Adherence to Antiretroviral Therapy in Children and Adolescents With HIV

Updated: September 30, 2025
Reviewed: September 30, 2025

Panel's Recommendations
• Strategies to maximize adherence should be discussed before and/or at initiation of antiretroviral therapy (ART) and before changing regimens (AIII). • Adherence to ART must be assessed and promoted at each visit, and strategies to maintain and/or improve adherence must be continually explored (AIII). • In addition to viral load monitoring, at least one other method of measuring adherence to ART should be used (AIII). • To facilitate adherence, simplified oral ART regimens (e.g., once daily, low pill burden) should be prescribed whenever feasible (AII*). • The option of long-acting injectable ART to facilitate and support adherence should be discussed with eligible children and adolescents and their caregivers (AIII).
Rating of Recommendations: A = Strong; B = Moderate; C = Optional *Rating of Evidence: I = One or more randomized trials in children† with clinical outcomes and/or validated endpoints; I* = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children† from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies in children† with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies in adults with long-term clinical outcomes with accompanying data in children† from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion* *† Studies that include children or children/adolescents, but not studies limited to postpubertal adolescents*

Background

Adherence to antiretroviral therapy (ART) is a principal determinant of virologic suppression. Suboptimal adherence may include missed or late doses, treatment interruptions and discontinuations, and subtherapeutic or partial dosing. Poor adherence will result in subtherapeutic plasma antiretroviral (ARV) drug concentrations, facilitating the development of resistance to one or more drugs in a given ARV regimen and possible cross-resistance to other drugs in the same class. Multiple factors—including regimen potency, pharmacokinetics, drug interactions, viral fitness, and the genetic barrier to ARV resistance—influence the adherence–resistance relationship.[1-3] In addition to compromising the efficacy of the current regimen, suboptimal adherence can limit the options for future effective ARV drug regimens in people who develop multidrug-resistant HIV; it also can increase the risk of secondary transmission of drug-resistant virus. Chronic nonadherence and persistent viremia can lead to immune dysfunction and clinical complications (see Recognizing and Managing Antiretroviral Treatment Failure).

With modern ART, the level of adherence needed to achieve viral suppression may be as low as 80% to 85%.[4, 5] However, emerging data indicate that less than 100% ARV adherence is associated with negative immunologic and clinical effects, even if the level of adherence is sufficient to achieve and sustain viral suppression.[6-9] A recent modeling analysis of data from studies in adults found that increasing adherence in persons who are virally suppressed could further reduce the risk of severe

non-AIDS events and death.[9] These data point out the need to prioritize addressing and maximizing adherence at visits for all children and adolescents, even those with viral suppression.

Poor adherence to ARV drugs is commonly encountered in the treatment of children and adolescents with HIV. Medication formulation and palatability, frequency of dosing, side effects, drug toxicities, and a child's age and developmental stage can affect adherence. In addition, many psychosocial, behavioral, and structural barriers for children and caregivers have also been associated with inadequate adherence. No consistent predictors of either good or poor adherence in children have been identified.[10-12] However, findings from the U.S. Pediatric HIV/AIDS Cohort Study (or PHACS) demonstrated that the prevalence of nonadherence increased with age. Among 381 children and adolescents with perinatally acquired HIV (PHIV), the prevalence of nonadherence increased from 31% to 50% ($P < 0.001$), and the prevalence of unsuppressed viral loads increased from 16% to 40% ($P < 0.001$) between preadolescence and late adolescence/young adulthood.[13] Similarly, in a report from the Early Pediatric Initiation Canada Cure Cohort, only 73% of the children with PHIV initiated on ART maintained viral suppression 3 years after it was first achieved.[14] Furthermore, several studies have demonstrated that adherence is not static and can vary with time on treatment.[15] In particular, adolescents often struggle to sustain adherence over time. In a study of 933 adolescents in South Africa aged 10 to 19 years who were followed for a 3- to 4-year period, adherence was assessed at baseline and two subsequent times via self-report of previous week ART adherence. Only 37% of participants reported consistent adherence at all three assessments. Both older age ($P = 0.007$) participants and those with horizontally acquired HIV ($P = 0.002$) were more likely to report inconsistent adherence across the three assessments.[16] These findings illustrate the difficulty of maintaining high levels of adherence and underscore the need to support children and their caregivers in developing strategies for long-term adherence to ART.

Specific Adherence Issues in Children

Adherence is a complex health behavior that is influenced by drug regimen, child and family factors, and the patient–provider relationship.[17, 18] Despite improvements over the last several years, the availability of once-daily, single-tablet ARV regimens and palatable formulations for infants and young children are still limited. Furthermore, infants and children are dependent on others for medication administration; adult caregivers may face barriers that undermine adherence in children, including forgetting doses, changes in routine, being too busy, and child refusal.[19, 20] Caregivers also may be inadequately prepared to support their child's adherence. In a study of communication strategies among caretakers of children with PHIV in rural South Africa, many caregivers used coercion and threats of grave consequences of nonadherence as a communication strategy to enforce adherence.[21] Some caregivers may place too much responsibility for managing medications on older children and adolescents before they are developmentally able to undertake such tasks.[22]

Adherence also may be jeopardized by social and health issues within a family (e.g., substance use, poor physical or mental health, death of a family member or friend, unstable housing, poverty, violence, involvement with the criminal justice system, limited social support).[23-26] Because stressful life events can disrupt adherence,[13] additional monitoring and adherence supports should be implemented at these times. Furthermore, children with PHIV and adolescents with non–perinatally acquired HIV typically enter care at different developmental stages with potentially different levels of caregiver support, which can affect adherence to ART in different ways. For adolescents transitioning from pediatric to adult care, the transition can be a vulnerable time for adherence. Such factors as changing providers, navigating the health care system as the primary medical decision-maker, and changes in insurance status and prescription access can precipitate interruptions in ART and barriers to optimal adherence. Immigrant children and families—particularly those who have

recently immigrated—may face social and cultural issues and language barriers, which can affect adherence.

Adherence Assessment and Monitoring

Providers should begin assessing potential barriers to adherence and discussing the importance of adherence at initiation of ART and when changing an ARV regimen. Evaluations should assess psychosocial and behavioral factors that may influence adherence, and interventions to help decrease these barriers should be supported. Providers should ask children and adolescents about their experiences with taking medications, as well as concerns and expectations about treatment, or address these issues with caregivers if the child is too young to engage in the conversation. Prior to treatment, it is important that the child/adolescent and/or caregiver explicitly agree to the treatment plan, which should include strategies to support adherence. It is also important to alert children/adolescents and caregivers to potential adverse effects (AEs) of ARV drugs (e.g., nausea, headaches, abdominal discomfort, sleep disturbances), explain how they can be managed, and emphasize the importance of informing the clinical team if they occur.

A routine adherence assessment should be incorporated into every clinical visit. Adherence is difficult to assess accurately; different methods of assessment have yielded different results, and each approach has limitations.[27-29] Viral load monitoring is the most useful indicator of adherence and is a routine component of monitoring individuals who are on ART (see Plasma HIV-1 RNA [Viral Load] and CD4 Count Monitoring in the Adult and Adolescent Antiretroviral Guidelines). It also can be used as positive reinforcement to encourage continued adherence.[30] With the introduction of long-acting injectable (LAI) ART, adherence is related to receiving scheduled injections on time. Therefore, barriers to LAI ART adherence have shifted from home management to retention barriers. Optimizing adherence requires assessment of such factors as transportation, appointment scheduling, and school or work absences. In addition to viral load monitoring, providers should use at least one other method to assess adherence, such as self-report of missed doses.[28] Table 15 below includes common approaches to monitoring medication adherence. When assessing adherence, a nonjudgmental approach and positive rather than negative feedback can be more successful in encouraging accurate reporting related to ART adherence.[31]

Strategies to Improve and Support Adherence

When concerns about adherence emerge, the child/adolescent and/or caregiver should be seen and/or contacted frequently to assess adherence. Strategies to improve and support adherence should be individualized to the child/adolescent and/or caregivers based on the barriers identified, developmental stage, and unique circumstances. Strategies should include simplifying the ARV drug regimen, developing treatment plans that integrate medication administration into daily routines (e.g., associating medication administration with daily activities, such as brushing teeth), optimizing the use of social and community support services, and addressing barriers to attending LAI ART administration appointments, if applicable. Multifaceted approaches that include regimen-related strategies; educational, behavioral, and supportive strategies focused on children and families; and strategies that focus on health care providers may be more effective than one specific intervention. Table 16 below summarizes some of the strategies that can be used to support and improve adherence to ARV medications. The Centers for Disease Control and Prevention offer the evidence-based Partnership for Health—Medication Adherence to HIV care providers.[32]

Regimen-Related Strategies

Oral ARV regimens should be simplified with respect to the number of daily doses and number of pills or volume of liquid prescribed. Efforts should be made to prescribe once-daily ARV regimens and single-tablet regimens whenever feasible (see Table 18 in Management of Children Receiving Antiretroviral Therapy). Several studies in adults have demonstrated better adherence with once-daily ARV regimens than with twice-daily regimens, as well as with single-tablet formulations than with multiple-tablet regimens.[33-37] See Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets or as a Co-packaged Formulation, by Drug Class and Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents for information about using fixed-dose combination tablets in children.

Long-acting injectable cabotegravir and rilpivirine (LA CAB/RPV) is an additional formulation option for adolescents ≥12 years of age who weigh at least 35 kg and who have sustained viral suppression but struggle with daily adherence (see the Cabotegravir and Rilpivirine sections for eligibility criteria). This formulation is not currently U.S. Food and Drug Administration approved for use in people who have not achieved sustained viral suppression. Using LA CAB/RPV in people who are not virally suppressed and are nonadherent is currently being studied in adults in the Long-Acting Therapy to Improve Treatment Success in Daily LifE (LATITUDE) trial.[38] A program in San Francisco demonstrated promising findings: adults with such barriers to ART adherence as housing instability, mental illness, and substance use who were treated with LA CAB/RPV despite not achieving viral suppression prior to initiation of therapy were able to attend injection appointments and achieve viral suppression with appropriate support and outreach.[39] Additionally, a small (n = 19) retrospective review of youth (aged 13–25) at a single location started LA CAB/RPV without achieving viral suppression first or using an oral lead-in therapy. Prior to enrollment, genotyping confirmed there was no resistance to cabotegravir or rilpivirine. All youth achieved viral suppression after 3 months on LA CAB/RPV and maintained viral suppression for 6 to 12 months when results were published.[40]

Drugs in the regimen should be chosen to minimize drug interactions and AEs (see Management of Medication Toxicity or Intolerance).[41] If drug-specific toxicities are thought to be contributing to nonadherence, efforts should be made to alleviate the AEs by changing the particular drug (or, if necessary, the drug regimen) when feasible. When nonadherence is related to the poor palatability of a liquid formulation or crushed pills, the offending taste can sometimes be masked with a small amount of flavoring syrup or food if simultaneous administration of food is not contraindicated (see Appendix A: Pediatric Antiretroviral Drug Information).[42] Unfortunately, the taste of lopinavir/ritonavir cannot be masked with flavoring syrup. A small study of children and youth aged 4 to 21 years found that training children to swallow pills was associated with improved adherence at 6 months post-training.[43] In poorly adherent children who are at risk of disease progression and who have severe and persistent aversion to taking medications, the use of a gastrostomy tube may be considered.[44]

Family-Related Adherence Strategies

Education is an essential component of establishing good medication adherence. Educating families about adherence should begin before initiating or changing ARV medications and should include a discussion of the goals of therapy, the importance of optimizing adherence, and the specific plans for supporting and maintaining a child's medication adherence. Caregiver adherence education strategies should include written and visual materials; a daily schedule illustrating times and doses of medications; and demonstration of the use of syringes, medication cups, and pill boxes. Additionally,

it may be helpful to assess the medication adherence of the caregiver or other household members who currently take ARV drugs or other chronic medications. Several behavioral tools can be used to integrate taking medications into a child's daily routine. The use of behavior modification techniques, especially the application of positive reinforcements and the use of small incentives (including financial incentives) for taking medications, can be effective tools to promote adherence.[45]

Because psychological issues and mental health disorders (e.g., depression, substance use) can affect ART adherence, recognition and treatment of these conditions is an essential part of preventing and treating nonadherence.[46, 47] The ability to talk with children about their medications is also important. If the child has not been informed of their HIV status, HIV disclosure should be discussed with the caregivers. In a systematic review of adolescents living in sub-Saharan Africa, 12 studies with 4,422 participants found that knowledge of HIV status was associated with adherence to ART (odds ratio [OR] 1.88; 95% confidence interval [CI], 1.21–2.94; P = <0.001).[48] In interviews with caregivers of children with HIV in South Africa, investigators found that caregivers who had disclosed to their child that they (i.e., the child) had HIV were truthful in their communications and named the disease as HIV, but communication about HIV was infrequent and focused on pill taking. By comparison, those who had not disclosed used deception, deflection, and coercion in response to health-related questions and to enforce adherence.[21] The decision to disclose HIV status should not necessarily be expected to improve adherence but should be based on a comprehensive assessment of psychosocial and developmental factors and the needs of the child and family. Additional data from the Democratic Republic of Congo show that disclosure of HIV status to youth by trained peers may lead to improved adherence, as measured by viral suppression, compared to disclosure by parent or health care workers.[49]

The growing use of telemedicine visits, which allow remote and often face-to-face interaction, provides new opportunities to support families and visualize ART handling/swallowing, as well as to conduct directly observed therapy (DOT) in the home setting. The evidence is mixed as to the efficacy of programs that are designed to improve adherence through DOT, but DOT may still be a useful strategy for some people.[50-52] A randomized controlled trial (RCT) of a 12-week multicomponent intervention—including remote coaching, electronic dose monitoring, and tailored outreach (Triggered Escalating Real-Time Adherence)—for viremic youth in the United States demonstrated improved adherence but not viral suppression compared with the standard of care.[25]

Other strategies to support adherence include using mobile applications that remind people to take medications; setting cell phone alarms to go off at medication times; sending text-message reminders; conducting motivational interviews; providing pill boxes, blister packaging, and other adherence support tools; and delivering medications to the home. An analysis using the Cost-Effectiveness of Preventing AIDS Complications (or CEPAC)–Adolescent model of HIV disease and treatment modeled the impact of a 12-month **hypothetical** adherence intervention (based on an interactive smartphone-based reminder system) among youth with HIV in the United States. Compared with the standard of care, the analysis showed that youth-targeted adherence interventions, even with modest efficacy to improve virologic suppression, could improve life expectancy, prevent onward HIV transmissions, and be cost effective.[53]

However, several systematic reviews evaluating the use of mobile phone technologies to improve ART adherence (mHealth) have been published and results continue to be inconclusive on the effectiveness of digital interventions to improve adherence in adolescents. A recent systematic review of digital interventions to improve adherence in youth with HIV who live in sub-Saharan Africa provided mixed evidence, with two of six trials finding significant improvement in viral suppression and the remaining four trials showing no significant improvement in adherence-related measures.[54] In another review, the authors found what they described as "ambiguous results with

high variability" about the effectiveness of mHealth interventions to improve adherence in low- and middle-income countries.[55] Of 17 studies, 56% reported a statistically significant positive impact of mHealth on adherence; 44% reported insignificant results. Another systematic review reported that the efficacy of mobile short message service (SMS) interventions varied depending on the specific SMS intervention tested.[56]

In a longitudinal cohort study, the association between medication-specific reactance—an aversive response to perceived threats against personal agency—and treatment failure was examined in a cohort of adolescents with HIV in Botswana. Reactant individuals may hear health messaging as a threat to their perceived freedom and respond by engaging in the opposed behavior. Adolescents, scoring >4 on a 5-point scale had 2.05-fold (95% CI, 1.23–3.41) greater odds of treatment failure than nonreactant youth ($P = 0.043$). Psychological reactance needs further study and may provide some insight into adherence behaviors among youth; it also may be important to consider in adherence counseling and in designing interventions.[57] Similarly, a cross-sectional analysis among youth in England with PHIV found that youth with greater concerns regarding ART had a reduced odds of adherence.[58]

Two studies provided evidence of the efficacy of peer-based interventions to improve ART adherence and viral suppression among adolescents and young people with HIV in Africa. In Project YES! in Ndola, Zambia, 273 youth aged 15 to 24 years receiving HIV care in four health facilities, including a pediatric clinic, were randomly assigned to monthly meetings with youth peer mentors. At 6 months, viral suppression improved in both study arms, but among participants in care at the pediatric clinic, the rate of viral suppression increased from 37.5% to 70.5% in the intervention arm versus 60.3% to 59.4% in the comparison arm (interaction term OR, 4.66; 95% CI, 1.84–11.78).[59] Another RCT tested the efficacy of a peer-led differentiated service delivery intervention on HIV clinical outcomes among adolescents with HIV aged 13 to 19 years in rural Zimbabwe. Sixteen clinics were randomized to standard of care or the enhanced intervention in which adolescents were assigned a community adolescent treatment supporter; attended monthly support group; and received text messages, calls, home visits, and clinic-based counseling. At 96 weeks, among 479 adolescents with data, 52 (25%) adolescents in the intervention arm versus 97 (36%) in the control arm had viral load >1,000 copies/mL or had died (adjusted prevalence ratio 0.58; 95% CI, 0.36–0.94; $P = 0.03$). These studies demonstrate that peer-based interventions have the potential to improve adherence and health outcomes among youth with HIV.[60]

In addition to clinic- and community-based programs, camp experiences can offer a source of peer support for children and youth with HIV and other chronic illnesses. Although data are limited,[61-63] many children and youth with HIV report attendance to camp programs to be empowering and helpful to learn about adherence to daily ART.

Further evidence of the efficacy of peer-support interventions for people with HIV comes from a recent systematic review and meta-analysis, including 20 RCTs comprising 7,605 participants from nine countries. The authors found superior retention in care (risk ratio 1.07; 95% CI, 1.02–1.12 at 12 months follow-up) and better ART adherence (risk ratio 1.06; 95% CI, 1.01–1.10 at 3 months of follow-up) but no statistically significant difference in viral suppression (risk ratio 1.02; 95% CI, 0.94–1.11 at 6 months of follow-up) among peer-support participants.[64]

Health Care Provider–Related Strategies

To improve and support ART adherence, providers should maintain a nonjudgmental attitude, establish trust with children and adolescents and their caregivers, and identify mutually acceptable goals for care. Providers can improve adherence through their relationships with the child/adolescent

and families, starting at the first visit together when they obtain explicit agreement on the medication and treatment plan, as well as strategies to support adherence. Fostering a trusting relationship and engaging in open communication are particularly important. Focus groups and semi-structured interviews were conducted with adolescents and their caregivers participating in a longitudinal adherence study. Participants who self-reported high adherence but for whom electronically monitored data reflected low adherence were selected. Adolescents described hiding and discarding pills and lying about their adherence. Adolescents and parents considered negative feedback for prior poor adherence as motivation for efforts to hide current poor adherence. The authors suggest that positive feedback for truth-telling may help develop family and staff alliances in support of adherence.[31]

Provider characteristics that have been associated with improved adherence in adults include consistency, willingness to give information and ask questions, technical expertise, and commitment to follow-up. Creating an environment in the health care setting that is child-centered and includes caregivers in adherence support also has been shown to improve treatment outcomes. Providing comprehensive multidisciplinary care (e.g., with nurses, case managers, pharmacists, social workers, psychiatric care providers) also may better serve more complex child/adolescent and family needs, including adherence. Provider-initiated education about viral load and counseling targeted at understanding viral load results, the health benefits of undetectable viral load, and the Undetectable = Untransmittable (U=U) concept are other strategies providers can use. Avoidant coping strategies or history of trauma may impact adherence. Although research is limited, use of trauma-informed care practices can be considered.[65]

Table 15. Approaches for Monitoring Medication Adherence

Routine Assessment of Medication Adherence in Clinical Care[a]	Description
Monitor viral load.	Viral load monitoring should be done more frequently after initiating or changing medications.[a]
Assess a quantitative self-report of missed doses.	Ask the child/adolescent and/or caregiver about the number of missed doses over a defined period (e.g., the last 1, 3, or 7 days). Alternatively, ask, "How many days did you take your medication during the past week?"
Request a description of the medication regimen.	Ask the child/adolescent and/or caregiver about the name, appearance, and number of medications and how often the medications are taken.
Assess barriers to medication administration.	Engage the child/adolescent and/or caregiver in a dialogue about potential barriers to adherence and strategies to overcome them.
Monitor pharmacy refills.	Approaches include a pharmacy-based or clinic-based assessment of on-time medication refills.
Employ telemedicine to monitor and support medication administration.	Telemedicine visits allow remote and often face-to-face contact and provide new opportunities to support families; to visualize ART preparation, handling, and swallowing; and to conduct DOT in the home setting.
Conduct pill counts.	Approaches include asking people to bring medications to the clinic, conducting home visits, or providing referrals to community health nursing.
Monitor attendance for ART injection appointments among adolescents on LAI regimens.	For individuals on LAI ART, adherence is related to receiving scheduled injections on time. Therefore, reducing barriers to adherence should focus on scheduling convenient appointments, minimizing school and work absences, and ensuring transportation to appointments.
Targeted Approaches to Monitoring Adherence in Special Circumstances	**Description**
Implement DOT in person and via telemedicine.	Include a brief period of hospitalization if indicated.
Measure drug concentration in plasma or DBS.	Measuring drug concentrations can be considered for particular drugs.
Approaches to Monitoring Medication Adherence in Research Settings	**Description**
Measure drug concentrations in hair.	Measuring hair drug concentrations can be considered for particular drugs; it provides a good measure of adherence over time.[27, 66, 67]
Use electronic monitoring devices.	Approaches include MEMS caps and Wisepill.
Use mobile phone–based technologies.	Approaches include interactive voice response, text messaging, and mobile apps.

[a] See Clinical and Laboratory Monitoring of Pediatric HIV Infection regarding the frequency of adherence assessment after initiating or changing therapy.

Key: app = application; ART = antiretroviral therapy; DBS = dried blood spot; DOT = directly observed therapy; LAI = long-acting injectable; MEMS = Medication Event Monitoring System

Table 16. Strategies to Improve Adherence to Antiretroviral Medications

Initial Intervention Strategies
• Establish trust and identify mutually acceptable goals for care. • Obtain explicit agreement on the need for treatment and adherence. • Determine whether the child is aware of their HIV status. Consider talking to the child's caregivers about disclosing this information to the child in a developmentally appropriate way. • Identify psychosocial, behavioral, or structural barriers that may affect adherence and help the child and/or family access resources to help eliminate these barriers. • Identify family, friends, health team members, and others who can support adherence. • Educate the child/adolescent and family about the critical role of adherence in therapy outcome, including the relationship between partial adherence and resistance and the potential impact on future drug regimen choices. • With the child/adolescent and family together, develop a treatment plan that they believe is achievable. • Address any concerns child/adolescent and caregivers have about the medications. • Work with the child/adolescent and family to make specific plans for taking medications as prescribed and for supporting adherence. Assist them in arranging administration during day care, school, and in other settings, when needed. Consider home delivery of medications. • Identify barriers—such as co-pays and insurance access—related to medication access to help prevent interruptions in ART. • Schedule a home visit or telemedicine visit to review medications and determine how they will be administered in the home setting. • In certain circumstances, consider a brief period of hospitalization for patient education and to assess the tolerability of the chosen medications.
Medication Strategies
• Choose the simplest regimen possible; reduce dosing frequency, pill size, and number of pills (see Appendix A, Table 1. Antiretrovirals Available in Fixed-Dose Combination Tablets or as a Co-packaged Formulation, by Drug Class and Appendix A, Table 2. Antiretroviral Fixed-Dose Combination Tablets and Co-packaged Formulations: Minimum Body Weights and Considerations for Use in Children and Adolescents). Consider LAI regimens (e.g., LA CAB/RPV) for eligible children and adolescents. • When choosing a regimen, consider the child/adolescent's routines and potential variations in individual and family activities. • Choose the most palatable medicine possible (pharmacists may be able to add syrups or flavoring agents to improve palatability). • Choose drugs with the fewest AEs; provide anticipatory guidance for managing AEs. • Simplify food requirements for medication administration. • Prescribe drugs carefully to avoid adverse drug–drug interactions. • Assess pill-swallowing capacity and offer pill-swallowing training and aids (e.g., pill-swallowing cup, pill glide). Adjust pill size as needed or check if the pill can be crushed. Consider dispersible formulations if possible. See drug sections in Appendix A: Pediatric Antiretroviral Drug Information for information about available formulations and administration of individual drugs. • Choose ARV regimens with high genetic barriers to resistance, when available, if there are concerns about adherence.

Table 16. Strategies to Improve Adherence to Antiretroviral Medications

Follow-Up Intervention Strategies
• Members of the multidisciplinary team should monitor adherence at each visit. In between visits, adherence can be monitored and supported by telephone, email, text, and other secure applications; confidentiality of any communication approach must be ensured. • Provide ongoing support, encouragement, and understanding of the difficulties associated with maintaining adherence to daily medication regimens. • Provide education and counseling that explain the meaning and significance of viral load results. • Use education aids, including pictures, calendars, and stickers. • Encourage the use of pill boxes, reminders, mobile apps, and alarms. • Provide follow-up clinic visits, telephone calls, text messages, and telemedicine visits to support and assess adherence. • Provide access to support groups, peer groups, summer camp programs, or one-on-one counseling for caregivers and individuals. • Provide referrals and support access to counseling and treatment services for individuals with identified mental health problems, including depression and substance abuse. • Provide pharmacist-based adherence support, such as medication education and counseling, blister packs, refill reminders, automatic refills, and home delivery of medications. • Consider DOT at home, in the clinic, or, in certain circumstances, during a brief period of inpatient hospitalization. • Consider gastrostomy tube use in certain circumstances. • Information on other interventions to consider can be found at the HIV Compendium of Best Practices on the CDC's website.

Key: AE = adverse effect; app = application; ART = antiretroviral therapy; ARV = antiretroviral; CDC = Centers for Disease Control and Prevention; DOT = directly observed therapy; LA CAB/RPV = long-acting injectable cabotegravir and rilpivirine; LAI = long-acting injectable;

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