HIV in Infants and Children

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Module 6: Key Populations
Lesson 1: HIV in Infants and Children

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Introduction

History of HIV in Children in the United States

The first reports of HIV in children in the United States emerged in December 1982, when the Centers for Disease Control (CDC) described four children under the age of 2 years who had unexplained immunodeficiency and opportunistic infections.[1] Several subsequent published reports described young children with AIDS.[2,3,4] In 1985, a highly publicized story emerged of a 13-year-old boy with hemophilia and AIDS who was banned from his middle school in Indiana because he had AIDS; this boy, Ryan White, captured the nation's attention as he courageously battled to maintain the right to attend school.[5] On August 18, 1990, the historic Ryan White Comprehensive AIDS Resources Emergency (CARE) Act was passed by the United States Congress, named in honor of Ryan White, who had died 4 months earlier at age 18.[6] In 1994, the Pediatric AIDS Clinical Trials Group (PACTG) 076 trial reported a three-part zidovudine regimen reduced perinatal HIV transmission by 67.5% when compared with placebo.[7] In the United States, due to the widespread implementation of highly effective measures to prevent perinatal HIV transmission, the number of children born with HIV has dramatically declined from a peak of more than 1,700 babies born with HIV per year in the early 1990s to fewer than 70 per year in recent years (Figure 1).[8,9,10,11,12]

Unique Aspects of Pediatric HIV

Clinicians who provide care for infants and children with HIV should be aware of the unique characteristics of these populations, integrate age-specific primary care measures with HIV management, and be sensitive to the social and developmental aspects involved in the care of young people living with HIV. Children living with HIV face unique challenges that necessitate special clinical care considerations. Although most principles and concepts related to the diagnosis and management of HIV are similar in adults and children, the following summarizes some key aspects of pediatric HIV care:

- Making a diagnosis of HIV in a newborn is confounded by the transfer of maternal anti-HIV antibodies to the baby.
- Interpretation of CD4 cell count values in children requires adjustment based on age-specific criteria.
- Urgent initiation of antiretroviral therapy is indicated for infants and young children with HIV as they are at risk for rapid disease progression and death.
- Antiretroviral medications have age-specific approvals with different dosing requirements.
- Children present special challenges in terms of adherence to antiretroviral therapy.

This Core Concept will focus on the diagnosis and management of HIV in infants and children through age 12 years of age. The topics of Preventing Perinatal HIV Transmission and HIV in Adolescents and Young Adults

are addressed in separate Topic Reviews.

Epidemiology of HIV in Children Younger than Age 13

Almost all children younger than 13 years of age with HIV in the United States have acquired HIV via perinatal transmission.[12,13] The following summarizes key epidemiologic features of children younger than 13 years of age in the United States (Figure 2).[12]

- At year-end 2022, in the United States, 1,124 children younger than age 13 were living with diagnosed HIV, which was approximately 0.1% of all persons living with diagnosed HIV.[12]
- In recent years, the number of children younger than age 13 living with diagnosed HIV in the United States has declined steadily.[12]
- Black children are disproportionately affected—at year-end 2022 among children younger than 13 years of age living with diagnosed HIV, 56% (629 of 1,124) were Black children.[12]

Staging of Pediatric HIV Disease

Staging

The initial evaluation of a child is an important time to determine the stage, or status, of the child's HIV disease. In the 2014 case definition, stage 0 indicates early HIV, inferred from a negative or indeterminate HIV test result within 6 months prior to a confirmed positive result.[14] Stages 1, 2, and 3 are determined based on the CD4 count, stratified by age (Table 1).[14] The presence of an AIDS-defining (stage 3) opportunistic infection confers a stage 3 diagnosis regardless of the CD4 cell count or percentage. Stage unknown refers to a person with laboratory confirmation of HIV, but no information about CD4 cell count or percentage (and no information about the presence of AIDS-defining clinical conditions). The absolute CD4 count takes precedence over the CD4 percentage, even in children, and the percentage is only considered if the corresponding CD4 count is unknown; this change was made because clinical evidence suggests the CD4 percentage has little effect on the prognosis and may actually overestimate the clinical stage.[14]

Real-Time Staging

In previous case definitions, a patient's stage of HIV was based on the most advanced stage ever experienced, or the "life-time stage." Once a patient progresses to a more advanced stage, their stage does not revert (or be upgraded) to any earlier stage. The updated 2014 staging system is more flexible, allowing for a patient's status to change in either direction after diagnosis; this is helpful in describing a patient's "real-time stage" or the status of HIV disease in the present moment. Admittedly, this new staging system is somewhat vague and it remains unclear how clinicians will utilize this more flexible component of staging for surveillance purposes.[14]

Clinical Criteria for HIV Diagnosis

According to the 2014 case definition, clinical criteria for a confirmed case of HIV are met when there is a note in a medical record by a physician or other qualified medical provider stating that the patient has HIV, followed by either laboratory criteria meeting the case definition, presumptive evidence of HIV infection (e.g., receipt of HIV antiretroviral therapy or prophylaxis for an opportunistic infection), an otherwise unexplained low CD4 count, or an otherwise unexplained diagnosis of an opportunistic illness.[14]

AIDS-defining Clinical Conditions

In children with laboratory-confirmed HIV, stage 3 (AIDS) is defined based on laboratory criteria (CD4 cell count) or clinical conditions. The list of AIDS-defining clinical conditions is extensive.[14,15] Note that lymphoid interstitial pneumonia (pulmonary lymphoid hyperplasia) has been removed from the list of AIDS-defining clinical conditions in children because this condition is associated with moderate rather than severe immunodeficiency.[14]

Diagnosis of HIV in Infants and Children

Recommended Diagnostic Tests

The greatest diagnostic challenges in young children occur with infants born to mothers with HIV. The diagnosis of HIV should be made as soon as possible in an infant exposed to HIV.[16] Note that, due to concerns for contamination with maternal blood, blood samples from the umbilical cord should not be used for diagnostic evaluation for HIV at birth. The following summarizes the tests to be utilized in the diagnosis of HIV in infants.[16]

- **Virologic Assays**: The diagnosis of HIV among infants and children younger than 18 months who are born to mothers with HIV is best made with the use of virologic assays (HIV nucleic acid testing [NAT]) that directly detect HIV RNA or HIV DNA.[16] The HIV RNA assays detect extracellular HIV RNA in plasma and the HIV DNA assays detect intracellular HIV DNA in peripheral blood mononuclear cells. Since false-positive tests can occur with both HIV DNA and RNA assays, repeat HIV NAT should be done if possible in order to verify the initial positive test.[16]
- **HIV Antigen-Antibody Tests and p24 Antigen Tests**: The use of HIV-1/2 antigen-antibody immunoassays or the HIV p24 antigen test alone is not recommended in the setting of perinatal HIV exposure because of the lower sensitivity and specificity in the first months of life when compared with virologic tests, such as HIV nucleic acid testing.[16,17] Serologic HIV-1/2 antigen-antibody immunoassay testing can be used for HIV diagnosis in infants and children with non-perinatal HIV exposure or for perinatally-exposed children older than 24 months of age.

Determining HIV Risk Status of Infants Born to Mothers with HIV

For infants born to mothers with HIV, the recommended HIV diagnostic evaluation varies based on the estimated perinatal HIV transmission risk. The Pediatric ART Guidelines identify two levels of HIV acquisition risk for infants: low risk and high risk.[16]

- ***Low Risk***: Infants born to mothers who—
    - Received antiretroviral therapy during pregnancy,
    - Had sustained suppression of HIV RNA levels (usually defined as less than 50 copies/mL), *and*
    - Were adherent to their antiretroviral regimen
- ***High Risk*****:** Infants born to mothers who—
    - Did not receive prenatal care,
    - Received no antepartum antiretroviral therapy or only intrapartum antiretroviral therapy,
    - Initiated antiretroviral therapy late in pregnancy (during the late second or third trimester),
    - Received a diagnosis of acute HIV infection during pregnancy or in labor, and/or
    - Had detectable HIV viral loads (≥50 copies/mL) close to the time of delivery, including those who received antiretroviral therapy but did not achieve sustained viral suppression.

HIV Testing Schedule of Infants Born to Mothers with HIV

The following summarizes Pediatric ART Guidelines recommendations or HIV testing of infants based on whether the infant is considered to be low-risk or high-risk for acquiring HIV (Figure 3).[16]

- **Recommended Testing Schedule for Infants at Low Risk**: For infants considered to be at low risk

of perinatal transmission, HIV NAT diagnostic testing should take place at 3 time points after birth: 14 to 21 days, 1 to 2 months, and 4 to 6 months.[16]

- **Recommended Testing Schedule for Infants at High Risk**: In general, HIV virologic testing (HIV NAT) for infants at high risk of perinatal HIV transmission should first be performed at birth, ideally prior to initiating an antiretroviral drug regimen. Regardless, presumptive HIV therapy should not be delayed. Additional virologic testing for infants considered to be at higher risk of perinatal HIV transmission and those receiving combination antiretroviral prophylaxis should be done at 14 to 21 days, 1 to 2 months, 2 to 3 months, and 4 to 6 months. Virologic testing (HIV NAT) is also indicated 2 to 6 weeks after cessation of antiretroviral prophylaxis (this is usually at 8 to 12 weeks of life).[16,18] The rationale for the extra testing 2 to 6 weeks after cessation of antiretroviral prophylaxis is that combination antiretroviral prophylaxis in infants exposed to HIV may diminish the sensitivity of diagnostic virologic assays normally performed at age 1 to 2 months.[16,18] If there are concerns that a newborn may be lost to follow-up for care, the infant should undergo virologic diagnostic testing at birth, even if they are at low risk for perinatal HIV transmission.[18]

Testing for Infants with Perinatal Exposure who are Breastfed

For a parent with HIV who breastfeeds, virologic testing should be done for the infant at birth, 14 to 21 days, 1 to 2 months, and 4 to 6 months of age.[16] In the event that a gap of longer than 3 months occurs between the testing at 1 to 2 months and 4 to 6 months, then one additional virologic test should be performed.[16] After 6 months of age, virologic testing should be done every 3 months during ongoing breastfeeding. The Perinatal HIV Clinical Guidelines acknowledge limited data exist to inform the appropriate frequency of HIV RNA testing for the breastfeeding parent, but they suggest one strategy is to perform maternal HIV RNA testing every 1 to 2 months during breastfeeding.[19] At any point, if there is a detectable maternal HIV RNA level, expert consultation should be obtained, and prompt testing of the infant with an HIV NAT should be performed.[19] If a person with a detectable HIV viral load continues to breastfeed, some experts recommend infant testing monthly for early detection of HIV in the setting of ongoing exposure.[19] Following cessation of breastfeeding, regardless of the child's age, virologic tests should be performed 4 to 6 weeks, 3 months, and 6 months post-cessation.[16,19]

Confirmatory Testing

Any infant with a positive virologic assay should have a confirmatory test performed as soon as possible after the initial positive test result. In children 24 months of age or older, the diagnosis of HIV can also be confirmed with an HIV-1/2 antigen-antibody immunoassay testing.[16,18]

Exclusion of HIV Diagnosis

The diagnosis of HIV can be excluded in a non-breastfed infant with:[16,18]

- Two negative virologic tests: one test at age 1 month or older (and at least 2 to 6 weeks after discontinuation of multi-drug antiretroviral prophylaxis) and a negative test at age 4 months or older,

or

- Two negative HIV antibody tests from separate specimens obtained at age 6 months or later

HIV Testing for Infants and Children Born to Mothers with Unknown HIV Status

Newborn infants or children whose maternal HIV status is not known, such as those in foster care or adoptees, should be promptly tested for HIV using age-appropriate diagnostic testing.[20]

Children Older than 24 Months or with Non-Perinatal HIV Exposure

For children with non-perinatal exposure to HIV or children with perinatal HIV exposure who are older than 24 months of age, the diagnostic testing approach should be the same as used to diagnose HIV in adolescents and young adults. This approach should utilize the approach outlined in the CDC/APHL HIV Laboratory Testing Guidelines.[13] The initial screening test consists of an HIV-1/2 antigen-antibody combination Immunoassay; positive screening tests should be followed by testing with an HIV-1/2 antibody differentiation immunoassay.[13] A positive screening test followed by a negative differentiation test warrants further testing with an HIV RNA assay.[13] For more details on HIV diagnostic testing in adolescents and adults, see Lesson HIV Diagnostic Testing in Module 1.

Clinical and Laboratory Monitoring

Baseline Evaluation

At entry to care, children with HIV should have a complete medical history, physical examination, and laboratory evaluation.[21] This history should include a detailed social history component (including immunizations, nutrition, physical and social/emotional environment) and evaluation for HIV-specific physical problems (e.g., growth delay, motor or cognitive neurological problems). Youth with perinatal acquisition of HIV appear to be particularly vulnerable to cognitive problems, especially in the executive function domain.[22,23,24] Baseline laboratory evaluation for all children diagnosed with HIV at entry into care should include the following:[21]

- **HIV-Specific Laboratory Studies**
  - HIV RNA level
  - CD4 cell count
  - HIV drug-resistance testing (genotype assay)
  - HLA-B*5701 test (if abacavir is being considered as part of the initial antiretroviral therapy regimen)
- **Screening for HIV-Associated Condition**s
  - Complete blood count
  - Serum creatinine
  - Serum glucose
  - Hepatic aminotransferase levels
  - Serum albumin
  - Urinalysis
- **Screening for Coinfections and Opportunistic Infections**
  - Hepatitis B virus (HBV), with HBV surface antigen, HBV surface antibody, and HBV core antibody
  - Hepatitis C virus (HCV), (using HCV RNA for children younger than 18 months of age and HCV antibody for children 18 months of age and older)
  - Cytomegalovirus antibody (for children older than 12 months of age)
  - Screening for tuberculosis infection (using a tuberculin skin test for children younger than 2 years of age and interferon-gamma release assay (IGRA) for children 2 years of age and older
- **Screening Children with HIV who Relocate to the United States from Other Countries**
  - Consider obtaining thyroid function tests, lead levels, and screening for gastrointestinal parasites.

Routine Monitoring

In general, all children living with HIV should undergo regular evaluation for growth and development, as well as for clinical signs and symptoms. At each visit, the medical provider should address the efficacy, safety and tolerability of the antiretroviral regimen as well as assess adherence. These visits can be in-person or using telehealth communication platforms at the provider's discretion and based on the comfort level of the child and guardian.[21]

- **Children Not Taking Antiretroviral Therapy**: For children who are not receiving antiretroviral therapy, absolute CD4 cell count and HIV RNA should be monitored every 3 to 4 months, regardless of whether they have HIV-related symptoms.[21]
- **Monitoring of Children after Initiating or Changing Antiretroviral Therapy**: After initiating or changing antiretroviral therapy, children should have an evaluation after 1 to 2 weeks and again after 2 to 4 weeks. Both of these evaluations should include a medical history, physical examination, and evaluation for medication adherence, mental health assessment and care coordination of multidisciplinary services, such as nutrition counseling and case management.[21] The 2- to 4-week

visit should include testing for an HIV RNA level and laboratory testing that varies depending on the antiretroviral regimen.[21]

- **Long-Term Monitoring of Children on Antiretroviral Therapy**: The long-term monitoring of children maintained on antiretroviral therapy should typically occur every 3 to 4 months and include the following: HIV RNA level, absolute CD4 cell count, chemistries, complete blood count with differential, medication toxicity, and adherence assessment, and antiretroviral medication dosage adjustment for growth and weight if needed.[21] Urinalysis, lipid panel, and random plasma glucose should be obtained every 6 to 12 months.[21] Monitoring of CD4 cell count and laboratory studies to detect antiretroviral medication toxicity can be done less frequently (every 6 to 12 months) in children who have been clinically stable for at least 2 years and (1) are adherent on a stable antiretroviral therapy regimen, (2) have sustained virologic suppression, with HIV RNA levels less than 50 copies/mL, and (3) have a CD4 count above the threshold for opportunistic infection risk.[21] In contrast, HIV RNA monitoring should continue to be performed every 3-4 months in order to assess adherence to the antiretroviral regimen.[21]
- **Type of Immunologic Monitoring**: The use of absolute CD4 cell count is preferred for monitoring the immunologic status of children. For children younger than 5 years of age, monitoring CD4 percentage is an acceptable alternative.[21] The risk of disease progression associated with a specific CD4 count or percentage varies with the age of the patient, with younger children (less than 1 year of age) experiencing a higher risk of progression and death.[25,26]
- **Children with Suspected Virologic, Immunologic, and/or Clinical Deterioration**: Evaluation of children with suspected virologic, immunologic, and/or clinical deterioration should ideally include expert consultation and, in the setting of virologic failure, undergo adherence assessment and HIV drug resistance testing.[21]

Interpreting Immunologic and Virologic Parameters in Children

When interpreting immunologic laboratory parameters in children with HIV, age is a crucial determinant because of widely variable age-appropriate norms for absolute CD4 count and CD4 percentage. Young children typically have CD4 counts that are much higher than those seen in adults. For example, among children younger than 12 months of age who do not have any immunologic deficiency, most will have a CD4 count of at least 1,500 cells/mm^3. The normal CD4 count declines during the first few years of life. Conceptually, it is very important to understand that children with HIV, especially very young children, can develop HIV-related opportunistic infections at significantly higher CD4 cell counts than adults who develop HIV-related opportunistic infections.[27] In addition, HIV RNA values are also typically higher in very young children who acquire HIV perinatally than in adolescents and adults. Although high HIV RNA levels correlate with more rapid disease progression in adults, the predictive value for HIV RNA concentration in a specific child is only moderate; the range of HIV RNA values overlaps in young children who experience rapid disease progression and those who do not.[21]

Antiretroviral Treatment for Children with HIV

Principles of Antiretroviral Therapy in Children

Antiretroviral therapy has been shown to significantly reduce morbidity, mortality, and hospitalizations among children with HIV in the United States.[28,29,30,31] A large clinical trial that randomized infants 6 to 12 weeks of age with HIV to receive early antiretroviral therapy versus deferred therapy (based on CD4-related criteria) found a 75% reduction in mortality when using the more aggressive policy of early treatment of infants.[31] Studies in children have demonstrated benefits to earlier initiation of antiretroviral therapy at higher CD4 counts, including improved immune response, reduction in proviral reservoirs, and more rapid growth reconstitution.[31,32,33,34,35] Similar to adults, ongoing viral replication in children is believed to cause a persistent inflammatory state that increases the risk of developing non-AIDS complications, such as renal disease, cancer, liver disease, and cardiovascular disease.[36,37] Several studies have shown that initiating antiretroviral therapy is associated with decreased systemic inflammation, lower risk of cardiomyopathy, and improved neurocognitive outcomes.[38,39,40]

Recommendations for When to Start Antiretroviral Therapy

Given data regarding the association of antiretroviral treatment initiation with benefits for immunity, as well as growth and neurodevelopmental outcomes in children, the Pediatric ART Guidelines now recommend rapid initiation of combination antiretroviral treatment for all children diagnosed with HIV infection, regardless of age, CD4 count, or HIV RNA level.[41] Exceptions include simultaneous diagnoses of cryptococcal meningitis, tuberculosis, or disseminated *Mycobacterium avium* complex infection in pediatric patients.[41] In these cases, initiation of antiretroviral therapy may be postponed to reduce the risk of immune reconstitution inflammatory syndrome (IRIS).[41] Consulting a pediatric HIV specialist is recommended in such clinical scenarios. In some instances, three-drug presumptive antiretroviral therapy is initiated for newborns who are at the highest risk of HIV acquisition, even prior to a confirmed diagnosis of HIV.[42] For infants younger than 12 months of age who are diagnosed with HIV, urgent initiation of antiretroviral therapy is critical since they have the greatest risk of accelerated HIV disease progression, clinical illness, and death.[41] For older asymptomatic children with diagnosed HIV, the data regarding the risks and benefits of immediate antiretroviral therapy are more limited. Since antiretroviral therapy initiated at a young age will be lifelong, simultaneously addressing barriers to adherence and assessing social support are particularly important to prevent the development of antiretroviral drug resistance that would limit future options. Accordingly, regular and frequent follow-up with the child and caregiver(s) may be necessary during the period immediately following the start of antiretroviral therapy.[41]

Principles of Antiretroviral Therapy in Children

The following factors should be considered when selecting an optimal HIV treatment regimen for children:[43]

- Age and weight
- Potential antiretroviral drug resistance
- Frequency of dosing
- Available formulations of drugs
- Medication preparation and administration requirements
- Potential drug Interactions
- Tolerance and drug toxicities
- Contraindications
- Co-morbidities that may impact choice of antiretrovirals
- Ability of patient to swallow medication
- Medication availability, cost and insurance coverage

Recommended Antiretroviral Regimens for Initial Therapy

The recommended antiretroviral therapy regimens in the Pediatric ART Guidelines are based on child's age, including gestational age and weight.[43] The following tables summarizes the preferred recommendations based on age and weight, including preferred initial regimens and preferred dual nucleoside reverse transcriptase inhibitor (NRTI) backbone regimens [43]

Table 2. HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Infants from Birth to <30 Days of Age[a,b]

Age	Regimens	Age/Weight Restrictions[c]
Preferred Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Infants ≥37 weeks of gestation and aged <30 days *and* Preterm infants with a postmenstrual age of ≥37 weeks at treatment initiation	**NNRTI (Nevirapine) or INSTI (Raltegravir) plus two NRTIs**	
	Nevirapine *plus* zidovudine *plus* (lamivudine *or* emtricitabine)	None
	Ralegravir *plus* zidovudine *plus* (lamivudine *or* emtricitabine)	≥2 kg
Preterm infants ≥32 to <37 weeks of gestation	**NNRTI (Nevirapine) plus two NRTIs**	
	Nevirapine plus zidovudine *plus* (lamivudine *or* emtricitabine)	None
Preterm infants <32 weeks of gestation	Consultation with a pediatric HIV expert or the National Perinatal HIV/AIDS Hotline (1-888-448-8765) is recommended	
Alternative Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Postmenstrual age ≥42 weeks *and* Postnatal age of >14 days	**PI (Lopinavir-ritonavir) plus two NRTIs**	
	Lopinavir-ritonavir *plus* zidovudine *plus* (lamivudine *or* emtricitabine)	None
Alternative NRTI Backbone Based on Age and Weight at Time of Treatment Initiation		
Infants ≥37 weeks of gestation	Abacavir *plus* (lamivudine *or* emtricitabine) if HLA-B*5701 negative[d]	None

[a] Panel recommendations summarized in this table are for children with HIV-1 infection.
[b] Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c] Fixed dose combinations may be available for some medication combinations.

[d] Abacavir is not approved by the U.S. Food and Drug Administration (FDA) for use in full-term neonates and infants aged <3 months. Recent data from the IMPAACT P1106 trial and two observational cohorts provide reassuring data on the safety of ABC in infants when initiated at the age of <3 months. Before abacavir administration, a negative HLA-B*5701 allele test result should be available.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: regimens recommended for initial therapy of antiretroviral-naive children. June 27, 2024. [HIV.gov]

Table 3. HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Infants and Children Aged ≥30 Days to <2 Years [a,b]

Age	Regimens [c]	Age/Weight Restrictions
Preferred Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Aged ≥30 Days to <2 Years	**INSTI (Dolutegravir) plus two NRTIs**	
	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	Dolutegravir ≥30 days and ≥3 kg to <25
	Dolutegravir *plus* abacavir *plus* (lamivudine or emtricitabine) if if HLA-B*5701 negative	Dolutegravir ≥30 days and ≥3 kg to <25
	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥3 months and ≥6 kg to <25 kg (in fixed combination pediatric pill) ≥25 kg if using dolutegravir-abacavir-lam fixed-dose combination pediatric pill
Alternative Anchor Drugs Based on Age and Weight at Time of Treatment Initiation		
Alternative anchor drugs to replace dolutegravir in an ART regimen with a *Preferred* NRTI backbone for Infants Aged ≥30 days to <2 Years	Lopinavir-ritonavir (boosted PI)	Postmenstrual age ≥42 weeks and postn days (lopinavir-ritonavir oral solution)
	Atazanavir plus ritonavir (boosted PI)	>15 kg to <25 kg
	Nevirapine	<3 years (nevirapine solution)
Alternative NRTI Backbone Based on Age and Weight at Time of Treatment Initiation		
Infants ≥37 weeks of	None	Abacavir *plus* (lamivudine or emtricitabin

gestation		B*5701 negative[d]

[a] Panel recommendations summarized in this table are for children with HIV-1 infection.
[b]Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c]xFixed dose combinations may be available for some medication combinations.
[d] Before abacavir administration, a negative HLA-B*5701 allele test result should be available.
[e] If dolutegravir dispersible tablets are not available, raltegravir can be administered using either the oral granules for suspension dispersed in water or as the chewable tablets dispersed in juice, formula, or milk.
[f] An NRTI backbone of zidovudine plus lamivudine twice daily or abacavir plus lamivudine twice daily allows for all medications to be administered at the same time when given in combination with lopinavir-ritonavir or raltegravir. There is considerable experience with zidovudine and lamivudine in this age group. Abacavir is associated with less bone marrow toxicity than zidovudine and may be the preferred NRTI for long-term use.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: regimens recommended for initial therapy of antiretroviral-naive children. June 27, 2024. [HIV.gov]

Table 4. HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Children Aged ≥2 Years to <12 Years[a,b]

Age	Regimens	Age/Weight Restrictions[c]
Preferred Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Aged ≥2 Years to <12 Years	**INSTI (Dolutegravir) plus two NRTIs[d]**	

and **Unable** to swallow pills	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥3 months and ≥3 kg to <25 kg (dolutegravir-abacavir-lamivudine fixed-d combination pediatric pill)
	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	≥30 days and ≥3 kg (dolutegravir)
	Dolutegravir *plus* (tenofovir DF-emtricitibine or tenofovir alafenamide-emtricitabine)	≥14 kg to <25 kg (tenofovir alafenamide-
Aged ≥2 Years to <12 Years *and* **Able** to swallow pills	**INSTI (Bictegravir or Dolutegravir) plus 2NRTIs**	
	Bictegravir-tenofovir alafenamide-emtricitabine (fixed-dose combination)[e,f]	Aged ≥2 years and ≥14 kg to <25 kg (bic tenofovir alafenamide 15 mg-emtricitabin ≥25 kg (bictegravir 50 mg-tenofovir alafe emtricitabine 200 mg)
	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	≥14 kg (dolutegravir tablets)
	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥25 kg
	Dolutegravir *plus* (tenofovir DF-emtricitibine or tenofovir alafenamide-emtricitabine)	Aged ≥30 days and ≥3 kg (dolutegravir) ≥14 kg (tenofovir alafenamide-emtricitab
Alternative Anchor Drugs in Regimen with Preferred NRTI Backbone Based on Age and Weight at Time of Treatment Initiation		
Aged ≥2 Years to <12 Years *and with* Preferred NRTI Backbone[g]	Atazanavir powder *plus* ritonavir powder (boosted PI)	≥15kg to ≤25 kg
	Atazanavir capsules *plus* ritonavir tablets (boosted PI)	≥15 kg
	Atazanavir plus cobicistat in fixed dose combination tablet (boosted PI)	≥35 kg
	Darunavir *plus* ritonavir (boosted PI)	≥20 kg
	Darunavir *plus* cobicistat in fixed dose combination tablet (boosted PI)	≥40 kg
	Nevirapine	None
	Nevirapine XR	Age ≥6 years
	Efavirenz	Age ≥3 years and ≥10 kg
	Doravirine	≥30 kg

Abbreviations
INSTI = Integrase strand transfer inhibitor; NRTIs = nucleoside reverse transcriptase inhibitors

[a] Panel recommendations summarized in this table are for children with HIV-1 infection.

[b] Recommendations for antiretroviral drugs or antiretroviral therapy

regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c] Fixed dose combinations may be available for some medication combinations.
[d] Before abacavir administration, a negative HLA-B*5701 allele test result should be available.
[e] There are two different strengths of bictegravir-tenofovir alafenamide-emtricitabine (*Biktarvy*), with the lower-strength tablet for children weighing ≥14 kg and <25 kg.
[f] The product label for bictegravir-tenofovir alafenamide-emtricitabine (*Biktarvy*) states that for children who are unable to swallow a whole tablet, the bictegravir-tenofovir alafenamide-emtricitabine tablet can be split and each part taken separately, as long as all parts are ingested within approximately 10 minutes.
[g] The tenofovir alafenamide plus emtricitabine is recommended as a *Preferred* NRTI combination for children and adolescents weighing ≥14 kg when used with an INSTI or NNRTI; a fixed dose tablet that contains tenofovir alafenamide plus emtricitabine (*Descovy*) is available in two strengths, with dosage determined by a child's weight. Tenofovir alafenamide-emtricitabine is approved by the FDA for children weighing ≥14 kg when used in the regimen bictegravir-tenofovir alafenamide-emtricitabine, which is also available in two strengths, with dosage determined by a child's weight. Tenofovir alafenamide-emtricitabine is a *Preferred* NRTI combination for children and adolescents weighing ≥35 kg when used with a boosted PI; tenofovir alafenamide-emtricitabine is not approved or recommended for use with a boosted PI in children weighing <35 kg.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for

the use of antiretroviral agents in pediatric HIV infection. What to start: regimens recommended for initial therapy of antiretroviral-naive children. June 27, 2024. [HIV.gov]

Antiretroviral Medication Information for Pediatric Use

For many of the approved antiretroviral agents, the FDA has stipulated specific age or weight restrictions based on limited available data in pediatric populations. Although starting regimens for children and adolescents typically consist of a select few of the best-studied regimens, a much more limited evidence base informs the assembly of salvage regimens. The Pediatric ART Guidelines maintain an excellent compendium of pediatric antiretroviral drug information that includes an overview of the FDA approval status of the antiretroviral medications in children, specific formulations, drug interactions, toxicities, and dosing recommendations in different aged children.[44] Although abacavir is presently not FDA-approved for use in infants younger than 3 months of age, it can be considered for use in newborns if zidovudine is not available or the infant has zidovudine-associated toxicity.[42] None of the preferred 2-NRTI backbones in children up to 12 years of age include tenofovir DF due to concerns about bone toxicity, especially since children with perinatally-acquired HIV already have reduced bone mineral density.[43,45,46,47] The Pediatric ART Guidelines are regularly updated as new data is available for dosing and the safety of antiretrovirals in infants and children and FDA approval status changes.[44]

Adherence with Antiretroviral Therapy

Poor adherence to antiretroviral therapy reduces the likelihood of virologic suppression, increases the risk of developing drug resistance mutations and virologic failure, limits future treatment options, and can lead to both disease progression and secondary transmission. Although the threshold for adherence associated with successful virologic suppression varies by individual drug as well as by individual patient characteristics, suboptimal adherence generally leads to poorer outcomes. Children with HIV often struggle with adherence due to complex dosing regimens, typical age-appropriate behaviors (toddlers, adolescents), dependency on an adult caregiver to reliably provide therapy, and social issues within the family unit, such as substance use or homelessness.[48] The Pediatric ART Guidelines recommend using antiretroviral regimens with reduced pill burden and once-daily dosing frequency whenever feasible to improve adherence. Eligible patients and their caregivers should be informed about the option of long-acting injectable antiretroviral therapy that can optimize adherence. Furthermore, it is recommended that providers monitor for adherence at every visit.[49] These strategies are organized into three categories: (1) initial intervention strategies, (2) medication strategies, and (3) follow-up intervention strategies.[49] To promote adherence, the Pediatric ART Guidelines recommend regular viral load monitoring and at least one other measure of medication adherence.[49]

Table 5. **Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection**

Evidence-Based Approaches for Monitoring Medication Adherence

Routine Assess	Description

Monitor viral load.	Viral load monitoring should be done more frequently after initiating or changing medications.
Assess quant	Ask patient and/or care

itative self-report of missed doses.	given about the number of missed doses over defined period (1, 3, or 7 days).
Request a description of the me	Ask the patient and/or caregiver about the nam

dication regimen.	e, appearance, and number of medications and how often the medications are taken.
Assess barriers to medi	Engage the patient and caregiver

cation administration.	individual or group counseling sessions to discuss barriers and challenges to adherence.				
Monitor pharmacy refills.	Approaches include pharmacy-based or clinic-based assessm				

	ent of on-time medication refills.
Employ telemedicine to monitor and support medication adherence	Telemedicine visits allow remote and often face-to-face contact and provide new oppo

istration.	rtunities to support families; to visualize ART preparation, handling, and swallowing; and to conduct DOT in the home setti		

	ng.
Conduct announced and unannounced pill counts.	Approaches include asking patients to bring medications to clinic, home visits, or referral to community health nursing

	.
Monitor attendance for injection clinic visits among adolescents on long-acting injectable antiretrovirals, adherence is related to receiving scheduled injections on time. Th	For individuals on long-acting injectable antiretrovirals, adherence is related to receiving scheduled injections on time. Th

ble regimens.	erefore, reducing barriers to adherence should focus on scheduling convenient appointments, minimizing school and work		

	absences, and ensuring transportation to appointments.
Targeted Approaches to Monitor Adhe	**Description**

rence in Special Circu	
Implement directly observed therapy (DOT) in person a	Include brief period of hospitalization if indicated.

ndviatelemedicine.	
Measuredrugconcentrationinplasmaordriedbloodspots.	Measuringdrugconcentrationscanbeconsideredforparticulardrugs.
Ap	**Des**

Approach to Monitor Medication Adherence in Research Settings	Description
Meas	Measurin

ured rug con cent rati ons in hai r.	g hair drug concentrations can be considered for particular drugs; it provides a good measure of adherence over time.
Us	Appr

electronic monitoring devices.	oaches include medication Event Monitoring System [MEMS] caps and Wisepill
Use mobile phone-based te	Approaches include interactive voice re

chnologies.	sponse, text messaging, and mobile apps.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Adherence to antiretroviral therapy in children and adolescents living with HIV. June 27, 2024. [HIV.gov]

Management of Antiretroviral Toxicity

Children taking lifelong antiretroviral therapy need to be monitored for both acute and chronic adverse effects, which can potentially involve different organ systems.[50,51,52] This is particularly important as new antiretroviral treatment options become available that do not have a long track record of pediatric use. The Pediatric ART Guidelines have compiled reference tables of potential adverse effects associated with different antiretroviral agents, and these guidelines provide detailed summaries for different types of adverse effects.[52] The implications of long-term exposure (from infancy or childhood) to antiretroviral medications remain an area of active study, and it is unclear whether life expectancy will be altered in individuals who survive into adulthood with perinatally-acquired HIV.[46]

Immunizations for Children Living with HIV

Immunization Guideline Resources

The Advisory Committee for Immunization Practices (ACIP) publishes annual guidelines for the use of vaccines for all children and adolescents, including specific recommendations for vaccines based on medical conditions.[53,54,55]

Immunization Recommendations for Children with HIV

All inactivated vaccines are safe to administer to children with HIV, irrespective of their immune status. Accordingly, all infants and children with HIV should receive inactivated vaccines per standard recommended pediatric schedules. Children with HIV may also need to receive additional vaccinations if the vaccines were not administered in infancy.[54,55] For routine immunization recommendations for children with HIV, see the most recent recommendations in the ACIP Adult Immunization Schedule.[55]

Use of Live Vaccines in Children with HIV

The ACIP defines high-level immunosuppression for children aged 18 years or younger as a CD4 percentage less than 15 or an absolute CD4 count less than 200 cells/mm^3.[55]

- **Live Influenza Virus Vaccine**: The live attenuated influenza vaccine is not recommended for children and adolescents with HIV, regardless of CD4 cell count or percentage.[55]
- **Live Measles Mumps-Rubella (MMR) Vaccine**: This vaccine is recommended for children or adolescents with HIV, unless they have high-level immunosuppression (CD4 cell count less than 200 cells/mm^3 or CD4 percentage less than 15%).[55]
- **Live Rotavirus Vaccine**: Although rotavirus is a live vaccine, it is recommended (with precaution) for all children with HIV, according to the usual dosing schedule.[55]
- **Live Varicella Vaccine**: This vaccine is recommended for children or adolescents with HIV, unless they have high-level immunosuppression (CD4 cell count less than 200 cells/mm^3 or a CD4 percentage less than 15%).[55]
- **Dengue Vaccine**: Dengue vaccine should not be administered to children or adolescents with HIV if they have high-level immunosuppression (CD4 cell count less than 200 cells/mm^3 or a CD4 percentage less than 15%); dengue vaccine can be administered with precaution to children with HIV if they have a CD4 count of at least 200 cells/mm^3 and they have a CD4 percentage of at least 15%.[55]

Opportunistic Infections in Children

It is beyond the scope of this review to address the prevention and treatment of all opportunistic infections that occur in children with HIV. The Pediatric OI Guidelines provide detailed information regarding prevention and treatment of the major opportunistic infections that occur in children.[56] The following discussion will focus on the prevention of three important opportunistic infections that can occur in children: *Pneumocystis* Pneumonia, *Toxoplasma* encephalitis, and disseminated *Mycobacterium avium* complex.[57,58,59] For additional information on the prevention of opportunistic infections in children and for information related to the treatment of opportunistic infections in children, see the detailed discussion in the Pediatric OI Guidelines.[56]

Pneumocystis Pneumonia Prophylaxis

Prophylaxis against *Pneumocystis jirovecii* pneumonia is an extremely beneficial intervention among infants with HIV, especially for those infants not yet on antiretroviral therapy. The incidence of *Pneumocystis* pneumonia in children with HIV is highest during the first year of life, with cases peaking at 3 to 6 months of age.[58] In resource-limited settings, *Pneumocystis* pneumonia has been shown in autopsy studies to cause up to 44% of HIV-associated deaths in children with HIV.[60]

Initiating *Pneumocystis* Pneumonia Prophylaxis in Children

The Pediatric OI Guidelines recommend administering *Pneumocystis* pneumonia prophylaxis in children with HIV who meet the following age-specific requirements:[58]

- **Age younger than 12 months (including those who are HIV indeterminate)**: All should receive *Pneumocystis* pneumonia prophylaxis, regardless of CD4 cell count or CD4 percentage.
- **Age 1 to 5 years**: CD4 count less than 500 cells/mm^3 or CD4 percentage is less than 15%.
- **Age 6 to 12 years**: CD4 count less than 200 cells/mm^3 or a CD4 percentage less than 15%

Recommended Regimens for *Pneumocystis* Pneumonia Prophylaxis in Children

Trimethoprim-sulfamethoxazole is the first choice for *Pneumocystis* pneumonia prophylaxis in infants and children.[58] This medication can be dosed daily or on three consecutive days per week. For those unable to take trimethoprim-sulfamethoxazole, acceptable alternatives include dapsone and atovaquone.[58] If the child is unable to tolerate any of these agents, aerosolized pentamidine can be used—if they are old enough to use nebulization with a Respirgard II nebulizer (typically older than 5 years of age).

Discontinuing *Pneumocystis* Pneumonia Prophylaxis in Children

All infants with confirmed HIV should continue *Pneumocystis* pneumonia prophylaxis until age 1 year and then undergo reassessment for the need for prophylaxis.[58] Infants who test HIV-indeterminate should continue *Pneumocystis* pneumonia prophylaxis until it is determined they do not have HIV infection.[58] For children with HIV who are older than 1 year of age, discontinuing *Pneumocystis* pneumonia prophylaxis should be considered if the child has received combination antiretroviral therapy for at least 6 months and has surpassed the original age-specific CD4 count and percentage threshold for initiating prophylaxis and maintained above that threshold for at least 3 consecutive months.[58] For children who do not have virologic suppression, the CD4 count and percentage should be reassessed every 3 months and prophylaxis should be restarted if the age-specific threshold for prophylaxis is once again met.

Prophylaxis Against Toxoplasma Encephalitis in Children

Toxoplasma gondii is a protozoan parasite that can infect humans and cause encephalitis and, more rarely, retinitis, pneumonitis, and disseminated disease. Risk factors for acquiring *T. gondii* include exposure to cats

(particularly cat feces), eating undercooked red meat, or ingesting raw shellfish.[57]

Indications for Prophylaxis Against *Toxoplasma* in Children

The Pediatric OI Guidelines recommend administering *Toxoplasma* encephalitis prophylaxis in toxoplasma-seropositive children with HIV who meet the following age-specific thresholds:[57]

- **Age younger than 6 years**: CD4 percentage less than 15%
- **Age 6 years and older**: CD4 count less than 100 cells/mm^3

Recommended Regimens for *Toxoplasma* Prophylaxis in Children

Trimethoprim-sulfamethoxazole is the preferred agent for *Toxoplasma* prophylaxis in all infants and children.[57] For those unable to take trimethoprim-sulfamethoxazole, the acceptable alternative is dapsone plus atovaquone.[57] Atovaquone with or without pyrimethamine can also be considered.

Discontinuing Toxoplasma Prophylaxis in Children

Discontinuing *Toxoplasma* prophylaxis should be considered if the child has received combination antiretroviral therapy for at least 6 months and for at least 3 consecutive months, has maintained a CD4 percentage above 15% for children younger than 6 years of age and greater than 200 cells/mm^3 for children 6 years of age and older.[57] For children who do not have virologic suppression, the CD4 percentage should be reassessed every 3 months and prophylaxis should be restarted if the age-specific threshold for prophylaxis is once again met.[57]

Prophylaxis Against *Mycobacterium avium* complex (MAC) in Children

Mycobacterium avium complex (MAC) is a ubiquitous organism that can cause disseminated disease in severely immunocompromised hosts. It is uncommon during the first year of life and its incidence increases with age and with declining CD4 count.

Indications for Prophylaxis Against MAC in Children

The Pediatric OI Guidelines recommend administering MAC prophylaxis to children with advanced immunosuppression, defined by age and CD4 count as:[59]

- **Children aged less than 1 year**: CD4 less than 750 cells/mm^3
- **Children aged 1 year to less than 2 years**: CD4 less than 500 cells/mm^3
- **Children aged 2 years to less than 6 years**: CD4 less than 75 cells/mm^3
- **Children aged 6 years or older**: CD4 less than 50 cells/mm^3

Recommended Regimens for MAC Prophylaxis in Children

The recommended regimen is azithromycin or clarithromycin (both available in suspensions).[59] Children who cannot take azithromycin or clarithromycin for prophylaxis may be offered rifabutin as an alternative, though clinicians should be aware of significant drug interactions associated with rifabutin, as well as a lack of pediatric data on its use.[59] Prior to initiating primary prophylaxis for MAC, a blood culture should be obtained to rule out preexisting disseminated disease.

Discontinuing MAC Prophylaxis in Children

For children older than 2 years of age with HIV, discontinuing MAC prophylaxis should be considered if the child has received combination antiretroviral therapy for at least 6 months and has surpassed the original age-specific CD4 count and percentage threshold for initiating prophylaxis (greater than 100 cells/mm^3 for

children at least 6 years of age and greater than 200 cells/mm^3 for children aged 2 years to less than 6 years) and maintained above that threshold for at least 3 consecutive months.[59] The Pediatric OI Guidelines do not make any specific recommendations for discontinuing prophylaxis in children younger than 2 years of age.

Summary Points

- In the United States, at year-end 2022, there was an estimated 1,124 children younger than 13 years of age living with diagnosed HIV in the United States; this number represents approximately 0.1 percent of all persons living with HIV in the United States.
- The 2014 CDC Revised Case Surveillance Definition for HIV specifies criteria for staging HIV in children by age and CD4 cell count, which is closely aligned with adult staging and differs from the prior pediatric classification system that was based on separate immunologic and clinical categories.
- A virologic assay (HIV nucleic acid testing, or NAT) that directly detects HIV RNA or HIV DNA is required to diagnose HIV among perinatally-exposed infants younger than 18 months of age.
- For infants born to mothers with HIV with a low risk of transmission, the recommended HIV diagnostic evaluation includes HIV nucleic acid testing at 3 time points after birth: 14 to 21 days, 1 to 2 months, and 4 to 6 months. For higher-risk infants, testing is also recommended at birth and 2 to 6 weeks after cessation of antiretroviral prophylaxis.
- The diagnosis of HIV can be excluded in a non-breastfed infant with (1) two negative virologic tests (at 1 month or later, and at 4 to 6 months or later) or (2) two or more negative antibody tests performed at 6 months of age or older.
- Monitoring for CD4 cell count and HIV RNA should be based on the child’s immune status, whether they are taking antiretroviral therapy, and whether they have suppressed HIV RNA levels.
- For women breastfeeding, most experts recommend maternal HIV RNA monitoring should be done every 1 to 2 months during breastfeeding. A detectable maternal HIV RNA level should prompt expert consultation.
- Antiretroviral therapy with rapid initiation is recommended for all infants and children, with special urgency for infants younger than 12 months of age.
- Preferred and alternative pediatric antiretroviral therapy regimens are based on a child’s age and special circumstances, and many antiretroviral agents have age restrictions based on limited data in pediatric populations.
- *Pneumocystis* pneumonia prophylaxis should be given to all children with HIV (or HIV indeterminate) who are less than 12 months of age, regardless of CD4 cell count or CD4 percentage. PCP prophylaxis in older children, as well as prophylaxis against *Toxoplasma* encephalitis *Mycobacterium avium* complex (MAC) disease in children of all ages, is based on the degree of immunosuppression.

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Figures

Figure 1 Annual Number of Perinatally-Acquired HIV Infections, United States, 1978–2022

During the years 1978-1993, the estimates were generated through a back calculation method.

Source: Centers for Disease Control and Prevention.

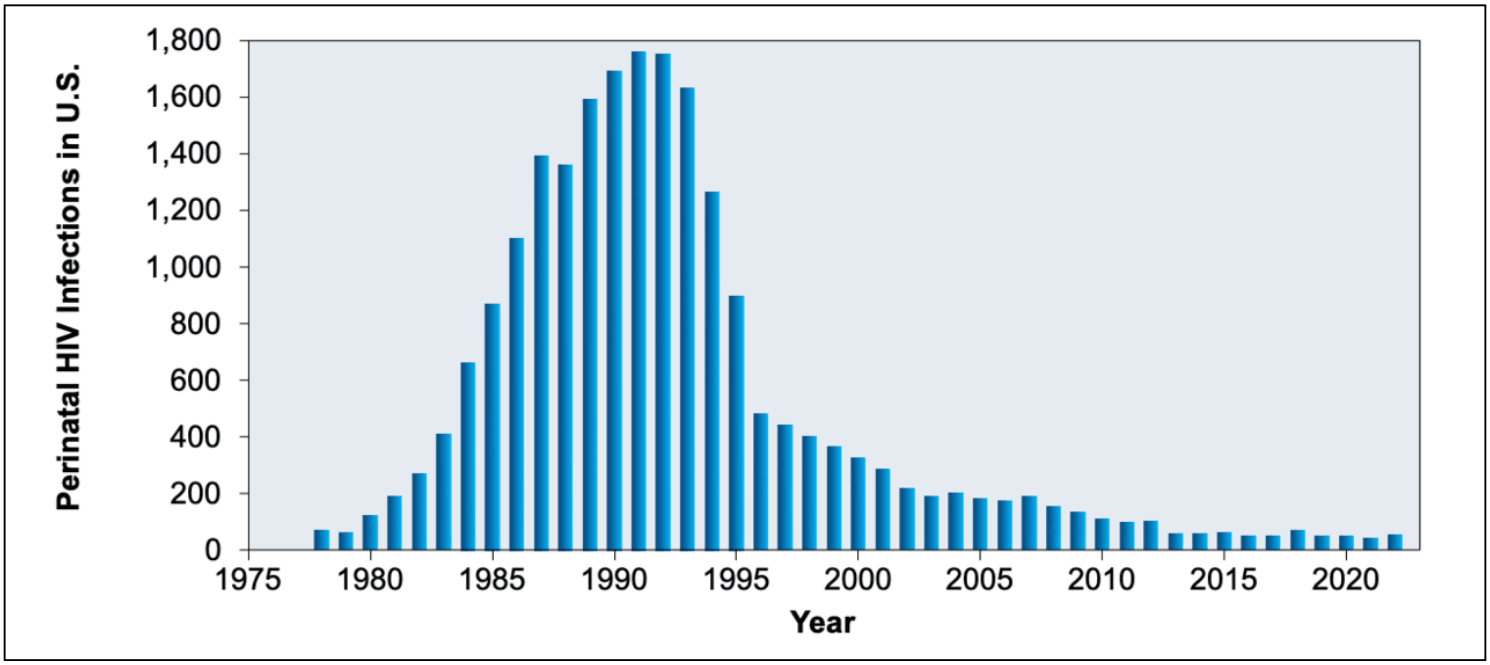


Figure 2 (Image Series) - HIV Epidemiology for Children in United States (Image Series) - Figure 2 (Image Series) - HIV Epidemiology for Children in United States
Image 2A: Persons Living with Diagnosed HIV. by Age, Year End 2022

Source: Centers for Disease Control and Prevention. Diagnoses, deaths, and prevalence of HIV in the United States and 6 territories and freely associated states, 2022. HIV Surveillance Report, 2022; vol. 35:1-177. Published May 2024.

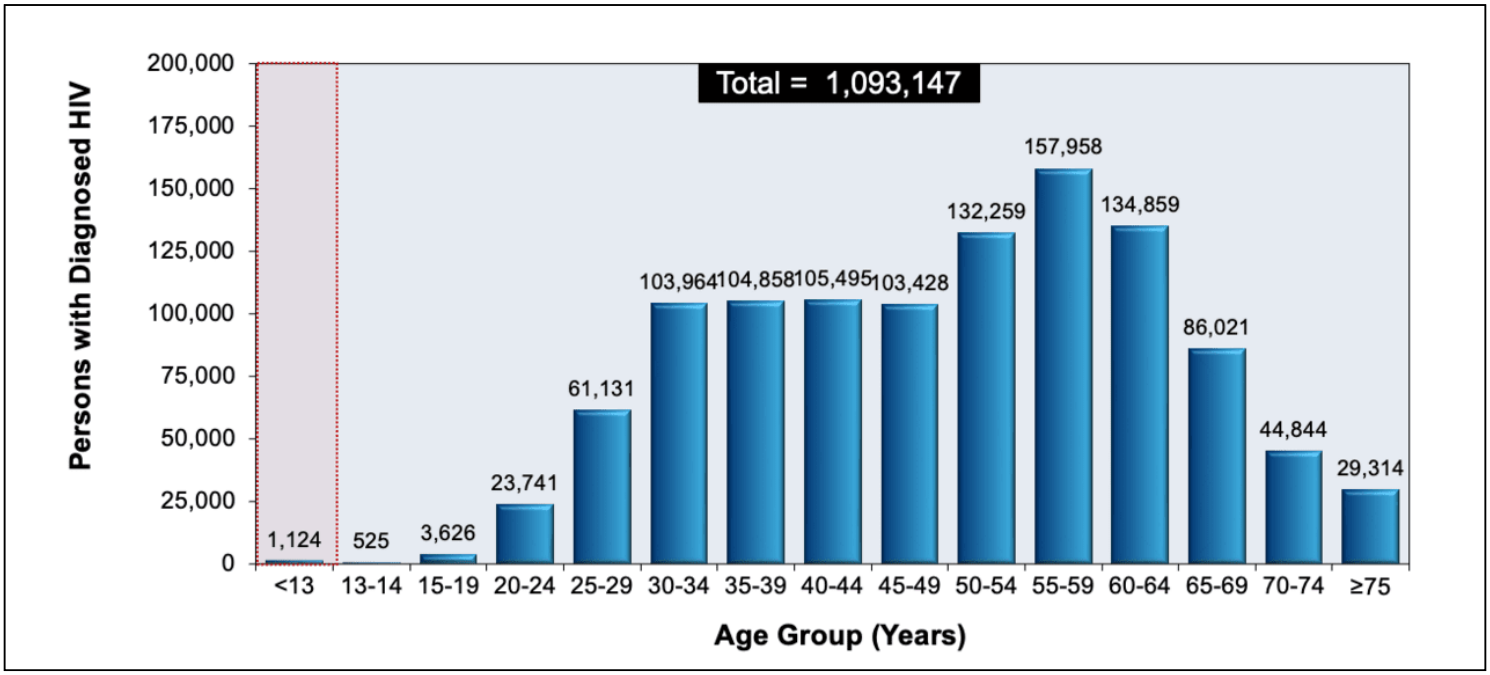


Figure 2 (Image Series) - HIV Epidemiology for Children in United States
Image 2B: Children

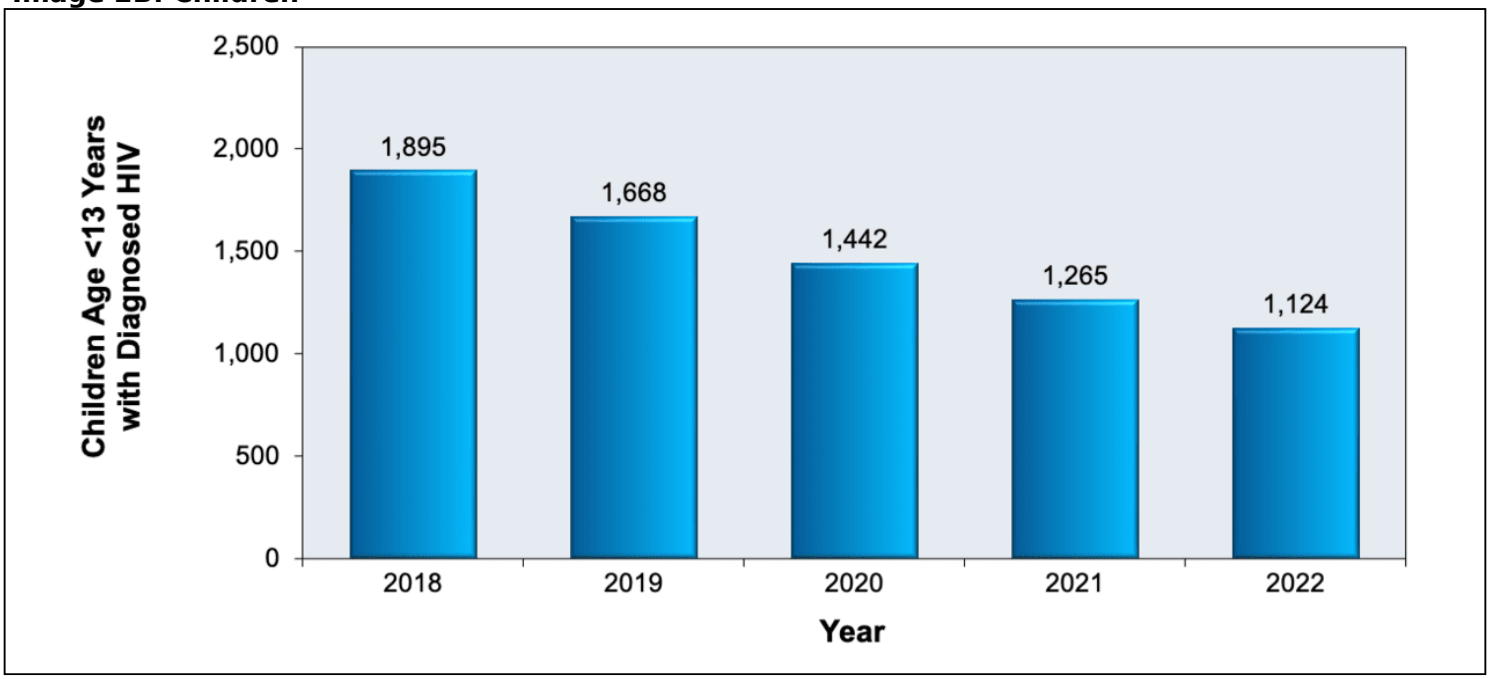


Figure 2 (Image Series) - HIV Epidemiology for Children in United States
Image 2C: Children

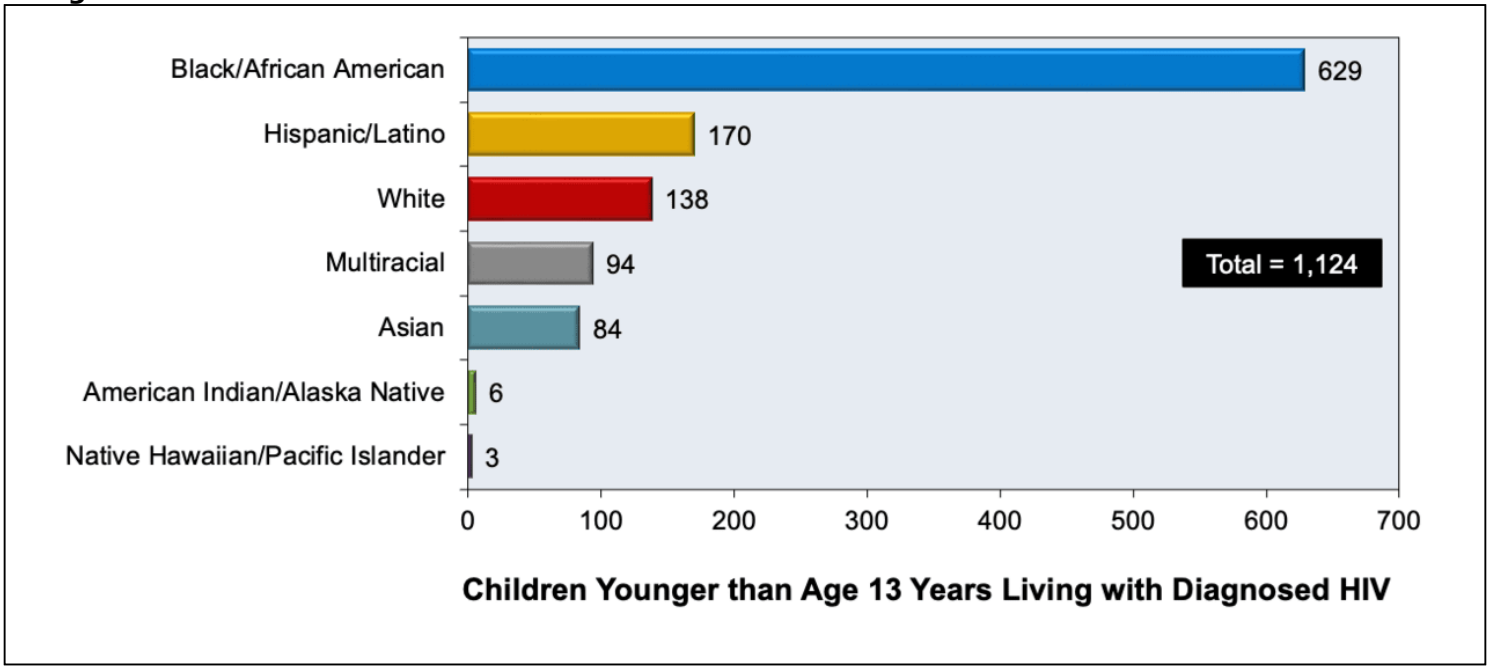
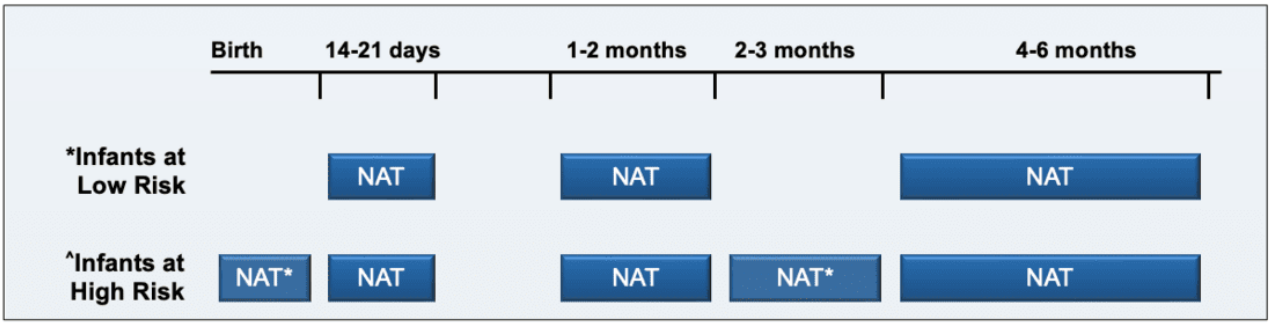


Figure 3 Recommended Virologic Testing Schedules for Infants Exposed to HIV by Perinatal HIV Transmission Risk

Abbreviation: NAT = nucleic acid test (e.g., HIV RNA or HIV DNA PCR)

Source: Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Diagnosis of HIV infection in infants and children. January 31, 2023.



*Low Risk refers to infants born to mothers with HIV who received standard antiretroviral therapy during pregnancy, had sustained suppression of HIV RNA levels, and were adherent to their antiretroviral regimen.

^High risk infants refers to infants born to mothers with HIV who did not receive prenatal care; received no antepartum antiretroviral therapy or only intrapartum antiretroviral therapy; initiated antiretroviral therapy late in pregnancy (during the late second or third trimester); received a diagnosis of acute HIV infection during pregnancy or in labor; and/or had detectable HIV viral loads (≥50 copies/mL) close to the time of delivery, including those who received antiretroviral therapy but did not achieve sustained viral suppression.

Table 1.

HIV Infection Stage[a] Based on Age-Specific CD4 Cell Count or Percentage

Stage	Age on Date of CD4 Test					
	<1 Year		1 to < 6 Years		≥6 Years	
	CD4 cells/µL	CD4%	CD4 cells/µL	CD4%	CD4 cells/µL	CD4%
1	≥1,500	≥34	≥1,000	≥30	≥500	≥26
2	750-1,499	26-33	500-999	22-29	200-499	14-25
3	<750	<26	<500	<22	<200	<14

[a] The stage is based primarily on the CD4 cell count; the CD4 cell count takes precedence over the CD4 percentage, and the percentage is considered only if the count is missing. If a Stage 3-defining opportunistic illness has been diagnosed, then the stage is 3 regardless of CD4 test results.

Source:

- Centers for Disease Control and Prevention. Revised surveillance case definition for HIV infection--United States, 2014. MMWR Recomm Rep. 2014;63:1-10. [PubMed Abstract]

Table 2. HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Infants from Birth to <30 Days of Age[a,b]

Age	Regimens	Age/Weight Restrictions[c]
Preferred Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Infants ≥37 weeks of gestation and aged <30 days *and* Preterm infants with a postmenstrual age of ≥37 weeks at treatment initiation	**NNRTI (Nevirapine) or INSTI (Raltegravir) plus two NRTIs**	
	Nevirapine *plus* zidovudine *plus* (lamivudine *or* emtricitabine)	None
	Ralegravir *plus* zidovudine *plus* (lamivudine *or* emtricitabine)	≥2 kg
Preterm infants ≥32 to <37 weeks of gestation	**NNRTI (Nevirapine) plus two NRTIs**	
	Nevirapine plus zidovudine *plus* (lamivudine *or* emtricitabine)	None
Preterm infants <32 weeks of gestation	Consultation with a pediatric HIV expert or the National Perinatal HIV/AIDS Hotline (1-888-448-8765) is recommended	
Alternative Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Postmenstrual age ≥42 weeks *and* Postnatal age of >14 days	**PI (Lopinavir-ritonavir) plus two NRTIs**	
	Lopinavir-ritonavir *plus* zidovudine *plus* (lamivudine *or* emtricitabine)	None
Alternative NRTI Backbone Based on Age and Weight at Time of Treatment Initiation		
Infants ≥37 weeks of gestation	Abacavir *plus* (lamivudine *or* emtricitabine) if HLA-B*5701 negative[d]	None

[a] Panel recommendations summarized in this table are for children with HIV-1 infection.
[b] Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c] Fixed dose combinations may be available for some medication combinations.
[d] Abacavir is not approved by the U.S. Food and Drug Administration (FDA) for use in full-term neonates and infants aged <3 months. Recent data

from the IMPAACT P1106 trial and two observational cohorts provide reassuring data on the safety of ABC in infants when initiated at the age of <3 months. Before abacavir administration, a negative HLA-B*5701 allele test result should be available.	

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: regimens recommended for initial therapy of antiretroviral-naive children. June 27, 2024. [HIV.gov]

Table 3. HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Infants and Children Aged ≥30 Days to <2 Years [a,b]

Age	Regimens [c]	Age/Weight Restrictions
Preferred Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Aged ≥30 Days to <2 Years	**INSTI (Dolutegravir) plus two NRTIs**	
	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	Dolutegravir ≥30 days and ≥3 kg to <25
	Dolutegravir *plus* abacavir *plus* (lamivudine or emtricitabine) if if HLA-B*5701 negative	Dolutegravir ≥30 days and ≥3 kg to <25
	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥3 months and ≥6 kg to <25 kg (in fixed combination pediatric pill) ≥25 kg if using dolutegravir-abacavir-lam fixed-dose combination pediatric pill
Alternative Anchor Drugs Based on Age and Weight at Time of Treatment Initiation		
Alternative anchor drugs to replace dolutegravir in an ART regimen with a *Preferred* NRTI backbone for Infants Aged ≥30 days to <2 Years	Lopinavir-ritonavir (boosted PI)	Postmenstrual age ≥42 weeks and postn days (lopinavir-ritonavir oral solution)
	Atazanavir plus ritonavir (boosted PI)	>15 kg to <25 kg
	Nevirapine	<3 years (nevirapine solution)
Alternative NRTI Backbone Based on Age and Weight at Time of Treatment Initiation		
Infants ≥37 weeks of gestation	None	Abacavir *plus* (lamivudine or emtricitabin B*5701 negative[d]

[a] Panel recommendations summarized in this table are for children with HIV-1 infection.
[b]Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c]xFixed dose combinations may be available for some medication combinations.
[d] Before abacavir administration, a negative HLA-B*5701 allele test result should be available.
[e] If dolutegravir dispersible tablets are not available, raltegravir can be

administered using either the oral granules for suspension dispersed in water or as the chewable tablets dispersed in juice, formula, or milk. [f] An NRTI backbone of zidovudine plus lamivudine twice daily or abacavir plus lamivudine twice daily allows for all medications to be administered at the same time when given in combination with lopinavir-ritonavir or raltegravir. There is considerable experience with zidovudine and lamivudine in this age group. Abacavir is associated with less bone marrow toxicity than zidovudine and may be the preferred NRTI for long-term use.	

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: regimens recommended for initial therapy of antiretroviral-naive children. June 27, 2024. [HIV.gov]

Table 4. HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Children Aged ≥2 Years to <12 Years[a,b]

Age	Regimens	Age/Weight Restrictions[c]
Preferred Initial Regimens Based on Age and Weight at Time of Treatment Initiation		
Aged ≥2 Years to <12 Years *and* **Unable** to swallow pills	**INSTI (Dolutegravir) plus two NRTIs**[d]	
	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥3 months and ≥3 kg to <25 kg (dolutegravir-abacavir-lamivudine fixed-d combination pediatric pill)
	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	≥30 days and ≥3 kg (dolutegravir)
	Dolutegravir *plus* (tenofovir DF-emtricitibine or tenofovir alafenamide-emtricitabine)	≥14 kg to <25 kg (tenofovir alafenamide-
Aged ≥2 Years to <12 Years *and* **Able** to swallow pills	**INSTI (Bictegravir or Dolutegravir) plus 2NRTIs**	
	Bictegravir-tenofovir alafenamide-emtricitabine (fixed-dose combination)[e,f]	Aged ≥2 years and ≥14 kg to <25 kg (bic tenofovir alafenamide 15 mg-emtricitabin ≥25 kg (bictegravir 50 mg-tenofovir alafe emtricitabine 200 mg)
	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	≥14 kg (dolutegravir tablets)
	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥25 kg
	Dolutegravir *plus* (tenofovir DF-emtricitibine or tenofovir alafenamide-emtricitabine)	Aged ≥30 days and ≥3 kg (dolutegravir) ≥14 kg (tenofovir alafenamide-emtricitab
Alternative Anchor Drugs in Regimen with Preferred NRTI Backbone Based on Age and Weight at Time of Treatment Initiation		
Aged ≥2 Years to <12 Years *and with* Preferred NRTI Backbone[g]	Atazanavir powder *plus* ritonavir powder (boosted PI)	≥15kg to ≤25 kg
	Atazanavir capsules *plus* ritonavir tablets (boosted PI)	≥15 kg
	Atazanavir plus cobicistat in fixed dose combination tablet (boosted PI)	≥35 kg
	Darunavir *plus* ritonavir (boosted PI)	≥20 kg
	Darunavir *plus* cobicistat in fixed dose combination tablet (boosted PI)	≥40 kg
	Nevirapine	None
	Nevirapine XR	Age ≥6 years
	Efavirenz	Age ≥3 years and ≥10 kg

	Doravirine	≥30 kg

Abbreviations
INSTI = Integrase strand transfer inhibitor; NRTIs = nucleoside reverse transcriptase inhibitors

[a] Panel recommendations summarized in this table are for children with HIV-1 infection.

[b] Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).

[c] Fixed dose combinations may be available for some medication combinations.

[d] Before abacavir administration, a negative HLA-B*5701 allele test result should be available.

[e] There are two different strengths of bictegravir-tenofovir alafenamide-emtricitabine (*Biktarvy*), with the lower-strength tablet for children weighing ≥14 kg and <25 kg.

[f] The product label for bictegravir-tenofovir alafenamide-emtricitabine (*Biktarvy*) states that for children who are unable to swallow a whole tablet, the bictegravir-tenofovir alafenamide-emtricitabine tablet can be split and each part taken separately, as long as all parts are ingested within approximately 10 minutes.

[g] The tenofovir alafenamide plus emtricitabine is recommended as a *Preferred* NRTI combination for children and adolescents weighing ≥14 kg when used with an INSTI or NNRTI; a fixed dose tablet that contains tenofovir alafenamide plus emtricitabine (*Descovy*) is available in two strengths, with dosage determined by a child's weight. Tenofovir alafenamide-emtricitabine is approved by the FDA for children weighing ≥14 kg when used in the regimen bictegravir-tenofovir alafenamide-emtricitabine, which is also available in two strengths, with dosage determined by a child's weight. Tenofovir alafenamide-emtricitabine is a *Preferred* NRTI

combination for children and adolescents weighing ≥35 kg when used with a boosted PI; tenofovir alafenamide-emtricitabine is not approved or recommended for use with a boosted PI in children weighing <35 kg.	

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: regimens recommended for initial therapy of antiretroviral-naive children. June 27, 2024. [HIV.gov]

Table 5. **Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection**

Evidence-Based Approaches for Monitoring Medication Adherence

Routine Assessment of Medication Adherence in Clinical Care	**Description**
Monitor viral load.	Viral load monitoring should be done more frequently after initiating or changing medications.
Assess quantitative self-report of missed doses.	Ask patient and/or caregiver about the number of missed doses over 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 dialogue around facilitators and challenges to adherence.
Monitor pharmacy refills.	Approaches include 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 announced and unannounced pill counts.	Approaches include asking patients to bring medications to clinic, home visits, or referral to community health nursing.
Monitor attendance for injection clinic visits among adolescents on long-acting injectable regimens.	For individuals on long-acting injectable antiretrovirals, 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 Monitor Adherence in Special Circumstances	**Description**
Implement directly observed therapy (DOT) in person and via telemedicine.	Include brief period of hospitalization if indicated.
Measure drug concentration in plasma or dried blood spots.	Measuring drug concentrations can be considered for particular drugs.
Approaches to Monitor 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.
Use electronic monitoring devices.	Approaches include medication Event Monitoring System [MEMS] caps and Wisepill
Use mobile phone-based technologies.	Approaches include interactive voice response, text messaging, and mobile apps.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Adherence to antiretroviral therapy in

children and adolescents living with HIV. June 27, 2024. [HIV.gov]