

# Limitations to Treatment Safety and Efficacy

## Adherence to the Continuum of Care

Updated: March 23, 2023

Reviewed: March 23, 2023

Key Considerations and Recommendations
<ul style="list-style-type: none"><li>• Linkage to care and adherence to both antiretroviral therapy (ART) and clinic appointments should be regularly assessed.</li><li>• An individual's barriers to adherence to ART and appointments should be assessed before or shortly after the initiation of ART and regularly thereafter.</li><li>• Rapid access to ART has become a pillar of the United States plan to end the HIV epidemic, and delays in access to ART should be addressed and treatment initiated as soon as possible.</li><li>• People with HIV having ART adherence problems should be placed on regimens with high genetic barriers to resistance, such as dolutegravir, bictegravir, or boosted darunavir. Side effects, out-of-pocket costs, convenience, and patient preferences also need to be considered.</li><li>• Adherence to ART should be regularly assessed by self-report at every clinic visit.</li><li>• People with HIV having difficulties with adherence to appointments or ART should be provided additional adherence support using a constructive, collaborative, nonjudgmental, and problem-solving approach.</li><li>• The approach taken to improve adherence should be tailored to each person's needs and barriers to care. Approaches could include, but are not limited to—<ul style="list-style-type: none"><li>○ Changing ART to simplify dosing or to reduce side effects</li><li>○ Allowing flexible appointment scheduling</li><li>○ Finding resources to assist with treatment costs to maintain uninterrupted access to both ART and appointments</li><li>○ Linking patients to resources to assist with unmet social and economic needs, such as transportation, food, housing, and support services</li><li>○ Linking patients to counseling to overcome stigma, substance use, or depression</li></ul></li><li>• Multidisciplinary approaches to finding solutions to problems of adherence to ART and appointments are often necessary, including collaborations with nursing, pharmacy, social work, and case management (to the extent available). The clinician's role is to help the patient understand the importance of adherence to the continuum of care, identify the barriers to adherence and address those that are within their purview, and link the patient to resources to overcome other barriers.</li><li>• Single-tablet regimens are generally recommended when clinically appropriate, but high-quality evidence to definitively recommend them is lacking, and shared decision-making with patients is essential (BIII).</li><li>• At this time, evidence does not support the use of financial incentives to engage patients in ongoing routine care.</li><li>• Methods to estimate adherence based on drug levels measured in plasma, dried blood spots, urine, and hair samples are available. Measuring adherence with these methods has not been shown in randomized studies to improve outcomes. However, if these methods are used, it should be in a collaborative manner to avoid promoting an adversarial relationship between the provider and patient.</li><li>• The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends against the use of long-acting ART in people who have detectable viral load due to suboptimal adherence to ART and in people who have ongoing challenges with retention in HIV care, except in a clinical trial (AIII).</li><li>• A summary of best practice interventions to improve linkage, retention, and adherence can be found at the Centers for Disease Control and Prevention's <a href="#">Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention</a>.</li></ul>
<p><b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Weak</p> <p><b>Rating of Evidence:</b> I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion</p>

## ***Introduction***

HIV treatment adherence includes initiating care with an HIV provider (linkage to care), regularly **engaging in** appointments (retention in care), and adhering to antiretroviral therapy (ART). The concept of a “continuum of care” has been used to describe the process of HIV testing, linkage to HIV care, initiation of ART, adherence to ART, retention in care, and virologic suppression.<sup>1-3</sup> The Centers for Disease Control and Prevention (CDC) estimates that HIV has not yet been diagnosed in about 13% of the people with HIV in the United States. **Based on 2019 data,** about 81% of individuals are linked to care within 30 days after receiving an HIV diagnosis. However, only **58%** of people with diagnosed HIV are retained in HIV care. It is estimated that only approximately 66% of people with diagnosed HIV are virally suppressed due to poor adherence to the continuum of care and to ART.<sup>4,5</sup> The data for adolescents and young adults **aged 13 to 14 years** are even more sobering: only 51% of youth with HIV receive a diagnosis, **79%** are linked to care within 1 month, and **59%** are retained in care. Outcomes along the continuum of care also vary by geographic region and other population characteristics, such as sex, race and ethnicity, and HIV risk factors.<sup>4</sup> To achieve optimal clinical outcomes and to realize the potential public health benefit of treatment as prevention, adherence to each step in the continuum of care is critical.<sup>6</sup> It is also important to realize that retention and adherence are not static states. Life events, changes in insurance status, comorbid conditions, and health system changes can cause people to shift back and forth on the continuum. Knowledgeable providers and high-quality system processes are vital in promoting rapid linkage and sustained retention in care and adherence to ART. **Finally, clinicians should recognize that adherence is a complex behavior requiring knowledge, motivation, memory, behavior change, external resources, and successful and persistent interaction with complex and, sometimes, challenging health care systems.**<sup>7-9</sup> The patient–provider relationship is central to improving patient engagement and adherence to treatment. **Providers must recognize that adherence is a collaborative effort between patients and their providers.**

This section provides guidance on linking patients to care, assessing and improving retention in care, and assessing and improving adherence to ART. The CDC maintains a [Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention](#) to improve linkage, retention, and adherence. In addition, a number of other groups and organizations have provided guidance for improving adherence to the steps in the care continuum.<sup>6,10</sup>

## ***Linkage to Care***

Receiving a diagnosis of HIV infection can be traumatic, and linkage to care efforts must be delivered with compassion and persistence. The time from diagnosis to linkage to care can be affected by many factors, including insufficient socioeconomic resources, active substance use, mental health problems, stigma, and disease severity (symptomatic HIV is associated with more successful linkage).<sup>11-15</sup> In the United States, youth, people who use injection drugs, and Black/African American persons have lower rates of linkage to care.<sup>4</sup> Some health system factors have also been associated with linkage success or failure. Co-location of testing and treatment services<sup>14</sup> and active linkage services (e.g., assisting the patient in setting up appointments, maintaining an active relationship with the patient until linkage is completed, providing linkage case management services)<sup>16-18</sup> bolster linkage to care. Conversely, passive linkage (e.g., only providing names and contact information for treatment centers) is associated with lower linkage to care.

## Monitoring Linkage to Care

Linking to HIV care after a new diagnosis of HIV infection is defined as completing an outpatient appointment with a clinical provider who has the skills and ability to treat HIV infection, including prescribing ART. Patients should be linked to care as soon as possible after diagnosis with HIV, preferably within 30 days. Monitoring linkage is a critical responsibility so that interventions can effectively reach people who are not linked to care. If the facilities that diagnose and treat an individual are the same or share the same electronic medical record system, it is relatively straightforward to monitor linkage to care. Monitoring linkage for people whose HIV is diagnosed outside the treatment provider's health care system is difficult and generally is the responsibility of the diagnosing provider or entity and the public health authority. However, once a patient makes contact with the treating clinical system, he or she should be engaged in linkage efforts and monitored for successful linkage to and retention in HIV care.

## Improving Linkage to Care

Strategies to improve linkage to care are summarized in Table 19 below. Linkage efforts should include immediate referral to care at diagnosis, appointment reminders, and outreach efforts if needed.<sup>16</sup> The only intervention shown to increase linkage to care in a randomized trial conducted in the United States is the Anti-Retroviral Treatment and Access to Services (ARTAS) intervention.<sup>17</sup> ARTAS is a strength-based intervention that aims to facilitate linkage to and retention in care for people with recently diagnosed HIV. The ARTAS intervention was tested in four cities and enrolled a diverse group of people. The participants in the ARTAS intervention trial were randomized to either an intervention arm or a control arm. Participants randomized to the control arm received information about HIV and care resources and a referral to a local HIV medical provider. Each participant in the intervention arm worked with an ARTAS interventionist for five sessions, 90 days, or until linkage—whichever came first. The interventionist helped participants to identify and use their strengths, abilities, and skills to link to HIV care; participants were also linked to community resources. Linkage to care, defined as completing at least one visit with an HIV clinician within the first 6 months, was greater among the ARTAS participants than the control participants (78% vs. 60%, adjusted risk ratio [RR] = 1.36,  $P < 0.001$ ). Furthermore, a greater percentage of ARTAS participants were retained in care, defined as visiting an HIV clinician at least once in each of the first two 6-month blocks after enrollment (64% vs. 49% for ARTAS and control participants, respectively; adjusted RR = 1.41,  $P = 0.006$ ). The results from the ARTAS intervention have been replicated in a community-based study.<sup>18</sup> The CDC supports free training in the ARTAS intervention. Other studies support the importance of post-test counseling to educate, motivate, and present positive messages about living with HIV,<sup>19</sup> peer support,<sup>20</sup> and engaging with the patient at the clinic in advance of the visit with the provider.<sup>21</sup> Financial incentives did not increase linkage to care within 90 days in a large randomized trial.<sup>22</sup>

## Retention in Care

Poor retention in HIV care is associated with greater risk of death.<sup>23,24</sup> Poor retention is more common in people who use substances, have serious mental health problems, have unmet socioeconomic needs (e.g., housing, food, transportation), lack financial resources or health insurance, have schedules that complicate adherence, have been recently incarcerated, or face stigma.<sup>25-28</sup> At the provider and health system level, low trust in providers and a poor patient-provider relationship have been associated with lower retention, as has lower satisfaction with the clinic experience.<sup>29-31</sup> Availability of appointments and timeliness of appointments (i.e., long delay

from the request for an appointment to the appointment's date) and scheduling convenience are also factors.

## Monitoring Retention in Care

Retention in care should be routinely monitored.<sup>6</sup> There are various ways to measure retention, including measures based on attended visits over a defined period of time (constancy measures) and measures based on missed visits.<sup>32</sup> Both approaches are valid and independently predict survival.<sup>33</sup> Missed visits and a prolonged time since the last visit are relatively easy to measure and should trigger efforts to retain or re-engage a person in care. Constancy measures (e.g., at least two visits that are at least 90 days apart over 1 year or at least one visit every 6 months over the last 2 years) can be used as clinic quality assurance measures.

## Improving Retention in Care

Strategies to improve retention in care are summarized in Table 19 below. The Retention through Enhanced Personal Contact (REPC) intervention was tested in a randomized trial in six clinics in the United States. The study enrolled people with HIV who had a history of inconsistent clinic attendance. Intervention relied on personal contact by an interventionist with at-risk patients. It included a brief face-to-face meeting upon returning to care and at each subsequent clinic visit, plus three types of phone calls: to check on patients between visits, to provide appointment reminders just before visits, and to attempt to reschedule missed visits. REPC resulted in small but significant improvements in retention in care, including in racial/ethnic minority populations and in people with detectable plasma HIV RNA.<sup>34</sup> In-clinic opioid replacement therapy helps opioid users remain in care.<sup>35</sup> An intervention using the electronic medical record to alert providers when patients had suboptimal follow-up or high viral loads also improved retention in care.<sup>36</sup>

Telehealth has emerged as an important modality to see and retain patients during the COVID-19 pandemic. A cluster-randomized study conducted in the Department of Veterans Affairs health facilities before the pandemic showed that the availability of telehealth resulted in improvements in viral suppression and the number of completed visits.<sup>37</sup> Reengaging and retaining people who are out-of-care remains particularly challenging. Patient navigation for out-of-care people with HIV in a New York City Medicaid health plan resulted in faster re-linkage to care but not improved retention in care.<sup>38</sup> In two randomized trials involving out-of-care, hospitalized patients with HIV, peer counselors and patient navigators did not improve re-linkage to care after hospital discharge.<sup>39,40</sup> In the only U.S.-based randomized study to test a “data to care” approach, which uses clinic and public health data to reach and reengage out-of-care people with HIV, the intervention did not result in significantly faster time to re-linkage or viral suppression.<sup>41</sup>

Data from nonrandomized studies are less conclusive, but there are many interventions that bear mentioning. Clinic-wide marketing (e.g., posters, brochures) and customer service training of patient-facing staff to promote attending scheduled visits and provide patients a welcoming and courteous experience have improved retention.<sup>42</sup> New patients who rated higher their experience with their doctor were more likely to stay in care.<sup>43</sup> Stepped case management and social and outreach services,<sup>44</sup> including mobile health applications that enhance communication and provide support, are beneficial, although the applications that have been developed and studied are not available for widespread public use. “Data to care” approaches have helped in some jurisdictions while yielding mixed results in others,<sup>45-47</sup> and they require substantial resources, and privacy concerns also must be adequately addressed. As noted above, a “data to care” approach did not improve outcomes in a

randomized controlled trial. Differentiated care approaches reduce the need for appointments and other expectations for patients doing well and allow extra resources to be devoted to patients not doing well. The evidence to support the use of differentiated care is strongest in low-resource settings, whereas in the United States, the evidence is limited to observational data, which suggest the approach has beneficial impact.<sup>48</sup>

Overall, these data support the concept that all clinic personnel, from the facilities staff to nurses to providers, play important roles in supporting retention in care by providing the optimal patient care experience, constructively affirming attendance rather than criticizing nonattendance, and collaboratively solving problems with patients to overcome barriers to care.<sup>30,34,42</sup> Flexible appointment schedules, expanded clinic hours, and copay and other financial or insurance assistance—such as that provided by the Ryan White HIV/AIDS Program—will also provide patients with uninterrupted access to clinical care. Patient navigation, telehealth, and engaging with patients through mobile health applications are likely to improve outcomes, although the evidence is not sufficient to support their use unequivocally.

The use of financial incentives or rewards to promote retention in care has been studied. A large study randomized clinic sites to financial incentives or standard of care. At baseline, 45% of the patients were retained in care in these clinics. The relative increase in the proportion of participants retained in care was 9% higher in clinics offering incentives than in standard-of-care clinics. Viral suppression also improved 4% at financial incentive clinics, from a baseline of 62%.<sup>22</sup> Evidence from a *post hoc* analysis of a subset of the sites involved in that trial shows a reduced but persistent improvement in retention in care after withdrawal of the incentives without a persistent effect on viral suppression.<sup>49</sup> In another large, randomized study of persons out of care and hospitalized, financial incentives plus patient navigation did not lead to sustained improvement in retention or viral load suppression over that achieved with standard care.<sup>39</sup> Data are not strong enough to support the routine use of financial incentives, and they, therefore, remain experimental for use in routine care at this time.

### ***Adherence to Antiretroviral Therapy***

Adherence to ART can be influenced by a number of factors, including the patient's social situation and clinical condition, the prescribed regimen, and the patient–provider relationship.<sup>50</sup> Poor adherence is often a consequence of one or more behavioral, structural, and psychosocial barriers (e.g., depression and other mental illnesses, neurocognitive impairment, low health literacy, low levels of social support, stressful life events including trauma, busy or unstructured daily routines, active substance use, homelessness, poverty, nondisclosure of HIV serostatus, denial, stigma, inconsistent access to medications due to financial and insurance status).<sup>51-54</sup>

Characteristics of one or more components of the prescribed regimen can affect adherence. Once-daily regimens,<sup>55</sup> including those with low pill burden (even if not one pill once daily), without a food requirement, and few side effects or toxicities, are associated with higher levels of adherence.<sup>56,57</sup> Single-tablet regimens (STRs) that include all antiretroviral (ARV) drugs in one pill taken once daily are easier for people to use. However, data to support or refute the superiority of an STR versus a once-daily multi-tablet regimen (MTR), as might be required for the use of some generic-based ARV regimens, are limited. Comparisons of these regimens are hampered because not all drugs and classes are available as STRs. There are demonstrated beneficial effects on virologic suppression in switch studies, in which persons on an MTR are randomized to stay on an MTR or switch to an STR.<sup>58</sup> Whether an STR is beneficial in people with HIV who are ART-naïve is not

known, with observational cohort studies showing benefit of a once-daily STR versus a once-daily MTR.<sup>57,59-62</sup> On the other hand, observational data from Spain showed that coformulated dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) resulted in similar viral suppression compared to DTG plus ABC/3TC when used both at treatment initiation and when people with viral suppression on STR were switched to the two-pill formulation as a cost-saving strategy.<sup>63</sup> Given these findings and their wide availability, STRs are generally recommended when clinically appropriate, but high-quality evidence to definitively recommend them is lacking, and shared decision-making with patients is essential (**BIII**).

Characteristics of the clinical setting can also have important structural influences on the success or failure of medication adherence. Settings that provide comprehensive multidisciplinary care (e.g., by case managers, pharmacists, social workers, mental health and substance use providers) support patients' complex needs, including their medication adherence-related needs. Treatment programs for substance use may offer services that promote adherence, such as directly observed therapy (DOT).

### **Monitoring Adherence to Antiretroviral Therapy**

Adherence to ART should be assessed and addressed in a constructive and nonjudgmental manner at every clinic visit. Given the potency of contemporary ART, a detectable viral load identified during chronic care for a patient with stable access to ART is most likely the result of poor adherence. Patient self-report, the most frequently used method for evaluating medication adherence, remains a useful tool. Carefully assessed patient self-report of high-level adherence to ART has been associated with favorable viral load responses.<sup>64-66</sup> Patient admission of suboptimal adherence is highly correlated with poor therapeutic response. The reliability of self-report often depends on how the clinician elicits the information. It is most reliable when ascertained in a simple, nonjudgmental, routine, and structured format that normalizes less-than-perfect adherence and minimizes socially desirable responses. To allow patients to disclose lapses in adherence, some experts suggest inquiring about the number of missed doses during a defined time period. For example, for a patient with a detectable viral load, a provider might state, "I know it is difficult to take medicine every day. Most people miss doses at least sometimes. Thinking about the last 2 weeks, how many times have you missed doses? Please give me a rough estimate so I can help you take the best care of yourself." Other research supports simply asking patients to rate their adherence during the last 4 weeks on a 5- or 6-point Likert scale<sup>67,68</sup> or using qualitative response categories.<sup>66</sup>

Other measures of adherence include pharmacy records and pill counts. Pharmacy records can be valuable when medications are obtained exclusively from a single source. Because pill counts can be altered by patients, are labor intensive, and can be perceived as confrontational, they are generally not used in routine care. Other methods of assessing adherence include the use of therapeutic drug monitoring and electronic measurement devices. However, these methods are costly and are generally reserved for research settings. Finally, methods to estimate adherence based on drug levels measured in plasma, dried blood spots, urine, and hair samples are available.<sup>69</sup> Some of these are commercially available, but none have been shown in randomized studies to improve outcomes. However, if these methods are used, it should be in a collaborative manner to avoid promoting an adversarial relationship between the provider and patient.

### **Improving Adherence to Antiretroviral Therapy**

Strategies to improve adherence to ART are summarized in Table 19 below. Just as they support retention in care, all health care team members play integral roles in successful ART adherence

programs.<sup>65,70-72</sup> An increasing number of interventions have proven effective in improving adherence to ART (for descriptions of the interventions, see the CDC's [Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention](#)). These interventions can be customized to suit a range of needs and settings. Many interventions that have been found to be efficacious in randomized trials require specialized training and resources before they can be implemented in routine care, and this has limited their impact. Nonetheless, these interventions have contributed to our knowledge in developing general principles of improving and maintaining adherence.

It is important that each new patient receives and understands basic information about HIV infection, including the goals of therapy (achieving and maintaining viral suppression, which will decrease HIV-associated complications and prevent transmission), the prescribed regimen (including dosing schedule and potential side effects), the importance of adherence to ART, and the potential for the development of drug resistance as a consequence of suboptimal adherence. Patients must also be positively motivated to initiate therapy, which can be assessed by simply asking patients if they want to start treatment for HIV infection. Clinicians should assist patients in identifying facilitating factors and potential barriers to adherence and develop multidisciplinary plans to attempt to overcome those barriers. Processes for obtaining medications and refills should be clearly described. Transportation to pharmacy and clinic visits should be assessed with linkage to appropriate services as needed. Plans to ensure uninterrupted access to ART via insurance, copay assistance, pharmaceutical company assistance programs, or AIDS Drug Assistance Programs (ADAP), for example, should be made and reviewed with the patient. Much of this effort to inform, motivate, and reduce barriers can be achieved by nonphysician members of the multidisciplinary team and can be accomplished concomitant with, or even after, starting therapy.<sup>73-76</sup> While delaying the initiation of ART is rarely indicated, some patients may not be comfortable starting treatment. Patients expressing reluctance to initiate ART should be engaged to understand and overcome barriers to ART initiation. Although homelessness, substance use, and mental health problems are associated with poorer adherence, they are not predictive enough at the individual level to warrant withholding or delaying therapy given the simplicity, potency, and tolerability of contemporary ART. Rapid ART initiation at the time of HIV diagnosis has been pursued as a strategy to increase viral load suppression and retention in care, but safety data, data on intermediate or long-term outcomes, and data from randomized controlled trials conducted in high-resource settings are currently lacking.<sup>73-76</sup> In low-resource settings, data from randomized trials suggest that rapid ART probably increases ART use and viral suppression at 12 months, but data on other important outcomes—such as retention in care, regimen switching, and mortality—are not sufficient to draw conclusions.<sup>77,78</sup> Rapid access to ART has become a pillar of the United States plan to end the HIV epidemic, and delays in access to ART should be addressed.<sup>79</sup> For more details, see [Initiation of Antiretroviral Therapy](#).

Successful treatment requires a regimen that the patient can adhere to.<sup>80,81</sup> It is important to consider the patient's daily schedule; tolerance of pill number, size, and frequency; and any issues affecting absorption (e.g., use of acid-reducing therapy, food requirements). As reviewed above, STRs have been associated with high rates of adherence. People with risk factors for poor adherence or a history of poor adherence should be offered regimens with high genetic barriers to resistance, if clinically appropriate. With the patient's input, a medication choice and administration schedule should be tailored to their daily activities. Clinicians should explain to patients that their first regimen is usually the best option for a simple regimen, which affords long-term treatment success. Establishing a trusting patient-provider relationship and maintaining good communication will help to improve adherence and long-term outcomes. Medication taking can also be enhanced using medication reminder aids. The evidence is strongest for text messaging, but pill box monitors, pill boxes, and alarms may also improve adherence.<sup>82-86</sup>

Positive reinforcement can greatly help patients maintain high levels of adherence. This technique to foster adherence includes informing patients of their low or suppressed viral load and increases in CD4 T lymphocyte cell counts. Motivational interviewing has also been used with some success.<sup>87-89</sup> Other effective interventions include nurse home visits, a five-session group intervention, and couples- or family-based interventions. Interventions involving several approaches are generally more successful than single-strategy interventions, and interventions based on cognitive behavioral therapy and supporter interventions have been shown to improve viral suppression.<sup>90</sup> Problem-solving approaches that vary in intensity and culturally tailored approaches also are promising.<sup>89,91,92</sup> To maintain high levels of adherence in some patients, it is important to provide therapy for substance use and mental health and to strengthen social support. DOT has been effective in providing ART to active drug users<sup>93</sup> but not to patients in a general clinic population<sup>94</sup> or in home-based settings with partners responsible for DOT.<sup>95,96</sup> The use of incentives or rewards to promote adherence has been studied, and they have been shown to improve adherence in one study conducted by the HIV Prevention Trials Network (HPTN)<sup>22</sup> and reduce viral load in another study that required very frequent viral load measurement and incentives.<sup>97</sup> Although the durability and feasibility of financial incentives are limited and behavior change is generally not sustained after the incentives are withdrawn, the HPTN study did find some evidence of sustained effect after 9 months.<sup>49</sup> Data are too limited to support the use of financial rewards for adherence in routine care.<sup>39,98,99</sup>

### ***Long-Acting Antiretroviral Therapy***

A long-acting ART (LA-ART) regimen (intramuscular cabotegravir and rilpivirine) has been studied and approved for use in populations with viral suppression. There are no data on the safety and efficacy of using LA-ART in people who currently do not have suppressed HIV replication. The long pharmacologic tail of LA-ART after last dose raises concerns for the emergence of resistant mutations in people who discontinue therapy without rapidly transitioning to an oral therapy. The Panel on Antiretroviral Guidelines for Adults and Adolescents, therefore, **recommends against the use of LA-ART in people who have detectable viral load due to suboptimal adherence to ART and in people who have ongoing challenges with retention in HIV care except in the context of a clinical trial (AIII).**

### ***Conclusion***

Clinicians can and must obtain relatively accurate information about a patient's adherence and barriers to ART and appointment adherence, and then engage patients in a productive conversation rather than simply telling patients to be adherent and offering warnings about what might ensue with continued poor adherence. The latter approach fails to acknowledge a patient's barriers to adherence, fails to provide the patient with actionable information, erodes rather than builds the patient-provider relationship, and has been demonstrated to not improve adherence.<sup>100,101</sup> At the same time, however, many of the interventions shown to improve adherence are difficult to implement in routine care. Nonetheless, effective lessons from this body of research can be applied to routine care to improve linkage to care, adherence to ART, and adherence to appointments. These lessons include the following:

- Regularly assess adherence to ART and appointments.
- Engage a patient who is struggling with adherence at any step on the care continuum with a constructive, collaborative, nonjudgmental, and problem-solving approach rather than reprimanding them or lecturing them on the importance of adherence.



- Elicit an individual's barriers to adherence, which may include personal, behavioral, medical, or structural barriers (e.g., substance use, housing instability, stigma, lack of transportation); clinic barriers (e.g., limited clinic hours, processes that make it more difficult to obtain prescriptions or schedule appointments); and system barriers (e.g., copays, prior approvals, processes that complicate maintaining pharmacy benefits or obtaining refills).
- Tailor approaches to improve adherence to an individual's needs and barriers, for example, by changing ART to simplify dosing or reduce side effects, finding resources to assist with copays or other out-of-pocket costs (see Table 19 **below**) to maintain an uninterrupted supply of ART and access to clinicians, or linking patients to counseling to overcome stigma, substance use, or depression.
- Place patients with apparent ART adherence problems on regimens with high genetic barriers to resistance, such as DTG, bictegravir, or boosted-darunavir regimens. When selecting the regimen, consider possible side effects, out-of-pocket costs, convenience, and patient preferences, because the only regimen that will work is the one the patient can obtain and is willing and able to take.
- Understand that multidisciplinary approaches and time to understand and address barriers are needed in many situations, and that the clinician's role is to help the patient to understand the importance of adherence to the continuum of care and identify any barriers to adherence, address those that are within their immediate purview, and link the patient to resources to overcome other barriers.

**Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy**

Strategies	Examples
Provide an accessible, trustworthy, nonjudgmental multidisciplinary health care team.	<ul style="list-style-type: none"> <li>• Include care providers, nurses, social workers, case managers, pharmacists, medication managers, and administrative staff on the care team; train all members on providing compassionate and patient-centered care.</li> </ul>
Strengthen early linkage to care and retention in care.	<ul style="list-style-type: none"> <li>• Encourage health care team participation in linkage to and retention in care.</li> <li>• Use ARTAS training (if available).</li> <li>• Actively support linkage to care with assistance in making appointments and linkage to services to overcome barriers to care.</li> <li>• Streamline Ryan White HIV/AIDS Program eligibility verification processes for uninsured and underinsured clients.</li> </ul>
Evaluate the patient's knowledge about HIV infection, prevention, and treatment and, based on this assessment, provide HIV-related information.	<ul style="list-style-type: none"> <li>• Keeping the patient's current knowledge base in mind, provide information about HIV, including the natural history of the disease, HIV viral load and CD4 count and expected clinical outcomes according to these parameters, therapeutic and prevention consequences of poor adherence, and importance of staying in HIV care.</li> </ul>
Identify facilitators, potential barriers to adherence, and necessary medication management skills both when starting ART and on an ongoing basis.	<ul style="list-style-type: none"> <li>• Assess the patient's cognitive competence and impairment.</li> <li>• Assess behavioral and psychosocial challenges, including depression, mental illnesses, trauma, levels of social support, levels of alcohol consumption and current substance use, nondisclosure of HIV serostatus, and stigma.</li> <li>• Identify and address language and literacy barriers.</li> <li>• Assess beliefs, perceptions, and expectations about taking ART (e.g., impact on health, side effects, disclosure issues, consequences of poor adherence).</li> <li>• Ask about medication-taking skills and foreseeable challenges with adherence (e.g., past difficulty keeping appointments, adverse effects from previous medications, issues managing other chronic medications, need for medication reminders and organizers).</li> <li>• Assess structural issues, including unstable housing, lack of income, unpredictable daily schedule, lack of prescription drug coverage, lack of continuous access to medications, and transportation problems.</li> </ul>
Provide needed resources.	<ul style="list-style-type: none"> <li>• Provide or refer for mental health and/or substance use treatment.</li> <li>• Provide resources to obtain prescription drug coverage (e.g., <a href="#">AIDS Drug Assistance Programs (ADAPs)</a>, <a href="#">Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs</a>).</li> <li>• Assist patients during insurance enrollment periods to facilitate enrollment in plans that cover antiretrovirals.</li> <li>• Provide resources about stable housing, social support, transportation assistance, and income and food security.</li> </ul>

**Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy**

Strategies	Examples
Involve the patient in ARV regimen selection.	<ul style="list-style-type: none"> <li>• Review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of poor adherence.</li> <li>• Assess daily activities and tailor regimen to predictable and routine daily events.</li> <li>• Consider preferential use of PI/r-based or DTG-based or BIC-based ART if poor adherence is anticipated.</li> <li>• Consider use of STR or fixed-dose-combination formulations to reduce pill burden.</li> <li>• Consider use of long-acting injectables in people with suppressed viral load if clinically appropriate.</li> <li>• Assess if the cost or copayment for drugs will affect adherence and access to medications.</li> </ul>
Assess adherence at every clinic visit.	<ul style="list-style-type: none"> <li>• Monitor viral load as a strong biologic measure of adherence.</li> <li>• Use a simple behavioral rating scale or self-reported assessment.</li> <li>• Employ a structured format that normalizes or assumes less-than-perfect adherence and minimizes socially desirable or “white-coat adherence” responses.</li> <li>• Ensure that other members of the health care team also assess and support adherence.</li> </ul>
Use positive reinforcement to foster adherence success.	<ul style="list-style-type: none"> <li>• Inform patients of benefits of low or nondetectable levels of HIV viral load (e.g., “Undetectable = Untransmittable”) and increases in CD4 cell counts.</li> <li>• Thank patients for attending their appointments.</li> </ul>
Identify the type of and reasons for poor adherence and target ways to improve adherence.	<ul style="list-style-type: none"> <li>• Failure to understand dosing instructions.</li> <li>• Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy).</li> <li>• Pill aversion or pill fatigue.</li> <li>• Adverse effects.</li> <li>• Inadequate understanding of drug resistance and its relationship to adherence.</li> <li>• The patient is unaware of appointments, or appointments are not scheduled with proper patient input.</li> <li>• Cost-related issues (e.g., copays for medications or visits, missed work time).</li> <li>• Depression, drug and alcohol use, homelessness, or poverty.</li> <li>• Stigma of taking pills or attending HIV-related appointments.</li> <li>• Nondisclosure of status or privacy concerns leading to missed doses, refills, or appointments.</li> </ul>

**Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy**

Strategies	Examples
Select from among available effective adherence and retention interventions.	<ul style="list-style-type: none"> <li>• See the CDC’s <a href="#">Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention</a> for a summary of best practice interventions to improve linkage, retention, and adherence.</li> <li>• Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms).</li> <li>• Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance, pharmacy delivery).</li> <li>• Use patient prescription assistance programs (see above in the table, under “Provide needed resources”).</li> <li>• Use motivational interviews.</li> <li>• Provide outreach for patients who drop out of care.</li> <li>• Use peer or paraprofessional treatment navigators.</li> <li>• Recognize positive clinical outcomes resulting from better adherence.</li> <li>• Arrange for DOT for persons in substance use treatment (if feasible).</li> <li>• Enhance clinic support and structures to promote linkage and retention (e.g., reminder calls, flexible scheduling, open access, active referrals, improved patient satisfaction).</li> <li>• Offer telehealth services for primary care, as well as supportive services when appropriate.</li> </ul>
Systematically monitor retention in care.	<ul style="list-style-type: none"> <li>• Record and follow up on missed visits.</li> </ul>

**Key:** ART = antiretroviral therapy; ARTAS = Anti-Retroviral Treatment and Access to Services; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; DOT = directly observed therapy; DTG = dolutegravir; PI/r = ritonavir-boosted protease inhibitor; STR = single-tablet regimen

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