Pediatric Treatment Scale-Up: The Unfinished Agenda of the Global Plan

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Abstract: Five million children have died of AIDS-related causes since the beginning of the epidemic. In 2011, the Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive (Global Plan) created the political environment to catalyze both the resources and commitment to end pediatric AIDS. Implementation and scale-up have encountered substantial hurdles, however, which have resulted in slow progress. Reasons include a lack of emphasis on testing outside of prevention of mother-to-child transmission services, an overall lack of integration and coordination with other services, a lack of training among providers, low confidence in caring for children living with HIV, and a lack of appropriate formulations for pediatric antiretrovirals. During the Global Plan period, we have learned that simplification is essential to successful decentralization, integration, and task shifting of services; that innovations require careful planning; and that the family is an important unit for delivering HIV care and treatment services. The post-Global Plan phase presents a number of noteworthy challenges that all stakeholders, national programs, and communities must tackle to guarantee universal treatment for children living with HIV. Accelerated action is essential in ensuring that HIV diagnosis and linkage to treatment happen as quickly and effectively as possible. As fewer infants are infected because of effective prevention of mother-to-child transmission interventions and the population of children living with HIV will age into adolescence adapting service delivery models to the epidemic context, and engaging the community will be critical to finding new efficiencies and allowing us to realize a true HIV-free generation—and to end AIDS by 2030.

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The authors have no funding or conflicts of interest to disclose.

The views and opinions expressed in the article are solely those of the authors and do not necessarily reflect those of the World Health organization, the U.S. Agency for International Development (USAID) or those of the United States Government.

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Key Words: HIV, Global Plan, pediatric, antiretroviral treatment, children

(*J Acquir Immune Defic Syndr* 2017;75:S59–S65)

BACKGROUND

By the end of 2015, an estimated 5 million (4.3–5.8 million) children had died of AIDS-related causes since the start of the HIV epidemic. Ninety-one percent of those children were living in sub-Saharan Africa.[1] In resource-limited settings, the funding and systems needed to achieve the same successes with pediatric HIV care and treatment that have been observed in Western countries were only introduced in the mid-2000s, and they were met with substantial challenges related to the complexity of treating children. The Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive (Global Plan) created the political environment to catalyze both the resources and commitment to end pediatric AIDS.[2] In 2011, the Global Task Team —which was called on to develop the Global Plan—endorsed the targets of 100% treatment coverage for infants and children younger than 2 years and a 50% reduction in AIDS-related deaths by 2015. These goals were recognized as part of Prong 4 of comprehensive prevention of mother-to-child transmission (PMTCT), which specified action on "providing appropriate treatment, care, and support to mothers living with HIV and their children and families."[3]

Global Plan implementation coincided with critical changes in World Health Organization (WHO) treatment guidelines that progressively promoted earlier diagnostic testing, earlier antiretroviral therapy, and use of more potent and tolerable drugs. Since 2010, implementation of early infant diagnosis was supported by recommendations for the use of dried blood spot samples to increase reach and access.[4] In the same year, infants and children under the age of 2 years were recommended to start treatment irrespective of their clinical and immunological conditions.[5] This age threshold was subsequently raised to 5 years in 2013 and then removed altogether to support treatment for all HIV-positive children in 2015.[6,7]

Although the normative platform has steadily evolved to capture new evidence and address programmatic needs, implementation and scale-up have nonetheless encountered substantial hurdles that have resulted in slow progress and

a concerning gap in treatment coverage. This study highlights the advancements made during the period of the Global Plan and explores potential reasons for the slow progress. We hereby highlight the experiences of countries that distinguished themselves by introducing innovations in testing, treatment, and service delivery. We also reflect on the lessons learned and the remaining challenges, and we propose key actions in the post-Global Plan phase within the evolving epidemic context.

PROGRESS DURING THE GLOBAL PLAN

The Global Plan's catalyzing efforts in PMTCT positively impacted pediatric treatment scale-up efforts and led to programmatic changes that resulted in earlier diagnosis and more rapid initiation of treatment for infants and children living with HIV. Several countries made significant progress scaling up early infant diagnosis and increasing the proportion of infants and children under the age of 2 years who were started on treatment.[8,9] The Global Plan's comprehensive 4-prong strategy acknowledged the need for family-centered care that ensures concomitant treatment for the mother, her children, and other family members. It also acknowledged that antiretroviral prophylaxis were neither completely effective nor universally accessible. As a result, children would continue to acquire HIV, and those who were infected would be in urgent need of prompt diagnosis and antiretroviral therapy.

A number of initiatives stemming from the Global Plan were launched to draw attention to the needs of children living with HIV. The United Nations Children's Fund, WHO, and the Elizabeth Glaser Pediatric AIDS Foundation launched the Double Dividend initiative in 2013 to mobilize the global political and community leadership to accelerate action toward the dual goals of ending pediatric HIV and improving child survival. In 2014, the United States government and the Children's Investment Fund Foundation jointly launched the Accelerating Children's HIV/AIDS Treatment initiative to double the number of children receiving antiretroviral therapy in 9 sub-Saharan African countries. The US $200 million initiative is being implemented in Cameroon, the Democratic Republic of Congo, Kenya, Lesotho, Malawi, Mozambique, the United Republic of Tanzania, Zambia, and Zimbabwe, and it will enable an additional 300,000 children in these countries to receive treatment. In addition, the Pediatric HIV Treatment Initiative also was launched in 2014 to ensure availability of better and more effective drugs for children: UNITAID, the Clinton Health Access Initiative, the Drugs for Neglected Diseases initiative and the Medicines Patent Pool aligned resources to accelerate the development, production, and availability of priority HIV medicines for children, with a focus on intellectual property, research and development, and market shaping.[10] On World AIDS Day 2014, the United States President's Emergency Plan for AIDS Relief, Pediatric HIV Treatment Initiative, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund) announced a new Global Pediatric Antiretroviral Commitment-to-Action to bring together leading organizations to accelerate the development of new, high-priority pediatric antiretroviral coformulations for first-line and second-line treatment by 2017.[11]

Despite these efforts, a clear divide remains at the end of the Global Plan between coverage for mothers and what is received by children. In 2015, only 50% (44%–59%) of children living with HIV in the 21 priority remaining countries of the Global Plan were receiving HIV treatment. Although this represents an increase from the 10% (9%–11%) baseline in 2009, children were significantly less likely to receive treatment than were pregnant women (50% compared with 74%; Fig. 1), and a widening treatment gap between adult and pediatric coverage has been observed in the West and Central African region. Countries such as Botswana, Namibia, and South Africa have been able to treat half or more of children living with HIV with antiretroviral therapy, whereas progress has been slowest in Cameroon, Chad, and Nigeria.[1]

REASONS FOR SLOW PROGRESS IN PAEDIATRIC TREATMENT SCALE-UP

Although incredible strides were made in preventing the vertical transmission of HIV during the Global Plan, improvements in access to treatment for those children already living with HIV was less robust. Despite progressive improvements in EID testing, efforts to identify HIV-positive children outside of the PMTCT context received less emphasis. This was partly attributed to a lack of provider training and to reduced confidence among health-care workers in both testing and caring for children living with HIV. For instance, a 2011 study in Côte d'Ivoire showed that most maternal, child health staff surveyed were not trained to test children or to provide HIV services.[12] In addition, although those who were trained believed in the importance of HIV testing, only 22% of routine immunization staff and 48% of general pediatric care staff were routinely testing children.

Another part of the challenge was that staffing levels in pediatric HIV programs did not increase to meet HIV testing needs. Additional staff was hired to ensure routine opt-out testing in PMTCT programs, which resulted in excellent testing coverage but this staffing increase was not mirrored in pediatric programming.[13] Caregiver concerns also affected pediatric testing: in a sample of more than 16,000 Zimbabwean adults, 91% felt that children would benefit from being tested for HIV, but 42% were concerned about

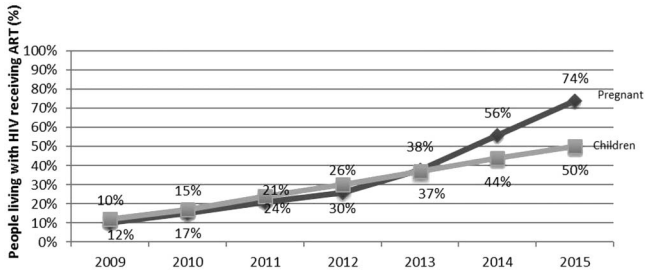


FIGURE 1. Percentage of pregnant women and children (0–14 years) living with HIV who received antiretroviral therapy in 21 Global Plan priority countries, 2009–2015.[2]

discrimination in the community if the testing result was positive.[14] The fear of violence or abandonment, along with stigma and discrimination also were factors that reduced the use of HIV services among caregivers.[15]

Access to services also proved to be a barrier to increasing the pediatric antiretroviral therapy coverage during the Global Plan. Caregivers cited long queues, negative staff attitudes, and health-care worker difficulties with pediatric counseling and venipuncture as reasons for not accessing HIV services.[16] Other reported factors included long wait times, lack of integration and coordination with other services, and drug shortages or stock-outs.[19] In addition, while integration of HIV testing into maternal newborn and child health (MNCH) programming has been found to be an effective case identification strategy, it has not been widely implemented.[17] Even when testing is being done, it is not systematic and provider-initiated testing and counseling practices are highly variable across and within facilities and service delivery points. Although routine opt-out testing was occurring in antenatal care and maternity wards, this strategy was not being used in many entry points where children at high risk of HIV come for services—malnutrition units, tuberculosis units, and in-patient wards—which represents another set of missed opportunities for identifying and placing HIV-positive children on antiretroviral therapy.[18]

Finally, the lack of appropriate pediatric antiretroviral formulations—along with challenges associated with ensuring availability of these drugs, preventing stock-outs, and supporting administration of the most effective drugs—affected the ability of programs to rapidly scale-up pediatric treatment and improve clinical outcomes. Of the 26 antiretroviral medications approved by the U.S. Food and Drug Administration as of January 7, 2016 have no pediatric indication, 8 have no pediatric formulation, and only 11 are approved for children below the age of 2 years.[19] Even with antiretroviral medicines that do have pediatric formulations, the number procured by countries was small, causing long delays and stock-outs that affected many children on antiretroviral therapy.[20]

INNOVATIONS DURING THE GLOBAL PLAN

The Global Plan provided political momentum in support of eliminating new HIV infections among children and keeping their mothers alive, allowing for notable innovations in diagnostics, drugs, and service delivery.

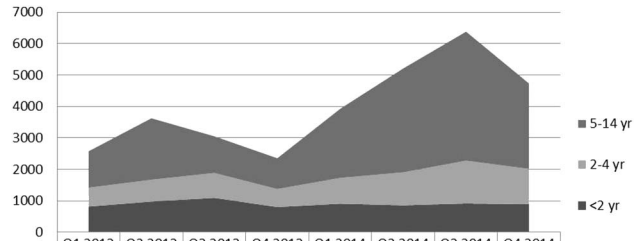
HIV Testing of Infants and Children

In many settings, identification of HIV-positive infants and children is the first critical step, and it is not easy. In most pediatric HIV programs, testing in infants is done through EID services; in children, it is done through rapid testing at various entry points throughout the facility and community. Another article in this supplement describes major progress in increasing coverage for EID services.[21] Despite this increase in EID service coverage, the numbers of HIV-positive children identified and started on treatment during the Global Plan were lower than expected. This issue is demonstrated through data from Zimbabwe; 70% of dried blood spot specimens collected in 2012 were obtained in PMTCT clinics, yet, most HIV-infected children identified in the same time period were from the pediatric wards.[22] Thus, most infected children were completely outside the PMTCT-EID cascade of care. In addition, children that were identified as positive were not being linked to care. More recently, as a result of the Accelerating Children's HIV/AIDS Treatment Initiative, a massive scale-up of testing across the full range of entry points is being implemented and more than 4 million additional children were tested in 2015 in 9 participating countries. Although the different epidemic context has resulted in significant diversity in terms of positivity rates, early findings suggest that index testing (testing children in families of HIV-positive adults) and testing at inpatient and malnutrition wards are the strategies with highest yield, and that they should be prioritized when scaling up HIV testing services for children.[23]

Antiretroviral Treatment

During the Global Plan, countries made significant efforts to scale-up pediatric treatment programming and provide children with the most effective medications in the optimal formulations. Simplified treatment initiation criteria and development of an ARV formulary by the Inter-agency Task Team (IATT) on the Prevention of HIV Infection in Pregnant Women, Mothers, and Children helped reduce the complexity of providing antiretroviral therapy to children.[24]

Several countries paved the way to earlier and broader use of antiretroviral medications by adopting policies to overcome the limited implementation of CD4 testing and simplify pediatric treatment management for health-care workers. Rwanda and South Africa moved first to treat all children under the age of 5 years; several other countries then opted to treat all children under the age of 15 years before WHO guidelines were updated in 2015. Uganda's goal of treating all children was instrumental to the 2015 WHO guidelines revision process, and it documented a number of important achievements within just 1 year of implementation: antiretroviral therapy coverage of children under 15 years of age increased from 22% in 2013 to 32% in 2014 (Fig. 2), and time to treatment initiation was reduced from 18 to 2 days.[25] The biggest increase in antiretroviral therapy initiation was



	Q1 2013	Q2 2013	Q3 2013	Q4 2013	Q1 2014	Q2 2014	Q3 2014	Q4 2014
5-14 yr	1158	1957	1167	983	2200	3306	4105	2719
2-4 yr	601	694	793	574	822	1048	1362	1125
<2 yr	819	979	1096	803	910	859	917	892

FIGURE 2. Scale-up of treat all children and adolescents under the age of 15 years in Uganda: number of children newly initiated on antiretroviral therapy.[30]

observed in lower-level health facilities (Health Center 3), suggesting that the simplification of treatment initiation criteria had potentially promoted task shifting and decentralization of pediatric antiretroviral therapy. A rapid assessment conducted in Uganda in July 2015 uncovered challenges with the "treat all" policy, such as the need to ensure reliable procurement of commodities and laboratory strengthening, as well as the importance of training, mentorship, and ongoing supportive supervision.[30]

Ensuring that commodities are in place and reliably procured is one of most critical conditions for safe treatment scale-up in the context of limited drug options available for children who need lifelong treatment. Although the WHO guidelines during the Global Plan have recommended increasingly potent and tolerable drugs to address some of the complexities of pediatric treatment—such as the need for different regimens for different ages and the need to revise dosing as the child grows and mechanisms to metabolize antiretroviral medicines mature—uptake of the optimal formulations has been poor in many countries.[26] Kenya is one of the first countries to introduce more effective pediatric regimens, prioritizing optimal formulations as indicated by the IATT formulary. Abacavir was first introduced in 2008 as the preferred nucleoside reverse transcriptase inhibitor in the first-line regimen in the Kenyan guidelines. Full optimization of the national pediatric regimen was achieved in 2015, when all the formulations procured by the country were included in the IATT formulary (Fig. 3). As a result, reports of stock-outs have plummeted and antiretroviral medicines were being reliably supplied to 75,489 children by the end of the Global Plan. The country also is rapidly introducing innovations such as lopinavir/ritonavir pellets, a new formulation of the recommended first-line infant treatment, which they are pilot-testing in the LIVING study.[27]

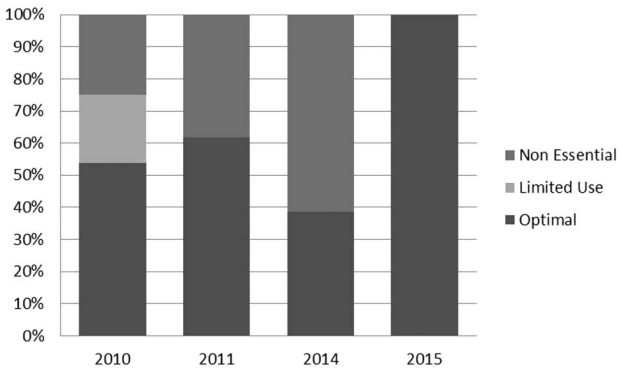


FIGURE 3. Adoption of optimal pediatric formulations procured in Kenya as defined by the IATT optimal formulary in any given year (2010–2015). Data for 2012 and 2013 are missing. In 2008, the Kenya Ministry of Health introduced abacavir as the preferred nucleoside reverse transcriptase inhibitors for children. At the same time, stavudine was removed from the list of antiretroviral medicines for the initiation of antiretroviral therapy among children, and its phase out among continuing patients was commenced. In 2009, Kenya transitioned from liquids to fixed-dose combination tablet formulations of abacavir and zidovudine for children (except for the very youngest), thus easing the treatment burden. This was supported by nationwide training of service providers. Minimal stock-outs were observed because of a robust system for commodity management and monitoring. By the end of 2015, 75,489 children aged below 15 years were receiving antiretroviral therapy in Kenya (source: courtesy of National AIDS & STI Control Program, Ministry of Health, Nairobi, Kenya–2016). Adaptations are themselves works protected by copyright. So to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

Service Delivery

The focus that the Global Plan brought to improving access to antiretroviral therapy and reducing pediatric mortality highlighted 2 key service delivery enablers: task shifting and the integration of pediatric antiretroviral therapy into other child health programs. Together, they contributed to achieving scale-up through decentralization (Fig. 4).

Task shifting seems to have played a significant role in the countries that achieved the greatest scale-up of pediatric antiretroviral therapy.[1] Nurse-managed pediatric antiretroviral therapy models—such as nurse-managed and nurse-initiated antiretroviral therapy in South Africa—have successfully empowered nurses and allied health workers to manage children with HIV. Swaziland and Zimbabwe also have implemented similar approaches, and in all cases, pediatric nurse-managed antiretroviral therapy was adopted after rollout of adult nurse-managed antiretroviral therapy. A systematic review of mortality and retention outcomes that compared nurse-managed pediatric HIV services with those where care is largely physician-led showed similar outcomes.[28] Optimal approaches to task shifting should emphasize task sharing between physicians and non-physicians, and they ensure that capacity building for nurses goes

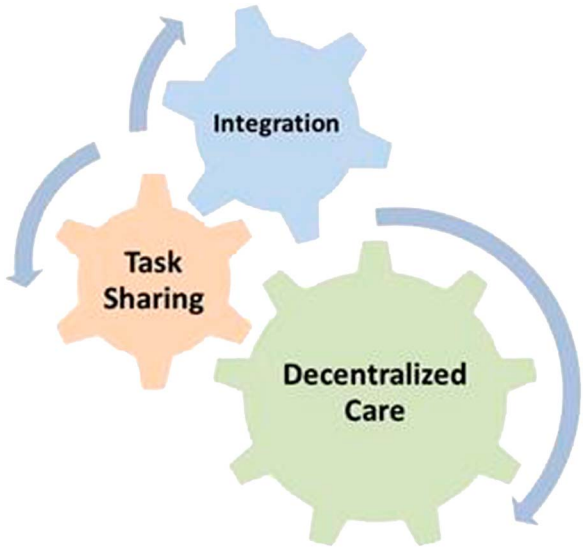


FIGURE 4. Three interlinked service delivery enablers contribute to pediatric scale-up.

beyond training to include ongoing supportive supervision and mentoring.

Decentralization and expansion of care to additional health facilities, including lower-level sites, becomes feasible as nurses become better able to manage pediatric treatment. Broadly speaking, there are 2 directions that the decentralization of HIV services for children can take: (1) pediatric antiretroviral therapy can be integrated into standard child health services, creating a pediatric primary care-type model; or (2) it can be integrated with adult antiretroviral therapy services through adoption of a family-based antiretroviral therapy program approach. In the United Republic of Tanzania, the integration of HIV services into under-5 clinics resulted in a doubling of the number of sites able to provide pediatric antiretroviral therapy and an associated increase in the number of children newly enrolled in treatment.[29] On the other hand, Uganda successfully implemented the family-based antiretroviral therapy care models and demonstrated a 40-fold increase in children enrolled in care and a 23-fold increase in children on antiretroviral therapy.[30] The family-based approach, pioneered by the multicountry Mother-to-Child Transmission-Plus Initiative and later implemented in Uganda,[31] used a community education model and set up family clinic days with tailored health education messages to improve adherence to clinic appointments for children.[32]

LESSONS LEARNED, REMAINING CHALLENGES, AND KEY OPPORTUNITIES

By examining the experience of the Global Plan, we learn the following:

- Simplification is essential. When interventions or policies are complex, progress can be slow because it is difficult to decentralize, integrate, and task shift.
- Innovations require careful planning. Although innovative approaches and technologies present enormous potential for change, only careful planning can ensure that fragile systems are not disrupted. Novel approaches must be safely introduced to have a positive impact on patients and program outcomes.
- The family is an important unit for delivering services. The family is not just a point of entry to HIV testing; it can also be a common denominator around which broader health services can be provided. Integration of adult and pediatric services maximizes the opportunities attached to any contact with a health facility.
- One size does not fit all. Adapting service delivery models to the epidemic context helps optimize the use of financial and human resources in already overburdened health systems.

The post-Global Plan phase presents a number of noteworthy challenges that the global community must tackle to ensure universal treatment for all children with HIV infection.

- Thirty-seven percent of all new pediatric infections are in Nigeria.[2] Nigeria is a striking example of a large country with diverse HIV prevalence across states and provinces that also has immature pediatric HIV programs. The best way to ensure that HIV services are provided equitably and efficiently to children in Nigeria and in other West and central African countries remains to be determined and demonstrated.
- Estimating the population of children with HIV accurately remains an enormous challenge, particularly across Africa. There also is a pressing need to obtain better age-disaggregated data, because they are essential to informing program planning and commodities forecasting, preventing stock-outs of testing kits and pediatric formulations, and monitoring progress toward treatment targets.
- Introduction of innovations is very much needed to improve pediatric antiretroviral therapy coverage, but data and thoughtful planning are imperative to guiding governments as they decide how best to adopt and implement these innovations. In general, careful documentation and dissemination of the early adoption of novel interventions is urgently needed.
- Lack of age-appropriate pediatric formulations continues to be a key barrier to starting and retaining children on suppressive treatment. Political input will be essential, because few market incentives exist to meet the needs of children. More effective mechanisms need to be identified to enable the rapid development and introduction of critical pediatric formulations.

MOVING FORWARD

Despite all the efforts under the Global Plan that are discussed here, a large pediatric treatment gap remains. The median age at initiation of treatment among children is 3.8 years, and while this age has declined from a peak of 5 years in, we know that children continue to die from HIV because they are not being identified and treated early enough.[33] Accelerated action is needed to ensure that HIV diagnosis and linkage to treatment happen as quickly and effectively as possible. This action will need to be coordinated and multifaceted, and it will require promoting service delivery models that are family-centered and/or integrated within maternal child health services. Decentralization through task sharing will need to be paired with robust training, mentorship, and supportive supervision to ensure the provision of quality services. In addition, the role of the community will need to be strengthened to support the continuum of HIV services and improve HIV education to reduce stigma. Finally, more work remains to ensure that the most effective and child-friendly medicines are available for children in the age-appropriate formulations, and that age-disaggregated data are available to inform forecasting and program effectiveness.

As fewer infants become infected with HIV and the cohort of children living with HIV on antiretroviral therapy ages into adolescence, global pediatric HIV stakeholders must focus on considerations for how services are provided to this population (Table 1). Either there will be a broader vision where children and adolescents are both critical parts of a life cycle approach housed in the

TABLE 1. Global Standards for Quality of Health-Care Services for Adolescents*

Adolescent health literacy	Standard 1. The health facility implements systems to ensure that adolescents are knowledgeable about their own health and that they know where and when to obtain health services.
Community support	Standard 2. The health facility implements systems to ensure parents, guardians, and other community members and community organizations recognize the value of providing health services to adolescents, and that they support the provision and utilization of services by adolescents.
Appropriate package of services	Standard 3. The health facility provides a package of information, counseling, diagnostic, treatment, and care services that fulfills the needs of all adolescents. Services are provided in the facility and through referral, linkages, and outreach.
Provider competencies	Standard 4. Health-care providers demonstrate the technical competence required to provide effective health services to adolescents. Both health-care providers and support staff respect, protect, and fulfill adolescents' rights to information, privacy, confidentiality, nondiscrimination, nonjudgmental attitudes, and respect.
Facility characteristics	Standard 5. The health facility has convenient operating hours, a welcoming and clean environment, and a commitment to privacy and confidentiality. It has the equipment, medicines, supplies, and technology needed to ensure effective service provision to adolescents.
Equity and non-discrimination	Standard 6. The health facility provides quality services to all adolescents, irrespective of their ability to pay, age, sex, marital status, education level, ethnic origin, sexual orientation, or other characteristics.
Data and quality improvement	Standard 7. The health facility collects, analyses, and uses age-disaggregated and sex-disaggregated data on service utilization and quality of care to support quality improvement. Health facility staff is supported to participate in continuous quality improvement.
Adolescent participation	Standard 8. Adolescents are involved in the planning, monitoring, and evaluation of health services, and in decisions regarding their own care, as well as in certain appropriate aspects of service provision.

*Data from WHO.[35]

maternal, newborn, child, and adolescent health platform, or health platforms will need to change how they handle caring for children with chronic conditions such as HIV, incorporating them into the adult platforms and creating family-centered chronic disease programs. One thing is clear: even as new pediatric HIV infections decline, programming platforms must continue to be vigilant and attentive to ensure that children living with HIV reach adolescence, and that those who are adolescents can become adults.

CONCLUSIONS

The Global Plan focused attention on pediatric HIV services, and its impact on current pediatric HIV programming is evident. The success of the Global Plan was generated through sustained leadership and focused action at the country level, and it benefited from regional and global partnerships that provided support to governments. As the global community strives to reach the impending treatment targets and start 1.6 million children on antiretroviral therapy by 2018, urgent action will be required at both the country and global levels.[34]

In this focused and coordinated action, we will need to ensure that mothers know their HIV status, that all of their children are tested in a timely manner, and that the services offered enable prompt initiation of antiretroviral therapy and retention in care. As fewer infants are infected because of successful PMTCT services, the large cohort of children living with HIV will age into adolescence; Therefore, it is essential that the global community ensures that services for these populations continue to address their needs in a thoughtful and successful manner. Adaptation of service delivery models to the epidemic context and engagement of the respective communities will be critical to finding new efficiencies, allowing us to end AIDS by 2030 and launch a true HIV-free generation.

REFERENCES

1. UNAIDS. *Global AIDS Update, 2016*. Geneva, Switzerland: UNAIDS; 2016.
2. UNAIDS. *On the Fast-Track to an AIDS-Free Generation*. Geneva, Switzerland: UNAIDS; 2016.
3. World Health Organization, United Nations Children's Fund. *Guidance on Global Scale-Up of the Prevention of Mother-To-Child Transmission of HIV*. Geneva, Switzerland: World Health Organization; 2007.
4. World Health Organization. *Diagnosis of HIV Infection in Infants and Children: WHO Recommendations*. Geneva, Switzerland: World Health Organization; 2010.
5. World Health Organization. *Antiretroviral Therapy for HIV Infection in Infants and Children. Recommendations for a Public Health Approach: 2010 Revision*. Geneva, Switzerland: World Health Organization; 2010.
6. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach*. Geneva, Switzerland: World Health Organization; 2013.
7. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach*. 2nd ed. Geneva, Switzerland: World Health Organization; 2016.
8. Leroy V, Tanser F, Vreeman R et al. Access to antiretroviral initiation among HIV infected children aged 0–19 years in the International Epidemiologic Databases to Evaluate AIDS Global Network [O_04]. Presented at: 8th International Workshop on HIV Paediatrics; 15–16 July, 2016; Durban, South Africa.
9. Goodall R, on behalf of the CIPHER Cohort Collaboration. Switching to second-line antiretroviral therapy in HIV infected children: a CIPHER cohort collaboration global analysis [O_05]. Presented at: 8th International Workshop on HIV Paediatrics; 15–16 July, 2016; Durban, South Africa.
10. Paediatric HIV Treatment Initiative (PHTI) to spur innovation and access to improve the lives of children living with HIV. Available at: http://unitaid.org/en/resources/press-centre/releases/1356-paediatric-hiv-treatment-initiative-phti-to-spur-innovation-and-access-to-improve-the-lives-of-children-living-with-hiv. Accessed May 19, 2014.
11. Global pediatric antiretroviral commitment-to-action to accelerate innovation and save children's lives. Available at: http://www.pepfar.gov/press/releases/2014/234543.htm. Accessed December 1, 2014.

12. Oga MA, Ndondoki C, Brou H, et al. Attitudes and practices of health care workers toward routine HIV testing of infants in Côte d'Ivoire: the PEDI-TEST ANRS 12165 Project. *J Acquir Immune Defic Syndr*. 2011; 57:S16–S21.
13. Wettstein C, Mugglin C, Egger M, et al. Missed opportunities to prevent mother-to-child-transmission: systematic review and meta-analysis. *AIDS*. 2012;26:2361–2373.
14. Buzdugan R, Watadzaushe C, Dirawo J, et al. Positive attitudes to pediatric HIV testing: findings from a nationally representative survey from Zimbabwe. *PLoS One*. 2012;7:e53213.
15. Scanlon ML, Vreeman RC. Current strategies for improving access and adherence to antiretroviral therapies in resource-limited settings. *HIV AIDS (Auckl)*. 2013;5:1–17.
16. Yeap AD, Hamilton R, Charalambous S, et al. Factors influencing uptake of HIV care and treatment among children in South Africa—a qualitative study of caregivers and clinic staff. *AIDS Care*. 2010;22:1101–1107.
17. Chamla DD, Essajee S, Young M, et al. Integration of HIV in child survival platforms: a novel programmatic pathway towards the 90-90-90 targets. *J Int AIDS Soc*. 2015;18:20250.
18. Ahmed S, Schwarz M, Flick RJ, et al. Lost opportunities to identify and treat HIV-positive patients: results from a baseline assessment of provider-initiated HIV testing and counselling (PITC) in Malawi. *Trop Med Int Health*. 2016;21:479–485.
19. Collaborative Initiative for Paediatric HIV Education and Research, Industry Liaison Forum, International AIDS Society. *ILF/CIPHER Thematic Roundtable on Paediatric ARVs Aligning, Coordinating and Accelerating Actions to Provide Better ARVs for Children*. Geneva, Switzerland; 2015. Available at: http://www.iasociety.org/Web/WebContent/File/ILF_CIPHER_Roundtable__ARVs__2015_Report.pdf.
20. Lee JS, Sagaon Teyssier L, Dongmo Nguimfack B, et al. An analysis of volumes, prices and pricing trends of the pediatric antiretroviral market in developing countries from 2004 to 2012. *BMC Pediatr*. 2016;16:41.
21. Essajee S, Bhairavabhotla R, Penazzato M, et al. Scale-up of early infant HIV diagnosis and improving access to pediatric HIV care in global plan countries: past and future perspectives. *J Acquir Immune Defic Syndr*. 2017;75(suppl 1):S51–S58.
22. Chamla D, Mbori-Ngacha D, Newman M, et al. Evidence from the field: missed opportunities for identifying and linking HIV-infected children for early initiation of ART. *AIDS*. 2013;27:S139–S146.
23. Siberry G. *Update on PEPFAR/Accelerate Children Treatment (ACT)*. Presented at: WHO/UNAIDS Annual Meeting with Pharmaceutical Companies and Stakeholders; March 8–9, 2016; Geneva, Switzerland (unpublished).
24. Inter-agency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children. *Update to the Optimal List of Paediatric ARV Formulations*. Geneva, Switzerland: Interagency Task Team on Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children; 2015.
25. Elyanu P. *Documenting the Implementation of Test and Treat for Children and Adolescents Less Than 15 Years: A Rapid Assessment*. Kampala, Uganda: Ministry of Health; 2015.
26. World Health Organization. Antiretroviral medicines in low- and middle-income countries: forecasts of global and regional demand for 2015–2020. In press.
27. Prospective study of lopinavir based antiretroviral therapyantiretroviral therapy for HIV infected children globally (LIVING Study). Available at: https://clinicaltrials.gov/ct2/show/NCT02346487. Published November 10, 2016. Accessed June 20, 2016.
28. Penazzato M, Lee J, Capparelli E, et al. Optimizing drugs to reach treatment targets for children and adolescents living with HIV. *J Int AIDS Soc*. 2015;18(suppl 6):20270.
29. Rwembera A. *Integrating Services in Tanzania*. Presented at: Regional workshop to step up the pace for HIV prevention in adolescent and HIV care and treatment in children and adolescents in the African Region; 15–18 September, 2015; Entebbe, Uganda (unpublished).
30. Luyirika E, Towle MS, Achan J. Scaling up paediatric HIV care with an integrated, family-centred approach: an observational case study from Uganda. *PLoS One*. 2013;8:e69548.
31. Abrams EJ, Myers L, Rosenfield A, et al. Prevention of mother-to-child transmission services as a gateway to family-based human immunodeficiency virus care and treatment in resource-limited settings: rationale and international experience. *Am J Obstet Gynecol*. 2007;197:S101–S106.
32. Graves JC, Schellack CJ, Margaret L. Family clinic day RCT in Uganda: child antiretroviral therapy retention and adherence [844]. Presented at: Conference on Retroviruses and Opportunistic Infections 2016; February 22–25, 2016; Boston, Mass.
33. International Epidemiologic Databases to Evaluate AIDS (IeDEA). 2005. Unpublished data.
34. UNAIDS. *Start Free, Stay Free, AIDS-Free. A Super Fast-Track Framework for Ending AIDS Among Children, Adolescents and Young Women by 2020*. Geneva, Switzerland: UNAIDS; 2016.
35. World Health Organization. *Global Standards for Quality Health Care Services for Adolescents*. Geneva, Switzerland: World Health Organization; 2015.