World Health Organization

GUIDELINES

UPDATED RECOMMENDATIONS ON

SERVICE DELIVERY FOR THE TREATMENT AND CARE OF PEOPLE LIVING WITH HIV

APRIL 2021

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Updated recommendations on service delivery for the treatment and care of people living with HIV

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II. ABBREVIATIONS AND ACRONYMS

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
CI	confidence interval
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HIV	human immunodeficiency virus
HR	hazard ratio
OR	odds ratio
RR	relative risk
SRHR	sexual and reproductive health and rights
TB	tuberculosis

III. DEFINITION OF KEY TERMS

Advanced HIV disease

For adults, adolescents and children five years and older, advanced HIV disease is defined as a CD4 cell count <200 cells/mm^3 or a WHO clinical stage 3 or 4 event at presentation for care. At presentation, all children living with HIV younger than five years should be considered as having advanced disease.

Age groups

The following definitions are used in these guidelines for the purpose of implementing recommendations for specific age groups. It is acknowledged that countries may have other definitions under national laws:

- An adult is a person older than 19 years of age (which includes young people 20–24 years old).
- An adolescent is a person 10–19 years of age inclusive.
- A child is a person one year to younger than 10 years of age.
- An infant is a child younger than one year of age.

Differentiated service delivery

An approach that simplifies and adapts HIV services to better serve the needs of people living with HIV and to optimize the available resources in health systems.

Integrated service delivery

Integrated health services are health services that are managed and delivered in a way that ensures people receive a continuum of health promotion, disease prevention, diagnosis, treatment, disease management, rehabilitation and palliative care services, at the different levels and sites of care within the health system and according to their needs, throughout the life course.

People-centred care

Care that is focused and organized around the health needs and expectations of people and communities rather than on diseases.

Key populations

Key populations are groups that have a high risk and disproportionate burden of HIV in all epidemic settings. They frequently face legal and social challenges that increase their vulnerability to HIV, including barriers to accessing HIV prevention, treatment and other health and social services. Key populations include men who have sex with men, people who inject drugs, people in prisons and closed settings, sex workers and transgender people.

Rapid ART initiation

Initiation of ART within seven days of HIV diagnosis.

Vulnerable populations

Vulnerable populations are groups of people that are vulnerable to HIV infection in certain situations or contexts, such as infants, children and adolescents (including adolescent girls and young men in sub-Saharan Africa), orphans, people with disabilities and migrant and mobile workers. They may also face social and legal barriers to accessing HIV prevention and treatment. These populations are not affected by HIV uniformly in all countries and epidemics and may include key populations. Each country should define the specific populations that are vulnerable and key to their epidemic and response, based on the epidemiological and social context.

IV. EXECUTIVE SUMMARY

WHO promotes a public health approach to programming and delivering antiretroviral therapy (ART), which has enabled access to treatment and care for people living with HIV to be scaled up in resource-limited settings.

The 2016 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection include a chapter that provides several recommendations for delivering HIV services across the cascade of care from HIV testing to long-term viral suppression.

These guidelines update provide updated recommendations and good practice statements in the following areas: starting ART, including initiating treatment outside the clinic and support for same-day ART start; frequency of clinical visits and ART refills; measuring adherence; tracing and re-engagement in care; psychosocial support for adolescents living with HIV; task sharing for diagnostic services; and service integration.

These guidelines were developed in accordance with procedures established by the WHO Guidelines Review Committee. The recommendations in the guidelines are based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to reviewing evidence and formulating recommendations.

The primary audience for these guidelines is national HIV programme managers and policy-makers in low- and middle-income countries. These updated guidelines will be a useful resource for clinicians and should help to shape the priorities of policy-makers in development agencies, international organizations, nongovernmental organizations and other implementing partners. These guidelines will also be of value to people living with HIV, communities and civil society organizations that will need to be engaged meaningfully to support their successful implementation.

These recommendations are intended to encourage continued improvements in access to ART, simplify care delivery for providers and end users and support return to care for those who have disengaged. Implementing these recommendations within the overall public health approach is anticipated to support further reductions in the number of people acquiring HIV and the number of people getting sick and dying from HIV-associated causes. The recommendations developed for these and other relevant guidelines developed since 2016 will be integrated with the updated consolidated HIV guidelines in 2021.

Many individuals contributed to the development of these guidelines including people living with HIV and representatives from affected communities, from ministry of health, researchers, implementers, and health care providers. WHO would like to acknowledge and thank the numerous contributors to these guidelines that were developed during the COVID-19 pandemic and will continue to engage with the global HIV community and Member States to ensure the continuity and quality of care for people living with HIV during and beyond the COVID-19 pandemic.

Summary of new recommendations

The following tables present the recommendations, including the strength of the recommendation and certainty of the evidence, as well as the good practice statements included in these guidelines. Clicking the hyperlink will take you straight to that section.

Recommendations

Recommendation	Update or new	Link to section
ART initiation may be offered outside the health facility *(Conditional recommendation; low- to moderate-certainty evidence)*	New	Section 3
People established on ART should be offered clinical visits every 3–6 months, preferably every six months if feasible *(Strong recommendation; moderate-certainty evidence)*	Update[a]	Section 5
People established on ART should be offered refills of ART lasting 3–6 months, preferably six months if feasible *(Strong recommendation; moderate- to low-certainty evidence)*	Update[b]	Section 5
HIV programmes should implement interventions to trace people who have disengaged from care and provide support for re-engagement *(Strong recommendation; low-certainty evidence)*	New	Section 6
Sexual and reproductive health services, including contraception, may be integrated within HIV services *(Conditional recommendation; very-low-certainty evidence)*	Update[c]	Section 8.1
Diabetes and hypertension care may be integrated with HIV services *(Conditional recommendation; very-low-certainty evidence)*	New	Section 8.2
Psychosocial interventions should be provided to all adolescents and young adults living with HIV *(Strong recommendation; moderate-certainty evidence)*	New	Section 9
Task sharing of specimen collection and point-of-care testing with non-laboratory personnel should be implemented when professional staffing capacity is limited *(Strong recommendation; moderate-certainty evidence)*	Update[d]	Section 10

[a] Updated from a strong recommendation made in 2016 that was based on moderate-certainty evidence. The evidence supporting this recommendation has been re-assessed but the recommendation itself has not changed.

[b] Updated from a strong recommendation made in 2016 that was based on low-certainty evidence. The evidence supporting this recommendation has been re-assessed but the recommendation itself has not changed.

[c] Updated from a conditional recommendation made in 2016 that was based on very low-certainty evidence.

[d] Updated from a good practice statement made in 2016.

Good practice statements

Good practice statement	Update or new	Link to section
Health systems should invest in people-centred practices and communication, including ongoing training, mentoring, supportive supervision and monitoring of health workers, to improve the relationships between patients and health-care providers.	New	Section 2
The offer of same-day ART initiation should include approaches to improve uptake, treatment adherence and retention, such as tailored patient education, counselling and support.	New	Section 4
Viral load for treatment monitoring should be complemented with non-judgemental, tailored approaches to assessing adherence.	New	Section 7
Disease programmes, especially those related to HIV and TB, should actively work towards balanced integration of diagnostic services.	New	Section 11

1. BACKGROUND

WHO's public health approach to delivering antiretroviral therapy (ART) has enabled access to treatment and care for people living with HIV to be scaled up, with an estimated 67% of people living with HIV receiving ART in 2020 – 25.4 million of 38 million people living with HIV, up from 7.8 million in 2010 *(1)*.

To reinforce the delivery of ART at scale, WHO promotes a public health approach to ART, using simplified and standardized ART that supports the decentralization of care, task sharing and community delivery and more efficient procurement and supply management *(2)*. The 2016 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection *(3)* included a chapter that provides several recommendations for delivering HIV services across the cascade of care from HIV testing to long-term viral suppression.

Despite the progress made in increasing access to treatment, challenges remain. Studies over the past decade have found that many people living with HIV disengage from care after starting treatment. In sub-Saharan Africa, about one third of adults disengaged from care within five years of starting treatment *(4)*. Long-term retention in care is an important challenge across geographical settings and age groups *(5–8)*, and those who have disengaged and stopped taking ART are at increased risk of transmitting HIV to other people, progressing to AIDS and dying.

Since the 2016 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection *(3)* was published and with the rapid scale-up of ART, emerging evidence and implementation experience and approaches justify reviewing and updating the service delivery guidance. Following a scoping meeting *(9)*, WHO convened a guideline development group to address several key questions to help national programmes in optimizing their delivery of care to all people living with HIV.

These guidelines provide updated recommendations and good practice statements in the following areas: starting ART, including initiating treatment outside the clinic and support for same-day ART initiation; frequency of clinical visits and ART refills; measuring adherence; tracing and re-engagement in care; psychosocial support for adolescents living with HIV; task sharing for diagnostic services; and service integration.

Applicability of service delivery recommendations

In contrast to most clinical interventions, service delivery interventions are generally highly context specific in terms of both relative effectiveness and relative importance in a given context. Consistent with the burden of disease, much of the evidence supporting the recommendations in these guidelines comes from studies undertaken in sub-Saharan Africa. Recognizing the importance of streamlined, standardized approaches to scaling up HIV services in settings with limited resources, the public health approach emphasizes strategies such as task sharing, decentralization, integrating HIV services with other public health programmes and patient and community empowerment. High-income countries with more resources and fewer HIV cases favour a more individualized approach to HIV care, although the overarching framework of the public health approach provides the setting within which this more personalized service delivery can occur.

Importantly, several populations are subject to structural barriers, including stigma, discrimination, criminalization and violence. This is especially important to women, young girls and adolescents and key populations, who are subject to these barriers across the HIV care cascade. Although service delivery is primarily aimed at developing programmatic guidance to help implement all the WHO recommendations, using primarily process-related outcomes and outputs, the basic principles for developing these WHO recommendations align with the concept of people-centred care, the public health approach and a rights-based approach.

The forthcoming WHO consolidated guidelines for HIV services for key populations describes essential strategies for an enabling environment, which includes developing supportive legislation and policy, including working towards decriminalizing behaviour, financial commitment, addressing stigma and discrimination, empowering communities and addressing violence against key populations. WHO also supports a strong emphasis on workforce training against stigma, discrimination and strategies to support people who are subject to violence and to ensure that all populations benefit from accessing better and safer health-care services.

1.1 Objectives

These guidelines are intended to contribute to achieving the Triple-Billion targets. These service delivery guidelines are expected to help meet UNAIDS commitments and the 95–95–95 targets *(10)*.

1.2 Target audience

These guidelines are intended for programme managers involved in implementing and adapting WHO guidelines in national HIV programmes, especially those in low- and middle-income countries. The guidelines will also be of interest to clinicians and other health-care providers, especially those working in primary care services that are the first point of contact for recipients of care. The guidelines will also be of interest to national HIV treatment advisory boards, national HIV and tuberculosis (TB) programme managers, people living with HIV, community- and faith-based organizations and international and bilateral agencies and organizations that provide technical and financial support to HIV programmes in resource-limited settings.

The recommendations in these guidelines are important for: people living with HIV of any age; clinicians and other health-care workers; HIV programme managers and programme managers of related programmes, including TB, sexually transmitted infections, sexual and reproductive health, noncommunicable diseases and viral hepatitis; donors; and nongovernmental organizations.

1.3 Guiding principles

The following principles have informed the development of these guidelines and should guide the implementation of the recommendations:

- The implementation of the guidelines should contribute to realizing the Sustainable Development Goals by achieving key global and national HIV goals.
- The guidelines are based on a public health approach to scaling up the use of antiretroviral drugs along the continuum of HIV prevention, care and treatment.
- Implementation of the guidelines needs to be accompanied by efforts to promote and protect the human rights of people who need HIV services, including ensuring informed consent, preventing stigma and discrimination in the provision of services and promoting gender equity and respectful care.
- Implementation of the recommendations in these guidelines should be informed by the local context, including HIV epidemiology and the prevalence of other comorbidities, the values and preferences of providers and beneficiaries, feasibility and acceptability, availability of resources, the organization and capacity of the health system and anticipated cost–effectiveness.

1.4 Methods for developing these guidelines

Annex 1 details the full methods for developing these guidelines. In summary, these guidelines were developed in accordance with procedures established by the WHO Guidelines Review Committee *(11)*. The recommendations in the guidelines are based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to reviewing evidence and formulating recommendations *(12)*. Consistent with previous WHO guidelines, these guidelines are based on a public health approach that considers feasibility and effectiveness across a variety of settings.

All external contributors to the guidelines, including members of the Guideline Development Group and the External Review Group, completed a WHO declaration of interests form in accordance with WHO policy for experts. The WHO Guideline Steering Group reviewed the declaration of interest forms and the results of the web-based search for each member of the Guideline Development Group and a management plan was agreed and recorded for each individual and presented at the guidelines meeting (Annex 1).

The systematic reviews and evidence-to-decision-making tables (web annexes[1]), prepared in accordance with the GRADE process, were shared in advance and presented at the meetings, and the methodologist facilitated discussions. For the updated recommendations, the Guideline Development Group met virtually on 5–9 October 2020.

[1] All supporting evidence that informed the development of these guidelines is available at: https://www.who.int/publications/i/item/9789240023581

All recommendations were made through consensus. Voting was not required, but the group agreed *a priori* that two thirds of the votes would be required for a decision. The draft guidelines were circulated for review to members of the Guideline Development Group and the External Review Group in November 2020.

1.5 Differentiated service delivery for HIV treatment

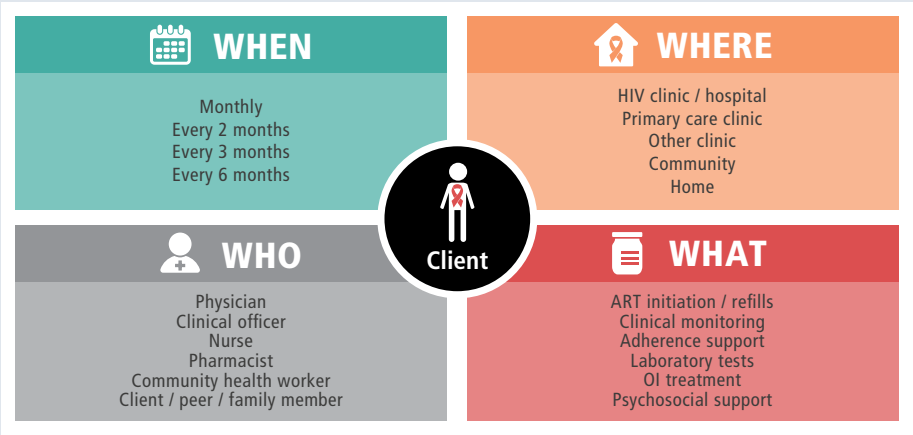
In nearly all countries, the delivery of HIV treatment in the initial phase of rapid scale-up was based on a one-size-fits-all, clinic-based model largely undifferentiated for individual needs *(13)*. As national guidelines have evolved towards initiating ART for all people living with HIV, differentiated service delivery for HIV treatment has become a critical component of recognizing the diversity of people living with HIV in adapting how HIV services are provided. Differentiated service delivery, previously referred to as differentiated care, is a person-centred approach that simplifies and adapts HIV services across the cascade in ways that both serve the needs of people living with and vulnerable to HIV and optimize the available resources in health systems *(14)*. The principles of differentiated service delivery can be applied to prevention, testing, linkage to care, ART initiation and follow-up and integration of HIV care and coinfections and comorbidities. This subsection focuses on differentiated service delivery for HIV treatment.

As national guidelines have evolved towards initiating ART for all people with HIV regardless of clinical and immune status, HIV programmes have been challenged to manage an increasingly diverse set of people's needs. The 2016 WHO consolidated guidelines *(3)* identified four groups of people with specific clinical needs: individuals presenting or returning to care with advanced HIV disease; individuals presenting or returning to care when clinically well; individuals established on ART; and individuals receiving an ART regimen that is failing *(15)*. Differentiated service delivery for HIV treatment has focused primarily on people who are clinically stable (established on ART – see Box 1). Subsequently, there has been recognition of the need to adapt services for those with advanced HIV disease, high viral load and comorbidities through simplified care packages and differentiated models of service delivery; the principles of differentiating service delivery according to the needs of different groups has also been extended to improving the uptake of HIV testing and prevention.

In addition to considering people's clinical needs, differentiated service delivery for HIV treatment should also consider the specific populations and contextual settings. For example, differentiated service delivery models should be designed to address the needs of children and adolescents, pregnant and breastfeeding women and key populations. There is also increasing experience of how such models have been adapted in settings with lower HIV prevalence, acute conflict or other emergency responses *(16)*.

Differentiated service delivery for HIV treatment considers and adapts four building blocks (Fig. 1). In any given differentiated service delivery model for HIV treatment, the building blocks need to be defined separately for clinical consultations, ART refills and psychosocial support.

Fig. 1. The building blocks of differentiated service delivery for HIV treatment



Since 2016, several countries have adopted and scaled up differentiated service delivery as part of national policy, especially in sub-Saharan Africa and for adults established on ART *(9)*. The definition of being established on ART (stability) should be applied to all populations, including those receiving second- and third-line regimens, those with controlled comorbidities, children, adolescents, pregnant and breastfeeding women and key populations. These populations often represent specific cohorts in which retention and suppression of viral loads has been challenging and hence may benefit more from differentiated service delivery for HIV treatment models adapted to their needs *(17)*.

Box 1. Criteria for determining whether a person is established on ART

To support the implementation of these recommendations, WHO has developed criteria for determining whether a person has been successfully established on ART:

- receiving ART for at least six months;
- no current illness, which does not include well-controlled chronic health conditions;
- good understanding of lifelong adherence: adequate adherence counselling provided; and
- evidence of treatment success: at least one suppressed viral load result within the past six months (if viral load is not available: CD4 cell count >200 cells/mm^3 or weight gain, absence of symptoms and concurrent infections). For children 3-5 years, CD4 cell count >350 cells/mm^3.

The provision of ART should not depend on receiving other services. Differentiated service delivery for HIV treatment aims to separate clinical consultations from other visits such as visits for ART refills and/or, if appropriate, psychosocial support. As outlined above, the building blocks for clinical consultations may differ from those for ART refills or psychosocial support. Psychosocial support may be aligned with clinical consultation, and ART refill visits or may be provided separately through additional community and peer support systems. Multi-month refills may be used alone or within any of the four categories of differentiated service delivery for HIV treatment listed below, each of which provides additional benefits to both the health system and clients. Multi-month refills may also be used for children older than two years, since dosage adjustments become less frequent beyond that age. The recommendations on the frequency of clinical visits and ART refills are outlined in the executive summary, with details in Section 5.

Differentiated service delivery models for HIV treatment described in practice and the literature can be described within one of the following four categories:

- group models managed by health-care workers;
- group models managed by clients;
- individual models based at facilities; and
- individual models not based at facilities.

Groups managed by health-care workers are people living with HIV, defined as those established on ART who meet at a defined time, either at the facility or in the community, and are facilitated by a health-care worker (including lay workers). The group environment provides peer support and education, and the lay health-care worker distributes medication. The most common example of a group managed by health-care workers is the ART adherence club. In a South African study including 3216 people across a large urban district, adherence club retention was 95% at 12 months and 89% at 24 months, and 88% of the members had viral loads taken, with viral load ≤400 copies/mL for 97% (95% confidence interval (CI) 97–98%) *(18)*. A high proportion of recipients of care remained in care (87%) and had suppressed viral loads (94%) up to three years after entering an adherence club, with attendance found to be highly protective against disengagement *(19,20)* compared with conventional care. Adherence club members receiving six-monthly ART refills had similar 24-month retention (93% versus 94%), higher viral load completion (94.5% versus 89.3%) and similar viral load suppression (96% versus 98%) versus those who received standard care (two-monthly refills and then four months at year end) *(21)*. In Zambia, rates of late drug pick-up are lower among participants in urban adherence clubs versus clinic-based participants. This model has also been demonstrated to be acceptable to both health-care workers and clients *(22)* and cost effective *(23)*. Positive outcomes of groups managed by health-care workers in terms of improved retention and viral suppression have also been reported across populations, including adolescents *(24)*, children and their caregivers *(25)*, postnatal women *(26)*, men who have sex with men *(27)* and, more recently, for those who have previously struggled with adherence *(28)*.

Groups managed by clients are groups of people living geographically close who meet at an agreed community location and nominate a member to collect ART for the group from the facility on a rotating basis. This member then distributes ART to the group at the agreed community location. Common examples include community adherence groups, community ART refill groups and community client-led ART delivery. Data from client-managed group models have shown improved retention across a range of settings in sub-Saharan Africa *(29–31)*. Qualitative evidence supports reduced costs, especially from the client perspective, and increased time savings and benefits of peer support available within this group model *(23,32–35)*. Health-care workers favoured client-managed groups because they can decongest the clinics and reduce workload *(36,37)*. Client-managed groups have also been implemented for family groups, key populations *(36)* and in unstable settings to support adherence *(33,38,39)*.

Individual models based at facilities are commonly known as fast-track or quick pick-up and go beyond extending the ART refill duration. Assigning a specific place (such as direct pick-up from a pharmacy) and time for ART refills that does not involve consultation with a health-care worker for clinical review or scripting minimizes time spent at the clinic. Evidence from such fast-track models has demonstrated reduced waiting times *(40,41)*, reduced missed appointments *(42)* and reduced costs from a limited societal and health ministry perspective *(43)*. A positive impact on retention and suppression of viral loads has also been documented. In Malawi, retention at five years after enrolment in their six-monthly appointment fast-track model was >86% versus 47% among those who were eligible but did not enrol *(44)*. In Zambia, those in the fast-track model were more likely to be retained at 12 months (relative risk (RR) 1.52) and maintain viral suppression (RR 1.07) *(45)*. The benefits of this approach have also been demonstrated in low-prevalence *(46)* and politically unstable settings *(39)* and in ART provision to children *(47,48)*. A study of extended ART refills for more than 22 000 children across six sub-Saharan African countries found that 66% had their ART refills extended beyond one month. Of those with extended refills, 2.6% were lost to follow-up and 2% died; suppression of viral loads remained high over five years, ranging by year from 79% to 85% *(47)*.

Individual models outside facilities vary according to where in the community services are provided and by whom. They can be divided into fixed community points (including private or community pharmacies), mobile outreach ART delivery and home delivery. The impact of fixed community points on retention and suppression of viral loads has been reported from several countries, including the Democratic Republic of the Congo, South Africa, Uganda and Zambia, reporting high retention rates across settings *(49–52)*. In the Democratic Republic of the Congo, ART refills are provided from community sites run by treatment-literate peers. Fixed community ART delivery points have also provided six-month ART refills *(30)* and been implemented for children *(53)* and key populations via drop-in centres *(54)*. Home delivery of ART has been studied in Kenya, South Africa and Uganda, with mixed results on retention and mortality *(55,56)*. In settings in which costs were analysed, health service and patient costs were lower for home delivery than for facility care *(57)*.

The relevance of home delivery within the model mix is context specific in relation to feasibility for the health system and factors such as distance and stigma. Less published evidence is available for mobile outreach approaches, but this approach does have the potential to support an integrated approach to the community delivery of other health services.

A recent rapid systematic review documenting outcomes of differentiated service delivery for HIV treatment *(58)* included 29 publications. Of the 37 models described, seven (19%) were facility-based individual models, 12 (32%) individual models based outside facilities, five (14%) groups led by clients and 13 (35%) groups led by health-care workers. Where a comparison with conventional care was provided, retention in most differentiated service delivery models was comparable to or better than for conventional care; where no comparison was provided, retention generally exceeded 80%. For suppression of viral loads, all those with a comparison to conventional care reported a small increase in suppression in the differentiated service delivery model; reported suppression exceeded 90% in 11 of 21 models *(59)*.

Information available about the costs and benefits of differentiated service delivery for HIV treatment for patients and the health system is scarce. A review of available literature suggests that differentiated service delivery for HIV treatment for those who are established on ART saved patients substantial money on travel costs and greatly reduced the time required to receive ART, including time spent on transport, waiting in the queue or having a clinic visit, and modestly reduced the resources the health system used *(23)*.

2. PEOPLE-CENTRED CARE

Good practice statement

Health systems should invest in people-centred practices and communication, including ongoing training, mentoring, supportive supervision and monitoring of health workers, to improve the relationships between patients and health-care providers.

Existing good practice statements

HIV programmes should:

- provide people-centred care that is focused and organized around the health needs, preferences and expectations of people and communities, upholding individual dignity and respect, especially for vulnerable populations, and engage and support people and families to play an active role in their own care by informed decision-making;
- offer safe, acceptable and appropriate clinical and non-clinical services in a timely fashion, aiming to reduce morbidity and mortality associated with HIV infection, and to improve health outcomes and quality of life in general; and
- promote the efficient and effective use of resources.

Background and rationale

People-centred health services are an approach to care that consciously adopts the perspectives of individuals, families and communities and sees them as participants and beneficiaries of trusted health systems that respond to their needs and preferences in humane and holistic ways *(3)*. This approach acknowledges the experiences and perspectives of health-care providers that may enable or prevent the delivery of people-centred care that is of high quality *(58)*.

In HIV care, several studies have shown that people are willing to travel longer distances to be seen by a health-care provider with a respectful and caring attitude, and negative health-care worker attitudes contribute to loss to care and poor programme outcomes *(60–62)*. For key populations in particular, experiencing stigma and discrimination in health-care settings is a structural barrier to accessing services *(63,64)*. WHO recommends addressing stigma and discrimination in health-care settings as an important component of ensuring access to HIV care *(65)*.

A systematic review was conducted up to 1 August 2020 to update guidance and identify practical ways to enhance people-centred care for people living with HIV *(66)* (see Box 2). The review identified 15 studies describing intervention strategies, including adults, adolescents *(67)* and children and the following key population groups: sex workers, men who have sex with men, transgender people and people who inject drugs.

Box 2. Interventions to improve relationships between clients and health-care providers

Interventions that were found to improve relationships between clients and health-care providers could be classified into the following approaches:

- providing friendly and welcoming services:
  - Such as by training providers to make general HIV services more welcoming, providing adolescent-friendly services outside school hours and training providers to welcome people back into care;
- conducting sensitization training for clinical and non-clinical health-care providers to improve care for key populations:
  - At both the primary care and community levels, which includes issues related to stigma and discrimination;
- offering individualized adherence counselling and client-centred communication:
  - Such as shared decision-making and planning for ART initiation and adherence and supporting change in provider attitudes towards those who have disengaged from care;
- facilitating client education in empowerment and communication skills; and
- providing feedback to health-care workers on client concerns and evaluation of service quality.
  - Such as community score cards and client feedback surveys combined with quality improvement exercises.

Overall, studies reported beneficial effects of these approaches across the HIV cascade outcomes, including improved ART uptake, adherence and suppression of viral loads. The evidence contributing to the systematic review was highly heterogeneous and evidence was insufficient to determine that any particular strategy was associated with better outcomes than another.

The Guideline Development Group formulated a new good practice statement considering the evidence showing that a health systems-based perspective and providing a variety of people-centred practices will improve relationships between clients and health-care providers. Not providing tools to improve provider services will likely be non-beneficial and potentially harmful, considering stigma, discrimination and violence against people living with HIV, especially among women, transgender people and other vulnerable groups. Health-care providers should be trained appropriately to ensure that, in addition to improving relationships with clients, they must also be capable of supporting women and vulnerable groups against gender or intimate partner violence and sexual health counselling and support.

3. INITIATING ART OUTSIDE THE HEALTH FACILITY

ART initiation may be offered outside the health facility

(Conditional recommendation; low- to moderate-certainty evidence)

This recommendation is additional to the routine offer of ART initiation at the health facility.

Background and rationale

Community-based HIV testing approaches are a key component of any HIV testing strategy *(68)*. In most settings, if a positive HIV diagnosis is made in the community – for example through mobile health services, community centres, services focusing on key populations and clients' homes – the individual is then referred to a health centre to start treatment *(68)*.

WHO recommends rapidly initiating ART, including starting on the same day of a positive diagnosis, partly because of the large losses previously observed between diagnosis and initiation *(15)*. A key implementation challenge was ensuring that rapid initiation of ART would be made available to people living with HIV in different settings and contexts.

Further, losses to care between community HIV testing and ART initiation are substantial. A 2018 systematic review of studies in sub-Saharan Africa found that the proportions linked to care could be as low as 14% for home-based testing and 10% for community-based testing; in some settings less than one quarter were known to have started treatment *(69)*. Reported reasons for not initiating treatment can include feeling healthy, insufficient social support, HIV stigma, high care-seeking costs and incomplete knowledge of treatment benefits *(70)*. This is of particular concern for vulnerable populations such as women, young girls and key populations, who are at heightened risk of stigma, discrimination and violence. WHO has provided recommendations on how national programmes should work to protect these populations *(65,71)*. A study from South Africa and Zambia found that people testing positive in the community often delayed starting ART because of issues related to the quality of care (including long waiting times, lengthy initiation procedures and lost clinic folders) and stigma associated with accessing care *(72)*. Other studies have cited lack of time *(73)* and concern about long clinic waiting times as the main reported reasons for not linking to care and starting treatment *(74)*.

A systematic review conducted up to 15 April 2020 identified three randomized trials and four observational studies providing evidence that offering ART initiation outside the health facility was associated with an increase in the proportion of people starting ART (RR 1.86, 95% CI 1.29–2.68), increased retention in care at 6–12 months following ART initiation (RR 1.44, 95% CI 1.33–1.56) and increased suppression of viral loads (RR 1.31, 95% CI 1.13–1.61) *(75)*; two studies included in this review included key populations *(76,77)*, and one study included adolescents and young adults *(78)*.

Benefits and harms

Early initiation of ART is associated with several health benefits, including reduced mortality and morbidity and reduced onward transmission *(79)*. The offer to start ART before referral to a health facility has the potential to reduce delays in starting treatment for individuals who are unwilling or unable to be referred to the health facility to start treatment. Although the studies that assessed community ART initiation reported no intervention-specific harm, ensuring that baseline assessments and support are provided either as part of the intervention or on referral to the health facility are important.

Feasibility, cost and cost effectiveness

When ART initiation is included as an additional component of existing community activities, additional expertise and resources are needed, as reflected by the studies *(75)*. A randomized trial of community-based ART in South Africa and Uganda included an activity-based microcosting study to estimate the annual per-client cost of community-based ART initiation. The study concluded that community-based ART could cost US$ 275–452 per person with suppressed viral loads, slightly more than the US$ 214–422 estimated for the facility-based initiation group *(80)*. Another study, from Malawi, assessed optional home initiation of ART following HIV self-testing and found that the average annual cost per participant who initiated ART was US$ 172 versus an annual cost of providing ART in facilities of US$ 858–1165 *(81)*.

Equity and acceptability

Implementing this recommendation could potentially increase access to treatment for individuals who may experience structural barriers such as criminalization, stigma and discrimination when attempting to access health-care services to initiate treatment. A study among female sex workers in the United Republic of Tanzania found that those receiving community ART initiation were more likely to have started treatment and be retained in care and less likely to have interrupted treatment or feel high levels of internalized stigma *(77,82)*. Evidence for adolescents was limited, and acceptability is uncertain.

Implementation considerations

WHO guidelines recommend a readiness assessment at ART start, including ART literacy, and a clinical assessment that includes CD4 cell count, to determine whether a person has advanced HIV disease and requires further diagnostic investigation and provision of prophylaxis *(15)*. WHO further recommends that nurses be able to initiate ART *(3)*, and this should be facilitated by supportive professional regulations.

Clients starting ART outside a health facility should be linked to a facility and enrolled in a long-term model of care. ART start should also be accompanied by appropriate counselling to ensure that individuals understand the importance of lifelong adherence and receive appropriate support. For those who are not ready to start, referral to care should be provided. Initiating ART outside a health facility needs to be accompanied by appropriate measures to ensure that risk assessment and counselling support are provided, including at the time of initiation and in the period thereafter.

This recommendation applies to all people living with HIV, including children and adolescents. However, there is very limited experience with ART initiation outside the facility for infants and young children; antiretroviral drug formulations, especially those for infants and younger children, may require additional practical advice on administration techniques and/or on storage conditions. Community health-care providers should be trained and provided with

the tools to deliver effective counselling to caregivers to support and oversee appropriate administration *(83)*. Additionally, it is important to ensure that adolescents are linked to psychosocial care and that children and parents are supported with disclosure and age-appropriate treatment literacy in the context of a holistic approach to family-based care.

Implementation of community ART initiation should consider health system requirements for supporting ART delivery at the community levels, including drug supply chain, laboratory services, training and supervising health personnel, providing preventive therapy and referral mechanisms for those who need higher-level care. Such adaptations may require a phased approach (for example, by starting implementation in settings in which community prevention and testing activities have been established). The provision of community HIV care should be included in national initiatives to ensure the quality of care.

Research gaps

Research is needed to improve understanding of client preferences about where to start ART and how to link to care by age, population and setting *(84,85)*. Tools to support initiation outside the health facility need to be designed and evaluated. Evidence shows substantial variability in the size of the community treatment team, and implementation research would be valuable in defining the optimum staffing complement and minimum set of skills required. Evidence on how ART initiation outside the facility affects household spending and catastrophic costs would also be of value.

4. RAPID INITIATION OF ART, INCLUDING SAME-DAY START

Existing recommendations

Rapid ART initiation[a] should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment

(Strong recommendation: high-certainty evidence for adults and adolescents; low-certainty evidence for children)

[a] Rapid initiation is defined as within seven days from the day of HIV diagnosis; people with advanced HIV disease should be given priority for assessment and initiation.

ART initiation should be offered on the same day to people who are ready to start

(Strong recommendation: high-certainty evidence for adults and adolescents; low-certainty evidence for children)

Source: Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy *(15)*.

Good practice statements

The offer of same-day ART initiation should include approaches to improve uptake, treatment adherence and retention such as tailored patient education, counselling and support.

Background and rationale

In 2017, WHO strongly recommended that rapid ART initiation be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment, with the offer of same-day start for people who are ready *(15)*. This recommendation was supported by evidence showing that rapidly initiating ART leads to an increased likelihood of starting treatment and improved suppression of viral loads and retention in care and may lead to reduced mortality *(86)*. WHO also strongly recommends that nurses be able to initiate and maintain ART *(3)*.

Uptake of this recommendation in national policy is variable. Several countries have not adopted this recommendation in national guidance, and some *(87)* but not all *(88,89)* studies have reported poorer retention in care when ART is started on the same day compared with less rapid ART initiation. Patient perspectives have highlighted the importance of good counselling and non-judgemental, respectful personnel *(90)*.

A systematic review was conducted up to 28 May 2020 to identify approaches that support accelerating the offer or uptake of ART after diagnosis among people living with HIV. The review identified 26 studies; 11 were conducted in general populations and three among pregnant women, 10 included key populations (seven included men who have sex with men, two people who inject drugs and one female sex workers) and two included adolescents.

Many strategies were examined, and these could be classified into (1) strategies targeting clients, (2) strategies targeting health-care providers and (3) strategies targeting the health system. Evidence indicated that all these approaches were associated with increased uptake of ART, suppression of viral loads at 12 months and retention in care at 12 months *(91)*.

The Guideline Development Group recognized the importance of implementing additional strategies to facilitate and improve same-day ART uptake and support good outcomes. The systematic review identified a diversity of interventions to improve uptake and outcomes following same-day ART initiation; some of these interventions provided indirect evidence of benefit for other aspects of HIV care. This diversity of direct and indirect evidence provided high certainty in the overall benefit of providing approaches to improve uptake, treatment adherence and retention and this led the Guideline Development Group to make a good practice statement. It was considered important to highlight strategies targeting clients, health-care providers and the health system. Table 1 outlines the most commonly assessed interventions.

Table 1. Evidence-informed approaches to supporting same-day ART initiation at the level of the client, provider and health system

Strategies targeting clients		Strategies targeting health-care providers	Strategies targeting the health system
Pre-ART initiation	Reduce administrative requirements to initiate ART	Provider training on rapid ART initiation	Reduce the number of pre-ART sessions
	Reduce pre-ART psychosocial requirements	Provider training on counselling	First ART counselling on the day of HIV testing
	Aim to improve pre-ART counselling content and delivery	Provider supervision, coaching and mentorship	Increase the duration of pre-ART sessions
	Promote shared decision-making	Provider performance feedback	Expedite the scheduling of appointments to initiate ART
	Increase duration of pre-ART sessions	Provide standard operating procedures and guidance documents	Provide ART first starter pack immediately with no pharmacy waiting time
	Navigation during ART initiation visit	Provide decision support tool (checklist or algorithm)	Point-of-care CD4, TB testing and diagnosis
	Incentives		
Post-ART initiation	Appointment reminders		
	Short-term ongoing navigation and support		
	Intensified post-ART counselling		
	Increased duration post-ART initiation clinical visit		
	Incentive to attend post-ART initiation visits		

5. FREQUENCY OF CLINICAL VISITS AND ART PICK-UP

Recommendations

People established on ART should be offered clinical visits every 3–6 months, preferably every six months if feasible

(Strong recommendation; moderate-certainty evidence)

People established on ART should be offered refills of ART lasting 3–6 months, preferably six months if feasible

(Strong recommendation; moderate- to low-certainty evidence)

Background and rationale

In 2016, WHO recommended clinical visits every 3–6 months and dispensing ART every 3–6 months for people established on ART *(3)*. Two distinct recommendations were made to underscore the point that clinical visits and medication pick-up should be considered separately. These recommendations have been broadly adopted by national guidelines, with clinical visits and medication pick-up every three months most commonly adopted according to country surveys *(47,92)*.

A systematic review conducted up to April 2020 assessed the evidence on outcomes associated with different frequencies of clinical visits and refills of ART *(93)*. The review identified three randomized trials and three observational studies comparing clinic visit frequency at three and six months and found no difference in retention in care (RR 0.99, 95% CI 0.94–1.03, low-certainty evidence) or suppression of viral load (RR 1.02, 95% CI 0.86–1.21, low-certainty evidence). The review also identified three studies, including one randomized trial, comparing ART dispensing frequency and found no difference in retention in care (RR 1.00, 95% CI 0.98–1.02, moderate-certainty evidence); suppression of viral load at six months was marginally reduced in one study *(31)* but was similar in the other two studies *(51,94)*. One study across six African countries reported that children and adolescents who transitioned to multi-month prescribing maintained favourable outcomes in terms of death, retention, adherence, immunosuppression and suppression of viral load *(47)*.

Benefits and harms

For people living with HIV who are established on ART, a frequency of clinical visits and dispensing of ART of 3–6 months is associated with improved outcomes compared with monthly schedules. The certainty of the evidence was low to moderate. Some of the evidence supporting these recommendations came from observational studies with methodological limitations, and there was important variability (heterogeneity) in outcomes across studies. No harm was identified.

Feasibility, cost and cost effectiveness

Many countries have adopted the previous WHO recommendation of clinic visits and ART dispensing every 3–6 months, demonstrating feasibility across a diversity of settings *(47,92)*. WHO has also recommended reducing client contact with health services as a way to maintain essential health services during periods of service disruption *(95)*. Differentiated service delivery for HIV treatment, including reduced visit frequency and increased ART refills, can save substantial patient travel costs and greatly reduced the time required to receive ART, including time spent on transport, waiting in the queue or having a clinic visit *(96)*. Reducing the visit frequency also reduces health system costs, making this a cost-saving intervention.

Equity and acceptability

A review of preferences among adults living with HIV found that, compared with monthly drug refills, people living with HIV preferred longer intervals but showed no strong preference for three-month compared with six-month refill frequency *(62)*. The Guideline Development Group judged that providing the option of less frequent health service interaction has the potential to increase equity by improving opportunities to access care for vulnerable and mobile populations.

Implementation considerations

Reducing the frequency of drug dispensing requires adequate drug supply and the possibility for appropriate storage for clients, including for community ART delivery. Consideration should be given to harmonize and optimize scheduling while ensuring patient choice and linkage to other key services, including viral load and other laboratory investigations, and dispensation of medications for TB preventive treatment and chronic conditions. Less frequent visits and less frequent drug pick-up should be implemented across subpopulations to promote a family-based approach to HIV service delivery. However, extended refills should be considered only for children older than two years when the frequency of dose adjustments becomes less frequent *(17)*, since younger children need to attend health services for routine services such as immunization. Additional models of community support may need to consider clinic visits for certain groups at greater risk of facing adherence challenges, such as adolescents, pregnant and postpartum women.

Research gaps

Evidence is needed on outcomes associated with less frequent clinical visits and/or drug refills (beyond six months) for various populations. In particular, there are contexts in which annual clinical visits are the standard of care and may both benefit clients and reduce costs for health systems.

6. TRACING AND RE-ENGAGEMENT IN CARE

Recommendation

HIV programmes should implement interventions to trace people who have disengaged from care and provide support for re-engagement

(Strong recommendation; low-certainty evidence)

Background and rationale

WHO guidelines strongly recommend that programmes provide community support for people living with HIV to improve retention in HIV care *(3)*. Poor retention undermines programme outcomes, including reducing mortality and achieving sustained population suppression of viral loads. Although many programmes have adopted these recommendations to support retention, loss to follow-up remains substantial in all regions, and especially high in southern Africa, affecting all age groups *(4,97,98)*. Although some individuals who are no longer engaged in care have died, recent data suggest that many individuals who are successfully traced are alive *(99)*, and many are willing to re-engage in care. WHO recommends tracing as one of a range of potential interventions that could improve linkage between diagnosis and ART initiation *(3)*. To date WHO has not made any recommendations on tracing activities after ART initiation.

A systematic review conducted up to April 2020 assessed the success of different activities to trace individuals who have disengaged and identify interventions to support re-engagement in care; the review identified 37 studies, eight of which included children and adolescents *(100)*. Overall, the review found that, among those who were alive, 58% (95% CI 51–65%) re-engaged in care. Tracing and re-engagement actions appeared to be more successful when people were traced soon after a missed visit compared with a longer period of disengagement. Approaches to tracing included remote communication (phone, text, mail and email), in-person tracing and a combination of both approaches.

Benefits and harms

Tracing activities can successfully re-engage people in care and achieve resuppression of viral load. The certainty of the evidence was judged to be low, mainly because of important heterogeneity in outcomes across studies leading to imprecise estimates of benefit. The literature did not identify any important harm. Although tracing activities carry the hypothetical risk of inadvertently disclosing HIV status that could lead to gender and intimate partner violence, discrimination and stigma, this risk is considered small and is outweighed by the benefits of re-engaging individuals into care and onto life-saving ART, without which there would be increased illness and death. The Guideline Development Group made a strong recommendation despite low-certainty evidence given the confidence in the health benefit for clients returning to care and minimal harm associated with tracing and re-engagement activities.

Feasibility, cost and cost effectiveness

Most reports described tracing activities undertaken by existing health facility personnel; in some cases, social workers and community health workers formed part of the tracing team, and personnel were trained. Other associated costs include establishing systems to trace and support re-engagement. In-person field tracing requires resources to support the travel of tracing teams, human resources with appropriate training and remuneration, including the potential need to undertake multiple tracing attempts.

Equity and acceptability

Tracing in the absence of consent may be considered intrusive and may not be accepted by clients who have disengaged from care (based on a range of motivations). Tracing must also be sensitive to the need to respect human rights and confidentiality and avoid inadvertently disclosing HIV status. The Guideline Development Group judged that the intervention would probably increase equity and is probably acceptable to most people living with HIV if delivered with a non-judgemental approach. Clients should be provided with the opportunity to consent to tracing when ART follow-up is discussed during patient counselling and at ART initiation.

Implementation considerations

Support for re-engagement in care can include interventions directed towards patients, such as peer- or provider outreach and navigation back to care, as well as toward health-care providers and health facilities, through systems to alert health-care providers that patients have disengaged. The nature of interventions could include reminders (such as phone calls or text messages), economic interventions (such as financial incentives or conditional cash transfers), case management or policy interventions, with steps taken to ensure complete confidentiality. Programme- or facility-level confidential client contact details should be kept up to date to ensure successful tracing if and when required. When tracing people who are not engaged in care is being considered, adequately assessing risks to vulnerable and key populations is critical. For example, women are subject to increased levels of both intimate partner and gender-based violence in the context of HIV, and appropriate training of health-care providers is therefore essential *(101)*. Client-reported reasons are critical to understanding both general and local reasons for failures of retention; these patient-reported reasons are far more predictive than sociodemographic factors such as age and sex *(102)*.

The criteria for tracing and recall should consider those who are seven or more calendar days late for a scheduled appointment. Although efforts should be made to trace everyone who has missed appointments and/or has abnormal laboratory test results, the following groups should be given priority: (1) people initiating treatment in the past six months with advanced HIV disease, (2) people with abnormal laboratory test results, (3) people not initiating treatment and (4) people overdue for clinical consultations or laboratory tests.

A non-judgemental approach is essential to supporting people to return to care; this requires reducing system barriers and improving interpersonal communication by developing the capacity of health-care providers. The Welcome Back service established by Médecins Sans Frontières and the Department of Health of South Africa provides a strong example of such an approach that combines medical and psychosocial support for people who have disengaged from care *(99,103)*.

Research gaps

Several studies have described the most common reasons for disengagement from care either before or after initiating ART *(70,102,104,105)*. Research is needed to tailor support that responds to these drivers to minimize disengagement and support re-engagement at different stages along the continuum of care. Qualitative research is important to understand the most acceptable and effective methods of tracing and re-engagement; this research should include disaggregation of approaches based on the population group (such as key populations), gender and age.

7. ASSESSING ADHERENCE

Good practice statement

Viral load for treatment monitoring should be complemented with non-judgemental, tailored approaches to assessing adherence.

Background and rationale

WHO strongly recommends that adherence-support interventions be provided to people receiving ART *(3)*. Viral load monitoring is the gold standard for monitoring adherence and confirming treatment response. Other approaches to monitoring adherence should be considered as a way to provide additional information about the risk of failure to suppress viral loads or to support daily tablet-taking behaviour in settings in which viral load testing is not available. Knowledge of adherence can support decisions about whether a recipient of care is eligible for simplified models of service delivery and whether to switch treatment regimens when viral load is unsuppressed.

Simple, affordable measures suggested by WHO to measure adherence include pill counts, pharmacy refill records and self reporting (Box 3) *(106)*. A systematic review conducted up to September 2020 identified 50 studies to assess the comparative diagnostic accuracy of these adherence measures *(107)*. Overall, the review found that all adherence measures had low sensitivity for identifying people who are non-adherent and have unsuppressed viral load. For self report, there was a tendency towards higher sensitivity in diagnosing viral non-suppression when five or more questions were asked as part of the assessment. Composite adherence measures, such as combining self report with pharmacy refill or tablet count, appeared to have higher sensitivity.

The Guideline Development Group issued a Good Practice Statement that viral load for treatment monitoring should be complemented with non-judgemental, tailored approaches to assessing adherence. This was based on indirect evidence that there is clear value in adherence measures as an opportunity to discuss issues relating to treatment with patients and identify potential barriers to maintaining adequate adherence and areas where support may be needed.

Box 3. Simple, low-cost approaches for measuring adherence

Pharmacy refill records provide information on when people pick up their antiretroviral drugs. Some studies *(108–110)* have found that pharmacy records are a more reliable measure than self-reported adherence.

Self-reported data are easy to collect and can be a useful adjunct to estimating non-adherence but are subject to recall bias *(106)*. Counselling on the importance of remembering ART doses and an environment that promotes and enables honest reporting of non-adherence are critical components. Self report has been found to be a more reliable predictor of failure to suppress viral loads when the recall period was within one week *(111)*.

Pill counts may help to assess adherence. Pill counts usually take place during routine health visits and may not be feasible in routine care settings. Pill count has been found to perform better when combined with self-reported adherence *(112)*.

A key value of all these approaches is that they encourage discussions about adherence with clients.

Specific population groups face additional challenges to adherence, and these should be considered when implementing the recommended interventions. People receiving ART face a range of individual, interpersonal, community and structural barriers to adherence, including issues related to social identity, gender norms, stigma and medical pluralism; unwelcoming health services; and the need for emotional, practical or financial support for long-term engagement and adherence *(113,114)*.

Effective monitoring of adherence requires a combination of approaches based on human and financial resource capacity, acceptability to clients and health workers and understanding of the local context.

Research is encouraged to identify the most accurate measures of adherence to ART that are feasible in settings with limited resources as a compliment to viral load testing.

8. INTEGRATING SERVICES

Chronic care requires integrating and linking related services to ensure comprehensive and consistent care provision over time, including providing related services in the same settings, systems to share information and effective referrals across settings and providers. Integrated services are likely to reduce missed opportunities for initiating ART, to enhance adherence support and to optimize retention in care.

8.1 Integrating sexual and reproductive health services, including contraception, within HIV services

Recommendation

Sexual and reproductive health services, including contraception, may be integrated within HIV services

(Conditional recommendation; very-low-certainty evidence)

Background and rationale

Among the 1.9 billion women of reproductive age (15–49 years old) worldwide in 2019, 1.1 billion need family planning and 270 million have an unmet need for contraception. Across regions, evidence indicates that sex workers have a greater unmet need for contraception than the general population, and there are reports of excessive reliance on using condoms alone instead of the recommended dual protection *(115–118)*. The proportion of the need for sexual and reproductive health including contraception services that was satisfied by modern methods was 76% globally in 2019, but this fell to less than 50% in western and central Africa. WHO emphasizes the importance of linking sexual and reproductive health and rights and HIV for adolescent girls and young women *(119)*. Since women living with HIV face unique challenges and human rights violations related to their sexuality and reproduction within their families and communities and from the health-care institutions in which they seek care, particular emphasis is placed on creating an enabling environment to support more effective health interventions and better health outcomes *(120)*.

In 2016, WHO made a conditional recommendation that sexually transmitted infection and family planning services can be integrated within HIV care settings *(3)*. Since that time, additional evidence has been published supporting the integration of sexual and reproductive health and HIV. A systematic review published in 2019 that considered linkage and integration found that the proportion of women receiving an HIV test during the study period ranged from 35% to 99% for integrated services and from 20% to 95% for non-integrated services or services integrated at a lower level *(121,122)*; the review summarized findings from several studies that included adolescent girls and young women. The proportion of women accessing HIV services using contraception ranged from 54% to 80% for integrated services and from 10% to 83% for non-integrated services *(121,122)*. Integrating HIV testing services with sexual and reproductive health services is feasible and has potential for positive joint outcomes. The review included six studies – one cluster randomized trial carried out in Uganda and five non-randomized cluster trials carried out in Kenya, eSwatini and the United States of America.

Two studies found that an increase in sexual and reproductive health services, including contraception, favoured integration; one study found an increase in the uptake of dual contraceptive methods. In the study that reported dual method use, the proportion of women using dual methods during the study period was 34% for integrated services and 0% for non-integrated services *(123)*. The overall certainty of evidence for all outcomes was very low, and the available evidence is limited *(122)*. In the other direction, another systematic review of 14 studies found that integrating family planning into HIV care and treatment settings was associated with higher levels of use and knowledge of modern methods of contraception among women living with HIV *(124)*.

Benefits and harms

Overall, integration is associated with increased offers and uptake of sexual and reproductive health services, including contraception, which is likely to result in improved downstream clinical outcomes. Given the nature of the intervention, the Guideline Development Group considered that the benefits likely outweighed any possible harm. One fear about integration is that tasking providers with too many services may reduce the quality of these services. However, it has been reported that integration can yield positive effects on service quality as well as client outcomes for contraceptive use, ART in pregnancy and HIV testing *(125)*. Integrating HIV and sexual and reproductive health services has been found to improve accessibility, the quality of antenatal care and nurse productivity while reducing stigma and without compromising uptake of care *(126)*.

Feasibility, cost and cost effectiveness

A study from Zambia found that integrated HIV testing and counselling and voluntary male medical circumcision services could be provided at a lower cost per client than segmented, vertical provision *(127)*. A study from Kenya *(128)* found decreased consultation times when services were integrated (10 versus 30 minutes); another study from Kenya *(129)* highlighted the need for sustained systems and health-care worker support over time. Integration may lead to increases in service efficiency, but this is likely to be highly context dependent *(130–132)*.

Equity and acceptability

A survey conducted among health-care providers and clients in support of these guidelines found that more than 90% of respondents considered that integration is important and feasible. Integration may improve access to sexual and reproductive health services, including contraception, among key populations. A study from Kenya found that access to sexual and reproductive health services, including contraception, for women who inject drugs can be improved by integrating contraceptive and other sexual and reproductive health interventions into existing outreach-based HIV prevention and harm-reduction programmes *(133)*. Another study among female sex workers in Kenya found that integration improved access to the use of non-condom contraception methods, which is important for these people, who may have difficulty negotiating condom use *(134)*. Integration also has the potential to reduce stigma. A survey of health-care providers in South Africa found that they considered integration important for reducing stigma and increasing access to and improving the quality of care *(135)*.

Implementation considerations

Implementing comprehensive and integrated sexual and reproductive health and rights and HIV programmes to meet the health needs and rights of the diverse group of women living with HIV requires that interventions be put into place to overcome barriers to service uptake, use and continued engagement. In all epidemic contexts, these barriers arise at the individual, interpersonal, community and societal levels. They may include challenges such as social exclusion and marginalization, criminalization, stigma, gender-based violence and gender inequality. Strategies are needed across health system building blocks to improve the accessibility, acceptability, affordability, uptake, equitable coverage, quality, effectiveness and efficiency of services for women living with HIV. If left unaddressed, such barriers undermine health interventions and the sexual and reproductive health and rights of women living with HIV *(120)*.

A focus on improving investment in the overall health system will be important to support the integration of sexual and reproductive health services, including contraception and HIV services. Laws and policy barriers to accessing sexual and reproductive health services, including for adolescents, need to be addressed. Although this applies to any integration effort, it is especially important since sexual and reproductive health programmes have historically been implemented as established vertical programmes within health systems. WHO strongly recommends that care for women experiencing intimate partner violence and sexual assault, as much as possible, be integrated into existing health services rather than being a stand-alone service *(120)*.

Training on human sexuality may facilitate greater understanding of sexually diverse communities, particularly those identifying as lesbian, gay, bi-sexual, transgender, questioning or intersex (LGBTQI), as well as adolescents and young people seeking accurate sexual and reproductive health and rights (SRHR) information and services *(68)*.

Since an increasing proportion of people living with HIV are receiving their HIV treatment through a differentiated service delivery model with extended ART refills and less frequent clinical visits, aligning the provision of sexual and reproductive health services, including contraception commodities – WHO recommends providing one year of oral contraception and supports community delivery and self-management – with differentiated service delivery for HIV treatment models should be considered.

Careful planning and coordination are important for both programme management and service delivery, including establishing integrated data systems and providing consistent cross-training of health-care providers. Political will, significant coordination, collaboration and integration across disease programmes are important *(136,137)*.

Research gaps

The evidence supporting approaches to integrating sexual and reproductive health services, including a range of contraception, with HIV services is limited. Research is encouraged to identify approaches to integration that lead to better uptake of sexual and reproductive health services, including contraception; such research should also consider integrating cervical cancer screening and vaccination. Implementation research is encouraged to evaluate different strategies of integration in different health systems and social contexts, including providing contraception in the context of less frequent clinical and ART refill visits.

8.2 Integrating diabetes and hypertension care with HIV care

Recommendation

Diabetes and hypertension care may be integrated with HIV services

(Conditional recommendation; very-low-certainty evidence)

Background and rationale

Low- and middle-income countries are facing an increasing burden of noncommunicable diseases. According to WHO, 15 million people 30–69 years old die prematurely from noncommunicable diseases every year, and 85% of these people live in low- and middle-income countries. Diabetes and hypertension are the major cardiovascular risk factors for target organ damage of the brain, heart and kidneys. An estimated 425 million people in low- and middle-income countries currently have diabetes. This number is expected to increase to 629 million in 2045. The prevalence of hypertension in low- and middle-income countries is estimated to exceed 20% *(138)*. Thanks to widespread access to ART, the life expectancy of people living with HIV has improved substantially, and this places them at risk of noncommunicable diseases that are common with increasing age. In addition to the elevated risks from modifiable factors for noncommunicable diseases such as smoking, poor diet and a sedentary lifestyle, people living with HIV have an independent increased risk of noncommunicable diseases (especially cardiovascular diseases, cervical cancer, depression and diabetes) related to HIV itself and to ART-related side effects *(139,140)*.

In April 2019, WHO convened an expert scoping consultation on noncommunicable diseases and mental health conditions with policy-makers, academics and partners from the HIV, noncommunicable disease and mental health communities to review existing WHO norms and policies for preventing and managing major noncommunicable diseases and mental health conditions. Participants identified the need to establish effective approaches identifying for integrating hypertension, diabetes and HIV services *(141)*.

A systematic review up to December 2019 identified five studies – two interrupted time-series studies *(142,143)* and three cluster randomized trials *(144–146)* – and found that integrated models of care that include hypertension or diabetes or multi-disease approaches may increase the number of people controlling both blood pressure and HIV. It also found that offering integrated care was unlikely to alter mortality (RR 0.90, 95% CI 0.79–1.02). The overall certainty of evidence was very low, and the available evidence is limited *(147)*.

Benefits and harms

The Guideline Development Group concluded that offering integrated services for managing hypertension and diabetes with HIV services will have a small beneficial effect and that any possible harm is small and related to increased workload that may impact the quality of services.

Feasibility, cost and cost effectiveness

The feasibility of integrating diabetes and hypertension care with HIV services may vary based on the setting and health system factors and should be supported at the planning and policy level. Involving the community may promote increased uptake of diagnostic, preventive, treatment and referral services for HIV and noncommunicable diseases *(148)*. One study found that engaging regulatory authorities early, considering work culture and building the capacity of a robust interdisciplinary workforce were critically important *(149)*. A comparative study in sub-Saharan Africa concluded that multi-disease services can be offered at relatively low marginal cost *(150)*.

Equity and acceptability

Implementing this recommendation may increase access to routine hypertension and diabetes services among those living with HIV with limited access to primary preventive services. The results of a WHO survey conducted to support these guidelines indicate that most respondents considered integrating HIV and diabetes (83%) or hypertension (78%) care to be very important or important. A systematic review reported high acceptability of integrated adherence clubs for people receiving chronic medication for controlling both HIV and noncommunicable diseases *(151)*. Another review found that most people would find it acceptable to receive noncommunicable disease services in an HIV care setting. HIV care providers were willing to provide noncommunicable disease services and recognized the potential benefits of doing so but highlighted concerns around space constraints, increased workload, training requirements, supply chain shortages and potential effects on other services as key factors to consider *(148)*.

Implementation considerations

A focus on improving investment in the overall health system will be important to support the integration of hypertension, diabetes and HIV services. Since an increasing proportion of people living with HIV are receiving their HIV treatment through a differentiated service delivery model with extended ART refills and less frequent clinical visits, aligning the provision of noncommunicable disease commodities with differentiated service delivery for HIV treatment models should be considered. Sustainable planning for lifelong health among people living with HIV, supply chain modifications, integration of data systems and consistent cross-training of health-care workers are also key considerations.

Careful planning and coordination are important for both programme management and service delivery, including establishing integrated data systems and providing consistent cross-training of health-care providers. Political will, significant coordination, collaboration and integration across disease programmes will be important.

Research gaps

The following research gaps were identified: long-term data on the health outcomes of people living with HIV who have noncommunicable diseases, cost–effectiveness data for various models of integrated care and implementation research on optimizing the supply chain. Research can help to define health promotion activities that encourage lifestyle changes and protect against noncommunicable diseases among people living with HIV, who may face stigma and other challenges to receiving health promotion through the usual channels. Research is also needed to inform how hypertension and diabetes care can be integrated with the common differentiated models of service delivery implemented for HIV. Qualitative research can inform the values and preferences of people living with HIV and noncommunicable diseases related to how care is delivered.

9. PSYCHOSOCIAL INTERVENTIONS FOR ADOLESCENTS AND YOUNG ADULTS LIVING WITH HIV

Recommendation

Psychosocial interventions should be provided to all adolescents and young adults living with HIV

(Strong recommendation; moderate-certainty evidence)

Background and rationale

The 2016 WHO consolidated HIV guidelines detailed the key elements of general care over the continuum of HIV care for people living with HIV *(3)*. However, adolescents and young adults living with HIV face distinct and interlinked challenges as they navigate the health-care system, take on responsibilities of managing their own care and treatment and confronting issues relating to stigma and disclosure *(152)*.

Adolescence entails biological, cognitive and social changes. It is a phase in the life-course of increased exploration of identity, vulnerability and experimentation, and navigating this phase can be particularly complex *(153)*. Adolescents and young adults living with HIV experience numerous mental and social issues, including depression, stigma, isolation, difficulties with treatment adherence and retention, sexual risk-taking practices and substance use *(154)*. In addition, evidence indicates that they are underserved by current HIV services and, compared with adults 25 years and older, have significantly worse access to and coverage of ART, worse suppression of viral loads and a high risk of loss to follow-up both before and after initiating ART *(3)*.

Psychosocial interventions, which adopt psychological, social and/or behavioural approaches to developing skills and knowledge, have been introduced across a variety of sociodemographic settings, but these interventions have not been adequately explored as a whole.

A systematic review up to July 2020 assessed the effect of psychosocial interventions on ART knowledge, linkage to care, adherence to ART, retention in care, viral load, sexual and reproductive health behaviour and knowledge and improved transitioning to adult services. Thirty randomized controlled trials of psychosocial interventions for adolescents and young adults were identified *(155)*. Psychosocial interventions improved adherence to ART (standardized mean difference 0.39, 95% CI 0.11–0.68); reduction in viral load (standardized mean difference – 0.26, 95% CI –0.45 to –0.07) and led to increased viral suppression (odds ratio (OR) 1.9, 95% CI 1.01–3.8) and undetectable viral load (OR 1.8, 95% CI 1.1–3.1). No undesirable effects were identified. The Guideline Development Group judged the certainty of evidence to be moderate.

The systematic review described the following psychosocial interventions:

- interventions that harnessed motivational interviewing, a collaborative, client-centred counselling style focused on increasing motivational readiness for behavioural change *(156–161)*:
- interventions that involved adolescents and their caregivers: family-based interventions to promote mental health and prevent negative behaviour (such as nonadherence) among adolescents with HIV, which are designed to strengthen communication, problem-solving and negotiation skills for both adolescents and caregivers *(162)*;
- interventions based around peer support and social networks, which are peer-driven interventions involving multiple intervention components to target adolescents and young adults living with HIV and improve outcomes, including adherence to treatment, retention in care and suppression of viral loads *(163–166)* and;
- digital means used to introduce new information and deliver behaviour change skills *(167–171)*.

Benefits and harms

Overall, the net effects on adherence and suppression of viral load were positive. There were no undesirable effects, and the interventions improved adherence and viral load outcomes. The Guideline Development Group judged the benefits to be moderate and harm trivial.

Feasibility, cost and cost effectiveness

Overall, psychosocial interventions for adolescents and young adults living with HIV were found to be feasible to implement *(166,172,173)*. Many studies reported low attrition rates, indicating that interventions were feasible and well accepted *(157,162,174,175)*. The location of the intervention also influenced feasibility, with interventions delivered digitally or at home considered more feasible because of convenience and flexibility *(164,176)*.

Comprehensive training of existing or new personnel and integrating interventions into existing health-care settings were important for successful implementation *(160,177,178)*. Other feasible interventions used existing peer support networks to improve engagement in care *(163)*.

A global consultation of adolescents and young adults living with HIV was conducted among 388 respondents across 45 countries supplemented by 10 focus group discussions with 61 adolescents and young adults with HIV across 10 countries (see Annex 1 for a report on the values and preferences survey). This consultation found that they want psychosocial support to be provided routinely and stressed the importance of continuous support.

There is potential for digital interventions and delivering support through virtual platforms *(179)*. There is an opportunity for delivering blended virtual and face-to-face psychosocial support to support access to equitable and widescale services.

The systematic review found that short-term increases in the costs of widespread implementation may offset the longer-term economic and social costs of failing to promote suppression of viral loads for adolescents living with HIV *(166)*. Psychosocial interventions designed to be implemented by lay counsellors or peer mentors are relatively inexpensive *(162,172,174,180)*. Costs may be reduced by using digital strategies for delivery *(167,173)*. The effects of digitally delivered interventions have been identified as being comparable to or even better than those of in-person interventions *(174)*. Conversely, labour-intensive interventions are more costly *(175)*.

Training and employing new personnel to deliver interventions also involve costs. The Guideline Development Group judged the certainty of evidence on costs and resource requirements to be moderate.

Equity and acceptability

Psychosocial interventions are likely to improve equity, especially for more vulnerable groups such as adolescent girls and young women, pregnant adolescents, adolescent mothers and key population groups and in contexts of high youth unemployment and persistent HIV stigma. The systematic review showed improvements in health equity when approaches are introduced to provide structural support, optimize the potential of peer support and networks and when gender preferences for psychosocial support interventions are considered *(166,181,182)*. The widespread provision of psychosocial services enables adolescents living with HIV to have a more equitable chance to benefit from optimal HIV outcomes by ensuring that each young person receives adequate support to enable them to live physically and mentally well with HIV.

The Guideline Development Group judged that offering psychosocial interventions to people living with HIV would increase equity. There was minimal uncertainty and little variability in how much adolescents and young adults living with HIV value the main outcomes. There was near universal agreement (95% of respondents) that psychosocial support interventions would help substantially across the HIV cascade and a range of outcomes. Psychosocial support was considered critical to both the mental and physical health of adolescents and young adults living with HIV. The findings demonstrate that psychosocial support is desired and preferred and described as being potentially transformative across HIV treatment outcomes (diagnosis and initiation onto ART, adherence, retention in care, suppression of viral load, mental health and sexual and reproductive health and rights). The findings show that adolescents and young adults living with HIV want to receive sustained psychosocial support at each stage of the HIV cascade.

Adolescents and young adults living with HIV prefer a varied package of psychosocial interventions, but they consider peer support especially important in managing their health. Interventions that focus on strengthening support from trusted family members and health-care workers are also desired.

Another survey was implemented among frontline health-care workers to assess a wide range of service delivery practices, gaps and enablers *(183)*; 324 health workers from 30 countries, primarily in sub-Saharan Africa, participated. At each step in the treatment cascade, the health-care workers reported psychosocial issues as major challenges and recommended psychosocial support strategies more than any other type of intervention.

The Guideline Development Group found no important variability on preferences and acceptability.

Implementation considerations

A package of services should be considered that is both acceptable and feasible within the context in which they are to be delivered. This package should be context specific and differentiated according to the needs and experiences of different subpopulations of adolescents and young adults living with HIV.

Some adolescents and young adults living with HIV may require adaptations to the content and/or delivery of psychosocial programming to meet their needs. These include adolescents and young adults with disabilities; who are living with mental health conditions or substance use; who are out of school; who are orphans; who are members of ethnic minority groups; who are lesbian, gay, bisexual, transgender and intersex (LGBTI); who are pregnant; and who

are living in contexts of adversity such as extreme poverty and/or humanitarian emergencies. In addition, differences in exposure to risks and protective factors depending on age, developmental stage, sex, health status, whether they belong to a key population and context need to be considered.

Evidence supports psychological approaches such as motivational interviewing and cognitive behavioural therapy. Programmes can include goal setting, problem solving, coping skills, healthy daily routines, interpersonal and communication skills and activation of social support, among other strategies. Interventions can be delivered through a range of delivery modalities and health-care workers, including clinic visits, home visits, support groups (including peer support and groups that link psychosocial support with ART delivery such as teen clubs), social media and telephone contact. These should be fully integrated within the package of clinical services to optimize impact. Facilitators should be able to develop supportive, trusting, non-judgemental relationships, to maximize engagement in programming; this requires investment in ongoing training, supervision and support for facilitators.

Interventions should be implemented in keeping with the global principles and standards for providing high-quality health-care services for adolescents. The highest ethical standards should be maintained, including voluntary participation, confidentiality, privacy and the best interests of each adolescent and young person. Failure to participate should not affect access to ART or other services.

The meaningful involvement of adolescents and young adults living with HIV in planning, developing, implementing and evaluating interventions would promote the acceptability and uptake of interventions.

Community support and the involvement of parents, parents, guardians and other community members in programmes may provide important support for programmes and promote their success.

Research gaps

Additional research is required to identify interventions that improve outcomes for different groups of adolescents and young adults living with HIV, such as those with disabilities; those with mental health conditions; those who acquired HIV perinatally versus horizontally; younger adolescents; those out of school; orphans; ethnic minority groups; key populations; those who are pregnant; and those living in contexts of adversity such as extreme poverty and/or humanitarian emergencies. Research is also needed on content and delivery strategies for interventions to involve parents and caregivers, for both younger and older adolescents, to assess the effectiveness of these programmes.

Further research is needed to inform feasible and effective training, supervision and implementation of support models at scale for facilitators of psychosocial interventions, including peer providers.

There is an ongoing need for research and programme evaluation from resource-constrained settings on psychosocial interventions for this group, which would be further supported with more data on the costs and cost effectiveness of interventions. To further inform implementation, intervention studies should aim to include methods to capture and report costs.

In addition, to enhance the comparability of study findings, intervention studies are encouraged to use standardized outcome definitions to report critical outcomes.

Lastly, follow-up beyond the immediate post-intervention period is needed to fully understand the long-term impact of psychosocial interventions.

10. TASK SHARING OF SPECIMEN COLLECTION AND POINT-OF-CARE TESTING

Recommendation

Task sharing of specimen collection and point-of-care testing with non-laboratory personnel should be implemented when professional staffing capacity is limited.

(Strong recommendation; moderate-certainty evidence)

Background and rationale

In the 2016 WHO consolidated guidelines *(3)*, a good practice statement stated that trained and supervised non-laboratory personnel, including laypeople, can undertake blood finger-pricks for collecting samples. This statement was made at a time when there were limited data comparing the performance of specimen collection and/or testing by non-laboratory personnel versus laboratory professionals. Most data before the 2016 consolidated guidelines focused on point-of-care diagnostic accuracy studies conducted in the laboratory by laboratory professionals.

Since 2016, several additional studies have been published, including the diagnostic accuracy of decentralized and task sharing of specimen collection and/or testing with non-laboratory professionals *(184)*. In addition, clinical studies examining how point-of-care testing by non-laboratory personnel affects patients have been published *(185)*. Together, this updated evidence has supported consideration of using point-of-care infant diagnosis and viral load testing to improve health outcomes.

In several settings, trained and supervised lay health-care providers are already conducting HIV testing and performing sample collection using the finger-prick method. In 2016, WHO strongly recommended that lay providers who are trained and supervised be able to independently conduct safe and effective HIV testing using rapid diagnostic tests *(3,68)*.

Access to diagnostic testing and sample collection remains low in many resource-limited settings, partly because of shortages of human resources, especially in rural settings. The lack of skilled laboratory professionals at health-care facilities and the need to scale up capacity may require sharing the tasks of point-of-care diagnostic testing and sample collection with lower cadres of health-care workers. Task sharing may also increase access to testing for key populations, who may have difficulty in accessing traditional health-care services regardless of professional staffing capacity.

A systematic review up to August 2018 identified 65 studies, mainly diagnostic accuracy studies *(184)*. Three randomized controlled trials assessed the clinical impact of point-of-care testing. Most studies (86%) were carried out in Africa. The certainty of the evidence was rated as moderate. The diagnostic accuracy analysis included about 15 000 data points. Ten types of non-laboratory health-care cadres performed nine types of point-of-care tests using 13 assays. Most studies included nurses. The primary outcome observed across most studies focused on the diagnostic accuracy of point-of-care testing when performed by non-laboratory personnel *(184)*.

Diagnostic accuracy of point-of-care CD4 testing

Compared with laboratory-based testing performed by laboratory professionals, point-of-care CD4 testing performed by non-laboratory health-care personnel had a mean bias of –35.72 cells/mm^3 (95% CI –57.10 to –14.33) *(184)*. Four studies compared the performance of point-of-care CD4 testing between laboratory professionals and non-laboratory personnel. The performance of each study was within the ±50 cells/mm^3 range, and the overall mean bias was –13.35 cells/mm^3 (95% CI –19.97 to –6.72). One study reviewed the performance of a device-free lateral flow CD4 assay when performed by nurses compared with laboratory-based CD4 testing performed by laboratory personnel *(186)* and found better performance of the test on venous blood (sensitivity: 81.7%, 95% CI 72.3–91.1%; specificity: 82.6%, 95% CI 77.1–88.1%) than on finger-prick specimens (sensitivity: 60.7%, 95% CI 45.0–76.3%; specificity: 89.5%, 95% CI 83.2–95.8%). No statistically significant difference in performance was detected by cadre of health-care worker ($p = 0.11$) or between point-of-care versus laboratory-based testing ($p = 0.11$).

Diagnostic accuracy and clinical impact of point-of-care infant diagnosis

A systematic review provided summary estimates of the diagnostic accuracy of technologies capable of being used at the point of care *(187)*. The performance overall was >98% sensitivity and >99% specificity. Seven of the 11 studies conducted the point-of-care test outside the laboratory. One study compared internal quality control rates and the return of results to caregivers for samples run on a point-of-care infant testing technology between nurses and laboratory-trained personnel to assess how task sharing affects the quality of testing. Failure rates did not differ significantly between non-laboratory testers (137 of 14 830 tests) and specialized laboratory-trained testers (28 of 364 tests) ($p = 0.35$) *(139)*.

Point-of-care same-day testing significantly reduced the time to deliver test results to caregivers *(185)*. In all seven studies *(185)*, the median time between sample collection and the results received by the infants' caregivers was 0 days (95% CI 0–0 days) for point of care, regardless of the test used, the age of the infant or the type of health-care facility. Same-day results were returned 97% of the time for point-of-care testing versus 0% for standard care. For laboratory-based testing, the median time between sample collection and results received by the caregiver ranged from 8 to 125 days, with a median of 35 days (95% CI 35–37 days). Five of seven studies had a median time to the caregiver receiving results exceeding 30 days.

The overall proportion of infants living with HIV initiating treatment within 60 days was 90.1% using point-of-care testing versus 53.7% using laboratory-based testing. The odds ratio of initiating treatment within 60 days was 7.9 (95% CI 5.4–11.5).

Three studies reviewed the performance of cryptococcal antigen lateral flow assays when used by non-laboratory personnel *(188–190)*. The non-laboratory personnel correctly identified cryptococcal antigen with 100% sensitivity and specificity in two of the studies. In the third study, when tested on serum samples, cryptococcal antigen lateral flow assays had sensitivity of 93% (95% CI 66–100%) and specificity of 100% (95% CI 88–100%). Two independent readers had strong agreement for all lateral flow assay results ($p < 0.001$). When trained nurses performed cryptococcal antigen lateral flow assays at the point of care, testing was feasible, had the highest accuracy on serum specimens and may accelerate prophylaxis and treatment of HIV-associated cryptococcal infections.

In addition, syphilis testing by non-laboratory personnel using the dual HIV/syphilis rapid diagnostic test had agreement of 0.67 (95% CI 0.36–0.97) and specificity of 99.9% (95% CI 99.8–100%) versus laboratory technicians *(191)*. Nursing personnel successfully tested external quality assurance panels using syphilis rapid tests, with sensitivity and specificity exceeding 90%.

Three studies compared the performance of alanine aminotransferase and haemoglobin enumeration tests operated by non-laboratory personnel with laboratory-based technologies operated by laboratory professionals *(192–194)*. Non-laboratory personnel operated both tests comparably to the laboratory-based technologies operated by laboratory professionals. A semiquantitative, visual point-of-care alanine aminotransferase assay performed by nurses had sensitivity of 87% and specificity of 77% compared with a laboratory-based technology operated by laboratory professionals. Finally, one study reviewed the performance of creatinine and lactate testing by non-laboratory personnel at two separate clinics. Creatinine testing had mean bias values of –4.5 µmol/L (95% CI –2.09 to –6.42 µmol/L) and –5.5 µmol/L (95% CI –4.49 to –6.42 µmol/L), and lactate testing had mean bias values of 0.01 mmol/L (95% CI –0.10 to 0.13 mmol/L) and 1.1 mmol/L (95% CI 1.04–1.18 mmol/L).

Clinical impact of point-of-care viral load testing

Using point-of-care tests, same-day viral load results were available to clinicians 99% of the time (median time to results being returned: 0 days) and to patients 99% of the time (median: 0 days) *(195,196)*. Using standard care, laboratory-based testing, same-day results were available for clinicians <25% of the time (median: 2 days) and for patients <1% of the time (median: 28 days). The observational studies also demonstrated substantially shorter time to return the results to both clinicians and patients using point-of-care testing versus laboratory-based testing. The hazard ratio (HR) comparing point-of-care with laboratory-based testing was 11.7 (95% CI 8.9–15.3) for returning the results to clinicians and 17.7 (95% CI 13.0–24.1) for returning the results to patients.

In the randomized controlled trial, 100% of patients identified with non-suppressed viral loads initiated second-line ART following point-of-care testing (median: 0 days) versus 44% (median: 76 days) following laboratory-based testing (risk difference 55.6%, 95% CI 23.1–88.0%; HR 10.9, 95% CI 2.1–57.5). The estimated time to any clinical action (either enhanced adherence counselling or initiating second-line ART) was also shorter following point-of-care testing versus laboratory-based testing in observational studies.

Benefits and harms

The Guideline Development Group formulated a strong recommendation based on their judgement of the overwhelming benefits of the intervention, including, but not limited to, the following.

- Most settings with limited resources and a high HIV burden lack laboratory professionals.
- Decentralized and task-shared specimen collection expands access to testing (dried blood spot specimens for infant diagnosis and viral load).
- Point-of-care testing leads to more rapid testing, return of results to clinicians and patients and clinical action.
- Fewer health facility visits are needed for caregivers to receive results and the timing of results is more reliable.

There was no major harm, but more extensive network support and maintenance were needed.

Feasibility, cost and cost effectiveness

Overall, task sharing of specimen collection and point-of-care testing with non-laboratory personnel was found to be feasible and acceptable. Task sharing would save costs with deployment of less trained personnel for diagnostic testing and sample collection. The most important cost will be training, ongoing supervision and remunerating non-laboratory personnel, albeit at a potentially lower cost compared with laboratory professionals. Decentralization will likely result in increased proportions of non-laboratory personnel required to perform the specimen collection and testing. This will require careful assessment and expansion of human resource capacity.

Equity and acceptability

Task sharing of specimen collection and point-of-care testing with non-laboratory personnel is likely to improve equity, since relying on specialized personnel favours populations in urban settings and increases the transport burden on rural populations, which generally have the lowest incomes. Task sharing may also increase access to testing for members of key populations, who may have difficulty in accessing traditional health services and facility-based services. Further, decentralizing specimen collection and testing may increase access to diagnostics, especially including interventions and technologies capable of returning the results on the same day or within a shorter time frame than laboratory-based testing.

In a systematic review conducted in 2019, 58% of non-laboratory personnel indicated that preparing dried blood spot specimens for viral load was very easy, 43% indicated that the specimen collection was easy and 85% of the respondents indicated that preparing dried blood spots was suitable for non-laboratory personnel *(184)*. Nurses had a 98% success rate of finger-prick blood specimen collection in South Africa. One study reported an ease-of-use score for task sharing point-of-care CD4 testing between 1.7 and 3 using a scale of 1 to 5 (5 being very difficult), and health-care worker trust in the test was measured at 82–100%. Another study found an odds ratio of 1.9 (95% CI 1.1–3.3) for more rational use of higher-level clinical personnel time with the introduction of point-of-care CD4 testing operated by lower-level personnel instead. Further, 94.7% (95% CI 92.9–95.9%) of lay health-care workers rated the point-of-care CD4 testing technology favourably. All non-laboratory personnel found the point-of-care viral load testing to be easy or very easy to use, and 85% of the respondents indicated that point-of-care viral load testing was suitable or very suitable for non-laboratory personnel. Ninety per cent of non-laboratory personnel said that a syphilis rapid diagnostic test was easy to use, while antenatal care personnel scored the dual HIV and syphilis rapid diagnostic test 2.41 (out of 3, being easiest) for ease of use and 2.27 (out of 3) for ease of interpretation.

A study in Cameroon, Côte d'Ivoire, Eswatini, Kenya, Lesotho, Mozambique, Rwanda and Zimbabwe conducted structured interviews with health-care workers providing infant testing services and semistructured interviews with national and regional laboratory managers or early infant diagnosis programme managers before and after point-of-care infant testing was implemented *(195)*. Health-care workers found point-of-care infant testing easy to use (74% said it was very simple to run the test) and were very satisfied with the fast turnaround time and ability to initiate treatment for infants living with HIV sooner (93%).

Implementation considerations

Access to high-quality diagnostic testing should be continually expanded across HIV and other molecular testing needs, ideally combining laboratory-based and point-of-care technologies in an integrated laboratory network. Implementing a wide network of decentralized and task-shared specimen collection and/or point-of-care testing will require centralized support from national laboratories and programmes to ensure adequate training, mentorship, service and maintenance, (continuous) quality assurance and accurate data entry at the point of care. In addition, decentralizing specimen collection and task sharing will require expanding human resource capacity. Legal and regulatory issues and policies may require adjustments in some countries to support the decentralization and task sharing of specimen collection and testing with non-laboratory personnel. Concurrently, scaling up and building human resource capacity, including strengthening laboratory personnel and capacity, will be critical to expanding diagnostic access. WHO has developed tools and guidelines for human resources for health and recommends an approach to systematically address the dynamics of the health workforce that includes assessing workload indicators among health-care providers.

Research gaps

Additional diagnostic accuracy studies directly comparing the performance of newer point-of-care technologies (infant diagnosis and viral load testing) between non-laboratory personnel and laboratory professionals would be valuable.

11. DIAGNOSTIC INTEGRATION

Good practice statement

Disease programmes, especially HIV and TB, should actively work towards balanced integration of diagnostic services.

Background and rationale

The aim of universal health coverage and related services is to deliver high-quality people-centred integrated service and care. Universal health coverage also emphasizes a fundamental shift in service delivery such that services are integrated and focused on the needs of people and communities. One intervention that shows promise in helping to achieve these goals is diagnostic integration. Significant unmet testing needs remain across diseases, including HIV, TB, hepatitis, sexually transmitted infections, emerging infections, and other infections. Programmatic integration (both sharing devices and integrating networks) is a priority intervention within the universal health coverage agenda to optimize the use of limited resources and improve care.

WHO developed guidance for countries on the key considerations of multi-disease testing in 2017 *(197)*. In 2019, WHO held a country consultation to share experiences and focus on some of the key aspects to diagnostic integration *(198)*: funding and resources; optimizing and mapping the diagnostic networks; integrating systems; and considerations related to patients.

Several countries across all WHO regions are already moving forward with diagnostic integration, seeing the benefits for programmes and patients. Some countries are also sharing devices and considering integrating HIV and TB diagnostic services and incorporating hepatitis C virus, human papillomavirus and emerging outbreak infections. Several technologies exist that can conduct multiple tests on the same technology and can be considered for diagnostic integration or device sharing *(199)*.

Numerous country pilot projects are ongoing or completed, including from the Central African Republic, the Democratic Republic of the Congo, India, Malawi, Mozambique and Zimbabwe. During the 2019 consultation *(198)*, countries reported the overall benefits diagnostic integration provides for all health programmes:

- more efficient and comprehensive patient care pathways;
- increased access for underserved or underfunded programmes;
- a more optimized and collaborative integrated diagnostic network with improved laboratory workflow;
- broader device footprints through shared technologies;
- overall more efficient laboratory services, including data management, sample transport, quality assurance, service and maintenance and supply chain;
- increased negotiating power with suppliers because of increased volumes and a stronger voice for lower, more inclusive, transparent and fair prices across programmes, countries and regions and reduced costs and more efficient use of limited resources by sharing operational costs;
- shared operational knowledge across programmes;
- streamlined diagnostic capabilities and approaches across stakeholders; and
- encouraging integrated cross-sectoral approaches to high-quality testing services and care.

In order to consider the utilization needs of all programs and continue to ensure the host programmes in particular have full access to device capacity, patient and test prioritization may be necessary. To ensure more rationale integrated testing, a number of countries have continued testing all people with presumptive TB with the addition of infant HIV diagnosis and targeted HIV viral load testing; HIV volumes were generally small and ensured no overutilization. Careful consideration for test volumes across diseases and how to set priorities among patients for point-of-care and laboratory referral testing will be critical through network optimization and mapping exercises.

The following challenges have been identified through pilots and programmes.

- Focus is required to adjust the laboratory and clinic workflow on implementing additional assays on the integrated platform.
- Systems considerations need to be implemented to ensure that results are returned on the same day, especially for more urgent tests and results, such as infant HIV diagnosis.
- Adequate human resource capacity is needed to manage additional patient demand.
- Service and maintenance contracts are often limited or challenging (this was specific to the technology implemented during pilots).
- Significant support is necessary to ensure that adequate infrastructure is introduced

Access to high-quality diagnostic testing should be continually expanded across testing needs, ideally combining laboratory-based and point-of-care technologies in an integrated diagnostic network without creating dependence on any one technology. Attention should also be paid to human resources, supply chain, quality assurance, monitoring and reporting and national regulatory components to develop sustainable and strong integrated networks.

Careful planning and coordination are important for both programme management and service delivery. Political will, significant coordination, collaboration and integration across disease programmes will be important.

Further, diagnostic integration and device sharing provide several potential mechanisms to reduce costs across assays, diseases and programmes *(198)*. Increased volumes and utilization will enable more efficient use of devices within cost and service and maintenance contracts, given the increase in the number of tests over which the fixed costs can be amortized. The cost per test decreases as utilization increases. Costs can be shared across numerous activities and programmes, including instruments, service and maintenance, logistics and commodity supply chain management, human resources, sample transport, training and mentoring, waste management, data management, quality assurance, and delivery of results.

Sharing costs between programmes could translate into cost savings for all programmes and more efficient use of resources. Costs can be shared between the host and beneficiary programmes under different allocation scenarios (such as by testing volumes, by allocating entire cost items to each respective programme or by accounting for already incurred investments). Costs are mainly saved by sharing device costs and service and maintenance costs *(200)*. Leveraging existing device fleets with available capacity is a feasible approach to increase access to testing in a cost-effective manner. Tools exist to support countries in understanding the savings available and determining the most efficient and effective strategy.

A systematic review up to June 2020 *(201)* found two observational studies reporting outcomes of integrating HIV and TB testing – one conducted by Médecins Sans Frontières in Zimbabwe *(202)* and another by the Clinton Health Access Initiative in Malawi and Zimbabwe *(203)*. Both studies reviewed the impact of integrating HIV testing with TB testing and how this affected TB testing, the programme that procured and set up the technology.

Even with the addition of HIV infant testing and targeted HIV viral load testing were considered, TB testing volumes accounted for about 60% of the total test volumes after integration. Despite the increase in overall testing volumes, device use never exceeded 75%. No adverse impact was observed on the turnaround time for results or outcomes after integration with HIV testing. The time to return results and proportion of people initiating TB treatment were the same before and after the addition of infant diagnosis testing and targeted viral load testing.

After integration with the TB-procured devices, HIV infant diagnosis and targeted HIV viral load testing experienced faster turnaround times and increased treatment initiation rates and the probability of clinical action for infants living with HIV and people living with HIV receiving ART experiencing viraemia. Offering TB, HIV infant diagnosis and targeted HIV viral load through integrated testing increased device use without exceeding capacity or affecting TB services. These studies show that integrated testing was operationally feasible with appropriate site selection to balance the expected demand. TB testing and treatment continued to be provided at the same rate.

Based on the available evidence and country experience, the Guideline Development Group determined that a good practice statement was indicated, since implementing the integration of diagnostic services across disease programmes is anticipated to result in net overall benefit. The Guideline Development Group agreed that programmes should consider integrating their diagnostic services, both for programmatic reasons and to ensure comprehensive care for people living with HIV. Increased efficiency is expected to be created, and diagnostic integration and sharing devices would enable more integrated health services and diagnostic networks.

Particular anticipated benefits include the potential to improve access to testing by increasing the device base; leveraging programme knowledge; and shared operational costs. Diagnostic integration is also expected to create a more optimized, efficient network across diseases, improve patient care and reduce the costs generated in vertical programmes. Diagnostic integration is also expected to ensure a more robust and reactive diagnostic network, particularly positioned to respond to outbreaks and pandemics as they arise.

Knowledge gaps were identified that could benefit from further research, including measuring the impact of diagnostic integration across disease types (including HIV, TB, hepatitis, sexually transmitted infections, cervical cancer and disease outbreaks). Implementation research to generate evidence supporting best practices for diagnostic integration and around the quality assurance approaches for sustainable delivery of diagnostic integration, especially in a broader, integrated network, would also be beneficial.

12. DISSEMINATING, ADAPTING AND IMPLEMENTING THE GUIDELINES

These updated guidelines will be made available on the WHO HIV website. The key findings and recommendations will be released in the form of a policy brief. This is in accordance with the plan to update the consolidated guidelines from 2016, and fully updated guidelines, including components of treatment and operational and service delivery guidelines, are planned for publication in mid-2021. The publication will be made available in English. Translations to other official languages will be developed in coordination with the regional and country offices.

Media and formats

The recommendations and supporting information will be integrated into the WHO HIV Tx App[2] which is a free mobile application for easy access and reference. The App is available globally for download on major App stores. Printed materials, pdfs and social media links will also be available to disseminate key messages of WHO recommendations. Key annexes containing information on the systematic reviews and other supporting information will be uploaded to the WHO website. Derivative products will be produced to assist countries in adapting and implementing guidelines into their own context in the form of slide sets, Q&A and webinars with key stakeholders.

Implementation

The Department of Global HIV, Viral Hepatitis and Sexually Transmitted Infection Programmes monitors the uptake of HIV-related recommendations through several mechanisms, including the Global AIDS Monitoring framework, country surveys and population-based HIV impact assessments, which provides indirect evidence of the impact of WHO recommendations. The Department will be working with WHO regional and country offices, major donors and implementing partners to support the uptake and implementation of these guidelines. Potential barriers include delays in dissemination because of increased time to translate the document and delayed uptake because of limited resources in countries to change existing policies.

Updating

Ongoing scoping reviews are carried out to anticipate what guidance might be required for the coming years. When necessary, rapid guidance and technical and operational updates will complement the guideline updates.

[2] Weblinks: www.hivtx.org/iphone, www.hivtx.org/android

References

1. 2020 Global AIDS update – seizing the moment – tackling entrenched inequalities to end epidemics. Geneva: UNAIDS, 2020 (https://www.unaids.org/sites/default/files/media_asset/2020_global-aids-report_en.pdf, accessed 5 March 2021).
2. Ford N, Ball A, Baggaley R, Vitoria M, Low-Beer D, Penazzato M et al. The WHO public health approach to HIV treatment and care: looking back and looking ahead. Lancet Infect Dis. 2018;18:e76–86.
3. 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 (https://www.who.int/hiv/pub/arv/arv-2016/en, accessed 5 March 2021).
4. Haas AD, Zaniewski E, Anderegg N, Ford N, Fox MP, Vinikoor M et al. Retention and mortality on antiretroviral therapy in sub-Saharan Africa: collaborative analyses of HIV treatment programmes. J Int AIDS Soc. 2018;21.
5. Wolff MJ, Cortes CP, Mejia FA, Padgett D, Belaunzaran-Zamudio P, Grinsztejn B et al. Evaluating the care cascade after antiretroviral therapy initiation in Latin America. Int J STD AIDS. 2018;29:4–12.
6. Kariminia A, Law M, Davies MA, Vinikoor M, Wools-Kaloustian K, Leroy V et al. Mortality and losses to follow-up among adolescents living with HIV in the IeDEA global cohort collaboration. J Int AIDS Soc. 2018;21:e25215.
7. Abuogi LL, Smith C, McFarland EJ. Retention of HIV-infected children in the first 12 months of anti-retroviral therapy and predictors of attrition in resource limited settings: a systematic review. PLoS One. 2016;11:e0156506.
8. Kaplan S, Nteso KS, Ford N, Boulle A, Meintjes G. Loss to follow-up from antiretroviral therapy clinics: A systematic review and meta-analysis of published studies in South Africa from 2011 to 2015. South Afr J HIV Med. 2019;20:984.
9. Ford N, Geng E, Ellman T, Orrell C, Ehrenkranz P, Sikazwe I et al. Emerging priorities in HIV service delivery. PLoS Med. 2020;17:e1003028.
10. United Nations Political Declaration on Ending AIDS. Geneva: UNAIDS; 2016 (https://www.unaids.org/sites/default/files/media_asset/fast-track-commitments_en.pdf, accessed 5 March 2021
11. Handbook of 2016 integrated HIV clinical care guidelines Botswana: Ministry of Health; 2016.
12. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A et al. Going from evidence to recommendations. BMJ. 2008;336:1049–51.
13. Duncombe C, Rosenblum S, Hellmann N, Holmes C, Wilkinson L, Biot M et al. Reframing HIV care: putting people at the centre of antiretroviral delivery. Trop Med Int Health. 2015;20:430–47.
14. Grimsrud A, Bygrave H, Doherty M, Ehrenkranz P, Ellman T, Ferris R et al. Reimagining HIV service delivery: the role of differentiated care from prevention to suppression. J Int AIDS Soc. 2016;19:21484.

15. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. Geneva: World Health Organization; 2017 (https://www.who.int/hiv/pub/guidelines/advanced-HIV-disease/en, accessed 5 March 2021).

16. Differentiated service delivery for HIV treatment: summary of published evidence. Geneva: International AIDS Society; 2020.

17. WHO, CDC, PEPFAR, USAID, IAS. Key considerations for differentiated antiretroviral therapy delivery for specific populations: children, adolescents, pregnant and breastfeeding women and key populations. Geneva: World Health Organization; 2017 (https://www.who.int/hiv/pub/arv/hiv-differentiated-care-models-key-populations/en, accessed 5 March 2021).

18. Tsondai PR, Wilkinson LS, Grimsrud A, Mdlalo PT, Ullauri A, Boulle A. High rates of retention and viral suppression in the scale-up of antiretroviral therapy adherence clubs in Cape Town, South Africa. J Int AIDS Soc. 2017;20(Suppl. 4):21649.

19. Kehoe K, Boulle A, Tsondai PR, Euvrard J, Davies MA, Cornell M. Long-term virologic responses to antiretroviral therapy among HIV-positive patients entering adherence clubs in Khayelitsha, Cape Town, South Africa: a longitudinal analysis. J Int AIDS Soc. 2020;23:e25476.

20. Kaplan SR, Oosthuizen C, Stinson K, Little F, Euvrard J, Schomaker M et al. Contemporary disengagement from antiretroviral therapy in Khayelitsha, South Africa: A cohort study. PLoS Med. 2017;14:e1002407.

21. Cassidy T, Keene C, Lebelo K, Grimsrud A, Wilkinson L. Twenty-four month retention and viral load outcomes from a non-inferiority cluster randomized trial of extending ART dispensing intervals to 6-monthly in adherence clubs. AIDS2020: Virtual, 6–10 July 2020 (http://programme.aids2020.org/Abstract/Abstract/11592, Accessed 5 March 2021).

22. Tshuma N, Mosikare O, Yun JA, Alaba OA, Maheedhariah MS, Muloongo K et al. Acceptability of community-based adherence clubs among health facility staff in South Africa: a qualitative study. Patient Prefer Adherence. 2017;11:1523–31.

23. Nicols B, Fatti G, Cele R, Leodeba N, Maotoe T, Sejana M. Economic evaluation of differentiated service delivery models for ART service delivery from a cluster-randomized trial in Lesotho: cost to provider and cost to patient. AIDS2020: Virtual, 6–10 July 2020 (https://programme.aids2020.org/Search/Search?search=PEE1626, accessed 5 March 2021).

24. Wilkinson L, Moyo F, Henwood R, Runeyi P, Patel S. Youth ART adherence clubs: outcomes from an innovative model for HIV positive youth in Khayelitsha, South Africa. AIDS 2016, 18–22 July 2016, Durban, South Africa.

25. Tsondai P, Wilkinson L, Henwood R, Ullauri A, Cassidy T. Retention and viral suppression outcomes of patients enrolled in family ART adherence clubs in Cape Town, South Africa. IAS 2017, 22–27 July 2017, Paris, France.

26. Lebelo K, Cassidy T, Duran L, Bhardwaj V, Mantangana N, Mdani L et al. Integrated postnatal clubs show improved maternal viral load completion and infant testing uptake compared to historical controls in Khayelitsha, South Africa. AIDS2020: Virtual, 6–10 July 2020 (http://programme.aids2020.org/Abstract/Abstract/7275, accessed 5 March 2021).

27. Athura S, Weikum D, Ajulong Cea. Leaving no one behind: assessing the impact of MSM community-based adherence clubs on retention and viral load suppression in Uganda. AIDS2020: Virtual, 6–10 July 2020 (http://programme.aids2020.org/Abstract/Abstract/5648, accessed 5 March 2021).

28. Finci I, Flores A, Gutierrez Zamudio AG, Matsinhe A, de Abreu E, Issufo S et al. Outcomes of patients on second- and third-line ART enrolled in ART adherence clubs in Maputo, Mozambique. Trop Med Int Health. 2020;25:1496–1502.

29. Decroo T, Koole O, Remartinez D, dos Santos N, Dezembro S, Jofrisse M et al. Four-year retention and risk factors for attrition among members of community ART groups in Tete, Mozambique. Trop Med Int Health. 2014;19:514–21.

30. Tukei BB, Fatti G, Tiam A, Ngorima-Mabhena N, Tukei VJ, Tshabalala I et al. Twelve-month outcomes of community-based differentiated models of multimonth dispensing of ART among stable HIV-infected adults in Lesotho: a cluster-randomized noninferiority trial. J Acquir Immune Defic Syndr. 2020;85:280–91.

31. Fatti G, Ngorima-Mabhena N, Mothibi E, Muzenda T, Choto R, Kasu T et al. Outcomes of three- versus six-monthly dispensing of antiretroviral treatment (ART) for stable HIV patients in community ART refill groups: a cluster-randomized trial in Zimbabwe. J Acquir Immune Defic Syndr. 2020;84:162–72.

32. Rasschaert F, Telfer B, Lessitala F, Decroo T, Remartinez D, Biot M et al. A qualitative assessment of a community antiretroviral therapy group model in Tete, Mozambique. PLoS One. 2014;9:e91544.

33. Auld AF, Shiraishi RW, Couto A, Mbofana F, Colborn K, Alfredo C et al. A decade of antiretroviral therapy scale-up in Mozambique: evaluation of outcome trends and new models of service delivery among more than 300,000 patients enrolled during 2004–2013. J Acquir Immune Defic Syndr. 2016;73:e11–22.

34. Bochner AF, Meacham E, Mhungu N, Manyanga P, Petracca F, Muserere C et al. The rollout of community ART refill groups in Zimbabwe: a qualitative evaluation. J Int AIDS Soc. 2019;22:e25393.

35. Mantell JE, Masvawure TB, Mapingure M, Apollo T, Gwanzura C, Block L et al. Engaging men in HIV programmes: a qualitative study of male engagement in community-based antiretroviral refill groups in Zimbabwe. J Int AIDS Soc. 2019;22:e25403.

36. Kagimu D, Egessa J, Oucul L, Senyonga E. Overcoming barriers to access of HIV/AIDS services among female sex workers through differentiated service delivery models, TASO Entebbe experience. AIDS 2018; 23–27 June 2018, Amsterdam, Netherlands.

37. Mwamba D, Herce M, Wa Mwanza M, Thulani R. Community adherence group (CAG) for HIV viremic patients: early lessons learnt from Lusaka, Zambia. IAS 2019, 21–24 July 2019, Mexico City, Mexico.

38. Jobarteh K, Shiraishi RW, Malimane I, Samo Gudo P, Decroo T, Auld AF et al. Community ART support groups in Mozambique: the potential of patients as partners in care. PLoS One. 2016;11:e0166444.

39. Ssonko C, Gonzalez L, Mesic A, da Fonseca MS, Achar J, Safar N et al. Delivering HIV care in challenging operating environments: the MSF experience towards differentiated models of care for settings with multiple basic health care needs. J Int AIDS Soc. 2017;20(Suppl. 4):21654.

40. Alamo ST, Wagner GJ, Ouma J, Sunday P, Marie L, Colebunders R et al. Strategies for optimizing clinic efficiency in a community-based antiretroviral treatment programme in Uganda. AIDS Behav. 2013;17:274–83.

41. Christ B, van Dijk J, Ballif M, Nyandoro T, Reichmuth M, Mukondwa W. Differentiated antiretroviral therapy delivery in rural Zimbabwe: availability, needs and challenges. OSF Preprints. 2020 August 12. doi:10.31219/osf.io/zpq2e.

42. Obua C, Kayiwa J, Waako P, Tomson G, Balidawa H, Chalker J et al. Improving adherence to antiretroviral treatment in Uganda with a low-resource facility-based intervention. Glob Health Action. 2014;7:24198.

43. Babigumira JB, Castelnuovo B, Stergachis A, Kiragga A, Shaefer P, Lamorde M et al. Cost effectiveness of a pharmacy-only refill program in a large urban HIV/AIDS clinic in Uganda. PLoS One. 2011;6:e18193.

44. Wringe A, Cawley C, Szumilin E, Salumu L, Amoros Quiles I, Pasquier E et al. Retention in care among clinically stable antiretroviral therapy patients following a six-monthly clinical consultation schedule: findings from a cohort study in rural Malawi. J Int AIDS Soc. 2018;21:e25207.

45. Bosomprah S, Zulu I, Herce M, Mulenga L, Shah M, Sikazwe Iea. Differentiated service delivery for HIV care: The fast track experience from Zambia. CROI 2020, 8–11 March 2020, Boston, MA, USA (https://www.croiconference.org/abstract/differentiated-service-delivery-for-hiv-care-the-fast-track-experience-from-zambia, accessed 5 March 2021).

46. Mesic A, Fontaine J, Aye T, Greig J, Thwe TT, Moreto-Planas L et al. Implications of differentiated care for successful ART scale-up in a concentrated HIV epidemic in Yangon, Myanmar. J Int AIDS Soc. 2017;20(Suppl. 4):21644.

47. Kim MH, Wanless RS, Caviness AC, Golin R, Amzel A, Ahmed S et al. Multimonth prescription of antiretroviral therapy among children and adolescents: experiences from the Baylor International Pediatric AIDS Initiative in 6 African Countries. J Acquir Immune Defic Syndr. 2018;78(Suppl. 2):S71–80.

48. Bacha JM, Aririguzo LC, Mng'ong'o V, Malingoti B, Wanless RS, Ngo K et al. The Standardized Pediatric Expedited Encounters for ART Drugs Initiative (SPEEDI): description and evaluation of an innovative pediatric, adolescent, and young adult antiretroviral service delivery model in Tanzania. BMC Infect Dis. 2018;18:448.

49. Mpima D, Birungi J, Makabayi R, Kanters S, Luzze C. Community antiretroviral therapy (ART) delivery models for high patient retention and sustaining good adherence: The AIDS Support Organisation (TASO) operational reseach findings, CDC/PEPFAR funded project in Uganda. IAS 2013, 30 June–3 July 2013, Kuala Lumpur, Malaysia.

50. Vogt F, Kalenga L, Lukela J, Salumu F, Diallo I, Nico E et al. Brief report: decentralizing ART supply for stable HIV patients to community-based distribution centers: program outcomes from an urban context in Kinshasa, DRC. J Acquir Immune Defic Syndr. 2017;74:326–31.

51. Fox MP, Pascoe S, Huber AN, Murphy J, Phokojoe M, Gorgens M et al. Adherence clubs and decentralized medication delivery to support patient retention and sustained viral suppression in care: results from a cluster-randomized evaluation of differentiated ART delivery models in South Africa. PLoS Med. 2019;16:e1002874.

52. Hendriksz F, Dube T, Strydom B, Banoo S. Centralized dispensing and alternative pick up points increases access to ARVs in Zambia. IAS 2019, 21-24 July 2019, Mexico City, Mexico.

53. Shoopala N, Baughman A, Mengistu A, Mitruka K, Woelk G, Mutandi G et al. Outcomes of community-based antiretroviral treatment program in Namibia. 28th Conference on Retroviruses and Opportunistic Infections, 8–11 March 2020, Boston, MA, USA (https://www.croiconference.org/abstract/outcomes-of-community-based-antiretroviral-treatment-program-in-namibia, accessed 5 March 2021).

54. Cornell M, Dovel K. Reaching key adolescent populations. Curr Opin HIV AIDS. 2018;13:274–80.

55. Selke HM, Kimaiyo S, Sidle JE, Vedanthan R, Tierney WM, Shen C et al. Task-shifting of antiretroviral delivery from health care workers to persons living with HIV/AIDS: clinical outcomes of a community-based program in Kenya. J Acquir Immune Defic Syndr. 2010;55:483–90.

56. Leisegang R, Calkins K, Cotton M, Cleary S, Karamchand S, Hammann F. HIV+ patients receiving ARVs through home delivery: does it matter? A causal analysis. 28th Conference on Retroviruses and Opportunistic Infections, 8–11 March 2020, Boston, MA, USA.

57. Vu L, Waliggo S, Zieman B, Jani N, Buzaalirwa L, Okoboi S et al. Annual cost of antiretroviral therapy among three service delivery models in Uganda. J Int AIDS Soc. 2016;19(5 Suppl. 4):20840.

58. Long L, Kuchukhidze S, Pascoe S, Nichols BE, Fox MP, Cele R et al. Retention in care and viral suppression in differentiated service delivery models for HIV treatment delivery in sub-Saharan Africa: a rapid systematic review. J Int AIDS Soc. 2020;23:e25640.

59. WHO global strategy on people-centred and integrated health services: interim report. Geneva: World Health Organization; 2015. (https://apps.who.int/iris/bitstream/handle/10665/155002/WHO_HIS_SDS_2015.6_eng.pdf?sequence=1, accessed 5 March 2021).

60. Zanolini A, Sikombe K, Sikazwe I, Eshun-Wilson I, Somwe P, Bolton Moore C et al. Understanding preferences for HIV care and treatment in Zambia: Evidence from a discrete choice experiment among patients who have been lost to follow-up. PLoS Med. 2018;15:e1002636.

61. Rabkin M, Strauss M, Mantell JE, Mapingure M, Masvawure TB, Lamb MR et al. Optimizing differentiated treatment models for people living with HIV in urban Zimbabwe: findings from a mixed methods study. PLoS One. 2020;15:e0228148.

62. Eshun-Wilson I, Kim HY, Schwartz S, Conte M, Glidden DV, Geng EH. Exploring relative preferences for HIV service features using discrete choice experiments: a synthetic review. Curr HIV/AIDS Rep. 2020;17:467–77.

63. Peitzmeier SM, Grosso A, Bowes A, Ceesay N, Baral SD. Associations of stigma with negative health outcomes for people living with HIV in the Gambia: implications for key populations. J Acquir Immune Defic Syndr. 2015;68(Suppl. 2):S146–53.

64. Kennedy CE, Baral SD, Fielding-Miller R, Adams D, Dludlu P, Sithole B et al. "They are human beings, they are Swazi": intersecting stigmas and the positive health, dignity and prevention needs of HIV-positive men who have sex with men in Swaziland. J Int AIDS Soc. 2013;16 (Suppl. 3):18749.

65. Consolidated guidelines on HIV prevention, diagnosis, treatment and care of key populations. Geneva: World Health Organization; 2016 (https://www.who.int/hiv/pub/guidelines/keypopulations/en, accessed 5 March 2021).

66. Beres L, Jingjia L, Aaron A, Khalifa B, Mody A, Schwartz S et al. Patient-centered interventions to improve patient–provider interactions for patients living with HIV in low- and middle-income countries. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

67. Global standards for quality health-care services for adolescents: a guide to implement a standards-driven approach to improve the quality of health care services for adolescents. Geneva: World Health Organization; 2015 (https://www.who.int/maternal_child_adolescent/documents/global-standards-adolescent-care/en, accessed 5 March 2021).

68. Consolidated guidelines on HIV testing services. Geneva World Health Organization; 2019 (https://www.who.int/hiv/pub/guidelines/hiv-testing-services/en, accessed 5 March 2021).

69. Sabapathy K, Hensen B, Varsaneux O, Floyd S, Fidler S, Hayes R. The cascade of care following community-based detection of HIV in sub-Saharan Africa – a systematic review with 90–90–90 targets in sight. PLoS One. 2018;13:e0200737.

70. Ahmed S, Autrey J, Katz IT, Fox MP, Rosen S, Onoya D et al. Why do people living with HIV not initiate treatment? A systematic review of qualitative evidence from low- and middle-income countries. Soc Sci Med. 2018;213:72–84.

71. Addressing violence against women. Key achievements and priorities. Geneva: World Health Organization; 2018 (https://www.who.int/reproductivehealth/publications/violence/adressing-vaw-achievements-priorities/en, accessed 5 March 2021).

72. Seeley J, Bond V, Yang B, Floyd S, MacLeod D, Viljoen L et al. Understanding the time needed to link to care and start ART in seven HPTN 071 (PopART) study communities in Zambia and South Africa. AIDS Behav. 2019;23:929–46.

73. Maughan-Brown B, Beckett S, Kharsany ABM, Cawood C, Khanyile D, Lewis L et al. Poor rates of linkage to HIV care and uptake of treatment after home-based HIV testing among newly diagnosed 15-to-49 year-old men and women in a high HIV prevalence setting in South Africa. AIDS Care. 2020:1–10.

74. Nhassengo P, Cataldo F, Magaco A, Hoffman RM, Nerua L, Saide M et al. Barriers and facilitators to the uptake of test and treat in Mozambique: a qualitative study on patient and provider perceptions. PLoS One. 2018;13:e0205919.

75. Eshun-Wilson I, Awotiwon A, Germann A, Amankwaa S, Ford N, Schwartz S et al. The effects of community-based antiretroviral therapy initiation on HIV cascade outcomes: a living systematic review and meta-analysis. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

76. Ibiloye O, Decroo T, Eyona N, Eze P, Agada P. Characteristics and early clinical outcomes of key populations attending comprehensive community-based HIV care: Experiences from Nasarawa State, Nigeria. PLoS One. 2018;13:e0209477.

77. Vu L, Tun W, Apicella L, Casalini C, Makyao N, Tsang S et al. Community-based antiretroviral therapy (ART) delivery for female sex workers in Tanzania: intervention model and baseline findings. AIDS Care. 2020;32:729–34.

78. Reif L BR, Rivera V, Jospeh B, Anglade B, Pape JW et al. A novel model of community cohort care for HIV-infected adolescents improves outcomes. Topics Antiviral Med. 2017;25(1 Suppl. 1):355s–6.

79. Eholie SP, Badje A, Kouame GM, N'Takpe J B, Moh R, Danel C et al. Antiretroviral treatment regardless of CD4 count: the universal answer to a contextual question. AIDS Res Ther. 2016;13:27.

80. Barnabas RV, Szpiro AA, van Rooyen H, Asiimwe S, Pillay D, Ware NC et al. Community-based antiretroviral therapy versus standard clinic-based services for HIV in South Africa and Uganda (DO ART): a randomised trial. Lancet Glob Health. 2020;8:e1305–15.

81. MacPherson P, Lalloo DG, Webb EL, Maheswaran H, Choko AT, Makombe SD et al. Effect of optional home initiation of HIV care following HIV self-testing on antiretroviral therapy initiation among adults in Malawi: a randomized clinical trial. JAMA. 2014;312:372–9.

82. Tun W, Apicella L, Casalini C, Bikaru D, Mbita G, Jeremiah K et al. Community-based antiretroviral therapy (ART) delivery for female sex workers in Tanzania: 6-month ART initiation and adherence. AIDS Behav. 2019;23(Suppl. 2):142–52.

83. Transitioning to an optimal paediatric ARV formulary: implementation considerations Geneva: World Health Organisation; 2018 (https://www.who.int/hiv/pub/paediatric/transition-paediatric-arv-formulary/en, accessed 5 March 2021).

84. Aung MN, Moolphate S, Kitajima T, Siriwarothai Y, Takamtha P, Katanyoo C et al. Perceived stigma of HIV patients receiving task-shifted primary care service and its relation to satisfaction with health service. J Infect Dev Ctries. 2017;11:697–704.

85. Aung MN, Moolphate S, Kitajima T, Siriwarothai Y, Takamtha P, Katanyoo C et al. Satisfaction of HIV patients with task-shifted primary care service versus routine hospital service in northern Thailand. J Infect Dev Ctries. 2015;9:1360–6.

86. Ford N, Migone C, Calmy A, Kerschberger B, Kanters S, Nsanzimana S et al. Benefits and risks of rapid initiation of antiretroviral therapy. AIDS. 2018;32:17–23.

87. Joseph Davey D, Kehoe K, Serrao C, Prins M, Mkhize N, Hlophe K et al. Same-day antiretroviral therapy is associated with increased loss to follow-up in South African public health facilities: a prospective cohort study of patients diagnosed with HIV. J Int AIDS Soc. 2020;23:e25529.

88. Mshweshwe-Pakela N, Hansoti B, Mabuto T, Kerrigan D, Kubeka G, Hahn E et al. Feasibility of implementing same-day antiretroviral therapy initiation during routine care in Ekurhuleni District, South Africa: retention and viral load suppression. South Afr J HIV Med. 2020;21:1085.

89. Lebelonyane R, Bachanas P, Block L, Ussery F, Abrams W, Roland M et al. Rapid antiretroviral therapy initiation in the Botswana Combination Prevention Project: a quasi-experimental before and after study. Lancet HIV. 2020;7:e545–53.

90. Scott NA, Maskew M, Fong RM, Olson IE, Brennan AT, Fox MP et al. Patient perspectives of quality of the same-day antiretroviral therapy initiation process in Gauteng Province, South Africa: qualitative dominant mixed-methods analysis of the SLATE II Trial. Patient. 2021;14:175–86.

91. Eshun-Wilson I, Wang S, Thompson R, Geng EH. The effects of co-interventions for rapid antiretroviral therapy initiation on HIV cascade outcomes: a living systematic review and metaanalysis. 2020. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

92. National Commitments and Policy Instrument (NCPI). Geneva: UNAIDS; 2021 (http://lawsandpolicies.unaids.org, accessed 5 March 2021).

93. Le Tourneau N, Eshun-Wilson I, German A, Thompson R, Geng EH. Reducing the frequency of appointments for clinical evaluation or medication pick-up among persons living with HIV: a living systematic review and meta-analysis. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

94. Grimsrud A, Patten G, Sharp J, Myer L, Wilkinson L, Bekker LG. Extending dispensing intervals for stable patients on ART. J Acquir Immune Defic Syndr. 2014;66:e58–60.

95. Maintaining essential health services: operational guidance for the COVID-19 context: interim guidance. Geneva: World Health Organisation, 2020 (https://apps.who.int/iris/handle/10665/332240, accessed 5 March 2021).

96. Patient benefits and costs associated with differentiated models of service delivery for HIV treatment in sub-Saharan Africa. Boston: Boston University School of Public Health; 2019. (AMBIT Project Report Number 01; https://www.heroza.org/wp-content/uploads/2019/09/AMBIT-report-01-patient-benefits-and-costs-Sept-03-2019-v1.1-1.pdf, accessed 5 March 2021).

97. Chammartin F, Dao Ostinelli CH, Anastos K, Jaquet A, Brazier E, Brown S et al. International epidemiology databases to evaluate AIDS (IeDEA) in sub-Saharan Africa, 2012–2019. BMJ Open. 2020;10:e035246.

98. Carlucci JG, Liu Y, Clouse K, Vermund SH. Attrition of HIV-positive children from HIV services in low and middle-income countries. AIDS. 2019;33:2375–86.

99. Zurcher K, Mooser A, Anderegg N, Tymejczyk O, Couvillon MJ, Nash D et al. Outcomes of HIV-positive patients lost to follow-up in African treatment programmes. Trop Med Int Health. 2017;22:375–87.

100. Mirzazadeh A, Thompson R, Bonyani A, Wilson I, Kahn J, Baral S et al. Systematic review and meta-analysis of interventions to reengage people living with HIV who are lost to follow-up. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

101. Li Y, Marshall CM, Rees HC, Nunez A, Ezeanolue EE, Ehiri JE. Intimate partner violence and HIV infection among women: a systematic review and meta-analysis. J Int AIDS Soc. 2014;17:18845.

102. Sikazwe I, Eshun-Wilson I, Sikombe K, Beres LK, Somwe P, Mody A et al. Patient-reported reasons for stopping care or switching clinics in Zambia: a multi-site, regionally representative estimate using a multi-stage sampling-based approach in Zambia. Clin Infect Dis. 2020 (online ahead of print).

103. Keene C, Cassidy T, Makeleni-Leteze T, Dutyulwa T, Dumile N, Flowers T et al. MSF's Welcome Service: supporting re-engagement with care. Cape Town: Southern Africa Medical Unit, 2019 (https://samumsf.org/sites/default/files/2019-06/Welcome%20services%20poster.pdf, accessed 5 March 2021).

104. Camlin CS, Neilands TB, Odeny TA, Lyamuya R, Nakiwogga-Muwanga A, Diero L et al. Patient-reported factors associated with reengagement among HIV-infected patients disengaged from care in east Africa. AIDS. 2016;30:495–502.

105. Amstutz A, Brown JA, Ringera I, Muhairwe J, Lejone TI, Klimkait T et al. Engagement in care, viral suppression, drug resistance and reasons for non-engagement after home-based same-day ART initiation in Lesotho: a two-year follow-up of the CASCADE trial. Clin Infect Dis. 2019;71:2608–14.

106. Mekuria LA, Prins JM, Yalew AW, Sprangers MA, Nieuwkerk PT. Which adherence measure – self-report, clinician recorded or pharmacy refill – is best able to predict detectable viral load in a public ART programme without routine plasma viral load monitoring? Trop Med Int Health. 2016;21:856–69.

107. Smith R. Measures of antiretroviral adherence for detecting viral nonsuppression in people living with HIV. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

108. Bisson GP, Gross R, Bellamy S, Chittams J, Hislop M, Regensberg L et al. Pharmacy refill adherence compared with CD4 count changes for monitoring HIV-infected adults on antiretroviral therapy. PLoS Med. 2008;5:e109.

109. Court R, Leisegang R, Stewart A, Sunpath H, Murphy R, Winternheimer P et al. Short term adherence tool predicts failure on second line protease inhibitor-based antiretroviral therapy: an observational cohort study. BMC Infect Dis. 2014;14:664.

110. Henegar CE, Westreich D, Maskew M, Brookhart MA, Miller WC, Majuba P et al. Comparison of pharmacy-based measures of adherence to antiretroviral therapy as predictors of virological failure. AIDS Behav. 2015;19:612–8.

111. Almeida-Brasil CC, Moodie EEM, Cardoso TS, Nascimento ED, Ceccato M. Comparison of the predictive performance of adherence measures for virologic failure detection in people living with HIV: a systematic review and pairwise meta-analysis. AIDS Care. 2019;31:647–59.

112. Wu P, Johnson BA, Nachega JB, Wu B, Ordonez CE, Hare AQ et al. The combination of pill count and self-reported adherence is a strong predictor of first-line ART failure for adults in South Africa. Curr HIV Res. 2014;12:366–75.

113. Eshun-Wilson I, Rohwer A, Hendricks L, Oliver S, Garner P. Being HIV positive and staying on antiretroviral therapy in Africa: a qualitative systematic review and theoretical model. PLoS One. 2019;14:e0210408.

114. Shubber Z, Mills EJ, Nachega JB, Vreeman R, Freitas M, Bock P et al. Patient-reported barriers to adherence to antiretroviral therapy: a systematic review and meta-analysis. PLoS Med. 2016;13:e1002183.

115. Long JE, Waruguru G, Yuhas K, Wilson KS, Masese LN, Wanje G et al. Prevalence and predictors of unmet contraceptive need in HIV-positive female sex workers in Mombasa, Kenya. PLoS One. 2019;14:e0218291.

116. Khan MR, Turner AN, Pettifor A, Van Damme K, Rabenja NL, Ravelomanana N et al. Unmet need for contraception among sex workers in Madagascar. Contraception. 2009;79:221–7.

117. Lim MS, Zhang XD, Kennedy E, Li Y, Yang Y, Li L et al. Sexual and reproductive health knowledge, contraception uptake, and factors associated with unmet need for modern contraception among adolescent female sex workers in China. PLoS One. 2015;10:e0115435.

118. Ochako R, Okal J, Kimetu S, Askew I, Temmerman M. Female sex workers experiences of using contraceptive methods: a qualitative study in Kenya. BMC Womens Health. 2018;18:105.

119. Global consultation on lessons from sexual and reproductive health programming to catalyse HIV prevention for adolescent girls and young women. Geneva: World Health Organization; 2016 (https://www.who.int/reproductivehealth/topics/linkages/WHO_Meeting_Rpt_HIV_Prevention_AGYW.pdf?ua=1, accessed 5 March 2021).

120. Consolidated guideline on sexual and reproductive health and rights of women living with HIV. Geneva: World Health Organization; 2017 (https://www.who.int/reproductivehealth/publications/gender_rights/srhr-women-hiv/en, accessed 5 March 2021).

121. Narasimhan M, Yeh PT, Haberlen S, Warren CE, Kennedy CE. Integration of HIV testing services into family planning services: a systematic review. Reprod Health. 2019;16 (Suppl. 1):61.

122. Rohwer A, van Wyk S, McCaul M. Integrated services for HIV testing and family planning: update of an existing systematic review. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

123. Rosenberg NE, Bhushan NL, Vansia D, Phanga T, Maseko B, Nthani T et al. Comparing youth-friendly health services to the standard of care through "Girl Power-Malawi": a quasi-experimental cohort study. J Acquir Immune Defic Syndr. 2018;79:458–66.

124. Haberlen SA, Narasimhan M, Beres LK, Kennedy CE. Integration of family planning services into HIV care and treatment services: a systematic review. Stud Fam Plann. 2017;48:153–77.

125. Warren CE, Abuya T, Askew I, Integra I. Family planning practices and pregnancy intentions among HIV-positive and HIV-negative postpartum women in Swaziland: a cross sectional survey. BMC Pregnancy Childbirth. 2013;13:150.

126. Zapata T, Forster N, Campuzano P, Kambapani R, Brahmbhatt H, Hidinua G et al. How to integrate HIV and sexual and reproductive health services in Namibia, the Epako Clinic Case Study. Int J Integr Care. 2017;17:1.

127. Hewett PC, Nalubamba M, Bozzani F, Digitale J, Vu L, Yam E et al. Randomized evaluation and cost-effectiveness of HIV and sexual and reproductive health service referral and linkage models in Zambia. BMC Public Health. 2016;16:785.

128. Siapka M, Obure CD, Mayhew SH, Sweeney S, Fenty J, Integra I et al. Impact of integration of sexual and reproductive health services on consultation duration times: results from the Integra Initiative. Health Policy Plan. 2017;32(Suppl 4):iv82–90.

129. Birdthistle IJ, Mayhew SH, Kikuvi J, Zhou W, Church K, Warren CE et al. Integration of HIV and maternal healthcare in a high HIV-prevalence setting: analysis of client flow data over time in Swaziland. BMJ Open. 2014;4:e003715.

130. Obure CD, Jacobs R, Guinness L, Mayhew S, Integra I, Vassall A. Does integration of HIV and sexual and reproductive health services improve technical efficiency in Kenya and Swaziland? An application of a two-stage semi parametric approach incorporating quality measures. Soc Sci Med. 2016;151:147–56.

131. Siapka M, Remme M, Obure CD, Maier CB, Dehne KL, Vassall A. Is there scope for cost savings and efficiency gains in HIV services? A systematic review of the evidence from low- and middle-income countries. Bull World Health Organ. 2014;92:499–511.

132. Obure CD, Guinness L, Sweeney S, Initiative I, Vassall A. Does integration of HIV and SRH services achieve economies of scale and scope in practice? A cost function analysis of the Integra Initiative. Sex Transm Infect. 2016;92:130–4.

133. Ayon S, Jeneby F, Hamid F, Badhrus A, Abdulrahman T, Mburu G. Developing integrated community-based HIV prevention, harm reduction, and sexual and reproductive health services for women who inject drugs. Reprod Health. 2019;16(Suppl. 1):59.

134. Dulli L, Field S, Masaba R, Ndiritu J. Addressing broader reproductive health needs of female sex workers through integrated family planning/ HIV prevention services: A non-randomized trial of a health-services intervention designed to improve uptake of family planning services in Kenya. PLoS One. 2019;14:e0219813.

135. Milford C, Greener LR, Beksinska M, Greener R, Mabude Z, Smit J. Provider understandings of and attitudes towards integration: Implementing an HIV and sexual and reproductive health service integration model, South Africa. Afr J AIDS Res. 2018;17:183–92.

136. Narasimhan M, Pillay Y, Garcia PJ, Allotey P, Gorna R, Welbourn A et al. Investing in sexual and reproductive health and rights of women and girls to reach HIV and UHC goals. Lancet Glob Health. 2018;6:e1058–9.

137. Call to action to attain universal health coverage through linked sexual and reproductive health and rights and HIV interventions. Geneva: World Health Organization; 2017 (https://www.who.int/reproductivehealth/publications/call-to-action-linked-srhr-hiv-interventions/en, accessed 5 March 2021).

138. Sarki AM, Nduka CU, Stranges S, Kandala NB, Uthman OA. Prevalence of hypertension in low- and middle-income countries: a systematic review and meta-Analysis. Medicine (Baltimore). 2015;94:e1959.

139. Adeloye D, Basquill C. Estimating the prevalence and awareness rates of hypertension in Africa: a systematic analysis. PLoS One. 2014;9:e104300.

140. Sarki AM, Nduka CU, Stranges S, Kandala N-B, Uthman OA. Prevalence of hypertension in low-and middle-income countries: a systematic review and meta-analysis. Medicine. 2015;94:e1959.

141. Scoping Consultation on Noncommunicable Diseases and Mental Health Conditions in People Living with HIV. Meeting report, Geneva, Switzerland, 9–10 April 2019. Geneva: World Health Organization; 2021.

142. Ameh S, Klipstein-Grobusch K, Musenge E, Kahn K, Tollman S, Gómez-Olivé FX. Effectiveness of an integrated approach to HIV and hypertension care in rural South Africa: controlled interrupted time-series analysis. J Acquir Immune Defic Syndr. 2017;75:472.

143. Rawat A, Uebel K, Moore D, Yassi A. Integrated HIV-care into primary health care clinics and the influence on diabetes and hypertension care: an interrupted time series analysis in Free State, South Africa over 4 years. J Acquir Immune Defic Syndr. 2018;77:476–83.

144. Fairall LR, Folb N, Timmerman V, Lombard C, Steyn K, Bachmann MO et al. Educational outreach with an integrated clinical tool for nurse-led non-communicable chronic disease management in primary care in South Africa: a pragmatic cluster randomised controlled trial. PLoS Med. 2016;13:e1002178.

145. Prabhakaran D, Jha D, Prieto-Merino D, Roy A, Singh K, Ajay VS et al. Effectiveness of an mHealth-based electronic decision support system for integrated management of chronic conditions in primary care: the mWellcare cluster-randomized controlled trial. Circulation. 2019;139:380–91.

146. Havlir DV, Balzer LB, Charlebois ED, Clark TD, Kwarisiima D, Ayieko J et al. HIV testing and treatment with the use of a community health approach in rural Africa. N Engl J Med. 2019;381:219–29.

147. Rohwer A, Uwimana-Nicol J, Toews I, Young T, Bavuma C, Meerpohl J. Effects of integrated models of care for diabetes and hypertension in low-and middle-income countries. A systematic review. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

148. Kemp CG, Weiner BJ, Sherr KH, Kupfer LE, Cherutich PK, Wilson D et al. Implementation science for integration of HIV and non-communicable disease services in sub-Saharan Africa: a systematic review. AIDS. 2018;32:S93–105.

149. Rabkin M, de Pinho H, Michaels-Strasser S, Naitore D, Rawat A, Topp SM. Strengthening the health workforce to support integration of HIV and noncommunicable disease services in sub-Saharan Africa. AIDS. 2018;32:S47–54.

150. Chang W, Chamie G, Mwai D, Clark TD, Thirumurthy H, Charlebois ED et al. Cost and efficiency of a hybrid mobile multi-disease testing approach with high HIV testing coverage in east Africa. J Acquir Immune Defic Syndr. 2016;73:e39.

151. Venables E, Edwards JK, Baert S, Etienne W, Khabala K, Bygrave H. "They just come, pick and go." The acceptability of integrated medication adherence clubs for HIV and noncommunicable disease (NCD) patients in Kibera, Kenya. PLoS One. 2016;11:e0164634.

152. Adolescent friendly health services for adolescents living with HIV: from theory to practice. Geneva: World Health Organization; 2019 (https://www.who.int/publications/i/item/adolescent-friendly-health-services-for-adolescents-living-with-hiv, accessed 5 March 2021).

153. Cluver LD, Orkin FM, Campeau L, Toska E, Webb D, Carlqvist A et al. Improving lives by accelerating progress towards the UN Sustainable Development Goals for adolescents living with HIV: a prospective cohort study. Lancet Child Adolesc Health. 2019;3:245–54.

154. Laurenzi CA, Skeen S, Gordon S, Akin-Olugbade O, Abrahams N, Bradshaw M et al. Preventing mental health conditions in adolescents living with HIV: an urgent need for evidence. J Int AIDS Soc. 2020;23:e25556.

155. Laurenzi CA, Du Toit S, Ameyan W, Melendez-Torres GJ, Kara T, Brand A et al. Psychosocial interventions for improving engagement in care and health and behavioural outcomes for adolescents and young people living with HIV: a systematic review and meta-analysis. J Int AIDS Soc. 2021.

156. Naar-King S, Wright K, Parsons JT, Frey M, Templin T, Lam P et al. Healthy choices: motivational enhancement therapy for health risk behaviors in HIV-positive youth. AIDS Educ Prev. 2006;18:1–11.

157. Naar-King S, Lam P, Wang B, Wright K, Parsons JT, Frey MA. Brief report: maintenance of effects of motivational enhancement therapy to improve risk behaviors and HIV-related health in a randomized controlled trial of youth living with HIV. J Pediatr Psychol. 2008;33:441–5.

158. Rongkavilit C, Wang B, Naar-King S, Bunupuradah T, Parsons JT, Panthong A et al. Motivational interviewing targeting risky sex in HIV-positive young Thai men who have sex with men. Arch Sex Behav. 2014;44:329–40.

159. Rongkavilit C, Naar-King S, Wang B, Panthong A, Bunupuradah T, Parsons JT et al. Motivational interviewing targeting risk behaviors for youth living with HIV in Thailand. AIDS Behav. 2013;17:2063–74.

160. Chen X, Murphy DA, Naar-King S, Parsons JT. A clinic-based motivational intervention improves condom use among subgroups of youth living with HIV. J Adolesc Health. 2011;49:193–8.

161. Naar-King S, Outlaw A, Green-Jones M, Wright K, Parsons JT. Motivational interviewing by peer outreach workers: a pilot randomized clinical trial to retain adolescents and young adults in HIV care. AIDS care. 2009;21:868–73.

162. Bhana A, Mellins CA, Petersen I, Alicea S, Myeza N, Holst H et al. The VUKA family program: piloting a family-based psychosocial intervention to promote health and mental health among HIV infected early adolescents in South Africa. AIDS Care. 2014;26:1–11.

163. Bouris A, Jaffe K, Eavou R, Liao C, Kuhns L, Voisin D et al. Project nGage: results of a randomized controlled trial of a dyadic network support intervention to retain young Black men who have sex with men in HIV care. AIDS Behav. 2017;21:3618–29.

164. Belzer ME, Naar-King S, Olson J, Sarr M, Thornton S, Kahana SY et al. The use of cell phone support for non-adherent HIV-infected youth and young adults: an initial randomized and controlled intervention trial. AIDS Behav. 2014;18:686–96.

165. Willis N, Milanzi A, Mawodzeke M, Dziwa C, Armstrong A, Yekeye I et al. Effectiveness of community adolescent treatment supporters (CATS) interventions in improving linkage and retention in care, adherence to ART and psychosocial well-being: a randomised trial among adolescents living with HIV in rural Zimbabwe. BMC Public Health. 2019;19:117.

166. Mavhu W, Willis N, Mufuka J, Bernays S, Tshuma M, Mangenah C et al. Effect of a differentiated service delivery model on virological failure in adolescents with HIV in Zimbabwe (Zvandiri): a cluster-randomised controlled trial. Lancet Global Health. 2020;8:e264–75.

167. Whiteley L, Brown LK, Mena L, Craker L, Arnold T. Enhancing health among youth living with HIV using an iPhone game. AIDS care. 2018;30(Suppl. 4):21–33.

168. Garofalo R, Kuhns LM, Hotton A, Johnson A, Muldoon A, Rice D. A randomized controlled trial of personalized text message reminders to promote medication adherence among HIV-positive adolescents and young adults. AIDS Behav. 2016;20:1049–59.

169. Linnemayr S, Huang H, Luoto J, Kambugu A, Thirumurthy H, Haberer JE et al. Text messaging for improving antiretroviral therapy adherence: no effects after 1 year in a randomized controlled trial among adolescents and young adults. Am J Public Health. 2017;107:1944–50.

170. Dulli L, Ridgeway K, Packer C, Murray KR, Mumuni T, Plourde KF et al. A social media–based support group for youth living with HIV in Nigeria (SMART Connections): randomized controlled trial. J Med Internet Res. 2020;22:e18343.

171. Spratt E, Papa C, Mueller M, Patel S, Killeen T, Maher E et al. Using technology to improve adherence to HIV medications in transitional age youth: research reviewed, methods tried, lessons learned. J Gen Med (Dover). 2017;1:1002.

172. Bermudez LG, Ssewamala FM, Neilands TB, Lu L, Jennings L, Nakigozi G et al. Does economic strengthening improve viral suppression among adolescents living with HIV? Results from a cluster randomized trial in Uganda. AIDS Behav. 2018;22:3763–72.

173. Christodoulou J, Abdalian SE, Jones AS, Christodoulou G, Pentoney SL, Rotheram-Borus MJ. Crystal clear with active visualization: understanding medication adherence among youth living with HIV. AIDS Behav. 2019;24:1207–11.

174. Nestadt DF, Saisaengjan C, McKay MM, Bunupuradah T, Pardo G, Lakhonpon S et al. CHAMP+ Thailand: pilot randomized control trial of a family-based psychosocial intervention for perinatally HIV-infected early adolescents. AIDS Patient Care STDs. 2019;33:227–36.

175. Kaihin R, Kasatpibal N, Chitreechuer J, Grimes RM. Effect of an empowerment intervention on antiretroviral drug adherence in Thai Youth. Behav Med. 2015;41:186–94.

176. Berrien VM, Salazar JC, Reynolds E, Mckay K. Adherence to antiretroviral therapy in HIV-infected pediatric patients improves with home-based intensive nursing intervention. AIDS Patient Care STDs. 2004;18:355–63.

177. Brown LK, Kennard BD, Emslie GJ, Mayes TL, Whiteley LB, Bethel J et al. Effective treatment of depressive disorders in medical clinics for adolescents and young adults living with HIV: a controlled trial. J Acquir Immune Defic Syndr. 2016;71:38.

178. Denison JA, Burke VM, Miti S, Nonyane BA, Frimpong C, Merrill KG et al. Project YES! Youth Engaging for Success: a randomized controlled trial assessing the impact of a clinic-based peer mentoring program on viral suppression, adherence and internalized stigma among HIV-positive youth (15–24 years) in Ndola, Zambia. PLoS One. 2020;15:e0230703.

179. Han HR, Hong H, Starbird LE, Ge S, Ford AD, Renda S et al. eHealth literacy in people living with HIV: systematic review. JMIR Public Health Surveill. 2018;4:e64.

180. Fatti G, Jackson D, Goga AE, Shaikh N, Eley B, Nachega JB et al. The effectiveness and cost-effectiveness of community-based support for adolescents receiving antiretroviral treatment: an operational research study in South Africa. J Int AIDS Soc. 2018;21(Suppl. 1).

181. Bermudez LG, Ssewamala FM, Neilands TB, Lu L, Jennings L, Nakigozi G et al. Does economic strengthening improve viral suppression among adolescents living with HIV? Results from a cluster randomized trial in Uganda. AIDS Behav. 2018;22:3763–72.

182. Brothers J, Hotton AL, Hosek SG, Harper GW, Fernandez MI. Young women living with HIV: outcomes from a targeted secondary prevention empowerment pilot trial. AIDS Patient Care STDs. 2016;30:229–35.

183. Mark D, Putta N, Essajee S, Rakhmanina N, Tall CT, Sugandhi N et al. Optimizing HIV service delivery for infants, children and adolescents: data from 324 facilities in 30 countries. 20th International Conference on AIDS and STIs in Africa, Kigali, Rwanda, 2–7 December 2019 (http://teampata.org/wp-content/uploads/2019/11/ICASA2019_Poster.pdf, accessed 5 March 2021).

184. Vojnov L, Taegtmeyer M, Boeke C, Markby J, Harris L, Doherty M et al. Performance of non-laboratory staff for diagnostic testing and specimen collection in HIV programs: a systematic review and meta-analysis. PLoS One. 2019;14:e0216277.

185. Luo R, Boeras D, Vojnov L. Systematic review on the clinical impact of point-of-care early infant diagnosis for HIV. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

186. Luchters S, Technau K, Mohamed Y, Chersich MF, Agius PA, Pham MD et al. Field performance and diagnostic accuracy of a low-cost instrument-free point-of-care CD4 test (Visitect CD4) performed by different health worker cadres among pregnant women. J Clin Microbiol. 2019;57:e01277-18.

187. Ochodo E, Guleid F, Mallett S, Deeks J. Point-of-care tests detecting HIV nucleic acids for diagnosis of HIV infection in infants and children aged 18 months or less. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

188. Drain PK, Hong T, Krows M, Govere S, Thulare H, Wallis CL et al. Validation of clinic-based cryptococcal antigen lateral flow assay screening in HIV-infected adults in South Africa. Sci Rep. 2019;9:2687.

189. Wake RM, Jarvis JN, Harrison TS, Govender NP. Brief report: point of care cryptococcal antigen screening: pipetting finger-prick blood improves performance of Immunomycologics lateral flow assay. J Acquir Immune Defic Syndr. 2018;78:574–8.

190. Williams DA, Kiiza T, Kwizera R, Kiggundu R, Velamakanni S, Meya DB et al. Evaluation of fingerstick cryptococcal antigen lateral flow assay in HIV-infected persons: a diagnostic accuracy study. Clin Infect Dis. 2015;61:464–7.

191. Olugbenga I, Taiwo O, Laverty M, Ngige E, Anyaike C, Bakare R et al. Clinic-based evaluation study of the diagnostic accuracy of a dual rapid test for the screening of HIV and syphilis in pregnant women in Nigeria. PLoS One. 2018;13:e0198698.

192. Gous N, Scott L, Potgieter J, Ntabeni L, Enslin S, Newman R et al. Feasibility of performing multiple point of care testing for HIV antiretroviral treatment initiation and monitoring from multiple or single fingersticks. PLoS One. 2013;8:e85265.

193. Gous NM, Scott LE, Potgieter J, Ntabeni L, Sanne I, Stevens WS. Implementation and operational research: implementation of multiple point-of-care testing in 2 HIV antiretroviral treatment clinics in South Africa. J Acquir Immune Defic Syndr. 2016;71:e34–43.

194. Jani IV, Sitoe NE, Chongo PL, Alfai ER, Quevedo JI, Tobaiwa O et al. Accurate CD4 T-cell enumeration and antiretroviral drug toxicity monitoring in primary healthcare clinics using point-of-care testing. AIDS. 2011;25:807–12.

195. Drain PK, Dorward J, Violette LR, Quame-Amaglo J, Thomas KK, Samsunder N et al. Point-of-care HIV viral load testing combined with task shifting to improve treatment outcomes (STREAM): findings from an open-label, non-inferiority, randomised controlled trial. Lancet HIV. 2020;7:e229–237.

196. Le Roux S, Myer L, Vojnov L. Clinical and operational impact of point-of-care compared to laboratory-based nucleic acid testing for routine HIV viral load monitoring: a systematic review and meta-analysis. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

197. Considerations for adoption and use of multidisease testing devices in integrated laboratory networks. Geneva, Switzerland. 2019. Geneva: World Health Organization, 2020. (https://www.who.int/tb/publications/2017/considerations_multidisease_testing_devices_2017/en, accessed 5 March 2021).

198. Molecular diagnostics integration global meeting report, Geneva, Switzerland. Geneva: World Health Organization, 2019 (https://www.who.int/publications/i/item/molecular-diagnostics-integration-global-meeting-report, accessed 5 March 2021).

199. Multi-disease diagnostic landscape for integrated management of HIV, HCV, TB and other coinfections. Geneva: Unitaid; 2018.

200. Obure CD, Gaitan-Duarte H, Losada Saenz R, Gonzalez L, Angel-Muller E, Laverty M et al. A comparative analysis of costs of single and dual rapid HIV and syphilis diagnostics: results from a randomised controlled trial in Colombia. Sex Transm Infect. 2017;93:482–6.

201. Khan S, Vojnov L. Patient impact and programmatic advantage of integrated testing. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

202. Ndlovu Z, Fajardo E, Mbofana E, Maparo T, Garone D, Metcalf C et al. Multidisease testing for HIV and TB using the GeneXpert platform: a feasibility study in rural Zimbabwe. PLoS One. 2018;13:e0193577.

203. Clinton Health Access Initiative. Patient impact, programmatic advantages, and cost savings of integrated testing. In preparation. [Abstract available in Web Annex C, https://www.who.int/publications/i/item/9789240023581]

Annex. Process of developing the guidelines

Background

Since the 2016 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection *(1)* were published and with the rapid scale-up of ART, emerging evidence and implementation experience and approaches justify reviewing and updating the service delivery guidance. A scoping exercise was held at the end of 2018 with national HIV programme managers, implementing partners and representatives from civil society and academia to define the priority questions *(2)*. A virtual Guideline Development Group meeting was convened in October 2020, guided by WHO standards for guideline development *(3)*. Fourteen systematic reviews were undertaken to address the PICO questions formulated and to inform an update of a definition. This was complemented by other information sources such as targeted literature searches, programmatic information and primary surveys. Many individuals contributed to the development of the guideline including people living with HIV and representatives of affected communities, representatives from ministry of health, researchers, implementers, and health care providers.

Retrieving, summarizing and presenting the evidence

Evidence synthesis and evidence to recommendations

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) method was used to rate the quality of the evidence and determine the strength of the recommendations. The GRADE approach to developing recommendations defines the certainty of evidence as the extent to which one can be confident that the reported estimates of effect (desirable or undesirable) available from the evidence are close to the actual effects of interest. After the evidence is collected and summarized, GRADE provides explicit criteria for rating the certainty of evidence that include study design, risk of bias, imprecision, inconsistency, indirectness and magnitude of effect *(4)*. The strength of a recommendation reflects the degree to which the Guideline Development Group is confident that the desirable effects (potential benefits) of the recommendation outweigh the undesirable effects (potential harm). Desirable effects may include beneficial health outcomes such as reduced morbidity and mortality, reduction of burden on the individual and/or health services and potential cost savings. Undesirable effects include those affecting individuals, families, communities or health services as well as the implementation of services that may not be cost effective within a particular context. Additional considerations include the resource use and cost implications of implementing the recommendations and clinical outcomes (such as drug resistance and drug toxicity).

Good practice statements are made when the Guideline Development Group has high confidence that indirect evidence supports greater net benefit relative to harms and when it would be unnecessarily burdensome and/or challenging to collect and summarize this evidence. (large opportunity cost). In addition, that equity and ethical considerations are favourable *(5)*. Good practice statements are made when it is considered that implementation would result in a large net positive benefit. Good practice statements would not generally be contested because not carrying out the best practice would be nonsensical or illogical and/or unethical. To inform the good practice statements made in these guidelines, efforts were made to gather the available evidence to inform the discussion and the decision of the group.

The PRECIS-2 tool was used to assess the extent to which the conduct of a given study reflects an explanatory (ideal situation) or a more pragmatic (usual care) context. PRECIS-2 has nine domains – eligibility criteria, recruitment, setting, organization, flexibility (delivery), flexibility (adherence), follow-up, primary outcome and primary analysis – scored from 1 (very explanatory) to 5 (very pragmatic) *(6)*.

All systematic reviews followed the PRISMA guidelines for reporting systematic reviews and meta-analyses.

Feasibility and acceptability

The pragmatism of studies provided indirect evidence on feasibility from the systematic reviews, obtained using PRECIS-2. Other sources of evidence for feasibility included the UNAIDS database on country adoption of relevant WHO recommendations. Key health ministry or partner stakeholders provided insights at the Guidelines Development Group meeting on feasibility in settings with a high burden of HIV infection. In addition, between July and September 2020, two online surveys of health-care workers, HIV programme managers and people living with HIV were carried out to assess the feasibility and acceptability of strategies for delivering HIV services and in parallel for the update of the clinical guidelines, submitted separately, which included questions that informed the diagnostic questions for these guidelines. Dissemination of this survey was supported by the HIV Coverage, Quality, and Impact Network (CQUIN) *(7)*. The results of these surveys were used to inform the acceptability and feasibility of the range of questions addressed. In addition, an online survey and 10 focus group discussions on psychosocial support intervention for adolescents and youth were conducted.

Resource use and cost effectiveness

The systematic reviews captured available published evidence on resource use including costing, cost effectiveness and affordability data. The Guideline Development and External Review Group included representatives from national programmes, who also provided perspectives on the resource implications in their countries.

Ethical considerations

Before the Guideline Development Group meeting, the proposed areas of intervention were reviewed by a WHO staff member with expertise in global health and ethics, and key issues with respect to equity were outlined to the Guideline Development Group for consideration when formulating recommendations.

Guideline Development Group meeting

For the updated recommendations in 2020, the Guideline Development Group met virtually on 5–9 October 2020. Using an electronic survey, the Guideline Development Group ranked the importance of each systematic review outcome using the GRADE rating scale from 1 to 9 *(3)*. The systematic reviews and evidence-to-decision-making tables, prepared in accordance with the GRADE process, were shared in advance and presented at the meetings, and the methodologist facilitated discussions. All recommendations were made through consensus. Voting was not required but the group agreed a priori that two thirds of the votes would be required for a decision. The Guideline Development Group formulated good practice principles based on their knowledge of the optimal approach to delivering HIV services, considering the absence of harm found in the evidence base and the inapplicability of the evidence to formal GRADE assessment.

Peer review

The draft guidelines were circulated for review to members of the Guideline Development Group and the External Review Group. The WHO Guideline Steering Group reviewed the comments and incorporated them into the final document with due consideration of any conflicts of interest of External Review Group members.

Declarations of interest

All external contributors to the guidelines, including members of the Guideline Development Group and the External Review Group, completed a WHO declaration of interests form in accordance with WHO policy for experts. A brief biography of each Guideline Development Group member was published on the WHO HIV website for a period of 14 days before the first meeting of the Guideline Development Group with a description of the objectives of the meeting. No public comments or objections were received. The responsible technical officer reviewed the declaration of interests forms as well as the results of the web-based search for each member of the Guideline Development Group. The results were shared with the WHO Guideline Steering Group, which reviewed the results, and a management plan was agreed and recorded for each individual. At the start of the guideline development meeting, all conflicts of interest identified and the management plan for any conflicts of interest were shared with the meeting participants. In accordance with the revised WHO policy for experts, a web-based search was conducted of Guideline Development Group members to identify any potential competing interest. The WHO Guideline Steering Group recorded and reviewed the results of the web-based search to identify any potential competing interest. The declared conflicts of interest were summarized and presented at the start of the Guideline Development Group meeting, and members were asked to vocalize any additional conflicts or undeclared conflicts. One member of the 2020 Guideline Development Group led one of the systematic reviews informing the meeting and was excluded from voting on the corresponding recommendation. No other conflicts of interest warranted exclusion from the discussion of specific recommendations.

External Review Group

The responsible technical officers reviewed the declaration of interest forms from members of the External Review Group in accordance with WHO guideline development policy, and the results were shared with the WHO Guideline Steering Group. Any conflicts of interest identified were considered when interpreting comments from External Review Group members during the external review process.

References

1. 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 (https://www.who.int/hiv/pub/arv/arv-2016/en, accessed 5 March 2021).
2. Ford N, Geng E, Ellman T, Orrell C, Ehrenkranz P, Sikazwe I et al. Emerging priorities in HIV service delivery. PLoS Med. 2020;17:e1003028.
3. WHO handbook for guideline development. 2nd ed. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/handle/10665/145714, accessed 5 March 2021).
4. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A et al. Going from evidence to recommendations. BMJ. 2008;336:1049–51.
5. Guyatt GH, Schunemann HJ, Djulbegovic B, Akl EA. Guideline panels should not GRADE good practice statements. J Clin Epidemiol. 2015;68:597–600.
6. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. BMJ. 2015;350:h2147.
7. About CQUIN [website]. New York: ICAP at Columbia University; 2021 (https://cquin.icap.columbia.edu/about-cquin, accessed 5 March 2021).

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