Target-Setting, Impact and Resource Needs for the Global AIDS Response

Technical consultation on testing and treatment

5-7 December 2018
Geneva, Switzerland

Summary

UNAIDS has recently launched a participatory process for the development of HIV programmatic targets for 2025 and resource needs estimates for 2021–2030. As in past years, the outputs from this process aim to serve as inputs to the next UNAIDS strategy, a possible future United Nations General Assembly High Level Meetings on the global HIV response, Global Fund replenishments, national target-setting and strategic planning and the decision-making of major global partners.

A multi-stakeholder Steering Group is guiding the process, and experts' technical inputs are being made within six consultative thematic groups on (1) testing and treatment, (2) primary prevention, (3) social enablers, (4) costs and resources, (5) integration and (6) longer-term technologies. The HIV testing and treatment consultative group met on 5-7 December 2018 in Geneva, Switzerland. The group was urged to achieve the following over the course of the meeting:

- Describe what testing and treatment would look like (including the introduction and rollout of innovations) within an ambitious AIDS response during the 2021-2030 period.
- Provide advice on how enabling factors interact with testing and treatment programmes.
- Provide advice on bundling of testing and treatment services with primary prevention HIV services and with other health services.
- Propose provisional targets for testing and treatment for 2025 and 2030.
- Propose how scale up to reach targets may differ by country, age/gender and population groups (including key populations).

Over the course of the meeting, participants reviewed progress to date, the models used to estimate the impact of future levels of service coverage, innovations that are currently being evaluated, implemented or are expected to be available in 2025–2030, the importance of social enablers on service coverage and outcomes, and the opportunities and challenges related to the integration of HIV services with the delivery of other health services. Consensus was achieved on the following:

Targets for testing and treatment

- The 2025 targets for both testing and treatment should not differ by country.
- Scale-up trajectories will need to be different. Countries with lower coverage and poorer outcomes should be encouraged to put in place and implement catch-up plans.
- Targets for all sub-populations should be at least 90–90–90 by 2025.

Testing strategies

- Countries need to employ a range of high-volume (e.g. provider-initiated testing and counselling) and high-yield (e.g. assisted partner notification) testing modalities, with a particular focus on:
 - Scaling up approaches for key populations, men and young people.
 - Linking people who test negative to HIV prevention services and people who test positive to treatment.

Treatment interventions

- Dolutegravir (DTG)-containing regimens and injectable antiretrovirals will make important contributions to the effectiveness of treatment in the near future, but will not be sufficient on their own.
- Adherence/retention support (including treatment literacy) is also needed, especially for key populations, other people who are marginalized and mobile populations.
- Reductions in the cost of viral load testing and wider rollout of assays that facilitate quicker return of results are expected to improve progress towards the third 90.
- Differentiated service delivery (DSD) and community-led services will play an important role in improving access to antiretroviral therapy, even beyond stable patients, and should thus be integrated into the modelling.
- Health systems strengthening will be required to manage the additional patient load, and also to avoid antiretroviral stockouts through improved procurement and supply chain management.
- The future frequency of viral load testing for stable patients and the use of 1000 copies/mL as the threshold for viral load suppression should be informed by the WHO guideline revision process during 2019.

Integration

- A careful and detailed unpacking of integration is needed.
- Efforts to integrate HIV services into broader health services should be people-centred focused on increasing access and uptake of quality services, not just achieving cost
- As the "how" and "when" of integration is more clearly defined, additional discussion will be needed on how to incorporate integration into the new set of targets, the expected impact of reaching those targets and the estimation of resource needs.

Introduction and background

Over the past two decades the Joint United Nations Programme on HIV/AIDS (UNAIDS) has played a central role in the development of impact-level and programmatic targets for the global AIDS response, as well as estimates of the financial resources required to reach these targets. UNAIDS estimations of targets, resource needs and impact have informed multi-year strategies for the global response, Global Fund replenishments and three General Assembly high-level meetings. The Fast-Track target-setting and modelling, begun in 2014, focused on the development of 2020 targets that would establish the momentum necessary to achieve the goal of "ending AIDS as a public health

90-90-90

The 90-90-90 targets required particular focus by the testing and treatment technical group. Launched by UNAIDS at the 20th International AIDS Conference in Melbourne, Australia, in 2014, the 90-90-90 targets reflect a fundamental shift in the world's approach to HIV treatment, moving it away from a focus on the number of people accessing antiretroviral therapy and towards the importance of a cascade of services that seek to maximize viral suppression among all people living with HIV. The targets, later included in the Fast-Track commitments made by the United Nations General Assembly in 2016, call on countries to achieve the following by 2020:

- 90% of people living with HIV know their HIV status.
- 90% of people living with HIV who know their status are on treatment.
- 90% of people on treatment are virally suppressed.

The targets have been largely successful in putting additional focus on HIV testing, linkage to care and helping people on treatment to achieve and sustain viral suppression. However, concerns have been expressed that 90–90–90 has become synonymous with Fast-Track, subsuming the other critical targets on HIV prevention and critical enablers such as human rights.

threat", which is defined in the 2030 Agenda on Sustainable Development as a 90% reduction in new HIV infections and AIDS-related deaths, compared to 2010 baseline estimates.

This modelling analysis determined that a "Fast-Track" approach was needed: a front-loading of investments to rapidly accelerate programme coverage and reach a set of targets by 2020 including the 90-90-90 testing and treatment targets¹, 95% coverage of services to prevent mother-to-child transmission of HIV, and access to a package of HIV prevention services to at least 90% of key populations.² Annual financial resources needed for this Fast-Track response for all low- and middle income countries (LMICs) peaked in 2020 at US\$26.2 billion—including US\$7.4 billion in low-income countries, US\$8.2 billion in lower middle-income countries and US\$10.5 billion in upper-middle-incomecountries—before declining approximately 9% by 2030. This resource needs estimate included savings of up to 35%; future efficiencies generated by economies of scale, price reductions and other technical and allocative efficiencies. The outputs of the model served as the basis for the UNAIDS 2016-2021 Strategy and the commitments within the United Nations General Assembly's 2016 Political Declaration on HIV/AIDS.3

New round of target-setting and resource needs estimation

From late 2018 to the middle of 2021, programmatic targets for 2025 and resource needs estimates for 2021–2030 will be developed by UNAIDS in close collaboration with its partners. As in past years, the outputs are timed to serve as inputs to the next UNAIDS strategy, a possible future United Nations General Assembly High Level Meetings on the

¹ 90% of people living with HIV know their status; 90% of people living with HIV who know their status are on treatment; and 90% of people on treatment are virally suppressed.

² Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD et al. What Is required to end the AIDS epidemic as a public health threat by 2030? The cost and impact of the Fast-Track approach. PLoS ONE. 2016;11(5):e0154893. doi:10.1371/journal.pone.0154893.

³ Fast-Track commitments to end AIDS by 2030. Geneva: Joint United Nations Programme on HIV/AIDS, 2016 (http://www.unaids.org/sites/default/files/media_asset/fast-track-commitments_en.pdf).

global HIV response, Global Fund replenishments, national target-setting and strategic planning and the decision-making of major global partners.

The multi-stakeholder Steering Committee guiding the process held its first face-to-face meeting on 10-12 October 2018 to define the scope of its work, to establish technical groups to inform the process, and to develop a plan for the dissemination of the outputs of the process. The Steering Committee's decisions on various operational and technical issues are contained in the report of its first meeting. Of particular note were decisions to focus the process on:

- Defining what is needed to reach the 2030 impact goals and guide countries to more efficiently and effectively achieve them.
- Setting programmatic targets to achieve high coverage of accessible and quality bundles of people-centred services.
- Ensuring that the contribution of social enablers and their costs are included in the target-setting and resource needs estimation.
- Capturing synergies between the HIV response and other health and development efforts.
- Project the impact of the introduction of new technologies on new HIV infections and AIDSrelated deaths.

Testing and treatment consultative group

Among the decisions was for pairs of Committee members to co-chair technical consultative groups on six thematic areas: (1) testing and treatment; (2) primary prevention; (3) social enablers; (4) costs and resources; (5) integration; and (6) longer-term technologies.

The main outputs of the technical groups may include, depending on the topic:

- An updated inventory of services with proven impact in the HIV response, including state-of-theart interventions, innovative approaches that will be rolled out during the 2020–2030 period, and those that will become available during 2030-2050.
- Identification and incorporation of newer methods to assess the impact of non-biomedical interventions, including the role of advocacy, social media, human rights enforcement and community engagement in increasing meaningful access to critical services.
- Exploration of the increased use of combination/bundled approaches to prevention, testing, treatment and support.
- Link service provision and social enablers.
- Identify synergies between HIV service delivery and efforts to deliver other health and social services.
- Propose ambitious yet feasible targets for 2025.
- Calculate the impact of reaching these targets by determining the size of populations, coverage
 of services within these populations and the effectiveness (impact on incidence and mortality) of
 each service.
- Update unit costs for service delivery, including feasible allocative, technical and productive efficiencies.
- Estimate resource needs, based on the targets, populations sizes and unit costs.
- Develop peer-reviewed scientific papers on the above topics, as appropriate.

The first technical consultative group, focused on HIV testing and treatment, was convened on 5-7 December 2018 in Geneva, Switzerland. The meeting was chaired by two Steering Committee members, Wafaa El-Sadr, Director of ICAP at Columbia University, and Omar Syarif, Treatment

Access Specialist Programme Manager of the Global Network of People Living with HIV (GNP+). Group members included experts from government programmes, civil society, research consortia and UNAIDS Cosponsors (see participants list).

Objectives of the meeting

At the start of the HIV testing and treatment consultative group meeting, the UNAIDS Secretariat briefed group members on the state of the HIV epidemic and the global response. It was noted that progress has been uneven. A growing number of countries have reached or are on track to reach the 90–90–90 testing and treatment targets, with particularly strong progress recently achieved in eastern and southern Africa. However, most countries will likely not achieve 90–90–90 by 2020, including the entire regions of western and central Africa, eastern Europe and central Asia and Middle East and North Africa. Progress is also uneven within countries. Service coverage and outcomes across the HIV testing and treatment cascade are often lower for children, young people, men and key populations at higher risk of HIV infection.

The Secretariat also briefed the group on the background of the target-setting process and the first meeting of the Steering Group. Reflecting the direction set by the Steering Group, the testing and treatment group was urged to achieve the following over the course of the meeting:

- Describe what testing and treatment would look like (including the introduction and rollout of innovations) within an ambitious HIV response during the 2021-2030 period.
- Provide advice on how enabling factors interact with testing and treatment programmes.
- Provide advice on bundling of testing and treatment services with primary prevention HIV services and with other health services.
- Propose provisional targets for testing and treatment for 2025 and 2030.
- Propose how scale up to reach targets may differ by country, age/sex and population groups (including key populations).

Group members discussed the heterogenous performance to date, including the particular challenges in western and central Africa and efforts to address them through a catch-up plan that aims to address bottlenecks, accelerate service delivery and reach a trajectory to achieve the 90–90–90 targets by 2020. It was stated that it would be useful to examine the experiences of strong-performing countries and distil them into advice for other countries. The HPTN 071 (PopART) trial has showed that first two 90s can be achieved in urban settings of southern Africa through annual interventions and health-care referrals by community health workers.

It was also noted that many—including modellers—initially reacted to the 90–90–90 targets with scepticism. Reaching them by 2020 did not appear feasible. But the fact that several countries have achieved the targets attests to the power of ambitious targets.

Expert advice

The STAC

The UNAIDS Scientific and Technical Advisory Committee (STAC) on 90–90–90 has supported UNAIDS efforts to advocate and provide advice to countries as they scale up HIV testing and treatment services and reach the 2020 targets. The STAC was asked to provide inputs to the target-setting and resource needs estimate process, and a summary of discussions from the last two meetings of the STAC were presented to the group.

The STAC called on the group to build on the 90–90–90 targets, and it considered several options for 2025 and 2030 targets. These options included:

- A simple target focused on a downstream outcome (e.g. 85% of people living with HIV achieve viral suppression).
- Breaking the three 90s into smaller pieces, such as individual targets for various modalities of HIV testing.
- A "90–90–90 plus" approach, with the "plus" potentially defined in a number of ways, such as including comprehensive HIV prevention, community engagement and/or optimized access to services for underserved sub-populations. The "plus" could also be interpreted to mean "more than 90".

The STAC acknowledged the differential achievement among countries and within countries to date, but it strongly disagreed with the possibility of adopting lower targets for poorer performing countries or regions, or for under-served sub-populations. It also supported the development of targets that would facilitate linkages among HIV prevention, testing and treatment services, and the integration of HIV services with other health services. It also called on the target-setting and resource needs estimation process to build investment cases for each of the three 90s or any newly developed targets.

Group members generally agreed with the STAC's analysis. The 90–90–90 targets have helped to galvanize action and accelerate progress, but they are not perfect. For example, these targets have inadvertently perpetuated a false divide between prevention and treatment. In addition, although the targets are meant to be achieved within each sub-population, the need for equitable achievement has not been explicit. Even in countries that are achieving 90-90-90, there are clear differences between the 90% who are being reached and the 10% who are being left behind. Moving forward it will be important to encourage countries to look at the 10% who are not being reached and address inequities. Many felt that differentiated targets—either among regions or countries or sub-populations—could perpetuate inequity. There were calls for specific targets for key populations, and efforts to ensure that HIV testing and treatment services are available and accessible across the lifespan, from infancy to old age.

Concern was also expressed by the group that the third 90 target for viral suppression has sometimes been misunderstood as a target for viral load testing coverage. Some members expressed concern that investment in viral load testing was too high relative to other aspects of HIV treatment service delivery. However, others warned that viral load testing was critical to rapid diagnosis of treatment failure, and that there is a real danger that drug resistance among people living with HIV will increase in the future, even if progress continues in other areas of the testing and treatment continuum.

There was a clear call for efforts to measure and ensure the quality of testing and treatment services. It was noted that the integration of HIV services with other health services is overwhelmingly viewed as a good thing as the world moves towards universal health coverage. However, integration does not always lead to better outcomes (see section on integration below).

World Health Organization

Rachel Baggaley and Meg Davis from the World Health Organization (WHO) presented the latest normative guidance on HIV testing and treatment, the evidence that has informed WHO guidelines, and the ongoing reviews of evidence and consultations that could lead to changes in WHO guidelines in the near future.

HIV testing programme data show that a mixture of facility-based and community-based testing modalities are needed to achieve 90% of all people living with HIV knowing their HIV status. All the tools required to reach this target are available, as evidenced by the range of countries that have achieved the first 90 or are on track to achieve the target by 2020. Partner notification and self-testing are under-used modalities in many countries, and there are other untapped opportunities to diagnose people living with HIV in health facility settings. For example, in some countries patients receiving services for sexually transmitted infection (STI) clinics, tuberculosis and antenatal care are not routinely tested for HIV. Linkages from testing to other HIV services are critical: initiation of treatment and partner notification for people who test positive, and linkage to prevention services (condoms, PrEP, VMMC, etc) for people who test negative. WHO also recommends additional focus on critical enablers for HIV testing—including stigma reduction, community empowerment, violence prevention and supportive laws and policies—as well as better use of data and increased focus on reaching key populations at high risk of HIV.

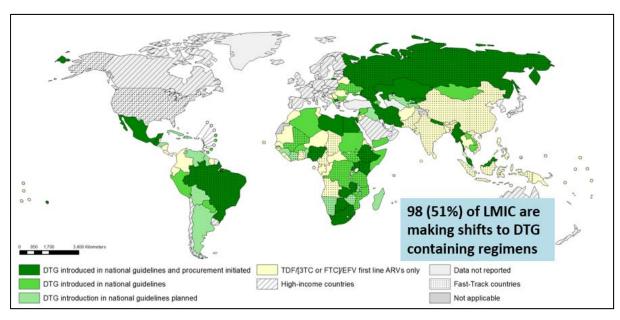


Figure 1. Transition to DTG, by country, July 2018

WHO guidelines for the immediate initiation of antiretroviral therapy after an HIV positive test, regardless of CD4 count, have been adopted by 84% of low- and middle-income countries and 100% of Fast-Track countries. However, not all of the countries that have adopted a treat-all policy have put that policy into practice. As resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) increases, WHO recommends the integrase strand transfer inhibitor (INSTI) Dolutegravir (DTG) as the preferred first-line treatment regimen (with a note of caution regarding women who

plan to become pregnant because of evidence of potential increased neural tube defects). Just over half of low- and middle-income countries are in the process of shifting to first-lines containing DTG (Figure 1). Efforts to develop paediatric, PEP, second-line and third-line regimens containing DTG are ongoing. Additional molecules—including new NNRTIs, nucleoside reverse transcriptase inhibitors (NRTIs) and entry blockers—have also been recently approved for clinical use.

Moving forward, WHO is increasingly viewing HIV treatment through the lens of universal health coverage. In addition, efforts to update HIV treatment guidelines based on the latest research and programme evidence may result in adjustments to the recommended viral load testing algorithm and revised recommendations for the treatment of HIV-associated tuberculosis.

Differentiated service delivery

Efforts to implement and scale-up <u>differentiated service delivery (DSD)</u> models were presented by Wafaa El-Sadr. DSD is a client-centred approach that simplifies and adapts HIV services to reflect the variety of preferences and expectations of people living with HIV, while reducing unnecessary burdens on the health system. Most DSD models to date have focused on stable patients, who have been on treatment for at least a year and have evidence of high adherence and/or viral load suppression. These patients are channelled into a variety of models, which are either individual or group-based, and are situated either at health facilities or in the community (Figure 2). These models aim is to improve clinical outcomes, improve the experiences of both patients and health-care workers, enhance the capacity of the health system to engage more people living with HIV, and reduce costs. They also allow health care workers to focus on patients who are not doing so well.

The Coverage, Quality and Impact Network (CQUIN), funded by the Bill and Melinda Gates Foundation, engages with ministries of health in sub-Saharan African countries and aims to support them in scale-up of various DSD models.

Figure 2. Illustrative DSD models for stable patients

	Individual	Group
Facility-based	Fast track Appointment spacing	ART clubs Teen clubs Family pick up
Community-based	Outreach model PODI model	Community ART Groups (CAGs)
		www.differentiatedcare.org

Modelling

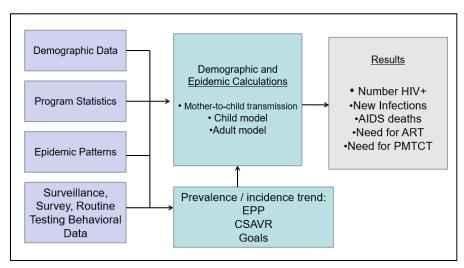
Efforts to refine HIV epidemic and response estimates modelling based on the latest available data were summarized in presentations by John Stover from Avenir Health, Jeffrey Eaton from Imperial

College London⁴ and Christophe Fraser on behalf of Oxford BDI Pathogen Dynamics, HPTN 071 (PopART) and the PANGEA-HIV consortium.

Spectrum and Goals

Avenir Health's Spectrum and Goals models will play a central role in the target-setting and resource needs estimate process. Spectrum uses demographic, programme and survey data to produce estimates of the number of people living with HIV, annual new HIV infections, annual AIDS-related deaths and the numbers of people in need of antiretroviral therapy and services for the prevention of mother-to-child transmission (Figure 3). It looks backwards in time. Recent model outputs for HIV incidence, HIV prevalence and treatment coverage are consistent with population-based HIV impact assessments (PHIAs), strengthening confidence in the accuracy of the estimates. However, the viral load suppression data from the PHIAs are somewhat higher than anticipated. Nonetheless, the modelled impacts of antiretroviral therapy on AIDS mortality are consistent with population mortality data.

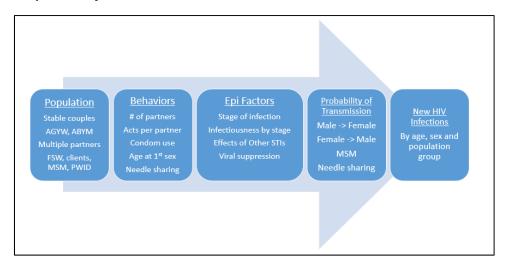
Figure 3. Inputs and outputs of the Spectrum model



The Goals model projects these same outputs forward based on future service coverage and behaviours among various population groups (Figure 4). HIV programme managers can use the Goals model to estimate the impact of various mixes of services as they aim to achieve the most impact with the available human and financial resources. A new HIV testing module is being developed for Goals. This model can help countries refine their mix of HIV testing modalities and improve efficiency, but there is no "optimize button" that will determine the most efficient mix for the user. Early outputs from the model suggest that after the first 90 has been achieved, it may be possible to cut back on HIV testing (especially high-volume, low-yield modalities such as voluntary counselling and testing sites) and still maintain the first 90. This would significantly reduce the cost of HIV testing. However, scaling back VCT in favour of a less expensive modality, such as self-testing, could reduce the availability of services. The modelling group will need guidance on whether this is indeed a viable strategy that should be encouraged in the new set of targets.

⁴ With support from Tim Hallett, Leigh Johnson, Matthias Egger, Nina Anderegg, the UNAIDS Reference Group on Estimates, Modelling and Projections, IeDEA Collaboration, ART-CC and ALPHA Network.

Figure 4. Components of the Goals model



<u>Treatment impact on mortality</u>

An important question moving forward is whether AIDS-related mortality rates will continue to decline or not. Estimates of AIDS-related mortality are derived from data from longitudinal studies of treatment cohorts. The data consistently and clearly show that considerable scale up of antiretroviral therapy over the last 15 years has led to a steep decline in AIDS-related deaths. The data also show that the biggest gains have already been made. The impact of antiretroviral therapy on mortality rates has been declining in recent years and may be levelling off. An increasing proportion of death among people living with HIV is not related to AIDS. At the same time, data from South Africa show that a growing number of patients in the country are interrupting treatment. Projections suggest that a growing percentage of AIDS-related deaths globally will be among those who interrupt treatment. During discussion it was noted that a substantial number of patients globally are lost to follow up, and among them many have died. The difficulty of tracking patients in low- and middle-income countries—for example if they interrupt treatment at one health facility and re-start in another facility—and weaknesses in the vital registration systems of many countries introduce uncertainty into mortality estimates. It will be important to gather additional data to better understand mortality trends among people living with HIV in order to improve estimates and projections.

<u>Treatment as prevention</u>

The evidence is conclusive about "U=U". People with an undetectable viral load will not transmit HIV. At a population level, available data show a "dose response" between antiretroviral therapy and HIV incidence—increasing the former reduces the latter. This impact is also reflected in models, informed by treatment coverage and viral load testing data.

Recent data from Rakai, Uganda, also confirms that voluntary medical male circumcision (VMMC) has an additive population-level prevention effect, and also that this treatment-plus-VMMC combination has (at least initially) a greater preventative benefit for men compared to women.⁵ Available data also suggest that the preventative impact of treatment at the population level is lower for people at high risk of HIV transmission. Model structures are designed to capture these nuances, but data are sparse and hard to quantify.

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⁵ Grabowski MK et al. HIV prevention efforts and incidence of HIV in Uganda. N Engl J Med, 2017;377:2154–66.

The prevailing transmission patterns in high-prevalence settings have been difficult to pin down. Phylogenetic data are being used to shed light on cycles of transmission and to inform ways to break them. Phylogenetic data from Kwa-Zulu Natal has suggested a "renewal cycle" of HIV transmission, where adult men acquire HIV from adult women of the same age, and then pass on their infections to younger women. As those younger women age, the cycle repeats. However, other phylogenetic data currently being analysed by PANGEA-HIV show a different "asymmetric cycle" of HIV transmission, where "youngish" adult men (aged 20 to mid-40s) transmit HIV to two "youngish" adult women (aged 18 to mid-40s), then one of the women passes on the infection to one adult man, and then the cycle repeats (Figure 5). These preliminary findings suggest that efforts to reach adult men within this age range in high-prevalence settings could accelerate incidence declines.

Modelling questions

As testing and treatment gaps close, there is increasing programmatic focus on achieving and sustaining viral suppression: for the health of the recipient of care, for prevention of HIV transmission and for the prevention of drug resistance. But there are limited data on the effectiveness of social enablers and various interventions that aim to improve HIV testing, treatment uptake and treatment adherence. The modelling group for the target-setting/resources needs process would like the testing and treatment group to answer the following questions:

- How to incorporate barriers (e.g. stigma) and enablers (e.g. efforts to address stigma)?
- How to incorporate quality of care?
- How to bring in other nuances of the dynamics of treatment, such as adherence, drug resistance and treatment failure?

During discussion there were a variety of views. Some felt that adherence interventions have minimal impact on viral suppression, and that drug stockouts were a bigger factor in treatment interruption. Others raise the issue of quality of care and the integration of HIV and tuberculosis services, as many people living with HIV are still dying of tuberculosis.

Innovations

The target-setting and resource needs process has the difficult challenge of predicting the speed and impact of the rollout of HIV response innovations. To inform this aspect of the process, Carl Dieffenbach, Director of the Division of AIDS at the U.S. National Institute of Allergy and Infectious Diseases, presented on the advances in approaches, molecules, regimens, diagnostics and monitoring that are expected to be available between 2025 and 2030.

Significant advances are expected in HIV, tuberculosis, hepatitis C (HCV) and hepatitis (HBV) treatment and prevention. These include long-acting PrEP and antiretroviral therapy, a tuberculosis vaccine, improved chemoprophylaxis as well as treatments for multi-drug-resistant and extensively drug-resistant tuberculosis. The availability of an effective HIV vaccine is less likely, with 2027 being the soonest possible availability for implementation. Diagnostic improvements expected in the coming years include additional point-of-care options that will enable data capture on smart

⁶ De Oliveira T et al. Transmission networks and risk of HIV infection in KwaZulu-Natal, South Africa: a community-wide phylogenetic study. Lancet HIV 2017; 4: e41–50. 30 November 2016. http://dx.doi.org/10.1016/ S2352-3018(16)30186-2.

phones/watches and viral load self-testing. The impact of all these tools, if they are indeed ready by 2025, will depend on countries willingness to adopt them and bring them to scale.

HIV attaches to a CD4 cell HIV enters a CD4 cell and HIV proteins and enzyme are released into the cell fostemsavir UB-421 (OD4 receptor) Reverse transcriptase (RT makes double strand HIV (GSK3732394) VRC01 (004 receptor) 3BNC117 and 10-1074 Integrase enables HIV to PGDM1400_{and}PGT121 join the cell DNA 10E8.4/iMab Protease cuts and reassembles new HIV. Each cell produces hundreds of new virions PRO-140 (00H EFdA (MK-8591) 3 GS-PS1

GS-CA1

GSK3640254

Figure 5. Targeting HIV throughout its lifecycle

Various drugs for HIV treatment that target the virus across its lifecycle (Figure 5) could be available by 2025, including capsid inhibitors, cell entry inhibitors, nuclear entry inhibitors, the next generations of INSTIs and immunotherapeutics. Adherence could be improved by a range of delivery (e.g. patches) and duration (e.g. injectables) innovations. Early experience with long-acting formulations suggest that fears of patient not returning for second or third doses have been overstated—a big drop-off was expected, but so far it seems that adherence is strong. During discussion, participants expressed concerns about safety windows for re-dosing and the long tail for long-acting PrEP. It was also noted that widespread rollout of these innovations will be dependent on their price, which could be more quickly lowered by the manufacture of generic varieties.

As health systems move towards UHC, it is important to make services available across the lifespan, from infants to children to adolescents to adults to older age. For the latter, efforts are ongoing to determine whether adding a statin to antiretroviral therapy regimens could improve outcomes for older people living with HIV, especially older women who tend to have higher incidence of cardiovascular disease.

Social enablers

From the community perspective, testing and treatment programmes are truly effective when they provide high quality services that are available, accessible, affordable and acceptable for all in need. Solange Baptiste, executive director of the International Treatment Preparedness Coalition (ITPC), stressed in a presentation that the reality at present falls short of this standard effectiveness. People living with HIV and key populations face a range of challenges across the testing and treatment cascade, including:

- Poverty-related barriers (unemployment, poor nutrition, etc)
- Poor service quality
- Inconvenience and high opportunity costs (long travel and wait times)

- Cost barriers—even when antiretrovirals are free, patients need to pay for travel costs, diagnostics, doctor's fees and so much more.
- Treatment illiteracy
- Stockouts
- Legal and policy barriers (e.g. criminalization)
- Stigma and discrimination

Social enablers may address these barriers. Community-led interventions are widely recognized by the international community as critical providers of services that address the individual health, social and behavioural barriers to services, but investment in community groups is sporadic, project-based and donor-dependent. Long-term investments are needed in community health and treatment education.

Treatment education is often misunderstood as a narrow, short-term effort to inform newly

Examples of informed questions about antiretrovirals

- How will this pill affect my other medications?
- What does my viral load test result mean?
- Do I still need to know my CD4 cell count?
- Can I get the pill for PrEP?
- At what viral load can I stop using a condom with my partner?
- I may have to shift to 2nd line, does this mean that I am drug resistant?
- Can I still get DTG even though I am planning to have a baby?
- What are my contraceptive options?
- I get more side effects if I don't eat when I take my medicines, but I sometimes I have only one meal per day – Is that OK?
- Can I give half of my pill to my daughter since the pediatric meds are out of stock?

diagnosed people living with HIV about what pills to take and when. Effective treatment education is broader and longer-term, helping patients to ask informed questions as they navigate a lifetime of treatment (see box). But in this test-and-start era, an ITPC global treatment access survey found that more than one third of people living with HIV reported that their healthcare professional did not give them enough time to think about if they were ready to start treatment, much less ask informed questions.

As well as an impassioned call to define and then support a robust community response, Baptiste called for as much data disaggregation as possible, and then setting service coverage targets that would not target people but still make it difficult for health systems to take a one-size-fits-all approach to case finding or to ignore the wrap-around services that are needed for high coverage and high adherence.

During discussion the huge service barriers faced by key populations were emphasized, such as the criminalization and imprisonment of gay men in sub-Saharan Africa. It was also agreed that poverty-related factors are significant barriers to HIV services, but that it will be difficult for the target-setting process to include poverty-reduction efforts within its package of services. Moving forward into the next session, the participants pondered the question: "What should the HIV response pay for?"

Integration

The 2016 Political Declaration on HIV/AIDS was the first to include a commitment to strengthen health systems through integration of HIV programmes into primary health care, sexual and reproductive health-care services and specialized infectious disease services, and to include targets for treatment of tuberculosis, cervical cancer and hepatitis B and C. This effort to "take AIDS out of isolation" is consistent with the findings of the IAS-Lancet Commission, which called for HIV services to be co-located with broader health services "where possible, with the aim of improving both HIV-related and non-HIV-specific health outcomes". The Commission stressed that greater integration of HIV and global health "must preserve and build on key attributes of the HIV response, including participatory community and civil society engagement and an ironclad commitment to human rights, gender equality, and equitable access to health and social justice".

The 2025 target-setting/resource needs estimation process has at least two integration-related challenges to address:

- The integration of HIV and non-HIV services, which aims to achieve economies of scale and/or economies of scope through technical or allocative efficiencies.
- The bundling or packaging of HIV prevention, testing and treatment services to improve linkages and overall HIV-related outcomes.

During discussion it was noted that key populations at highest risk of HIV infection often don't access mainstream health services. An alternative approach would be to build client-centred platforms for the delivery of multiple health and HIV services to these populations. Similarly, past efforts to integrate the tuberculosis programme into the broader health system in Zambia and other countries were associated with poorer TB outcomes. If the primary health care system is weak, it may not be wise to integrate a disease response into it. Investment in primary health care is needed as well, and it's not clear where that funding should come from. The HIV response? The complications of costing integrated services could be done through two approaches:

- Take a proportion of the full integrated service cost and assign it to HIV.
- Assign the full cost to HIV, but also the full benefit of the service (both HIV and non-HIV).

The consensus was that one needs to be cautious about integration—it shouldn't be done simply for integration's sake. Integration should be done for a purpose: to improve the functioning of the health system; to improve outcomes for the patients; and to improve efficiency.

Way forward

The meeting concluded with group work sessions followed by group presentations and discussions that aimed to achieve consensus on the outputs of the meeting. These sessions were guided by the following questions:

- HIV testing
 - Should targets and the rate of scale up of testing differ by country, population, age and/or sex?
 - o What should be the upper limits of the targets?
 - o What are the testing strategies that should be pursued in different situations?
- HIV treatment

- Should targets and the rate of scale up of testing differ by country, population, age and/or sex?
- For countries or groups that have achieved the second 90 by 2020, what should their target be for 2025?
- o What interventions are required to achieve the viral suppression target?
- Will Dolutegravir and injectable treatment be part of a future response, and will their availability (or non-availability) affect the feasibility to achieve target sand effectiveness?
- o How will DSD likely evolve over 2020-2030 given current assumptions?
- What is the likely time-course of linkage to treatment for those found to be living with HIV for different population groups?

Targets for testing and treatment

There was consensus that 2025 targets for both testing and treatment should not differ by country. Because progress has been uneven to date, scale-up trajectories will need to be different. Countries with lower coverage and outcomes should be encouraged to put in place and implement catch-up plans. Targets for sub-populations should be at least 90–90–90 (see box). As coverage for several sub-populations is likely to remain below the national average, the effect of reaching the 90s for each sub-population would likely be an aggregate that exceeds 90–90–90 and potentially approaches or even achieves 95–95–95.

It was not clear whether the three 90s were sufficient targets for testing and treatment, or whether additional, operational-level targets would be needed to guide countries to put in place the range of facility-based and community-based service delivery mechanisms and support systems required to achieve high levels of service coverage (outputs) and outcomes.

Testing strategies

Sub-populations for target-setting

- Key populations (people who inject drugs, transgender people, sex workers, incarcerated people and gay men and other men who have sex with men)
- Men and women under the age of 35
- Men and women aged 35 and over
- Children (<13, but recognising the fluidity of this definition)
- Sub-national (as defined and appropriate for the country)
- Pregnant women (95% target)

There was consensus that the target-setting and resource needs process should capture the need for countries to employ a range of high-volume (e.g. provider-initiated testing and counselling) and high-yield (e.g. assisted partner notification) testing modalities that match the epidemic situation, with a particular focus on:

• Scaling up approaches for key populations, men and young people.

• Linking people who test negative to HIV prevention services and people who test positive to treatment.

The group felt that more information was needed before making a recommendation on whether voluntary counselling and testing could be scaled back or replaced by other strategies such as self-testing after a country achieves the first 90.

Treatment interventions

The group agreed that DTG and injectables are likely to make important contributions to the effectiveness of treatment in the near future, but that these bio-medical innovations will not be sufficient on their own. Adherence/retention support (including treatment literacy) is also needed, especially for key populations, other people who marginalized and mobile populations. Reductions in the cost of viral load testing and wider rollout of assays that facilitate quicker return of results will be important factors in improving progress towards the third 90. DSD is expected to play an important role in improving the accessibility of antiretroviral therapy, even beyond stable patients, and there were consistent calls for community-led services to be integrated into the target-setting/resource needs estimation process. Health systems strengthening will be required to manage to the additional patient load, and also to avoid stockouts through improved procurement and supply chain management.

The group was less certain about the future frequency of viral load testing for stable patients and the use of 1000 copies/mL as the threshold for viral load suppression; something that will need to be informed by the WHO guideline process over 2019. There was also lingering concern about the long tails of long-acting injectable antiretrovirals, and whether the use (or perhaps misuse) of injectables could lead to the development of drug resistance.

Integration

The group called for a more careful and detailed "unbundling" of integration, as the term can be used to mean so many things. There was strong consensus that efforts to integrate HIV services into broader health care should ensure that such services are people-centred—focused on increasing access and uptake of quality services, not just achieving cost efficiencies. Integration should increase coordination and collaboration across the various levels of the health system, including community-led services.

As the "how" and "when" of integration is more clearly defined, additional discussion will be needed on how to incorporate integration into the new set of targets, the expected impact of reaching those targets and the estimation of resource needs. For example, will the costs of integrated services be shared across vertical disease programmes? Or will the HIV response pick up all the costs of integrated services, and then also be credited for all the results?