

ADHERENCE TO ARVS IN CHILDREN AND YOUTH LIVING WITH HIV



IMPORTANCE OF ADHERENCE

- Adherence to ARVs is a principal determinant of virologic suppression, prevention of HIV resistant strain, and reduced HIV transmission risk^{1,2}
- $\geq 95\%$ adherence is needed to adequately suppress viral replication³
- Estimated adherence rate among Youth (age 13-24) living with HIV is 28%-69%³
- Suboptimal adherence includes missed or late doses, interruptions and discontinuations, subtherapeutic or partial dosing^{4,5}

1. Sethi AK, Celentano DD, Gange SJ, et al. Association between adherence to antiretroviral therapy and human immunodeficiency virus drug resistance. *Clin Infect Dis*. 2003; 37:1112-1118.

2. Gardner EM, Burman WJ, Steiner JF, et al. Antiretroviral medication adherence and the development of class-specific antiretroviral resistance. *AIDS*. 2009;23:1035-1046.

3. Reisner SL, et al. *Top HIV Med*. 2009;17(1):14-25.

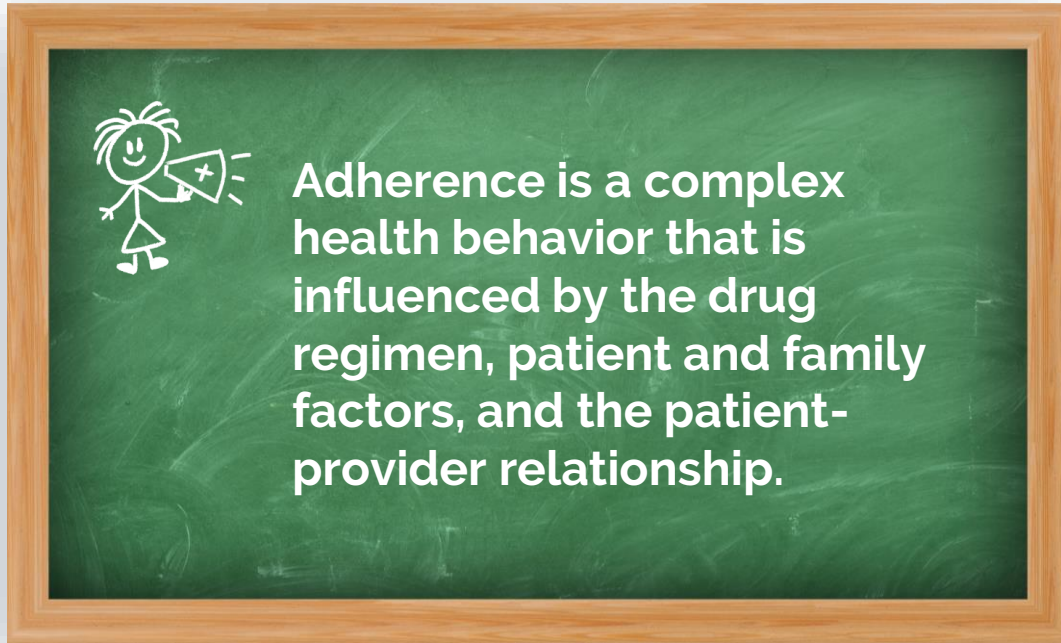
4. Vreeman RC, Nyandiko WM, Liu H, et al. Measuring adherence to antiretroviral therapy in children and adolescents in western Kenya. *J Int AIDS Soc*. 2014;17:19227. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25427633>.

5. Hawkins A, Evangeli M, Sturgeon K, Le Prevost M, Judd A, Aalphi Steering Committee. Episodic medication adherence in adolescents and young adults with perinatally acquired HIV: a within-participants approach. *AIDS Care*. 2016;28 Suppl 1:68-75. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26886514>.

CONSEQUENCES OF POOR ADHERENCE

- Incomplete virologic response, virologic rebound or virologic failure
- High viral load and low CD4 increase risk of progression to AIDs/HIV-related complications
- Subtherapeutic plasma ARV drug concentrations
- Development of resistance to one or more drugs in a given regimen
- Possible cross-resistance to other drugs in same class
- Regimen changes and limited options for future effective drug regimens especially in the pediatric population
- Increased risk of secondary transmission of drug-resistant virus

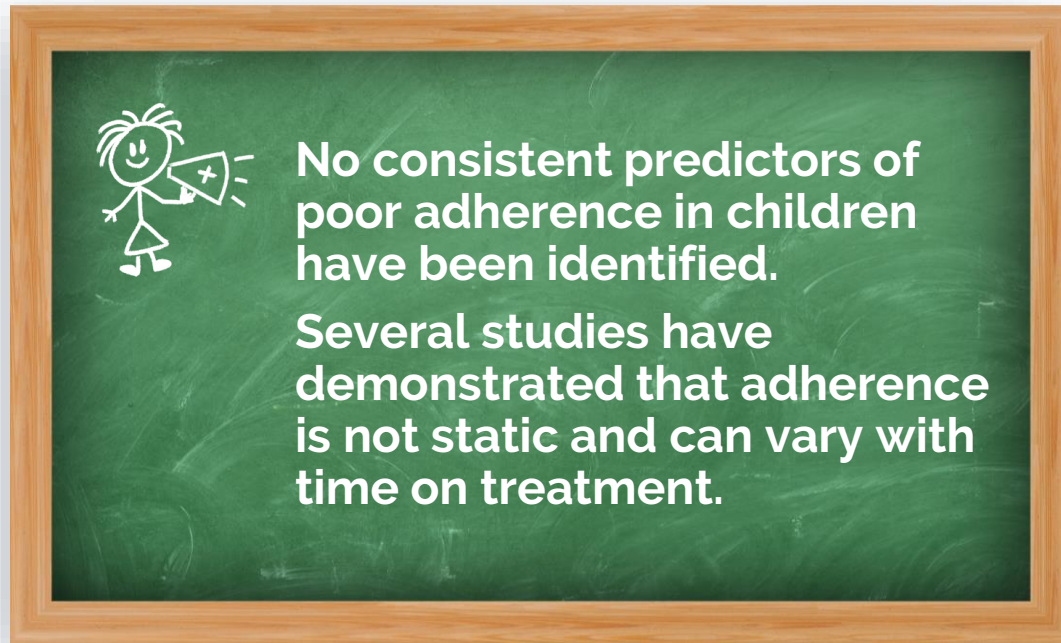
BARRIERS TO ADHERENCE



Factors Affecting Adherence:

- Medication formulation/palatability
- Frequency of dosing
- Drug toxicities and side effects
- Child's age and developmental stage
- Infant and children dependence on others for medication administration
- Psychosocial, behavioral and sociodemographic characteristics of children and caregivers

PREDICTORS OF POOR ADHERENCE



- Findings from the U.S. Pediatric AIDS/HIV Cohort Study (PHACS) demonstrated that the prevalence of nonadherence increased with age.
- Among 381 children and adolescents with perinatal HIV infection, 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 pre-adolescence and late adolescence/young adulthood.
- These findings illustrate the difficulty of maintaining high levels of adherence and underscore the need to work with patients and their families to ensure that adherence education, support, and assessment are integral components of care.



DHHS GUIDELINES RECOMMENDATIONS ON ADHERENCE ASSESSMENT AND MONITORING

- Strategies to maximize adherence should be discussed before and/or at initiation of antiretroviral therapy (withing 1-2 weeks) and again before changing regimens (AIII).
- Adherence to therapy 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).
- Once-daily antiretroviral regimens and regimens with a low pill burden should be prescribed whenever feasible (AI*).

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 post-pubertal adolescents

METHODS OF ADHERENCE ASSESSMENT¹

Routine Assessment of Medication Adherence in <u>Clinical Care</u> ^{**}	Description
Monitor viral load.	Viral load monitoring should be done more frequently after initiating or changing medications.
Assess a quantitative self-report of missed doses.	Ask the patient and/or caregiver about the number of missed doses over a defined period (1,3, or 7 days).
Request a description of the medication regimen.	Ask the patient 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 patient and 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.
Conduct announced and unannounced pill counts.	Approaches include asking patients to bring medications to the clinic, home visits, or referral to community health nursing.

1. Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf>. Access April 2022.
 2. Pintye J, Bacchetti P, Teeraananchai S, et al. Brief report: lopinavir hair concentrations are the strongest predictor of viremia in HIV-infected Asian children and adolescents on second-line antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2017;76(4):367-371. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28825944>.
 3. Al-Hassany L, Kloosterboer SM, Dierckx B, Koch BC. Assessing methods of measuring medication adherence in chronically ill children—a narrative review. *Patient Prefer Adherence*. 2019;13:1175-1189. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31413546>.
 4. Craker L, Tarantino N, Whiteley L, Brown L. Measuring antiretroviral adherence among young people living with HIV: observations from a real-time monitoring device versus self-report. *AIDS Behav*. 2019;23(8):2138-2145. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30888573>.

^{**}Adherence is difficult to assess accurately; different methods of assessment have yielded different results, and each approach has limitations.²⁻⁴

METHODS OF ADHERENCE ASSESSMENT CONTINUED...

Targeted Approaches to Monitoring Adherence in <i>Special Circumstances</i> **	Description
Implement directly observed therapy	Include a brief period of hospitalization if indicated.
Measure drug concentration in plasma or dried blood spot.	Measuring drug concentrations can be considered for particular drugs
Approaches to Monitoring Medication Adherence in <i>Research Settings</i> **	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.
Use electronic monitoring devices.	Approaches include medication event monitoring system and Wisepill.*
Use cell phone-based technologies.	Approaches include interactive voice response, text messaging and mobile apps.

1. Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf>. Access April 2022.
 2. Pintye J, Bacchetti P, Teeraananchai S, et al. Brief report: lopinavir hair concentrations are the strongest predictor of viremia in HIV-infected Asian children and adolescents on second-line antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2017;76(4):367-371. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28825944>.
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 4. Craker L, Tarantino N, Whiteley L, Brown L. Measuring antiretroviral adherence among young people living with HIV: observations from a real-time monitoring device versus self-report. *AIDS Behav*. 2019;23(8):2138-2145. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30888573>.

*www.wisepill.com

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DHHS GUIDELINES: STRATEGIES TO IMPROVE ADHERENCE

MEDICATION STRATEGIES

- Reduce dosing frequency, pill size, and number of pills
- Assess pill-swallowing capacity and offer pill-swallowing training and aids (e.g., pill-swallowing cup, pill glide). Adjust pill size as needed.
- Choose the most palatable medicine possible (consider addition of syrups or flavoring agents to increase palatability).
- Consider the patient's daily and weekly routines and potential variations in patient and family activities.
- Choose drugs with the fewest AEs; provide anticipatory guidance for managing AEs
- Simplify food requirements
- Prescribe drugs carefully to avoid adverse drug-drug interactions.

INITIAL INTERVENTIONAL STRATEGIES

- Establish trust and identify mutually acceptable goals for care.
- Obtain explicit agreement on the need for treatment and adherence.
- Identify mental health issues that may affect adherence. Evaluate and initiate treatment for mental health issues before starting ARV drugs, if possible
- Determine if 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 people who can support adherence.
- Educate on the critical role of adherence, including the relationship between partial adherence and resistance and the potential impact on future drug regimen choices.
- Establish readiness to take medication by staging practice sessions.
- Work to make specific plans. Arrange administration during day care, school, and in other settings, when needed. Consider home delivery of medications.
- Schedule a visit to review medications and determine how they will be administered in the home setting.

FOLLOW-UP INTERVENTION STRATEGIES

- At each visit have multiple team members monitor adherence and between visits by telephone, email, text, & social media, as needed.
- Provide ongoing support, encouragement, and understanding of the difficulties associated with maintaining adherence to daily medication regimens.
- Use patient education aids, including pictures, calendars, and stickers.
- Encourage the use of pill boxes, reminders, mobile apps, alarms, and timers.
- Provide clinic or telehealth visits, telephone calls, & text messages to support and assess adherence.
- Provide access to support groups, peer groups, or one-on-one counseling
- Provide pharmacist-based adherence support, such as medication education and counseling, blister packs, refill reminders, automatic refills, and home delivery of medications.
- Consider DOT in certain circumstances.
- Consider gastrostomy tube use in certain circumstances.

HELPFUL RESOURCES

[Complete List](#) | [Medication Adherence Chapter](#) | [Compendium](#) | [Intervention Research](#) | [Research](#) | [HIV/AIDS](#) | [CDC](#)

[Partnership for Health - Medication Adherence](#) | [Treat](#) | [Effective Interventions](#) | [HIV/AIDS](#) | [CDC](#)

[Every Dose Every Day toolkit](#)