Scaling Up Pediatric HIV Care and Treatment in Africa: Clinical Site Characteristics Associated With Favorable Service Utilization

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Background: To improve pediatric enrollment and retention in HIV treatment programs in Africa, we examined factors associated with service utilization within the Elizabeth Glaser Pediatric AIDS Foundation program in Côte d'Ivoire, Mozambique, South Africa, Tanzania and Zambia.

Methods: We retrospectively reviewed characteristics of clinical sites providing HIV treatment services within our program. For each site, favorable pediatric program outcomes were defined as a cumulative number or percentage of pediatric enrollment in care or antiretroviral therapy (ART) more than the pooled median value or an attrition rate less than 10%. We compared proportions of sites with favorable outcomes among those with or without selected characteristics. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were determined using logistic regression analyses, accounting for potential confounding factors.

Results: Over 4 years, 33,331 children were enrolled, including 18,255 on ART, across 220 sites. Characteristics associated with favorable pediatric enrollment were nutritional support (aOR = 8.9; CI: 2.8 to 28.4), linkages with associations of people living with HIV (aOR = 4.2; CI: 1.8 to 9.5), early infant diagnosis (aOR = 3.3; CI: 1.5 to 7.1), and on-site prevention of mother-to-child transmission services (aOR = 3.1; CI: 1.0 to 11.1). Similarly, linkages with people living with HIV, early infant diagnosis, and prevention of mother-to-child transmission were associated with high proportion of children on ART younger than 2 years of age. Home-based care was associated with low pediatric attrition rates (aOR = 2.9; CI: 1.4 to 5.8).

Conclusions: Certain site characteristics were associated with favorable pediatric enrollment and retention in our program. Expanding these characteristics to improve pediatric HIV treatment in Africa warrants further evaluation.

Key Words: pediatric, HIV, AIDS, care and treatment, health systems, Africa

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INTRODUCTION

Sub-Saharan Africa bears the highest burden of pediatric HIV/AIDS, with 90% of children with HIV infection in the world.[1] Early access to antiretroviral therapy (ART) is critical to saving the lives of children with HIV. However, the timely diagnosis of HIV infection in children and their enrollment and retention in long-term care are critical challenges in Africa, despite increasing efforts toward establishing universal access to treatment.

The lack of ART has disastrous consequences for children with HIV. Approximately 50% of these children die before the age of 2 years and 75% before reaching 5 years if not on treatment.[2,3] In contrast, several studies have demonstrated that early ART within the first 12 weeks of life results in significant reduction in early mortality,[4–11] with a greater than 90% probability of survival into adulthood.[12]

Barriers of access to pediatric HIV treatment services, particularly for infants in Africa, include poor access to early infant diagnosis (EID) using DNA polymerase chain reaction (PCR) testing, limited training of clinicians in the management of pediatric AIDS, limited pediatric ARV drug formulations, poor health care infrastructure, and sociocultural factors.[13–16] In addition, minimizing attrition rates in clinical settings providing HIV treatment is a critical issue across all HIV programs in Africa, with overall attrition rates ranging from 10% to more than 50% at 24 months,[17–22] mainly because of loss to follow-up (LTFU) or AIDS-related death.[19,23] It is therefore a critical public health priority to address these challenges for a successful expansion of pediatric HIV treatment in Africa.

Since 2004, the Elizabeth Glaser Pediatric AIDS Foundation has provided technical support for the implementation of HIV care and treatment and prevention of mother-to-child transmission (PMTCT) services via Project HEART (Help

Expand Anti-Retroviral Therapy), a President's Emergency Plan for AIDS Relief funded initiative through the Centers for Disease Control and Prevention. The program was rolled out in a wide range of public, faith-based, and private health care facilities in 5 African countries: Côte d'Ivoire, Mozambique, Tanzania, South Africa, and Zambia. These 5 countries, located in western, eastern, and southern Africa, have a high prevalence of HIV infection. However, despite a rapid increase in the number of HIV-positive patients enrolled into care since the inception of this large-scale program, children continue to be underrepresented, and attrition from clinical care has been an ongoing challenge, similar to experiences in other HIV care programs in Africa.[18,23]

After reviewing various clinical site characteristics associated with enrollment or retention of children within this multicountry HIV treatment and PMTCT programs of Project HEART, we postulated that specific site characteristics or gaps in essential services may account for the differences in service utilization between sites. The objective of this analysis was to identify which site characteristics were associated with favorable pediatric HIV service utilization.

METHODS

Data Sources

Clinical Facilities Survey

We conducted a retrospective review of all clinical facilities providing HIV treatment services, within the 5 Project HEART countries, from August 2008 to April 2009. A standard questionnaire was designed for the purpose of the survey, and covered more than 120 fields of information relevant to services within a comprehensive HIV care and treatment program. Information on the site's characteristics included, but were not limited to: (1) general characteristics, including geographic setting (urban or rural), site level (primary care clinics or tertiary hospitals), and type of facility (public or private); (2) a site's access to various essential services, such as basic laboratory services, EID DNA PCR testing (either via an on-site laboratory or through referral), provision of cotrimoxazole prophylaxis and nutritional support services (either nutrition assessment, nutrition counseling, the provision of vitamin supplement, and food support); (3) level of human resources available and trained in HIV care, (4) linkages with associations of people living with HIV (PLHIV) (as either adherence support staff or volunteers); (5) On-site PMTCT services, located within the same heath center as the HIV treatment site, and (6) provision of home-based care services via the site. Home-based care was defined as a set of palliative care or of social services that are delivered at home by a health worker. These care services were limited to treatment adherence counseling and psychological support. The questionnaire was tested and validated after a pilot in each country, before the implementation of the overall site review.

This review was conducted at all sites providing HIV treatment services within Project HEART from 2004 to 2008, which had submitted data summary reports for the relevant outcome indicators. Information describing HIV care and treatment site characteristics was collected on a standard questionnaire by in-country program staff and transmitted electronically for data management. Data were checked for gaps and inconsistencies, and further inquiries to the respective sites were made and corrections were done accordingly.

Program Outcome Indicators

Project HEART site-level routinely collected program data are transferred electronically to a central data warehouse developed to monitor project PMTCT and care and treatment activities, and to generate quarterly program reports. For the purposes of this analysis, select outcome indicators were extracted from the central database and merged to the clinical facilities survey database. Site-specific outcome indicators of interest included (1) the cumulative number of children in care, (2) the percentage of all patients on ART who were younger than 15 years, (3) the percentage of children started on ART in 2008 who were younger than 2 years of age, and the total pediatric attrition rate. Total pediatric patient attrition was measured as a proportion of the total number of children who started ART at the clinical site who were LTFU, dead, or stopped ART. LTFU was defined as a patient who was not seen at scheduled clinic visits for at least 3 consecutive months.

Statistical Analyses

Statistical analysis was done using SAS 9.1 software. Descriptive statistics were used to summarize frequency distributions of general clinical site characteristics and proportions of sites with specific health services. For each outcome indicator, we computed the median value and interquartile range (IQR), and the proportion of sites with an outcome indicator more than the pooled median value across all sites. Because of the relatively low median values for the outcome indicators, higher threshold above the median values were selected. For each site, favorable pediatric program outcomes were defined as having more than 100 children in care (including those on ART) and at least 8% of all patients in care were younger than 15 years, at least 10% of the children on ART in 2008 were younger than 2 years of age, or a total attrition rate less than 10% for the children on ART.

Potential explanatory variables for favorable pediatric enrollment included geographic setting, site type, outpatient care services for HIV-infected children, access to EID DNA PCR testing, having an associated pediatrician, a nurse or pediatrician specifically trained in HIV care, colocated PMTCT services, nutritional support services, and linkages with PLHIV associations. Explanatory variables considered for low attrition rate included geographic setting, site type, outpatient care services for HIV-infected children, provision of cotrimoxazole prophylaxis, nutritional support services, associated pediatrician, a pediatrician or a nurse specifically trained in HIV care, home-based care services, psychosocial support, linkages with PLHIV associations, and having a computerized patient tracking system. For each analysis, a specific country subgroup analysis was not possible because of the smaller sample size when each country was considered individually.

We compared the proportion of clinical sites with favorable pediatric program outcomes as defined among those with or without specific site characteristics. χ^2 test for association and odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were used to identify characteristics that were significantly associated with the respective outcome indicators. Finally, we assessed the association of clinical site characteristics with the outcome indicators using multivariate logistic regression models. Selected explanatory variables that were included in the final models were those significantly associated with the favorable outcome indicators in univariate analysis. Clinical site type, geographic setting, site level, and program start year were included in each model as potential confounding variables. Our objective was to assess the program as a whole. Therefore, the country was not included as a variable of interest. Adjusted ORs (aORs) and respective 95% CIs were computed to assess the independent association of the clinical site characteristics with either pediatric enrollment or attrition rates.

RESULTS

Completed questionnaires were received from 222 (96%) of the 231 of Project HEART clinical sites, including 76 sites in Côte d'Ivoire, 59 sites in Zambia, 52 sites in Tanzania, 20 sites in Mozambique, and 15 sites in South Africa. Of these 222 sites, 2 sites were excluded for missing information for the outcome indicators. A total of 33,331 children were enrolled into care, including 18,255 on ART across these sites.

Distribution of Clinical Site Characteristics

Table 1 presents the distribution of clinical site characteristics and pediatric patient enrollment and attrition rates across our program in the 5 countries. Most sites were urban, public, and primary health care centers. Similar proportions of clinical sites (50%) started a care and treatment program before or after 2006. Most clinical sites (88%) reported offering outpatient care for children with HIV. However, only 21% and 19% of clinical sites reported having an associated pediatrician or a pediatrician specifically trained in HIV care, respectively. Most HIV-treatment sites (84%) were located within an antenatal care center providing PMTCT services. The majority of these clinical sites had at least one nurse specifically trained in HIV care (82%).

Regarding clinical services, most sites reported providing cotrimoxazole prophylaxis (77%) and offering some form of nutritional support services (73%) consisting of assessment of nutritional status, nutrition counseling, provision of vitamins or food. The main gaps in essential pediatric HIV care services were access to EID, representing only 58% of all sites, and individual nutritional support services. A small proportion of sites reported systematically providing nutritional assessment (34%), food support (32%), or vitamins (50%) to HIV-positive children. Home-based care service was reported by 51% of sites and 58% of the sites reported having linkages with PLHIV associations. The number of children enrolled into care varied widely across sites, with a median of 56 children (IQR: 10–197). Similarly, the percentage of pediatric patient enrollment varied, with children younger than 15 years representing a median of 7% of all patients including adults in care (IQR: 4%–10%) and a median of 6% of children on ART were younger than 2 years. Only 37% of clinical sites had at least 100 children in care and 48% of sites had at least 10% of children on ART younger than 2 years of age, whereas 32% of the sites had a total attrition rate for pediatric patients less than 10%.

TABLE 1. Distribution of Select Clinical Site Characteristics and Pediatric Enrollment

Site Characteristics	Number of Sites (N = 220)	Percentage
Urban	155	71
Rural	65	29
Public/government site	174	79
Nongovernment site	46	21
Tertiary health facility	22	10
Primary care facility	198	90
Older sites: 2004–2006	109	50
Newer sites: 2007–2008	111	50
Outpatient care for HIV-infected children	195	88
Access to EID DNA PCR testing	105	48
Pediatrician on site ≥1	47	21
Pediatrician trained in HIV care ≥1	42	19
Nurses trained in HIV care ≥1	180	82
PMTCT services provided on site	186	84
Nutritional support provided on site	161	73
Nutritional assessment	76	34
Nutritional counseling	151	68
Multivitamins supplements	111	50
Food support	72	32
Cotrimaxazole prophylaxis	172	77
Home-based care	112	51
Computerized tracking system	127	60
PLHIV linked to the site	128	58

Favorable Outcome Indicators (Enrollment or Attrition)	Sites With Favorable Outcome Indicators	
Cumulative number of children in care ≥ DNA PCR 100	82	37
Percent of total patients in care <15 years ≥8%	82	37
Percent of new children on ART in 2008 <2 years ≥10%	106	48
Total attrition rate of children on ART <10%	70	32

PMTCT, prevention of mother-to-child transmission of HIV; EID, early infant HIV diagnosis DNA PCR.

Site Characteristics Associated With Favorable Pediatric Enrollment

Table 2 shows selected site characteristics that were significantly associated with a high number of children in care. In multivariate analysis, tertiary sites (aOR = 5.1; CI: 1.5 to 17.1), older sites (aOR = 3.9; CI: 1.7 to 9.1), nutritional support services (aOR = 8.9; CI: 2.8 to 28.4), and linkages

TABLE 2. Clinical Site Characteristics Associated With a Large Number of Children in Care

Site Characteristics	Sites with Cumulative Number of Children in Care ≥100, n (%)	Crude OR (95% CI)	aOR (95% CI)
Setting		**2.0 (1.1 to 3.9)**	2.0 (0.9 to 4.4)
Urban	65/155 (42)		
Rural	17/65 (26)		
Type		1.5 (0.7 to 2.9)	2.1 (0.8 to 5.9)
Public	68/174 (39)		
Private	14/46 (30)		
Level		**2.7 (1.1 to 6.6)**	**5.1 (1.5 to 17.1)**
Tertiary hospital	13/22 (50)		
Primary care	69/198 (35)		
Start year		**3.2 (1.8 to 5.6)**	**3.9 (1.7 to 9.1)**
Older sites: 2004–2006	55/109 (50)		
Newer sites: 2007–2008	27/111 (24)		
Access to EID DNA PCR		**4.3 (2.4 to 7.7)**	**3. 3 (1.5 to 7.1)**
Yes	57/105 (54)		
No	25/115 (22)		
Pediatrician trained in HIV care		1.4 (0.7 to 2.8)	—
Yes	18/41 (44)		
No	64/179 (36)		
Nurse trained in HIV care		**2.8 (1.2 to 6.4)**	2.1 (0.7 to 6.1)
Yes	74/180 (41)		
No	8/40 (20)		
PMTCT service on site		**2.6 (1.1 to 6.3)**	**3.1 (1.1 to 11.1)**
Yes	75/186 (40)		
No	7/34 (21)		
Pediatric nutritional support		**7.6 (3.1 to 18.6)**	**8.9 (2.8 to 28.4)**
Yes	75/161 (47)		
No	6/58 (10)		
PLHIV linked to site		**3.3 (1.8 to 6.2)**	**4.2 (1.8 to 9.5)**
Yes	60/128 (47)		
No	18/86 (21)		

PMTCT, prevention of mother-to-child transmission of HIV.
Values in bold indicate statistically significant Crude or adjusted Odds Ratios (OR).

with PLHIV associations (aOR = 4.2; CI: 1.8 to 9.5). Access to EID DNA PCR testing (aOR = 3.1; CI: 1.7 to 9.1) and on-site PMTCT services (aOR = 3.1; 1.1 to 11.1) were associated with having at least 100 children in care. Having an associated pediatrician or a nurse specifically trained in HIV care was not significantly associated with pediatric patient enrollment in the program.

We also assessed the association of site characteristics with pediatric enrollment in terms of the percentage of the total number of patients (including adults) in care younger than 15 years of age. There was a significant association of pediatric enrollment with PMTCT services (aOR = 4.0; CI: 1.3 to 12.0) and nutritional support (aOR = 3.3; CI: 1.5 to 7.2). However, there was no association with access to EID or having an associated pediatrician or nurse specifically trained in HIV care.

Clinical site characteristics that were significantly associated with a high percentage of new children on ART younger than 2 years (Table 3) included access to EID (aOR = 2.6; CI: 1.3 to 4.9) having a nurse specifically trained in HIV care (aOR = 3.9; CI: 1.6 to 9.8), PMTCT services on site (aOR = 2.9; CI: 1.1 to 8.1), and linkages with PLHIV associations (aOR = 2.6; CI: 1.4 to 4.9).

Clinical Site Characteristics Associated with Low Pediatric Attrition Rates

Table 4 highlights site-specific characteristics that were significantly associated with low attrition of children on ART in univariate and multivariate analyses. Public and newer sites tended to have low attrition compared with private and older sites. Similarly, sites that reported offering home-based care services were more likely to have low attrition rates compared with sites that did not provide those services (aOR = 2.9; CI: 1.4 to 5.8). Surprisingly, sites that reported having a computerized patient tracking system were less likely to have low attrition rates compared with sites that had a paper-based system. This result cannot be explained by site size because larger and smaller sites had similar attrition rates. However, sites with a computerized tracking system tended to be private sites, older sites, and larger sites with home-based care services.

DISCUSSION

Although there are assumptions and anecdotal evidence suggesting a positive impact of the quality of health systems on HIV service utilization in developing countries, to our knowledge, limited research has been done in this area.[24] We attempted to address this knowledge gap, using data from our large HIV program in 5 countries in Africa with a high burden of HIV infection.

This assessment demonstrated associations of certain services with favorable program outcomes for children and poses the question that if these services were expanded, perhaps pediatric HIV service utilization would also expand and improve in similar developing country populations. The results presented here have shown that enrollment of children in HIV care services was far below the international target of 15% of all HIV-positive patients in care, which underscores the need for more aggressive strategies to increase enrollment of children in such settings.

The findings have also demonstrated that a number of essential services are associated with high enrollment and retention of children in the program. First, sites that reported offering EID or nutritional support services and those having

TABLE 3. Clinical Site Characteristics Associated With Increased Infants on ART

Site Characteristics	Sites with ≥10% of Children on ART Who are <2 Years n (%)	Crude OR (95% CI)	aOR (95% CI)
Setting		1.1 (0.6 to 1.9)	1.3 (0.6 to 2.6)
Urban	76/157 (48)		
Rural	30/65 (46)		
Type		1.7 (0.9 to 3.4)	1.5 (0.7 to 3.4)
Public	89/176 (51)		
Private	17/46 (37)		
Level		1.4 (0.6 to 3.3)	0.9 (0.3 to 2.6)
Primary hospital	97/200(49)		
Tertiary hospital	9/22 (41)		
Start year		1.2 (0.7 to 2.0)	1.4 (0.6 to 2.5)
Older sites: 2004–2006	55/111 (50)		
Newer sites: 2007–2008	51/111 (46)		
Access to EID DNA PCR		**3.5 (2.0 to 6.1)**	**2.6 (1.3 to 4.9)**
Yes	67/105 (64)		
No	39/117 (33)		
Pediatrician trained in HIV care		1.1 (0.6 to 2.2)	—
Yes	21/47 (45)		
No	85/175 (49)		
Nurse trained in HIV care		**4.7 (2.0 to 10.7)**	**3.9 (1.6 to 9.8)**
Yes	96/182 (54)		
No	8/40 (20)		
PMTCT service on site		**4.3 (1.8 to 10.3)**	**2.9 (1.1 to 8.1)**
Yes	99/188 (53)		
No	7/43 (21)		
Pediatric nutritional support		**2.9 (1.9 to 1.5-5.5)**	1.4 (0.7 to 31)
Yes	86/161 (53)		
No	17/60 (28)		
PLHIV linked to site		**2.0 (2.1 to 3.5)**	**2.6 (1.4 to 4.9)**
Yes	68/128 (53)		
No	32/88 (36)		

Analysis included all 222 sites that reported data on new children younger than 2years started on ART in 2008, when program started to be disaggregated by age group.
PMTCT, prevention of mother-to-child transmission of HIV.
Values in bold indicate statistically significant Crude or adjusted Odds Ratios (OR).

TABLE 4. Clinical Sites Characteristics Association With Low Attrition of Children on ART

Characteristics	Sites With Total Attrition <10%	Crude OR (95% CI)	aOR (95% CI)
Setting		1.8 (1.9 to 3.3)	1.9 (0.9 to 3.9)
Rural	28/61 (46)		
Urban/ semiurban	42/130 (32)		
Site type		**2.8 (1.3 to 6.2)**	**2.5 (1.1 to 6.0)**
Public	61/147 (42)		
Private	9/44 (21)		
Level		1.6 (0.5 to 4.5)	2.6 (0.8 to 8.7)
Tertiary	7/15 (47)		
Primary/ secondary	63/176 (36)		
Start year		**2.7 (1.3 to 4.3)**	**2.4 (1.2 to 4.9)**
New site	47/99 (47)		
Old site	24/92 (26)		
Site size		0.81 (0.4 to 1.5)	—
Large ≥100	28/81 (36)		
Small <100	45/114 (39)		
Pediatrician on site		0.6 (0.2 to 1.5)	—
Yes	33/39 (85)		
No	116/152 (76)		
Nurses trained in HIV care		0.7 (0.3 to 1.6)	—
Yes	57/161 (35)		
No	13/30 (47)		
Nutrition support services		0.7 (0.3 to 1.4)	—
Yes	53/151 (35)		
No	17/39 (44)		
Home-base care		**2.0 (1.1 to 3.6)**	**2.9 (1.4 to 5.8)**
Yes	46/106 (43)		
No	24/85 (28)		
Computerized system		**0.4 (0.2 to 0.7)**	**0.4 (0.2 to 0.9)**
Yes	34/120 (28)		
No	36/71 (52)		
PLHIV linked to site		0.9 (0.5 to 1.7)	—
Yes	44/118 (37)		
No	26/67 (39)		

Values in bold indicate statistically significant Crude or adjusted Odds Ratios (OR).

a linkage with PLHIV associations are more likely to have a favorable enrollment of children. A small percentage of the clinical sites, however, reported having EID services or having linkages with PLHIV associations, suggesting that expanding these services and associations or linkages may have a beneficial impact. For example, increasing access to DNA PCR testing is likely to improve timely treatment of infants with HIV.[25] Even in remote rural clinical facilities, organizing the collection and transportation of dried blood spot specimens to a referral laboratory for DNA PCR testing has proved feasible.[25–27] However, the widespread implementation of EID throughout HIV programs has been a slow process, as shown by the small proportion of sites with access to DNA PCR in our program data.

Second, providing nutritional services was associated with favorable pediatric enrollment in care, in this study,

which might be explained by the common occurrence of malnutrition in children with HIV. Malnutrition and failure to thrive are common manifestations of HIV infection and AIDS among children and one of the main reasons for hospital admissions.[28–30] No association was observed with infant on ART. The discrepancies in our results could be explained by delays in HIV diagnosis and ART because of the limited access to EID. Given the retrospective nature of our data, it is unclear whether there is a direct causal relationship between provision of nutritional support services and enrollment of pediatric patients.

Other interesting findings were the high enrollment of children and infants at sites that were located in a center providing PMTCT services or that had linkages with PLHIV association. These findings support the current strategy of integration of pediatric HIV treatment and PMTCT services and the involvement of PLWH in HIV program.

With regard to attrition rates, sites that reported offering home-based care services tended to have low attrition of children from the program. This finding is consistent with the result of a pediatric HIV cohort study that found a lower risk of LTFU for sites with an associated outreach service.[31] Provision of nutritional support services were not associated with low attrition, suggesting a possible advanced disease stage and high attrition because of death among children receiving nutritional support. Surprisingly, sites that reported having a computerized patient tracking system had high attrition rates. These results could not be explained by differences in the general site characteristics, such as geographic setting, type, level, or program year, because those factors were adjusted for in multivariate analysis. In addition, this association could not be the result of differences in the site size, defined as the number of children in care. Although larger sites tended to have a computerized patient tracking system, the proportion of sites with low attrition rates did not differ between larger and smaller sites. One possible explanation of the higher attrition rates for sites with a computerized tracking system could be differences in the quality of the data collection and reporting systems, which is a common challenge of health information systems in resource-limited settings.[32–34] Having a computerized tracking system may improve the site's capacity for systematic monitoring and accurate reporting of the number of patients LTFU, which tend to be underreported by sites that rely on paper-based monitoring systems. That is, for sites having a paper-based monitoring system, potential misclassification of patients may result through an overreporting of the status "currently in care." As a result, attrition rates could be underestimated.

There are a few limitations to our assessment. First, in an effort to have a comprehensive review of the program, the questionnaire was not specific enough and the use of aggregate program outcome data limited our ability to interpret the findings, to make any causal inference. Second, our results may not be representative of the entire program in the countries, because the analysis was limited to Project HEART supported clinical sites, which are not a random sample of HIV treatment sites within the respective countries. However, the likelihood of a systematic bias may be limited because the sites that were evaluated represent a wide range of health facilities from diverse geographic settings, types, and levels of the health care pyramid in these countries. Third, it was not possible to account for other unmeasured potential confounding factors such as pediatric HIV care policies, or the availability of pediatric drug formulations that may influence enrollment or retention of children in care. Finally, although our questionnaire was piloted in each country and used only by program staff working most directly with each site, further validation of the results obtained was only done by multiple queries back to the program staff and sites themselves.

Nevertheless, our findings suggest a set of potential interventions, which may improve pediatric HIV service utilization. These types of interventions might be introduced or strengthened at sites with suboptimal HIV treatment uptake or retention rates for children, and operations research performed to determine potential benefits. In addition, high performing sites need to be supported to sustain activities that are found to have a significant association with improved program outcomes. For example, increasing systematic access to EID may increase early treatment initiation of infants diagnosed with HIV infection. Integrating nutritional support of any kind with HIV services could improve enrollment and retention of HIV-positive children with malnutrition who are in urgent need of ART. Integration of PMTCT with pediatric HIV care services, strengthening linkage with PLWH might improve enrollment of younger children. Finally, according to this analysis, developing or strengthening home-based care services could be a way to improve retention of pediatric patients in HIV care and treatment programs in resource-poor settings.

Despite its limitations, this review of our large multicountry HIV care and treatment program in Africa has provided some insights into the gaps in clinical services for pediatric HIV care and treatment and suggests areas of clinical site activities that could be strengthened, to improve pediatric HIV care and treatment services in resource-limited settings.

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REFERENCES

1. WHO/UNAIDS/UNICEF. *Toward Universal Access: Scaling Up Priority HIV/AIDS-Interventions in the Health Sector. Progress report*. 2010. Available at: http://www.who.int/hiv/pub.
2. Newell ML, Brahmbhatt H, Ghys PD. Child mortality and HIV infection in Africa: a review. *AIDS*. 2004;18(suppl 2):S27–S34.
3. Newell ML, Coovadia H, Cortina-Borja M, et al. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet*. 2004;364:1236–1243.
4. Matida LH, Marcopito LF, Succi RC, et al. Improving survival among Brazilian children with perinatally-acquired AIDS. *Braz J Infect Dis*. 2004;8:419–423.

5. Song R, Jelagat J, Dzombo D, et al. Efficacy of highly active antiretroviral therapy in HIV-1-infected children in Kenya. *Pediatrics*. 2007;120: e856–e861.
6. Wamalwa DC, Farquhar C, Obimbo EM, et al. Early response to highly active antiretroviral therapy in HIV-1-infected Kenyan children. *J Acquir Immune Defic Syndr*. 2007;45:311–317.
7. Violari A, Cotton MF, Gibb DM, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med.* 2008;359: 2233–2244.
8. Patel K, Hernan MA, Williams PL, et al. Long-term effectiveness of highly active antiretroviral therapy on the survival of children and adolescents with HIV infection: a 10-year follow-up study. *Clin Infect Dis.* 2008;46:507–515.
9. Chiappini E, Galli L, Tovo PA, et al. Five-year follow-up of children with perinatal HIV-1 infection receiving early highly active antiretroviral therapy. *BMC Infect Dis.* 2009;9:140.
10. Dollfus C, Le Chenadec J, Faye A, et al. Long-term outcomes in adolescents perinatally infected with HIV-1 and followed up since birth in the French perinatal cohort (EPF/ANRS CO10). *Clin Infect Dis.* 2010; 51:214–224.
11. Edmonds A, Yotebieng M, Lusiama J, et al. The effect of highly active antiretroviral therapy on the survival of HIV-infected children in a resource-deprived setting: a cohort study. *PLoS Med.* 2011;8:e1001044.
12. McConnell MS, Byers RH, Frederick T, et al. Trends in antiretroviral therapy use and survival rates for a large cohort of HIV-infected children and adolescents in the United States, 1989-2001. *J Acquir Immune Defic Syndr.* 2005;38:488–494.
13. Committee on Pediatric AIDS, Section on International Child Health. Increasing antiretroviral drug access for children with HIV infection. *Pediatrics*. 2007;119:838–845.
14. Cherutich P, Inwani I, Nduati R, et al. Optimizing paediatric HIV care in Kenya: challenges in early infant diagnosis. *Bull World Health Organ.* 2008;86:155–160.
15. Castelli F, Pietra V, Diallo I, et al. Antiretroviral (ARV) Therapy in Resource Poor Countries: What do we need in real life? *Open AIDS J.* 2010;4:28–32.
16. Waning B, Diedrichsen E, Jambert E, et al. The global pediatric antiretroviral market: analyses of product availability and utilization reveal challenges for development of pediatric formulations and HIV/AIDS treatment in children. *BMC Pediatr.* 2010;10:74.
17. Williams PL, Van Dyke R, Eagle M, et al. Association of site-specific and participant-specific factors with retention of children in a long-term pediatric HIV cohort study. *Am J Epidemiol.* 2008;167:1375–1386.
18. Braitstein P, Katshcke A, Shen C, et al. Retention of HIV-infected and HIV-exposed children in a comprehensive HIV clinical care programme in Western Kenya. *Trop Med Int Health.* 2010;15:833–841.
19. Anaky MF, Duvignac J, Wemin L, et al. Scaling up antiretroviral therapy for HIV-infected children in Côte d'Ivoire: determinants of survival and loss to programme. *Bull World Health Organ*. 2010;88:490–499.
20. Hassan AS, Sakwa EM, Nabwera HM, et al. Dynamics and constraints of early infant diagnosis of HIV infection in Rural Kenya. *AIDS Behav.* 2012; 16:5–12.
21. Barth RE, Tempelman HA, Moraba R, et al. Long-Term Outcome of an HIV-Treatment Programme in Rural Africa: Viral Suppression despite Early Mortality. *AIDS Res Treat.* 2011;2011:ID434375.
22. Sutcliffe CG, Bolton-Moore C, van Dijk JH, et al. Secular trends in pediatric antiretroviral treatment programs in rural and urban Zambia: a retrospective cohort study. *BMC Pediatr.* 2010;10:54.
23. Davies MA, Keiser O, Technau K, et al. Outcomes of the South African National Antiretroviral Treatment Programme for children: the IeDEA Southern Africa collaboration. *S Afr Med J.* 2009;99:730–737.
24. Barker PM, McCannon CJ, Mehta N, et al. Strategies for the scale-up of antiretroviral therapy in South Africa through health system optimization. *J Infect Dis.* 2007;196(suppl 3):S457–S463.
25. Chatterjee A, Tripathi S, Gass R. Implementing services for Early Infant Diagnosis (EID) of HIV: a comparative descriptive analysis of national programs in four countries. *BMC Public Health.* 2011;11:553.
26. Sherman GG, Stevens G, Jones SA, et al. Dried blood spots improve access to HIV diagnosis and care for infants in low-resource settings. *J Acquir Immune Defic Syndr.* 2005;38:615–617.
27. Fischer A, Lejczak C, Lambert C, et al. Simple DNA extraction method for dried blood spots and comparison of two PCR assays for diagnosis of vertical human immunodeficiency virus type 1 transmission in Rwanda. *J Clin Microbiol.* 2004;42:16–20.
28. Marston M, Zaba B, Salomon JA, et al. Estimating the net effect of HIV on child mortality in African populations affected by generalized HIV epidemics. *J Acquir Immune Defic Syndr.* 2005;38:219–227.
29. Sunguya BF, Poudel KC, Otsuka K, et al. Undernutrition among HIV-positive children in Dar es Salaam, Tanzania: antiretroviral therapy alone is not enough. *BMC Public Health.* 2011;11:869.
30. Madec Y, Germanaud D, Moya-Alvarez V, et al. HIV prevalence and impact on renutrition in children hospitalised for severe malnutrition in Niger: an argument for more systematic screening. *PLoS One.* 2011;6:e22787.
31. Anema A, Zhang W, Wu Y, et al. Availability of nutritional support services in HIV care and treatment sites in sub-Saharan African countries. *Public Health Nutr.* 20138–47.
32. Mate KS, Bennett B, Mphatswe W, et al. Challenges for routine health system data management in a large public programme to prevent mother-to-child HIV transmission in South Africa. *PLoS One*. 2009;4:e5483.
33. Kiragga AN, Castelnuovo B, Schaefer P, et al. Quality of data collection in a large HIV observational clinic database in sub-Saharan Africa: implications for clinical research and audit of care. *J Int AIDS Soc.* 2011;14:3.
34. Garrib A, Stoops N, McKenzie A, et al. An evaluation of the District Health Information System in rural South Africa. *S Afr Med J.* 2008;98:549–552.