

SERVICE DELIVERY

6

6.1	Introduction	238
6.2	Differentiated care	239
6.3	Models of community ARV delivery	242
6.4	Linkage from HIV testing to enrolment in care	243
6.5	Retention in care	251
6.6	Adherence	255
6.7	Frequency of clinic visits and medication pickup	259
6.8	Task shifting and task sharing	262
6.9	Decentralization	266
6.10	Integrating and linking services	268
6.11	Delivering HIV services to adolescents	274
6.12	Improving the quality of HIV care services	279
6.13	Procurement and supply management systems for HIV health products	283
6.14	Laboratory and diagnostic services	294

6 SERVICE DELIVERY

6.1 Introduction

Less than 30% of people diagnosed with HIV in resource-limited settings navigate the full continuum of care (1,2). Worldwide, less than 50% of adults are retained in care four years after initiation of antiretroviral therapy (ART) (3). Simple and standardized first-line ART now directly supports adherence, decentralization, task shifting to nurse-led teams and community delivery and more efficient procurement and supply management. In 2013, for the first time, WHO published operational recommendations on how to implement clinical recommendations on the use of antiretroviral (ARV) drugs. These guidelines further expand on the implementation aspects of the clinical recommendations and present 10 new recommendations, three good practices, consensus-derived definitions and a new framework for ART service delivery intended to help countries and programme managers improve the quality and efficiency of services.

This chapter provides guidance in three service delivery areas:

1. Differentiated care:
 - addressing the diversity of needs of people in care
 - community ARV drug delivery approaches.
2. Recommendations to strengthen the continuum of treatment and care:
 - linkage from HIV testing to enrolment in care
 - retention
 - adherence
 - frequency of clinic visits and medication pickup
 - task shifting
 - decentralization
 - integration
 - adolescent-friendly health services.
3. Considerations for continuity and high quality of service delivery:
 - quality service delivery
 - ensuring a stable supply chain of ARV drugs
 - laboratory and diagnostic services.

New service delivery recommendations made in 2015 are included with recommendations from the 2013 WHO *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection*. The inclusion criteria of all systematic reviews conducted to support the decision-making process included adults, key populations, pregnant and breastfeeding women, children and adolescents. In general, there were limited data to inform specific recommendations for these important populations. However, learning from programme implementation has helped to highlight specific challenges and some potential solutions to improve service delivery.

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 this chapter comes from studies undertaken in sub-Saharan Africa. Nevertheless, for the majority of interventions, evidence was also available from other regions. Where this is not the case, the need for evidence from a broader range of settings has been indicated in the corresponding section as a research gap.

Many of the recommendations in the service delivery section are conditional and represent interventions that have been shown to have benefit in some settings and thus represent approaches that programme managers can consider in designing their care packages.

6.2 Differentiated care

It is estimated that 95% of HIV service delivery is currently facility based (4). In nearly all countries, the delivery of HIV care in the initial phase of rapid scale-up has been based on a “one-size-fits-all”, clinic-based model, largely undifferentiated for individual needs (5). As national guidelines evolve towards initiating ART for all people living with HIV regardless of clinical and immunological status (6), HIV programmes will be challenged to manage an increasingly diverse set of patient needs. There is now a growing cohort of patients who have been on treatment for several years. At the same time, there is a need to expand timely access to ART for those who have yet to start. While implementation of the recommendations in these guidelines will mean that more people will start earlier, programmes must also retain the capacity to respond to the needs of patients who present with advanced disease, and are at heightened risk of morbidity and mortality (7).

During a scoping consultation on care packages for people living with HIV, WHO reviewed the growing diversity of patient needs and assessed how programmes can treat and care for people differentially within a public health approach (8). Broadly, four groups of patients with specific needs can be identified. First, people who present when well, potentially with higher CD4 cell counts, may require additional and targeted

adherence and retention support in order to commit to lifelong ART. Second, people presenting to care with advanced disease require a fast-tracked clinical and care package to initiate ART and prevent death and reduce ill health. A third group of individuals are those who are already on ART but need careful monitoring to ensure timely action as required; this may include clinical care, additional adherence support and timely switch to second-line ART regimens in the case of treatment failure. A final group of stable individuals are likely to represent the majority of people on ART and they can safely reduce the frequency of clinic visits, potentially receiving ART in community settings. Such an approach can relieve overburdened health-care settings and enable more attention to be paid to patients with more complex conditions who require prompt diagnosis and treatment of opportunistic infections, enhanced adherence support, viral load testing and potential changes of regimen, HIV drug resistance testing or other specialized care (8). Receiving care closer to their home can also reduce direct and indirect costs related to transport and long facility waiting time for patients and their families. While these four groups have distinct needs, patients may move between the groups over the course of their lifetime in care.

Table 6.1. Diversity of care needs for people living with HIV

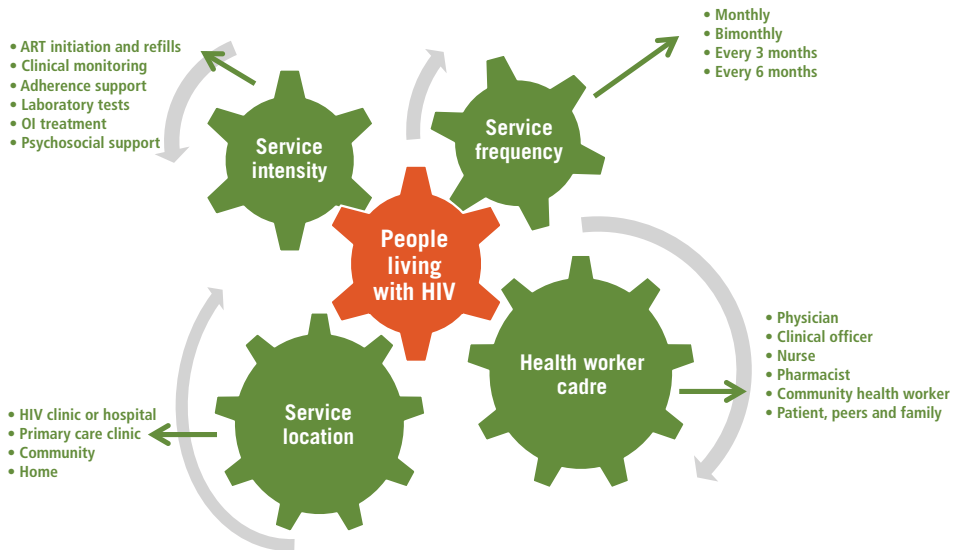
People living with HIV	Care package elements
People presenting when well	Adherence and retention support
People with advanced disease	Clinical package to reduce mortality and morbidity
Stable individuals	Reduced frequency of clinic visits and community ART delivery models
Unstable individuals	Adherence support, viral load testing, switch to second- or third-line ART if indicated, monitoring for HIV drug resistance (HIV-DR)

The care package elements for people living with HIV (Table 6.1) are a minimum and may be expanded according to the epidemic, clinical setting and health-care system. These packages are further supported by the differentiated care framework, which proposes the delivery of care in facilities for those who need clinic-based services, with less frequent clinical contact for those who are stable. Differentiating between the service needs of those who are unwell – either because they present late for care or due to treatment failure – and those who are stable on ART, and determining where and how those services are to be delivered, are key to maximizing treatment outcomes and efficiencies. A number of national HIV programmes have already adopted differentiated approaches to care as they scale up ART.

The differentiated care framework (Fig. 6.1) is characterized by four delivery components: (i) the types of services delivered; (ii) the location of service delivery; (iii) the provider of services; and (iv) the frequency of services. How these components are combined into a service delivery framework will vary across countries and populations, but the common intention should be to improve acceptability and care outcomes (5).

Two key groups of people require specific approaches that will involve different resource requirements – people who present late to care and people who are stable on ART. To

Figure 6.1. Key factors in differentiated approaches to HIV care (5)



support differentiated care approaches for these two groups, the following WHO consensus definitions and related package of care were reached in a Delphi survey of experts.¹

People with advanced disease are defined as those presenting to care with a CD4 count below 200 cells/mm³ or WHO disease stages 3 and 4. The package of care for these people should include the following:

- rapid initiation of ART (once the risk of immune reconstitution inflammatory syndrome [IRIS]² is ruled out);
- systematic screening for *Cryptococcus* antigen;
- screening and treatment for tuberculosis (TB) or isoniazid preventive treatment (IPT) as indicated;³
- screening for toxoplasmosis and co-trimoxazole (CTX) prophylaxis; and
- intensive follow-up.

Stable individuals are defined as those who have received ART for at least one year and have no adverse drug reactions that require regular monitoring, no current illnesses or pregnancy, are not currently breastfeeding and have good understanding of lifelong adherence and evidence of treatment success (i.e. two consecutive viral load measurements below 1000 copies/mL). In the absence of viral load monitoring, rising

¹ The Delphi technique is aimed at generating consensus. It solicits opinions from groups in an iterative process of questions. After each round, the responses are summarized and redistributed for discussion in the next round. Through a process of convergence involving the identification of common trends and inspection of outliers, a consensus is reached.

² Immune reconstitution inflammatory syndrome (IRIS): IRIS is a spectrum of clinical signs and symptoms thought to be associated with immune recovery brought about by a response to ART. It occurs among 10–30% of the people initiating ART, usually within the first 4–8 weeks after starting therapy.

³ This is recommended for all people living with HIV but should be prioritized for patients presenting with advanced disease.

CD4 cell counts or CD4 counts above 200 cells/mm³, an objective adherence measure, can be used to indicate treatment success. The package of care for stable individuals can include the following:

- less frequent (3–6-monthly) clinic visits;
- less frequent (3–6-monthly) medication pickup;
- community-based care; and
- cessation of CD4 count monitoring if viral load testing is available.

While less frequent clinic visits are recommended for stable individuals, rapidly growing children (0–5 years old) and adolescents will need to be monitored more frequently for treatment dosing/weight changes and adherence support.

6.3 Models of community ARV delivery

To accommodate the growing number of stable individuals on ART and improve retention in care and health outcomes, innovative models of community ARV delivery have been developed. WHO reported on their emerging importance in 2014 (9), and they are shown in Table 6.2. Several implementing organizations – notably Médecins Sans Frontières (MSF) together with health ministries – have been pioneers in developing these models. Outcomes have been reported for four countries in sub-Saharan Africa and

Table 6.2. Summary of strategies for alternative community delivery of long-term ART (10)

Key objective	Appointment spacing and fast-track ARV refill	At enrolment into care		Community ART distribution points	Community ART groups
		Facility-based clubs	Community-based clubs		
Health service driven ←					
→ Patient driven					
Patient perspective					
Reduce costs (time and transport)	Yes	Yes	Yes	Yes	Yes
Increase peer support	No	Yes	Yes	Yes	Yes
Enhance community participation	No	Potentially	Potentially	Potentially	Yes
Health-care perspective					
Reduce workload					
Nurse	Yes	Yes	Yes	Yes	Yes
Pharmacist	Yes	Yes	No	Yes	Yes
Counsellor/health-care worker/peer supporter	N/A	No	No	No	No
Maintain and improve health care					
Retention	Yes	Yes	Yes	Yes	Yes
Improve self-management of patients	Yes	Yes	Yes	Yes	Yes

the impact assessed through routine programme data (10). Models of interest include appointment spacing for clinical and drug refill visits in Malawi, peer educator-led ART refill groups in South Africa, community ART distribution points in the Democratic Republic of the Congo and patient-led community ART groups in Mozambique. All these approaches were found to reduce the burden for patients (reduced time and cost of travel to clinic and less income loss) and the health system (reduced clinic attendance), while maintaining high retention in care (more than 90% retained in care across multiple time points). The success of community ART models depends on sufficient and reliable support and resources, including a flexible and reliable drug supply, access to quality clinical management, a reliable monitoring system that can follow patients in and out of the community to the clinic and a nationally supported cadre of lay health workers.

6.4 Linkage from HIV testing to enrolment in care

6.4.1 Interventions to ensure timely linkage



Recommendation

Following an HIV diagnosis, a package of support interventions should be offered to ensure timely linkage to care for all people living with HIV (strong recommendation, moderate-quality evidence).

The following interventions have demonstrated benefit in improving linkage to care following an HIV diagnosis:

- streamlined interventions to reduce time between diagnosis and engagement in care, including (i) enhanced linkage with case management, (ii) support for HIV disclosure, (iii) patient tracing, (iv) training staff to provide multiple services and (v) streamlined services (moderate-quality evidence);
- peer support^a and navigation approaches for linkage (moderate-quality evidence); and
- quality improvement approaches using data to improve linkage (low-quality evidence).

^a Peer support includes peer counselling.

Background

Patient attrition following an HIV diagnosis is a huge global challenge, contributing to delayed ART initiation, avoidable morbidity and mortality, suboptimal treatment outcomes, increased cost of care and preventable HIV transmission. In sub-Saharan Africa, it is estimated that 57% (42–70%) of people who are diagnosed are linked to HIV care (11). A retrospective cohort analysis in South Africa identified that 25% of newly diagnosed people were not linked to care, and 35% who were linked never initiated ART (12,13). Data from community-based cohorts in seven African countries suggest that the majority of deaths among people with HIV occur prior to starting

ART (14). Decreasing loss to follow-up by early initiation of ART is estimated to reduce mortality by 6–14% (13).

Multiple factors may hinder successful linkage to care, including distance from HIV care sites, transport costs, disclosure-related concerns, stigma and long waiting times at the facility (15). Men and young people tend to be less likely to be linked to HIV care. As programmes expand access to HIV testing services, it is essential that linkage to HIV care be improved through interventions that support people in the initial steps of the continuum of care. Such interventions may vary based on the local context, including the health-care delivery system, geography and target population.

Rationale and supporting evidence

A systematic review identified 60 studies from 16 countries that evaluated the effect of 63 interventions on improving linkage of newly diagnosed patients to HIV care (16). The majority of the studies were observational and targeted adults and pregnant women living with HIV in Africa (80%). Three main areas of intervention were identified: (i) streamlined interventions; (ii) peer support and navigation approaches; and (iii) quality improvement approaches. Almost all the studies reviewed were conducted in the context of 2013 WHO ART eligibility criteria, which by definition was characterized by longer pre-ART care prior to ART initiation. Initiating all people living with HIV will significantly reduce the period of time between HIV diagnosis and ART initiation; as such, many of the interventions outlined below may need to refocus on accelerating ART initiation as well as engagement in care.

Streamlined interventions

Four studies evaluated packages of service delivery interventions to streamline care; two were randomized controlled trials and two observational studies with pre–post designs. Overall, there was moderate-quality evidence of increased ART initiation and engagement in care among those eligible.

Multifaceted interventions to reduce time between diagnosis and engagement in care and ART initiation included (i) enhanced linkage with case management, (ii) support for HIV disclosure, (iii) patient tracing for those who failed to engage in care, (iv) training staff to provide multiple services and (v) streamlined services to accelerate time to initiation. These were shown to be associated with increased rates of ART initiation (16). Such promising approaches should be considered as part of routine care to improve ART uptake. However, because the studies evaluated multiple system interventions, the improvements reported cannot readily be attributed to any specific action but rather to the multifaceted interventions as a whole. Due to high variability surrounding equity and the feasibility of the use of incentives to improve linkage, this intervention was not included in the recommendation; however, it should be noted that multifaceted, streamlined services may employ incentives to improve linkage to care and initiation of ART in selected populations.

Peer support and navigation

The systematic review identified seven cohort studies demonstrating that peer support and navigation interventions were effective in increasing linkage to care (16). The specific interventions evaluated included home visits, peer support, including for navigating the health-care system, and enhanced counselling. The evidence for peer support and

navigation interventions was overall of moderate-quality for increasing linkage to care due to the observational nature of the studies. In the reviewed studies, peer navigators assisted patients to link from community-based testing services to health-care settings where HIV care is provided. No studies identified any significant harmful effect of the interventions.

Counselling interventions were identified in eight included studies (seven cohort studies and one individual randomized controlled trial). Specific interventions included one-on-one post-test counselling, group counselling and counselling delivered by trained community members. All interventions demonstrated a significant increase in clinic enrolment, although none demonstrated any increase in ART initiation.

Quality improvement

Five quality improvement (QI) intervention studies (one cluster randomized controlled trial and four cohort studies) demonstrated significant benefits for linkage to care. Four of these studies with the largest benefits were all implemented in programmes to prevent mother-to-child transmission of HIV (16). All QI initiatives employed in the interventions focused on the use of facility data and addressing locally specific barriers to linkage. Overall quality was low due to the risk of bias in the individual studies. Interventions included educational outreach training sessions for health workers, policy and protocol changes and improved data collection.

Other approaches

The systematic review also identified very low-quality evidence demonstrating the effect of integrating services within HIV care settings – provision of ART in TB treatment settings and maternal and child health settings – on reducing time between diagnosis and ART initiation. These findings are consistent with existing WHO recommendations (see section 6.10 “Integrating and linking services”). CD4 cell count testing at the point of care can also be used to prioritize patients for urgent linkage to care and ART initiation (see section 6.4.2 “CD4 cell count testing at the point of care”).

The WHO Consolidated guidelines on HIV testing services also identify good practices to increase linkage to care, developed by reviews of published studies and programmatic experience (17). These are valuable and are consistent with the new recommendations listed above to improve linkage and are derived from the testing perspective. WHO recommends that all HIV testing services should adhere to the five C’s – consent, confidentiality, counselling, correct test results and connection (linkage to prevention, treatment and care services) (see section 2.1 “Clinical guidelines: HIV diagnosis – Introduction”). Taken together, the new recommendations and good practices outline a comprehensive set of interventions with demonstrated benefit to improve linkage from testing to care and ART initiation.

Cost and cost-effectiveness

The costs of specific interventions will vary depending on the components of the intervention and the context for implementation. None of the studies identified in the systematic review reported estimates of the direct cost or cost-effectiveness of interventions. Effective linkage to HIV care following an HIV diagnosis potentially improves programme effectiveness, supports earlier ART initiation and reduces loss to

Good practices for linkage from HIV testing services (17)

- Comprehensive home-based HIV testing, which includes offering home assessment and home-based ART initiation
- Integrated services, where HIV testing, HIV prevention, treatment and care, TB and sexually transmitted infection (STI) screening and other relevant services are provided together at a single facility or site
- Providing on-site or immediate testing for CD4 cell count with same-day results
- Providing assistance with transport, such as transportation vouchers, if the ART site is far from the HIV testing service site
- Decentralized ART provision and community-based distribution of ART
- Support and involvement of trained lay providers who are peers and act as peer navigators, expert patients/clients and community outreach workers to provide support, and identify and reach people lost to follow-up
- Intensified post-test counselling by community health workers
- Using communication technologies, such as mobile phones and text messaging, which may help with disclosure, adherence and retention, particularly for adolescents and young people
- Providing brief strengths-based case management, which emphasizes people's self-determination and strengths, is client-led and focuses on future outcomes, helps clients set and accomplish goals, establishes good working relationships among the client, the health worker and other sources of support in the community and provides services outside of office settings
- Promoting partner testing may increase rates of HIV testing and linkage to care, as may approaches that encourage male involvement in prevention of mother-to-child transmission (PMTCT) settings
- Intimate partner notification by the provider, with permission, is feasible in some settings; it identifies more HIV-positive people and promotes their early referral to care

follow-up before treatment initiation, thus resulting in potential cost savings along the continuum of care.

Equity and acceptability

A qualitative evidence synthesis identified 25 studies of interventions to support linkage to care (18). Key areas of convergence included counselling and support interventions that highlighted the importance of positive interactions with health-care workers and case managers (high confidence) and family and peer support (moderate confidence). For service delivery interventions, process and discussion of implementation of interventions

(high confidence) and task-shifting interventions (high confidence) all were acceptable to improve linkage. HIV programmes need to address barriers to linkage to HIV care and ART initiation. This is particularly important for populations that face multiple barriers, both structural and individual, to accessing HIV services.

Population considerations

Children

There is historically poor linkage and retention among children, especially for infants tested using early infant diagnosis (EID) within programmes for PMTCT of HIV. Of the two studies identified in the systematic review (16) that evaluated interventions delivered at the time of EID (one individually randomized controlled trial and one cohort study), both demonstrated significantly increased ART initiation with the use of technology (automated text messages to providers and mothers and provision of rapid results using short message service/Global System for Mobile Communications/General Packet Radio Service (SMS/GSM/GPRS) printers [see section 6.4.3 “Laboratory connectivity”]). The recommendation and good practice statements should be considered relevant for this population, given the lack of demonstrated harm and potential benefit. In addition, point-of care EID should be utilized to improve linkage to care (see section 2.5.3 “Point-of-care technologies for the diagnosis of HIV infection in infants and children”) and family-centred service delivery models considered.

Adolescents

Developmental changes during adolescence may mean that not all adolescents have the ability to come to terms with an HIV diagnosis. Adolescents may also have limited awareness of their own health needs and of the availability of services, in addition to limited experience and confidence in navigating the health services. Consent requirements can also restrict access to treatment and care. One randomized controlled trial was identified in the systematic review (16) demonstrating that peer support groups resulted in significantly increased linkage to care for this age group. Other linkage mechanisms involving outreach to the adolescent patient should also be considered for this population. These include peer-based interventions, community-based services, support groups and use of mobile technology, social media or call centres. All linkage mechanisms should be introduced at the point of HIV testing for young people living with HIV.

Research gaps

Evaluation is needed of packages of strategies aimed at improving linkage to care to build a stronger evidence base, including packages developed in the era of initiating ART for all people living with HIV regardless of CD4 cell count. Future studies should disaggregate effects of these strategies by sex, key populations and age. Costing studies and cost-effectiveness analyses are needed to better inform national policy decisions.

6.4.2 CD4 cell count testing at the point of care

NEW

Recommendation

CD4 cell count testing at the point of care can be used to prioritize patients for urgent linkage to care and ART initiation (conditional recommendation, low-quality evidence).

Background

WHO and national guidelines have progressively recommended earlier initiation of ART at higher CD4 cell counts, and in all regions, ART is being started at increasingly higher CD4 cell counts (19,20). Nevertheless, it is recognized that it may not be possible to immediately implement the recommendation to initiate ART for all people with HIV regardless of CD4 count in all settings. In addition, across all regions, many people start ART too late, with median CD4 cell counts at ART initiation in sub-Saharan Africa still below 200 cells/mm³ (21). This is partly explained by late HIV diagnosis and delays in linking people to care following a positive diagnosis. Once linked to care, long turnaround times for laboratory results have contributed to delays in ART initiation and loss to follow-up (1,17,22). Therefore, while there may be a reduction in the need for CD4 count testing over time, CD4 count testing at the point of care remains a potentially important approach to increase access to clinical monitoring and decrease turnaround times. Many countries in sub-Saharan Africa have implemented CD4 count testing at the point of care, and several reports suggest that it can reduce loss to follow-up and time to ART initiation (22).

Rationale and supporting evidence

A systematic review identified 30 studies, mainly conducted in Africa, which assessed the impact of CD4 count testing at the point of care on turnaround time of results, loss to follow-up, ART initiation rate and timing compared to conventional laboratory-based CD4 count testing (23). The review identified significant reductions in turnaround times for results returned to the provider using CD4 count testing at the point of care (median 0.1 day) compared to conventional laboratory-based CD4 testing (11 days). Time between HIV diagnosis and ART initiation was also lower (9 days compared to 32 days) (23). The findings were heterogeneous, with a variable degree of risk of bias in the studies. Overall, low-quality evidence indicated that CD4 testing at the point of care improves each step of the treatment cascade from testing to ART initiation.

Studies of cost-effectiveness in low-income settings have concluded that CD4 count testing at the point of care is cost-effective, even in settings where an initial investment in point-of-care devices is required, as this is offset by the health benefits of reduced morbidity and mortality (24,25). Many countries have piloted or implemented at-scale strategies for CD4 count testing at the point of care, including through task-shifting approaches. A number of studies have also reported that trained and supervised non-laboratory staff, including laypeople, can undertake blood finger-prick testing and

carry out point-of-care diagnostic tests (19), including point-of-care CD4 count testing (26), and this can facilitate the conduct of CD4 count testing at the point of care.

A conditional recommendation was made acknowledging that the use of this intervention will be highly context specific. Consideration was given to the forecasted reduction in the need for CD4 cell count testing over time as the recommendation to initiate ART regardless of CD4 cell count is fully implemented.

Equity and acceptability

Providing CD4 count testing at the point of care is judged to improve equity by bringing it closer to where patients reside and improving access to testing in rural settings. CD4 count testing at the point of care is acceptable to people living with HIV and preferred to laboratory-based testing (27,28). The acceptability to health workers is similarly positive due to the ease of use and interpretation of results (28).

Implementation considerations

It is anticipated that many countries will adopt a phased approach to implementing the policy of ART initiation at any CD4 cell count recommended in these guidelines. Nevertheless, HIV programmes should retain the capacity to perform CD4 cell count assays at baseline and in case of treatment failure, as this remains one of the best predictors of disease progression and mortality risk (29).

Appropriate placement of point-of-care instruments is a key factor, based on considerations such as volume, distance, loss to follow-up and cost. Careful consideration should be given to human resource requirements and quality assurance (QA). The connectivity functions of point-of-care CD4 testing instruments are critical to monitoring QA as well as supply management and programme monitoring and evaluation. Point-of-care programmes should be integrated into existing laboratory and clinical programmes to ensure synergy, strengthening and linkage to care and treatment.

Research gaps

Given the changing role of CD4 count measurement for initiation and monitoring recommended in these guidelines, models for how best to use existing CD4 count testing equipment, including point-of-care CD4 count testing, will be important.

6.4.3 Laboratory connectivity

NEW

Recommendation

Electronic communication can be considered to transfer test results and reduce delays in acting on the results of early infant diagnosis and other essential laboratory tests (conditional recommendation, low-quality evidence).

The decentralization of HIV care services to primary-care settings has allowed for expanded access to treatment and improved outcomes. One challenge to delivery of care at peripheral facilities has been to ensure rapid and reliable turnaround of laboratory results. Sample transportation networks can result in delays in or losses of results, which in turn can delay clinical decision-making. While this can be partly overcome through the use of devices at the point of care, in situations where these devices are unavailable, alternative approaches are needed to ensure that delays in turnaround time of essential laboratory results, in particular for EID, are minimized. Early identification of HIV-infected infants is critical to enable timely initiation of ART.

SMS/GSM/GPRS printers represent a potential solution, whereby laboratories can transmit messages to the clinic site in real time via standard telecommunication networks. A number of countries have well-established programmes using SMS/GSM/GPRS printers, including Kenya, Mozambique, Rwanda, South Africa, Zambia and Zimbabwe. Several other countries are in the implementation and pilot phases of SMS/GSM/GPRS printer use.

Rationale and supporting evidence

A systematic review was conducted focusing on the potential for electronic result delivery systems to reduce turnaround time of early infant HIV diagnostic test results (30). Mortality among HIV-positive infants is highest during the first three months, and early HIV diagnosis and prompt ART initiation can significantly reduce this risk (31). Turnaround times using traditional paper-based systems can extend to around two months, leading to loss to follow-up of mothers and their infants and increased infant mortality if treatment is delayed.

The review identified 11 retrospective cohort studies, all conducted in Africa. The use of SMS/GSM/GPRS printers reduced average turnaround time by 17 days (from 68 to 51 days), with several studies reporting a turnaround time of less than 20 days (30). The evidence was graded as low quality due to the absence of randomized study designs and lack of data on clinical impact. Because it is possible that similar efficiencies could be gained for other laboratory test results, electronic result delivery systems could be used for other tests such as CD4 count testing, viral load testing and other non-HIV-related testing.

No formal cost–effectiveness analysis has been conducted; however, the cost of the intervention is likely to be offset by the substantial health benefits related to earlier identification of HIV-positive infants. This premise is also considered relevant for other essential laboratory tests.

Equity and acceptability

SMS/GSM/GPRS printers have been well accepted and widely implemented in many countries for return of laboratory results. The technology has the potential to improve access to results in rural settings and, as such, could improve equity. Focus groups conducted with women living with HIV who had given birth within the past 3 years suggest that any intervention to speed up identification of HIV-infected infants has the potential to reduce anxiety of mothers and is therefore highly acceptable (32).

Implementation considerations

Adequate cellular phone network coverage, maintenance, troubleshooting and systems for ensuring the supply of sufficient credit and printer consumables are all key to ensuring coverage and uninterrupted service. Implementation should take into account the need to ensure data security and patient confidentiality. Resources for adequate training of health workers and provision of consumables need to be allocated to avoid interruption of service.

Research gaps

Further studies should assess the clinical impact of SMS/GSM/GPRS printers on infant ART initiation rates, loss to follow-up, mortality and morbidity. It would be useful to assess the utility and impact of the use of SMS/GSM/GPRS printers and other technologies that return results for a range of essential laboratory results.

6.5 Retention in care



Recommendations

Programmes should provide community support for people living with HIV to improve retention in HIV care (strong recommendation, low-quality evidence).

The following community-level interventions have demonstrated benefit in improving retention in care:

- package of community-based interventions^a (children: low-quality evidence; adults: very low-quality evidence)
- adherence clubs^b (moderate-quality evidence)
- extra care for high-risk people (very low-quality evidence)

^a Patient advocates, treatment and peer support interventions providing adherence and psychosocial support in the community.

^b Peer support, distribution of ARV drugs and assessment by non-clinical or lay providers.

Background

Poor patient retention undermines programme and patient outcomes, including achieving sustained viral suppression. The global effort to increase the number of people on ART needs to ensure that people taking ART are retained in chronic care for life. Systematic reviews show that retention rates are estimated to be as low as 64% to as high as 94% at 12 months after ART initiation (33,34). Several countries report a lower than 60% retention rate after 3 years on ART, with high loss to follow-up representing unknown outcomes. Retention in ART programmes is a major challenge in all settings and across populations, specifically paediatric and adolescent populations, postpartum women and men. Multiple factors may play a role in loss to follow-up, including distance to health facilities, lack of transport or inability to cover travel expenses, stigma and disclosure-related issues, being too sick and lack of understanding of the need for lifelong care.

Rationale and supporting evidence

A systematic review (35) identified six studies (one randomized controlled trial and five cohort studies) that evaluated community-level interventions to strengthen retention in HIV care: a package of community-based interventions, adherence support clubs and provision of extra care for high-risk patients. A strong recommendation was made despite the overall low quality of evidence due to the balance of benefit greatly outweighing potential harm, the degree of acceptability to people living with HIV and the programmatic benefits of implementing interventions that result in positive patient and programmatic outcomes.

Package of community-based interventions

Community-based interventions identified with beneficial impact on retention in HIV care included: support centred on the needs of the individual, counselling and psychosocial support by lay adherence counsellors or patient advocates and family and peer support. The lay counsellors or patient advocates assisted patients by linking health facilities with communities, providing counselling and patient-centred support and visiting patients in their home environment. One cohort study (36) included children and adolescents (aged <16 years) and demonstrated significantly increased retention at 36 months with overall low quality of evidence. Bringing services closer to communities through decentralization has also improved retention in HIV care and has been recommended by WHO since 2013 (see section 6.9 “Decentralization”) (37).

Adherence clubs

The systematic review identified one retrospective cohort study (38) evaluating the impact of facility-based adherence clubs on loss to follow-up or death at 40 months, with a significant reduction compared to standard care. No studies were identified in the review evaluating the impact of adherence clubs on outcomes for adolescents or children.

Extra care for high-risk people

The systematic review identified one cohort study from Kenya that evaluated the impact of nurses and non-clinical health workers providing weekly or biweekly contact with patients with advanced HIV infection (i.e. CD4 count <100 cells/mm³) on mortality (39). Stable individuals on ART met for brief assessments by a non-clinical health worker, referral to a nurse where necessary, in addition to peer support and distribution of ART every 2 months. The study also included a yearly follow-up review with a clinician. Long-term follow-up and death were significantly reduced at 40 months, with an overall very low quality of evidence.

Cost and cost-effectiveness

The cost of implementing community-level interventions varies by setting and depends on whether community-based health programmes are already established. Generally, costs related to training and remunerating lay providers are much less than the cost of care provided at facility level and care provided by health workers. Cost related to community support, peer support and support by patient advocates is often related to training and orienting these cadres and support groups.

Equity and acceptability

A qualitative evidence synthesis (40) highlighted key interventions that were acceptable, related to improving retention in HIV care. These included lay health workers providing support (moderate confidence), particularly if they were also living with HIV; family and friend support (moderate confidence); mobile health (mHealth) interventions (moderate confidence) and developing positive and non-judgemental relationships with those implementing the intervention (moderate confidence).

Population considerations

Pregnant and breastfeeding women

For pregnant women living with HIV, the transition from antenatal care and maternal, newborn and child health (MNCH) services to ART care is a potential point for loss to follow-up. A systematic review (41) identified 10 studies (one cluster randomized controlled trial, three individual randomized controlled trials and six cohort studies) that evaluated interventions to improve postpartum retention of women living with HIV. The majority of the studies reported outcomes in the immediate postpartum period. There was moderate-quality evidence to support the use of phone calls and SMS/GSM/GPRS to improve retention in the early postpartum period (6–10 weeks). Given the paucity of data on the long-term impact of these interventions, limited conclusions can be derived from this result. There is also very limited evidence on the cost-effectiveness of interventions to improve retention in care of postpartum women. However, a systematic review attests to the positive impact of various mHealth approaches (42). Given the low costs of technologies such as SMS or phone, it can be inferred that this would likely be a cost-effective intervention.

A review of country programme experience of delivery of ART in antenatal care settings shows a range of practices to address women who transition from MNCH-based services to HIV care clinics. This transition period is often a critical point in which a substantial number of women and their infants discontinue care. Several countries are implementing interventions with evidence of benefit, including assigning district-level focal points, active patient tracing and financial support for transportation. Many programmes are implementing community-based interventions: peer support such as mothers-to-mothers programmes and peer adolescent support groups for adolescent pregnant women living with HIV. Structured counselling sessions and telephone reminders may also have the potential to support the process of transition.

Children

Caregivers are responsible for understanding the importance of retaining children in care, especially younger children. Disclosure to children typically occurs late, making it challenging to discuss the importance of follow-up. WHO recommends age-appropriate disclosure to children (43). Solutions include:

- supporting caregivers to attend for regular follow-up; and
- reinforcing to caregivers the importance of the process of disclosing to the child, which can begin early with age-appropriate messaging and tools.

Adolescents

Frequent clinic visits, time spent waiting for services and having to miss school discourages adolescents' engagement in care. Negative attitudes of health workers, concerns regarding privacy and confidentiality and limited opportunity to discuss their concerns also act as barriers to retention for younger people. Distance to facilities and out-of-pocket expenses may restrict their engagement. Service delivery models beyond the facility, which support adolescents to engage in care, such as peer-based interventions and community-based services, should be considered. Peer interventions are highly valued by young people. Adolescent-friendly health services should be implemented to improve quality (see section 6.11 "Delivering HIV services to adolescents").

Consider:

- providing adolescent services at specific times or in separate areas with flexible appointment systems that accommodate school hours;
- comprehensive services that address multiple needs, including psychosocial support and sexual and reproductive health (SRH); and
- close monitoring of adolescents' engagement in care, rapid proactive follow-up and implementation of strategies for re-engagement.

Men

A systematic review (44) identified 69 studies demonstrating that men had a 37% increased risk of death while on ART compared to women, after adjusting for baseline characteristics. This is partly explained by the fact that men tend to be diagnosed later and are more likely to start ART late. In several settings, initiatives to improve men's engagement in care have focused on engaging them in services for PMTCT. Innovative service delivery models are essential to improve men's access to HIV care services and ART initiation. Programmes need to routinely disaggregate data by sex in order to better monitor access to and outcomes of treatment for both men and women.

Implementation considerations

There is no single model of community or peer support that works in all settings, and programmes need to adapt such interventions to the local context. Some patients may choose not to receive services in the community due to concern over stigma and discrimination. Community interventions require linkage with health facilities for smooth transfer and referral of patients, when necessary, and strategic planning and resourcing for sustainability. Community-level programmes still need to be integrated into national health sector plans in many settings.

Research gaps

Implementation research and evaluation of the different models of community-level support in different contexts are necessary to further guide programmes. Innovative approaches and effective strategies are needed to support transitioning across different care-delivery points for men, postpartum women, adolescents and children. Further data on the cost of implementing community-level interventions in different settings will guide national policy.

6.6 Adherence

NEW

Recommendations

Adherence support interventions should be provided to people on ART (strong recommendation, moderate-quality evidence).

The following interventions have demonstrated benefit in improving adherence and viral suppression:

- peer counsellors (moderate-quality evidence)
- mobile phone text messages (moderate-quality evidence)
- reminder devices (moderate-quality evidence)
- cognitive-behavioural therapy (moderate-quality evidence)
- behavioural skills training and medication adherence training (moderate-quality evidence)
- fixed-dose combinations and once-daily regimens (moderate-quality evidence).^a

^a Refer to section 4.4.2 “Fixed-dose combinations and once-daily regimens” for detail.

Background

Adherence to ART is the primary determinant of viral suppression and the risk of transmission, disease progression and death (45–47). Suboptimal adherence is a major challenge worldwide and is associated with a diversity of patient- and programme-related causes. Individual factors may include forgetting doses, being away from home, changes in daily routine, depression or other illness and substance or alcohol use. Adherence to ART may also be challenging in the absence of supportive environments for people living with HIV and in the presence of HIV-related stigma and discrimination. Medication-related factors may include adverse events and the complexity of dosing regimens, such as those for children. Health system factors include distance to health services, long waiting times to receive care and obtain prescription refills, receiving only one month’s supply of drugs, pharmacy stock-outs and the burden of direct and indirect costs of care (48,49).

Specific population groups face additional challenges to adherence, and these should be considered when implementing the recommended interventions.

Pregnant and postpartum women

The pregnancy and postpartum period presents significant biological, social and economic challenges that may affect treatment adherence. It is estimated that around a quarter of pregnant women have inadequate ART adherence, and this is higher during the postpartum period (50). Pregnancy-related conditions such as nausea and vomiting may negatively affect treatment adherence. Other individual factors include suboptimal understanding of HIV, ART and PMTCT, lack of partner disclosure and support, and fear

of stigma and discrimination. Service delivery barriers include poor-quality clinical practices, gaps in provider knowledge and training, poor access to services and health worker attitudes (51,52).

Adolescents

It is estimated that over one third (38%) of adolescents globally are suboptimally adherent to ART, with substantial regional variation (53). In addition to common challenges to adherence, adolescents face specific challenges, including psychosocial issues such as peer pressure, the perceived need to conform and inconsistent daily routine (54,55). Adolescents are often left out of decisions and have limited opportunities to discuss their concerns, and there is limited availability of adolescent-specific treatment literacy and adherence counselling tools. For adolescents who are transitioning from paediatric to adolescent care, additional challenges may include assuming increased responsibility for their own care, issues relating to disclosure to peers or partners, difficulties in navigating the health-care system, lack of links between adult and paediatric services and inadequately skilled health workers (56).

Infants and young children

Successfully treating a child requires the commitment and involvement of a responsible caregiver. Parents and other family members of children living with HIV may themselves be living with HIV, and suboptimal HIV care and treatment for family members could result in suboptimal care for the child. Other challenges include lack of nutrition support, limited choice of paediatric formulations, poor palatability of liquid formulations, high pill or liquid volume burden, large pill size, frequent dosing requirements and difficulties in swallowing tablets (57–59).

People with mental health conditions and substance use

People with HIV with uncontrolled depressive symptoms are more likely to have poor adherence to ART (60,61). Adherence is complicated by mental health comorbidity that results in forgetfulness, poor organization and poor comprehension of treatment plans. Counselling for HIV and depression and appropriate medical therapies for people with mental disorders can help to improve adherence. WHO recommends that assessment and management of depression should be included in care services for all people living with HIV (see section 5.3.2 “Assessment and management of depression in people living with HIV”).

Use of alcohol and other substances may also contribute to poor adherence to ART. Alcohol and substance use can lead to forgetfulness, poor organization and diversion of monetary resources (62,63). Treatment of depression and management of substance use disorders can improve HIV treatment outcomes (64,65). WHO recommends treatment of depression and substance use disorders regardless of HIV status. Other key services for people with HIV who use drugs, such as needle and syringe programmes and drug substitution therapy, provide further opportunities to support adherence.

Key populations

In many settings, key populations face multiple challenges related to stigma and discrimination that can affect access to health services, all of which may impact negatively on adherence (66,67). WHO Consolidated guidelines on HIV prevention,

diagnosis, treatment and care for key populations include specific considerations for adherence support for these populations.

Rationale and supporting evidence

A systematic review and network meta-analysis identified 84 randomized controlled trials of interventions to improve adherence (68). Forty-seven trials reported on overall viral suppression and 71 on adherence. The review found overall moderate-quality evidence to support a range of interventions that demonstrate the benefits of improving adherence and viral suppression. Interventions were grouped by components of similarity, given below:

- Peer counsellors: there is direct evidence of higher levels of adherence compared to standard care.
- Mobile phone text messages: text messages sent to the client's phone one way or two ways. There is direct evidence that text messages result in higher adherence compared to standard care.
- Reminder devices: interventions using calendars, alarms, system devices for disease management assistance and pagers. There is direct evidence that supporters and device reminders result in increased viral suppression.
- Cognitive-behavioural therapy: there is direct evidence of a higher rate of viral suppression compared to standard care.
- Behavioural skills training: provision of training or medication adherence training sessions. These included module-based interventions and those designed to improve life skills, attitudes, behaviour and knowledge.

The benefits significantly outweigh any potential harm for all interventions identified. Peer counsellors are generally considered to be a low-cost intervention and, in some settings, have been highly cost-effective. Interventions such as cognitive-behavioural therapy and behavioural skills training require initial increased investment for training and resources. Reminder devices, telephone interventions and mobile phone text messages are low cost in the majority of low- and middle-income countries. Cost-effectiveness will vary depending on the setting and epidemic context. A strong recommendation was made by the Operational Guideline Development Group, given the potential benefits for patient outcomes, feasibility in a variety of settings and low cost.

Supportive interventions

Several interventions may also be of value in addressing specific challenges that impact on adherence and/or viral suppression. Nutritional assessment, care and support are essential components of HIV care. HIV programmes should ensure that existing national policies on nutritional support are observed to maximize adherence to ART and achieve optimal health outcomes, particularly in food-insecure settings. Nutritional support could include nutritional counselling, cash transfers, subsidizing food costs and/or food vouchers. Studies suggest that providing nutritional support to people receiving ART reduces the risk of non-adherence among food-insecure individuals (69).

Financial support can reduce the risk of non-adherence (70). Programmes and care providers should consider a broader programmatic approach to reducing the costs of care for people living with HIV. This includes avoiding out-of-pocket payments at the

point of care (such as drugs, diagnostics and clinical services), supporting transport costs, decentralizing care and reducing the frequency of health facility visits. Programmes need to consider the ethical and equity implications of providing financial support and non-monetary incentives for people living with HIV. Standardized criteria for supporting people receiving ART may need to be developed based on national income levels.

Equity and acceptability

A qualitative evidence review (71) of the acceptability of interventions to improve adherence identified intervention-specific themes. These included educational programmes for individuals and families (high confidence), mobile phone text messages (high confidence), health worker outreach (moderate confidence) and complex interventions (low confidence). Confidentiality and privacy and strengthening social networks were identified as cross-cutting themes from a total of 31 studies. Interventions may be more acceptable if they consider local cultural customs and religious beliefs. Peer-based interventions are generally well accepted, in particular among adolescents, who find that hearing experiences and learning from others facing the same challenges is critical for supporting adherence and engagement in care (72).

Implementation considerations – monitoring adherence

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

Viral load monitoring

Viral load monitoring is considered the gold standard for monitoring adherence and confirming treatment response. Although treatment failure is often caused by lapses in adherence to ART, it may also result from other factors, including drug resistance, malabsorption, drug–drug interactions and other patient-, disease- and drug-associated effects. Other approaches to monitoring adherence should therefore be considered as a way to provide additional information about possible causes of virological failure or to support adherence monitoring in settings where viral load testing is not available. WHO recommends that, following an initial high viral load (>1000 copies/mL), an adherence intervention be carried out prior to conducting a second viral load test. This has been shown to lead to re-suppression in over 70% of patients (73). Viral load monitoring also has a high potential to motivate adherence.

Pharmacy refill records

Pharmacy refill records provide information on when people pick up their ARV drugs (74,75). Pharmacy records are more reliable than self-reporting (76) and are already a part of national monitoring and evaluation frameworks in many settings.

Self-reporting

Self-reported data are easy to collect and can be a useful adjunct to estimating non-adherence but are subject to recall bias (77). Counselling on the importance of remembering ART doses and an environment that promotes and enables honest reporting of non-adherence are critical components of monitoring adherence to ART in routine care settings.

Pill counts

Counting the remaining pills in bottles may help to assess adherence. Pill counts usually take place at routine health-care visits. However, some people discard tablets prior to health-care visits, leading to overestimated adherence. Counting pills also requires health-care personnel to invest significant time and may not be feasible in routine care settings. Pill count has been found to perform better when combined with self-reported adherence (78).

Research gaps

Further research is needed to determine:

- optimal ways to proactively monitor adherence and identify through simple triage those patients in greatest need of adherence support;
- interventions to support adherence in populations at heightened risk of suboptimal adherence (children and adolescents, pregnant women, men who have sex with men, people who inject drugs);
- potential synergistic effects of combining two or more interventions that could impact individual, social support and health system factors; and
- the effectiveness of long-acting ART in improving adherence and viral suppression.

6.7 Frequency of clinical visits and medication pick-up



Recommendations

- Less frequent clinical visits (3–6 months) are recommended for people stable on ART (strong recommendation, moderate-quality evidence).^a
- Less frequent medication pickup (3–6 months) is recommended for people stable on ART (strong recommendation, low-quality evidence).^b

^a When routine clinical consultations are due, they should be coordinated with planned medication pickup to reduce visit frequency.

^b ARV supply management should be strengthened to ensure availability of ARV medicines and prevent stock-outs in the context of less frequent medication pickup.

Background

In the early period of ART scale-up in low- and middle-income settings, the majority of people seeking HIV care presented with advanced disease, often requiring intensive clinical management (79). This led to the typical practice of monthly visits to health facilities for clinical review (80). As guidelines now recommend treatment at earlier stages of the disease, there is a growing appreciation that, with effective ART and good adherence, people can have a near-normal life expectancy (81–83). HIV programmes are providing ART to increasing numbers of people who are stable on ART, and there is a need to rationalize the delivery of care to reduce the burden on health systems, particularly in countries with a high HIV prevalence. Frequent clinical visits also place a

burden on people taking ART, and the opportunity and financial costs of travelling to the clinic have been associated with an increased risk of poor adherence and poor retention in care (84). Correspondingly, approaches to reducing the frequency of clinical visits, including community ART dispensing, have been associated with improved retention (85,86).

Rationale and supporting evidence

Because clinical visits and medication pickup are often linked, both were assessed in a combined systematic review that found eight studies (one cluster randomized controlled trial, two randomized controlled trials and five cohort studies) from Kenya, Malawi, South Africa, Uganda and the United States, providing comparative data on the impact of reduced frequency of clinical visits. Overall, the review found that reduced frequency of clinical visits among stable individuals was associated with significantly better retention, with no difference in mortality outcomes. The same review identified three studies from Malawi, South Africa and Spain, which reported that reduced frequency of ART refills was also associated with improved retention in care. The studies also reported a positive trend towards improved adherence (87). There was no evidence that reduced frequency of ART refills led to additional complications or disengagement from care.

The strong recommendation to reduce the frequency of clinical visits and drug refills is supported by the expanding availability of ART and the fact that people are presenting to care earlier and require less intensive clinical care. This trend is expected to continue as countries move towards initiating ART for all people living with HIV regardless of CD4 cell count. In addition, there is substantial cost to people and health services of monthly clinical visits for those who are stable on ART. Reducing the frequency of clinical and ART pickup visits will be cost saving for both patients and health services. All cost analyses conducted within the systematic review point towards reduced cost per patient with reduced visits.

Equity and acceptability

Implementation of these recommendations is likely to improve equity as it relieves the burden placed on people to attend for frequent clinical assessments and to pick up drugs. This burden is greatest on people in rural areas (distance to travel) and those with very low income (costs associated with time off work). This recommendation is supported by the reported acceptability by young people and adults, citing increased convenience and fewer interruptions of daily schedules.

Implementation considerations

Reduced frequency of clinical and ART pickup visits has already been implemented for HIV and other chronic diseases in a variety of low- and middle-income settings. In implementing these recommendations, programmes need to consider coordinating routine clinical consultations with planned medicine pickup to reduce visit frequency. ARV drug procurement and supply management should be strengthened to ensure availability of ARV drugs and prevent stock-outs in the context of less frequent medication pickup (see section 6.10 "Integrating and linking services").

In some settings, consideration is being given to implementing even less frequent (i.e. annual) clinical visits for people who are stable on ART. While there is currently no published evidence to support this approach as a formal recommendation in these guidelines, it is recognized that this may be a reasonable approach in certain contexts and for certain populations.

Population considerations

Pregnant and breastfeeding women

Pregnant or breastfeeding women on ART may require closer follow-up and more frequent visits than other populations. Psychosocial support and counselling requirements may need to be considered, especially with regard to infant feeding and postpartum care. Differential care models should be used from the beginning of pregnancy until the end of the breastfeeding period.

Children

The needs of the children evolve as they grow, especially during rapid phases of growth and development, early adolescence and around the time of disclosure. Differential care models should be modified to the child's needs. Growth monitoring is an important component of paediatric HIV care and is necessary for dose adjustment of ART. This should be emphasized within the differential care model.

Adolescents


Rapid development may impact on adherence, retention and support requirements for adolescents. The evolving capacities and emerging independence of adolescents need to be recognized as well as the involvement of caregivers. Busy and changing daily routines and competing priorities can make frequent visits challenging for adolescents. Close monitoring of adolescents' engagement in care, rapid and proactive follow up and implementation of strategies for re-engagement are critical. Facilitating independence and self-management can support differential care for adolescents. Peers and other community-based services can also facilitate early identification of adolescents requiring additional support and follow-up. (See section 6.11 "Delivering HIV services to adolescents".)

Research gaps

Further evidence of the feasibility and benefits of increasingly spaced clinical visits and medication pickup (greater than 6 months) is needed, and this should be studied across various patient populations.

6.8 Task shifting and task sharing

Recommendations

- **Trained and supervised lay providers can distribute ART to adults, adolescents and children living with HIV (strong recommendation, low-quality evidence).** 
- Trained non-physician clinicians, midwives and nurses can initiate first-line ART (strong recommendation, moderate-quality evidence).
- Trained non-physician clinicians, midwives and nurses can maintain ART (strong recommendation, moderate-quality evidence).
- Trained and supervised community health workers can dispense ART between regular clinical visits (strong recommendation, moderate-quality evidence).

These recommendations apply to all adults, adolescents and children living with HIV.

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/arv2013/download/en>).

Background

The number of available health workers remains inadequate in many settings with a high burden of HIV. Task shifting and task sharing involve the redistribution of tasks within health workforce teams. Specific tasks are reassigned to health workers with shorter training and fewer qualifications to optimize the available human resources. Although increasing the number of health-care personnel is also crucial, clinical tasks need to be shared and shifted to ensure that enough health workers are available.

In 2013, WHO made recommendations on task shifting relating to initiation, maintenance and dispensing of ART. These recommendations are supported by a systematic review of four randomized controlled trials and six observational studies (88). Overall, the data showed no difference in mortality and some evidence of reduced rates of loss to follow-up when nurses or non-physician clinicians initiated or maintained people on ART or when community health workers maintained people on ART relative to physicians performing these tasks. The quality of care in these studies was ensured by providing training, mentoring and supervision for nurses, non-physician clinicians and community health workers, clear referral pathways and effective monitoring and evaluation systems (88).

These guidelines provide a new recommendation for trained and supervised lay providers to distribute ART to adults, adolescents and children living with HIV. Several high HIV-burden settings are experiencing a critical shortage of pharmacy personnel to undertake this task. Apart from the absolute shortage of such staff, pharmacy personnel tend to be concentrated in urban settings, large hospitals and private pharmacies,

accentuating shortages in rural and primary-care settings (89–91). Community distribution of ART for stable individuals can ease the burden of care on people with HIV and health services by reducing the frequency of clinical consultation and drug pick-up visits. Additionally, retrospective cohort studies from Uganda, the United Republic of Tanzania and Zambia demonstrate that community ARV distribution results in significantly less patient attrition than health facility-based services (92).

Rationale and supporting evidence

Indirect evidence from a systematic review comparing dispensing of ARV drugs by non-pharmacists compared to pharmacists identified two cluster randomized trials that compared the outcomes of community-based HIV care with clinic-based care (93). The first trial evaluated patient outcomes (viral load, CD4 count, opportunistic infections and change in ART regimen) when ART was provided in community settings by community care counsellors living with HIV compared to clinic-based ART delivery where care was provided by health professionals. In the community-based settings, ART was distributed by community care counsellors who were trained and mentored for patient triaging, referral when necessary and distribution of ARV drugs prefilled by pharmacy personnel. People receiving community-based care had been on ART for more than six months and had no clinical conditions and high levels of self-reported adherence to treatment (94). People in the standard-of-care arm visited health facilities on a monthly basis, picked up their ARV drugs from a health facility pharmacy and were provided care by health workers. The second trial evaluated virological failure among those accessing ART from lay providers in the community compared to the standard ART care delivery by health professionals at health facilities (95).

The meta-analysis identified no difference in mortality and virological failure between people who received care from a community-based team and those who received care from health professionals at a health facility. Fewer people were lost to follow-up in the community-based care group. Both groups demonstrated high levels of self-reported medication adherence, with no statistical differences between the groups. The overall quality of evidence is low. The lay providers were also part of a wider community-based intervention with additional confounders that supported the success of the intervention, not solely the distribution of ART.

A strong recommendation was made that trained and supervised lay providers can distribute ART to adults, adolescents and children living with HIV despite the low quality of evidence, considering existing programme experience of trained and supervised community health workers and lay workers providing and performing other tasks within the HIV testing, treatment and care continuum. Additionally, there are important examples within the broader health sector where community health workers, with minimal training, are entrusted to provide curative and preventive care in maternal and child health services, malaria diagnosis and treatment and TB care.

Potential benefits and harm

The public health benefits of lay providers distributing ART are an overall increase in the number of providers to overcome the shortage of facility personnel, reduced clinic congestion and services provided closer to communities, which support retention in care. Where ARV drug supply and stock management are not reliable, distributing ARV drugs outside health facilities may increase distribution sites and potentially aggravate stock-

outs. Neither of the two studies in the systematic review included people with comorbidities or children. While the recommendation is relevant to these populations, necessary dose adjustments, as the child grows, can be safely done during clinic visits, with maintenance treatment provided at the community level.

Cost and cost–effectiveness

There may be initial increased costs for training and other costs associated with introduction of community ART distribution. However, studies report substantial costs to patients when they are required to travel to centralized health services to collect medication. A study from Uganda reported that the cost to people receiving hospital-based care was three times higher than for people who received home-based care (95).

Equity and acceptability

A qualitative evidence synthesis identified that task shifting can enhance linkage to care and treatment adherence and assists HIV programmes to cope with shortages of professional health workers (18). Strengthened relationships between people with HIV and local communities can empower individuals. In Malawi, people from the community were hired as pharmacy attendants to pre-package and distribute ARV drugs to enhance the capacity of pharmaceutical services, an approach that has facilitated visit spacing and reduced waiting times and health providers' workload at health facilities (96).

Implementation considerations

Both initial and ongoing training and mentoring, supportive supervision and administrative planning have been critical to the success of programmes that have implemented task shifting. Programmes adopting these recommendations need to train and establish a system for routine supportive supervision of health workers, including lay providers. Adopting task shifting and sharing strategies often requires the revision of regulatory frameworks and national policies so that new cadres of health workers can perform new tasks. WHO recommends that all health workers, including lay providers, should be adequately remunerated (97), and programme experience indicates that it is difficult to sustain health services based on volunteerism alone. National regulatory bodies, professional associations and other stakeholders need to be involved when addressing the scope of practice, roles and responsibilities of health workers.

It is important that the local supply chain system take into account task shifting and sharing responsibilities, and community models of ARV drug delivery to ensure adequate stock. The supply management logistic information system needs to incorporate all ARV drug distribution outlets, including community lay providers' distribution sites (see section 6.13 "Procurement and supply management systems for HIV health products").



Good practice statement

Trained and supervised non-laboratory staff, including laypeople, can undertake blood finger-prick for sample collection.

WHO recommends that trained and supervised lay providers be used to provide safe and effective HIV testing services using rapid diagnostic tests (see section 2.3.1 “Pre- and post-test services: overview”). A systematic review (98) was conducted to evaluate the outcomes of shifting tasks of finger-prick specimen collection for HIV-related diagnostic tests to non-laboratory staff (i.e. clinicians, nurses and midwives) and lay providers compared to laboratory professionals doing the same task. The review identified 27 studies (observational and technical evaluations), the majority based in sub-Saharan Africa (88%). The study results were inconsistent due to various cadres of health workers, test types utilized and the outcomes assessed. All of the studies reported a high degree of acceptability by clients and health workers, which was consistent with findings from the qualitative evidence synthesis on the acceptability of task shifting (see recommendations for task shifting). The inconsistent study results, high risk of bias and limitations of the reported data reduce the ability to make definitive conclusions from the systematic review alone.

A good practice statement was developed on task shifting for conducting blood samples by finger-prick testing, due to the overall benefits outweighing any potential harm. Nurses, midwives and clinicians readily perform HIV testing and are involved in EID sample collection and CD4 point-of-care testing in many settings, which form the basis of this good practice statement. Expanding finger-prick testing to lay providers will support increased access to essential diagnostics and decentralization of HIV care. In several settings, trained and supervised lay providers are already conducting HIV testing and performing sample collection using the finger-prick method. No harm was identified from this approach; however, a system of quality assurance is necessary for effective and safe implementation. The WHO *Consolidated guidelines on HIV testing services* provide additional considerations and key steps for successful implementation related to performing testing and sample collection by lay providers (<http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en>).

Building human resource capacity

As HIV treatment and care have been scaled up in the past decade, in-service training has assumed a key role in rapidly upgrading the competencies of health-care providers. All health workers, including community health workers and lay providers, need to be regularly trained, mentored and supervised to ensure high-quality care and timely implementation of updated national policies. Given the rapidly evolving knowledge on HIV care and treatment, countries need to consider a system for supporting health workers' continuing education, including through clinical mentoring and regular supportive supervision (99). The use of new technologies, such as computer-based self-learning, distance education, online courses and phone-based consultation, may supplement classroom in-service training and enable efficient use of health workers' time and other resources. It is equally important to strengthen the HIV treatment and care components of existing pre-service courses for health workers graduating and receiving certification in a range of disciplines. Health-care workers also need to be equipped to manage HIV as a chronic condition, work in a team and implement new national guidelines and protocols.

Programme managers should also support the development and implementation of policies to create a suitable environment for recruiting, retaining, remunerating and motivating health workers in rural or remote areas, where turnover and attrition may be considerably higher than in urban settings.

In many countries, people living with HIV, community workers and volunteers are involved in delivering HIV testing, counselling, care, treatment and social support services. People with HIV are also involved in training health workers as expert trainers. Involving people living with HIV in both training health workers and delivering HIV services may have the additional benefit of overcoming HIV-related stigma and discrimination.

Research gaps

Research is needed to determine the feasibility and safety of further task shifting to improve access to treatment, including initiation and maintenance of ART at the community level, with spaced clinical visits to a health facility.

High-quality evidence is lacking for the initiation of second-line ART by trained non-physician clinicians, midwives and nurses. Further research in this area would identify the benefits and harm of implementing this approach in settings where there are clinician shortages.

6.9 Decentralization

Recommendations

Decentralization of HIV treatment and care should be considered as a way to increase access to and improve retention in care:

- initiation of ART in hospitals with maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence);
- initiation and maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence); and
- initiation of ART at peripheral health facilities with maintenance at the community level (strong recommendation, moderate-quality evidence).^a

^a Community level includes external outreach sites, health posts, home-based services or community-based organizations. Frequency of clinical visits will depend on health status.

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/arv2013/download/en/>).

Background

The rapid scale-up of ART programmes has posed significant challenges to health systems in high-burden, resource-limited settings. In many settings with a high burden of HIV infection, clinics have long waiting times due to the volume of patients needing care. Decentralizing

HIV treatment and care reduces waiting times for people receiving care in facilities and brings HIV services closer to people's homes. Decentralizing HIV treatment and care also strengthens community engagement by linking community-based interventions with health facilities and can optimize access to services, care-seeking behaviour and retention in care. People living with HIV, affected communities and community-based interventions play a key role in providing HIV testing, treatment, care and support.

Rationale and supporting evidence

This recommendation, made in 2013, is supported by a systematic review identifying 16 studies (two cluster randomized trials and 14 cohort studies) assessing models of decentralized HIV treatment and care. The review provides evidence that decentralization of HIV care, either from hospitals to health centres or from health centres to community-based care, improves patient access and retention in care without compromising clinical outcomes. All but one of the studies was carried out in sub-Saharan Africa, and the benefits of decentralization may differ in different contexts (100).

Implementation considerations

The optimal model for ART decentralization (partial or full) depends on the local context, including the burden of HIV infection and the health-care delivery system. Programmes should determine which clinical and laboratory services will be available at what level of the health-care delivery system.

Programme managers should consider the values and preferences of those receiving care, the number of people likely to attend decentralized settings and whether decentralization brings services closer to people who would otherwise travel long distances to receive ART.

Decentralization should be accompanied by efforts to strengthen linkage and referral systems. Community-based treatment programmes should be linked with regular care at health facilities and with adequate laboratory facilities, diagnostics, monitoring and evaluation and drug and supply management systems.

Standards of care should be defined for each level of the health system. The role of each level should match its capacity, and the lines of authority and accountability should be clear and well understood. In many settings, decentralizing ART requires task shifting to ensure an appropriate mix of health workers at peripheral facilities. An appropriate regulatory framework (laws, regulations, policies and guidelines) is needed to allow tasks to be performed by different cadres of health workers.

Adaptations may be needed for specific populations. HIV care and treatment services for pregnant and postpartum women and HIV-exposed and -infected children can be provided in decentralized settings and is a preferred option where the HIV burden is high and a large number of women and children access health services in primary care settings. In settings with a low HIV burden, a centralized service delivery model with community linkage may be more appropriate. Some groups, such as adolescents and key populations, may choose to receive HIV services in a facility that is not close to their homes due to stigma and disclosure-related concerns. In such settings, programme managers should incorporate the values and preferences of their clients in designing appropriate service delivery models.

6.10 Integrating and linking services

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

6.10.1 Delivering ART in maternal and child health-care settings

Recommendation

In generalized epidemic settings, ART should be initiated and maintained in eligible^a pregnant and postpartum women and in infants at maternal and child health-care settings, with linkage and referral to ongoing HIV care and ART, where appropriate (strong recommendation, very low-quality evidence).

^a All people living with HIV are now eligible for initiating ART at any CD4 cell count.

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/arv2013/download/en>).

Background

Access to ART for pregnant and breastfeeding women with HIV remains a challenge, as does provision of essential services to HIV-exposed and -infected infants and ensuring that services for PMTCT reach pregnant adolescents, female sex workers and women who inject drugs.

Because many women living with HIV access health services only at the time of pregnancy, maternal and child health settings provide a key opportunity to provide access to ART (101,102). In most generalized HIV epidemic settings, maternal and child health services are provided at the primary care level, where pregnant women and children predominantly access health services. WHO recommends offering HIV testing to pregnant women through provider-initiated approaches as an essential component of MNCH services (see section 2.6.2 “Other priority populations: pregnant women”). WHO also recommends couple and partner HIV testing for all pregnant women and their partners in maternal and child health-care services in generalized HIV epidemics, and that such testing should be considered for key populations in concentrated and low-level epidemics (17).

ART should be available in maternal and child health clinics or easily accessible in a linked model of service delivery. Countries with generalized epidemics may consider a phased approach to providing ART in maternal and child health settings, which may effectively transform such settings into ART sites, giving priority to facilities with the largest burden of HIV, and building health systems to ensure uninterrupted ART and adherence and retention.

Not all maternal and child health settings will have the capacity to provide long-term HIV treatment and care for women, their partners and children. These settings will need to assess the best time for transitioning and linking mothers and their infants to chronic HIV care. Issues to consider in the assessment may include the capacity and quality of HIV care in the maternal and child health-care setting, acceptability and proximity of alternative HIV care settings and HIV burden.

Rationale and supporting evidence

The systematic review conducted to support this recommendation in 2013 evaluated the impact of providing HIV treatment and care to women in maternal and child health-care settings compared to referral to ART clinics in generalized epidemic settings. One cluster randomized trial and three observational studies showed that integrated services improved uptake of and adherence to ART during pregnancy, but outcomes for maternal mortality, morbidity, immune response, infant HIV testing uptake and mother-to-child transmission were comparable (103–107). Providers felt that integrated services increased efficiency, decreased waiting time for clients and improved relationships between providers and patients, resulting in less stigmatization and improved care and adherence to treatment (108). Given the potential to improve access and provide acceptable services to increase adherence and retention, this is a strong recommendation despite the very low quality of evidence. The alternative to providing ART in maternal and child health settings is to refer women and infants to HIV care facilities. Referral-based models may further require women and infants to receive care at separate service delivery points, potentially resulting in decreased linkage and coverage of ART.

6.10.2 Delivering ART in TB treatment settings and TB treatment in HIV care settings

Recommendations

In settings with a high burden of HIV and TB, ART should be initiated for people living with HIV in TB treatment settings, with linkage to ongoing HIV care and ART (strong recommendation, very low-quality evidence).

In settings with a high burden of HIV and TB, TB treatment may be provided for people living with HIV in HIV care settings where a TB diagnosis has also been made (strong recommendation, very low-quality evidence).

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/arv2013/download/en>).

Background

In 2014, ART coverage was less than 40% among the total number of people estimated to have fallen ill with HIV-associated TB in 20 of the 41 countries with the highest burden of HIV and TB (109).

Since 2010, WHO has recommended that ART be initiated for all people living with HIV and active TB patients, regardless of CD4 cell count. TB treatment should be initiated first, followed by ART as soon as possible within the first eight weeks of starting TB treatment (see section 4.3.5 “Timing of ART for adults and children with TB”). CTX prophylaxis is also recommended for all people living with HIV and active TB, regardless of CD4 cell count (see, section 5.2.1 “Co-trimoxazole prophylaxis”). These recommendations are intended to facilitate expanded ART coverage for people living with HIV and TB and to support the diagnosis and treatment of active TB. TB infection control measures (see Annex 16) are crucial in HIV care settings to minimize the risk of nosocomial transmission of TB.

Rationale and supporting evidence

A systematic review conducted to support these recommendations in 2013 (110) evaluated the effectiveness of delivering ART in TB treatment settings. The review identified 19 observational studies, many of which showed increased uptake and timeliness of ART initiation. However, data on mortality and TB treatment success were inconsistent. The systematic review evaluating the effectiveness of delivering TB treatment in HIV care settings identified five observational studies. Two studies reported decreased mortality and another showed comparable mortality rates. TB treatment success rates and ART uptake were comparable across studies (110). In making the recommendations, the quality of evidence was considered along with programmatic risks and benefits.

6.10.3 ART in settings providing opioid substitution therapy

Recommendation

ART should be initiated and maintained in eligible^a people living with HIV at care settings where opioid substitution therapy (OST) is provided (strong recommendation, very low-quality evidence).

^a All people living with HIV are now eligible for initiating ART at any CD4 cell count.

Source: Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/arv2013/download/en>).

Background

These guidelines recommend the same ART eligibility criteria for all individuals living with HIV, regardless of drug use behaviour. WHO recommends opioid substitution therapy (OST) (with methadone or buprenorphine) for the treatment of opioid dependence, combined with psychosocial support (111). Where available, treatment of opioid dependence should be integrated and administered in conjunction with ART for those who need it. Although there is some evidence to suggest that OST improves HIV treatment outcomes among people living with HIV who inject drugs, OST should not be a

prerequisite for initiating or maintaining ART for people who use opioids. The provision of ART in settings providing OST may expand access to ART for people who inject drugs.

Given the high incarceration rates of people who inject drugs, efforts should be made to ensure that ART is available as part of prison health services. Continuity of treatment and care need to be maintained through appropriate referrals when people return to the community.

Rationale and supporting evidence

A systematic review conducted to support this recommendation in 2013 identified one randomized trial and three observational studies evaluating the effect of delivering ART in settings providing OST. Most of these studies had small sample sizes. Some studies observed trends of improved viral suppression and reduced mortality, while others found comparable rates of viral suppression and mortality (112–114).

This recommendation supports expansion of ART by delivering the service in settings providing OST. OST should be provided free of charge or covered by public health-care insurance and should be accessible to all those in need, including in prisons and other closed settings. HIV programmes will need to continue to work closely with other service providers to ensure successful implementation of this recommendation. Guidance on maintaining effective OST programmes is available in the WHO Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations (http://apps.who.int/iris/bitstream/10665/128048/1/9789241507431_eng.pdf?ua=1&ua=1).

6.10.4 STI and family planning services in HIV care settings

NEW

Recommendation

Sexually transmitted infection (STI) and family planning services can be integrated within HIV care settings (conditional recommendation, very low-quality evidence).

Background

There is significant overlap in the demographics and risk profile among people accessing HIV treatment and care services and SRH services. WHO recommends the routine offer of HIV testing services for people with an STI in all epidemic settings and for family planning clients in generalized epidemic settings. Data from countries across sub-Saharan Africa confirm high rates of unintended pregnancy (51–84%) among women living with HIV (115–118). There is also a higher unmet need for family planning services among women living with HIV enrolled in HIV care compared to the general population.

A study in Uganda found that 75% of women living with HIV had an unmet need for family planning, more than double the unmet need reported by women who did not have HIV (34%) (119). A limited but growing body of evidence suggests that many women in

Asia who are living with HIV lack access to family planning services and experience disproportionately high rates of unintended pregnancy and abortion (120). Adolescent women are more likely to have unintentional pregnancies, detectable viral loads during pregnancy and higher mother-to-child transmission rates compared to adult mothers (121). Access to adolescent-friendly family planning services should be prioritized for this group.

STI and family planning services can be delivered in conjunction with chronic HIV care at primary care settings. Integration and linkage of these services potentially expands access to all of them. The diagnosis of syphilis in pregnant women is increasingly integrated with HIV testing services, and the dual elimination of mother-to-child transmission of HIV and syphilis is a global public health objective.

Rationale and supporting evidence

A systematic review identified three studies (one retrospective cohort and two comparative cross-sectional studies) from low- and middle-income countries. These evaluated the impact of providing family planning services on contraceptive use in HIV care settings and the rate of unplanned or unintended pregnancy among people enrolled in HIV care (122). All the studies reported improved contraceptive use compared to referral to an external maternal and child health or family planning clinic. One cluster randomized trial examining the integration of family planning into HIV care and treatment services in Kenya found that integration was feasible, inexpensive to implement and cost-effective (123). The review did not identify any studies that evaluated delivery of STI services in HIV care settings. The overall quality of evidence is very low due to the observational nature of the studies and the lack of data on delivery of STI services in HIV care settings in low- and middle-income countries. There is evidence that integrated service delivery is cost-effective and leads to economies of scale (124–126).

A conditional recommendation was made that STI and family planning services can be integrated within HIV care settings, considering existing programme experience, potential for cost savings and evidence of feasibility and acceptability. Provision of integrated services will improve access and expand the opportunity to provide STI and family planning services to a key population of adults and adolescents.

Equity and acceptability

A qualitative evidence review identified 10 studies from Uganda, Ghana, Kenya, Malawi, Swaziland and Zambia (127–136). A global community dialogue and focus groups were also conducted in Bangladesh, Burundi, Ethiopia, Myanmar and Uganda to evaluate the perceptions of people living with HIV about the delivery of STI and family planning services in HIV care settings. Three studies evaluated the perceptions of health-care providers. Overall, integration of STI and family planning services into HIV care settings is the acceptable and preferred model of service delivery by people living with HIV and service providers. Many people living with HIV expressed a preference to receive family planning services in an “HIV-only” environment.

Feasibility

Delivery of comprehensive, integrated HIV and SRH services is already part of national policy in several high HIV-burden settings (137). Feasibility and models of integrating STI and family planning services in HIV care settings is often context specific. Effective implementation of integrated services at national scale requires an enabling environment, including collaboration across programmes, particularly in human resources and supply management, supportive supervision and joint programme planning, monitoring and evaluation. Major challenges cited by health-care providers and programme managers include poor patient record-keeping, key commodity stock-outs, client misconceptions about the side-effects of some contraceptive methods and an increased workload for health workers, especially in database management.

Implementation considerations

It is essential to provide follow-up to postpartum women living with HIV and their HIV-exposed infants, both for HIV and for routine postpartum and child health care. Initial follow-up of the infant is usually scheduled at the first immunization visit at 4–6 weeks. Follow-up for the mother should ideally be scheduled at the same time and should include a postpartum check-up, family planning counselling and review of ARV drug regimen and adherence support (138). Family-based care, in which the mother, her baby and partner receive care in the same place, should be promoted as much as possible.


For adolescents living with HIV, HIV care presents an opportunity for the provision of comprehensive SRH information and services, including safe sex practices, prevention and management of other STIs, sex and sexuality education and family planning services. Sex and sexuality should be treated in a positive, non-judgemental way with all adolescents, regardless of their HIV status. Integrated service delivery models also present an opportunity to provide comprehensive services to key populations.

6.10.5 Care transition

An effective continuum of HIV care ensures that patients are retained as they transition between different health-care services and providers. Care transitions may be negatively affected by stigma and discrimination, fear of disclosure to new providers and anxiety or inconvenience resulting from changes in providers, their practice style and location. Examples of such changes include adolescents transitioning from paediatric care to adult care; pregnant and postpartum women transitioning from maternal and child health services to HIV care; patients transitioning from hospitals to primary care facilities; patients transitioning from facility-based to community-based services; and patients in correctional facilities transitioning to general outpatient care. Effective planning and support for patients are needed to ensure that these transitions occur as smoothly as possible.

6.11 Delivering HIV services to adolescents

Recommendations

- **Adolescent-friendly health services should be implemented in HIV services to ensure engagement and improved outcomes (strong recommendation, low-quality evidence).** 
- Community-based approaches can improve treatment adherence and retention in care of adolescents living with HIV (conditional recommendation, very low-quality evidence).
- Training of health-care workers can contribute to treatment adherence and improvement in retention in care of adolescents living with HIV (conditional recommendation, very low-quality evidence).
- Adolescents should be counselled about the potential benefits and risks of disclosure of their HIV status to others and empowered and supported to determine if, when, how and to whom to disclose (conditional recommendation, very low-quality evidence).

Source: HIV and adolescents: guidance for HIV testing and counselling and care for adolescents living with HIV. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/adolescents/en>).

Background

These guidelines recommend ART initiation in all adolescents (10–19 years old) living with HIV, regardless of CD4 count or clinical stage of disease (see section 4.3.3 “When to start ART in adolescents (10–19 years of age)”). There is a growing cohort of adolescents living with HIV, which includes those infected from birth and those who have acquired HIV later in childhood and adolescence. While there is still a lack of health outcome data for this age group, emerging evidence indicates that adolescents living with HIV are underserved by current HIV services and have significantly worse access to and coverage of ART (139). Adolescents are at high risk of loss to follow-up both before and after ART initiation; people aged 15–24 years and those attending services for the PMTCT of HIV are particularly at risk (140–146).

Rationale and supporting evidence

All adolescents, including those living with HIV, face significant barriers to accessing health services, due to inadequate health literacy, limited ability to navigate health systems, legal requirements for parental or caregiver consent, and insufficient resources to pay direct and associated service costs (147,148). Adolescents face significant levels of stigma and discrimination, particularly those from key populations, among whom criminalization of behaviour such as sex work, drug use and same-sex activity further perpetuates social exclusion and hinders access to health and support services (149,150).

Poor quality of services also limits adolescent engagement in health care. Adolescents often perceive health services as unacceptable due to concerns about confidentiality and

negative health provider attitudes (150,151,153). Services are often not organized to accommodate adolescent needs and routines and have inconvenient service schedules, inflexible appointments and unwelcoming environments (150,151). Without sufficient consideration and support, adolescents can be lost between paediatric and adult services. The rapid developmental and social changes that occur during adolescence exacerbate the impact of such barriers and can have a profound impact on the way adolescents engage with health services (151).

Due to their unique needs, adolescents living with HIV require quality comprehensive services and care to support access, retention and adherence. This includes psychosocial support, SRH and mental health care (151,152). The WHO quality-of-care framework provides a useful working definition of adolescent-friendly health services (Box 6.1) (153,154). Additionally, global standards for quality health-care services for adolescents have been developed to support implementation (Box 6.2) (155).

Box 6.1. WHO-defined characteristics of adolescent-friendly health services

Equitable: all adolescents, not just certain groups, are able to obtain the health services they need.

Accessible: adolescents are able to obtain the services that are provided.

Acceptable: health services are provided in ways that meet the expectations of adolescent clients.

Appropriate: the right health services that adolescents need are provided.

Effective: the right health services are provided in the right way and make a positive contribution to the health of adolescents.

A systematic review (156) was conducted to assess the effectiveness of adolescent-friendly health services for adolescents living with HIV compared to standard care. Due to the limited evidence available, the review was expanded to include the general adolescent population and young people up to and including 24 years of age. Adolescent-friendly health services were defined according to the WHO characteristics and the global standards for quality health-care services for adolescents. Eleven randomized control trials (157–167) and eight observational studies (168–175) from four of the six WHO regions were identified. Four studies focused on adolescents living with HIV; the remainder focused on SRH, HIV prevention, mental health, diabetes, general health and smoking cessation. All studies included two or more of the WHO characteristics, and global standards for quality health-care services for adolescents. Only one study included all WHO characteristics and no study addressed all global standards.

Young people engaged in adolescent-friendly health services compared to standard care showed small but significant improvements in various outcomes, including health

outcomes (lower pregnancy rates); health-care utilization (presentation at a clinic for mental health, HIV counselling and testing and outpatient visits); uptake (HIV testing); knowledge (HIV and STI acquisition, pregnancy prevention and sexual health); attitudes (towards sex and HIV testing); sexual risk-reduction behaviour (condom use); self-efficacy (condom use or diabetes management); and service acceptability. No differences were seen with respect to healthy lifestyle or quality of life outcomes. Among HIV-positive young people exposed to adolescent-friendly health services compared to the standard care, there were small but significant improvements with respect to short-term viral load reduction and long-term ART adherence. The overall quality of evidence is low. A strong recommendation was made despite low-quality data, citing the promising improvement in outcomes, the existing programme experience, and evidence of feasibility and acceptability by the end users.

Cost and cost–effectiveness

No studies have assessed the resource requirements or cost–effectiveness of adolescent-friendly health services within HIV service settings. However, a cost modelling study and a retrospective cost analysis for adolescent-friendly health services in low- and middle-income countries reported that, although additional resources are required to ensure delivery of quality adolescent-friendly health services, investments to implement and scale up these services – in particular, services providing multiple interventions – appear to have value and impact for adolescents (176,177).

Equity and acceptability

Adolescent-friendly approaches aim to ensure that all adolescents obtain the health services that they need, that policies and procedures are in place to facilitate provision of health services to adolescents and that all health service providers treat adolescents with equal care and respect, regardless of HIV status, behaviour or other characteristics.

A global consultation of 470 young people living with HIV and a situational analysis of over 200 facilities in the WHO African Region was undertaken to prepare for the development of these guidelines (150,178). Additional inputs were also considered from two unpublished, multicountry longitudinal qualitative studies with 147 adolescents living with HIV (179).

Key acceptability themes and suggested strategies for improving service delivery focused on empowered and solution-oriented information and support; opportunities for open and honest discussion; skills development on SRH and HIV disclosure from an early age; comprehensive care that addresses issues beyond HIV, including support for adolescents from key populations; flexible scheduling of clinic visits to accommodate school hours; free services closer to home and community-based services; dedicated hours and spaces for adolescents; peer-led interventions and services; and an adolescent-competent workforce.

Feasibility

The programmatic and facility-level feasibility of adolescent-friendly health services was explored. The situational analysis of facilities assessed the availability of appropriate HIV treatment services for adolescents (181). Thirty-five per cent of facilities reported that adolescent patients were attended to separately from adult and/or paediatric patients through the use of dedicated schedules, staff or spaces. A case study of a government

ART clinic in KwaZulu-Natal province in South Africa found that it is feasible to provide adolescent-friendly health service approaches in an HIV service setting. Although financial costs were low, consideration needs to be given to ensure engagement of stakeholders, including adolescents, adolescent-specific training, minimal provider rotation and adequate time for planning of restructured services. A survey of HIV programme managers highlighted the lack of appropriately trained health service providers and the need for greater preparation of health-care services as key challenges in delivering HIV services to adolescents (180).

Experience in Zimbabwe has identified several requirements for scaling up adolescent-friendly HIV services. These include a national, multisectoral, coordinated response; adolescent-sensitive policies and guidelines; meaningful involvement of adolescents; training and sustained mentorship of health service providers; community systems strengthening; linking community interventions with health facilities; and a national monitoring and evaluation framework with disaggregation and clear indicators for adolescents.

Implementation considerations

The global standards for quality health-care services for adolescents provide an approach to implementing health-care services for adolescents (Box 6.2) (152). The standards outline the desired level of care and what needs to be done for the standards to be achieved.

Further actions to implement the standards at the national, district and facility levels are outlined within the implementation guide (158). These standards and actions are relevant to HIV services for adolescents.

HIV-specific implementation considerations include the following:

- aligning approaches for HIV service delivery with WHO and national adolescent-friendly health service standards, protocols and activities;
- including implementation of adolescent-friendly approaches in HIV health service supervisory and monitoring systems;
- ensuring training, research and personal development opportunities for health service providers on adolescent HIV treatment and care;
- engaging service providers, adolescents and other key stakeholders to identify acceptable and feasible activities;
- implementing adolescent-friendly health service approaches in all HIV services used by adolescents, including antenatal care for pregnant adolescents living with HIV;
- establishing linkages and referral pathways to ensure a comprehensive continuum of care, especially for the transition from paediatric to adult HIV services; and
- addressing the needs and vulnerabilities of adolescents from key populations (181).

Box 6.2. Global standards for quality of health-care services for adolescents

Adolescent health literacy	Standard 1. The health facility implements systems to ensure that adolescents are knowledgeable about their own health and that they know where and when to obtain health services.
Community support	Standard 2. The health facility implements systems to ensure that parents, guardians and other community members and community organizations recognize the value of providing health services to adolescents and support the provision and utilization of services by adolescents.
Appropriate package of services	Standard 3. The health facility provides a package of information, counselling, diagnostic, treatment and care services that fulfil the needs of all adolescents. Services are provided in the facility and through referral, linkages and outreach.
Provider competencies	Standard 4. Health-care providers demonstrate the technical competence required to provide effective health services to adolescents. Both health-care providers and support staff respect, protect and fulfil adolescents' rights to information, privacy, confidentiality, non-discrimination, non-judgemental attitude and respect.
Facility characteristics	Standard 5. The health facility has convenient operating hours, a welcoming and clean environment and maintains privacy and confidentiality. It has the equipment, medicines, supplies and technology needed to ensure effective service provision to adolescents.
Equity and non-discrimination	Standard 6. The health facility provides quality services to all adolescents irrespective of their ability to pay, age, sex, marital status, education level, ethnic origin, sexual orientation or other characteristics.
Data and quality improvement	Standard 7. The health facility collects, analyses and uses data on service utilization and quality of care, disaggregated by age and sex, to support quality improvement. Health facility staff is supported to participate in continuous quality improvement.
Adolescents' participation	Standard 8. Adolescents are involved in the planning, monitoring and evaluation of health services and in decisions regarding their own care as well as in certain appropriate aspects of service provision.

Source: http://www.who.int/maternal_child_adolescent/documents/global-standards-adolescent-care/en

Additional guidance

Adolescent HIV testing, counselling and care: implementation guidance for health providers and planners. Geneva: World Health Organization; 2014 (http://www.who.int/maternal_child_adolescent/documents/hiv-testing-counselling/en).

HIV and adolescents: guidance for HIV testing and counselling and care for adolescents living with HIV. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/adolescents/en>).

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 (http://www.who.int/maternal_child_adolescent/documents/global-standards-adolescent-care/en).

Interagency Working Group on Key Populations: technical brief series on young key populations (<http://www.who.int/hiv/pub/toolkits/hiv-young-msm/en>).

Research gaps

Research should contribute to a better understanding of how to implement adolescent-friendly health services at a programmatic level and the cost-effectiveness of these approaches in HIV services in low- and middle-income countries. Research on the service delivery needs of adolescents living with HIV should examine the minimum package of care; models of delivery at different service levels, including for key populations and pregnant adolescents living with HIV; the integration of SRH in ART services for adolescents; interventions to support safe disclosure; treatment literacy; interventions to address mental health; and the impact of provider training and peer interventions.

6.12 Improving the quality of HIV care services

Background

This section provides brief guidance for programme managers and health-care providers on improving the quality of HIV care services. It focuses on key principles, approaches and interventions, highlighting QA and quality improvement (QI) practices based on implementation and programme experience. HIV programmes should also be innovative in addressing local challenges and aim to strengthen programme monitoring and the routine use of programme data to improve the quality of services. Quality of care emphasizes that services should be effective in achieving desired health outcomes and that health-care practices should be people-centred and safe (182). The *WHO global strategy on people-centred and integrated health services* outlines the strategy and provides an overview of evidence and good practices (183,184). Strategies to improve the quality of HIV care services are needed both at the programme management level and at health facility and community levels where HIV care services are provided (185). If an intervention is to achieve the desired health outcomes, it needs to be evidence based, of high quality and achieve a level of coverage that brings desired outcomes at the population level.

Rationale for strengthening the quality of HIV care services

Quality care means that people living with HIV receive the care they require to maintain their health and quality of life. For HIV programmes and health-care providers, quality HIV care optimizes programme effectiveness and efficiency. For policy-makers and funding agencies, quality care is an important requirement for maintaining health at the population level and ensuring the optimal use of available resources.

HIV programmes should plan to provide quality HIV care services from the outset by incorporating quality in the national policy, strategic plan, strategic information framework and operational and service delivery plans. Quality of care should not be seen as an additional activity to routine HIV services or a short-term project to redress implementation issues and gaps; it should be incorporated into daily activities at all levels, from service delivery to national programme management.

The WHO global strategy on people-centred and integrated health services

The *WHO global strategy on people-centred^a and integrated health services^b* represents a fundamental shift in the way health services should be funded, managed and delivered. Without a people-centred and integrated health services approach, health care will become increasingly fragmented, inefficient and unsustainable. The strategy proposes that all people have access to health services provided in a way that responds to their needs and that are equitable, safe, effective, efficient, timely and of an acceptable quality.

Within the context of HIV care service delivery, people-centred care includes:

- building health-care providers' skills for effective communication with people;
- providing information and supporting people to make informed decisions and for their active engagement in their own care and self-management;
- offering a patient appointment system and acceptable frequency of facility visits;
- avoiding long health facility waiting times during clinical consultations, medication pick-up or laboratory services;
- coordinating care when people require multiple services (e.g. TB and HIV treatment, family-centred care); and
- providing comprehensive integrated services, as appropriate and relevant.

^a People-centred health services involve an approach to care that consciously adopts the perspectives of individuals, families and communities and sees them as participants as well as beneficiaries of trusted health systems that respond to their needs and preferences in humane and holistic ways. People-centred care requires that people have the education and support they need to make decisions and participate in their own care. It is organized around the health needs and expectations of people rather than diseases.

^b Integrated health services are health services that are managed and delivered in a way that ensures that 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 their whole life.

Source: WHO global strategy on people-centred and integrated health services (<http://www.who.int/servicedeliverysafety/areas/people-centred-care/en>).

WHO, the participants of a scoping consultation on strengthening quality of HIV clinical services and members of the Operational Guideline Development Group developed the following good practice statements for HIV care services that are reflective of the broader WHO global strategy on people-centred and integrated health services (187).

NEW

Good practice statements

HIV programmes should:

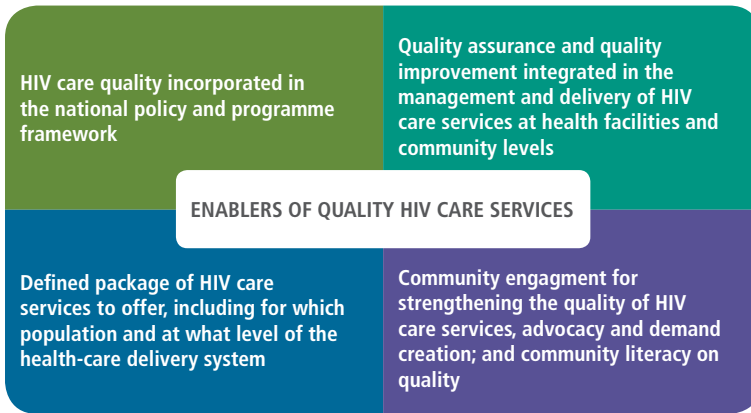
- provide people-centred care that is focused and organized around the health needs, preferences and expectations of people and communities, upholding individual dignity and respect, especially for vulnerable populations, and engage and support people and families to play an active role in their own 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 efficient and effective use of resources.

Components of quality assurance and quality improvement

QI is the process of improving services and care through the routine use of patient and programme data. Several contextual factors, such as leadership and teamwork, also have a bearing on the quality of HIV care. Programme managers and health-care providers need to continuously monitor the quality of HIV care services (Fig. 6.2). This can be done by comparing implementation against set standards, analysis and use of routinely collected data at facility level and consultation with service users or community networks on the needs, values and preferences related to HIV care services that they receive. Some quality interventions require broader system-level interventions to ensure sustained improvement. For example, the delivery of community ART, triaging patients to reduce clients' waiting time for clinical consultation and use of lay providers in patient education and counselling all require a supportive programme and resources for sustained implementation. Lessons from the QI process in HIV care service delivery and management should feed back into subsequent policy and programme formulation and planning processes.

Enablers of quality improvement

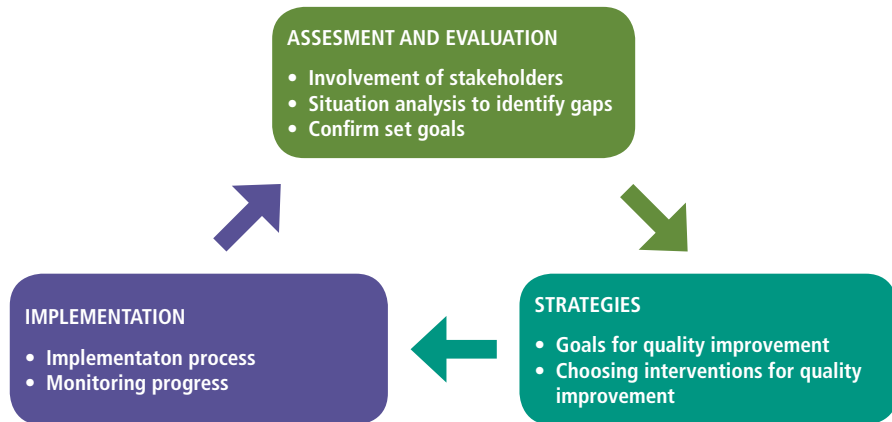
HIV programmes should provide a national framework for strengthening the quality of HIV care services. The framework should also facilitate accountability and resource mobilization at different levels of the health-care delivery system. Integration of quality HIV care in national policies and strategic plans can also facilitate partnership with other health programmes and stakeholders, including professional associations, funding agencies, research institutions, communities and networks of people living with HIV. A national framework should also highlight the needs of marginalized people or groups, address resource needs to reach underserved populations and address health worker capacity to bridge gaps in quality. Comprehensive quality-of-care activities should include both QA and QI activities. Fig. 6.2 summarizes enablers for delivering high-quality HIV care services.

Fig. 6.2. Key enablers of quality HIV care services

Several key considerations for integrating QI of HIV care into national policies, programmes and strategic plans are given below.

- Ensure involvement of stakeholders, including networks of people with HIV, communities and health-care workers, for building a common understanding on strengthening quality HIV care services and efficient use of resources.
- Identify elements of national policies and strategies to address the quality of HIV care services and HIV-related stigma and its impact on accessing HIV care services.
- Prioritize strategies for QA and QI of HIV care (Fig. 6.3).
- Identify nationally harmonized key indicators and reporting requirements for monitoring the quality of HIV care.
- Define roles and responsibilities of stakeholders at different levels of the health-care delivery system in strengthening the quality of HIV care services.
- Allocate resources for the development of mechanisms to support QI; for management and information systems that report, monitor and improve the quality of HIV care services; and for alignment of performance with implementation of evidence-based good practices.
- Include high-quality, people-centred HIV care service delivery in the principles, values and strategies of national policies and the HIV strategic plan.
- Set standards for evidence-based HIV care through national guidelines by defining the package of HIV care services to be offered, including at what level of the health-care delivery system and for which population or geographical location.
- Provide a national monitoring framework for continuous QI of HIV care services and assure that the practice of care adheres to national, evidence-based guidelines and standards.

Fig. 6.3. Process of building a strategy for continuous quality improvement



6.13 Procurement and supply management systems for HIV health products

6.13.1 Overview

This section provides operational guidance on procurement and supply management (PSM), with a focus on how PSM systems can respond to new recommendations in these guidelines. Comprehensive advice on the general management of PSM systems is readily available in existing publications and training materials. References to relevant publications and materials are provided at the end of this section.

The overarching objective of PSM systems is to support national policy with the adequate and continuous availability of the most effective, heat-stable, fixed-dose, quality-assured ARV drug formulations, diagnostics and other consumables at service delivery sites, in the right quantities, at the lowest possible cost and in a timely manner.

The new recommendation that ART should be initiated in all people living with HIV regardless of CD4 cell count will require an integrated national strategic response that considers the resources available and enables strong PSM systems at all levels of the health system. In addition, the fact that all people living with HIV need to be on ART will accelerate the scaling up of ART programmes. Procurement managers and ART programme managers will need to work together to ensure that the national supply system is forecasting, procuring and distributing the quantities of ARV drug and other health commodities required to meet the increasing national demand and the 90–90–90 target.

While there are no major changes in the ART regimens recommended in these guidelines, new drugs are recommended as components of alternative regimen choices, with potentially important implications for PSM.

6.13.2 Implementation considerations

Most national HIV programmes will need to plan a phased approach to the adoption of the new recommendations, notably the expansion of ART to all people living with HIV and the introduction of pre-exposure prophylaxis (PrEP) for groups at substantial risk of HIV infection. Where programme resources are already stretched, unplanned adoption of these new recommendations with the associated increase in demand for drugs and diagnostics may lead to stock-outs and imbalances.

Challenges and opportunities associated with implementing new WHO recommendations include the following:

- product selection;
- quantification and demand forecast;
- procurement planning and execution, including delivery and timeliness of orders;
- the ability of global supply to cope with the increasing global demand;
- storage and distribution, including logistics constraints;
- monitoring of consumption and demand changes;
- frequency of ARV drug pickup;
- information flow between stakeholders at different levels;
- costs and opportunities for cost saving;
- shelf-life of ARV drugs;
- risk of stock-outs if procurement does not meet demand; and
- risk of expired health products if the quantities procured have been overestimated.

National HIV programmes should consider establishing a stakeholder working group to develop a plan to address these issues, with participation by health policy-makers, implementers, PSM specialists and representatives from central medical stores management and the finance ministry.

Selecting pharmaceutical and diagnostic products

- Medicines should be selected in accordance with national ART guidelines and programme needs.
- National ART guidelines should provide guidance on alternative regimens in case of drug toxicities and treatment failure or stock-outs (e.g. lopinavir/ritonavir [LPV/r] versus atazanavir (ATV)/r; lamivudine (3TC)-containing versus emtricitabine (FTC)-containing formulations).
- It is recommended that the overall number of ARV drug regimens be minimized in order to optimize treatment and sourcing. According to WHO country surveys conducted in

2015, 30% of reporting countries use over 10 different first-line ARV drug regimens in adults and adolescents.

- Before new products are included in national essential medicines lists, registration and intellectual property status should be verified to ensure that the product can be imported.
- If a selected ARV drug is not on the national list and/or registered in the country, HIV programme managers should coordinate with the national drug regulatory authority and request that these drugs be put on the list and registered. Pharmaceutical companies also have a responsibility to register products in countries where they market their products.
- Drugs no longer recommended by WHO for any ARV drug treatment regimen should be removed from the national ART guidelines and essential medicines lists, and plans should be made to transition patients to more effective regimens, using existing stocks as appropriate.
- The synchronized introduction of new guidelines with planning for forecasting, procurement and distribution will minimize the wastage of products that are being phased out and shortages of newly recommended products.
- National essential medicines lists should be optimized for paediatric ARV drug formulations following the detailed guidance on preferred paediatric products provided in the Interagency Task Team (IATT) Paediatric ARV Optimal Formulary available at <http://www.emtct-iatt.org/wp-content/uploads/2015/05/Updated-Formulary-04012015.pdf>.

Quantification and forecasting of demand

To assess the volume of products required to meet programme demand, PSM managers need to know:

- the number of patients on treatment, disaggregated by age group;
- the ARV drug regimens in use by those patients;
- proposed changes in ARV drug regimens, if any;
- the expected rate of scale-up of treatment, i.e. the increase in numbers of patients on each regimen in a given period of time;
- the numbers of rapid test kits required to identify people with HIV in line with scale-up targets;
- the forecasted uptake of PrEP; and
- the frequency of ARV drug pickup by patients.

The process of quantification of needs can be highly complex. Good practice suggests that quantification should be undertaken annually, projecting for at least two years with a quarterly or semi-annual review to determine if any significant upward or downward adjustments are needed. Assuming that financial resources are available, PSM managers can then plan ahead and place long-term orders while allowing sufficient flexibility to adjust for potential changes in the pace of scale-up, regimen switching and/or other unforeseen events affecting consumption.

When demand for a specified period has been quantified, procurement managers should develop a supply plan that takes into account:

- the months of stock currently available;
- the existing orders yet to be fulfilled by vendors;
- the budget available for new orders;
- the volume of new orders required to satisfy the forecasted demand, including provision of a safety buffer stock; and
- the required delivery dates for new shipments.

It is recommended that this process of supply planning be conducted on a quarterly or half-yearly basis to accommodate changes in demand and any delivery delays from suppliers.

Procurement

A uniform and harmonized procurement system is required to efficiently procure quality-assured, affordable ARV drugs and diagnostics. Procurement should be based on selection of appropriate products and forecasted needs, considering consumption, expanding services, phasing in and phasing out of formulations and implementing new recommendations. Transparent procedures should be adopted to achieve best-value procurement and a QA system implemented to procure, store and distribute quality-assured pharmaceuticals, diagnostics and other health products.

National procurement programmes should:

- request that partners supporting the national HIV programme consolidate PSM systems and pool procurement for ARV drugs and diagnostics;
- consider joining other pooled procurement mechanisms to increase economies of scale and minimize the risk of long delivery times observed with small orders (second-line regimens and paediatric ART);
- establish agreed specifications for selected products to ensure a common basis for procurement competition, QA standards of the products, and any special needs such as packaging or identification, with special requirements likely leading to price increases;
- use a competitive process to ensure value for money;
- establish long-term framework contracts against which call-down orders can be placed for commodities in regular and repeated demand, such as medicines and diagnostics. This will reduce procurement transaction costs as well as the time taken from identification of need to fulfilment of order and help to build collaborative relationships between buyers (national procurement managers) and sellers (suppliers);
- wherever possible, implement a multisupplier procurement strategy to support a healthy market and avoid dependence on a single supplier, which will also provide flexibility during periods of supply constraints or where individual suppliers face production or logistical difficulties that lead to delays;
- use a publicly accessible database to facilitate access to information about prices and to support competition; and

- follow the principles described in the United Nations interagency guidelines for donated drugs and WHO model quality assurance system for procurement (MQAS) (186).

National HIV programmes should be aware that other countries and programmes will be ordering the same or similar formulations at the same time, and manufacturers may already have orders that will account for current production, possibly for several months ahead. Working with their suppliers, procurement managers will be able to place their orders according to agreed volumes and delivery schedules. Advice on current production and any existing supply constraints and opportunities may also be available from the organizations and contacts provided at the end of this chapter (see section 6.13.6 “Useful PSM resources”).

Storage and distribution

Appropriate storage and distribution of HIV medicines, diagnostics and other commodities is essential. The recommendation to offer ART to people with HIV regardless of CD4 cell count will significantly increase commodity volumes and the demands on storage and distribution. Countries may need to plan for new public facilities or examine alternative approaches, including leveraging additional resources by outsourcing to private sector facilities, provided that they are appropriate for storing pharmaceuticals. Neither of these options is a quick fix; contracting with private sector providers may take many months to complete the appropriate tendering, contracting and QA of providers before available facilities can be activated for use. Countries may also wish to explore the potential of existing parallel systems, such as cold-chain facilities in immunization programmes for products that require temperature control.

PSM systems should consider planned programmatic changes in service delivery related to the frequency of clinical visits and location where patients receive their ARV drugs. For example, community distribution of ARV drugs to stable patients and community-based HIV testing may involve another step in the local supply chain and potentially increase the quantity of ARV drugs and diagnostics to be procured and distributed. Changes that impact positively on the amount of stock retained at each level, including by the patient, need to take into account the shelf-life of the ARV drugs. For example, the most common first-line ARV drugs currently have a 24-month shelf-life only, and many rapid test kits have a 12- to 18-month shelf-life only, which may impact storage and distribution plans.

Storage and distribution plans should include:

- QA of products on receipt at the warehouse;
- secure storage facilities appropriate for pharmaceuticals;
- cold storage for products that require temperature control;
- rationalization of the number of storage levels to reduce the length of the supply pipeline;
- inventory control systems with appropriate minimum and maximum levels that trigger reordering;
- regular distribution patterns to service facilities, with increased frequency of potentially smaller deliveries supporting more effective use of existing limited space and distribution capacity; and

- routine data reporting from facilities to monitor usage and identify changes in predicted consumption patterns that may risk excess stocks (which can be reallocated to avoid expiry) or stock-outs.

Ensuring a secure supply for programme flexibility and to avoid stock-outs and expired health products

It is essential to avoid stock-outs in order to prevent treatment discontinuation and achieve ART targets. Recommended actions to avoid the risk of stock-outs include the following.

- There should be close coordination with HIV programme managers and policy-makers to understand the planned progression towards “treat all” targets. Programme managers and clinicians should agree on the speed at which new patients will be started on treatment to ensure that the required commodities are available. A faster-than-planned introduction of new patients will exhaust stocks and cause an increased risk of stock-out; a slower-than-planned introduction risks overstocking and wastage due to expiry of medications.
- A clear understanding is needed of the supply chain implications of any proposed changes in the service delivery model (e.g. community distribution of ARV drugs).
- It is important to ensure that the ARV drug and diagnostics supply chain – especially its distribution system and allocation of commodities by facility – reflects the geography of the HIV epidemic.
- New patients should be initiated on the preferred first-line regimen, unless clinically contraindicated.
- Quantification and ordering should include a rotating safety buffer to compensate for errors in forecasting and potential delivery delays. It is recommended that the buffer be part of the normal stock rotation, not a separate stockpile, to avoid the risk of retaining aged or expiring products. The level of buffer may vary but should cover at least one round of planned deliveries so that any delivery delay will not lead to a stock-out. Forecasts should be revisited at least semi-annually to adjust for variances between forecasts and actual demand and to review demand for the next 12–18 months, adjusting orders as necessary.
- Orders should be placed in advance for timely delivery. Procurement managers should work closely with their suppliers to understand the suppliers’ normal delivery periods and plan accordingly. It is recommended that orders be placed at least six months ahead of the required date of delivery, as this will allow adequate time for production and – where volumes allow delivery by sea freight – reduce the cost of shipping. It is also recommended that, where practical, deliveries be staged rather than arriving as a large shipment containing six months or more of stock. Staged deliveries allow for more flexible delivery schedules and enable PSM managers to make the best use of existing storage and distribution capacity.
- PSM managers should be aware of potential and actual constraints in the global market. In 2015, there were some constraints in the availability of important active pharmaceutical ingredients. This impacts the ability of formulators to manufacture and deliver finished products and must be factored into requested delivery times for new orders.

- Special consideration should be given to products that have a low demand, as in the case of many drugs used by adults or adolescents in second- or third-line ART and many paediatric ART regimens. Production of these medicines will be less frequent and many countries will require only low volumes, usually less than a full production batch. Pooled procurement at the national level and cooperation between countries and with suppliers may be appropriate in the case of these products. Buffer stocks may need to be higher to compensate for less regular deliveries and challenges in accurate forecasting of usage and uptake. Examples of such mechanisms include the Pan American Health Organization regional drug facility and the Paediatric ARV Procurement Working Group.
- Where procurement regulations allow, it is recommended that framework contracts be placed to allow for call-down orders. This maximizes the flexibility in delivery schedules, which can be adapted to actual consumption, and reduces the need for frequent repeat procurement and bidding exercises without compromising value for money.
- Several of the above actions will limit the risks of stock-outs as well as expired products (e.g. moving ARV drugs from low-volume treatment sites to high-volume treatment sites). However, when products expire, they should be destroyed according to the approaches and various disposal methods outlined in the WHO *Guidelines for safe disposal of unwanted pharmaceuticals in and after emergencies* (http://apps.who.int/iris/bitstream/10665/42238/1/WHO_EDM_PAR_99.2.pdf).

Use and monitoring

Robust information systems ensure the availability of accurate and timely consumption data on ARV drugs and diagnostics and other information required to effectively monitor the performance of the entire supply system and forecast the ARV drugs and diagnostics needed. Monitoring PSM through the effective use of early warning indicators prevents stock-outs and overstocks leading to expiry. Reliable capture and analysis of usage and consumption data from facilities will support a robust bottom-up approach to quantification and forecasting that will reflect changes in demand and support a flexible approach to the introduction of new recommendations in these guidelines.

6.13.3 Special considerations for adult and adolescent ART regimens

The preferred first-line ART regimen remains tenofovir (TDF) in combination with lamivudine and efavirenz, or TDF in combination with FTC and efavirenz (EFV), preferably as fixed-dose combinations (see section 4.4 “What to start: first-line ART”). Regimens containing nevirapine (NVP) are retained in the guidelines as an alternative option where clinically required for patients who cannot tolerate or have contraindications to TDF or EFV.

Key changes compared to 2013 are:

- dolutegravir (DTG) and EFV 400 mg/day are recommended as alternative first-line agents;
- darunavir/ritonavir (DRV/r) (as part of a heat-stable fixed-dose combination [FDC]) and DTG are recommended as alternative second-line options (see section 4.8.1 “Second-line ART for adults and adolescents”); and

- DTG and raltegravir (RAL) are recommended as potential third-line options (see section 4.8.3 “Third-line ART”).

Four key challenges for the supply chain arise as a result of the recommended ARV drug regimens.

- The currently approved suppliers of preferred first-line FDC formulations are expected to have sufficient production capacity to satisfy the increased demand for these formulations as the number of patients on treatment increases, provided that increases are carefully phased to avoid sudden spikes in demand. However, short-term supply constraints may arise, highlighting the need for proper planning and maintenance of buffer stocks at the national level.
- Delivery lead times for the recommended first-line drugs may become extended during peak periods of demand. PSM managers should be aware of current lead times and plan their orders and deliveries accordingly.
- Purchasers and implementing partners who are distributing zidovudine (AZT)-based and NVP-based regimens to patients and have stocks and orders in process should consider how to manage their stocks to avoid stock-outs or wastage due to expiry of usable products from overstocking.
- There may initially be limited demand for alternative first-line, second-line or third-line regimens, particularly those containing the newer medicines DTG, DRV/r and RAL. Pooling orders from several buyers is recommended to increase the volumes to be ordered and ensure that suppliers can deliver and adequately respond to the demand.

Transitioning to the recommended preferred regimens and preferred formulations

Programmes should plan carefully and discuss with their suppliers the pace at which increased quantities of TDF- and EFV-based products can be made available. This will require a graduated process of transition to the “test and offer” paradigm and for alternative scale-up targets. To ensure that supply is available to meet the anticipated demand, a phased programme is highly recommended. Suggested approaches are the following.

- Initiate new patients eligible for ART on TDF-based regimens, with preference for FDCs of TDF + 3TC + EFV or TDF + FTC + EFV.
- Include buffer stocks in supply plans and liaise closely with suppliers and the major pooled procurement mechanisms to understand global demand patterns and act accordingly.

Programmes should stop procuring the following:

- Stavudine (d4T): in light of the cumulative mitochondrial toxicity of d4T, it should no longer be procured, and people currently receiving d4T-based regimens should transition to a TDF-based regimen.
- Didanosine (ddI): ddI should no longer be procured as it is no longer recommended as an alternative nucleoside reverse-transcriptase inhibitor (NRTI) in adult and adolescent second-line regimens due to toxicity, lower efficacy and inconvenient dosing requirements.

People currently receiving first-line AZT- and/or NVP-based regimens should be transitioned to the preferred first-line FDCs in a phased manner to enable the use of current stocks and orders and taking into account the speed at which increased deliveries of TDF products can be ordered and delivered.

In areas with a high prevalence of HIV-2 infection, the procurement and use of formulations with two-drug FDCs (TDF with 3TC, TDF with FTC and AZT with 3TC) might be a preferred option, as this provides the flexibility to combine the NRTI backbone with protease inhibitors (PIs) or integrase strand transfer inhibitors (INSTIs) in first- and second-line therapy for people living with HIV-2 infection.

In the case of newer products such as DTG, DRV/r and RAL or existing products of low demand (e.g. for second- or third-line regimens), where feasible and practicable, procurement managers should consider pooling their demand with other domestic programmes, neighbouring countries or other regional programmes and/or collaborating with major purchasers to form a part of total orders that meet manufacturers' production batch sizes. Shelf-life, storage facilities and consumption patterns permitting, PSM managers should also plan to hold larger buffer stocks for essential products in low demand. In the case of newly introduced products, it should also be assumed that initial orders may require longer lead times.

Supply chain considerations for implementation of less frequent ARV drug refills, community ART delivery and lay providers distributing ARV drugs

There are several supply chain issues that programme managers and policy-makers need to consider when adopting and implementing new service delivery recommendations regarding less frequent ARV drug pickup, the use of community ART delivery models and lay providers distributing ARV drugs. PSM managers and policy-makers should examine the current ARV drug supply chain model and its performance to see what adaptations are needed to enable the supply chain to support these new recommendations. As no "one-size-fits-all" supply approach will meet the needs of differentiated care models, the local supply chain must be agile enough to serve a variety of service delivery models, including at the community level. In addition, programme managers should consider taking a phased approach that takes into account the following:

- the additional ARV drugs needed at pickup sites, including the provision of a safety buffer stock;
- the number of patients to be served by multi-month (3- to 6-month) prescribing and the regimens they currently use;
- the capacity of local distribution sites to safely and securely store and handle the additional ARV drugs;
- the additional reporting needed by the logistics information system to track the ARV drugs through these sites, including at community level;
- any ARV drug shelf-life constraints;
- overall supply chain performance where the recommendations will be implemented; and
- incorporation of additional ARV drug requirements in the country's annual quantification, financing, procurement and supply plans.

Besides the quantity of additional products required to implement new recommendations, the manufacturing lead time may influence the pace at which programmes can take new recommendations to national scale.

6.13.4 Special considerations for paediatric ART

These guidelines make no changes to the first-line paediatric ART regimen recommended in 2013 (see section 4.4.4 “First-line ART for children three to ten years of age” and section 4.4.5 “First-line ART for children younger than three years of age”). RAL is newly recommended in second-line paediatric ART for children younger or older than 3 years after failure of a first-line regimen containing LPV/r (see section 4.8.3 “Third-line ART”).

Transitioning to recommended preferred regimens and preferred formulations

In general, these guidelines recommend once-daily FDCs to facilitate procurement and supply chain management, logistics and adherence. Additional logistic and programme factors should be addressed for national programmes to select optimal formulations. To ensure smooth implementation of recommended first-line regimens for children, it is critical for policy-makers and implementers to consider the availability of paediatric ARV drug formulations.

National programmes are urged to limit the procurement of ARV drug products for children to formulations on the Optimal Paediatric Formulary of the IATT on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and their Children. Complying with the IATT Optimal Formulary based on WHO recommendations will help to simplify the supply chain and aggregate global demand to stabilize the global supply of ARV drugs for children.

Programmes should not procure the following paediatric formulations:

- Stavudine (d4T): d4T is no longer recommended due to its cumulative mitochondrial toxicity. Children currently receiving d4T-based regimens should transition to preferred paediatric ART regimens.
- Didanosine (ddI): ddI should no longer be procured as it is no longer recommended as an alternative NRTI in paediatric second-line regimens due to toxicity, lower efficacy and inconvenient dosing requirements.

When available, age-appropriate FDCs for any recommended regimen are preferable.

Dispersible tablets (also known as tablets for oral solution) are the preferred solid oral formulations.

Oral liquid formulations should be avoided in favour of solid oral dosage forms when available:

- FDCs of abacavir (ABC) + 3TC (60 mg + 30 mg and 120 mg + 60 mg) are available as dispersible scored tablets recommended as the preferred option in the Optimal Paediatric Formulary.
- Three formulations of lopinavir (LPV)/r are available for use among young children: LPV/r 100 mg/25 mg heat-stable tablet for children >10 kg who are able to swallow whole tablets; LPV/r pellets 40 mg/10 mg to be taken with soft food such as porridge

(newly available in 2015); and LPV/r oral liquid 80 mg/20 mg per 1 ml for use among infants. The IATT has produced a fact sheet on how to administer and use the new dosage form of oral pellet LPV/r 40 mg/10 mg (187).

In light of the continuing challenges of ensuring the availability of ARV drug formulations for children, the IATT provides guidance on optimal ARV drug products for children to promote a secure and sustainable supply. A new revision took place in December 2015 after these guidelines were finalized, and an updated version will be available at <http://www.emtct-iatt.org/resources>.

6.13.5 Checklist for introducing new products and phasing out old ones

These guidelines recommend new ARV drug formulations for adults and adolescents as well as for paediatric ART. Introduction of new medicinal or diagnostic products is one of the most complex and unpredictable activities in any HIV programme and, as such, presents a heightened challenge for policy-makers, PSM managers and manufacturers. When planning the introduction of new products, the following PSM-related factors should be taken into account.

- Is the product subject to patent or other intellectual property protection that would restrict access to generic formulations of the product in your country? In many middle-income countries, access to generic versions of ARV drugs is restricted. Should this be the case, advice is available from the Public Health, Innovation and Intellectual Property Team of the WHO Department of Essential Medicines and Health Products.
- Is the product registered for use in your country? If not, consider obtaining a temporary waiver and, in the meantime, accelerate the official registration processes for future procurement. This information should be available from the national drug regulatory authority. While it is the responsibility of the manufacturer to arrange registration, registering a drug can be a lengthy and expensive process.
- What is the forecasted demand for the product, including the anticipated pace of adoption? The pace of adoption is very difficult to forecast accurately, and ordering and delivery schedules must take into account this unpredictability. Faster adoption may lead to stock-outs if the procurement plan has not taken this into account, whereas a slower pace could lead to expiry of stocks if the procurement plan assumed a faster adoption. PSM managers will need to monitor consumption closely and have risk mitigation strategies in place. In case of faster adoption, suppliers should be asked to be prepared to respond to urgent orders. In case of slower adoption, suppliers should be asked to deliver quantities gradually according to country requests until all the quantities ordered are consumed. Ordering in large volumes has the advantage of economies of scale, but suppliers should be flexible enough to send deliveries according to national demand to prevent wastage by expiry. PSM managers are encouraged to work with HIV programme managers in formulating risk mitigation plans to account for the difficulty of accurate forecasting of demand and the pace of adoption.
- How will introduction of the new product impact the use of existing medicines or diagnostics? Unless it is recommended that a product be stopped due to severe toxicity or other reasons, PSM managers should always plan to optimize the use of existing stocks and orders before a full switchover to new products, in order to avoid wastage.

- How will purchase of the new product affect procurement budgets? PSM managers may wish to consult with major global purchasers to gauge the expected price so that quantities of existing and new products can be accommodated within the available budget. In some cases, lack of sufficient funds has delayed a full transition to new products that were more expensive or led to stock-outs of existing products.
- What is the shelf-life of the product and how might this affect the procurement strategy and the in-country distribution of the product? The “first expiry, first out” principle should be applied in stock management and distribution. Products with a shorter shelf-life should be distributed to treatment sites and dispensed as quickly as possible to allow their consumption before their expiry.
- Does the new product require any special handling or storage, such as temperature control? Consider adjusting the capacity and storage conditions of current facilities.
- What is the production status of the new product? What minimum order will the supplier accept and what is the anticipated lead time from order placement to delivery? In the case of products in lower demand, manufacturers may be willing to only commit to production once they are assured of commercially viable orders.
- If small volumes of new products are required, PSM managers should consider collaborating with neighbouring countries or global pooled procurement mechanisms to reach total order volumes that are viable for the manufacturers. This strategy may be particularly appropriate for second- and third-line formulations and for paediatric ARVs.
- Policy-makers and PSM managers may wish to consult with global purchasers and other knowledgeable entities to gain market intelligence on new formulations while they develop strategies to introduce these new formulations through national procurement.

6.13.6 Useful PSM resources

This document does not cover all technical issues related to PSM. The PSM Toolbox contains PSM tools that can be searched by technical area and by publishing organization: <http://psmtoolbox.org/en>.

6.14 Laboratory and diagnostic services

6.14.1 Overview

Implementing recommendations in these guidelines will require increased access to laboratory and diagnostic services.

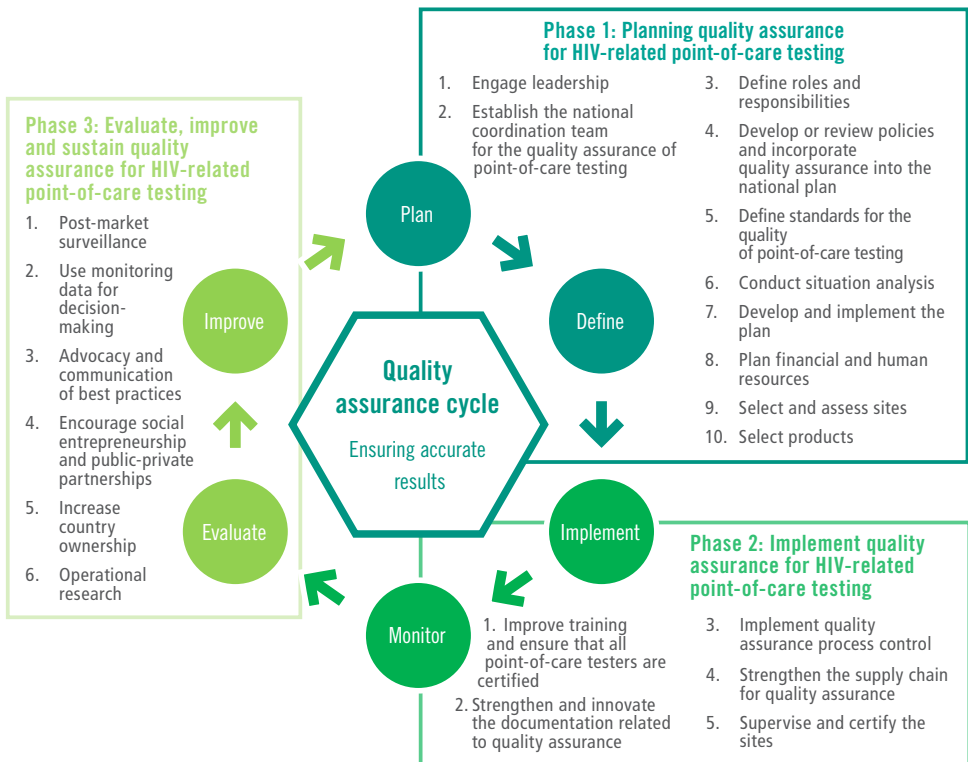
To ensure that diagnostic services are accurate and reliable, relevant QA systems need to be developed and strengthened. Within a country, a multiplicity of diagnostic settings may exist, such as laboratories, maternal and child health clinics, HIV testing and counselling sites and community-based testing. A multipronged and networked approach to selecting diagnostics and laboratory systems should therefore be planned and adopted. Because many new diagnostic tests and point-of-care systems are entering the market, the use of only high-quality diagnostics and equipment needs to be ensured. Strategic planning for proper placement and harmonization of testing platforms should be carried out to ensure appropriate use and cost-effectiveness.

Effective laboratory and diagnostic services require sound leadership and governance to enable the following activities (188):

- strengthening and expanding laboratory and diagnostic services;
- supporting a dedicated specimen referral system;
- appropriate availability of CD4 count testing;
- increased access to HIV viral load testing for all people on ART, for monitoring purposes;
- supporting the expansion of diagnostic services to include testing at the point of care;
- training and certifying health-care workers who perform testing;
- ensuring high-quality diagnostics and plans for implementing these, including QA; and
- ensuring appropriate deployment of diagnostic technologies to increase their efficient and optimal use.

WHO and the United States Centers for Disease Control and Prevention (CDC) have developed a handbook on QA approaches to point-of-care testing and for laboratories in low- and middle-income countries (191). Figure 6.4 shows the three-phase approach to QA of laboratory programmes.

Fig. 6.4. Three phases of laboratory quality assurance



Source: WHO, US CDC. Improving the quality of HIV-related point-of-care testing: ensuring the reliability and accuracy of test results. Geneva: World Health Organization; 2015 (<http://www.who.int/hiv/pub/toolkits/handbook-point-of-care-testing/en>).

6.14.2 Strengthening and expanding laboratory and diagnostic services

The following areas are important for strengthening the network of laboratory and diagnostic services in order to implement the recommendations in these guidelines:

- national laboratory strategic plans and policies;
- evaluating diagnostics for their performance and operational characteristics to validate testing algorithms (with backup options) before introduction;
- carrying out strategic planning in order to properly place and harmonize testing platforms to ensure appropriate use and cost-effectiveness;
- expanding current laboratory networks to support and monitor the decentralization and integration of testing services and to provide access to testing when diagnostic services are unavailable at service delivery sites;
- allocating appropriate resources to ensure the availability of testing services, including human and financial resources; and
- guidance on operations and service delivery.

6.14.3 Supporting a dedicated specimen referral system

Laboratory referral systems and procedures for collecting and processing specimens need to be strengthened to increase access to viral load and other testing (e.g. CD4 testing at the point of care and EID). Providing for and strengthening a dedicated, efficient, safe and cost-effective specimen referral system requires reliable specimen transport with adequate conditions for whole blood, plasma and dried blood spot specimens as well as for rapidly and dependably reporting test results back to the referring site with linkage to care. Rapid reporting of results is essential for timely care.

6.14.4 Increasing access to HIV viral load testing

These guidelines recommend the use of viral load testing to monitor treatment response and diagnose treatment failure and the use of dried blood spot samples for viral load testing. This will require ongoing strengthening of existing laboratory services and phased expansion of monitoring services in peripheral facilities. It may involve:

- strengthening and leveraging existing EID networks;
- ensuring that laboratories have adequate infrastructure, technical expertise and QA and QI programmes;
- ensuring an appropriate mix of high-volume centralized laboratory testing and testing at the point of care for facilities in remote locations; and
- use of dried blood spot specimens to increase access to viral load testing.

6.14.5 Planning for appropriate use of CD4 count testing as access to viral load testing increases

As countries move to eliminate CD4 count-dependent treatment initiation thresholds and viral load monitoring replaces monitoring with CD4 cell count, it is anticipated that the

demand for CD4 count testing will decrease. As this transition takes place, programme, laboratory and PSM staff should take into account the following programmatic considerations.

- As demand decreases, reductions in CD4 count testing capacity can be staged through several strategies based on site-level demand, age of the instrument and failure rates.
- Although sample referral networks for CD4 cell count and viral load testing may overlap, the sample types require different transport capabilities. Programmes need to ensure adequate network capability for sample referral for viral load testing prior to scaling down CD4 count testing.
- Programme planning should include a realistic transition of financial support from CD4 count testing to viral load monitoring. Cost savings may not be evident immediately, as the cost per test for CD4 count testing will increase as volumes decrease.
- Quantification and forecasting (active supply planning) will be essential to account for commodity shifts. This is particularly important in the early phases of the transition when historical data will not reflect current commodity needs. Supply chain needs, including cold-chain transport and storage, must also be considered during the transition.
- Even in settings with full access to viral load testing, CD4 cell count testing capability will continue to be needed as part of HIV programmes for baseline risk and other clinical assessments. Depending on the context, as the transition to viral load monitoring from CD4 count testing for initiation and monitoring progresses, programmes may wish to consider centralizing the continued use of CD4 count testing.

6.14.6 Expanding diagnostic services to point-of-care settings

Decentralizing laboratory and diagnostic services requires that all aspects of testing be in place before services are implemented. This includes:

- using only high-quality, evaluated and reliable diagnostic tests;
- supervising and monitoring point-of-care testing for quality and reliability;
- implementing a strategy for managing the supply chain and equipment service;
- establishing data management systems for timely identification of quality issues; and
- regional and national data reporting.

6.14.7 Ensuring appropriate deployment of diagnostic technologies

The WHO diagnostic use survey demonstrated that several technologies are available in the countries that reported their diagnostic usage. Their utilization is lower than 50% of their capacity for several reasons:

- Deployment of high-throughput instruments in low-volume settings with no appropriate plan for sample transportation: CDC and WHO have produced a strategic planning manual since the Maputo Declaration on Strengthening of Laboratory Systems to ensure that equipment is deployed in a tiered laboratory network based on the volume of tests at the testing sites (Table 6.3).

Table 6.3. Tiered laboratory network at various levels of the health-care delivery system

Health-care delivery level	Laboratory service	Quality assurance actions	Human resources
National reference laboratory	<ul style="list-style-type: none"> • Enzyme immunoassays for diagnosis • Higher throughput CD4 count testing • HIV molecular technologies, including HIV viral load testing and quantitative and qualitative early infant diagnosis • HIV resistance testing 	<ul style="list-style-type: none"> • Validating point-of-care testing • Training and certification • Coordinating quality assurance • Proficiency testing • Confirmatory testing • Collecting and analysing data • Taking corrective action 	<ul style="list-style-type: none"> • Senior laboratory specialists • Senior laboratory supervisors • Trainers • Senior technicians
Regional or provincial reference laboratory	<ul style="list-style-type: none"> • Enzyme immunoassays for diagnosis • Higher throughput CD4 count testing • HIV molecular technologies, including HIV viral load testing and quantitative and qualitative early infant diagnosis 	<ul style="list-style-type: none"> • Rapid diagnostic tests, point-of-care tests for CD4 count, early infant diagnosis and viral load • Coordinating regional training and quality assurance • Collecting and analysing data • Taking corrective action 	<ul style="list-style-type: none"> • Laboratory supervisors • Trainers • Senior technicians
District-level laboratory	<ul style="list-style-type: none"> • Enzyme immunoassays for diagnosis • Low-throughput CD4 count testing • Chemistry, haematology and microbiology 	<ul style="list-style-type: none"> • HIV rapid diagnostic tests, point-of-care tests for CD4 count testing, early infant diagnosis and viral load • Supervising sites • Corrective action 	<ul style="list-style-type: none"> • Laboratory technicians • Laboratory assistants
Primary care setting	<ul style="list-style-type: none"> • HIV rapid diagnostic tests and other point-of-care tests • Collecting dried blood spots 	<ul style="list-style-type: none"> • HIV rapid diagnostic tests, point-of-care tests for CD4 count testing • Collecting dried blood spots for point-of-care tests and early infant diagnosis 	<ul style="list-style-type: none"> • First-level trained health workers such as nurses and clinical officers
Community-based and community outreach	<ul style="list-style-type: none"> • HIV rapid diagnostic tests • Collecting finger-prick samples for testing 	<ul style="list-style-type: none"> • HIV rapid diagnostic tests 	<ul style="list-style-type: none"> • Community health workers

Source: WHO expert meeting report on short, medium, longer term product development priorities for HIV-related diagnostics, 6–7 June 2012, Geneva, Switzerland (http://www.who.int/hiv/pub/meetingreports/hiv_diagnostics/en) and Handbook for improving the quality of HIV-related point-of-care testing: ensuring the reliability and accuracy of test results, 2015 (<http://www.who.int/hiv/pub/toolkits/handbook-point-of-care-testing/en>).

- Frequent stock-out of reagents: WHO has developed a manual for efficient procurement of essential equipment and laboratory commodities to support national programme managers when they are estimating their procurement (http://apps.who.int/iris/bitstream/10665/180980/1/9789241509183_eng.pdf?ua=1).
- Lack of maintenance and repair needs: maintenance should be embedded in the contractual agreement with the manufacturers supplying diagnostics.
- Lack of installation of purchased equipment due to lack of trained personnel or adequate space for the size of the equipment: prior strategic planning is essential to ensure that appropriate space and a trained laboratory technician are ready when the procured equipment is delivered for use in the country.

References

- 1 Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. *PLoS Med*. 2011;8(7):e1001056.
- 2 Mugglin C, Estill J, Wandeler G, Bender N, Egger M, Gsponer T et al. Loss to programme between HIV diagnosis and initiation of antiretroviral therapy in sub-Saharan Africa: systematic review and meta-analysis. *Trop Med Int Health*. 2012;17(12):1509–20.
- 3 IeDEA-WHO Collaboration. Global analysis of retention in care in initial HIV care and treatment programmes in the IeDEA regions. 2015.
- 4 Fast-Track – ending the AIDS epidemic by 2030. Geneva: UNAIDS; 2014 (http://www.unaids.org/en/resources/documents/2014/JC2686_WAD2014report, accessed 1 November 2015).
- 5 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(4):430–47.
- 6 Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. Geneva: World Health Organization; 2015 (<http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/>, accessed 10 December 2015).
- 7 Braitstein P, Brinkhof MW, Dabis F, Scheter M, Boule A, Miotti A, Miotti P et al. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *Lancet*. 2006;367(9513):817–24.
- 8 Scoping consultation on care packages for people living with HIV. Meeting report, 24–26 September 2014. Geneva: World Health Organization (<http://www.who.int/hiv/pub/arv/consultation-carepackages-plhiv/en/>, accessed 1 November 2015).
- 9 March 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bitstream/10665/104264/1/9789241506830_eng.pdf?ua=1, accessed 15 October 2015).
- 10 Bemelmans M, Baert A, Goemaere E, Wilkinson L, Vanendyck M, van Cutsem G et al. Community-supported models of care for people on HIV treatment in sub-Saharan Africa. *Trop Med Int Health*. 2014;19 (8):968–77.
- 11 Kranzer K, Govindasamy D, Ford N, Johnston V, Lawn SD. Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic review. *J Int AIDS Soc*. 2012;15:17383.
- 12 Boule A, Zinyakтира N, Evans J, Osler M, Coetzee D, Groenewald P et al. Understanding high ongoing HIV-associated mortality in the era of antiretroviral therapy in the Western Cape Province of South Africa. In: 20th IEA World Congress of Epidemiology. Anchorage, Alaska, 17–21 August 2014 (<https://wce.confex.com/wce/2014/webprogram/Paper2516.html>, accessed 11 February 2016).
- 13 The HIV modelling consortium. Priorities for HIV care in Sub-Saharan Africa: A population perspective 2015. (http://www.hivmodelling.org/sites/default/files/uploads/documents/meeting-reports/WSI%20HIVMC%20GRC%20report_2015-09-29.pdf, accessed 15 February 2016).

- 14 Slaymaker E, Zaba B, Mclean E, Hosegood V, Nakiyingi-Miiri J, Crampin M et al. Scale and distribution of excess deaths among HIV positive adults by diagnosis, care and treatment history in African population based cohorts 2007–2011. In: 20th International AIDS Conference, Melbourne, Australia, 20–25 July 2014. [Abstract MOPE120].
- 15 Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: a systematic review. *AIDS*. 2012;26(16):2059–67.
- 16 Fox M, Rosen S. Systematic review of interventions to facilitate linkage to care to support development of the WHO 2015 Consolidated guidelines for the use of antiretroviral drugs for treating and preventing HIV infection, Boston University, 2015. Web Supplement B.
- 17 Consolidated guidelines on HIV testing services: 5Cs: consent, confidentiality, counselling, correct results and connection. Geneva: World Health Organization; 2015 (http://apps.who.int/iris/bitstream/10665/179870/1/9789241508926_eng.pdf?ua=1&ua=1, accessed 31 October 2015).
- 18 Best J, Tso L, Bin Y, Tucker J, Lackey M. Barriers and facilitators to interventions improving linkage to care: a meta-synthesis of qualitative research studies, 2015. Protocol (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017252, accessed 15 February 2016).
- 19 leDea and ART Cohort Collaborations, Avila D, Althoff KN, Mugglin C, Woos-Kaloustian K, Koller M et al. Immunodeficiency at the start of combination antiretroviral therapy in low-, middle-, and high-income countries. *J Acquir Immune Defic Syndr*. 2014;65(1):e8–16.
- 20 Davies MA, Phiri S, Wood R, Wellington M, Cox V, Bolton-Moore C et al. Temporal trends in the characteristics of children at antiretroviral therapy initiation in southern Africa: the leDEA-SA Collaboration. *PLoS One*. 2013;8(12):e81037.
- 21 Siedner MJ, Ng CK, Bassett IV, Katz IT, Bangsberg Dr, Tsai AC. Trends in CD4 count at presentation to care and treatment initiation in sub-Saharan Africa, 2002–2013: a meta-analysis. *Clin Infect Dis*. 2015;60(7):1120–7.
- 22 Wynberg E, Cooke G, Shroufi A, Reid SD, Ford N. Impact of point-of-care CD4 testing on linkage to HIV care: a systematic review. *J Int AIDS Soc*. 2014;17:18809.
- 23 Vojnov L, Markby J, Boeke C, Harris L, Ford N, Peter T. POC CD4 testing improves linkage to HIV care and timeliness of ART initiation in a public health approach: a systematic review and meta-analysis. *PLoS One*. 2016;11:e0155256.
- 24 Hyle E, Jani I, Lehe J, Su A, Wood R, Quevedo J et al. The clinical and economic impact of point-of-care CD4 testing in Mozambique and other resource-limited settings: a cost-effectiveness analysis. *PLoS Med*. 2014;11(9):e1001725. doi: 10.1371/journal.pmed.1001725 .
- 25 Larson B, Schnippel K, Ndibongo B, Long L, Fox MP, Rosen D. How to estimate the cost of point-of-care CD4 testing in program settings: an example using the Alere Pima™ analyzer in South Africa. *PLoS One*. 2012;7(4):e35444. doi: 10.1371/journal.pone.0035444.
- 26 Gous N, Scott L, Potgieter J, Ntabeni L, Enslin S, Newman R et al. Feasibility of performing multiple point of care testing for HIV anti-retroviral treatment initiation and monitoring from multiple or single fingersticks. *PLoS One*. 2013;8(12):e85265.
- 27 Herbert S, Edwards S, Carrick G, Copas A, Sandford C, Amphlett M et al. Evaluation of PIMA point-of-care CD4 testing in a large UK HIV service. *Sex Transm Infect*. 2012;88:413–417.
- 28 Pinto IC, Sabidó M, Pereira AB, Mello MB, de Melo Xavier Shimizu A, Protti BL et al. Field evaluation of a point-of-care CD4 analyzer for monitoring HIV patients in the interior of the Amazon Region, Brazil. *PLoS One*. 2015;10(4):e0121400.
- 29 Ford N, Meintjes G, Pozniak A, Bygrave H, Hill A, Peter T et al. The future role of CD4 cell count for monitoring antiretroviral therapy. *Lancet Infect Dis*. 2015;15(2):241–7.
- 30 Vojnov L, Clinton Health Access Initiative. In HIV-exposed infants less than 18 months, is returning EID results by SMS/GPRS printer more effective than routine result retrieval? 2015. Web Supplement B.
- 31 Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med*. 2008;359(21):2233–44.
- 32 International Community of Women Living with HIV (ICW), Global Network of People Living with HIV (GNP+). Early infant diagnosis: understanding the perceptions, values and preferences of women living with HIV in Kenya, Namibia and Nigeria. 2015 (http://www.gnpplus.net/assets/wbb_file_updown/4894/ICW%20GNP+Early%20Infant%20Diagnosis-%20Perspectives%20of%20Women%20Living%20with%20HIV.pdf, accessed 20 January 2016).

- 33 Fox MP, Rosen S Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007–2009: a systematic review. *Trop Med Int Health*. 2010;15(s1):1–15.
- 34 Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. *PLoS Med*. 2011;8(7):e1001056.
- 35 Penn A, Azman H, Horvath A, Taylor K, Hickey M, Rajan J et al. Interventions for improving retention in antiretroviral therapy (ART) programs for people with HIV infection in resource-limited settings: a systematic review. Protocol. (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017017, accessed 16 February 2016)..
- 36 Grimwood A, Fatti G, Mothibi E, Malahlela M, Shea J, Eley B. Community adherence support improves programme retention in children on antiretroviral treatment: a multicentre cohort study in South Africa. *J Int AIDS Soc*. 2012;15:17381.
- 37 Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (<http://www.who.int/hiv/pub/guidelines/arv2013/en/>, accessed 1 November 2015).
- 38 Luque-Fernandez MA, Van Cutsem G, Goemaere E, Hilderbrand K, Schomaker M, Mantangana N et al. Effectiveness of patient adherence groups as a model of care for stable patients on antiretroviral therapy in Khayelitsha, Cape Town, South Africa. *PLoS One*. 2013;8:e56088.
- 39 Braitstein P, Siika A, Hogan J, Kosgei R, Sang E, Sidle J et al. A clinician-nurse model to reduce early mortality and increase clinic retention among high-risk HIV-infected patients initiating combination antiretroviral treatment. *J Int AIDS Soc*. 2012;15:7.
- 40 Hall BJ, Sou KL, Tucker JD, Beanland RL. Barriers and facilitators to interventions improving HIV retention in care: a qualitative evidence review. 2015. Protocol (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017328, accessed 15 February 2016).
- 41 Geldsetzer P, Bärnighausen T. Systematic review of interventions to improve retention of women in HIV care during the postpartum period. Harvard School of Public Health. 2015. Web Supplement B.
- 42 Catalani C, Philbrick W, Fraser H, Mechael P, Israelski DM. mHealth for HIV treatment and prevention: a systematic review of the literature. *Open AIDS J*. 2013;7:17–41.
- 43 Guideline on HIV disclosure counselling for children up to 12 years of age. Geneva: World Health Organization; 2011 (http://www.who.int/hiv/pub/hiv_disclosure/en/, accessed 1 November 2015).
- 44 Beckham S, Baral S, Negussie E, Doherty M, Beyrer C. Differential HIV treatment outcomes by gender: a systematic review & meta-analysis of mortality. 2015 Web Supplement B.
- 45 Bangsberg DR, Perry S, Charlebois ED, Clark RA, Robertson M, Zolopa AR et al. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS*. 2001;15(9):1181–3.
- 46 Nachega JB, Hislop M, Dowdy DW, Chaisoon RE, Regensberg L, Maartens G. Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes. *Ann Intern Med*. 2007;146(8):564–73.
- 47 Wood E, Hogg RS, Yip B, Harrigan PR, O'Shaughnessy MV, Montaner JS. Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when the CD4⁺ cell count is 0.200 to 0.350 × 10⁹ cells/L. *Ann Intern Med*. 2003;139(10):810–16.
- 48 Mills EJ, Nachega JB, Bangsberg DR, Singh S, Rachlis B, Wu P et al. Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS Med*. 2006;3(11):e438.
- 49 Martin S, Elliott-DeSorbo DK, Wolters PL, Toledo-Tamula MA, Roby G, Zeichner S et al. Patient, caregiver and regimen characteristics associated with adherence to highly active antiretroviral therapy among HIV-infected children and adolescents. *Pediatr Infect Dis J*. 2007;26(1):61–7.
- 50 Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. *AIDS*. 2012;26(16):2039–52.
- 51 Colvin CJ, Konopka S, Chalker JC, Jonas E, Albertini J, Amzel A et al. A systematic review of health system barriers and enablers for antiretroviral therapy (ART) for HIV-infected pregnant and postpartum women. *PLoS One*. 2014;9(10): e108150.
- 52 Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J et al. A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women. *PLoS One*. 2014;9(11):e111421.

- 53 Kim SH, Gerber SM, Fidler S, Ward H. Adherence to antiretroviral therapy in adolescents living with HIV: systematic review and meta-analysis. *AIDS*. 2014;28(13):1945–56.
- 54 Murphy DA, Sarr M, Durako SJ, Moscicki AB, Wilson CM, Muenz LR et al. Barriers to HAART adherence among human immunodeficiency virus-infected adolescents. *Arch Pediatr Adolesc Med*. 2003;157(3):249–55.
- 55 Lowenthal ED, Bakeera-Kitaka S, Marukutira T, Chapman J, Goldrath K, Ferrand RA. Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: a review of emerging challenges. *Lancet Infect Dis*. 2014;14(7):627–39.
- 56 Hussien SA, Chahroudi A, Boylan A, Camacho-Gonzalez AF, Hackett S, Chakraborty R. Transition of youth living with HIV from pediatric to adult-oriented healthcare: a review of the literature. *Future Virol*. 2015;9(10):921–9.
- 57 Fetzer BC, Mupenda B, Lusiana J, Kitetele F, Golin C, Behets F. Barriers to and facilitators of adherence to pediatric antiretroviral therapy in a sub-Saharan setting: insights from a qualitative study. *AIDS Patient Care STDs*. 2011;25(10):611–21.
- 58 Ivanovska V, Rademaker CM, van Dijk L, Mantel-Teeuwisse AK. Pediatric drug formulations: a review of challenges and progress. *Pediatrics*. 2014;134(2):361–72.
- 59 Bagenda A, Barlow-Mosha L, Bagenda D, Sakwa R, Fowler MG, Musoke PM. Adherence to tablet and liquid formulations of antiretroviral medication for paediatric HIV treatment at an urban clinic in Uganda. *Ann Trop Paediatr*. 2011;31(3):235–45.
- 60 Uthman OA, Magidson JF, Safren SA, Nachega JB. Depression and adherence to antiretroviral therapy in low-, middle- and high-income countries: a systematic review and meta-analysis. *Curr HIV/AIDS Rep*. 2014;11(3):291–307.
- 61 Gonzalez JS, Batchelder AW, Psaros C, Safren SA. Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. *J Acquir Immune Defic Syndr*. 2011;58(2):181–7.
- 62 Nakimuli-Mpungu E, Bass JK, Alexandre P, Mills EJ, Musisi S, Ram M et al. Depression, alcohol use and adherence to antiretroviral therapy in sub-Saharan Africa: a systematic review. *AIDS Behav*. 2012;16(8):2101–18.
- 63 O'Neil CR, Palmer AK, Coulter S, O'Brien N, Shen A, Zhang W et al. Factors associated with antiretroviral medication adherence among HIV-positive adults accessing highly active antiretroviral therapy (HAART) in British Columbia, Canada. *J Int Assoc Physicians AIDS Care (Chic)*. 2012;11(2):134–41.
- 64 Pyne JM, Fortney JC, Curran GM, Tripathi S, Akinson JH, Kilbourne AM et al. Effectiveness of collaborative care for depression in human immunodeficiency virus clinics. *Arch Intern Med*. 2011;171(1):23–31.
- 65 Lucas GM, Mullen BA, Weidle PJ, Hader S, McCaul ME, Moore RD. Directly administered antiretroviral therapy in methadone clinics is associated with improved HIV treatment outcomes, compared with outcomes among concurrent comparison groups. *Clin Infect Dis*. 2006;42(11):1628–35.
- 66 Mountain E, Mishra S, Vickerman P, Pickles M, Gilks C, Boily MC. Antiretroviral therapy uptake, attrition, adherence and outcomes among HIV-infected female sex workers: a systematic review and meta-analysis. *PLoS One*. 2014;9(9):e105645.
- 67 Graham SM, Mugo P, Gichuru E, Thiong'o A, Macharia M, Okuku HS et al. Adherence to antiretroviral therapy and clinical outcomes among young adults reporting high-risk sexual behavior, including men who have sex with men, in coastal Kenya. *AIDS Behav*. 2013;17(4):1255–65.
- 68 Mills E, Kanters S, Socias ME, Global Evaluation Services. Systematic literature review report: which interventions enhance adherence to ART for people living with HIV? 2015. Web Supplement B.
- 69 Cantrell RA, Sinkala M, Megazinni K, Lawson-Marriott S, Washington S, Chi BH et al. A pilot study of food supplementation to improve adherence to antiretroviral therapy among food-insecure adults in Lusaka, Zambia. *J Acquir Immune Defic Syndr*. 2008;49(2):190–5.
- 70 Munoz M, Finnegan K, Zeladita J, Caldas A, Sanchez E, Callacna M et al. Community-based DOT-HAART accompaniment in an urban resource-poor setting. *AIDS Behav*. 2010;14(3):721–30.
- 71 Qingyan M, Rich Z, Haochu L, Fengyu H, Weiping C, Lackey M et al. ARV Interventions improving ARV adherence: a systematic review of global qualitative evidence. 2015 Web Supplement C.

- 72 Pangaea Global AIDS Foundation. Preliminary report of the community led consultation for WHO 2015 Consolidated treatment guidelines update. Acceptability of early initiation of antiretroviral therapy (ART) and viral load monitoring: values and preferences of service users and providers 2015 2015. (http://apps.who.int/iris/bitstream/10665/189977/1/WHO_HIV_2015.36_eng.pdf?ua=1, accessed 15 February 2016).
- 73 Bonner K, Mezocho A, Roberts T, Ford N, Cohn J. Viral load monitoring as a tool to reinforce adherence: a systematic review. *J Acquir Immune Defic Syndr*. 2013;64(1):74–8.
- 74 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.
- 75 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(4):612–18.
- 76 Sangeda RZ, Mosha F, Prosperi M, Aboud S, Vercauteren J, Camacho RJ et al. Pharmacy refill adherence outperforms self-reported methods in predicting HIV therapy outcome in resource-limited settings. *BMC Public Health*. 2014;14:1035.
- 77 Kagee A, Nel A. Assessing the association between self-report items for HIV pill adherence and biological measures. *AIDS Care*. 2012;24(11): 1448–52.
- 78 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(5):366–75.
- 79 ART-LINC Collaboration of International Databases to Evaluate AIDS (IeDEA) Keiser O, Anastos K, Schecter M, Balestere E, Myer L et al. Antiretroviral therapy in resource-limited settings 1996 to 2006: patient characteristics, treatment regimens and monitoring in sub-Saharan Africa, Asia and Latin America. *Trop Med Int Health*. 2008;13(7):870–9.
- 80 Scaling up antiretroviral therapy in resource-limited settings. Guidelines for a public health approach. Geneva: World Health Organization; 2002 (http://www.who.int/hiv/pub/prev_care/en/ScalingUp_E.pdf, accessed 1 November 2015).
- 81 Johnson LF, Mossong J, Dorrington RE, Schomaker M, Hoffmann CJ, Keiser O et al. Life expectancies of South African adults starting antiretroviral treatment: collaborative analysis of cohort studies. *PLoS Med*. 2013;10(4):e1001418.
- 82 Mills EJ, Bakanda C, Birungi J, Chan K, Ford N, Cooper CL et al. Life expectancy of persons receiving combination antiretroviral therapy in low-income countries: a cohort analysis from Uganda. *Ann Intern Med*. 2011;155(4): 209–16.
- 83 Nsanzimana S, Remera E, Kanters S, Chan K, Forrest JI, Ford N et al. Life expectancy among HIV-positive patients in Rwanda: a retrospective observational cohort study. *Lancet Glob Health*. 2015;3(3):e169–77.
- 84 Mills EJ, Nachega JB, Bangsberg DR, Singh S, Rachlis B, Wu P et al. Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS Med*. 2006;3(11):e438.
- 85 Koole O, Tsui S, Wabwire-Mangen F, Kwasigabo G, Menten J, Mulenga M et al. Retention and risk factors for attrition among adults in antiretroviral treatment programmes in Tanzania, Uganda and Zambia. *Trop Med Int Health*. 2014;19(12):1397–410.
- 86 Bemelmans M, Baert S, Goemaere E, Wilkinson L, Vandendyck M, van Cutsem G et al. Community-supported models of care for people on HIV treatment in sub-Saharan Africa. *Trop Med Int Health*. 2014;19(8):968–77.
- 87 Apollo T, Ford N, Socias E, Wiens M, Mills E, Kanters S. Effect of frequency of clinic visits and medication pick-up antiretroviral therapy outcomes: a systematic review and meta-analysis. In: 18th International Conference on AIDS and STIs in Africa. Harare, Zimbabwe, 29 November–04 December 2015. [Abstract THUAE0804].
- 88 Kredo T, Adeniyi FB, Bateganya M, Pienaar ED. Task shifting from doctors to non-doctors for initiation and maintenance of antiretroviral therapy. *Cochrane Database Syst Rev*. 2014;(7):CD007331.

- 89 The world of medicines situation 2011: pharmaceutical human resources. Geneva: World Health Organization; 2012 (<http://apps.who.int/medicinedocs/en/m/abstract/Js20054en/>, accessed 1 November 2015).
- 90 FIP Global Pharmacy: workforce report 2012. The Hague, Netherlands: FIP; 2012 (http://www.fip.org/files/members/library/FIP_workforce_Report_2012.pdf, accessed 11 February 2016).
- 91 Pharmaceutical human resources assessment tools. World Health Organization: Geneva; 2011 (<http://apps.who.int/medicinedocs/en/cl/CL5.23.35/clmd,50.html>, accessed 1 November 2015).
- 92 Koole O, Tsui S, Wabwire-Mangen F, Kwasigabo G, Menten J, Mulenga M et al. Retention and risk factors for attrition among adults in antiretroviral treatment programmes in Tanzania, Uganda and Zambia. *Trop Med Int Health*. 2014;19(12):1397–410. doi: 10.1111/tmi.12386
- 93 Mbeye NM, Adetokunboh O, Negussie E, Kreda T, Wiysonge CS. The effects of shifting responsibility from pharmacy to non-pharmacy personnel for dispensing antiretroviral medications to patients infected with HIV: a systematic review and meta-analysis. *South African Cochrane*. 2015. Web Supplement B. Protocol. (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017034, accessed 15 February 2016).
- 94 Selke HM, Kimaiyo S, Sidle JE, Vedantahn R, Teirney 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(4):483–90.
- 95 Jaffar S, Amuron B, Foster S, Birungi J, Levin J, Namara G et al. Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial. *Lancet*. 2009;374(9707):2080–9.
- 96 Harries AD, Zachariah R, Lawn SD, Rosen S. Strategies to improve patient retention on antiretroviral therapy in sub-Saharan Africa. *Trop Med Int Health*. 2010;15 (Suppl 1):70–5.
- 97 Task shifting: global recommendations and guidelines. Geneva: World Health Organization; 2008 (<http://www.who.int/healthsystems/TTR-TaskShifting.pdf>, accessed 1 November 2015).
- 98 Vojnov L, Clinton Health Access Initiative. Does specimen collection and performing diagnostic tests by non-lab professionals, including lay providers, compared to laboratory professionals have comparable patient and programme outcomes? 2015. Web Supplement B.
- 99 WHO recommendations for clinical mentoring to support scale-up of HIV care, antiretroviral therapy and prevention in resource-constrained settings. Geneva: World Health Organization; 2006 (<http://www.who.int/hiv/pub/guidelines/clinicalmentoring.pdf>, accessed 1 November 2015).
- 100 Kreda T, Ford N, Adeniyi FB, Garner P. Decentralising HIV treatment in lower- and middle- income countries. *Cochrane Database Syst. Rev.* 2013;(6):CD009987. doi: 10.1002/14651858.CD009987.pub2.
- 101 Duff P, Kipp W, Wild TC, Rubaale T, Okech-Ojony J. Barriers to accessing highly active antiretroviral therapy by HIV-positive women attending an antenatal clinic in a regional hospital in western Uganda. *J Int AIDS Soc*. 2010;13:37.
- 102 Mucedzi A, Chandisarewa W, Keatinge J, Stranix-Chibanda L, Woelk G, Mbizvo E et al. Factors associated with access to HIV care and treatment in a prevention of mother to child transmission programme in urban Zimbabwe. *J Int AIDS Soc*. 2010;13:38.
- 103 Killam WP, Tambatamba BC, Chintu N, Rouse D, Stringer E, Bweupe M et al. Antiretroviral therapy in antenatal care to increase treatment initiation in HIV-infected pregnant women: a stepped-wedge evaluation. *AIDS*. 2010;24(1):85–91.
- 104 Ong'ech JO, Hoffman HJ, Kose J, Audo M, Matu L, Savosnick P et al. Provision of services and care for HIV-exposed infants: a comparison of maternal and child health clinic and HIV comprehensive care clinic models. *J Acquir Immune Defic Syndr*. 2012;61(1):83–9.
- 105 Turan JM, Steinfeld RI, Onono M, Bukusi EA, Woods M, Shade SB et al. The study of HIV and antenatal care integration in pregnancy in Kenya: design, methods, and baseline results of a cluster-randomized controlled trial. *PLoS One*. 2012;7(9):e44181.
- 106 Vo Bn, Cohen CR, Smith RM, Bukusi ES, Onono MA, Scharwtz K et al. Patient satisfaction with integrated HIV and antenatal care services in rural Kenya. *AIDS Care*. 2012;24(11):1442–7.
- 107 Tsague L, Tsiouris FO, Carter RJ, Mugisha V, Tene G, Nyankesha E et al. Comparing two service delivery models for the prevention of mother-to-child transmission (PMTCT) of HIV during transition from single-dose nevirapine to multi-drug antiretroviral regimens. *BMC Public Health*. 2010;10:753.

- 108 Winestone LE, Bukusi EA, Cohen CB, Kwaro D, Schmidt NC, Turan JM. Acceptability and feasibility of integration of HIV care services into antenatal clinics in rural Kenya: a qualitative provider interview study. *Glob Public Health*. 2012;7(2):149–63.
- 109 Global tuberculosis report 2015, 20th edition. Geneva: World Health Organization; 2015 (http://www.who.int/tb/publications/global_report/en/, accessed 19 January 2016).
- 110 Integration of HIV and TB services. Web annex. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: World Health Organization; 2013 (http://apps.who.int/iris/bitstream/10665/94591/1/WHO_HIV_2013.82_eng.pdf?ua=1, accessed 1 November 2015).
- 111 Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. Geneva: World Health Organization; 2009 (http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf, accessed 1 November 2015).
- 112 Achmad YM, Istiqomah AN, Iskandar S, Wisaksana R, van Crevel R, Hidayat T. Integration of methadone maintenance treatment and HIV care for injecting drug users: a cohort study in Bandung, Indonesia. *Acta Med Indones*. 2009;41(Suppl 1):23–7.
- 113 Lucas GM, Chaudhry A, Hsu J, Woodson T, Lau B, Olsen Y et al. Clinic-based treatment of opioid-dependent HIV-infected patients versus referral to an opioid treatment program: a randomized trial. *Ann Intern Med*. 2010;152(11):704–11.
- 114 Zaller N, Gillani FS, Rich JD. A model of integrated primary care for HIV-positive patients with underlying substance use and mental illness. *AIDS Care*. 2007;19(9):1128–33.
- 115 Rochat TJ, Richter LM, Doll HA, Buthelezi NP, Tomkins A, Stein A. Depression among pregnant rural South African women undergoing HIV testing. *JAMA*. 2006;295(12):1376–8.
- 116 Suryavanshi N, Erande A, Pisal H, Shankar AV, Bhosale RA, Bollinger RC et al. Repeated pregnancy among women with known HIV status in Pune, India. *AIDS Care*. 2008;20(9):1111–18.
- 117 Schwartz SR, Mehta SH, Taha TE, Rees HV, Venter F, Black V. High pregnancy intentions and missed opportunities for patient–provider communication about fertility in a South African cohort of HIV-positive women on antiretroviral therapy. *AIDS Behav*. 2012;16(1):69–78.
- 118 Wanyenze RK, Tumwesigye NM, Kindyomunda R, Beyeza-Kashesya J, Atuyambe L, Kansiime A et al. Uptake of family planning methods and unplanned pregnancies among HIV-infected individuals: a cross-sectional survey among clients at HIV clinics in Uganda. *J Int AIDS Soc*. 2011;14:35.
- 119 Jhangri GS, Heys J, Alibhai A, Rubaale T, Kipp W. Unmet need for effective family planning in HIV-infected individuals: results from a survey in rural Uganda. *J Fam Plann Reprod Health Care*. 2012;38(1):23–9.
- 120 Petruney T, Minichiello SN, McDowell M, Wilcher R. Meeting the contraceptive needs of key populations affected by HIV in Asia: an unfinished agenda. *AIDS Res Treat*. 2012;2012:792649.
- 121 C Horwood, L M Butler, L Haskins, Phakathi S, Rollins N. HIV-infected adolescent mothers and their infants: low coverage of HIV services and high risk of HIV transmission in KwaZulu-Natal, South Africa. *PLoS One*. 2013;8(9):e74568
- 122 Horvath H. Integration of family planning or sexually-transmitted infection prevention & care services in antiretroviral therapy clinics. University of California, San Francisco. Web Supplement B.
- 123 Grossman D, Onono M, Newmann SJ, Blat C, Bukusi EA, Shade SB et al. Integration of family planning services into HIV care and treatment in Kenya: a cluster-randomized trial. *AIDS*. 2013;27(Suppl 1):S77–85.
- 124 Shade SB, Kevany S, Onono M, Ochieng G, Steinfeld RL, Grossman D et al. Cost, cost-efficiency and cost-effectiveness of integrated family planning and HIV services. *AIDS*. 2013;27(Suppl 1):S87–92.
- 125 Sweeney S, Obure CD, Maier CB, Greener R, Dehne K, Vassall A. Costs and efficiency of integrating HIV/AIDS services with other health services: a systematic review of evidence and experience. *Sex Transm Infect*. 2012;88(2):85–99.
- 126 Dudley L, Garner P. Strategies for integrating primary health services in low- and middle-income countries at the point of delivery. *Cochrane Database Syst Rev*. 2011;(7):CD003318.
- 127 Adamchak SE, Grey TE, Otterness C, Katz K, Janowitz B. Introducing family planning services into antiretroviral program in Ghana: an evaluation of a pilot intervention. *Family Health International*; 2007 (<http://www.popline.org/node/199913>, accessed 1 November 2015).

- 128 Asiimwe D, Kibombo R, Matsiko J, Hardee K. Study of the integration of family planning and VCT/ PMTCT/ART programs in Uganda. USAID; 2005 (<http://www.policyproject.com/pubs/corepackages/uganda%20TOO%20Final%2012%2020%2005.pdf>, accessed 1 November 2015).
- 129 GNPLWA, The Network of Zambian People Living with HIV/AIDS, UK aid. Positive health, dignity and prevention in Zambia. 2013 (http://www.gnplplus.net/assets/PHDP_Zambia-copy.pdf, accessed 1 November 2015).
- 130 Harrington EK, Newmann SJ, Onono M, Schwartz KD, Bukusi EA, Cohen CR et al. Fertility intentions and interest in integrated family planning services among women living with HIV in Nyanza Province, Kenya: a qualitative study. *Infect Dis Obstet Gynecol.* 2012;2012:809682.
- 131 Integration Initiatives. Making sense of complexity: key findings from the Integra Initiative [newsletter]. 2013 (<http://www.integrainitiative.org/blog/wp-content/uploads/2013/08/IntegraNewsletterIssue6-1.pdf>, accessed 1 November 2015).
- 132 International HIV/AIDS Alliance. Visions, voices, and priorities of young people. 2013 (http://www.aidsalliance.org/assets/000/001/588/LinkUpVVP_original.pdf?1424964366, accessed 1 November 2015).
- 133 Newmann SJ, Grossman D, Blat C, Onono M, Steinfeld R, Bukusi EA et al. Does integrating family planning into HIV care and treatment impact intention to use contraception? Patient perspectives from HIV-infected individuals in Nyanza Province, Kenya. *Int J Gynaecol Obstet.* 2013;123(Suppl 1):e16–23.
- 134 Patel R, Baum S, Grossman D, Steinfeld R, Onono M, Cohen C et al. HIV-positive men's experiences with integrated family planning and HIV services in western Kenya: integration fosters male involvement. *AIDS Patient Care STDs.* 2014;28(8):418–24.
- 135 Steinfeld RL, Newmann SJ, Onono M, Cohen C, Bukusi EA, Grossman D. Overcoming barriers to family planning through integration: perspectives of HIV-positive men in Nyanza Province, Kenya. *AIDS Res Treat.* 2013;2013:861983.
- 136 The ACQUIRE PROJECT. Searing H, Farrell B, Gutin S, Johri N, Subramanian L et al. Evaluation of a family planning and antiretroviral therapy integration pilot in Mbale, Uganda. Evaluation and Research Study No. 13. New York: EngenderHealth/The ACQUIRE Project; 2008 (http://www.acquireproject.org/archive/files/11.0_research_studies/er_study_13.pdf, accessed 1 November 2015).
- 137 Hope R, Kendall T, Langer A, Barnighausen T. Health system integration of sexual and reproductive health and HIV services in sub-Saharan Africa: a scoping study. *J Acquir Immune Defic Syndr.* 2014;67(Suppl 4):S259–70.
- 138 WHO recommendations on postnatal care of the mother and newborn. Geneva: World Health Organization; 2013 (http://www.who.int/maternal_child_adolescent/documents/postnatal-care-recommendations/en/, accessed 1 November 2015).
- 139 All in to #EndAdolescentAIDS. Launch document. Geneva: Joint United Nations Programme on HIV/AIDS; 2014 (<http://allintoendadolescentaids.org/wp-content/uploads/2015/02/ALL-IN-Launch-Document.pdf>, accessed 1 November 2015).
- 140 Auld AF, Agolory SG, Shiraishi RW, Wabwire-Manger F, Kwesigabo G, Mulenga M et al. Antiretroviral therapy enrollment characteristics and outcomes among HIV-infected adolescents and young adults compared with older adults—seven African countries, 2004–2013. *MMWR Morb Mortal Wkly Rep.* 2014;63(47):1097–103.
- 141 Lamb MR, Fayorsey R, Nuwagaba-Biribonwoha H, Viola V, Mutabazi V, Alwar T et al. High attrition before and after ART initiation among youth (15–24 years of age) enrolled in HIV care. *AIDS.* 2014;28(4):559–68.
- 142 Grimsrud A, Balkan S, Casas EC, Lujan J, Van Cutsem G, Poulet E et al. Outcomes of antiretroviral therapy over a 10-year period of expansion: a multicohort analysis of African and Asian HIV programs. *J Acquir Immune Defic Syndr.* 2014;67(2):e55–66.
- 143 Koech E, Teasdale CA, Wang C, Fayorsey R, Alwar T, Mukui IN et al. Characteristics and outcomes of HIV-infected youth and young adolescents enrolled in HIV care in Kenya. *AIDS.* 2014;28(18):2729–38.
- 144 Vinikoor MJ, Joseph J, Mwale J, Marx MA, Goma FM, Mulenga LB et al. Age at antiretroviral therapy initiation predicts immune recovery, death, and loss to follow-up among HIV-infected adults in urban Zambia. *AIDS Res Hum Retroviruses.* 2014;30(10):949–55.

- 145 Berheto TM, Haile DB, and Mohammed S. Predictors of loss to follow-up in patients living with HIV/AIDS after initiation of antiretroviral therapy. *N Am J Med Sci*. 2014;6(9):453–9.
- 146 Bygrave H, Mtangirwa J, Ncube K, Ford N, Kranzer K, Munyaradzi D. Antiretroviral therapy outcomes among adolescents and youth in rural Zimbabwe. *PLoS One*. 2012;7(12):e52856.
- 147 Ngoksin E, Ninahazwe C, Bhila J, Musah L, Beryl CA, Watson K, Armstrong A. “Taking them forever and taking them on time”: the treatment and care needs of adolescents living with HIV. 2015. In: 18th International Conference on AIDS and STIs in Africa. Harare, Zimbabwe 29th Nov–4th Dec 2015. [Poster A-751-0002-01669].
- 148 Health for the world’s adolescents: a second chance in the second decade. Geneva: World Health Organization; 2014 (http://www.who.int/maternal_child_adolescent/topics/adolescence/second-decade/en/ accessed 1 November 2015).
- 149 Interagency Working Group on Key Populations. HIV and young key populations: a technical brief series – annex 6 of Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva: World Health Organization; 2014 (<http://www.who.int/hiv/pub/guidelines/keypopulations/en>, accessed 1 November 2015).
- 150 Lost in transition: current issues faced by adolescents living with HIV in Asia Pacific. Bangkok: Asia Pacific Network of People Living with HIV/AIDS; 2013 (http://www.unicef.org/eapro/Lost_in_Transitions.pdf, accessed 1 October 2015).
- 151 Mavhu W, Berwick J, Chirawu P, Makamba M, Copas A, Dirawo J et al. Enhancing psychosocial support for HIV positive adolescents in Harare, Zimbabwe. *PLoS One*. 2013;8(7):e70254.
- 152 Denison JA, Banda H, Dennis AC, Packer C, Nyambe N, Stalter RM et al. “The sky is the limit”: adhering to antiretroviral therapy and HIV self-management from the perspectives of adolescents living with HIV and their adult caregivers. *J Int AIDS Soc*. 2015;18(1):19358.
- 153 Making health services adolescent friendly: developing national quality standards for adolescent friendly health services. Geneva: World Health Organization; 2012 (http://apps.who.int/iris/bitstream/10665/75217/1/9789241503594_eng.pdf, accessed 1 November 2015).
- 154 Quality assessment guidebook. A guide to assessing health services for adolescent clients. Geneva: World Health Organization; 2009 (http://www.who.int/maternal_child_adolescent/documents/fch_cah_9789241598859/en/, accessed 1 November 2015).
- 155 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. Volume 1: standards and criteria. Geneva: World Health Organization; 2015 (http://apps.who.int/iris/bitstream/10665/183935/1/9789241549332_vol1_eng.pdf?ua=1, accessed 15 September 2015).
- 156 Butler L, Linderfren M, Katz I, Armstrong A. Are adolescent-friendly health services compared to standard health services more effective at ensuring engagement and improved outcomes for adolescents? Web Supplement B.
- 157 Asarnow JR, Jaycox LH, Duan N, LaBorde AP, Rea MM, Murray P et al. Effectiveness of a quality improvement intervention for adolescent depression in primary care clinics: a randomized controlled trial. *JAMA*. 2005;293(3):311–19.
- 158 Barnett B, Liu J, DeVoe M, Duggan AK, Gold MA, Pecukonis E. Motivational intervention to reduce rapid subsequent births to adolescent mothers: a community-based randomized trial. *Ann Fam Med*. 2009;7(5):436–45.
- 159 Belzer ME, Naar-King S, Olsen 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(4):686–96.
- 160 Charron-Prochownik D, Sereika SM, Becker D, White NH, Schmitt P, Powell AB 3rd et al. Long-term effects of the booster-enhanced READY-Girls preconception counseling program on intentions and behaviors for family planning in teens with diabetes. *Diabetes Care*. 2013;36(12):3870–4.
- 161 Cohen D, Lises C, Williams WR, Brunson CF, Batstone T. Exploratory study to evaluate the provision of additional midwifery support to teenage mothers. *Public Health*. 2011;125(9):632–8.
- 162 Colby SM, Monti PM, O’Leary Tevyaw T, Barnett NP, Spirito A et al. Brief motivational intervention for adolescent smokers in medical settings. *Addict Behav*. 2005;30(5):865–74.

- 163 Cowan FM, Pascoe SJ, Langhaug LF, Mavhu W, Chidiya S, Jaffar S et al. The Regai Dzive Shiri project: results of a randomized trial of an HIV prevention intervention for youth. *AIDS*. 2010;24(16):2541–52.
- 164 Doyle AM, Ross D, Maganja K, Baisley K, Masesa C, Andreasen A et al. Long-term biological and behavioural impact of an adolescent sexual health intervention in Tanzania: follow-up survey of the community-based MEMA kwa Vijana Trial. *PLoS Med*. 2010;7(6):e1000287.
- 165 Ross DA, Changalucha J, Obasi AI, Todd J, Plummer ML, Cleophas-Mazige B et al. Biological and behavioural impact of an adolescent sexual health intervention in Tanzania: a community-randomized trial. *AIDS*. 2007;21(14):1943–55.
- 166 Harper CC, Cheong M, Rocca CH, Darney PD, Raine TR. The effect of increased access to emergency contraception among young adolescents. *Obstet Gynecol*. 2005;106(3):483–91.
- 167 Franklin VL, Waller A, Pagliari C, Greene SA. A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes. *Diabet Med*. 2006;23(12):1332–8.
- 168 Chernick LS, Westhoff C, Ray M, Garcia M, Garth J, Santelli J et al. Enhancing referral of sexually active adolescent females from the emergency department to family planning. *J Womens Health (Larchmt)*. 2015;24(4):324–8.
- 169 Elliott L, Henderson M, Nixon C, Wight D. Has untargeted sexual health promotion for young people reached its limit? A quasi-experimental study. *J Epidemiol Community Health*. 2013;67(5):398–404.
- 170 Funck-Brentano I, Dalban C, Veber F, Quartier P, Hefez S, Costagliola D et al. Evaluation of a peer support group therapy for HIV-infected adolescents. *AIDS*. 2005;19(14):1501–8.
- 171 Gilmer TP, Ojeda VD, Fawley-King K, Larson B, Garcia P. Change in mental health service use after offering youth-specific versus adult programs to transition-age youths. *Psychiatr Serv*. 2012;63(6):592–6.
- 172 Ngo AD, Ha TH, Rule J, Dang CV. Peer-based education and the integration of HIV and sexual and reproductive health services for young people in Vietnam: evidence from a project evaluation. *PLoS One*. 2013;8(11):e80951.
- 173 Olson AL, Gaffney CA, Lee PW, Starr P. Changing adolescent health behaviors: the healthy teens counseling approach. *Am J Prev Med*. 2008;35(5 Suppl):S359–64.
- 174 Teasdale CA, Chege D, Fayorsey R, Abrams EJ. Impact of youth and adolescent friendly services on retention of 10-24 year olds in HIV care and treatment programs in Kenya. *J Acquir Immune Defic Syndr*. 2016;71(2):e56–9.
- 175 Davila JA, Miertschin N, Sangsriy S, Schwarzwald H, Henley C, Giordano TP. Centralization of HIV services in HIV-positive African-American and Hispanic youth improves retention in care. *AIDS Care*. 2013;25(2):202–6.
- 176 Deogan C, Ferguson J, Stenberg K. Resource needs for adolescent friendly health services: estimates for 74 low- and middle-income countries. *PLoS One*. 2012;7(12):e51420.
- 177 Kempers J, Ketting E, and Lesco G. Cost analysis and exploratory cost-effectiveness of youth-friendly sexual and reproductive health services in the Republic of Moldova. *BMC Health Serv Res*. 2014;14:316.
- 178 Mark D, Andrade C, Armstrong A, Runciman T, Penazzato M, Hatane L et al. Availability of appropriate HIV treatment and care services for adolescents in sub-Saharan Africa: a situational analysis. Conducted Sept 2014. (http://apps.who.int/iris/bitstream/10665/189977/1/WHO_HIV_2015.36_eng.pdf?ua=1, accessed 15 February 2016).
- 179 Bernays S, Papparini S, Rhodes T, Seeley J. Summary report to address PICO questions for young people living with HIV: findings from the ARROW and BREATHER qualitative research projects in Uganda, Zimbabwe, USA, UK and Ireland. On behalf of BreatHER and ARROW social science teams. May 2015.
- 180 Wolmarans L, Van der Kwaak A, Beanland R. National HIV programme managers' perspectives on implementing interventions for treating and preventing HIV infection. Conduct of a survey to update the World Health Organization's consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection 2015. Royal Tropical Institute KIT Health and Education. Web Supplement B.

- 181 Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva; World Health Organization; 2015 (<http://www.who.int/hiv/pub/guidelines/keypopulations/en/>, accessed 1 November 2015).
- 182 Brown C, Lilford R. Evaluating service delivery interventions to enhance patient safety. *BMJ*. 2008;337:a2764.
- 183 WHO global strategy on people-centred and integrated health services. Geneva: World Health Organization; 2015 (<http://www.who.int/servicedeliverysafety/areas/people-centred-care/global-strategy/en/>, accessed 15 February 2016).
- 184 People-centred and integrated health services: an overview of the evidence. Geneva; World Health Organization; 2015 (<http://www.who.int/servicedeliverysafety/areas/people-centred-care/evidence-overview/en/>, accessed 1 November 2015).
- 185 Heiby J. The use of modern quality improvement approaches to strengthen African health systems: a 5-year agenda. *Int J Qual Health Care*. 2014;26(2):117–23.
- 186 A model quality assurance system for procurement agencies: recommendations for quality assurance systems focusing on prequalification of products and manufacturers, purchasing, storage and distribution of pharmaceutical products. Geneva: World Health Organization; 2007 (Technical Report Series, No. 937; <http://www.who.int/medicines/publications/ModelQualityAssurance.pdf>, accessed 31 October 2015).
- 187 WHO, Interagency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Their Children (IATT), UNICEF. Factsheet on lopinavir and ritonavir oral pellets 40 mg/10 mg. UNICEF, WHO; 2015 (<http://www.emtct-iatt.org/wp-content/uploads/2015/09/IATT-LPVr-Factsheet-Final-30-September-2015.pdf>, accessed 16 October 2015).
- 188 WHO, US CDC. Improving the quality of HIV-related point-of-care testing: ensuring the reliability and accuracy of test results. Geneva: World Health Organization; 2015 (<http://www.who.int/hiv/pub/toolkits/handbook-point-of-care-testing/en/>, accessed 18 January 2016).

