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Strategies for Identifying and Linking HIV-Infected Infants, Children, and Adolescents to HIV Treatment Services in Resource Limited Settings

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Abstract

Many children living with HIV in resource-limited settings remain undiagnosed and at risk for HIV-related mortality and morbidity. This article describes 5 key strategies for strengthening HIV case finding and linkage to treatment for infants, children, and adolescents. These strategies result from lessons learned during the Accelerating Children's HIV/AIDS Treatment Initiative, a public-private partnership between the President's Emergency Plan for AIDS Relief (PEPFAR) and the Children's Investment Fund Foundation (CIFF). The 5 strategies include (1) implementing a targeted mix of HIV case finding approaches (eg, provider-initiated testing and counseling within health facilities, optimization of early infant diagnosis, index family testing, and integration of HIV testing within key population and orphan and vulnerable children programs); (2) addressing the unique needs of adolescents; (3) collecting and using data for program improvement; (4) fostering a supportive political and community environment; and (5) investing in health system-strengthening activities. Continued advocacy and global investments are required to eliminate AIDS-related deaths among children and adolescents.

Keywords

pediatrics; HIV case finding; HIV treatment; adolescents; resource-limited settings

INTRODUCTION

Although new HIV infections among children have declined by 47% since 2010,¹⁻³ an estimated 160,000 children younger than 15 years acquire HIV annually.³ Without

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treatment, HIV infection is often rapidly progressive and fatal among infants, with an estimated 52% dying within 12 months of birth.⁴ Antiretroviral treatment (ART) can reduce this mortality by up to 75%.^{5–8} Beyond infancy, long-term survivors can remain undiagnosed throughout childhood and into adolescence.⁹ Although early mortality is very high among untreated infants infected prenatally and intrapartum, evidence suggests that infants infected during breastfeeding can survive much longer without treatment.¹⁰

The Accelerating Children's HIV/AIDS Treatment (ACT) Initiative was a \$200 million public–private partnership between the President's Emergency Plan for AIDS Relief (PEPFAR) and the Children's Investment Fund Foundation (CIFF) that aimed to dramatically scale-up pediatric HIV treatment coverage in 9 countries in Africa. Between 2014 and 2016, ACT successfully improved children's access to HIV testing services and increased the number of children and adolescents living with HIV (C/ALHIV) on ART by 44%.¹¹ Table 1 presents the percent increase in the number of children tested and diagnosed over the 2-year initiative in the 4 countries with complete data across all the finer age bands. The number of diagnosed children was highest during the first year of the initiative and tapered off because programs successfully identified the easiest to reach children and new pediatric cases became harder to find. ACT also improved the use of age-disaggregated data to better monitor HIV treatment coverage among infants, children, and adolescents.¹¹

This article describes 5 key strategies for improving pediatric case finding and linkage to treatment based on lessons learned during the ACT initiative.

WHAT ARE EXISTING GAPS IN HIV CASE FINDING AMONG CHILDREN AND ADOLESCENTS?

Although diagnosis of C/ALHIV has significantly improved through ACT and other initiatives, there remain specific subpopulations with unique challenges.

HIV-Exposed Infants

Current WHO guidelines recommend virologic testing for HIV-exposed infants (HEIs) using a DNA polymerase chain reaction test at 4–6 weeks of age to optimize detection of intrauterine, intrapartum, and early postnatal HIV transmission.¹² In 2016, only 50% of HEI in 21 priority countries received early infant diagnostic (EID) testing by 2 months.¹³ Lack of efficient systems for sample collection, transport, and processing lead to long turnaround times between laboratories and facilities, prolonging diagnosis and increasing the likelihood that infected infants will die or become lost-to-follow-up.^{14–16} Poor retention of HIV-infected mothers also contributes to low EID coverage.¹⁷ Even when mothers do return for clinical appointments, lack of systems for linking mothers to their infants creates missed opportunities for testing infants.

About half of new infant infections are estimated to occur during the breastfeeding period (Fig. 1).^{13,18} Improving adherence and retention support to ensure that women remain virally suppressed, and strengthening routine HIV testing throughout pregnancy and breastfeeding to detect incident maternal HIV infection are key to preventing these infections. Offering sexual partner testing can also reduce HIV acquisition among pregnant

and breastfeeding women involved in serodiscordant relationships.¹⁹ Finally, ensuring that infants receive an HIV test and final diagnosis once breastfeeding has ceased is critical to identify infants infected during the breastfeeding period.

Perinatally Infected Children

Up to a third of HIV-infected infants are slow progressors, with a median survival of 16 years without treatment.²⁰ These perinatally infected children may only receive HIV testing and diagnosis when they develop severe illness. Although provider-initiated testing and counseling (PITC) at health facilities is recommended to identify these children, barriers that prevent optimal implementation include lack of clarity on the definition of a legal guardian, age of consent, limited trained staff, and shortages of rapid test kits.²¹ Facility-based PITC may also be insufficient on its own to identify all undiagnosed C/ALHIV. In Zimbabwe, a substantial burden of undiagnosed C/ALHIV was found in the community even after 2 years of optimized PITC at nearby facilities.²²

Adolescents

The number of ALHIV (aged 10–19 years) is growing because of the “aging up” of children perinatally infected in the early 2000’s and to the population boom resulting in the largest generation of adolescents in history.³ Although a third of new HIV infections occur in young people aged 15–24 years, data from recent population-based HIV impact assessment (PHIA) surveys in Lesotho, Malawi, Swaziland, Uganda, Tanzania, Zambia, and Zimbabwe support a growing body of evidence that adolescents have lower rates of HIV diagnosis, ART initiation, and viral suppression than other populations (Fig. 2).²³ Barriers to adolescent uptake of HIV testing include stigma, poor health care provider attitudes, parental consent requirements, and inadequate risk perception.²⁴

FIVE KEY STRATEGIES FOR ADDRESSING GAPS IN PEDIATRIC AND ADOLESCENT CASE FINDING AND LINKAGE TO TREATMENT

The ACT initiative sought to address these gaps through a variety of interventions. Below, we summarize 5 key strategies for improving pediatric case finding and linkage to treatment based on lessons learned from this initiative.

Strategy 1: Implement a Targeted Mix of Approaches to Strengthen HIV Case Finding and Linkage to Treatment

Approaches for strengthening pediatric case finding are summarized in Table 2 and in the text below.

Scale-Up PITC Within Health Facilities—Routinely testing all children and adolescents attending clinics where HIV may be an underlying cause of illness is highly effective for identifying C/ALHIV who were either missed during the early postnatal period, or who acquired HIV during breastfeeding.⁹ Several systematic reviews have found high prevalence rates among children tested in TB clinics, pediatric inpatient wards, malnutrition centers, and outpatient departments.^{9,25}

In high-prevalence settings (>5% adult HIV prevalence), screening mothers or infants attending immunization or under-5 clinics may be another approach for identifying HEI.^{26,27} Mothers (preferably) or newborns can be screened for HIV infection or exposure, respectively, using an HIV rapid serologic test. An HIV virologic test can then be offered to all infants who test positive or whose mothers are HIV infected. Although this strategy was found to be effective in high-prevalence settings such as South Africa,²⁸ it may not be as effective in settings with low HIV prevalence and/or high PMTCT coverage.

Risk screening tools may help optimize PITC by identifying high-risk children in need of an HIV test.²⁹ In Zimbabwe, a risk screening tool increased the percent of children testing HIV-positive from 1.4% to 4.7%. It also reduced the number of children required to be tested to identify one CLHIV from 22 to 10.³⁰ This tool, however, was designed to diagnose perinatally infected adolescents who are symptomatic from untreated, longstanding HIV infection. It may not effectively identify asymptomatic perinatally infected children or newly infected adolescents who are likely to be asymptomatic. Adolescent risk screening tools may need additional questions on sexual health. Sensitive questions on sexual behavior or genitourinary symptoms have been challenging to operationalize in busy clinics, while still maintaining client privacy and confidentiality.^{29,30} Further operational research is needed to validate tools for different populations and contexts and on how best to implement this approach.

Optimize EID for HIV-Exposed Infants

Several approaches have improved EID including point of care (POC) EID testing, establishing sample transport hubs, deploying mentor mothers to increase retention of mother–infant pairs, and using mobile health strategies to return results to facilities.^{31,32} In Malawi, POC EID testing was shown to increase the proportion of HIV-positive infants initiating ART within 60 days of sample collection from 41.9% to 91.1%,³³ suggesting the need to evaluate strategies for increasing the availability of POC EID testing. This includes use of GeneXpert platforms, which have not been used to full capacity for TB diagnosis. Adding infant testing information to the monitoring tools used to track HIV-infected mothers can help link mother–infant pairs and facilitate identification of HEI in need of an HIV test.³¹ The World Health Organization (WHO) recommends consideration of a virologic test at birth (known as “birth testing”) to detect in utero infections.¹⁹ Birth testing is not a replacement for the 4- to 6-week test and should only be adopted by countries who have achieved at least 80 percent coverage of the 4- to 6-week test, with timely return of results.

Test All Biologic Children of Adults and Siblings Receiving ART Through Family Index Testing

Family index testing (FIT) involves health service providers actively offering HIV testing to the biologic children of adults and siblings receiving HIV services.^{34,35} In a systematic review of 21 studies, FIT resulted in a 3.3% yield among CLHIV.²⁵ In Malawi, 90% of CLHIV identified through FIT linked to treatment.³⁶ FIT may also facilitate disclosure and communication within the family and improve adherence and retention in HIV clinical care.³⁴

Despite its demonstrated effectiveness, FIT remains inadequately scaled-up. In Malawi, only 20% of children of adult patients with ART had received HTS,³⁷ and only 36% of hospitalized children with HIV-infected parents received HTS in Uganda.³⁸ Parents may be reluctant to have their children tested for fear of disclosing their own status. In Kenya, 42% of HIV-infected adults had children with unknown status. Only 14% of these adults allowed HTS for their children. Yet, high HIV prevalence rates (7.4%) were observed among the children tested.³⁹

Reinforcing the importance of testing partner(s) and biologically exposed children at every clinic visit and offering facility- or home-based family HTS can help improve uptake of FIT. In the Malawi-based Tingathe Program, community health workers offer home-based HTS to partners and family members of ART clients, leading to a 10-fold increase in the number of CLHIV enrolled in pediatric treatment.⁴⁰ A recent pooled analysis from Demographic and Health Surveys in sub-Saharan Africa found that adolescents aged 15–17 years who had lost their mother, lost both parents, or had an HIV-infected mother were 2–3 times more likely to test HIV-positive.^{36,41} Testing adolescents up to 15 years as part of household-based FIT can be a targeted strategy for diagnosing ALHIV.

Test the Children of Key and Vulnerable Populations

Testing the infants and children of key population (KP) living with HIV, particularly HIV-infected female sex workers and injection drug users, is another important strategy for improving pediatric case finding among hard-to-reach populations. Although this is an aspect of family index testing, many programs fail to include KP children in their index testing efforts, and many KP programs do not systematically provide counseling about the need to test infants and children as part of their routine services. In Cameroon, a program to test the children of HIV-positive female sex workers at community-based drop-in centers found a 6.1% prevalence, highlighting the potential utility of this approach (G. Fouda, personal communication, 4 May 2017). No studies on this approach seem to have been published, however.

Implement Risk Screening for All Orphan and Vulnerable Children

Orphaned children are at high risk for HIV from vertical transmission and, because of their economic vulnerability, may also be at risk from horizontal HIV transmission through sexual abuse or early sexual debut.^{42,43} In Zimbabwe, 18% of orphaned children attending a community-based orphan and vulnerable children (OVC) program tested HIV-positive, suggesting many undiagnosed children may be enrolled in these programs.⁴³ HIV risk screening tools, based on behavioral and clinical factors, may help identify OVC in need of an HIV test, as described above.³⁰

Link All HIV-Infected Infants, Children, and Adolescents to HIV Treatment Services

An HIV diagnosis without linkage to treatment confers no benefit to C/ALHIV. Strengthening linkage to treatment requires close coordination between HIV testing and treatment programs for a successful “hand-off.” After diagnosis, HTS programs can assume responsibility for linking C/ALHIV to treatment. After linkage, HIV treatment programs then assume responsibility for retaining C/ALHIV through ART initiation, clinical

monitoring, and viral suppression. Designating specific linkage navigators or counselors within HTS and ART programs can facilitate communication between the 2 programs and ensure linkage takes place.¹¹

Several promising practices to improve linkage to treatment among adults have been identified (Table 2), although further evaluation is needed to understand their utility among C/ALHIV. These include same day ART initiation,^{44–46} POC EID technologies,³³ intensified pre- and post-test counseling,^{47,48} tracking mother–infant pairs,^{41,49} patient escorts from HTS to ART services,^{50,51} and family-based ART services.^{52,53} Follow-up phone calls or home visits, mobile text appointment reminders, and case management can also help link children who fail to enroll in ART services within 14 days of diagnosis.^{53–56} Use of 2-week ART starter packs within community testing programs has been proposed to improve linkage in adults but has not been widely evaluated among children.⁵⁷ Patient-level registers and indicators allow for HTS programs to actively track whether C/ALHIV link to treatment and identify those who may need additional linkage support.⁵⁸ These tools can also ensure that minimum benchmarks for linkage to treatment are being met and trigger quality improvement efforts in the event of underperformance.

Strategy 2: Address the Unique Needs of Adolescents to Support HIV Case Finding and Linkage to Treatment

Adolescents remain the only age group for which HIV-related deaths are increasing.³ To improve HIV case finding among adolescents, it is important to address identification of undiagnosed perinatally infected children and newly infected adolescents, who may be asymptomatic when diagnosed. Improving coverage of facility-based PITC, with the addition of entry points for sexual and reproductive health services, is critical for identifying ALHIV. Effective community-based testing is also needed because adolescents may not present to facilities unless they are very sick or become pregnant.

Partner notification is another strategy for targeted testing among adolescents.⁵⁹ Active notification, whereby a health care provider assists ALHIV to notify and test their sexual partner(s), should be prioritized because passive strategies that rely solely on the adolescent to bring their partner(s) to the facility for an HIV test are less likely to be effective among adolescents who do not feel empowered to disclose to their partner(s). This is especially true if the partner is older.⁶⁰

HIV self-testing (HIVST) has a high acceptance rate among older adolescents,⁶¹ and adolescents are more likely to accurately use oral self-test kits.⁶² Although HIVST holds potential to increase HTS coverage among adolescents, OraQuick, the most common HIVST kit, is only recommended for persons 17 years and older.⁶³ Operational research will be needed to identify dissemination strategies and ensure that adolescents screening positive are linked to diagnostic HTS and treatment services, if confirmed positive.

Community campaigns pairing mobile HIV testing with other wellness services, such as SEARCH and POP-ART-Y, identified large numbers of previously undiagnosed adolescents.^{64,65} The proportion of ALHIV who knew their HIV-positive status increased 3-fold during the POP-ART-Y study in Zambia,⁶⁴ and the majority (58%) of adolescents

diagnosed during Project SEARCH in Uganda and Kenya were new diagnoses.⁶⁵ Pairing HTS with other services may help destigmatize HIV testing.⁶⁶ However, because of lower HIV prevalence among adolescents and the high cost of these campaigns, this strategy may need to be limited to “hot spots” (areas of high prevalence and low HTS coverage) and/or very remote areas.

HIV testing in schools has been widely accepted by parents.⁶⁷ Yet, some countries face challenges with coordination between the Ministries of Health and Education, with HIV testing not allowed on school property.⁶⁸ In studies, HIV prevalence was quite variable across schools, ranging from 1.9% to 8.3% in South Africa to only 1.4% in Botswana.^{69–72} Further evaluation of school-based testing models is needed to better understand the utility of this approach.

Other innovative approaches for improving adolescent HTS coverage should be explored, including demand creation through use of edutainment and social media.⁷³ Social network testing, in which HIV-positive and high-risk, HIV-negative individuals recruit others from their social, sexual, and drug-using networks for HTS, is an effective approach among KPs.^{74,75} It may also be effective among adolescents. Although economic incentives to caregivers increased HIV testing uptake among children and adolescents,^{76,77} more research is needed on the scalability and sustainability of this approach.

Adolescents have lower rates of linkage to and retention in ART services than adults. Providing a comprehensive set of adolescent-friendly HIV testing and treatment services including adherence counseling and support, sexual and reproductive health services, and mental health support can help improve linkage and retention among adolescents.⁷⁸ Support from health care workers is also critical.⁶⁸ Involving adolescents in the design, delivery, and evaluation of HIV testing, treatment, and support services can ensure these programs address their unique needs.⁷⁹

Strategy 3: Collect and Use Data to Strengthen Programming

Developing effective tools and systems to collect and review strategic information including epidemiologic, program, costing, and surveillance data will further optimize pediatric case finding. This information can be used to conduct real-time analyses and shift programs toward effective approaches.^{80,81} Information to track includes coverage and absolute number of new diagnoses to identify where there may be capacity to expand services, the yield (proportion of children who test HIV-positive), and cost per diagnosis. Disaggregation of data by age and sex allows for programs to concentrate services on populations with low testing coverage and greatest unmet need for treatment. Subnational and site-level data analysis can identify hot spots where new diagnoses of C/ALHIV are occurring and enable geographic targeting of HTS.

Strategic information can also inform quality improvement. HTS programs can set benchmarks around diagnosis and linkage to treatment for pediatric populations, use their programmatic data to monitor their progress toward achieving these benchmarks, and develop interventions to improve performance, as needed. Program managers at regional

and district levels can provide supportive supervision and mentoring to health facilities and HTS programs struggling to meet performance targets.⁸²

Strategy 4: Foster a Supportive Political and Community Environment

Supportive policy implementation is crucial to improve access to HIV testing and treatment services among C/ALHIV. In many countries, the age of consent for HTS is 18 years, which can limit access among younger adolescents.⁸³ In some settings, the age of consent for HTS is lower than the age of consent for HIV treatment, hindering linkage to treatment for ALHIV.^{24,84} Continued advocacy for policies that lower the age of consent for testing and treatment is needed to improve adolescent access to these services. Clarification within national guidelines on who can consent for a minor to receive HIV testing and treatment is also needed. In many cases, the biological parent is not available to consent due to death or work-related travel. Health care providers are often reluctant to test children without the consent of one or both biologic parents, which can lead to missed opportunities for pediatric testing.⁸³ Policies allowing for task shifting of rapid HIV testing among children over 18 months to lay counselors and community health workers can help ease human resource constraints and improve HTS access.⁸⁴

Collaboration with community leaders and members, ALHIV networks, and civil society organizations is also essential to ensure that HIV testing and treatment services meet the needs of C/ALHIV and their caregivers.⁸⁵ Community members can advocate for policy change, drive demand for services, and assist with linkage to and retention in ART services. Community scorecards can bridge the demand side (“service user”) and the supply side (“service provider”) to jointly address service delivery barriers.⁸⁶ In Mozambique, community scorecards improved pediatric treatment services through reduced wait times and increased ARV availability.¹¹

Strategy 5: Invest in Health Systems Strengthening

Pediatric HTS requires an adequate supply of essential commodities, including rapid test kits and EID materials. Yet, many HTS programs report frequent commodity stock-outs.⁸⁷ Regular monitoring and management of the entire supply chain system—including stock levels, forecasting, procurement, storage, and delivery—is critical to address supply chain gaps and to ensure that the right commodities are in the right place at the right time.⁸⁷

Avoiding misdiagnosis of HIV—both false positive and false negative results—among children and adolescents is critically important to prevent mistakenly placing an HIV-uninfected child on ART or missing a lifesaving diagnosis.^{88,89} Inconclusive results, while an issue at all ages, can be fatal for infants. In one study, 17% of infants with inconclusive results died due to delayed delivery of a final HIV-positive diagnosis.⁹⁰ Collaboration between HTS programs and laboratory personnel to implement quality assurance measures including competency-based certification of testers, proficiency testing, and retesting for verification before ART initiation is needed to prevent incorrect or inconclusive results.⁹¹

CONCLUSIONS

In summary, despite recent success in improving pediatric case finding, many C/ALHIV in resource-limited settings remain undiagnosed and at substantial risk for HIV-related mortality and morbidity. To achieve epidemic control, national and regional programs will need to measure their progress toward achieving international benchmarks across all age and sex categories. This includes ensuring 90% of C/ALHIV have been diagnosed, 90% of those diagnosed are initiated on ART, and 90% of those on ART achieve viral suppression.⁹² The strategies described in this article result from lessons learned from the ACT initiative, which successfully improved pediatric case finding and treatment in 9 African countries. These strategies, if implemented at scale and with fidelity, can assist countries to achieve international benchmarks for pediatric populations. Continued advocacy and global investments are required to eliminate AIDS-related deaths among children and adolescents.

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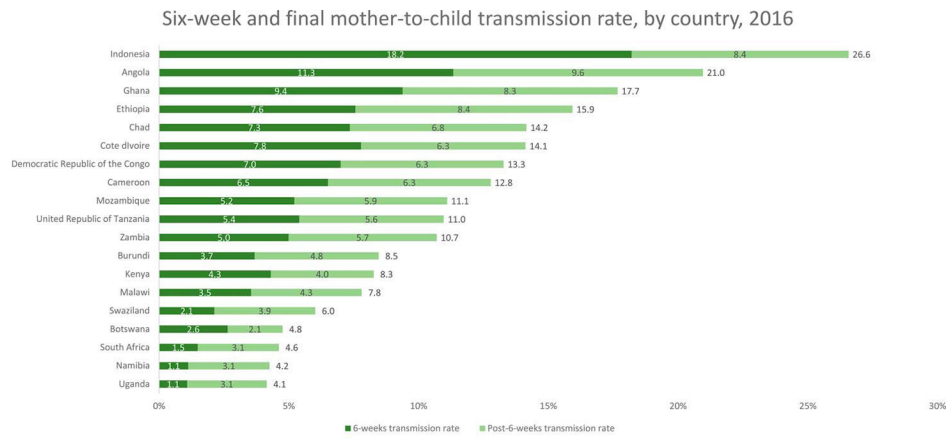
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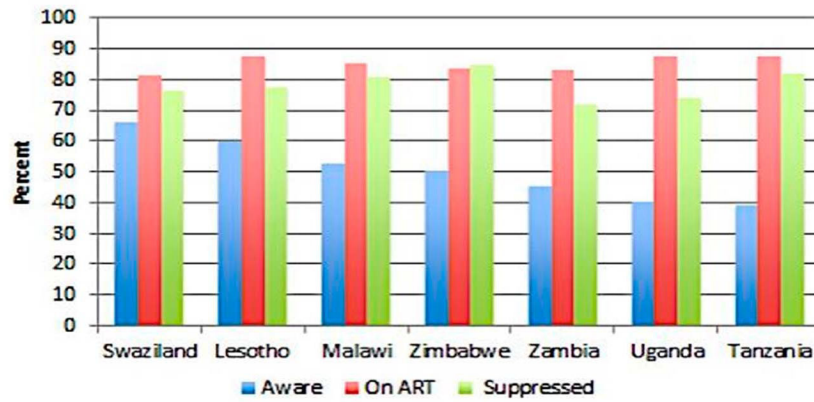
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Source: UNAIDS 2017 estimates.

FIGURE 1. Mother-to-child HIV transmission rates at 6 weeks and after cessation of breastfeeding by country, 2016.

Progress to 90/90/90 in 15 to 24 year olds



Note: Results based on self-report of HIV awareness and ART status (plus ARV testing in Malawi and Zambia), and on viral load testing.

Source: PEPFAR PHIA

FIGURE 2. Progress to 90/90/90 among 15- to 24-year-olds in Swaziland, Lesotho, Malawi, Zimbabwe, Zambia, Uganda, and Tanzania (2016 population-based HIV impact assessments).

TABLE 1.

Trends in the Number of Children Tested and Diagnosed Under the ACT Initiative

Country	Age of Child	No. of Children Tested for HIV				No. of Children Diagnosed HIV-Positive			Percent Increase from October 2014 to September 2017	
		FY15	FY16	FY17	FY15	FY16	FY17	Tested	Diagnosed	
Democratic Republic of the Congo	<01*	2839	2558	3227	52	148	130	14%	150%	
	01-09	48,405	64,641	89,279	1120	1228	1448	84%	29%	
	10-14	24,492	30,192	31,535	451	540	442	29%	-2%	
Lesotho	15-19	106,059	108,631	98,577	1194	951	755	-7%	-37%	
	<01*	9369	6716	8603	321	149	152	-8%	-53%	
	01-09	50,761	85,851	121,366	934	728	685	139%	-27%	
Zambia	10-14	38,919	51,454	69,165	752	521	490	78%	-35%	
	15-19	66,118	76,020	97,141	2131	1741	1741	47%	-18%	
	<01*	50,008	56,256	65,190	2626	1914	1925	30%	-27%	
Zimbabwe	01-09	145,126	263,136	491,206	9650	6667	7696	238%	-20%	
	10-14	138,291	183,059	412,674	6162	4476	5223	198%	-15%	
	15-19	487,734	425,937	736,369	25,266	16,256	15,880	51%	-37%	
Zimbabwe	<01*	52,148	37,324	34,306	2023	1331	1103	-34%	-45%	
	01-09	20,788	95,790	116,658	1692	3872	3915	461%	131%	
	10-14	52,591	104,295	163,275	972	2410	2934	210%	202%	
Zimbabwe	15-19	205,290	288,968	354,440	8198	9817	9626	73%	17%	

* <01 results from the PEPFAR monitoring, evaluation, and reporting (MER) indicator on HIV testing was replaced with results from the indicator on early infant diagnosis.

TABLE 2.

Strategies for Improving HIV Case Finding and Linkage to Treatment Among Infants, Children, and Adolescents

Strategies for Improving HIV Case Finding Among Infants, Children, and Adolescents
Scale-up PITC within health facilities in TB clinics, nutrition centers, and pediatric inpatient clinics
Consider HIV risk screening tools to optimize testing in facilities
In high-prevalence settings (>5% adult HIV prevalence), test mothers or infants attending immunization or under-5 clinics to identify HEIs
Use strategies that identify HIV-exposed children through connection to adults and other children living with HIV
Optimize PMTCT and EID for HEIs
Test all biologic children of adults and siblings receiving any HIV service (PMTCT and ART) through facility- or home-based family index testing
Test the children of key and vulnerable populations
Implement risk screening for all OVC
Offer partner notification services to adolescents
Consider other innovative approaches, such as HIVST, social network testing, and the use of incentives
Collaborate with community leaders, ALHIV networks, community members, and civil society organizations to ensure that HTS and linkage strategies meet the needs of infants, children, adolescents, and caregivers
Strategies for Strengthening Linkage to HIV Treatment for Infants, Children, and Adolescents
Provide same day ART initiation
Offer intensified post-test counseling on importance of starting ART
Provide patient escort between HIV testing and ART services
Offer peer navigation/case management services
Conduct follow-up (phone/home visit) for clients who fail to link within 14 d
Use ART starter packs in remotely located HIV testing sites
Systematically document and monitor linkage to treatment using individual-level registers and indicators