estill J, Keiser O, Cornell M, Moolla H, Schomaker M et al. Do increasing rates of loss to follow-up in antiretroviral treatment programs imply deteriorating patient retention? Am J Epidemiol. 2014;180(12):1208–12. doi: 10.1093/aje/kwu295.

Programme and economic factors assessed for association with LTFU

Clinic size. Significantly lower LTFU was observed amongst medium-sized clinics (250–1000 patients on ART), when compared to smaller clinics ($p<0.001$) and larger clinics ($p<0.001$). Most observations were from the African region. As the size of a clinic's population increases, available resources may become strained; likewise, clinics with fewer patients on ART may lack the needed human or financial resources to trace and re-engage defaulters back into care. A similar relationship between clinic size and retention at 12 months was noted, as described in **Box 1**.

ART coverage. No relationship was observed between levels of LTFU and change in national ART coverage across EWI rounds repeated in the same country. This observation suggests that even with rapid scale-up of ART, programmes can manage to keep levels of LTFU relatively steady. Other programme factors are therefore likely to explain the observed global increase in LTFU.

Gross national income. Significant heterogeneity in round-level prevalence estimates at all income levels was observed. There was no evidence of a relationship between gross national income per capita and LTFU ($p>0.1$).

Increasing global estimates of LTFU are concerning, and may signal strain on the health sector as access to ART is rapidly expanded. Minimizing LTFU will maximize population-level retention on ART, thereby maximizing long-term reductions in AIDS-related morbidity and mortality.

Retention on ART at 12 months

KEY FINDINGS

Countries: 50

ART clinics: 7062

Patients: 368 364

Period: 2004–2014

Finding: 73.5% (95% CI: 66.5–79.6%) of individuals were retained in care 12 months after initiating ART, a result that falls short of the WHO-suggested retention target of over 85% at 12 months.

Global trend: Variability observed in retention estimates over time and across regions does not permit assessment for trends over time.

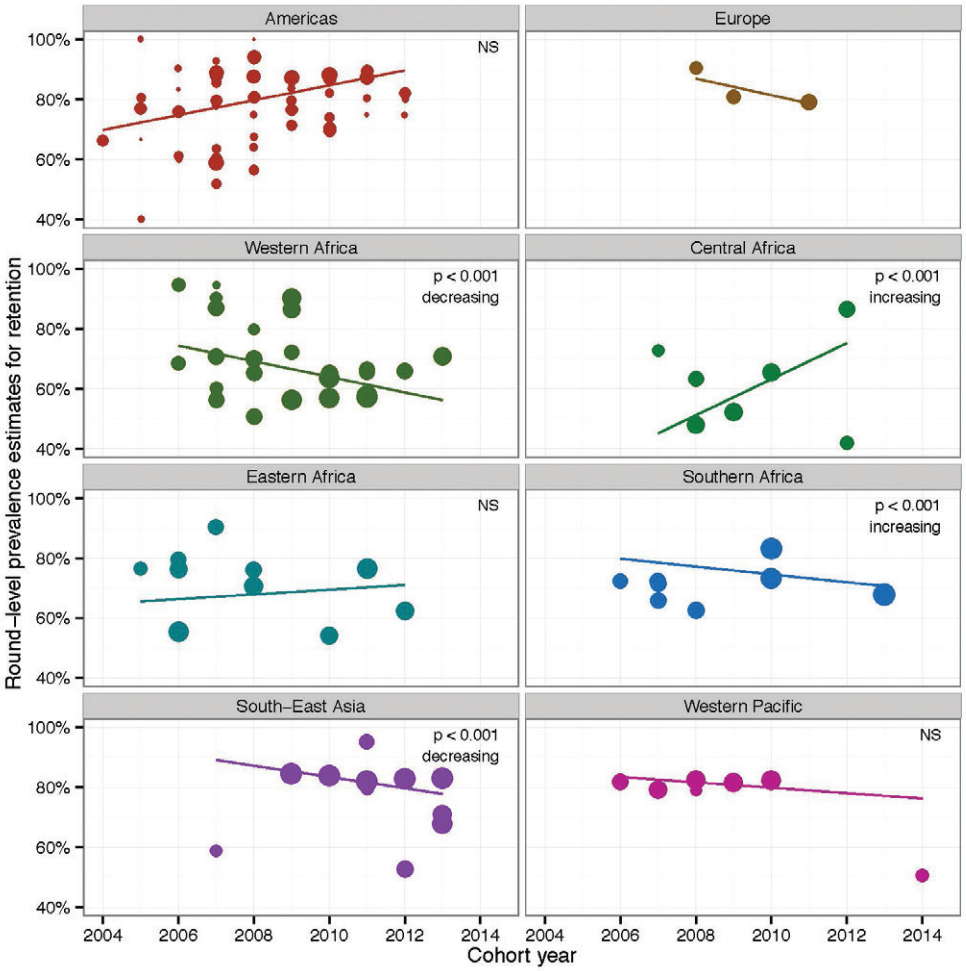
High levels of retention on ART are critical to the long-term success of global ART scale-up. Important regional variations were noted (see **Table 5**), with lower retention observed amongst clinics reporting EWI data in the African Region (67.6% (95% CI: 60.7–73.8%)) when compared to all other regions combined (81.0% (95% CI: 77.3–84.3%)). Within Africa, the lowest level of retention was noted in Central Africa, with an average of 59.1% (95% CI: 48.3–69.0%) of patients retained on ART at 12 months amongst the EWI surveys reported. No individual region had an average retention that exceeded the WHO-suggested target of 85%.

Table 5. Percentage of patients retained in care 12 months after ART initiation by region, 2004–2014

Region	No. of countries reporting data	No. of clinics	No. of records	% of patients retained in care 12 months after ART initiation (mean)	95% confidence interval
Americas	18	133	10 948	80.9%	74.0–86.3%
Europe	1	33	2 651	81.3%	74.5–86.6%
Western Africa	9	1 055	86 645	64.3%	54.5–73.0%
Central Africa	3	221	14 826	59.1%	48.3–69.0%
Eastern Africa	6	355	38 481	68.3%	55.8–78.6%
Southern Africa	5	332	65 533	73.5%	62.0–82.5%
South-East Asia	5	4 695	123 860	81.0%	72.2–87.5%
Western Pacific	3	238	25 420	81.2%	74.1–86.6%
Total	**50**	**7 062**	**368 364**	**73.5%**	**66.5–79.6%**

Regional trends in retention over time are shown in **Fig. 8**. Considerable variability observed in retention estimates over time and across regions does not permit assessment for global trends in retention over time. However, global results are broadly consistent with a recent large meta-analysis assessing more than 1 million records, which observed 78% retention at 12 months.[1]

Fig. 8. Retention on ART at 12 months – regional time trends, 2004–2014



Each dot represents the round-level prevalence estimate for this EWI. The size of the dots is proportional to the log of the total number of patients monitored. Results from statistical testing are reported for each region, including the statistical significance and the direction of the temporal trend. NS – not significant; p >0.05.

When assessing time trends within regions, only regions reporting data from at least three different countries, and with two or more rounds reported per country, were tested.

Programme and economic factors assessed for association with retention

ART coverage. A positive relationship was observed between retention and ART coverage, with countries with higher proportions of HIV-infected individuals on ART experiencing higher retention at 12 months ($p<0.001$). While countries able to provide higher ART coverage may be better equipped in other ways to retain patients, thereby driving this association, there is concern that rapid expansion of ART may lead to a decline in programme quality. In a sub-analysis measuring retention and restricted to countries with multiple rounds, a positive relationship was observed between change in ART coverage and change in retention ($p<0.05$), suggesting that countries expanding faster have greater improvements in retention.

Gross national income. On univariate analysis, retention is positively correlated with gross national income per capita ($p<0.001$). On average, countries with higher gross national incomes reported higher levels of retention. This correlation is likely driven by higher levels of ART coverage in upper-middle- and high-income countries, as the relationship between gross national income and retention does not persist after adjusting for ART coverage ($p>0.1$). This finding is consistent with the absence of a correlation between LTFU and gross national income. The finding is not surprising given that ART is available free of charge in most countries; therefore, measures of individual wealth (such as income per capita) may be expected to have limited impact on ART uptake. ART coverage is therefore likely a proxy for system capacity. For example, in earlier reporting years, countries that had high ART coverage (e.g. the Americas) all had considerably stronger health systems compared to countries with low coverage.

[1] Fox MP, Rosen SJ. Retention of adult patients on antiretroviral therapy in low- and middle-income countries: systematic review and meta-analysis 2008-2013. J Acquir Immune Defic Syndr. 2015;69(1):98–108.

Clinic size. When estimates of retention are assessed with corresponding clinic size, medium-sized clinics appear to have superior retention compared to very small and very large clinics. This finding is particularly apparent in the South-East Asia Region (**Box 1**).

Box 1. Retention and relationship to clinic size in South-East Asia

Retention of patients in care 12 months after ART initiation is a critical marker of ART clinic and programme success. As access to ART expands, an ever larger number of patients will initiate and be maintained on ART. Inevitably, during this process, some clinics will grow in size, while others will become smaller through decentralization. Four countries provided data on ART clinic size from the South-East Asia Region: India, Myanmar, Nepal and Thailand. The majority of the clinics were from Thailand. Results within Thailand suggest that ART clinics smaller than 250 patients and larger than 1000 patients receiving ART report significantly poorer retention than clinics within these bounds ($p<0.001$ for both bounds). Although fewer clinics reported data, this pattern was replicated in Myanmar, but not in India and Nepal. As the size of clinic populations increase, available resources may become overstretched leading to a drop off in retention. Likewise, clinics with fewer patients on ART may lack the necessary human or financial resources to actively trace and re-engage defaulters back into care.

In summary, available data for this report suggest varying trends in retention across clinics within regions, with a lack of any clear global trend. Observations may be due to selected countries and clinics reporting data; nonetheless, many ART clinics are falling well below the WHO-suggested target of over 85% of patients retained on ART at 12 months.

As ART programmes expand, improving retention on ART at 12 months, and indeed in the long term, is critical, as many countries have only one second-line regimen and very limited (if any) salvage regimens. LTFU accounts for the majority of all attrition, thus retention cannot be improved without significant strengthening of defaulter tracing, death registries and record-keeping systems (as described previously), combined with a reduction in mortality amongst patients on ART. The ability to trace defaulters is crucial to ensuring uninterrupted treatment of HIV infection, and will become increasingly important as "Treat All" is scaled up. However, many clinics lack the financial or human resources for tracing, and for robust and sustainable mechanisms to link patients back into treatment.

On-time pill pick-up

KEY FINDINGS

Countries: 9
ART clinics: 5027
Patients: 492 145
Period: 2010–2014
Finding: 85.5% (95% CI: 72.1–93.1%) of pill pick-ups were on time, falling short of the WHO goal of over 90% of patients picking up pills on time, i.e. within two days of the run-out date if taken according to schedule.
Global trend: Due to limited data, no assessment for global trends over time was performed.

On-time pill pick-up is an objective measure of population adherence to ART and is associated with LTFU, virological failure, HIVDR and increased mortality. Region-specific prevalence estimates of on-time pill pick-up are shown in **Table 6**. Data are heavily weighted to the South-East Asia Region.

Table 6. On-time pill pick-up by region, 2010–2014

Region	No. of countries reporting data	No. of clinics	No. of records	EWI mean	95% confidence interval
Africa	4	438	132 688	69.9%	55.0–81.1%
South-East Asia	4	4 588	359 315	91.4%	84.9–95.2%
Western Pacific	1	1	142	70.4%	56.0–81.7%
Total	**9**	**5 027**	**492 145**	**85.5%**	**72.1–93.1%**

This analysis presents the revised 2011 cross-sectional definition of the indicator, and assesses on-time pill pick-up amongst patients on ART regardless of treatment duration or regimen line. "On time" is defined as pills picked up within two days of the run-out date, if taken according to schedule. Africa is combined into a single region due to paucity of data (1 country in Western Africa, 1 country in Central Africa, and 2 countries in Southern Africa).

Amongst the clinics reporting data in the South-East Asia Region, 91.4% (95% CI: 84.9–95.2%) of pill pick-ups were on time, exceeding the WHO-recommended target of over 90%. Amongst countries reporting data in the African Region, however, only 69.9% (95% CI: 55.0–81.1%) of pill pick-ups were on time, falling short of the WHO-recommended target. In other regions (excluding Africa), 90.7% (95% CI: 88.9–92.3%) of pill pick-ups were on time. These findings suggest that the clinics reporting data in Asia have succeeded in minimizing barriers to adherence; while in Africa, greater attention to adherence support is required.

As illustrated in **Box 2**, on-time pill pick-up is correlated with clinic-level viral load suppression, as exemplified by data from Thailand.

Box 2. Illustration of correlation between clinic-level on-time pill pick-up and viral load suppression

High levels of viral load suppression (HIVDR prevention) are a goal of every ART programme. Thailand is a country in South-East Asia with 240 088 people receiving ART as of September 2013; this represents 80.1% of those eligible for treatment (CD4 $\leq$ 350cells/mm^3).

National guidelines recommend viral load testing of all patients six months after initiating ART and annually thereafter[1]. Overall, for cohorts spanning 2010 to 2014, high levels of adherence as measured by on-time pill pick-up were observed in Thailand. During the reporting period, 89.9% of all pill pick-ups were on time, using the revised 2011 on-time pill pick-up EWI. Approximately one third (34%) of clinics did not achieve the 90% target of patients picking up ART on time (within two days of the run-out date, if taken according to schedule). **Of all the EWIs reported in Thailand (ART prescribing practices, retention, and on-time pill pick-up), on-time pill pick-up was found to be the strongest predictor of clinic-level viral load suppression ($p<0.001$), after adjusting for cohort year and clinic size**. Clinic-level prescribing practices and retention were not significantly predictive ($p>0.1$). As routine individual patient-level viral load testing is not available in all settings, this observation suggests that identifying clinics with less-than-desirable pill pick-up, then targeting their patient populations for adherence interventions, may lead to improvements in overall population-level viral load suppression, and therefore improved health outcomes.

When assessing 87 153 records from 833 clinics in 29 countries, where a more conservative pre-2011 definition of on-time pill pick-up[2] was used, 52.5% (95% CI: 36.8–67.7%) of individuals picked up ART on time between 2006 and 2013. More details are available in the *Epidemiological methods* section of the **Annex**.

On-time pill pick-up is an important proxy measure of population adherence to ART. Maintaining high levels of adherence to ART is essential for sustained long-term virological suppression and prevention of HIVDR.

Programme and economic factors assessed for association with on-time pill pick-up

Due to marked heterogeneity of data, programme and economic factors were not assessed for association with on-time pill pick-up.

[1] National guidelines on HIV/AIDS diagnosis and treatment. Bangkok: Bureau of AIDS, TB and STIs (BATS); 2010.

[2] Prior to 2011, "on time" was defined as a pill pick-up that occurred on or before the pills ran out if taken according to schedule. No grace period was allowed, and patient buffer supply was not considered. After 2011, a pill pick-up was considered "on time" if medication was picked up within two days of the run-out date, if taken according to schedule, and buffer supply (if known) was considered.

On-time appointment keeping

KEY FINDINGS

Countries: 19

ART clinics: 1388

Patients: 113 957

Period: 2006–2012

Finding: 60.3% (95% CI: 40.4–77.2%) of individuals attended scheduled appointments on time (within seven days of a scheduled appointment), a result falling short of WHO's suggested target of over 80%.

Global trend: On-time appointment keeping was one of the least frequently reported EWIs, thus global and regional trends are not reported.

On-time clinical appointment keeping has been correlated with other measures of ART adherence.[1,2] Amongst clinics reporting, on-time appointment keeping in the African Region was 49.8% (95% CI: 35.5–64.1%) versus 86.0% (95% CI: 83.9–87.9%) for all other regions combined. Notably, performance in Southern Africa was 81.3% (95% CI: 66.8–90.4%), considerably higher than in the other African subregions. The average in Western Africa was 40.7% (95% CI: 24.2–59.7%), in Central Africa was 54.8% (95% CI: 36.4–71.9%), and in Eastern Africa was 50.4% (95% CI: 23.6–77.0%). The highest averages for on-time appointment keeping were observed in Europe, the Western Pacific and South-East Asia, at 89.2% (95% CI: 79.7–94.6%), 86.5% (95% CI: 75.0–93.2%) and 83.5% (95% CI: 70.5–91.5%), respectively. Moderate performance was observed in the Americas, with an average of 70.1% (95% CI: 52.5–83.2%) (see **Table 7**).

Table 7. On-time appointment keeping by region, 2006–2012[1]

Region	No. of countries reporting data	No. of clinics	No. of records	EWI mean	95% confidence interval
Americas	4	21	1 080	70.1%	52.5–83.2%
Europe	1	33	2 651	89.2%	79.7–94.6%
Western Africa	4	579	41 303	40.7%	24.2–59.7%
Central Africa	1	133	4 208	54.8%	36.4–71.9%
Eastern Africa	4	243	24 786	50.4%	23.6–77.0%
Southern Africa	2	73	10 813	81.3%	66.8–90.4%
South-East Asia	1	32	2 135	83.5%	70.5–91.5%
Western Pacific	2	274	26 981	86.5%	75.0–93.2%
Total	**19**	**1 388**	**113 957**	**60.3%**	**40.4–77.2%**

[1] On-time appointment keeping was dropped as an EWI of HIVDR in 2011 in favour of on-time pill pick-up.

Significant heterogeneity across countries was observed at all time points. On-time appointment keeping was one of the least frequently reported EWIs, thus global and regional trends are not reported.

Programme and economic factors assessed for association with on-time appointment keeping

Due to heterogeneity of data, it was not possible to test for association between on-time appointment keeping and clinic and programme factors.

[1] Chalker JC, Andualem T, Gitau LN, Nitaganira J, Obua C, Tadeg H et al. Measuring adherence to antiretroviral treatment in resource-poor settings: the feasibility of collecting routine data for key indicators. BMC Health Serv Res. 2010;10:43. doi: 10.1186/1472-6963-10-43.

[2] White YR, Pierre RB, Steel-Duncan J, Palmer P, Evans-Gilbert T, Moore J et al. Adherence to antiretroviral drug therapy in children with HIV/AIDS in Jamaica. West Indian Med J. 2008;57(3):231–7.

Drug stock outs

KEY FINDINGS

Countries:	35*
ART clinics:	1703*
Period:	2005–2014
Finding:	35.7% of clinics had at least one stock out during their respective reporting year, a result falling below the WHO target of 0% of months with a stock out during a 12-month reporting period.
Time trend analysis:	Considerable variability observed in estimates of drug stock outs over time and across regions does not allow for estimation of global trends over time.

* Includes 553 clinics in 5 countries reporting aggregate-level data only.

Procurement of ARV drugs and robust supply chain management within countries are critical to maintaining populations on ART. Globally, amongst 1703 clinics monitored, there is considerable variability in the frequency of stock outs for routinely dispensed ARV drugs.

On average, clinics experiencing drug stock outs reported two stock-out episodes in different months within a year; each episode lasted one or more days. Restricting analysis to clinics that reported detailed level data, 67.9% (781/1150) of clinics experienced no drug stock outs, while 5.3% (61/1150) of clinics observed a stock out of at least one day during each of the 12 months during the reporting period.

Table 8. Drug stock outs by region, 2005–2014

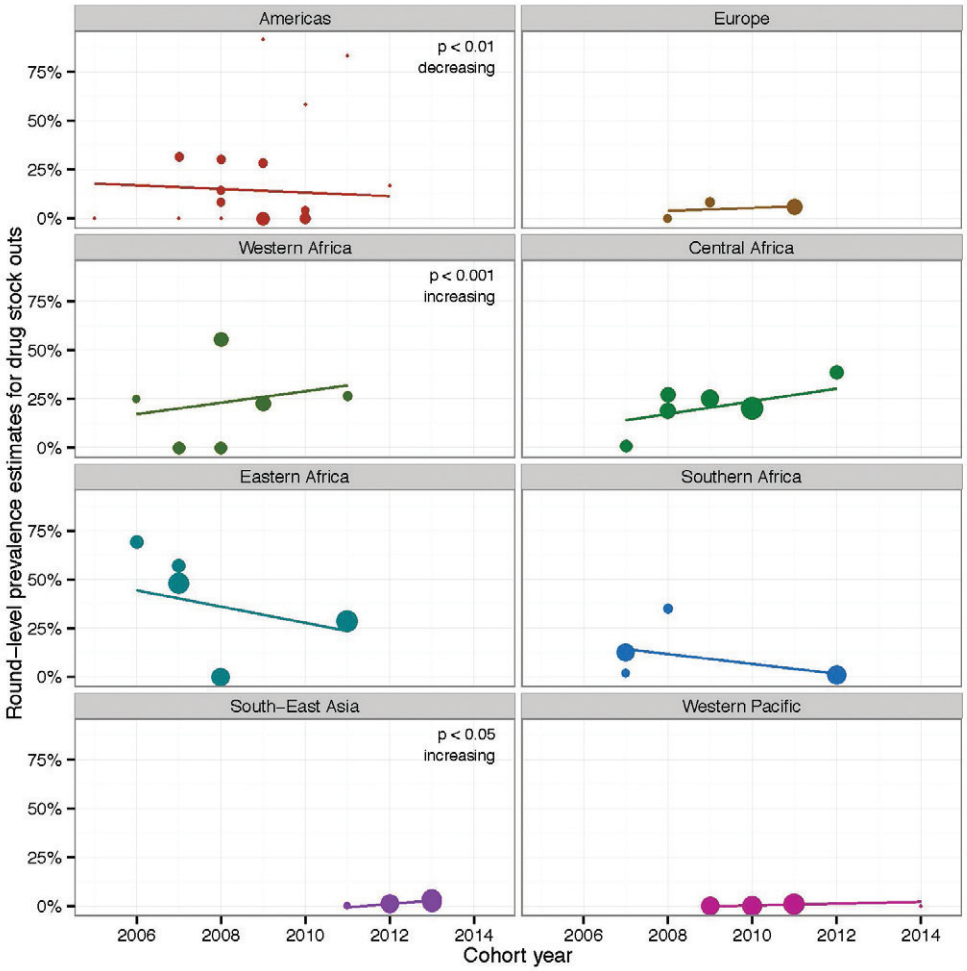
Region	No. of countries reporting data	No. of clinics	EWI mean[1]	95% confidence interval
Americas	9	56	14.3%	5.3–33.3%
Europe	1	33	5.6%	1.9–14.9%
Western Africa	4	76	23.9%	6.0–60.9%
Central Africa	2	215	21.9%	8.5–46.0%
Eastern Africa	3	268	33.1%	11.9–64.4%
Southern Africa	4	98	7.7%	1.7–29.2%
South-East Asia	4	182	2.1%	0.6–6.9%
Western Pacific	3	222	0.4%	0.1–1.2%
Total	**30**	**1 150**	**14.8%**	**7.2–28.0%**

[1] % months with stock out of any routinely dispensed ARV drug.

ARV drug stock outs were more frequently observed amongst clinics reporting in Eastern and Western Africa, averaging 33.1% (95% CI: 11.9–64.4%) and 23.9% (95% CI: 6.0–60.9%) of months in a year with at least one stock out, respectively. Reported stock outs were higher in Africa (all subregions combined) compared to all other global regions – specifically, 24.2% (95% CI: 9.4–49.6%) compared to 2.9% (95% CI: 1.2–7.3%) of months in a year with at least one stock out. Low levels of stock outs were reported from clinics monitored in South-East Asia and the Western Pacific, averaging 2.1% (95% CI: 0.6–6.9%) and 0.4% (95% CI: 0.1–1.2%) of months in a year with at least one stock out, respectively (see **Table 8**).

Regional time trends of ARV drug stock outs are presented in **Fig. 9**.

Fig. 9. Drug stock outs – regional time trends, 2005–2014



Each dot represents the round-level prevalence estimate for this EWI. Results from statistical testing are reported for each region, including the statistical significance and the direction of the temporal trend.

When assessing time trends within regions, only regions reporting data from at least three different countries, and with two or more rounds reported per country, were tested.

In the Americas, there was an overall decrease in stock outs ($p<0.01$) amongst clinics reporting data, despite some countries having high levels of stock outs (e.g. as high as 11/12 months in one country). Western Africa and South-East Asia observed an increase in stock outs over time ($p<0.001$ and $p<0.05$, respectively) amongst clinics reporting data. The considerable variability observed in estimates of drug stock outs over time and across regions does not allow for assessment of global changes in this indicator over time.

Programme and economic factors assessed for association with drug stock outs

ART coverage. No relationship was observed between the speed with which ART coverage expanded and reported ARV drug stock outs within countries ($p>0.1$), suggesting that rapid expansion of ART is not associated with an increase in frequency of stock outs.

Gross national income. A statistically significant relationship was observed between drug stock outs and gross national income per capita in current US dollars, with higher-income countries experiencing less frequent stock outs ($p<0.05$). After adjusting for cohort year, this relationship reduces to a non-significant trend ($p<0.1$).

On-time appointment keeping. When associations between clinic-level on-time appointment keeping and drug stock outs are explored, higher levels of appointment keeping are observed at clinics with fewer or no drug stock outs, compared to clinics with more frequent stock outs ($p<0.001$). This relationship persists even after adjusting for regional differences. Among clinics with no stock outs, 38.6% met the target of over 90% of appointments on time; by contrast, among clinics with at least one stock out during the reporting period, only 15.9% met the on-time appointment keeping target; finally, among clinics with stock outs in at least six of the 12 months during the reporting period, only 11.1% met the on-time appointment keeping target.

Retention. Similar relationships were observed between stock outs and retention on ART at 12 months ($p<0.001$), and stock outs and on-time pill pick-up ($p<0.001$). It may be that clinics with fewer stock outs have more resources and are better equipped to support adherence than clinics with more stock outs. Although adherence is generally recognized as reflecting patient behaviour with regard to drug pick-up, this behaviour needs to be understood within the broader programmatic context, i.e. that adherence can be influenced by external factors. Notably, drug stock outs have been identified as determinants of non-adherence in Nigeria[1] and India,[2] and have been shown to be associated with a doubled risk of interruption in care and even death in Côte d'Ivoire.[3] These findings may signify that at clinics with more frequent ARV drug stock outs, people become discouraged and do not return to the clinic on time.

Clinic size. No association was observed between drug stock outs and clinic size ($p>0.05$).

In summary, considerable variability of drug stock outs was reported across regions, and the overall extent to which stock outs of routinely used ARV drugs were reported is worrisome. Although the WHO drug stock out indicator does not capture patient-level treatment interruptions, substitutions, or switches of ARV drugs due to stock outs, it should be emphasized that a stock out of any routinely dispensed ARV drug has the potential to significantly impact patient and population-level outcomes.

Viral load suppression and viral load completion

High levels of sustained population HIV viral load suppression are critical to achieving the WHO/UNAIDS 90-90-90 target by 2020 and the elimination of AIDS as a public health threat by 2030. Viral load suppression was monitored in 18.8% of all EWI rounds by 13 countries: Antigua and Barbuda (2010–2012), Barbados (2009), Colombia (2009), Dominica (2010–2012), Ecuador (2009–2010), El Salvador (2007–2008), Mali (2009), Nicaragua (2009–2010), Niger (2008), Papua New Guinea (2015), South Africa (2013), Suriname (2009–2012), and Thailand (2009–2014). Its low uptake likely reflects the limited availability of routine viral load testing during the period monitored. For this reason, global and regional estimates of viral load suppression and viral load completion are not presented. However, in South Africa and Thailand, relatively high levels of viral load suppression were observed amongst patients receiving viral load testing, with variable success in achieving high levels of viral load testing completion (**see Box 3**).

Box 3. Viral load suppression and viral load completion in Thailand and South Africa

Thai national ART guidelines[4] recommend viral load testing of all patients six months after initiating ART and annually thereafter. If viral load test results show more than 50 copies/ml, guidelines stipulate intensive adherence counselling with a follow-up viral load test after three months. In Thailand, the proportion of clinics achieving the target of over 90% for viral load suppression remained stable from 78.0% (638 of 818 clinics) in 2009 to 74.7% (646 of 865 clinics) in 2013. In all years, high levels of viral load suppression were reported amongst those alive and on ART 12 months after treatment initiation: in 2009 viral load suppression was 93.9% (95% CI: 93.4–94.3%); in 2010 it was 94.6% (95% CI: 94.1–95.0%); in 2011 it was 94.7% (95% CI: 94.3–95.1%); in 2012 it was 93.3% (95% CI: 92.9–93.7%); and in 2013 it was 93.6% (95% CI: 93.2–94.0%).[5,6] Coverage of viral load testing increased during the same period, from 53.8% in 2009 to 79.8% in 2013 ($p<0.001$).

South Africa, one of three African countries to report viral load suppression, monitored this indicator at 115 clinics distributed amongst two provinces participating in EWI monitoring during 2013-1014. Overall, viral load done and recorded was 44.5%; that is, just under half of eligible patients received viral load testing and had a result available in a provider accessible record at the clinic level. Of clinics monitored, 21.6% reported completion of viral load testing for over 70% of eligible patients, while the remaining 78.4% of clinics fell below the WHO-recommended target, with levels of completion below 70%. At 12 months, 80.7% (95% CI: 77.9–83.4%) of patients on ART had a viral load below 1000 copies/ml. Only 10.4% of clinics were classified as achieving the target of over 90% viral load suppression at 12 months, while 54.8% achieved a level of 80–90%, and 34.8% reported levels below 80%.

Success in achieving levels of viral load suppression greater than 90% were documented at clinics in both Thailand and South Africa, suggesting that reaching the target of 90% of people taking ART have suppressed viral load is feasible.

---

[1] Uzochukwu BSC, Onwujekwe OE, Onoka AC, Okoli C, Uguru NP, Chukwuogo OI. Determinants of non-adherence to subsidized anti-retroviral treatment in southeast Nigeria. Health Policy Plan. 2009;24(3):189–96. doi:10.1093/heapol/czp006.

[2] Sarna A, Pujari S, Sengar AK, Garg R, Gupta I, Dam Jv. Adherence to antiretroviral therapy and its determinants amongst HIV patients in India. Indian J Med Res. 2008;127(1):28–36.

[3] Pasquet A, Messou E, Gabillard D, Minga A, Depoulosky A, Deuffic-Burban S et al. Impact of drug stock-outs on death and retention to care among HIV-infected patients on combination antiretroviral therapy in Abidjan, Côte d'Ivoire. PLoS ONE. 2010;5(10):e13414.

[4] National guidelines on HIV/AIDS diagnosis and treatment. Bangkok: Bureau of AIDS, TB and STIs (BATS); 2010.

[5] Percentage of patients receiving ART whose viral load was less than 1000 copies/ml during the first 12 months of ART (latest viral load result during the first 3–12 months of ART).

[6] Lertpiriyasuwat C, Teeraratkul A, Suchonwanich Y et al. Monitoring HIV drug resistance early warning indicators to assess performance of Thailand's antiretroviral treatment program. (Unpublished manuscript)

As countries strive for an AIDS-free generation, it is imperative that viral load testing become the standard of care in LMIC. Increasing viral load monitoring for ART patients will require lowering costs associated with viral load testing and improving access in LMIC. In 2014, UNAIDS launched a global diagnostic access initiative, which challenged the global community to work with manufacturers to provide reasonably priced viral load testing, reducing the price of test kits to as low as US$ 10 per test.[1] More countries and clinics will need to take advantage of this pricing to reach the EWI and 90-90-90 targets.

As viral load testing is scaled up, the timely use and appropriate response based on patient viral load results must be considered. Viral load monitoring provides a means to differentiate care, such that frequency of clinic visits is reduced for patients with viral suppression and increased attention is given to those with virological failure. A reduction in clinic visits based on viral suppression has been shown to make viral load monitoring cost effective.[2] The majority of LMIC are in the early stages of initiating viral load testing as a national monitoring strategy for patients on ART. Numerous health system challenges to viral load scale-up have been encountered, including difficulties with specimen transport, equipment breakdown, personnel shortages, and weak laboratory information management systems and laboratory infrastructure.[3] Solutions to these challenges must urgently be found.

To maximize the impact of increased access to viral load testing, the identification and timely management of patients failing therapy will be critical. These objectives are essential if the 90-90-90 global target is to be attained, and unnecessary HIVDR prevented.

[1] UNAIDS and partners launch initiative to improve HIV diagnostics. Geneva: Joint United Nations Programme on HIV/AIDS; 2014. Available at: http://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2014/september/20140925prviralload.

[2] Working Group on Modelling of Antiretroviral Therapy Monitoring Strategies in Sub-Saharan Africa. Sustainable HIV treatment in Africa through viral-load-informed differentiated care. Nature. 2015;528, S68–S76. doi: 10.1038/nature16046.

[3] Lecher S, Ellenberger D, Kim AA, Fonjungo PN, Agolory S, Borget MY et al. Scale-up of HIV viral load monitoring – seven sub-Saharan African countries. MMWR Morbidity and Mortality Weekly Report. 2015;64(46):1287–90.

AGGREGATE EWI RESULTS BY REGION

In total, 59 countries reported any EWI data; while 15 countries reported national aggregate-level data only for at least one round: Antigua and Barbuda (2009), Bahamas (2007), Botswana (2008–2009), Cambodia (2007, 2008, 2010, 2011), China (2013–2014), Ethiopia (2009), Grenada (2009), Indonesia (2011), Kenya (2011), Malawi (2005–2006), Myanmar (2013), Nigeria (2007), Rwanda (2007), Saint Kitts and Nevis (2008), and Zimbabwe (2008, 2012). These data have therefore been analysed separately. The proportion of all clinics monitoring EWIs achieving or exceeding WHO-suggested targets for desirable performance is presented in **Table 9**.

Table 9. Proportion of clinics monitored achieving target by region (clinic-level and aggregate data from n=59 countries)

Region	Prescribing practices (Target=100%)	LTFU (Target<15%)	Retention (Target>85%)	On-time pill pick-up (Target>90%)	On-time appointment keeping (Target>80%)	Drug stock outs (Target=0%)
Americas	40.8% (152)	67.3% (110)	52.2% (138)	28.0% (50)	40.9% (22)	58.6% (58)
Europe	87.9% (33)	87.9% (33)	48.5% (33)	63.6% (33)	93.9% (33)	72.7% (33)
Western Africa	61.2% (1 608)	20.8% (583)	18.0% (1 055)	7.7% (443)	24.0% (579)	60.0% (85)
Central Africa	96.9% (223)	35.1% (208)	19.0% (221)	3.8% (210)	30.1% (133)	56.3% (215)
Eastern Africa	89.4% (564)	60.6% (561)	26.5% (505)	2.3% (215)	19.0% (290)	60.1% (371)
Southern Africa	88.7% (559)	51.3% (263)	33.3% (526)	17.5% (416)	68.2% (85)	13.2% (17 268)
South-East Asia	85.2% (4 855)	50.8% (63)	51.6% (4 745)	65.3% (4 719)	75.0% (44)	88.4% (232)
Western Pacific	95.5% (6 626)	89.0% (2 948)	82.3% (6 092)	67.2% (3 679)	67.3% (388)	94.9% (336)
Total	**84.6% (11 542)**	**53% (2 219)**	**53.8% (10 765)**	**58.4% (9 765)**	**39.8% (1 574)**	**64.3% (1 703)**

Targets as per Table 1. Values are percentages of clinics meeting target, with number of clinics indicated in parentheses.

Overall, analyses based on this increased data set corroborate the results from the previous sections. Globally, 84.6% of clinics monitored prescribed ART appropriately, following national or international guidelines. Only 53.0% of clinics monitored achieved the target of less than 15% LTFU 12 months after ART initiation, and only 53.8% achieved the target of over 85% retention at 12 months.

Amongst the clinics reporting data, 58.4% achieved the global target of over 90% on-time pill pick-up, while 39.8% of clinics achieved the target of over 80% on-time appointment keeping. Finally, 64.3% of clinics reported one or more drug stock outs.

Based on an assessment of **Table 9**, variability in regional performance is readily apparent. High levels of performance for all EWIs are observed for clinics in the Western Pacific Region. Somewhat lower levels of performance are observed amongst clinics monitored in South-East Asia, Eastern Africa and the Americas. The lowest levels of overall performance for all indicators are observed in Western Africa. Even in the best performing regions, not all clinics achieved the WHO-recommended targets for each indicator, suggesting that even in high-performance regions there is room for programme and clinic improvement. Excluding the Western Pacific Region, clinics in all other regions struggled to minimize LTFU and achieve optimal levels of retention on ART. Levels of adherence, as measured by on-time pill pick-up and on-time appointment keeping, are concerning in Africa. Drug stock outs occur in all regions; however, data suggest that more clinics are having stock outs in Africa compared to other regions.

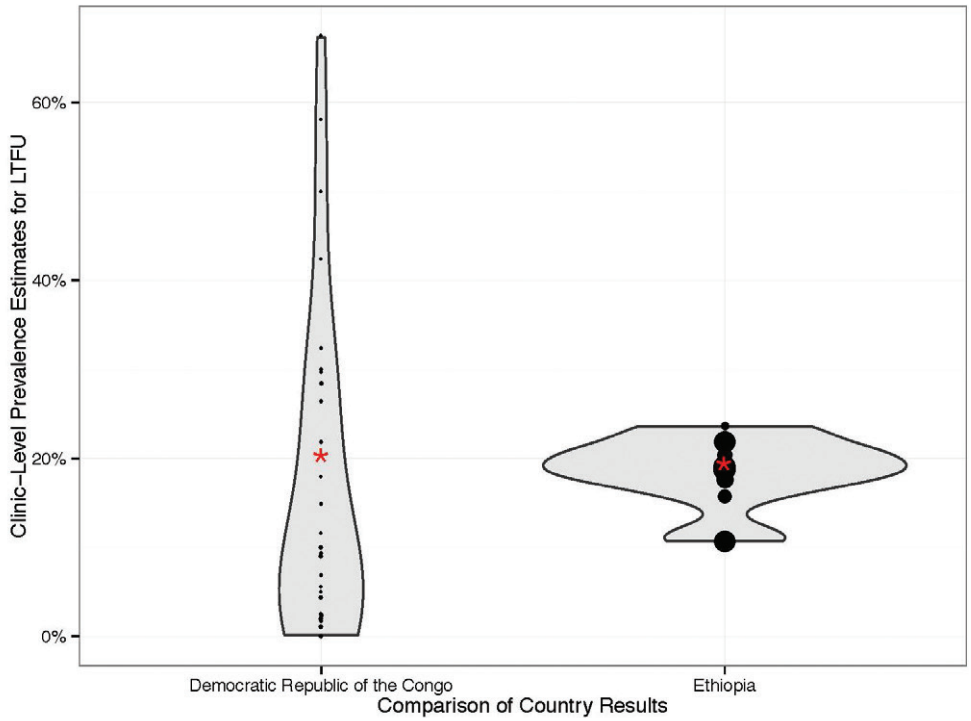
VARIABILITY OF CLINIC PERFORMANCE WITHIN COUNTRIES

National and regional prevalence estimates allow comparison of performance within and between countries, and over time. However, aggregated national prevalence estimates may mask important underlying variability in clinic-level performance. More specifically, national averages do not convey information that is necessary to improve the quality of programme performance. This concept is discussed using country examples.

DRC and Ethiopia: a comparison between country variability of clinic-level LTFU at 12 months

The DRC and Ethiopia monitored LTFU at 12 months in 2010 and 2006, respectively, with similar country-level prevalence estimates. The prevalence of LTFU was 19.1% in the DRC and 18.3% in Ethiopia. The DRC monitored LTFU in 112 clinics (of 344 in the country) with a median of 19 records assessed per clinic (range: 2–114). Ethiopia monitored LTFU in 14 clinics (of 272 in the country) with a median of 665 records assessed per clinic (range: 76–1122). To compare variability in clinic-level performance across these two countries, analysis was restricted to clinics with at least 30 records assessed, because results from clinics with fewer records are more statistically unstable. The range of LTFU amongst clinics monitored in the DRC was 0–67.5%, while in Ethiopia it was 10.7–23.6% (see **Fig. 10**). While the two countries have very similar national averages, Ethiopia has larger clinics that tightly cluster around the mean, while the DRC reports smaller clinics with a wide range of performance.

Fig. 10. Comparison of between country variability of clinic-level LTFU at 12 months



Violin plot showing clinic-level prevalence estimates for LTFU amongst clinics with 30 or more patients monitored. Each clinic is denoted by a dot and the size of the dot corresponds to the number of patients monitored at that clinic. The national average is denoted by the red asterisk. The violin shape is widest where the greatest number of clinics (and patients) are located on the 0–100% scale.

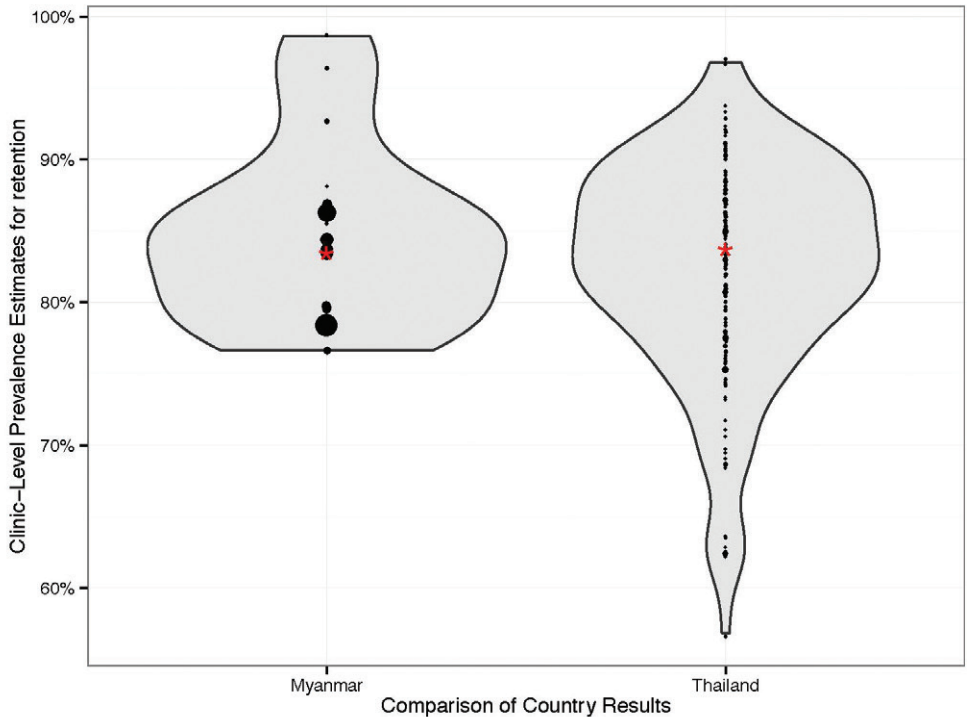
Generally, strong centralized authority may lead to clustering around a mean, while diffuse and decentralized management of health systems may lead to greater variability. The significant intra-country variation of LTFU at 12 months in the DRC may be due to: differences in the way clinics maintain records; the availability or use of death registries; the availability of additional resources for defaulter tracing to maximize retention; and other patient or clinic-level factors. Therefore, an approach based on clinic performance is likely to be most effective, and focusing on

the largest clinics with the lowest performance is a wise use of resources. Specifically, the observed variation in the DRC should prompt clinic-level investigations. Initial qualitative investigations at clinics with high functioning (i.e. low LTFU) and clinics with poor functioning (i.e. high LTFU) are likely to yield valuable information regarding determinants of LTFU, from which lessons can be more broadly applied to other clinics. In some cases, additional operational research or investigation, such as case control or case series, may be useful to clarify the source of problems and identify solutions. Approaches seeking to identify and optimize existing resources and solutions within the ART programme or health planning unit are likely to be both required and beneficial. In Ethiopia, however, because clinic-level retention estimates cluster around the mean, lessons learned from the highest functioning clinics and applied to all clinics may well be highly effective in decreasing LTFU.

Myanmar and Thailand: a comparison between country variability of clinic-level retention at 12 months

A second example compares levels of retention on ART for Myanmar and Thailand in 2012. Myanmar reported retention from 22 clinics (of 103 in the country) with a median of 353 records assessed per clinic (range: 10–1258). Thailand reported retention from 926 clinics (of 978 in the country) with a median of 20 records assessed per clinic (range: 1–255). The national aggregate prevalence of retention in Myanmar was 82.7%, compared to 82.9% in Thailand. Despite having very similar national averages, clinic-level retention estimates varied widely. Restricting analysis to clinics with at least 30 records assessed, outcomes ranged from 76.6% to 98.7% in Myanmar, and from 56.6% to 97% in Thailand (see **Fig. 11**). As discussed earlier, the considerable variability in clinic-level estimates of retention observed in Thailand suggest that optimization of overall performance will focus on understanding and addressing clinic-level determinants of retention, and that resources should be focused on clinics most in need. By contrast, Myanmar reported data from fewer but also larger clinics. Although there is some evidence of clinic-level variability in Myanmar, less is observed than in Thailand. This finding may reflect a more centralized health structure; therefore, appropriate investigations at the highest functioning clinics may yield valuable lessons that can be applied to all clinics.

Fig. 11. Comparison of between-country variability of clinic-level retention on ART at 12 months



Violin plot showing clinic-level prevalence estimates for retention amongst clinics with 30 or more patients monitored. Each clinic is denoted by a dot and the size of the dot corresponds to the number of patients monitored at that clinic. The national average is denoted by the red asterisk. The violin shape is widest where the greatest number of clinics (and patients) are located on the 0–100% scale.

NATIONAL AND CLINIC-LEVEL RESPONSE TO RESULTS OF EWI MONITORING

The monitoring of ART programme factors alerts clinics and national programme planners to situations that may favour the emergence of population-level HIVDR or virological failure. EWI results form the basis of recommendations for quick action, either at the 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 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.

The identification of local solutions best tailored to individual country scenarios is likely to require a mix of qualitative and quantitative investigation, which may be informed by analysis of cost effectiveness. EWI monitoring is designed to signal areas of clinic and programme service delivery requiring interventions to improve programme quality. Thus, it is critical that their monitoring be routine, and that appropriate resources be budgeted for investigation, capacity-strengthening and interventions in order to effect needed quality improvements. Creative and sustainable funding mechanisms will likely be required to implement locally identified best practices and innovative solutions.

General actions may include: increased training and resources for specific aspects of care; strengthening of record-keeping systems; provision of targeted support for adherence; changes in service delivery model and reduction of barriers to continuous access to care; development of novel supply chain management and drug procurement techniques; and building of laboratory infrastructure. General examples of programme and clinic-level responses to suboptimal EWI performance are listed in **Table 10**.

Table 10. Examples of responses to suboptimal EWI performance

EWI	Response
Prescribing practices	• Training of providers in appropriate triple-drug prescribing practices and in national and international treatment guidelines • Assuring continuous drug supply at clinic level to prevent the need to substitute, switch or dispense mono- or dual-therapy due to drug shortages or stock outs
LTFU	• Defaulter tracing to characterize the contribution of deaths and silent transfers, and to re-engage patients into care – Losses due to transfer of care without knowledge of the original clinic (i.e. silent transfers) require: -- improved processes to report and record transfers, defaulter tracing, and use of national unique patient identifiers – Losses due to unascertained deaths require: -- clinical improvements to minimize mortality and strengthened ascertainment of deaths (e.g. engaging families to report deaths, linking ART records to death registries) – Losses due to disengagement from care require: -- strengthened and better resourced defaulter tracing mechanisms; and -- initiation of patient tracing as close to the date of last missed clinic or pharmacy appointment as possible • Strengthened community outreach and counselling, SMS appointment reminders, alternative clinic appointment times, decentralization of ART care delivery, and alternative models of care, such as home-based care • Provision of more than a one-month supply of ART to decrease the frequency of clinic visits (may support engagement in care)
Retention	• *Recommendations as per LTFU* • Defaulter tracing to re-engage patients who have defaulted back into care • Reduction of HIV-associated stigma • Extra care for high-risk people[1] • Provision of community support for people living with HIV[2,3,4] – Community-level interventions include adherence clubs and use of non-clinical or lay patient advocates and peer support partners to encourage adherence and provide psychological support
On-time pill pick-up	• Adherence support[5] – This includes peer counselling, SMS services, reminder devices, cognitive behavioural therapy, behavioural skills, fixed-dose combinations and once-daily regimens • Decentralization of ART services • Reduction of HIV-associated stigma • Provision of more than a one-month supply of ARV drugs • Use of objective measures of adherence to counsel patients • Electronic or paper based pharmacy registers
On-time appointment keeping	• *Recommendations as per on-time pill pick-up* • Electronic or paper based appointment scheduling • SMS or telephone call reminders
Drug stock outs	• Strengthening of drug forecasting, procurement, and supply information and distribution systems[6] • Global and regional planning prior to and during change of preferred ARV regimens
Viral load suppression	• Interventions to improve adherence linked to improved virological suppression[7] – This includes peer counsellors, SMS and reminder devices, behavioural skills training, medication adherence training, use of fixed-dose combinations and once-daily regimens. • Routing viral load at 6 months, 12 months then annually thereafter and prompt response to virological failure
Viral load completion	• Lowering costs associated with viral load testing and development of laboratory infrastructure • Addressing logistical challenges associated with specimen transport, equipment breakdown, personnel shortages and weak laboratory information management systems • Demand creation among clinicians and people living with HIV

[1] Braitstein P, Siika A, Hogan J, Kosgei R, Sang E, Sidle J et al. A clinician-nurse model to reduce early mortality and increase clinic retention among high-risk HIV-infected patients initiating combination antiretroviral treatment. J Int AIDS Soc. 2012;15:7.
[2] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016. Section 6.5. Available at: http://www.who.int/hiv/pub/en/.
[3] Penn A, Azman H, Horvath A, Taylor K, Hickey M, Rajan J et al. Interventions for improving retention in antiretroviral therapy (ART) programs for people with HIV infection in resource-limited settings: a systematic review. 2014. Protocol. Available at: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017017.
[4] Luque-Fernandez MA, Van Cutsem G, Goemaere E, Hilderbrand K, Schomaker M, Mantangana N et al. Effectiveness of patient adherence groups as a model of care for stable patients on antiretroviral therapy in Khayelitsha, Cape Town, South Africa. PLoS ONE. 2013;8:e56088.
[5] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016. Section 6.5. Available at: http://www.who.int/hiv/pub/en/.
[6] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016. Section 6.13. Available at: http://www.who.int/hiv/pub/en/.
[7] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016. Section 6.6. Available at: http://www.who.int/hiv/pub/en/.

EXAMPLES OF ART PROGRAMME ACTIONS TAKEN BY COUNTRIES IN RESPONSE TO EWI RESULTS

This section presents a series of case studies to demonstrate how countries have used EWIs of HIVDR to optimize clinic and programme performance.

Argentina: EWI case study

An example of suboptimal provider compliance with ART prescribing guidance is illustrated by data reported from Argentina. Argentina is an upper-middle-income country in Latin America with HIV prevalence of 0.5% (0.3–0.6%) amongst adults aged 15–49 years, equalling 130 000 (78 000–170 000) people living with HIV as of 2014. During the period of EWI monitoring, the programme was in the process of phasing out stavudine and didanosine, in favour of tenofovir, due to concerns about toxicity. The country chose to capture provider compliance with its national directives.

Therefore, the Argentine national ART programme defined any regimen containing stavudine, didanosine, indinavir, nelfinavir, or two or more PIs (with the exception of low-dose ritonavir) as "inappropriate". Additionally, the prescribing of any unboosted PI – except when acceptable according to the treatment guidelines in effect at the time of the EWI round – and the prescribing of any mono- or dual-drug regimen were classified as "inappropriate". None of the four clinics monitored in 2010, and only one of the four clinics monitored in 2011, achieved the goal of 100% appropriate prescribing.

Despite national directives, clinics continued to prescribe ARV drugs inconsistent with national guidelines. For example, one large hospital in the national capital, Buenos Aires, reported that only 71.7% of prescribing followed national guidelines in 2010. In 2011, the same hospital reported a very modest improvement, with appropriate prescribing reaching 75.6%. As a result of these findings, the national ART programme investigated further and determined that the vast majority of inappropriate prescribing was due to the use of stavudine. The programme conducted educational activities related to ARV drug toxicities and worked with clinics to fast-track substitution of stavudine and didanosine with tenofovir.

Namibia: EWI case study

Namibia is a resource-limited country in sub-Saharan Africa that has been severely affected by the HIV epidemic. There are approximately 260 000 people living with HIV in Namibia, from a population of 2.3 million (Namibia Ministry of Health and Social Services, unpublished data, 2015). Among people aged 15–49 years, approximately 16.9% are infected with HIV. The epidemic is predominantly spread via heterosexual contact. Prevalence estimates vary by region, with up to 37.7% of people infected with HIV-1 in the most heavily affected areas in the north.[1]

During the pilot of its first round of EWIs in 2009, the Namibia national ART programme realized that existing pharmacy records did not capture ARV drug supply at the clinic-dispensary level, but rather at a more central level. Contemporary anecdotal reports from some clinics in Namibia documented occurrences of stock outs of certain ARV drugs, necessitating drug substitutions in order to prevent treatment interruptions. Significantly, these suspected stock outs at the clinic level were not captured by assessment of stock at higher levels. Based on this EWI pilot exercise,[2] programming changes were made to the national electronic pharmacy record, which allowed it to capture stock at the clinic-level dispensary.

Despite these changes, during the next round of EWI monitoring in 2010, it was noted that ART pharmacies were not correctly using the revised records. Specifically, pharmacists were expected to update the system to reflect the new stock as it arrived; however, this did not always happen, and the default of the electronic system allowed dispending of ART to patients on "0" stock. Thus, at the start of the 2010 round, it appeared that many drug stock outs had occurred, when in reality drugs had been available to patients at clinics. Recognizing the importance of this EWI, Namibia retrained pharmacists in best practices, and developed a new system for reporting significant drug stock outs at the dispensary level. As a result of these interventions, the country was able to confidently monitor ARV drug stock outs in 2011, demonstrating that only five out of 49 sites monitored had any stock out of a routinely dispensed ARV drug.

This example is important because it illustrates the value of monitoring drug supply continuity at the level where stock outs most impact patient care. Additionally, it illustrates how a national ART programme successfully modified existing record-keeping systems and trained staff to improve documentation, leading to a sustained improvement in record keeping, and allowing on going routine monitoring of this EWI.

Namibia also investigated clinics not achieving 100% appropriate prescribing practices. Less than 1% of patients were found to be receiving mono- or dual-therapy; most of these patients had transferred from the private sector on the inappropriate regimen and been continued on it by clinic staff. Identification of inappropriate prescribing practices in Namibia contributed to the establishment of clinical mentors to investigate inappropriate regimens and teach clinic staff about optimal prescribing and the risks of HIVDR. It also prompted the national ART programme to engage with the private sector to assess and standardize prescribing practices in line with national and international guidelines.[3]

EWI monitoring also led to the realization that Namibia needed to improve retention in care. Consequently, the Namibia Ministry of Health and Social Services initiated several operational research studies to assess the efficacy and cost effectiveness of defaulter tracing. It also provided additional resources to clinics failing to achieve desirable levels of retention. In addition, the country identified low levels of adherence as a possible barrier to long-term population-level success. As a result, an SMS system to remind patients to take their pills and return to clinic appointments was implemented at pilot sites.

[1] Republic of Namibia Ministry of Health and Social Services. Directorate of Special Programmes. Surveillance report of the 2014 national HIV sentinel survey. November 2014. Available at: http://www.mhss.gov.na/files/downloads/12f_2014%20National%20HIV%20Sentinel%20Survey.pdf.

[2] Hong SY, Jonas A, Dumeni E, Badi A, Pereko D, Blom A et al. Population-based monitoring of HIV drug resistance in Namibia with early warning indicators. J Acquir Immune Defic Syndr. 2010;55(4):27–31.

[3] Jonas A, Sumbi V, Mwinga S, DeKlerk M, Tjituka F, Penney S et al. HIV drug resistance early warning indicators in Namibia with updated World Health Organization guidance. PLoS ONE. 2014.

Zimbabwe: EWI case study

Zimbabwe is experiencing a generalized HIV epidemic, with an adult prevalence rate of 14.7% according to its 2012 National HIV/AIDS Estimates. An estimated 1 328 535 (1 269 818–1 434 422) Zimbabweans were living with HIV and AIDS at the end of 2011. In 2012, approximately 581 801 adults received ART through the Ministry of Health and Child Care ART rollout programme, which started in 2004.

Zimbabwe monitored EWIs in cohort years: 2006, 2007, 2008, 2010 and 2012. In all rounds, data abstraction, verification and validation posed challenges due to multiple paper-based record-keeping systems, which proved laborious to use. This challenge highlights the need for simple, standardized paper records and the scale-up of simple electronic patient record-keeping systems. Incomplete source documents compromised the integrity of data; a recommendation was therefore made to set up data quality management committees, to ensure records are properly maintained and to achieve congruity between clinic and pharmacy registers.

In its last EWI round in 2012, which included 74 clinics, Zimbabwe identified suboptimal retention and unacceptably high rates of LTFU as barriers to achieving the UNAIDS 90-90-90 target. A recommendation was made to implement defaulter tracing at clinics in an attempt to link people back into care. This process also aims to strengthen the use of existing patient referral forms during decentralization, in order to document transfers of care from one clinic to another.

IMPROVING MONITORING AND RESPONSE FOR EWIs OF HIVDR

In many LMIC, HIVDR testing is neither routinely available nor recommended for individual patient management. Genotyping is expensive and complex, and available regimens remain limited. However, the monitoring of patient and clinic factors associated with the emergence of preventable HIVDR is comparatively inexpensive and can be used to recognize situations favouring the emergence of HIVDR in order to reduce its harmful consequences. Even if HIVDR were not an issue, the monitoring of programmes for quality of service delivery would be critical.

Initially developed in 2007, EWIs of HIVDR were amongst the first clinic-level quality-of-care indicators that were tied to performance targets and designed to alert programmes to differences in clinic-level performance for the purpose of stimulating investigation and identifying local and sustainable solutions to complex problems.

By 2011, it had become clear that the plethora of stakeholder promulgated indicators, however well intentioned, had reached proportions that deterred their implementation. That year, EWIs underwent a simplification process, during which they were reduced from seven indicators with 15 different versions to five indicators with only one version each.[1] During the revision process, EWIs were harmonized with definitions from the United Nations General Assembly and the United States President's Emergency Plan for AIDS Relief, and targets were soundly grounded in available scientific evidence. Further revisions to EWIs were taken in 2015, during their integration into WHO's *Consolidated strategic information guidelines for HIV in the health sector.*[2]

Several factors may have influenced the observed decline in clinic-level EWI reporting in recent years. It may be partly due to interruption of donor funding for this activity, as well as the widespread misperception that EWI monitoring was a research activity, rather than a locally driven assessment for the purpose of improving clinic performance. It is equally possible that several years of direct donor seed funding contributed to the perception that this was a research activity, rather than a vital part of routine monitoring and evaluation. It is also likely that many countries have clinic-level "EWIs of HIVDR" data as part of their care and treatment cascade, but did not report it to WHO due to misperceptions. With the integration of EWIs into WHO's *Consolidated strategic information guidelines*, it is anticipated that indicator reporting will increase, and that streamlined processes will be developed to support reporting and the use of clinic-level data for programme optimization.

Despite vigorous attempts to investigate actions taken by countries based on EWI findings, and the impacts of these actions on future outcomes or levels of HIVDR, findings were limited. Nevertheless, the investigation revealed some unsettling facts. Several countries had a backlog of EWI data that had neither been analysed nor validated, or for which no action had been taken. At the country level, lack of training within ART programmes on qualitative epidemiological methods hampered programme led investigations, as did lack of funding for implementation of possible remedies. From a global perspective, it was not feasible to monitor individual clinic-level outcomes over time, as clinic-level data were often submitted in a blinded fashion – this process should happen at a country level, and is anticipated to be reinvigorated through the HIVDR GAP.

Finally, whether countries are implementing EWI monitoring as a specific activity or, more appropriately, routinely assessing objective measures of adherence, retention, LTFU, drug stock out, viral load suppression and viral load coverage, it is vital not to lose sight of the relationship between these factors and preventable HIVDR. Even as new drugs are introduced in the future, it will remain essential to redouble collective efforts to be responsible stewards of ARV drugs, and to seek new ways to minimize preventable HIVDR and maximize the quality of ART service delivery.

[1] Using early warning indicators to prevent HIV drug resistance. Report of the Early Advisory Indicator Panel meeting (11–12 August 2011). Geneva: World Health Organization; 2012. Available at: http://www.who.int/hiv/pub/meetingreports/ewi_meeting_report/en/.

[2] Consolidated strategic information guidelines for HIV in the health sector. Geneva: World Health Organization; 2015. Available at: http://www.who.int/hiv/pub/guidelines/strategic-information-guidelines/en/.

CONCLUSION

Enormous strides have been made in the scale-up of ART over the last decade. To achieve the ambitious global targets of 90-90-90 by 2020 and the elimination of AIDS as a public health threat by 2030, not only do millions of people need to be started on ART, but the quality of service delivery in many countries needs be strengthened. This report highlights common gaps in ART service delivery, including excess LTFU, suboptimal retention, drug stock outs and inadequate support for population adherence to ART. The report should be seen as a call to action to improve the quality of ART service delivery in LMIC.

Given increasing levels of HIVDR in LMIC, it is essential to optimize programme- and clinic-level function in order to minimize situations favourable to the emergence of HIVDR. Routine EWI monitoring provides crucial information about the quality of service delivery at clinics providing ART. National aggregate data can highlight broader programmatic issues hampering the achievement of desired treatment outcomes, and results can be instrumental in prioritizing actions and allocating resources to clinics most in need.

Since 2011, monitoring and reporting of EWIs of HIVDR has decreased globally. In 2015, only a handful of countries reported implementing EWI monitoring – a fact that may place many countries at serious risk of unknowingly creating situations favourable to the emergence of preventable HIVDR. Although called by different names, many EWIs are, in fact, integrated into a country's care and treatment cascade or other quality improvement efforts. More clinic-level data are undoubtedly available at country level, but were not reported to WHO. What is uncertain is whether the relationship between these indicators and unnecessary HIVDR is recognized, and whether data available within countries are being used proactively to make adjustments to service delivery in an effort to guard against unnecessary HIVDR.

In light of the findings in this report, as well as increasing levels of HIVDR in LMIC, heightened vigilance and rapid response to clinic and programme situations favouring HIVDR are imperative. Clinic-level data must be proactively exploited and lessons in best practice learned and applied, in order to ensure that the maximum population benefits of ART are attained – thus, ultimately ensuring the elimination of AIDS as a public health threat.

ANNEX

Epidemiological methods

EWIs monitor factors related to patient care (appropriate prescribing and viral load suppression at 12 months); patient behaviour (adherence); and clinic-level and programme management (follow-up, retention on ART, and procurement and supply management of ARV drugs). EWIs use standardized definitions and targets, which have evolved over time as programmes matured, lessons were learned, and public health actions were refined. The original targets proposed in 2008 were revised in 2011; all targets are grounded in medical and scientific literature. This report uses 2011 targets.

While no substantial changes were made to the definitions for appropriate prescribing, retention and drug stock outs, changes were made to the on-time pill pick-up indicator. The definition for this indicator evolved in response to emerging literature assessing pill-based methods of adherence, and reflected a desire for a simple yet precise definition. Prior to 2011, WHO recommended that pill pick-up be assessed amongst a cohort of ART initiators during their first 12 months of therapy, or amongst a sample (cross-sectional method) of patients on ART for any length of time. Pill pick-up was classified as "on time" if it occurred on or before the pill run-out date, if pills had been taken according to schedule. No grace period was allowed and any existence of a patient buffer stock was ignored. The cohort method assessed all pill pick-ups during the first 12 months, while the cross-sectional approach assessed two consecutive pill pick-ups after an established "baseline".

In 2011, acknowledging that existing definitions did not adequately account for the possibility of patients accumulating pills over time, or sufficiently reflect NNRTI pharmacokinetics, a revised definition was recommended. Like the previous version, the 2011 definition is cross-sectional and assesses on-time pill pick-up amongst patients on ART regardless of treatment duration or regimen line. However, unlike the previous version, "on time" is defined as pills being picked up within two days of the run-out date, if taken according to schedule. Additionally, the revised definition assesses only one pill pick-up after an established "baseline".

Prior to 2011, two definitions existed for the on-time appointment keeping indicator. One measured on-time appointment keeping amongst a cohort of treatment initiators during their first 12 months of therapy; the other assessed whether two consecutive appointments were on time, after a baseline appointment, amongst patients on ART for any duration. For both definitions, an appointment was classified as "on time" if it was within seven days of the scheduled appointment. This indicator was dropped in 2011, due to weaker evidence of its association with HIVDR or virological failure when compared to on-time pill pick-up.[1]

WHO-recommended EWI methods are designed to provide results generalizable to the clinic from which they were obtained. Sample sizes are calculated based on the relevant eligible population size to achieve point prevalence estimates with confidence intervals ±7%. Sample size calculations and data abstraction are supported by an electronic data abstraction tool available from WHO.[2] Recommended reporting uses stratified targets to provide clinic-specific and programme-level benchmarks, against which to assess performance and compare variability in clinic performance. Individual clinic-level EWI prevalence estimates are classified using score cards. In the context of EWI monitoring, score cards yield three classifications: red (poor performance, below desired target); amber (fair performance, not yet at desired target); and green (excellent performance, achieving desired target). More detailed information about EWIs, their definitions and changes over time, their indicator targets, and score card reporting is available in the 2011 *Report of the EWI Advisory Indicator Panel*, available at: http://www.who.int/hiv/pub/meetingreports/ewi_meeting_report/en/.

Statistical methods

Point estimates and confidence intervals were extracted from generalized estimating equation (GEE) models, which accounted for correlation within countries through the use of a sandwich estimator. As GEEs are marginal models, they return point estimators that are nearly identical to those derived by adding clinic-level numerators and dividing by clinic-level denominators. Their advantage is the appropriately inflated confidence intervals they return as a reflection of the within country variability.

Tests for regional differences, time trends, clinic size and associations between EWIs were conducted using mixed-effects logistic regression models, with clinic-level outcomes as binomial observations weighted by clinic-specific denominators. Random effects were included at the country level, to account for expected correlation among clinics within the same country. When assessing time trends within regions, only regions reporting data from at least three different countries, and with two or more rounds reported per country, were tested. When assessing the relationship with clinic size, the size of a clinic was either transformed to a log scale or divided into categories (e.g. small clinics <250 patients, medium clinics 250–1000 and large clinics >1000).

[1] Using early warning indicators to prevent HIV drug resistance. Report of the Early Advisory Indicator Panel meeting (11–12 August 2011). Geneva: World Health Organization; 2012. Available at: http://www.who.int/hiv/pub/meetingreports/ewi_meeting_report/en/.

[2] The EWI data abstraction tool may be downloaded at: http://www.who.int/hiv/pub/meetingreports/ewi_meeting_report/en/.

ART coverage was estimated as the number of people on ART divided by the number of people living with HIV in the cohort year. The relationship between ART coverage and EWI national prevalence estimates was evaluated using ART coverage in the year of the EWI cohort. Sensitivity analyses were conducted using the year prior to the EWI cohort and two years prior to the EWI cohort; no differences were observed. To evaluate the hypothesis that rapid scale-up of ART was associated with a decline in EWI outcomes, change scores were generated as the difference in ART coverage and the difference in EWI outcomes between two consecutive EWI monitoring rounds. The relationship between these change scores was then tested using a simple linear model.

The relationship between gross national income and EWI outcomes was assessed using GEE models allowing for correlations within countries, transforming gross national income per capita to a log scale, and controlling for EWI cohort. Gross national income per capita in current US dollars is a country's gross national income, converted to US dollars using the World Bank Atlas method, and divided by the mid-year population.[1]

Some EWI results were excluded because of recognized data quality issues. The decision to exclude these results was reached with the help of the country.

Regional and subregional country groupings[2]

Americas:
Antigua and Barbuda; Argentina; Bahamas; Barbados; Belize; Bolivia (Plurinational State of); Colombia; Dominica; Dominican Republic; Ecuador; El Salvador; Grenada; Guatemala; Guyana; Honduras; Jamaica; Nicaragua; Saint Kitts and Nevis; Saint Lucia; Saint Vincent and the Grenadines; Suriname

Central Africa:
Cameroon; Central African Republic; Democratic Republic of the Congo

Eastern Africa:
Burundi; Ethiopia; Kenya; Malawi; Mozambique; Rwanda; Uganda; United Republic of Tanzania

Southern Africa:
Angola; Botswana; Lesotho; Namibia; South Africa; Swaziland; Zimbabwe

Western Africa:
Benin; Burkina Faso; Côte d'Ivoire; Ghana; Guinea; Mali; Niger; Nigeria; Senegal; Togo

South-East Asia:
India; Indonesia; Myanmar; Nepal; Thailand

Western Pacific:
Cambodia; China; Papua New Guinea; Viet Nam

Eastern Europe:
Ukraine

1 World Bank Group. GNI per capita, Atlas method (current US$). 2016. Available at: http://data.worldbank.org/indicator/NY.GNP.PCAP.CD.
2 The subregional country groupings for Africa used in this report are available at: www.unicef.org/wcaro/WCARO_SOAC08_Fig011.pdf (accessed 16 June 2016).

Table 1A. Top 15 EWI rounds contributing data for analysis, 2004–2014

Country	Cohort year	No. of clinics monitored	No. of clinics in country	% of clinics monitored
Thailand	2013–2014	929	993	93.6%
Thailand	2012–2013	926	978	94.7%
Thailand	2011–2012	923	949	97.3%
Thailand	2010–2011	921	937	98.3%
Thailand	2009–2010	916	943	97.1%
South Africa[1]	2013–2014	156	3 817	4.1%
Ghana	2011–2012	133	162	82.1%
Ghana	2011	132	162	81.5%
Ghana	2009–2010	119	133	89.5%
DRC	2010	112	344	32.6%
Ghana	2010–2011	109	150	72.7%
Ghana	2010	100	150	66.7%
Uganda	2011	95	465	20.4%
Ghana[2]	2009	88	133	66.2%
Viet Nam	2011	83	590	14.1%

[1] Sampling performed in two provinces.
[2] One of two different EWI rounds performed in Ghana in 2009.

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Americas	Antigua and Barbuda	2010			82.3% (62, 1)			
		2011			80.6% (31, 1)			
		2012			80.0% (25, 1)			
		Total			81.4% (118, 3)			
	Argentina	2010	76.4% (785, 4)	5.4% (37, 2)		75.5% (110, 1)		4.2% (48)
		2011	84.2% (304, 4)	24.3% (304, 4)		33.6% (304, 4)	91.1% (304, 4)	
		Total	78.6% (1089, 8)	22.3% (341, 6)		44.7% (414, 5)	91.1% (304, 4)	4.2% (48)
	Barbados	2005	94.0% (83, 1)	1.2% (83, 1)	80.8% (78, 1)			
		2006	87.1% (101, 1)	7.9% (101, 1)	61.4% (88, 1)			
		2007	84.1% (69, 1)	4.3% (69, 1)	63.8% (58, 1)			
		2008	96.3% (81, 1)	18.6% (43, 1)	64.3% (42, 1)			0% (12)
		2009	97.3% (74, 1)	6.2% (32, 1)	83.9% (31, 1)			
		Total	91.7% (408, 5)	6.7% (328, 5)	69.7% (297, 5)			0% (12)
	Belize	2007	100% (100, 1)	16.0% (100, 1)	52.0% (100, 1)			
		Total	100% (100, 1)	16.0% (100, 1)	52.0% (100, 1)			
	Bolivia (Plurinational State of)[8]	2010	90.7% (259, 1)	33.0% (264, 1)	69.7% (264, 1)	13.3% (249, 1)		
		Total	90.7% (259, 1)	33.0% (264, 1)	69.7% (264, 1)	13.3% (249, 1)		
	Colombia	2007	100% (113, 1)	14.2% (113, 1)	85.8% (113, 1)		64.6% (113, 1)	
		2008	100% (24, 1)	25.0% (24, 1)	75.0% (24, 1)		70.8% (24, 1)	
		2009	100% (127, 1)	14.2% (127, 1)	79.5% (127, 1)		79.5% (127, 1)	
		Total	100% (264, 3)	15.2% (264, 3)	81.8% (264, 3)		72.3% (264, 3)	

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014 (continued)

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Americas	Dominica	2007	50.0% (4, 1)					
		2008	100% (3, 1)	0% (3, 1)	100% (3, 1)			
		2009	100% (5, 1)	0% (5, 1)				
		2010	71.4% (7, 1)		71.4% (7, 1)			
		2011	75.0% (8, 1)		75.0% (8, 1)			
		2012	100% (16, 1)		75.0% (16, 1)			
		Total	86.0% (43, 6)	0% (8, 2)	76.5% (34, 4)			
	Dominican Republic	2009	85.5% (975, 14)	10.8% (1004, 16)	87.3% (855, 15)			
		2010	88.3% (1311, 20)		88.3% (1311, 20)			
		Total	87.1% (2286, 34)	10.8% (1004, 16)	87.9% (2166, 35)			
	Ecuador	2009	95.7% (235, 2)	14.4% (90, 1)	76.6% (235, 2)	77.0% (235, 2)	64.4% (90, 1)	
		2010	98.8% (260, 2)	26.0% (100, 1)	74.0% (100, 1)	69.0% (100, 1)	62.0% (100, 1)	
		Total	97.4% (495, 4)	20.5% (190, 2)	75.8% (335, 3)	74.6% (335, 3)	63.2% (190, 2)	
	El Salvador	2007	89.6% (460, 5)	7.1% (421, 5)	88.3% (394, 5)			31.6% (57)
		2008	91.2% (509, 5)	4.0% (478, 5)	94.2% (450, 5)			30.0% (60)
		2009	89.5% (560, 5)					28.3% (60)
		Total	90.1% (1529, 15)	5.5% (899, 10)	91.5% (844, 10)			29.9% (177)
	Grenada	2005	100% (3, 1)	0% (3, 1)	66.7% (3, 1)			0% (12)
		2006	100% (6, 1)	0% (6, 1)	83.3% (6, 1)			
		2007	100% (14, 1)	0% (14, 1)	85.7% (14, 1)			
		2008	100% (3, 1)	0% (3, 1)	100% (3, 1)			
		Total	100% (26, 4)	0% (26, 4)	84.6% (26, 4)			0% (12)
	Guatemala	2008	100% (37, 1)	21.6% (37, 1)	67.6% (37, 1)	64.9% (37, 1)		
		Total	100% (37, 1)	21.6% (37, 1)	67.6% (37, 1)	64.9% (37, 1)		

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014 (continued)

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Americas	Guyana	2004		11.9% (226, 1)	66.4% (226, 1)			
		2005		6.9% (303, 1)	77.2% (303, 1)			
		2006		12.6% (277, 1)	76.2% (277, 1)			
		2007		18.5% (184, 1)	60.3% (184, 1)			0% (12)
		2009						0% (156)
		Total		11.8% (990, 4)	71.3% (990, 4)			0% (168)
	Honduras	2007	99.0% (629, 5)	8.8% (628, 5)	89.0% (629, 5)	84.3% (521, 5)		
		2008	98.8% (575, 5)	13.1% (574, 5)	87.8% (575, 5)	87.6% (461, 5)		
		2009	99.4% (616, 5)	12.2% (613, 5)	87.5% (616, 5)	82.3% (538, 5)		
		2011	98.4% (618, 11)	11.1% (610, 11)	87.3% (616, 11)	74.1% (456, 11)		
		Total	98.9% (2438, 26)	11.3% (2425, 26)	87.9% (2436, 26)	82.2% (1976, 26)		
	Jamaica	2007	92.1% (969, 5)	30.4% (969, 5)	59.0% (892, 5)			8.3% (48)
		2008	93.2% (687, 5)					
		Total	92.5% (1656, 10)	30.4% (969, 5)	59.0% (892, 5)			8.3% (48)
	Nicaragua	2008	100% (106, 4)	41.5% (106, 4)	56.6% (106, 4)	48.0% (98, 4)	58.5% (106, 4)	14.6% (48)
		2009	100% (137, 2)	28.5% (137, 2)	71.5% (137, 2)	58.4% (137, 2)		
		2010	100% (238, 8)	22.2% (216, 8)	70.6% (238, 8)	77.3% (216, 8)	49.5% (216, 8)	0% (96)
		Total	100% (481, 14)	28.5% (459, 14)	67.8% (481, 14)	65.2% (451, 14)	52.5% (322, 12)	4.9% (144)
	Saint Lucia	2005	92.9% (14, 1)	0% (14, 1)	100% (13, 1)			
		2006	95.5% (22, 1)	0% (22, 1)	90.5% (21, 1)			
		2007	96.6% (29, 1)	3.4% (29, 1)	92.9% (28, 1)			
		2008	96.7% (30, 1)	16.7% (30, 1)	93.1% (29, 1)			
		2009	88.5% (26, 1)		85.7% (7, 1)			
		2010	100% (10, 1)					
		Total	94.7% (131, 6)	6.3% (95, 4)	92.9% (98, 5)			

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014 (continued)

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Americas	Saint Vincent and the Grenadines	2005		3.8% (26, 1)	40.0% (25, 1)			
		2006	100% (20, 1)	10.0% (20, 1)	60.0% (20, 1)			
		2007	97.1% (35, 1)	12.1% (33, 1)	78.1% (32, 1)			
		2008	94.3% (35, 1)					0% (12)
		Total	96.7% (90, 3)	8.9% (79, 3)	61.0% (77, 3)			0% (12)
	Suriname	2007	100% (228, 1)	35.6% (264, 1)	79.8% (228, 1)			
		2008	94.7% (283, 1)		80.8% (271, 1)			
		2009	100% (247, 1)		87.4% (247, 1)			91.7% (12)
		2010	100% (248, 1)		86.7% (248, 1)			58.3% (12)
		2011	100% (270, 1)		89.6% (270, 1)			83.3% (12)
		2012	100% (225, 1)		82.2% (225, 1)			16.7% (12)
		Total	99.0% (1501, 6)	35.6% (264, 1)	84.6% (1489, 6)			62.5% (48)
Western Africa	Benin	2007	99.8% (400, 5)		60.2% (400, 5)	36.3% (369, 5)	49.5% (396, 5)	
		Total	99.8% (400, 5)		60.2% (400, 5)	36.3% (369, 5)	49.5% (396, 5)	
	Burkina Faso	2006–2007	95.7% (744, 9)	18.2% (751, 9)	68.6% (724, 9)	4.3% (751, 9)		
		2007–2008	98.9% (1593, 21)	18.3% (1215, 20)	70.8% (1555, 21)	1.1% (1499, 20)		
		2008–2009	99.1% (2221, 23)	20.6% (1697, 22)	70.0% (2165, 23)	29.7% (2666, 23)		
		2010–2011	92.9% (2088, 25)	20.8% (1882, 24)	65.3% (1990, 25)	23.7% (3291, 25)		
		2012–2013	97.6% (1840, 25)	20.2% (1650, 25)	66.0% (1761, 25)			
		2013			70.8% (3564, 23)			
		Total	96.9% (8486, 103)	19.9% (7195, 100)	68.9% (11759, 126)	19.7% (8207, 77)		
	Côte d'Ivoire	2006–2007						25.0% (40)
		2008–2009	98.1% (1841, 19)	34.2% (1413, 18)	50.8% (1467, 18)	21.9% (2008, 18)		55.4% (204)
		Total	98.1% (1841, 19)	34.2% (1413, 18)	50.8% (1467, 18)	21.9% (2008, 18)		50.4% (244)

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014 (continued)

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Western Africa	Ghana	2007	86.8% (2225, 27)		87.0% (1784, 22)		74.8% (2298, 27)	
		2009–2010	90.1% (10218, 119)	35.5% (9375, 119)	56.3% (9410, 119)		23.5% (9410, 119)	
		2009 a	97.2% (6037, 74)		90.3% (5818, 72)		98.4% (4158, 71)	
		2009 b	97.2% (4096, 88)		86.7% (3365, 87)		70.0% (3365, 87)	
		2010	92.2% (9751, 100)	30.2% (8911, 100)	63.5% (8958, 100)		27.1% (8958, 100)	
		2010–2011	94.2% (11387, 109)	36.7% (10460, 109)	56.9% (10512, 109)		22.0% (10512, 109)	
		2011	95.7% (51500, 132)		57.3% (13094, 129)	75.3% (50674, 132)		
		2011–2012	97.5% (54959, 133)		57.7% (12181, 132)	74.1% (54113, 133)		
		Total	95.6% (150173, 782)	34.3% (28746, 328)	63.3% (65122, 770)	74.7% (104787, 265)	39.1% (38701, 513)	
	Guinea	2008–2009	100% (229, 4)	25.8% (229, 4)	79.9% (229, 4)	65.9% (229, 4)		
		Total	100% (229, 4)	25.8% (229, 4)	79.9% (229, 4)	65.9% (229, 4)		
	Mali	2009	95.6% (570, 2)	6.1% (505, 2)		90.5% (505, 2)		
		Total	95.6% (570, 2)	6.1% (505, 2)		90.5% (505, 2)		
	Niger	2007	98.8% (1285, 11)	37.9% (1257, 11)	56.2% (1257, 11)			0% (132)
		2008	99.6% (1420, 11)	31.9% (1527, 11)	65.4% (1502, 11)			0% (132)
		Total	99.2% (2705, 22)	34.6% (2784, 22)	61.2% (2759, 22)			0% (264)
	Nigeria	2011	96.1% (1376, 9)	18.6% (1320, 9)	66.6% (1348, 9)			26.4% (72)
		Total	96.1% (1376, 9)	18.6% (1320, 9)	66.6% (1348, 9)			26.4% (72)
	Senegal	2006–2008	98.7% (1034, 19)	10.0% (932, 19)	94.8% (575, 19)			
		2007–2008	100% (96, 4)	3.3% (122, 4)	94.4% (36, 4)	100% (68, 4)	41.2% (68, 4)	
		2011–2012	99.5% (1536, 37)	30.7% (1344, 37)	65.7% (1381, 37)	62.3% (1381, 37)	63.0% (1361, 37)	
		Total	99.2% (2666, 60)	21.3% (2398, 60)	74.6% (1992, 60)	64.0% (1449, 41)	62.0% (1429, 41)	
	Togo	2007	97.2% (466, 10)	21.2% (325, 10)	90.5% (306, 10)	72.6% (420, 10)	78.5% (368, 10)	
		2007–2008	100% (706, 10)		57.5% (365, 10)		81.4% (409, 10)	
		2009	100% (926, 21)	6.9% (896, 21)	72.2% (898, 21)	23.0% (984, 21)		22.6% (252)
		Total	99.4% (2098, 41)	10.7% (1221, 31)	72.3% (1569, 41)	37.8% (1404, 31)	80.1% (777, 20)	22.6% (252)

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014 (continued)

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Western Africa	Cameroon	2007–2008	100% (300, 10)	25.0% (300, 10)	73.0% (300, 10)	36.3% (300, 10)		0.8% (120)
		2008	99.4% (3445, 19)	35.9% (3322, 19)	48.1% (3392, 19)	21.7% (3429, 19)		27.2% (228)
		2009	99.8% (4807, 40)	35.3% (4547, 40)	52.3% (4687, 40)	24.8% (4329, 36)		25.2% (456)
		2012–2013	100% (2165, 15)		86.6% (1724, 13)	80.7% (1584, 12)		38.7% (168)
		Total	99.7% (10717, 84)	35.2% (8169, 69)	57.4% (10103, 82)	33.3% (9642, 77)		25.0% (972)
Central Africa	Central African Republic	2012	100% (580, 5)	29.7% (468, 5)	42.1% (468, 5)	41.2% (325, 2)		
		Total	100% (580, 5)	29.7% (468, 5)	42.1% (468, 5)	41.2% (325, 2)		
	DRC	2008	100% (1108, 22)	18.2% (1111, 22)	63.4% (1108, 22)	43.2% (1047, 21)	57.9% (1109, 22)	18.9% (264)
		2010	100% (3239, 112)	19.1% (3105, 112)	65.5% (3147, 112)	32.8% (3175, 110)	53.6% (3099, 111)	20.2% (1340)
		Total	100% (4347, 134)	18.9% (4216, 134)	65.0% (4255, 134)	35.3% (4222, 131)	54.8% (4208, 133)	20.0% (1604)
Eastern Africa	Burundi	2007	99.1% (1387, 19)	4.3% (1387, 19)	90.5% (1326, 18)	35.3% (1326, 18)		57.1% (156)
		2008	97.8% (1827, 45)	10.7% (1827, 45)	76.0% (1827, 45)	23.9% (1827, 45)		
		Total	98.4% (3214, 64)	7.9% (3214, 64)	82.1% (3153, 63)	28.7% (3153, 63)		57.1% (156)
	Ethiopia	2006	100% (8568, 14)	18.3% (8568, 14)	55.3% (8568, 14)			
		2008	100% (6302, 45)	17.6% (6302, 45)	70.7% (6302, 45)		89.6% (6302, 45)	0% (540)
		Total	100% (14870, 59)	18.0% (14870, 59)	61.8% (14870, 59)		89.6% (6302, 45)	0% (540)
	Kenya	2006	98.3% (1324, 18)	15.8% (1108, 18)	79.5% (1181, 18)		41.3% (1031, 17)	
		2012	98.8% (3811, 49)	26.7% (3804, 49)	62.3% (3803, 49)		30.8% (3819, 49)	
		Total	98.7% (5135, 67)	24.3% (4912, 67)	66.4% (4984, 67)		33.1% (4850, 66)	
	Mozambique	2006	99.8% (2599, 4)	12.4% (516, 4)	76.6% (516, 4)	88.5% (15099, 4)		
		Total	99.8% (2599, 4)	12.4% (516, 4)	76.6% (516, 4)	88.5% (15099, 4)		
	Rwanda	2009	100% (2974, 55)	8.0% (2974, 55)		19.0% (2953, 53)		
		Total	100% (2974, 55)	8.0% (2974, 55)		19.0% (2953, 53)		

Table 2A. **Detailed summary of EWI results from 55 countries, 2004–2014 (continued)**

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Eastern Africa	Uganda	2006	97.9% (3308, 41)	7.1% (2968, 39)	76.3% (2968, 39)		30.0% (1644, 9)	69.2% (156)
		2007						47.9% (912)
		2011	99.8% (9125, 95)	18.2% (9125, 95)	76.4% (9125, 95)	43.8% (9125, 95)	39.9% (9125, 95)	28.6% (1140)
		Total	99.3% (12433, 136)	15.5% (12093, 134)	76.4% (12093, 134)	43.8% (9125, 95)	38.4% (10769, 104)	39.4% (2208)
	United Republic of Tanzania	2010	100% (3020, 29)	23.7% (2865, 28)	54.1% (2865, 28)		38.6% (2865, 28)	
		Total	100% (3020, 29)	23.7% (2865, 28)	54.1% (2865, 28)		38.6% (2865, 28)	
Southern Africa	Angola	2008	100% (1045, 9)	50.8% (1045, 9)				34.7% (72)
		Total	100% (1045, 9)	50.8% (1045, 9)				34.7% (72)
	Lesotho	2007	100% (1828, 27)	21.0% (1540, 27)	71.6% (1633, 27)	86.4% (1825, 25)	87.6% (1700, 24)	
		Total	100% (1828, 27)	21.0% (1540, 27)	71.6% (1633, 27)	86.4% (1825, 25)	87.6% (1700, 24)	
	Namibia	2007	99.8% (1620, 9)	17.2% (1537, 9)	65.8% (1537, 9)			
		2008–2009	99.6% (3863, 33)	19.7% (3710, 33)				
		2012	100% (9442, 48)		83.2% (19299, 49)	87.1% (9573, 48)		1.0% (588)
		Total	99.8% (14925, 90)	19.0% (5247, 42)	81.9% (20836, 58)	87.1% (9573, 48)		1.0% (588)
	South Africa[9]	2013–2014	100% (13905, 95)		67.8% (25562, 111)	27.2% (16744, 113)		
		Total	100% (13905, 95)		67.8% (25562, 111)	27.2% (16744, 113)		
	Swaziland	2007–2008	83.7% (4752, 4)	26.4% (4534, 4)		76.4% (3579, 4)		2.1% (48)
		2008–2009	99.0% (2080, 14)	24.6% (2080, 14)	62.6% (2080, 14)			
		Total	88.4% (6832, 18)	25.8% (6614, 18)	62.6% (2080, 14)	76.4% (3579, 4)		2.1% (48)
	Zimbabwe	2006	97.7% (1069, 15)	14.3% (1062, 15)	72.4% (926, 15)			
		2007	99.5% (1941, 40)	19.7% (1936, 40)	72.3% (1861, 40)			12.6% (468)
		2010	100% (14624, 67)	15.1% (11851, 64)	73.3% (12635, 67)	41.2% (10779, 54)	80.1% (9113, 49)	
		Total	99.8% (17634, 122)	15.7% (14849, 119)	73.1% (15422, 122)	41.2% (10779, 54)	80.1% (9113, 49)	12.6% (468)

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014 (continued)

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Europe	Ukraine	2008	100% (396, 4)	9.4% (392, 4)	90.6% (392, 4)	83.2% (392, 4)	87.8% (392, 4)	0% (48)
		2009	97.5% (676, 6)	9.7% (659, 6)	81.0% (659, 6)	86.5% (659, 6)	87.7% (659, 6)	8.3% (72)
		2011	100% (1600, 23)	3.5% (1600, 23)	79.1% (1600, 23)	87.1% (1600, 23)	90.2% (1600, 23)	5.8% (276)
		Total	99.4% (2672, 33)	5.9% (2651, 33)	81.3% (2651, 33)	86.4% (2651, 33)	89.2% (2651, 33)	5.6% (396)
South-East Asia	India	2013–2014	100% (11482, 62)		67.8% (9849, 62)	85.2% (11482, 62)		3.6% (744)
		Total	100% (11482, 62)		67.8% (9849, 62)	85.2% (11482, 62)		3.6% (744)
	Indonesia	2007	99.3% (304, 4)	23.7% (304, 4)	58.9% (292, 4)	38.0% (137, 4)	67.6% (136, 4)	
		2012	99.8% (2445, 50)	22.1% (1668, 45)	52.7% (1983, 46)	34.6% (1677, 26)	84.6% (1999, 28)	1.3% (528)
		2013	99.9% (5238, 48)		71.0% (5692, 49)	84.6% (5149, 49)		1.9% (588)
		Total	99.9% (7987, 102)	22.4% (1972, 49)	66.0% (7967, 99)	71.6% (6963, 79)	83.5% (2135, 32)	1.6% (1116)
	Myanmar	2011	100% (1030, 2)	4.8% (1030, 2)	95.2% (1030, 2)	97.7% (1030, 2)		0% (24)
		2012	100% (3109, 22)		82.7% (7699, 22)	96.3% (3109, 22)		0.4% (264)
		Total	100% (4139, 24)	4.8% (1030, 2)	84.2% (8729, 24)	96.6% (4139, 24)		0.3% (288)
	Nepal	2011–2012	100% (325, 3)		79.8% (435, 3)	72.0% (325, 3)		0% (36)
		Total	100% (325, 3)		79.8% (435, 3)	72.0% (325, 3)		0% (36)
	Thailand	2009–2010	99.7% (127851, 916)		84.6% (20060, 897)	91.7% (60520, 894)		
		2010–2011	99.8% (145705, 920)		83.9% (19675, 901)	91.9% (63766, 893)		
		2011–2012	99.9% (159955, 923)		82.1% (20137, 911)	90.6% (67621, 903)		
		2012–2013	99.9% (174268, 926)		82.9% (18102, 896)	91.6% (74112, 907)		
		2013–2014	99.9% (185485, 929)		83.0% (18906, 902)	91.9% (78380, 904)		
		Total	99.8% (793264, 4614)		83.3% (96880, 4507)	91.6% (344399, 4501)		
Western Pacific	Cambodia	2009						0% (408)
		2012					81.4% (2855, 50)	
		Total					81.4% (2855, 50)	0% (408)
	China	2006–2007	100% (258, 4)	4.3% (258, 4)	82.0% (233, 4)	46.9% (258, 4)		
		Total	100% (258, 4)	4.3% (258, 4)	82.0% (233, 4)	46.9% (258, 4)		

Table 2A. Detailed summary of EWI results from 55 countries, 2004–2014 (continued)

Region	Country[1]	Cohort year	Prescribing practices[2]	LTFU[3]	Retention[4]	On-time pill pick-up[5]	On-time appointment keeping[6]	Drug stock outs[7]
Western Pacific	Papua New Guinea	2008	100% (200, 2)	29.5% (193, 2)	79.0% (195, 2)	48.5% (200, 2)		
		2014–2015	100% (143, 1)		50.8% (398, 1)	70.4% (142, 1)		0% (12)
		Total	100% (343, 3)	29.5% (193, 2)	60.0% (593, 3)	57.6% (342, 3)		0% (12)
	Viet Nam	2007	99.6% (1383, 18)	2.6% (1858, 17)	82.0% (1792, 17)		83.0% (1329, 14)	
		2008	99.9% (4577, 27)	5.6% (4531, 27)	79.3% (4303, 27)		89.7% (2547, 25)	
		2009	99.9% (5122, 42)	5.4% (5631, 42)	82.5% (5594, 42)		90.2% (4365, 42)	0% (504)
		2010	100% (5745, 62)	5.6% (5942, 62)	81.7% (5906, 62)		86.2% (6837, 61)	0% (744)
		2011	100% (7326, 83)	6.2% (7022, 83)	82.4% (6999, 83)		86.3% (9048, 82)	1.0% (996)
		Total	99.9% (24153, 232)	5.5% (24984, 231)	81.7% (24594, 231)		87.2% (24126, 224)	0.4% (2244)

[1] Data may not be representative of the country or region reporting.
[2] Percentage of patients prescribed regimens per national guidelines. The numbers in parenthesis are the number of patient records, followed by the number of clinics reporting.
[3] Percentage of patients LTFU 12 months after ART initiation. The numbers in parenthesis are the number of patient records, followed by the number of clinics reporting.
[4] Percentage of patients retained in care 12 months after ART initiation. The numbers in parenthesis are the number of patient records, followed by the number of clinics reporting.
[5] Percentage of patients picking up pills on time. The numbers in parenthesis are the number of patient records, followed by the number of clinics reporting.
[6] Percentage of patients attending scheduled appointments on time. The numbers in parenthesis are the number of patient records, followed by the number of clinics reporting.
[7] Percentage of clinics with stock outs of any routinely dispensed ARV drug. The number of clinics reporting is in parenthesis.
[8] Bolivia (Plurinational State of) reported aggregate data from four clinics serving over 90% of all patients on ART in the country.
[9] South Africa reported data from two provinces.

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

ISBN 978 92 4 151117 9