

# Differentiated Care for Adults at High Risk of HIV Disease Progression



## A Call to Action

**HIV LEARNING NETWORK**  
**The CQUIN Project for Differentiated Care**



**ICAP**

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Mailman School of Public Health

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The goal of the HIV Coverage, Quality, and Impact Network (CQUIN) is to increase the number of people living with HIV initiating and sustaining highly effective HIV treatment with sustained viral suppression. Towards this end, ICAP at Columbia University aims to catalyze the delivery of high quality differentiated care at scale by supporting a network of countries at various stages of implementing differentiated care services, enabling experience sharing, joint learning, and collaborative problem solving. More information about CQUIN can be found at [cquin.icap.columbia.edu](http://cquin.icap.columbia.edu).

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## Abbreviations

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AFB	Acid-fast bacillus
AIDS	Acquired immunodeficiency syndrome
ALUP	Advanced, Late, and Unstable Patients
ART	Antiretroviral therapy
CM	Cryptococcal meningitis
CPT	Cotrimoxazole prophylactic treatment
CrAg	Cryptococcal antigen
DC	Differentiated care
DSD	Differentiated service delivery
EAC	Enhanced adherence counseling
HCW	Health care worker
HF	Health facilities
HIV	Human immunodeficiency virus
HIVST	HIV self-testing
HTS	HIV testing services
IAS	The International AIDS Society
ICAP	ICAP at Columbia University
IPT	Isoniazid preventive therapy
IRIS	Immune reconstitution inflammatory syndrome
LMIC	Low- and middle-income countries
MDT	Multidisciplinary team
NCD	Non-communicable disease
NIMART	Nurse-initiated and managed ART
OI	Opportunistic infection
PEPFAR	The U.S. President's Emergency Fund for AIDS Relief
PITC	Provider-initiated testing and counseling
PLHIV	People living with HIV
PWID	People who inject drugs
RVLT	Routine viral load testing
SIPOC	Severely immunosuppressed package of care
SOPs	Standard operating protocols
SMS	Short message service
TASO	The AIDS Support Organization
TB	Tuberculosis
VL	Viral load
WHO	World Health Organization

## Background/Rationale

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The scale-up of antiretroviral therapy (ART) is one of the world's great public health success stories. The number of people living with HIV (PLHIV) accessing ART in low- and middle-income countries rose from 400,000 in 2003 to 18.2 million in 2016, and an estimated 7.8 million deaths have been prevented by the scale-up of HIV treatment.<sup>1</sup> Increased access to prevention and treatment has led to a 35 percent drop in new HIV infections since 2000, including a 58 percent decrease amongst children.<sup>2</sup>

Despite these remarkable successes, there are challenges to continuing business as usual when it comes to the design and delivery of HIV programs. Changing clinical guidelines and ambitious global targets have markedly expanded the number of people eligible for ART. In order to meet the UNAIDS 90-90-90 targets, for example, the number of people on ART would need to double by 2020.<sup>3</sup> Unfortunately, global funding for HIV has plateaued, and many countries are being asked to do more with less when it comes to HIV programming. A second challenge is that the growing numbers of patients on ART have led to overcrowding at health facilities, increasing wait times for patients, overwhelming clinicians, and consequently compromising patient satisfaction. Finally, gaps in program quality, such as suboptimal retention rates, threaten both individual patient outcomes and public health goals.<sup>4</sup>

In response to these challenges, new global guidelines support the use of *differentiated service delivery* (DSD), moving away from a “one-size-fits-all” facility-based model towards different algorithms and programmatic design for diverse groups of PLHIV while maintaining the principles of the public health approach.<sup>5 6</sup> By varying the design and delivery of services offered to different groups of patients, DSD aims to enhance quality, efficiency and patient satisfaction. It puts the client at the center of service delivery while ensuring the health system is functioning in a clinically and programmatically-relevant and efficient manner. Key elements of this approach include re-assessing the “when, where, who, and what” of HIV services for patient groups with different clinical, psychosocial, and contextual characteristics.<sup>7</sup> The World Health Organization (WHO), the President's Emergency Plan for AIDS Relief (PEPFAR), and an increasing number of national ministries of health have endorsed the DSD strategy.

In recent years, the evidence base for differentiated care for stable patients has grown. Innovative pilot programs have explored approaches such as fast-track appointments, multi-month ART prescribing, decreased visit frequency, clinic-based ART clubs, and community-based ART groups.<sup>8</sup> In contrast, there has been less attention to developing differentiated models of care for patients with advanced or unstable HIV disease. Clinical guidelines and policies regarding optimal packages of care for high-risk patients exist,<sup>9</sup> but most suggest (or imply) that these services should be delivered as per usual facility-based models. They give few or no recommendations about how, by whom, or where they should be delivered for optimal impact.

Thus, although WHO and a number of national HIV treatment guidelines recommend specific interventions for which interventions and services to provide to patients with advanced or unstable HIV, differentiated models of care addressing the “how” rather than the “what” have not been tested, and these elements are rarely specified in guidelines (Appendix A). We reviewed the evidence base on optimal programmatic models for high-risk patients to identify best practices and resources for the “how” of differentiated HIV services for these populations. We found very few examples in

either the published or grey literature. This suggests a need for innovative thinking and pilot projects designed to optimize program design for patients with advanced or unstable HIV disease.

Development of differentiated models for unstable patients and those with advanced HIV disease will be a priority as differentiated service delivery expands and matures. This document defines the target populations of interest, describes the currently recommended packages of care, and reviews available differentiated care models. It will serve as a call to action to motivate stakeholders to share their experiences, generate new evidence, and to advocate for attention to this high-risk population.

## Defining High-Risk Patients

People living with HIV on ART that are at high risk of poor clinical outcomes include (1) patients with advanced disease who have initiated ART within the past year, and (2) patients who have been on ART for a year or more but are considered “unstable” due to a range of challenges, including unsuppressed viral load, adverse drug reactions, advanced immunosuppression, active opportunistic infections, nonadherence with ART, substance use, mental illness and other comorbidities requiring close follow-up (Fig. 1, Table 1).

Figure 1: Overview of Patient Classification for Differentiated Care (*ICAP Approach to Differentiated Care*, 2017)

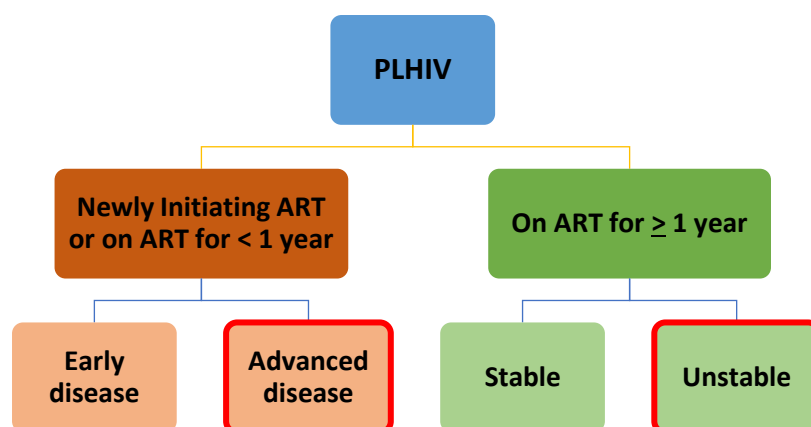


Table 1: Defining High-Risk Patients

New to ART / Advanced Disease	On ART for > 1 year / Unstable
Newly initiating ART or on ART for <1 year and	<i>On ART for &gt;1 year and any of the following:</i>
CD4 <200/mm <sup>3</sup> and/or	Not virally suppressed*
WHO stage III/IV	CD4 <200/mm <sup>3</sup>
	Adverse drug reaction requiring ongoing monitoring
	Active opportunistic infection, including TB
	Non-adherent with ART**
	Substance use
	Comorbid condition(s) requiring frequent follow up
*Not virally suppressed = most recent VL >1,000 and/or no VL in the past 6 months	
**Non-adherent = 2+ missed doses a month for patients on once-daily regimens, 4+ missed doses a month for patients on twice-daily regimens; and/or misses drug pickups	

The *ICAP Approach to Differentiated Care*<sup>10</sup> provides detailed recommendations for the management of patients in each of the four groups identified in Figure 1. This review document builds upon that resource to provide a closer look at the evidence base informing models of care for patients at risk for poor clinical outcomes as defined above. We first describe the package of care for such patients (the “what”), and then summarize our findings on programmatic models (the “how”).

## The Package of Care: Identifying the “What”

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In this section, we describe the recommended packages of care – the “what” for patients who are new to ART with advanced disease and for unstable patients on ART, noting that updated WHO guidance is expected in April of 2017.

### New to ART with Advanced Disease

Although definitions vary, a WHO 2016 consensus document based on a Delphi study of 73 respondents from 28 countries defines presentation with advanced disease as: persons presenting for care with a CD4 count  $<200$  cells/mm<sup>3</sup> or presenting with an AIDS-defining diagnosis (WHO disease stage 3 or 4) regardless of CD4 cell count.<sup>11</sup>

Adult PLHIV with CD4 cell counts  $<200$  cells/mm<sup>3</sup> are at significantly higher risk of mortality than less immunosuppressed patients, and mortality is even more strongly associated with patients whose CD4 cell counts are  $<50$  cells/mm<sup>3</sup>.<sup>12 13</sup> Although many global and national guidelines recommend starting ART for all PLHIV, the majority of individuals initiating ART do so with advanced immunosuppression.<sup>14</sup> The latter patients have a less favorable response to ART compared to those initiating treatment earlier in the course of HIV infection, and have a less robust CD4 count recovery on treatment.<sup>15 16</sup> In addition, they are at high risk of opportunistic infections (OI). For example, the incidence of tuberculosis (TB) in untreated PLHIV is between 10 and 30 times higher in those with a CD4 count  $<50$  cells/mm<sup>3</sup> compared to those with a CD4 count of  $\geq 500$  cells/mm<sup>3</sup>.<sup>17</sup> CD4 cell count at the time of ART initiation is one of the strongest predictors of mortality,<sup>18 19 20</sup> and mortality within a year of HIV diagnosis is ten times higher for patients presenting with advanced disease.<sup>21</sup>

### The Package of Care

Achieving immune system recovery with ART is the primary means to reduce morbidity and mortality related to HIV disease, and delays in ART initiation result in avoidable suffering and deaths.<sup>22</sup> Strategies to reduce early mortality and morbidity among PLHIV presenting to care with advanced disease include prompt initiation of OI prophylaxis, screening and treatment for co-morbid conditions, swift initiation of ART for those without active cryptococcal infection, and close follow-up and monitoring so that adherence can be supported and complications, such as adverse drug reactions and/or immune reconstitution inflammatory syndrome (IRIS) can be diagnosed and appropriately managed.<sup>23</sup>

Cumulative evidence from observational data and randomized clinical trials supports the value of cotrimoxazole prophylactic treatment (CPT) in resource-limited settings in reducing hospitalizations, morbidity, and mortality among PLHIV.<sup>24</sup> Despite an increasing understanding of the potential impact of CPT in resource-limited settings, wide-scale implementation of CPT programs has been slow and suboptimal.<sup>25</sup>

Tuberculosis and HIV are intimately related. Tuberculosis is the most common serious OI in PLHIV, and the leading cause of AIDS-related deaths in adults and children in sub-Saharan Africa.<sup>26</sup> The World Health Organization strongly recommends that all PLHIV should be screened for TB symptoms at each clinic encounter, with expedited TB diagnosis and treatment for presumptive TB cases and prompt initiation of isoniazid preventive therapy (IPT) if active TB is excluded. In recent years, WHO has endorsed the use of molecular diagnostics such as Xpert MTB/RIF; urine testing



for mycobacterial lipoarabinomannan (LAM) has also been endorsed by WHO for use in symptomatic patients with advanced HIV and signs or symptoms of TB (e.g., hospitalized patients with CD4 cell counts <100 cells/mm<sup>3</sup>.)<sup>27 28</sup>

The use of IPT and ART has been shown to have additive benefits on reducing TB incidence and mortality compared to IPT or ART alone.<sup>29 30</sup> Unfortunately, IPT coverage remains low, with fewer than 25 percent of eligible patients receiving IPT.<sup>31</sup> Based on evidence of the efficacy of ART initiation on reducing mortality among patients with HIV-related TB, WHO recommends early initiation of ART in HIV-positive TB patients, specifically within the first eight weeks of TB treatment, and within the first two weeks of initiating TB treatment for HIV-positive TB patients with CD4 counts <50 cells/mm<sup>3</sup>.

In sub-Saharan Africa, cryptococcal meningitis (CM) is a leading cause of death among people with advanced HIV, both before and after ART is initiated. The risk of CM is highest among severely immunocompromised patients and is most common in those with a CD4 count less than 100 cells/mm<sup>3</sup>.<sup>32</sup> Routine serologic screening for cryptococcal antigen (CrAg) in PLHIV with CD4 cell count less than 100 cells/mm<sup>3</sup>, early detection of cryptococemia, and pre-emptive treatment with fluconazole prior to initiation of ART has been shown to decrease overall mortality among this population as well as the risk of CM-associated IRIS.<sup>33</sup> WHO has recommended CrAg screening in ART-naïve adults with advanced disease.

Table 2 illustrates the package of interventions recommended for PLHIV with advanced disease in the 2016 *WHO Guidelines on the Use of Antiretroviral Therapy for HIV Prevention and Treatment*;<sup>8</sup> these recommendations are also included in several national HIV treatment guidelines, including those from Kenya, Uganda, and Lesotho. Updated WHO guidance is expected in April, 2017. The *ICAP Approach to Differentiated Care* and some national guidelines also specify the need for intensive management of any presenting illnesses, close monitoring for IRIS, and ongoing adherence counseling.

**Table 2. WHO Package of Care for Patients with Advanced Disease**

- |  |
|--|
| <ul style="list-style-type: none"><li>✓ Rapid initiation of ART</li><li>✓ Screening for Cryptococcus antigen in the blood</li><li>✓ Screening and treatment for tuberculosis, or IPT, as indicated</li><li>✓ Cotrimoxazole prophylaxis</li><li>✓ Intensive follow-up</li></ul> |
|--|

Additional OI prophylaxis interventions were evaluated in the 2016 REALITY trial. Preliminary results published in abstract form demonstrate a 27 percent reduction in mortality among patients with CD4 <100 cells/mm<sup>3</sup> receiving an enhanced prophylaxis package, compared to those receiving CPT alone.<sup>34</sup> The enhanced package included five days of azithromycin (500 mg), single-dose albendazole (400 mg), 12 weeks of INH/pyridoxine (300/25 mg), and 12 weeks of fluconazole (100 mg) in addition to continuous CPT. While no national guidelines currently recommend the use of enhanced prophylaxis, some programs are piloting the approach. The Lighthouse Trust in Malawi, for example, will include the enhanced prophylaxis package in its Advanced, Late and Unstable Patients (ALUP) protocol starting in 2017.<sup>35</sup>

Optimal adherence to ART is critical for HIV treatment success, including sustained HIV viral suppression, reduced risk of drug resistance, improved quality of life and survival, and decreased risk

of HIV transmission. To avoid treatment failure, adherence preparation, monitoring, and support are strongly recommended as critical components of the package of care for all patients initiating ART. In many countries, key services include adherence counseling, patient education, support groups, and community-based outreach, although these vary in design, intensity and availability. Adherence is often challenging during the first few months of treatment, and most guidelines recommend intensive multidisciplinary support until patients achieve virologic suppression. Given the urgency to start ART in patients presenting with advanced disease, and the recommendation for same-day ART initiation for some individuals, accelerating delivery and developing innovative methods of delivering adherence and psychosocial support concurrently with ART are programmatic priorities (see below).

### **“Unstable” Patients on ART**

Although more than 90 percent of PLHIV achieve viral suppression within a year of starting ART,<sup>36</sup> <sup>37</sup> viral suppression is not always achieved or maintained. In addition, some patients who have been on ART for a year or more may face other challenges that lead to characterizing them as “unstable.” As seen in Table 1, this includes patients on ART with a CD4+ count <200 cells/mm<sup>3</sup>, active opportunistic infections, adverse drug reactions requiring monitoring, non-adherence with ART, substance use, mental illness, and/or other comorbid condition(s) requiring frequent follow up and intensive support.

Unstable patients on ART are a heterogeneous group, but all are at high risk for poor clinical outcomes including complications and/or treatment failure. People living with HIV on ART who continue to have evidence of advanced immunosuppression require close monitoring because of their high risk for OIs. Patients with active opportunistic infections, adverse drug reactions, and/or comorbid condition(s) such as cardiovascular, renal or hepatic disease, require intensive clinical management to avoid morbidity and mortality due to those conditions, and to assure adherence to ART during their management. People living with HIV with viral load >1,000 copies/ml, adherence challenges, and psychosocial challenges such as substance use and mental illness require enhanced adherence support to avoid treatment failure.

Patients on ART who do not achieve and maintain plasma HIV RNA <1000 copies/ml, or who experience virologic rebound, may develop ART resistance mutations. Managing patients with ART resistance usually requires consultation with an HIV expert or a multidisciplinary team (MDT). In some programs, a second line committee reviews patients with suspected first line failure to approve for second line regimen use.

### **The Package of Care**

The package of care for unstable patients on ART generally falls into several overlapping categories: (a) intensive and/or advanced clinical care for individuals with acute opportunistic infections, drug reactions, and co-morbid condition(s); (b) enhanced adherence support with frequent virologic and immunologic monitoring for patients with viral load >1000 copies/ml and known or suspected nonadherence, and (c) advanced ART management for patients with known or suspected drug resistance. In addition, common elements for unstable patients include the need for more frequent visits (generally every one to two months), service delivery by specialist clinicians (particularly in case of suspected ART resistance), and intensive psychosocial/adherence support.

Adherence assessment should be conducted for all patients with suspected or confirmed treatment failure (e.g., those on ART for at least six months who have a viral load >1,000 copies/ml, a decline in CD4+ count, or lack of improvement or worsening clinical condition). Suboptimal adherence is often, but not always, the reason for treatment failure, and a careful multidisciplinary assessment should always be conducted in this context. Ideally, a multidisciplinary team will assess all potential causes of treatment failure including non-adherence, inadequate dosing, drug-drug interactions, drug-food interactions, impaired absorption (e.g., chronic severe diarrhea), and drug resistance, if available. Adherence assessment should include a supportive discussion with the patient about medication usage, review of medication pick-ups, consideration of pill counts, a home visit, and discussions with treatment supporters, caretakers and/or spouse/partners, if the patient agrees.

Enhanced adherence counseling (EAC) aims to assess adherence barriers in a nonjudgmental way, and to help the patient construct a personalized adherence plan with concrete objectives. It is important not to focus solely on knowledge of HIV and ART but also to review psychological, emotional, and socio-economic factors that may contribute to poor adherence. In addition, exploring the patient's motivation for taking medication often highlights reasons for poor adherence. Several national guidelines recommend at least three EAC sessions, followed by a repeat viral load testing, although no definitive comparison of EAC approaches has been conducted.<sup>38</sup>

## Differentiating Services: Identifying the “How”

The previous section briefly reviewed the packages of care recommended for high-risk patients – the what. To understand how these services are delivered, and to identify differentiated models of care for PLHIV at high risk for poor clinical outcomes, we reviewed the published and grey literature, and reached out to diverse implementers to learn more about the “where, when, and who” of program design for this subgroup of patients. We also reviewed national ART guidelines from ten countries in sub-Saharan Africa (see Appendix A). In order to synthesize the findings, we categorized key challenges and barriers to effective service delivery for high-risk patients (Table 3) and describe innovations and best practices developed to address them. In some cases, programs have developed and piloted these approaches, such as the Severely Immunosuppressed Package of Care (SIPOC) model in Kenya described below. Other innovations have been identified in the context of implementation science studies, such as the SEARCH study in Uganda,<sup>39</sup> and Link4Health in Swaziland, among others.<sup>40</sup>

**Table 3: Key challenges and barriers to service delivery for high-risk patients**

Challenge	Illustrative Barriers/Challenges
Identification of high-risk patients	Delayed ART eligibility assessment
	Delayed identification of failing regimens
	Delayed linkage from testing to treatment
ART initiation and management	Delayed switch to 2 <sup>nd</sup> /3 <sup>rd</sup> line regimens
	Lack of standard operating protocols (SOPs) for high risk patients
Prevention and management of acute co-morbid conditions(s)	Insufficient or absent OI screening/prophylaxis
	Weak linkages for up-referral to more specialized site/providers
	Discontinuity between inpatient, outpatient, and community-based services
	Siloed HIV and NCD services
Management of chronic co-morbid condition(s)	Lack of strong home care systems
	Need for specialized adherence support

### Timely Identification of High-Risk Patients

As noted above, the majority of PLHIV initiate ART with advanced immunosuppression, missing a critical opportunity to prevent complications of HIV and to maximize the chance of sustained treatment success. Optimizing HIV testing services (HTS) to identify PLHIV early in the course of HIV infection is an essential element of effective HIV programming, and a wealth of innovative program models have been piloted in recent years. The use of point-of-care CD4 testing, able to provide same-day results, has enabled programs to rapidly identify patients with advanced disease and to accelerate their linkage to treatment.<sup>41 42 43</sup> Expansion of routine viral load testing (RVLT) services has also improved programs’ ability to identify unstable patients on ART.

### ART Initiation and Management

Failed linkage from HIV testing to treatment is a leading cause of delayed ART initiation. Other systems barriers include requirements for multi-visit assessments prior to starting ART, and/or laboratory testing that may have long turn-around times and/or be unavailable. In addition to point-

of-care CD4 testing and swift preparation, several national guidelines now have streamlined visit schedules, and emphasize that availability of laboratory test results should not be a pre-requisite for starting ART.

## ART Initiation

Developing “fast-track” protocols for patients with advanced immunosuppression is a key element of several national strategies. Kenya’s national guidelines recommend ART initiation within two weeks of diagnosis for all patients, and specify weekly visits until ART is initiated, twice monthly visits during the first month, and monthly visits thereafter.<sup>44</sup> South Africa’s national guidelines recommend fast track ART initiation (within seven days of diagnosis) for patients with CD4 cell count <200 cells/mm<sup>3</sup> and/or clinical stage four disease.<sup>45</sup> Lesotho’s national guidelines recommend same-day ART initiation for patients who demonstrate “clear readiness to begin ART”<sup>46</sup> and highlight the urgency of rapid ART initiation in patients with low CD4 cell counts, as do the Swaziland national guidelines, which further emphasize that unavailability of laboratory tests should not delay ART.<sup>47</sup>

Decentralized ART services and task shifting are also important facilitators of rapid ART initiation for high-risk patients. Moving ART services closer to patients, whether to primary health facilities or to community settings, is a critical step towards accelerating ART access. In order to achieve such decentralization, non-specialist clinicians such as nurses and medical officers must be able to prescribe ART; many national guidelines now support nurse-initiated and managed ART (NIMART).

The *ICAP Approach to Differentiated Care* outlines step-by-step guidance for the management of PLHIV who present with advanced disease, defining key clinical, laboratory and psychosocial services needed by clinic visit (Table 4) and key considerations (Table 5).

**Table 4: ICAP Guidance for Patients Presenting with Advanced Disease**

When	What	By Whom	Where
<b>First Visit (Time 0)</b>	<i>Clinical visit:</i> Confirm HIV diagnosis; CD4 test (baseline); WHO Staging; screen for CrAg and TB Adherence support and counseling <i>Drug:</i> ART and CTX initiation	Clinician <sup>+</sup>	HIV Clinic
<b>Week 2</b>	<i>Clinical visit:</i> Management of OIs, monitor side effects/toxicity Adherence assessment, support and counseling <i>Drug:</i> ART and CTX refill for 1 month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 1-2</b>	<i>Clinical visit:</i> Monitor side effects/toxicity; manage OIs; initiate IPT Adherence assessment, support and counseling <i>Drug:</i> ART, INH, and CTX refill for 1 month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 3</b>	<i>Clinical visit:</i> Monitor side effects/toxicity Adherence assessment, support and counseling <i>Drug:</i> ART, INH, and CTX refill for 1 month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 4-5</b>	<i>Clinical visit:</i> Monitor side effects/toxicity Adherence assessment, support and counseling <i>Drug:</i> ART, INH, and CTX refill for 1 month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 6 Milestone Visit</b>	<i>Clinical visit:</i> Monitor side effects/toxicity <i>Lab:</i> VL sample collection Adherence assessment, support and counseling <i>Drug:</i> ART, INH, and CTX refill for 1 month	Clinician <sup>+</sup>	HIV Clinic

<b>Month 7</b>	<i>Clinical visit:</i> VL results delivered to patient; monitor clinical symptoms via symptom checklist and check for side effects/toxicity Adherence assessment, support and counseling Stepped up counseling and support as needed, based on VL results <i>Drug:</i> INH refill for 1 mo, ART and CTX refill for 3 months	Clinician <sup>+</sup>	HIV Clinic
<b>Month 8-11</b>	<b>VL &gt;1000</b> <i>Clinical visit:</i> Monitor side effects/toxicity Adherence support ; Stepped up counseling <i>Drug:</i> ART and CTX refill for 1 month <i>Lab:</i> Repeat VL between M9 and M11 after good adherence has been achieved	Clinician <sup>+</sup>	HIV Clinic
	<b>VL &lt;1000</b> <i>Clinical Visit:</i> Monitor side effects/toxicity Adherence assessment, support and counseling <i>Drug:</i> ART and CTX refill for 3 months	Clinician <sup>+</sup>	HIV Clinic
<b>Month 12 Milestone Visit</b>	<i>Clinical visit:</i> Monitor side effects/toxicity <i>Lab:</i> Second VL sample collection Adherence counseling and support <i>Drug:</i> ART and CTX refill for 1 month Reclassify patients as stable vs. unstable based on clinical evolution and VL results	Clinician <sup>+</sup>	HIV Clinic

<sup>+</sup> Clinician includes physicians, nurses, clinical officers and medical technicians

\* At every contact with patients, health care worker (clinician, nurse or lay counselor) should assess the patient and reclassify him/her as “early” or “advanced” disease, and refer to the appropriate follow-up if indicated.

**Table 5: Key Considerations for Service Delivery for Patients who Present with Advanced HIV Disease**

<b>Patients who Present with Advanced HIV Disease (WHO Stage 3 or 4, or CD4+ count &lt;200cells/mL )</b>	
Location of Service	<ul style="list-style-type: none"> <li>• Management at any ART service delivery point; all facility levels</li> <li>• Initial management and ART initiation by trained and experienced HCW</li> <li>• Consultation with MDT, TWG, mentors, and senior clinicians as needed (including telephone consultation, HIV information hotline)</li> <li>• Referral to a higher-level facility when feasible if consultation is not adequate to stabilize the patient</li> </ul>
Focus of Treatment Preparation Counseling	<ul style="list-style-type: none"> <li>• ART is required to prevent further damage to the immune system</li> <li>• Starting ART soon will decrease risk of disease progression, including wasting and OIs</li> <li>• ART is the most important treatment to restore health</li> </ul>
Frequency of Follow-up	<ul style="list-style-type: none"> <li>• Weekly follow-up until ART initiation, and then at week 2 and 4 after ART initiation, and then monthly until confirmed viral suppression</li> <li>• More frequent visits or in-patient hospitalization may be required to stabilize acute medical conditions and address psychosocial and other concerns</li> </ul>

## Switching to 2<sup>nd</sup>/3<sup>rd</sup> line Regimens

High-risk patients on ART may require 2<sup>nd</sup> or 3<sup>rd</sup> line ART regimens. Bottlenecks to such treatment adjustments include the lack of specialist clinicians, a situation that has engendered the use of “2<sup>nd</sup> line committees” that review all proposed regimen changes, ensuring specialist review and consistent application of national guidelines. Because some countries have few – or only one – committee, this process can be time-consuming, and decentralizing decision-making has become a priority in a number of countries, including Lesotho, Kenya and Mozambique.

Other barriers include the lack of familiarity with 2<sup>nd</sup> line regimens on the part of front line staff, who may require mentoring and supervision by more experienced clinicians. In many settings, nurses have not been trained to manage even first line regimens, despite the implementation of NIMART in their countries of practice. For example, in a survey in Eastern Kenya, only two-thirds of nurses had been trained in comprehensive HIV care and treatment and less than half had been trained to prescribe first-line ART.<sup>48</sup> Innovative models to support less experienced clinicians include Kenya’s Uliza! Hotline for telephone consultations,<sup>49</sup> and pilot telemedicine programs.<sup>50</sup>

## Prevention and Management of Acute Comorbidities

In contrast to stable patients, whose differentiated care requires fewer clinical assessments and fewer visits to health facilities, high-risk patients often need close follow-up by multi-disciplinary teams including specialist clinicians. Experience suggests that clinicians do not always identify high-risk patients, and that there is a need for heightened vigilance and specialized protocols to support the identification and management of these individuals.

## Protocols/Procedures for High-Risk Patients

In addition to fast track protocols, some programs have well-defined packages of care for patients with advanced HIV disease. In Kenya, ICAP is piloting an approach called the Severely Immunosuppressed Package of Care (SIPOC), which includes standard operating protocols, checklists, and other job aids designed to support delivery of a defined set of staging, prophylaxis and ART services (Table 6). The charts of patients with CD4 cell counts less than 100 cells/mm<sup>3</sup> are flagged with a SIPOC sticker, and a SIPOC patient assessment form is added to each chart; health workers are trained to be vigilant in identifying and managing high-risk patients, and facility-level supplies and equipment are defined in advance.

**Table 6: The SIPOC package**

Staging	Clinical staging and same-day CD4 testing
Prevention	TB symptom screening at every clinical visit; TB testing with Xpert MTB/Rif assay and/or X-ray as indicated; CrAg screening (if CD4 <100 cells/mm <sup>3</sup> or WHO stage 4); Cotrimoxazole preventive therapy (CPT)
Additional screening	Hepatitis B screening, stool for parasites and AFB in anyone with persistent diarrhea
Support	Intensive follow-up (twice-monthly visits for one month after ART initiation, then monthly visits); active tracking; nutritional assessment, counseling, and supplementation; adherence counseling; linkage to peer educator with weekly phone calls; home visits.

Other models of care for high-risk patients include the systematic use of case managers. For example, Kenya’s national ART guidelines recommend case managers, home visits, consideration of directly-observed ART treatment, and both group and individualized counseling for PLHIV with suspected or confirmed ART failure.<sup>51</sup> A 2015 study in Tanzania and Zambia found that the addition of a short period of lay worker home visits to clinic-based services for patients initiating ART with fewer than 200 CD4 cells/mm<sup>3</sup> was associated with significantly lower mortality.<sup>52</sup>

Differentiating visit schedules for PLHIV with advanced disease is another approach to managing acute illness or complex comorbidities.<sup>8</sup> At least one study has shown that more frequent visits for patients with advanced disease leads to improved outcomes.<sup>53</sup> Many national guidelines recommend more intense follow up for high-risk patients, although few specify an exact visit schedule. The *ICAP Approach to Differentiated Care* details recommended schedules for patients presenting with advanced disease and unstable patients on ART (Tables 4 and 7).

**Table 7. Differentiated Care for Patients who are Unstable on ART for > 1 year**

What	By Whom	Where
Clinical assessments every 1-2 months	Clinician <sup>+</sup>	HIV Clinic
Lab: VL monitoring 3 months after enhanced adherence support*	Clinician	HIV clinic
Psychosocial/Adherence support** every 1-2 months	Lay counselor, adherence counselor or pharmacist	HIV Clinic
Drug pick up every 1-2 months	Lay counselor or adherence counselor	HIV clinic
<sup>+</sup> Clinician includes physicians, nurses, clinical officers and medical technicians <sup>*</sup> Reclassify patients after each viral load and/or clinical assessment <sup>**</sup> Refer to ICAP Enhanced Adherence Plan of Care		

Specialized clinics – on specific days and/or at specific locations – are also used to support the differentiated management of high-risk patients. For example, Kenya’s national ART guidelines recommend the creation of a specialized clinic day for patients on 2<sup>nd</sup> and 3<sup>rd</sup> line regimens in health facilities with sufficient volume. Clinics for patients with TB/HIV, Kaposi’s sarcoma, cervical cancer and other co-morbid conditions requiring specialized care and treatment are another approach; these are more common at secondary and tertiary hospitals, but are also found at less-specialized facilities, who may host a visiting specialist on specific clinic days.

Another intervention to support patients requiring intensive outpatient follow up is the provision of temporary housing near health facilities for patients making frequent visits.<sup>54</sup>

### Prophylaxis of Opportunistic Infections

As noted in Table 2 above, WHO guidelines recommend the use of CPT for all PLHIV, as well as IPT for those who screen negative for TB and screening for Cryptococcus for those with CD4 cell counts <100 cells/mm<sup>3</sup>. Several pilot programs go further, including SIPOC, and an initiative recently launched by Lighthouse Trust, a non-governmental organization in Malawi, which has developed a differentiated package of care for Advanced, Late and Unstable patients (ALUP). The ALUP package will include screening for Cryptococcus with serum testing for Crptyococcal antigen



(CrAg) and the addition of urine LAM (urine lipoarabinomannan) testing to TB screening protocols. Patients with CD4 cell counts  $<100$  cells/mm<sup>3</sup> will receive the enhanced prophylaxis package used in the REALITY trial, as well as vitamins and therapeutic nutrition as needed.<sup>55</sup> Lighthouse has developed a flow chart for patient management and launched the ALUP services in early 2017.

## Facilitating Up-Referral to More Specialized Health Facilities

Differentiated care for stable patients often includes down-referral and decentralization of care and treatment to front-line health facilities and to the community. Corresponding up-referral for patients who become unstable is a high-priority need. Swift identification of newly unstable patients and robust linkages to higher-level and/or more specialized care are critical for patient safety and long-term treatment success, as is accurate documentation and communication between facilities and health care providers. We found no published or grey literature examples of differentiated referral processes, however.

## Linking Inpatient and Outpatient Care

Patients with advanced disease are more likely to require inpatient treatment than stable patients, making smooth referrals and linkages between inpatient and outpatient settings an essential element of high-quality care. We found no published examples of differentiated linkages processes for unstable patients.

## Management of Co-Morbid Chronic Conditions

In some cases, high-risk patients require more frequent monitoring because of chronic, not acute, health challenges. These may be HIV-related conditions, such as renal or hepatic insufficiency, or other chronic co-morbidities, such as non-communicable diseases (NCDs).

## Integrating HIV and NCD Services

The rising burden of cardiovascular disease (CVD), cardiovascular disease risk factors, and other chronic NCDs in sub-Saharan Africa has led to dual epidemics of HIV and NCDs in many countries. People living with HIV may be at higher risk of CVD than the general population, due to the effects of HIV replication on inflammatory and coagulation markers as well as the increased risk of hyperlipidemia and diabetes associated with some antiretroviral drugs. Studies in South Africa and Swaziland, for example, show hypertension rates of 30%-40% amongst older PLHIV enrolled in care and treatment.<sup>56 57</sup> Hepatitis C, other co-infections, medications, and the direct effects of HIV can also raise the risk of renal and hepatic insufficiency amongst PLHIV. Although integrated HIV and NCD services have been piloted in several countries, models of *differentiated* care for individuals with both HIV and NCDs are rare. In Kenya, Médecins sans Frontières initiated Medication Adherence Clubs for patients with HIV as well as HIV-negative patients with stable hypertension and/or diabetes, providing proof of concept for the use of nurse-facilitated community-based care and treatment for mixed chronic diseases.<sup>58</sup> In several countries, however, patients with both HIV and NCDs may receive differentiated care for their HIV – in the form of visit spacing, multi-month prescription, and community-based services – but find that they must still come to a health facility each month for clinical assessment and to pick up medications for NCDs.

## Specialized Education, Counseling, and Community Antiretroviral Groups

Although high-risk patients have diverse characteristics, many share specific challenges with regards to treatment access, adherence, and retention. Designing differentiated peer education or community antiretroviral groups is one way to provide enhanced support. Kenya's national guidelines suggest that patients on second-line ART or those not virally suppressed will benefit from co-scheduling them on specific days, simplifying access to specialized clinical care but also to specialized support groups. In some countries, community ART groups include both stable and unstable patients; in others, groups are designed specifically for unstable patients. Neither approach has undergone robust evaluation.

Enhanced adherence counseling (EAC) for patients with viral load  $>1,000$  copies is recommended in many national ART guidelines. Typically, two to three EAC sessions are delivered over three months, followed by a repeat viral load test. No single best approach has been identified.

## Strengthening Home Care Systems

Home-based care for high-risk PLHIV has been a staple of HIV programs for decades, although the earliest efforts focused on palliation, rather than treatment. The AIDS Support Organization (TASO) and partners conducted a cluster-randomized trial of clinic- vs. home-based ART services in rural Uganda, focusing on patients with CD4 cell counts  $< 250$  cells/mm<sup>3</sup> and/or WHO stage 3 or 4 disease. Home-based services included monthly visits from trained laypeople who delivered ART and used a structured checklist to review adherence and check for symptoms. Counselors also visited quarterly. The home-based model was shown to be both cost-effective<sup>59</sup> and non-inferior to clinic based care,<sup>60 61</sup> even amongst patients with CD4 cell counts  $< 50$  cells/mm<sup>3</sup>.<sup>62</sup> The availability of mobile health applications has expanded the possibilities for home-based care and treatment.

## Summary/Way Forward

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The package of care recommended for high-risk patients is evolving, as new evidence is developed regarding the “what” of patient care. In contrast, there is limited information regarding the “how” – the optimal models of delivering these services at scale. As more and more stable patients initiate ART, the specialized needs of unstable patients and those with advanced HIV disease may be overlooked. Differentiated care for stable patients has the potential to decompress health facilities, enabling health workers to provide targeted attention to patients with advanced or unstable disease. However, our review indicates that guidelines, resources, and tools for differentiated care of high-risk patients are scarce.

Programmatic priorities include ways to rapidly identify high-risk patients, such as screening and risk stratification tools. In addition, the use of standard operating protocols, clinical support tools, and job aids may ensure that unstable patients receive the appropriate level of care, as in the SIPOC program in Kenya and the ALUP protocol in Malawi. Attention to linkages and transfers will be particularly important for high-risk patients.

Additional research priorities include exploration of *where* to deliver care for unstable patients – to what extent can this be decentralized and delivered outside of hospital settings? Will community-based and/or home-based models of care work for unstable patients? Although the tacit assumption may be that specialist physicians will treat high-risk patients, the *who* of differentiated care may also be a fruitful line of enquiry. Innovative training and supervision strategies may enable non-physician clinicians to provide care for unstable patients, although this evidence base needs to be developed.

Fostering stakeholder exchange around the issue of differentiated care for high-risk patients is a priority for the CQUIN network, which seeks to facilitate joint learning, exchange of protocols and tools, and co-creation of program resources. Updates and resources will be available on CQUIN’s website [cquin.icap.columbia.edu], in addition to related webinars and workshop reports.

## Appendix A: Design and Delivery of Interventions for High Risk Patients in National ART Guidelines

Country	Title of Guideline(s)	Recommendations for Patients Presenting w/ Advanced Disease	Recommendations for Unstable Patients on ART
<b>WHO</b>	Consolidated Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV infections, 2015	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>• Specifies clinical package, including: rapid ART initiation, screening for CrAg, toxoplasmosis (screening method not specified) and TB, OI management if indicated, IPT if indicated, CYX prophylaxis, “intensive follow up”</li> <li>• Also mentions “desirable” services, including pregnancy testing, HBV and HCV serology, screening for STIs, and assessment for NCDs</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>• Not specified, but implication is at health facility</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>• No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>• No specific guidance for this population</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>• Adherence and retention support</li> <li>• Viral load testing</li> <li>• Switch to second- or third-line ART if indicated</li> <li>• HIV drug resistance testing</li> <li>• OI screening and management. TB screening, diagnosis and treatment, CTX, IPT</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>• Not specified, but implication is at health facility</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>• No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>• No specific guidance for this population</li> </ul>
<b>Botswana</b>	Handbook of The Botswana 2016 Integrated HIV Clinical Guidelines	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>• In addition to standard recommendations, screening for CrAg, and CMV retinitis (via referral to ophthalmologist)</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>• No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>• Specifies that unstable patients must be seen by Medical Officer (not nurse)</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>• Specifies visit and lab schedule for unstable patients</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>• For patients with treatment failure, guideline specifies assessment for all non-resistance causes (e.g., non-adherence, incorrect dosing, drug-drug interaction, malabsorption, etc.) and retesting in 4-6 weeks</li> <li>• If not suppressed, repeat VL is recommended in another 4-6 weeks; if not trending down by at least one log, switch ART regimen</li> <li>• Specifies indications for viral resistance testing</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>• No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>• Specifies that unstable patients must be seen by medical officer (not nurse), suggests consultation with HIV Specialist</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>• Specifies visit and lab schedule for unstable patients</li> </ul>

Country	Title of Guideline(s)	Recommendations for Patients Presenting w/ Advanced Disease	Recommendations for Unstable Patients on ART
Kenya	Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV infections in Kenya, 2016 Edition	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>• Standard Package of Care (rapid initiation of ART, CrAg screening, screening and treatment for tuberculosis, or IPT as indicated, screening for toxoplasmosis, [method not specified], CTX)</li> <li>• Intensive follow up</li> <li>• Close monitoring for development of immune reconstitution inflammatory syndrome (IRIS)</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>• At any ART service delivery point; all facility levels</li> <li>• Initial management and ART initiation by trained and experienced HCW</li> <li>• Consultation with MDT, TWG, mentors, and senior clinicians as needed (including telephone consultation such as <i>Uliza! Clinicians' HIV Hotline</i>)</li> <li>• Referral to a higher-level facility when feasible if consultation is not adequate to stabilize the patient</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>• Initial management and ART initiation by trained and experienced HCW Consultation with MDT, TWG, mentors, and senior clinicians as needed (including telephone consultation such as <i>Uliza! Clinicians' HIV Hotline</i>)</li> <li>• Referral to a higher-level facility when feasible if consultation is not adequate to stabilize the patient</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>• Weekly follow-up until ART initiation, and then at week 2 and 4 after ART initiation, and then monthly until confirmed viral suppression</li> <li>• More frequent visits or hospitalization may be required to stabilize acute medical conditions and address psychosocial and other concerns</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>• Enhanced Adherence Counselling (EAC)</li> <li>• Enhanced Adherence Support Interventions (for patients failing or at high-risk of failing treatment)</li> <li>• Directly Observed Therapy (DOT) for patients with suspected/confirmed treatment failure</li> <li>• Special Support Groups for patients who failing treatment or who are on 2nd line ART.</li> <li>• Treatment preparation for 2nd Line or 3rd Line ART</li> <li>• Targeted counselling and education to prepare them for the new regimen and to support ongoing adherence</li> <li>• Organization of patients on 2<sup>nd</sup>/3rd line ART to be booked on the same day and seen by a dedicated MDT clinic.</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>• Clinician not specified, but notes that management of unstable patients on ART is multifaceted and may include: <ul style="list-style-type: none"> <li>- Care giver</li> <li>- Family member</li> <li>- Treatment buddy</li> <li>- Case manager</li> <li>- Special support groups such as putting patients with similar challenges into peer-support groups</li> <li>- Community support groups (CHWs, VHWs...)</li> <li>- MDT</li> </ul> </li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>• ART Clinics with trained HCWs</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>• For patients with an initial VL <math>\geq 1,000</math> copies/ml, the patient should have DOTs (somebody watching the patient actually swallow their medicine every day) to confirm good adherence for 3 months before repeating the viral load.</li> </ul>

Country	Title of Guideline(s)	Recommendations for Patients Presenting w/ Advanced Disease	Recommendations for Unstable Patients on ART
Lesotho	National Guidelines on the Use of Antiretroviral for HIV Prevention and Treatment, 5th Edition, 2016	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>Rapid ART initiation (ideally within 1 week if no OI present requiring delay), serum cryptococcal antigen screening test for all with CD4 &lt;100 cells/mm<sup>3</sup>, TB screening and prompt initiation of TB treatment TB-HIV coinfection, IPT for patients screening negative for TB, CXR in patients with advanced HIV, CTX prophylaxis, nutritional assessment and support</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>ART facilities: Low threshold for admitting patients presenting with advanced HIV to the hospital for stabilization, nutritional support, and observation during the initial stages of ART and any needed OI treatments.</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>Not specified, but notes need for intensive follow-up with more frequent clinical visits to rescreen for OIs and signs of IRIS.</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>Enhanced adherence counselling sessions as soon as treatment failure is identified and a minimum of 3 EAC sessions are recommended over a period of 8-12 weeks.</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>Patients with treatment failure should have close follow-up at the health facility and possibly the home.</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>HIV expert clinician</li> <li>Consultation with 2<sup>nd</sup> line committee</li> <li>Referral to community health workers; support groups; Community ART Groups (CAGS) (once eligible to join a CAG)</li> <li>Identifying supportive family/community members</li> <li>Nutritionist: Linkage to social support services – transportation, food</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>Not precisely specified—states that individuals with treatment failure should be evaluated regularly at frequent intervals by a MDT</li> </ul>
Namibia	National Guidelines for Antiretroviral Therapy Fourth Edition, 2014	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>

Country	Title of Guideline(s)	Recommendations for Patients Presenting w/ Advanced Disease	Recommendations for Unstable Patients on ART
Rwanda	National Guidelines for Prevention and Management of HIV and STIs, 2016	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population, notes that individuals with advanced disease are not eligible for visit spacing</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>Enhanced adherence counseling recommended for individuals with VL &gt;1000</li> <li>Guidance for 2<sup>nd</sup> and 3<sup>rd</sup> line ART regimens provided</li> <li>Genotypic recommended prior to 3<sup>rd</sup> line ART</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>
South Africa	National Consolidated Guidelines for the Prevention of Mother to Child Transmission of HIV (PMTCT) and the Management of HIV in Children, Adolescents and Adults, 2015	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>For patients with &lt;80% adherence at any visit and those with first VL &gt;1000 copies/ml. <ul style="list-style-type: none"> <li>The ART counsellor/nurse or doctor re-educates the patient, caregiver and their 'buddy' about the importance of adherence</li> <li>Evaluation of the support structures in place and how they can be improved; Encouraging patients to participate in a support groups</li> <li>Assessment for mental health issues/substance misuse</li> <li>Investigating the family situation through a social worker and actively address food security</li> </ul> </li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>Increasing home visits by therapeutic counsellors/patient advocates to daily or weekly at a minimum</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>There is <b>third-line review committee</b> set up to coordinate the management of patients failing on the second-line regimen.</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>

Country	Title of Guideline(s)	Recommendations for Patients Presenting w/ Advanced Disease	Recommendations for Unstable Patients on ART
Tanzania	National Guidelines for the Management of HIV and AIDS, 2015	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>
Uganda	Consolidated Guidelines for Preventing and Treating HIV Infections in Uganda, <i>Draft 2016</i>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>	<p><b>What?</b></p> <p>After assessment, and is non-suppressed PLHIV, repeat the VL test within 6 months after the last non-suppressed test. Within this period, the following should have been done:</p> <ul style="list-style-type: none"> <li>Contact the patient to return to facility within one week after facility receives results</li> <li>The facility ART Team should hold a case discussion on patients with non-suppressed VLs to determine possible causes of non-suppression.</li> <li>Discuss results with the patient and assess for barriers to adherence</li> <li>Do intensive adherence counseling support monthly for three months</li> <li>Repeat VL test one month after the last (3rd) intensive adherence counseling session.</li> <li>If the repeat VL is suppressed, follow the standard algorithm.</li> <li>If repeat VL is not suppressed, and the ART team is confident that the patient is adherent, then the patient is failing on the current ARV regimen and should be switched according to the guidance</li> </ul> <p>Intensive adherence counseling (IAC) is offered to patients with a non-suppressed viral load. IAC helps a client develop a comprehensive plan for adhering to ARVs by; identifying their barriers to adherence; gaining insight of the barriers, and exploring possible ways to overcome barriers and making a plan to adhere to medicine (5As).</p>



Country	Title of Guideline(s)	Recommendations for Patients Presenting w/ Advanced Disease	Recommendations for Unstable Patients on ART
Zambia	Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection 2016	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for individuals presenting with advanced disease, but clearly describes levels of referral</li> <li>All newly-diagnosed patients should be treated at health facility (not community) level</li> <li>ART initiation may take place at Health Centre level</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for individuals presenting with advanced disease</li> <li>Certified nurse/midwives can prescribe 1<sup>st</sup> line ART</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>Specifies ART regimen for selected co-morbidities, including renal insufficiency and severe mental illness</li> <li>Specifies algorithm for suspected treatment failure</li> <li>Specifies indications for referral to next level</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>Advanced Treatment Centres (ATCs) should manage complex and advanced patients, including those failing 2<sup>nd</sup> line ART; can also provide consultations to clinicians at other levels of the health system</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>Diverse cadres can prescribe second line ART with appropriate training and supervision (nurse prescribers, clinical officers, medical licentiates, medical officers); only medical specialists can prescribe 3<sup>rd</sup> line ART.</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>
Zimbabwe	Operational and Service Delivery Manual for Prevention, Care and Treatment of HIV in Zimbabwe, 2015	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>	<p><b>What?</b></p> <ul style="list-style-type: none"> <li>Counseling preparation for 2nd line</li> <li>Devising an Action Plan for clients with a first VL (targeted or routine) more than 1000 copies/ml</li> <li>Enhanced Adherence Counseling Notebooks</li> <li>Assessment of OIs</li> <li>Home visits and/or Community support</li> <li>Assigning a "Treatment Buddy"</li> <li>Establishing "Clinic Case Discussion" meetings</li> </ul> <p><b>Where?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>Who?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul> <p><b>When (visit frequency)?</b></p> <ul style="list-style-type: none"> <li>No specific guidance for this population</li> </ul>

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