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Evaluating Global HIV Prevention, Care, and Treatment Services for Children in the International Epidemiology Databases to Evaluate AIDS (IeDEA)

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	HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PAEDIATRICS





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Title: Evaluating Global HIV Prevention, Care, and Treatment Services for Children in the International Epidemiology Databases to Evaluate AIDS (IeDEA)

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Key Words: HIV/AIDS, health policy, international health services, pediatrics

ABSTRACT

Objectives: To assess access children with HIV have to comprehensive HIV care services, to evaluate the implementation and scale-up of services over time, and to compare site services with clinical cohort data to explore whether access to these services influences retention in care.

Design: A cross-sectional standardized survey was completed in 2014-2015 by sites providing HIV care to children across regions of the International epidemiology Databases to Evaluate AIDS (IeDEA) consortium. We developed a comprehensiveness score based on the World Health Organization (WHO)'s nine categories of essential services to categorize sites as "low" (0-5), "medium" (6-7), or "high" (8-9). When available, comprehensiveness scores were compared with scores from a 2009 survey. We compared patient-level data with site services to investigate the relationship between the comprehensiveness of services and retention in care.

Results: Data from 174 IeDEA sites in 32 countries were analyzed. Of the WHO essential services, sites were most likely to offer ART provision and counseling (99%), co-trimoxazole prophylaxis (97%), prevention of mother-to-child transmission services (96%), outreach for patient engagement and follow-up (95%), CD4 cell count testing (88%), tuberculosis screening (87%), and select immunization (72%) services. Sites were less likely to offer nutrition/food support (56%), viral load testing (69%), and HIV counseling and testing (40%). 10 percent of sites rated "low," 59% "medium," and 31% "high" in the comprehensiveness score. The mean comprehensiveness of services score increased significantly from 5.6 in 2009 to 7.3 in 2014 ($p<0.001$; $n=30$). Loss to follow-up after ART initiation was highest in clinics with a "low" level of services and lowest in clinics with a "high" level of services.

Conclusion: This global assessment suggests the potential care impact of continuing to scale-up and sustain comprehensive pediatric HIV services. Meeting recommendations for comprehensive services for HIV care should remain a global priority.

STRENGTHS AND LIMITATIONS:

- This study fills a critical gap in the literature, given the lack of similar assessments of the trend and impact of changes in pediatric HIV care services across a broad global geography.
- This study was able to disaggregate by age, allowing a more comprehensive assessment across the range of pediatric care.
- The data for this study were collected from September 2014 to January 2015 and may not represent the current state of HIV pediatric care.
- Limitations in the available patient-level data meant that certain analyses were only done for the East Africa region and may not be generalizable to other regions within IeDEA or at non-IeDEA sites.

MANUSCRIPT

INTRODUCTION

In 2020, there were an estimated 1.7 million children with HIV between the ages of 0-15 years.(1) New infections among children declined by 53% from 2010 to 2020, with most new infections occurring in African countries. Access to combination antiretroviral therapy (ART), however, remains an important challenge for this population. In 2020, only 54% of children with HIV globally were accessing ART, which is substantially lower than the percentage of adults with HIV accessing ART (74%).(1) Barriers to scale-up of pediatric treatment include inadequate access to early infant diagnosis, lack of provider experience in delivering pediatric care, limited availability of pediatric antiretroviral formulations, and weak health care infrastructure, but there are few data on the extent to which these specific pediatric HIV services are available globally.(2-5) For children with HIV who are in care, losses to follow-up from care and deaths while in care appear to remain high, though these rates are difficult to accurately report.(6, 7) It is important to document the capacity of HIV care and treatment programs to deliver comprehensive, integrated HIV prevention, care, and treatment services to children across multiple regions in order to identify gaps in services and target resources appropriately.(8-12)

Data on clinical capacity and services are also needed to ensure that pediatric services continue to improve their quality and comprehensiveness, in line with global guidelines for the care of children living with and exposed to HIV. An assessment of global pediatric HIV care capacity at sites of the International Epidemiology Databases Evaluating AIDS (IeDEA) consortium from 2009 revealed that only 38% of sites had capacity for routine viral load monitoring, and that 89% had direct access to infant HIV DNA PCR testing.(13) Over time, the World Health Organization (WHO) has continued to revise its guidelines for the care of children with HIV, including initiation of ART for all children under 5 years of age, initiation of ART for all children >5 years of age with a CD4 cell count <500 cells/μl, routine viral load monitoring for all patients,(14) and then the expansion to recommend treatment of all children and adults with HIV with lifelong ART regardless of immunologic status.(15) The ultimate goal of these guidelines is to improve pediatric morbidity and mortality related to HIV through expanded prevention, treatment, and monitoring services.

Examining whether and how the availability of more comprehensive HIV prevention and treatment services improve patient-level pediatric outcomes are important steps in ensuring that global care services ultimately improve the care of children. Here, we draw on site-level survey assessments administered to a consortium of HIV care programs worldwide to assess the extent to which children with HIV have access to comprehensive HIV care services, to evaluate the implementation and scale-up of these services over time, and to compare these survey findings with clinical cohort data to explore whether access to these services influences the retention in care of children with HIV.

METHODS

Population

The IeDEA research consortium was established in 2005 with support from the U.S. National

Institute for Allergy and Infectious Diseases to develop a global resource of clinical data from people with HIV (www.iedea.org). IeDEA collects data from seven international regional data centers: the Asia-Pacific, CCASAnet (encompassing the Caribbean Central and South America), Central Africa, East Africa, NA-ACCORD (encompassing Canada and the U.S.), Southern Africa, and West Africa. Each IeDEA region collaborates with clinical sites to define key variables and harmonize large datasets to address research questions around the impact of the global ART rollout on HIV-related clinical services and outcomes. Pediatric clinical and ART resources across the Africa and Asia-based HIV care sites were previously evaluated in 2009.⁽¹³⁾

Study design and data collection

We surveyed the IeDEA sites that provide HIV treatment and prevention services to children, in any configuration of stand-alone pediatric services or combined care for children and adults. The standardized site assessment tool was adapted from the site assessment survey done in 2009.⁽¹³⁾ Study data were collected and managed using a web-based survey on the REDCap (Research Electronic Data Capture) platform (www.project-redcap.org) hosted at the Vanderbilt Institute for Global Health at Vanderbilt University. Site clinical directors or managers were asked to complete the survey, providing information about the sites' physical and clinical characteristics and capacity to deliver WHO-recommended pediatric HIV prevention, care, and treatment services.

We created a measure of comprehensiveness of pediatric care services based on the WHO's nine categories of essential services: 1) ART access with psychosocial and adherence counseling; 2) nutrition or food support or counseling; 3) prevention of mother-to-child transmission (PMTCT) services, including medication; 4) CD4 cell count and HIV viral load testing; 5) tuberculosis screening; 6) counseling and testing for HIV, 7) co-trimoxazole prophylaxis, 8) immunization access for select vaccine-preventable diseases (hepatitis B, pneumococcal, influenza vaccine, or yellow fever vaccines); and 9) outreach for patient engagement and follow-up.⁽¹⁶⁾ In calculating the comprehensiveness score, one point was awarded for each service adequately provided by the site, with a total score range between 0 (no services offered) and 9 (all services offered). Sites were then categorized into "low" (0-5), "medium" (6-7), or "high" (8-9) service levels, as was done in prior global site assessment evaluations, from similar site assessment surveys done in 2009.⁽¹³⁾

In order to investigate the relationship between the comprehensiveness of available services and retention in care, patient-level data were also extracted from the IeDEA global cohort database. Patient inclusion criteria were: (1) documented HIV infection; (2) age <16 years of age at enrollment; (3) enrolled into care in 2001 or later at least 6 months prior to site-specific database closure; and (4) either enrolled at a site which completed the 2009 survey or enrolled within six months of the 2014 site assessment survey. Due to high amount of missing data for items from site surveys, only patients seen at sites with missing data for at most 1 item (n=62 sites) were included in the analysis (n=28,378). The sample was further restricted by including only patients enrolled within six months of the 2014 survey if they were affiliated with sites only completing that round of surveys (n=18,487). Since the resulting patient-level dataset was overwhelmingly from East Africa (n=17,596 (95.2%)) and less than 5% of the sample consisted of patients from

the IeDEA regions of Asia-Pacific, CCASAnet, Central Africa, and West Africa, we selected only sites in East Africa (52 sites) for the patient-level analyses. Then, the dataset was further restricted to patients with non-missing ART start date (n=12,401 in 35 centers.)

Statistical analysis

Data were analyzed using SAS (SAS Institute Inc., Cary, NC, U.S.). Descriptive analyses were performed, with site characteristics stratified by region. We analyzed differences in the mean comprehensive of services scores for clinics that participated in both the 2009 and 2014 IeDEA site assessments using a paired t-test.

The analyzed patient-level outcome of interest was time from ART start to loss to program due to either death, transfer, or loss to follow up. Loss to follow-up was defined as no record of death or transfer and no visit between the date of the last clinic visit attended and six months or more of database closure. This was a competing risk model with the two competing events being death and loss to follow-up and being transferred coded as censored. Kaplan-Meier plots and bivariate Cox proportional hazard models were used to assess the association between comprehensive care category and loss to program. A multivariable Cox proportional hazards model which included clinically important patient-level variables – age at ART start (categorical, 0 to <5 years, 5 to <10, 10 to <15, 15 to 16); categorical immune status at ART start as defined by the WHO, based on age and CD4 cell count or percentage depending on age, WHO clinical stage at enrollment, and clinic location (urban, mostly urban, mostly rural or rural) – was used to investigate the relationship between level of comprehensiveness of services (low, medium, high) and patient retention in care. Hazards ratios and 95% confidence intervals (CI) were reported. As a sensitivity analysis, the model was refit using data obtained from multiple imputation for missing values for CD4 percentage (24.0%), WHO clinical stage (13.8%), and age at ART start (0.1%) using the Markov Chain Monte Carlo (MCMC) method.(17)

Patient and Public Involvement

Patients or the public were not involved in the design or conduct of our research. In the East Africa region, briefings on the findings were done in clinics to patients, including both study participants and non-participants.

RESULTS

All 536 sites providing HIV care in the IeDEA global regions received the survey, and 287 (53.5%) sites completed the survey between September 2014 and January 2015. Out of those 287 sites, 174 (61%) provided pediatric care. Site characteristics by IeDEA region are shown in Table 1. Overall, most sites providing pediatric HIV care (82%) saw both children and adult patients, including almost 17,000 children with HIV. The majority of the sites were in African countries, with 88 sites (51%) from Southern Africa, 34 sites (20%) from East Africa, 17 sites (10%) from Central Africa, 16 sites (9%) from the Asia-Pacific, 12 sites (7%) from West Africa, and 7 sites (4%) from CCASAnet. Most of the care sites were located in urban (39%) or mostly urban (8%) settings, and almost all were public facilities (93%). Overall, the HIV care sites were well distributed across different levels of health care services; 40% were primary care sites, 25%

were secondary care sites, and 34% were tertiary care sites. However, the participating sites from the Asia-Pacific, CCASAnet, and Central Africa regions were almost exclusively tertiary facilities.

Table 1. Site Characteristics by International Epidemiology Databases to Evaluate AIDS (IeDEA) Region (n=174 sites)*

		Asia-Pacific (n=16)	CCASAnet (n=7)	Central Africa (n=17)	East Africa (n=34)	Southern Africa (n=88)	West Africa (n=12)	Total (n=174)
Number of Pediatric and Adolescents in Care, 2014		70 (2 sites)	611 (7 sites)	1748 (13 sites)	8165 (33 sites)	3113 (12 sites)	3076 (10 sites)	16783 (77 sites)
Age at Enrollment for Patients in Care in 2014	0 to <5	47 (67.1)	356 (58.3)	567 (32.4)	3519 (43.1)	1934 (62.1)	1666 (54.2)	8089 (48.2)
	5 to <10	17 (24.3)	150 (24.5)	628 (35.9)	2844 (34.8)	685 (22.0)	989 (32.2)	5313 (31.7)
	10 to <15	6 (8.6)	89 (14.6)	461 (26.4)	1514 (18.5)	427 (13.7)	389 (12.6)	2886 (17.2)
	15 to 16	0 (0.0)	16 (2.6)	92 (5.3)	288 (3.5)	67 (2.2)	32 (1.0)	495 (2.9)
Patient Population	Children Only	16 (100.0)	3 (42.9)	0 (0.0)	0 (0.0)	3 (3.4)	10 (83.3)	32 (18.4)
	Both Children and Adults	0 (0.0)	4 (57.1)	17 (100.0)	34 (100.0)	85 (96.6)	2 (16.7)	142 (81.6)
Site Location	Urban	0 (0.0)	7 (100.0)	16 (94.1)	9 (26.5)	32 (36.4)	3 (25.0)	67 (38.5)
	Mostly Urban	0 (0.0)	0 (0.0)	0 (0.0)	8 (23.5)	0 (0.0)	6 (50.0)	14 (8.0)
	Mostly Rural	0 (0.0)	0 (0.0)	0 (0.0)	12 (35.3)	0 (0.0)	0 (0.0)	12 (6.9)
	Rural	0 (0.0)	0 (0.0)	0 (0.0)	5 (14.7)	51 (58.0)	0 (0.0)	56 (32.2)
	Unknown	16 (100.0)	0 (0.0)	1 (5.9)	0 (0.0)	5 (5.7)	3 (25.0)	25 (14.4)

Type of Facility	Public	15 (93.8)	6 (85.7)	16 (94.1)	31 (91.2)	83 (94.3)	11 (91.7)	162 (93.1)
	Private	1 (6.3)	1 (14.3)	1 (5.9)	3 (8.8)	5 (5.7)	1 (8.3)	12 (6.9)
Level of Facility	Primary	2 (12.5)	0 (0.0)	0 (0.0)	13 (38.2)	54 (61.4)	1 (8.3)	70 (40.2)
	Secondary	0 (0.0)	0 (0.0)	0 (0.0)	16 (47.1)	25 (28.4)	2 (16.7)	43 (24.7)
	Tertiary	14 (87.5)	7 (100.0)	17 (100.0)	5 (14.7)	9 (10.2)	7 (58.3)	59 (33.9)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)	2 (1.1)
Academic Affiliation	No	4 (25.0)	0 (0.0)	14 (82.4)	22 (64.7)	77 (87.5)	4 (33.3)	121 (69.5)
	Yes	12 (75.0)	7 (100.0)	3 (17.6)	12 (35.3)	10 (11.4)	8 (66.7)	52 (29.9)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.6)
Pediatrician on Site	Available every day clinic open	15 (93.8)	7 (100.0)	6 (35.3)	2 (5.9)	5 (5.7)	10 (83.3)	45 (25.9)
	Available some days	1 (6.3)	0 (0.0)	4 (23.5)	12 (35.3)	7 (8.0)	1 (8.3)	25 (14.4)
	Not available	0 (0.0)	0 (0.0)	7 (41.2)	20 (58.8)	76 (86.4)	1 (8.3)	104 (59.8)

*Findings other than “Pediatric and Adolescents in Care” are listed as n(%)

Site-specific characteristics

Most sites (60%) reported that pediatricians were not available, although this varied significantly by region. A majority of sites within the Asia Pacific, CCASAnet, and West Africa regions had a pediatrician either available all days or some days, while most sites in the East and Southern Africa regions (which had the largest pediatric patient populations) reported that a pediatrician was not available on any day.

Out of the nine essential services, we found that sites were most likely to offer ART access (99% of sites), co-trimoxazole prophylaxis (97%), comprehensive PMTCT services (96%), outreach services for patient follow-up (95%), tuberculosis screening (87%), and immunization services (72%) (Table 2). During this time period, providing either or both CD4 cell count and viral load testing was considered an essential service, and 88% of sites report CD4 cell count testing and 69% reported viral load testing. Sites were less likely to report offering nutrition counseling or food support (56%), and HIV counseling and testing (40%). The median comprehensive care score was 7 (interquartile range [IQR], 6-7). Among the 174 sites, 18 sites (10%) offered a “low” level of services, 103 sites (59%) offered a “medium” level of services, and 53 (31%) offered a

“high” level of services. Sites offering a “high” level of services were more likely to be in the Asia-Pacific (56% of sites in the region), CCASAnet (43%), or East Africa (44%) regions, with the Central Africa (29%) and West Africa (25%) regions having lower proportions of sites reporting a “high” level of services.

Table 2. Site Capacity and Comprehensiveness of Services Score by IeDEA Region (n=174 sites)*

WHO Essential Services		Asia-Pacific (n=16)	CCASAnet (n=7)	Central Africa (n=17)	East Africa (n=34)	Southern Africa (n=88)	West Africa (n=12)	Total (n=174)
ART Access with Counseling		16 (100.0)	6 (85.7)	17 (100.0)	34 (100.0)	88 (100.0)	12 (100.0)	173 (99.4)
Nutrition		12 (75.0)	4 (57.1)	4 (23.5)	25 (73.5)	45 (51.1)	7 (58.3)	97 (55.7)
PMTCT		13 (81.3)	7 (100.0)	17 (100.0)	34 (100.0)	87 (98.9)	9 (75.0)	167 (96.0)
CD4 Testing and/or Viral Load Testing	CD4	15 (93.8)	5 (71.4)	13 (81.3)	19 (65.5)	62 (96.9)	12 (100.0)	126 (87.5)
	Viral Load	11 (68.8)	4 (57.1)	12 (75.0)	26 (89.7)	37 (57.8)	9 (75.0)	99 (68.8)
TB screening		16 (100.0)	7 (100.0)	12 (70.6)	32 (94.1)	77 (87.5)	7 (58.3)	151 (86.8)
HIV counseling and testing		11 (68.8)	6 (85.7)	4 (23.5)	16 (47.1)	26 (29.5)	6 (50.0)	69 (39.7)
Co-trimoxazole		16 (100.0)	7 (100.0)	17 (100.0)	31 (91.2)	85 (96.6)	12 (100.0)	168 (96.6)
Immunizations		13 (81.3)	7 (100.0)	12 (70.6)	24 (70.6)	65 (73.9)	5 (41.7)	126 (72.4)
Outreach		14 (87.5)	4 (57.1)	15 (88.2)	34 (100.0)	88 (100.0)	11 (91.7)	166 (95.4)
Comprehensiveness Score	Low (0-5)	0 (0.0)	0 (0.0)	5 (29.4)	2 (5.9)	8 (9.1)	3 (25.0)	18 (10.3)
	Medium (6-7)	7 (43.8)	4 (57.1)	10 (58.8)	17 (50.0)	58 (65.9)	7 (58.3)	103 (59.2)
	High (8-9)	9 (56.3)	3 (42.9)	2 (11.8)	15 (44.1)	22 (25.0)	2 (16.7)	53 (30.5)

*Findings are listed as n(%)

Thirty sites providing pediatric care responded to both the 2009 and 2014-2015 assessments. The mean comprehensiveness of services score increased significantly from 5.6 (standard deviation [SD], 1.4) in 2009 to 7.3 (SD, 1.4) in 2014 ($p<0.001$) (Table 3). A greater proportion of sites

reported offering services in the 2014 survey compared to the 2009 survey for each of the nine essential services except for CD4 cell count testing and immunization; 80% of sites reported CD4 cell count testing in 2009 and only 60% reported testing in 2014. Similarly, 80% of sites in 2009 reported offering immunization services, but only 70% of these same sites reported offered immunizations in 2014. From 2009 to 2014, we found that the largest increases were for nutrition services (13% to 80%), viral load testing (7% to 83%), HIV counseling and testing (13% to 43%), and outreach (70% to 100%).

Table 3. Changes in Site Capacity and Comprehensiveness of Services from 2009 to 2014 (n=30)

		Site Assessment 1.0 (2009)	Site Assessment 2.0 (2014)
Comprehensiveness score	Mean ± Standard Deviation	5.571 ± 1.372	7.333 ± 1.373*
ART Access with Counseling	N (%)	24 (80.0)	30 (100.0)
Nutrition		4 (13.3)	24 (80.0)
PMTCT		26 (86.7)	30 (100.0)
CD4 Testing		24 (80.0)	18 (60.0)
Viral Load Testing		2 (6.7)	25 (83.3)
TB Screening		25 (83.3)	28 (93.3)
HIV Counseling and Testing		4 (13.3)	13 (43.3)
Co-trimoxazole		26 (86.7)	27 (90.0)
Immunizations		24 (80.0)	21 (70.0)
Outreach		21 (70.0)	30 (100.0)

*There was a statistically significant increase in the mean comprehensive care score from 2009 to 2014 among pediatric sites with at most 1 care item missing. Differences in mean comprehensiveness scores were tested by paired t-test.

Patient-level analyses

A total of 12,401 children at 35 sites in the East Africa region were included in the patient-level analysis, of which 192 (1%) were at clinics reporting a “low” level of services, 10,386 (84%) were at clinics reporting a “medium” level of services, and 1,823 (15%) were at clinics reporting a “high” level of services. The probability of loss to follow-up after ART initiation was highest in clinics with a “low” level of services and lowest in clinics with a “high” level of services (Figure 1). In multivariable Cox proportional hazard models, compared with children in care at clinics providing a “low” level of services, children in care at clinics providing “medium” and

“high” levels of services had hazard ratios of loss to follow-up of 0.58 (95% CI: 0.47, 0.72) and 0.12 (95% CI: 0.07, 0.23), respectively, adjusting for age at ART start, immunologic status, WHO clinical stage at enrollment, and clinic location. Results from models using imputation of missing covariate data were not substantially different from what is presented here.

DISCUSSION

With only 54% of children with HIV on treatment globally in 2021 and 40% of children with HIV virally suppressed,⁽¹⁾ it is essential that we understand the capacity of global HIV care and treatment sites to provide comprehensive care to children. In this evaluation of a broad range of global care sites providing services to children with HIV, we noted significant improvement in the sites’ provision of essential HIV care and prevention services for children and pregnant people between assessments done in 2009 and 2014. Access to ART and provision of PMTCT services increased substantially – providing the necessary backdrop to achieving an AIDS-free generation through both prevention and treatment. Moreover, there was a dramatic scale-up in access to routine viral load monitoring (from 6.7% to 83.3%), reflecting success in policy shifts to improve access to viral load monitoring and supporting the global efforts to achieve viral suppression. As routine viral load monitoring increased, these data already showed a parallel drop in CD4 cell count testing services by 2014.

Even though the comprehensiveness of essential pediatric HIV services grew substantially in the five years between the assessments, we can still see critical gaps in access to broader services for children and adolescents. While services such as providing nutrition support and counseling for HIV testing generally increased, these services remained absent from many sites. Perhaps even more concerning from a child health perspective, particularly in the face of the ongoing COVID-19 pandemic, fewer sites reported offering immunizations in the 2014 survey. Addressing potential gaps in access to immunizations for children and adolescents at risk of immune-compromise merits close attention. There is a defined need to catch up on the delayed childhood immunizations missed for 23 million children worldwide related to the COVID-19 pandemic.⁽¹⁸⁾ Moreover, many health systems might consider the potential for these care sites to bolster broader coverage of vaccinations for human papillomavirus to prevent cervical cancer, and to provide SARS-CoV-2 vaccination. The urgency in moving more pediatric care sites globally to provide the full range of essential services is also highlighted by the potential clinical impact. Our findings, from analyses performed in East Africa, one of our constituent regions, suggest that sites providing more comprehensive services also have more children with HIV retained in care, which may in turn result in less HIV-related disease and fewer adverse clinical outcomes. These sites may also be those with the most robust resources or sites where care is more accessible. Rather than pushing all sites to expand their range of services without attention to the available resources or access to care, attention must be given to expanding and sustaining the resources needed for providing comprehensive care.

There are several limitations to these data. The data were collected from September 2014 to January 2015 and may not represent the current state of HIV pediatric care. On the other hand, these data do highlight the trajectory of HIV care systems as global pediatric HIV treatment guidelines shift. Moreover, our observations fill a critical gap in the literature, given the lack of similar assessments of the trend and impact of changes in pediatric HIV care services across a

broad global geography. We also were able to disaggregate by age, allowing a more comprehensive assessment across the range of pediatric care, including for varying definitions of “child”, whether those less than 15 years or less than 16 years. While the impact of the comprehensiveness of services level was significant for patient-level care engagement outcome, et While we acknowledge the potential lack of generalizability of the East Africa observations to the IeDEA Network, particularly outside of African countries, we are less concerned about the same between IeDEA-affiliated sites and their ambient environment in their respective countries or other similar sites in Africa. For example, in other patient-level analyses from global IeDEA, the East Africa IeDEA cohort demographics have been representative of broader African settings, both within and outside of IeDEA.(19-22) Another concern arises due to shifts in the sites participating in the surveys between 2009 and 2014. Because of this shift, we did not have longitudinal data for all sites, in order to assess changes in the services provided over the 5-year period of the study. Nevertheless, a sufficient number of sites did have complete surveys on both occasions. The large number of these sites and the consistency of the longitudinal trends in (increasing) comprehensiveness of HIV-related services, provides a broad look at the state of the global pediatric HIV care in these regions during this period.

CONCLUSIONS

As global programs work to expand the availability and quality of pediatric HIV treatment and prevention services, understanding the capacity of global sites caring for this population to provide services for children and adolescents with HIV, can guide targets for improving care access and quality. This global survey of IeDEA cohort sites demonstrates significant gains in the comprehensiveness of HIV treatment and prevention services available for children between 2009 to 2014, while identifying important remaining gaps. Data from the East Africa region further suggest that sites providing a comprehensive array of HIV-related services experience higher retention in care among their clients, compared to sites offering lower levels of the essential services for HIV treatment and prevention. Achieving global treatment success for children and adolescents with HIV and eliminating mother-to-child transmission of HIV requires that we continue to prioritize strengthening the healthcare systems available for these populations with HIV worldwide.

Competing interests

The authors declare that they have no competing interests.

Authors’ Contributions

RCV, CTY, CWW, and KWK designed and provided scientific oversight for the study. Material preparation and data collection were performed by NKNY, CWW, AE, MD, VL, PL, RS, CT, CBM, OOT, and MS. CTY led data analysis in collaboration with SO and SB. The first draft of the manuscript was written by RCV. All authors reviewed and contributed to subsequent versions. All authors read and approved the final manuscript.

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Data Availability

The data that support the findings of this study are available on request from the corresponding author. All data requests must be approved by IeDEA.

Ethical Approval

The patient-related data presented here are based on retrospective deidentified information collected on a routine basis in sites participating in the IeDEA consortium. These data were approved for use by the local institutional review boards in each of the IeDEA countries included in the analysis and consent requirements were deferred to the local institutional review boards. All sites and IeDEA regional coordinating centres also had Institutional Review Board approvals in place permitting the collection of site-level data for the survey.

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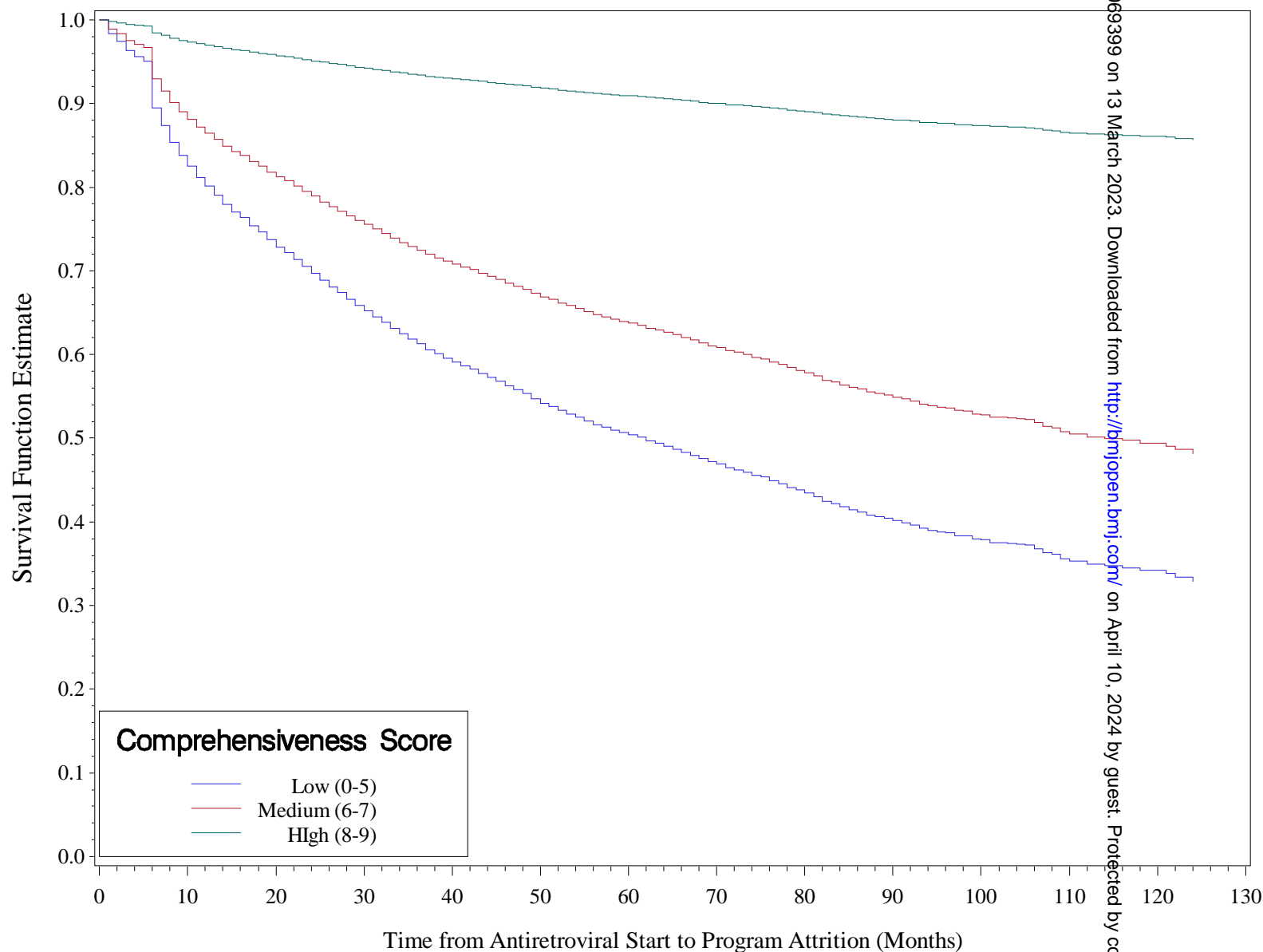
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Figure 1. Kaplan-Meier Plots of Time from Antiretroviral Therapy Initiation to Loss to Follow-up by Site-Level Comprehensive Services Score among 12,401 Children in East Africa IeDEA Enrolled in Care from 2001 to 2014.



Reporting checklist for quality improvement in health care.

Based on the SQUIRE guidelines.

*Note from the authors: The SQUIRE guidelines/checklist does not perfectly align with our manuscript, but we selected it since it focuses on health service evaluation. This was not an evaluation of a specific intervention and therefore the reporting items do not always apply. We felt this checklist was the most appropriate for our objectives.

	Reporting Item	Page Number
Title	#1 Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	Pg 1 (this manuscript does not seek to improve an initiative, but to understand the current landscape of pediatric health services)
Abstract	#02a Provide adequate information to aid in searching and indexing	Pg. 2
	#02b Summarize all key information from various sections of the text using the abstract format	Pg. 2

of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions

Introduction

Problem description	#3	Nature and significance of the local problem	Pg. 3
Available knowledge	#4	Summary of what is currently known about the problem, including relevant previous studies	Pg. 3
Rationale	#5	Informal or formal frameworks, models, concepts, and / or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	Pg. 3 (does not look at a specific intervention, but did provide rationale for the assessment)
Specific aims	#6	Purpose of the project and of this report	Pg. 3
Methods			
Context	#7	Contextual elements considered important at the outset of introducing the intervention(s)	Pg. 4 (since no intervention, context is given to how the assessment was developed)

Intervention(s)	#08a	Description of the intervention(s) in sufficient detail that others could reproduce it	Pg. 4 (since no intervention, context is given to how the assessment was developed)
Intervention(s)	#08b	Specifics of the team involved in the work	Pg. 4
Study of the Intervention(s)	#09a	Approach chosen for assessing the impact of the intervention(s)	Pg. 4-5
Study of the Intervention(s)	#09b	Approach used to establish whether the observed outcomes were due to the intervention(s)	N/A (no intervention was evaluated)
Measures	#10a	Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	Pg. 4-5
Measures	#10b	Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	Pg. 4-5
Measures	#10c	Methods employed for assessing completeness and accuracy of data	Pg. 5
Analysis	#11a	Qualitative and quantitative methods used to draw inferences from the data	Pg. 5

Analysis	#11b	Methods for understanding variation within the data, including the effects of time as a variable	Pg. 5
Ethical considerations	#12	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	Pg. 5
Results	#13a	Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project	N/A (there was no intervention, but does describe when the survey was conducted)
	#13b	Details of the process measures and outcome	Pgs 7-10
	#13c	Contextual elements that interacted with the intervention(s)	
	#13d	Observed associations between outcomes, interventions, and relevant contextual elements	Pg. 9
	#13e	Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	N/A (no intervention)

	#13f	Details about missing data	Pg. 7
Discussion			
Summary	#14a	Key findings, including relevance to the rationale and specific aims	Pg. 10
Summary	#14b	Particular strengths of the project	Pg. 10
Interpretation	#15a	Nature of the association between the intervention(s) and the outcomes	Pg. 10 (described the association between comprehensive score and patient-level outcome)
Interpretation	#15b	Comparison of results with findings from other publications	Pg. 11 (limited similar assessments to compare)
Interpretation	#15c	Impact of the project on people and systems	Pg. 10
Interpretation	#15d	Reasons for any differences between observed and anticipated outcomes, including the influence of context	Pg. 10
Interpretation	#15e	Costs and strategic trade-offs, including opportunity costs	Pg. 10-11
Limitations	#16a	Limits to the generalizability of the work	Pg. 10-11
Limitations	#16b	Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis	Pg. 11

1	Limitations	#16c	Efforts made to minimize and adjust for	Pg. 11
2			limitations	
3				
4				
5				
6	Conclusion	#17a	Usefulness of the work	Pg. 11
7				
8				
9	Conclusion	#17b	Sustainability	N/A
10				
11				
12	Conclusion	#17c	Potential for spread to other contexts	Pg. 11
13				
14				
15	Conclusion	#17d	Implications for practice and for further	Pg. 11
16			study in the field	
17				
18				
19	Conclusion	#17e	Suggested next steps	Pg. 11
20				
21				
22	Other			
23	information			
24				
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28				
29	Funding	#18	Sources of funding that supported this work.	Pg. 12
30			Role, if any, of the funding organization in	
31			the design, implementation, interpretation,	
32			and reporting	
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None The SQUIRE 2.0 checklist is distributed under the terms of the Creative Commons Attribution License CC BY-NC 4.0. This checklist can be completed online using <https://www.goodreports.org/>, a tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)

BMJ Open

Survey Evaluating Global HIV Prevention, Care, and Treatment Services for Children Links Comprehensiveness to Retention in Care among International Epidemiology Databases to Evaluate AIDS (IeDEA) Consortium

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Title: Survey Evaluating Global HIV Prevention, Care, and Treatment Services for Children Links Comprehensiveness to Retention in Care among International Epidemiology Databases to Evaluate AIDS (IeDEA) Consortium

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ABSTRACT

Objectives: To assess access children with HIV have to comprehensive HIV care services, to longitudinally evaluate the implementation and scale-up of services, and to use site services and clinical cohort data to explore whether access to these services influences retention in care.

Methods: A cross-sectional standardized survey was completed in 2014-2015 by sites providing pediatric HIV care across regions of the International epidemiology Databases to Evaluate AIDS (IeDEA) consortium. We developed a comprehensiveness score based on the World Health Organization (WHO)'s nine categories of essential services to categorize sites as "low" (0-5), "medium" (6-7), or "high" (8-9). When available, comprehensiveness scores were compared with scores from a 2009 survey. We used patient-level data with site services to investigate the relationship between the comprehensiveness of services and retention.

Results: Survey data from 174 IeDEA sites in 32 countries were analyzed. Of the WHO essential services, sites were most likely to offer antiretroviral therapy (ART) provision and counseling (n=173; 99%), co-trimoxazole prophylaxis (168; 97%), prevention of perinatal transmission services (167; 96%), outreach for patient engagement and follow-up (166; 95%), CD4 cell count testing (126; 88%), tuberculosis screening (151; 87%), and select immunization services (126; 72%). Sites were less likely to offer nutrition/food support (97; 56%), viral load testing (99; 69%), and HIV counseling and testing (69; 40%). 10% of sites rated "low," 59% "medium," and 31% "high" in the comprehensiveness score. The mean comprehensiveness of services score increased significantly from 5.6 in 2009 to 7.3 in 2014 ($p<0.001$; $n=30$). Patient level analysis of loss to follow-up after ART initiation estimated the hazard was highest in sites rated "low" and lowest in sites rated "high".

Conclusion: This global assessment suggests the potential care impact of scaling-up and sustaining comprehensive pediatric HIV services. Meeting recommendations for comprehensive HIV services should remain a global priority.

STRENGTHS AND LIMITATIONS:

- This study fills a critical gap in the literature, given the lack of similar assessments of the trend and impact of changes in pediatric HIV care services across a broad global geography.
- This study provides a comprehensive assessment across the range of actual pediatric HIV care practice globally.
- A comparison of site-level assessments and patient-level data reveals the clinical impact of a lack of comprehensive services for children living with HIV.
- The data for this study were collected from September 2014 to January 2015 and may not represent the current state of HIV pediatric care; however, these are still some of the only data on this topic available.
- Limitations in the available patient-level data meant that certain analyses were only done for the East Africa region.

MANUSCRIPT

INTRODUCTION

In 2020, there were an estimated 1.7 million children with HIV between the ages of 0-15 years.(1) New infections among children declined by 53% from 2010 to 2020, with most new infections occurring in African countries. Access to combination antiretroviral therapy (ART), however, remains an important challenge for this population. In 2020, only 54% of children with HIV globally were accessing ART, which is substantially lower than the percentage of adults with HIV accessing ART (74%).(1) Barriers to scale-up of pediatric treatment include inadequate access to early infant diagnosis, lack of provider experience in delivering pediatric care, limited availability of pediatric antiretroviral formulations, and weak health care infrastructure, but there are few data on the extent to which these specific pediatric HIV services are available globally.(2-5) For children with HIV who are in care, losses to follow-up from care and deaths while in care appear to remain high, though these rates are difficult to accurately report.(6, 7) It is important to document the capacity of HIV care and treatment programs to deliver comprehensive, integrated HIV prevention, care, and treatment services to children across multiple regions in order to identify gaps in services and target resources appropriately.(8-12)

Data on clinical capacity and services are also needed to ensure that pediatric services continue to improve their quality and comprehensiveness, in line with global guidelines for the care of children living with and exposed to HIV. An assessment of global pediatric HIV care capacity at sites of the International Epidemiology Databases Evaluating AIDS (IeDEA) consortium from 2009 revealed that only 38% of sites had capacity for routine viral load monitoring, and that 89% had direct access to infant HIV DNA PCR testing.(13) Over time, the World Health Organization (WHO) has continued to revise its guidelines for the care of children with HIV, including initiation of ART for all children under 5 years of age, initiation of ART for all children >5 years of age with a CD4 cell count <500 cells/μl, routine viral load monitoring for all patients,(14) and then the expansion to recommend treatment of all children and adults with HIV with lifelong ART regardless of immunologic status.(15) The ultimate goal of these guidelines is to improve pediatric morbidity and mortality related to HIV through expanded prevention, treatment, and monitoring services.

Examining whether and how the availability of more comprehensive HIV prevention and treatment services improve patient-level pediatric outcomes are important steps in ensuring that global care services ultimately improve the care of children. Here, we draw on site-level survey assessments administered to a consortium of HIV care programs worldwide to assess the extent to which children with HIV have access to comprehensive HIV care services, to evaluate the implementation and scale-up of these services over time, and to compare these survey findings with clinical cohort data to explore whether access to these services influences the retention in care of children with HIV.

METHODS

Population

The IeDEA research consortium was established in 2005 with support from the U.S. National

Institute for Allergy and Infectious Diseases to develop a global resource of clinical data from people with HIV (www.iedea.org). IeDEA collects data from seven international regional data centers: the Asia-Pacific, CCASAnet (encompassing the Caribbean Central and South America), Central Africa, East Africa, NA-ACCORD (encompassing Canada and the U.S.), Southern Africa, and West Africa. Each IeDEA region collaborates with clinical sites to define key variables and harmonize large datasets to address research questions around the impact of the global ART rollout on HIV-related clinical services and outcomes. Pediatric clinical and ART resources across the Africa and Asia-based HIV care sites were previously evaluated in 2009.(13)

Study design and data collection

We surveyed the IeDEA sites that provide HIV treatment and prevention services to children, in any configuration of stand-alone pediatric services or combined care for children and adults. The standardized site assessment tool was adapted from the site assessment survey done in 2009.(13) Study data were collected and managed using a web-based survey on the REDCap (Research Electronic Data Capture) platform (www.project-redcap.org) hosted at the Vanderbilt Institute for Global Health at Vanderbilt University. Site clinical directors or managers were asked to complete the survey, providing information about the sites' physical and clinical characteristics and capacity to deliver WHO-recommended pediatric HIV prevention, care, and treatment services. In 2009, 26 sites in Asia Pacific, 16 sites in Central Africa, 52 sites in East Africa, 19 sites in Southern Africa, and 21 sites in Western Africa were surveyed (N=143). In 2014, an additional 31 sites were surveyed (see Table 1 for regional breakdown.) Between 2009 and 2014, 30 sites both 1) provided care for children and/or adolescents with HIV and 2) had consistent site IDs between 2009 and 2014, and therefore these sites' survey findings were used to compare care services.

We created a measure of comprehensiveness of pediatric care services based on the WHO's nine categories of essential services: 1) ART access with psychosocial and adherence counseling; 2) nutrition or food support or counseling; 3) prevention of perinatal transmission (PMTCT) services, including medication; 4) CD4 cell count and HIV viral load testing; 5) tuberculosis screening; 6) counseling and testing for HIV, 7) co-trimoxazole prophylaxis, 8) immunization access for select vaccine-preventable diseases (hepatitis B, pneumococcal, influenza vaccine, or yellow fever vaccines); and 9) outreach for patient engagement and follow-up.(16) In calculating the comprehensiveness score, one point was awarded for each service adequately provided by the site, with a total score range between 0 (no services offered) and 9 (all services offered). Sites were then categorized into "low" (0-5), "medium" (6-7), or "high" (8-9) service levels, as was done in prior global site assessment evaluations, from similar site assessment surveys done in 2009.(13)

In order to investigate the relationship between the comprehensiveness of available services and retention in care, patient-level data were also extracted from the IeDEA global cohort database. Patient inclusion criteria were: (1) documented HIV infection; (2) age <16 years of age at enrollment; (3) enrolled into care in 2001 or later at least 6 months prior to site-specific database closure; and (4) either enrolled at a site which completed the 2009 survey or enrolled within six months of the 2014 site assessment survey. Due to high amount of missing data for items from

site surveys, only patients seen at sites with missing data for at most 1 item (n=62 sites) were included in the analysis (n=28,378). The sample was further restricted by including only patients enrolled within six months of the 2014 survey if they were affiliated with sites only completing that round of surveys (n=18,487). Since the resulting de-identified patient-level dataset was overwhelmingly from East Africa (n=17,596 (95.2%)) and less than 5% of the sample consisted of patients from the IeDEA regions of Asia-Pacific, CCASAnet, Central Africa, and West Africa, we selected only sites in East Africa (52 sites) for the patient-level analyses. Then, the dataset was further restricted to patients with non-missing ART start dates (n=12,401 in 35 centers.) See Figure 1.

Statistical analysis

Data were analyzed using SAS (SAS Institute Inc., Cary, NC, U.S.). Descriptive analyses of the 2014 survey were performed, with site characteristics stratified by region. We were able to link data for 30 clinics which responded to both the 2009 and 2014 IeDEA site assessments surveys and analyzed differences in the mean comprehensive of services scores by using paired t-tests.

The analyzed patient-level outcome of interest was time from ART start to loss to program due to either death, transfer, or loss to follow up. Loss to follow-up was defined as no record of death or transfer and no visit between the date of the last clinic visit attended and six months or more of database closure. This was a competing risk model with the two competing events being death and loss to follow-up and being transferred coded as censored. Bivariate Cox proportional hazard models were used to assess the association between comprehensive care category (obtained from the 2014 or earlier 2009 surveys) and loss to program. A multivariable Cox proportional hazards model which included clinically important patient-level variables – age at ART start (categorical, 0 to <5 years, 5 to <10, 10 to <15, 15 to 16); categorical immune status at ART start as defined by the WHO, based on age and CD4 cell count or percentage depending on age, WHO clinical stage at enrollment, and clinic location (urban, mostly urban, mostly rural or rural) – was used to investigate the relationship between level of comprehensiveness of services (low, medium, high) and patient retention in care. Hazards ratios and 95% confidence intervals (CI) were reported. As a sensitivity analysis, the model was refit using data obtained from multiple imputation for missing values for CD4 percentage (24.0%), WHO clinical stage (13.8%), and age at ART start (0.1%) using the Markov Chain Monte Carlo (MCMC) method.(17)

Patient and Public Involvement

Patients or the public were not involved in the design or conduct of our research. In the East Africa region, briefings on the findings were done in clinics to patients, including both study participants and non-participants.

RESULTS

All 536 sites providing HIV care in the IeDEA global regions received the survey, and 287 (53.5%) sites completed the survey between September 2014 and January 2015. Out of those 287 sites, 174 (61%) provided pediatric care. Site characteristics by IeDEA region are shown in

Table 1. Overall, most sites providing pediatric HIV care (82%) saw both children and adult patients, including almost 17,000 children with HIV. The majority of the sites were in African countries, with 88 sites (51%) from Southern Africa, 34 sites (20%) from East Africa, 17 sites (10%) from Central Africa, 16 sites (9%) from the Asia-Pacific, 12 sites (7%) from West Africa, and 7 sites (4%) from CCASAnet. Most of the care sites were located in urban (39%) or mostly urban (8%) settings, and almost all were public facilities (93%). Overall, the HIV care sites were well distributed across different levels of health care services; 40% were primary care sites, 25% were secondary care sites, and 34% were tertiary care sites. However, the participating sites from the Asia-Pacific, CCASAnet, and Central Africa regions were almost exclusively tertiary facilities.

Table 1. 2014 Survey Site Characteristics by International Epidemiology Databases to Evaluate AIDS (IeDEA) Region (n=174 sites)*

		Asia-Pacific (n=16)	CCASAnet (n=7)	Central Africa (n=17)	East Africa (n=34)	Southern Africa (n=88)	West Africa (n=12)	Total (n=174)
Number of Pediatric and Adolescents in Care, 2014		70 (2 sites)	611 (7 sites)	1748 (13 sites)	8165 (33 sites)	3113 (12 sites)	3076 (10 sites)	16783 (77 sites)
Age at Enrollment for Patients in Care in 2014	0 to <5	47 (67.1)	356 (58.3)	567 (32.4)	3519 (43.1)	1934 (62.1)	1666 (54.2)	8089 (48.2)
	5 to <10	17 (24.3)	150 (24.5)	628 (35.9)	2844 (34.8)	685 (22.0)	989 (32.2)	5313 (31.7)
	10 to <15	6 (8.6)	89 (14.6)	461 (26.4)	1514 (18.5)	427 (13.7)	389 (12.6)	2886 (17.2)
	15 to 16	0 (0.0)	16 (2.6)	92 (5.3)	288 (3.5)	67 (2.2)	32 (1.0)	495 (2.9)
Patient Population	Children Only	16 (100.0)	3 (42.9)	0 (0.0)	0 (0.0)	3 (3.4)	10 (83.3)	32 (18.4)
	Both Children and Adults	0 (0.0)	4 (57.1)	17 (100.0)	34 (100.0)	85 (96.6)	2 (16.7)	142 (81.6)
Site Location	Urban (officially designated to be city with city administration and political bodies)	0 (0.0)	7 (100.0)	16 (94.1)	9 (26.5)	32 (36.4)	3 (25.0)	67 (38.5)

	Mostly Urban (big and small towns, peri-urban areas, growth points, mining communities)	0 (0.0)	0 (0.0)	0 (0.0)	8 (23.5)	0 (0.0)	6 (50.0)	14 (8.0)
	Mostly Rural (large and small scale commercial farming areas)	0 (0.0)	0 (0.0)	0 (0.0)	12 (35.3)	0 (0.0)	0 (0.0)	12 (6.9)
	Rural (subsistence farming areas)	0 (0.0)	0 (0.0)	0 (0.0)	5 (14.7)	51 (58.0)	0 (0.0)	56 (32.2)
	Other/Mixed urban-rural (e.g., small town, peri-urban area, growth points, mining community, etc.)	16 (100.0)	0 (0.0)	1 (5.9)	0 (0.0)	5 (5.7)	3 (25.0)	25 (14.4)
Type of Facility	Public	15 (93.8)	6 (85.7)	16 (94.1)	31 (91.2)	83 (94.3)	11 (91.7)	162 (93.1)
	Private	1 (6.3)	1 (14.3)	1 (5.9)	3 (8.8)	5 (5.7)	1 (8.3)	12 (6.9)
Level of Facility	Primary	2 (12.5)	0 (0.0)	0 (0.0)	13 (38.2)	54 (61.4)	1 (8.3)	70 (40.2)
	Secondary	0 (0.0)	0 (0.0)	0 (0.0)	16 (47.1)	25 (28.4)	2 (16.7)	43 (24.7)
	Tertiary	14 (87.5)	7 (100.0)	17 (100.0)	5 (14.7)	9 (10.2)	7 (58.3)	59 (33.9)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)	2 (1.1)
Academic Affiliation	No	4 (25.0)	0 (0.0)	14 (82.4)	22 (64.7)	77 (87.5)	4 (33.3)	121 (69.5)
	Yes	12 (75.0)	7 (100.0)	3 (17.6)	12 (35.3)	10 (11.4)	8 (66.7)	52 (29.9)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.6)
Pediatrician on Site	Available every day clinic open	15 (93.8)	7 (100.0)	6 (35.3)	2 (5.9)	5 (5.7)	10 (83.3)	45 (25.9)
	Available some days	1 (6.3)	0 (0.0)	4 (23.5)	12 (35.3)	7 (8.0)	1 (8.3)	25 (14.4)

Not available	0 (0.0)	0 (0.0)	7 (41.2)	20 (58.8)	76 (86.4)	1 (8.3)	104 (59.8)
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*Findings other than “Pediatric and Adolescents in Care” are listed as n(%)

Site-specific characteristics

Most sites (60%) reported that pediatricians were not available, although this varied significantly by region. A majority of sites within the Asia Pacific, CCASAnet, and West Africa regions had a pediatrician either available all days or some days, while most sites in the East and Southern Africa regions (which had the largest pediatric patient populations) reported that a pediatrician was not available on any day.

Out of the nine essential services, we found that sites were most likely to offer ART access (99% of sites), co-trimoxazole prophylaxis (97%), comprehensive PMTCT services (96%), outreach services for patient follow-up (95%), tuberculosis screening (87%), and immunization services (72%) (Table 2). During this time period, providing either or both CD4 cell count and viral load testing was considered an essential service, and 88% of sites report CD4 cell count testing and 69% reported viral load testing. Sites were less likely to report offering nutrition counseling or food support (56%), and HIV counseling and testing (40%). The median comprehensive care score was 7 (interquartile range [IQR], 6-7). Among the 174 sites, 18 sites (10%) offered a “low” level of services, 103 sites (59%) offered a “medium” level of services, and 53 (31%) offered a “high” level of services. These “high” levels of services or more comprehensive services were clustered at sites in Asia-Pacific (56% of sites in the region), CCASAnet (43%), and East Africa (44%).

Table 2. 2014 Survey Site Capacity and Comprehensiveness of Services Score by IeDEA Region (n=174 sites)*

WHO Essential Services		Asia-Pacific (n=16)	CCASAnet (n=7)	Central Africa (n=17)	East Africa (n=34)	Southern Africa (n=88)	West Africa (n=12)	Total (n=174)
ART Access with Counseling		16 (100.0)	6 (85.7)	17 (100.0)	34 (100.0)	88 (100.0)	12 (100.0)	173 (99.4)
Nutrition		12 (75.0)	4 (57.1)	4 (23.5)	25 (73.5)	45 (51.1)	7 (58.3)	97 (55.7)
PMTCT		13 (81.3)	7 (100.0)	17 (100.0)	34 (100.0)	87 (98.9)	9 (75.0)	167 (96.0)
CD4 Testing and/or Viral Load Testing	CD4	15 (93.8)	5 (71.4)	13 (81.3)	19 (65.5)	62 (96.9)	12 (100.0)	126 (87.5)
	Viral Load	11 (68.8)	4 (57.1)	12 (75.0)	26 (89.7)	37 (57.8)	9 (75.0)	99 (68.8)
TB screening		16 (100.0)	7 (100.0)	12 (70.6)	32 (94.1)	77 (87.5)	7 (58.3)	151 (86.8)

HIV counseling and testing		11 (68.8)	6 (85.7)	4 (23.5)	16 (47.1)	26 (29.5)	6 (50.0)	69 (39.7)
Co-trimoxazole		16 (100.0)	7 (100.0)	17 (100.0)	31 (91.2)	85 (96.6)	12 (100.0)	168 (96.6)
Immunizations		13 (81.3)	7 (100.0)	12 (70.6)	24 (70.6)	65 (73.9)	5 (41.7)	126 (72.4)
Outreach		14 (87.5)	4 (57.1)	15 (88.2)	34 (100.0)	88 (100.0)	11 (91.7)	166 (95.4)
Comprehensiveness Score	Low (0-5)	0 (0.0)	0 (0.0)	5 (29.4)	2 (5.9)	8 (9.1)	3 (25.0)	18 (10.3)
	Medium (6-7)	7 (43.8)	4 (57.1)	10 (58.8)	17 (50.0)	58 (65.9)	7 (58.3)	103 (59.2)
	High (8-9)	9 (56.3)	3 (42.9)	2 (11.8)	15 (44.1)	22 (25.0)	2 (16.7)	53 (30.5)

*Findings are listed as n(%)

From among pediatric care sites which responded to the 2009 survey (n=143) and 2014 survey (n=714), we were able to link data for 30 sites: East Africa (26 sites), Asia Pacific (3 sites) and Southern Africa (1 site). The mean comprehensiveness of services score increased significantly from 5.6 (standard deviation [SD], 1.4) in 2009 to 7.3 (SD, 1.4) in 2014 ($p<0.001$) (Table 3). A greater proportion of sites reported offering services in the 2014 survey compared to the 2009 survey for each of the nine essential services except for CD4 cell count testing and immunization; 80% of sites reported CD4 cell count testing in 2009 and only 60% reported testing in 2014. Similarly, 80% of sites in 2009 reported offering immunization services, but only 70% of these same sites reported offered immunizations in 2014. From 2009 to 2014, we found that the largest increases were for nutrition services (13% to 80%), viral load testing (7% to 83%), HIV counseling and testing (13% to 43%), and outreach (70% to 100%).

Table 3. Changes in Site Capacity and Comprehensiveness of Services from 2009 to 2014 (n=30)

		Site Assessment 1.0 (2009)	Site Assessment 2.0 (2014)
Comprehensiveness score	Mean ± Standard Deviation	5.571 ± 1.372	7.333 ± 1.373*
ART Access with Counseling	N (%)	24 (80.0)	30 (100.0)
Nutrition		4 (13.3)	24 (80.0)
PMTCT		26 (86.7)	30 (100.0)
CD4 Testing		24 (80.0)	18 (60.0)
Viral Load Testing		2 (6.7)	25 (83.3)

	Site Assessment 1.0 (2009)	Site Assessment 2.0 (2014)
TB Screening	25 (83.3)	28 (93.3)
HIV Counseling and Testing	4 (13.3)	13 (43.3)
Co-trimoxazole	26 (86.7)	27 (90.0)
Immunizations	24 (80.0)	21 (70.0)
Outreach	21 (70.0)	30 (100.0)

*There was a statistically significant increase in the mean comprehensive care score from 2009 to 2014 among pediatric sites with at most 1 care item missing. Differences in mean comprehensiveness scores were tested by paired t-test.

Patient-level analyses

A total of 12,401 children at 35 sites in the East Africa region were included in the patient-level analysis, of which 192 (1%) were at clinics reporting a “low” level of services, 10,386 (84%) were at clinics reporting a “medium” level of services, and 1,823 (15%) were at clinics reporting a “high” level of services. Care classification was based on either the 2014 or 2009 surveys. Mean age at enrollment was 5.9 years, with median age of 5 years and range from 0 to 16 years. The probability of loss to follow-up after ART initiation was highest in clinics with a “low” level of services and lowest in clinics with a “high” level of services (Figure 2). Hazard ratios from bivariate and multiple regression Cox proportional hazard models are presented in Table 4. In multivariable Cox proportional hazard models, compared with children in care at clinics providing a “low” level of services, children in care at clinics providing “medium” and “high” levels of services had hazard ratios of loss to follow-up of 0.58 (95% CI: 0.47, 0.72) and 0.12 (95% CI: 0.07, 0.23), respectively, adjusting for age at ART start, gender, immunologic status, WHO clinical stage at enrollment, and clinic location. Results from models using imputation of missing covariate data were not substantially different from what is presented here.

Table 4 Hazard Ratios from Cox Proportional Hazard Models of Time to Loss to Program

		Bivariate Models				Multiple Regression			
	Level	Hazard Ratio	95% Confidence Interval	Overall Test	p-value	Hazard Ratio	95% Confidence Interval	Overall Test	p-value
Age at ART start	0-<1	1.715	(1.460,2.015)	<.0001	<.0001	2.298	(1.530,3.552)	<.0001	<.0001
	1-<2	1.388	(1.236,1.559)			1.413	(1.139,1.753)		
	2-<5	reference				reference			
	5-<7	0.906	(0.820,1.002)			1.042	(0.907,1.197)		
	7-<10	0.857	(0.780,0.941)			0.989	(0.866,1.130)		
	10-<13	0.941	(0.851,1.040)			1.064	(0.926,1.222)		
	13-<16	1.186	(1.067,1.318)			1.309	(1.132,1.514)		
	16-<23	1.495	(1.258,1.777)			1.716	(1.400,2.103)		
Comprehensive Care Score	(4-5)	reference		<.0001	<.0001	reference		<.0001	<.0001
	(6-7)	0.657	(0.562,0.768)			0.584	(0.472,0.722)		
	(8-9)	0.139	(0.084,0.230)			0.124	(0.066,0.233)		
Gender	Female	1.026	(0.966,1.089)	0.4056	0.4056	1.022	(0.949,1.100)	0.5679	0.5679
	Male	reference				reference			
Immune Status	Not Significant	reference		<.0001	<.0001	reference		<.0001	<.0001
	Advanced immunosuppression	1.026	(0.899,1.172)			0.943	(0.818,1.086)		
	Mild immunosuppression	0.915	(0.781,1.072)			0.901	(0.763,1.064)		
	Severe immunosuppression	1.227	(1.104,1.365)			1.141	(1.019,1.278)		
Facility Location	Mostly rural	0.663	(0.607,0.724)	<.0001	<.0001	0.721	(0.636,0.816)	<.0001	<.0001
	Mostly urban	0.571	(0.524,0.623)			0.575	(0.508,0.650)		

		Bivariate Models				Multiple Regression			
	Level	Hazard Ratio	95% Confidence Interval	Overall Test	p-value	Hazard Ratio	95% Confidence Interval	Overall Test	p-value
WHO/CDC stage at ART start	Rural	0.480	(0.411,0.560)		<.0001	0.440	(0.354,0.546)		<.0001
	Urban	reference				reference			
	1	reference				reference			
	2	1.104	(1.035,1.177)	0.0025	0.0025	1.095	(1.014,1.182)	0.0200	0.0200

DISCUSSION

With only 54% of children with HIV on treatment globally in 2021 and 40% of children with HIV virally suppressed,(1) it is essential that we understand the capacity of global HIV care and treatment sites to provide comprehensive care to children. In this evaluation of a broad range of global care sites providing services to children with HIV, we noted significant improvement in the sites’ provision of essential HIV care and prevention services for children and pregnant people between assessments done in 2009 and 2014. Access to ART and provision of PMTCT services increased substantially in the 30 sites with both assessments– providing the necessary backdrop to achieving an AIDS-free generation through both prevention and treatment. Moreover, there was a dramatic scale-up in access to routine viral load monitoring (from 6.7% to 83.3%), reflecting success in policy shifts to improve access to viral load monitoring and supporting the global efforts to achieve viral suppression. As routine viral load monitoring increased, these data already showed a parallel drop in CD4 cell count testing services by 2014.

Even though the comprehensiveness of essential pediatric HIV services grew substantially in the five years between the assessments, we can still see critical gaps in access to broader services for children and adolescents. While services such as providing nutrition support and counseling for HIV testing generally increased, these services remained absent from many sites. Perhaps even more concerning from a child health perspective, particularly in the face of the ongoing COVID-19 pandemic, fewer sites reported offering immunizations in the 2014 survey. Addressing potential gaps in access to immunizations for children and adolescents at risk of immune-compromise merits close attention. There is a defined need to catch up on the delayed childhood immunizations missed for 23 million children worldwide related to the COVID-19 pandemic.(18) Moreover, many health systems might consider the potential for these care sites to bolster broader coverage of vaccinations for human papillomavirus to prevent cervical cancer, and to provide SARS-CoV-2 vaccination. The urgency in moving more pediatric care sites globally to provide the full range of essential services is also highlighted by the potential clinical impact. Our findings, from analyses performed in East Africa, one of our constituent regions, suggest that sites providing more comprehensive services also have more children with HIV retained in care, which may in turn result in less HIV-related disease and fewer adverse clinical outcomes. These sites may also be those with the most robust resources or sites where care is more accessible. In considering how to expand the range of services available in a health system, attention must also be given to what specific resources are already available to adapt to care expansion and how access to even more basic levels of care might be improved.

There are several limitations to these data. The data were collected from September 2014 to January 2015 and may not represent the current state of HIV pediatric care. On the other hand, these data do highlight the trajectory of HIV care systems as global pediatric HIV treatment guidelines shift. Moreover, our observations fill a critical gap in the literature, given the lack of similar assessments of the trend and impact of changes in pediatric HIV care services across a broad global geography. We are able to show the age distribution by region (table 1), allowing a the comprehensive assessment of services to be compared across the range of pediatric care, including for varying definitions of “child”, whether those less than 15 years or less than 16 years. While we acknowledge the potential lack of generalizability of the East Africa observations to the IeDEA Network, particularly outside of African countries, we are less

concerned about the same between IeDEA-affiliated sites and their ambient environment in their respective countries or other similar sites in Africa. For example, in other patient-level analyses from global IeDEA, the East Africa IeDEA cohort demographics have been representative of broader African settings, both within and outside of IeDEA.⁽¹⁹⁻²²⁾ Another concern arises due to shifts in the sites participating in the surveys between 2009 and 2014. Because of this shift, we did not have longitudinal data for all sites, in order to assess changes in the services provided over the 5-year period of the study. Nevertheless, a sufficient number of sites did have complete surveys on both occasions. Moreover, the estimation that only 53% of sites completed the survey is a conservatively low estimate because some of the sites changed their consortium identifiers in the course of the follow-up, making it impossible to pair their data conclusively. Despite the fact that the longitudinal data were only available for 17% of the sites surveyed in 2014, this is still some of the only data on this topic available within these years. The large number of these sites and the consistency of the longitudinal trends in (increasing) comprehensiveness of HIV-related services, provides a broad look at the state of the global pediatric HIV care in these regions during this period.

CONCLUSIONS

As global programs work to expand the availability and quality of pediatric HIV treatment and prevention services, understanding the capacity of global sites caring for this population to provide services for children and adolescents with HIV can guide targets for improving care access and quality. This global survey of IeDEA cohort sites demonstrates significant gains in the comprehensiveness of HIV treatment and prevention services available for children between 2009 to 2014, while identifying important remaining gaps. Data from the East Africa region further suggest that sites providing a comprehensive array of HIV-related services experience higher retention in care among their clients, compared to sites offering lower levels of the essential services for HIV treatment and prevention. Achieving global treatment success for children and adolescents with HIV and eliminating perinatal transmission of HIV requires that we continue to prioritize strengthening the healthcare systems available for these populations with HIV worldwide.

Competing interests

The authors declare that they have no competing interests.

Authors' Contributions

RCV, CTY, CWW, and KWK designed and provided scientific oversight for the study. Material preparation and data collection were performed by NKNY, CWW, AE, MD, VL, PL, RS, CT, CBM, OOT, and MS. CTY led data analysis in collaboration with SO and SB. The first draft of the manuscript was written by RCV. NKNY, CWW, AE, MD, VL, PL, RS, CT, CBM, OOT, MS, CTY, KWK, SO, SB, RM, and RCV reviewed and contributed to subsequent versions. All authors read and approved the final manuscript.

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Data Availability

The data that support the findings of this study are available on request from the corresponding author. All data requests must be approved by IeDEA.

Ethical Approval

The patient-related data presented here are based on retrospective deidentified information collected on a routine basis in sites participating in the IeDEA consortium. These data were approved for use by the local institutional review boards in each of the IeDEA countries included in the analysis and consent requirements were deferred to the local institutional review boards. As the patient-level data was collected from routine patient care, consent was not required. All sites and IeDEA regional coordinating centres also had Institutional Review Board approvals in place permitting the collection of site-level data for the survey. The Institutional Review Board (IRB) of Indiana University, Indianapolis, IN, USA (approval numbers: 1105005574 and 1105005572) approved this study for the East Africa region, which is the leading and coordinating site for this site assessment.

Figures

Figure 1: Consort Diagram of Inclusion Criteria for Patient Level Analysis

Figure 2: Predicted Survival of Time from Antiretroviral Therapy Initiation to Loss to Follow-up by Site-Level Comprehensiveness of Services among 12,401 Children in East Africa IeDEA Enrolled in Care from 2001 to 2014

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Figure 1 Consort Diagram of Inclusion Criteria for Patient Level Analysis

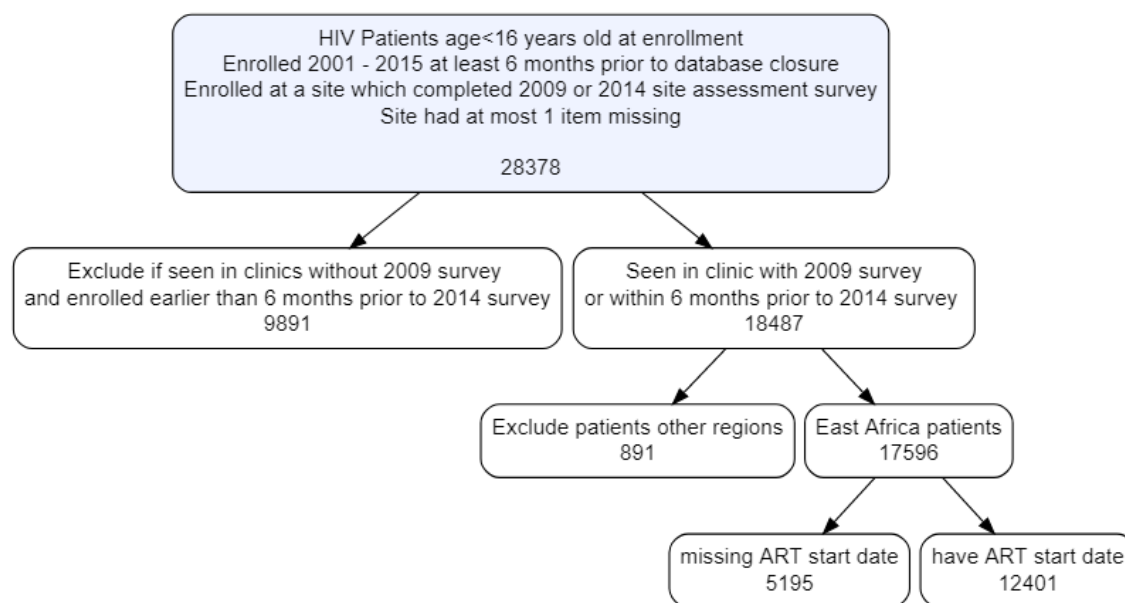
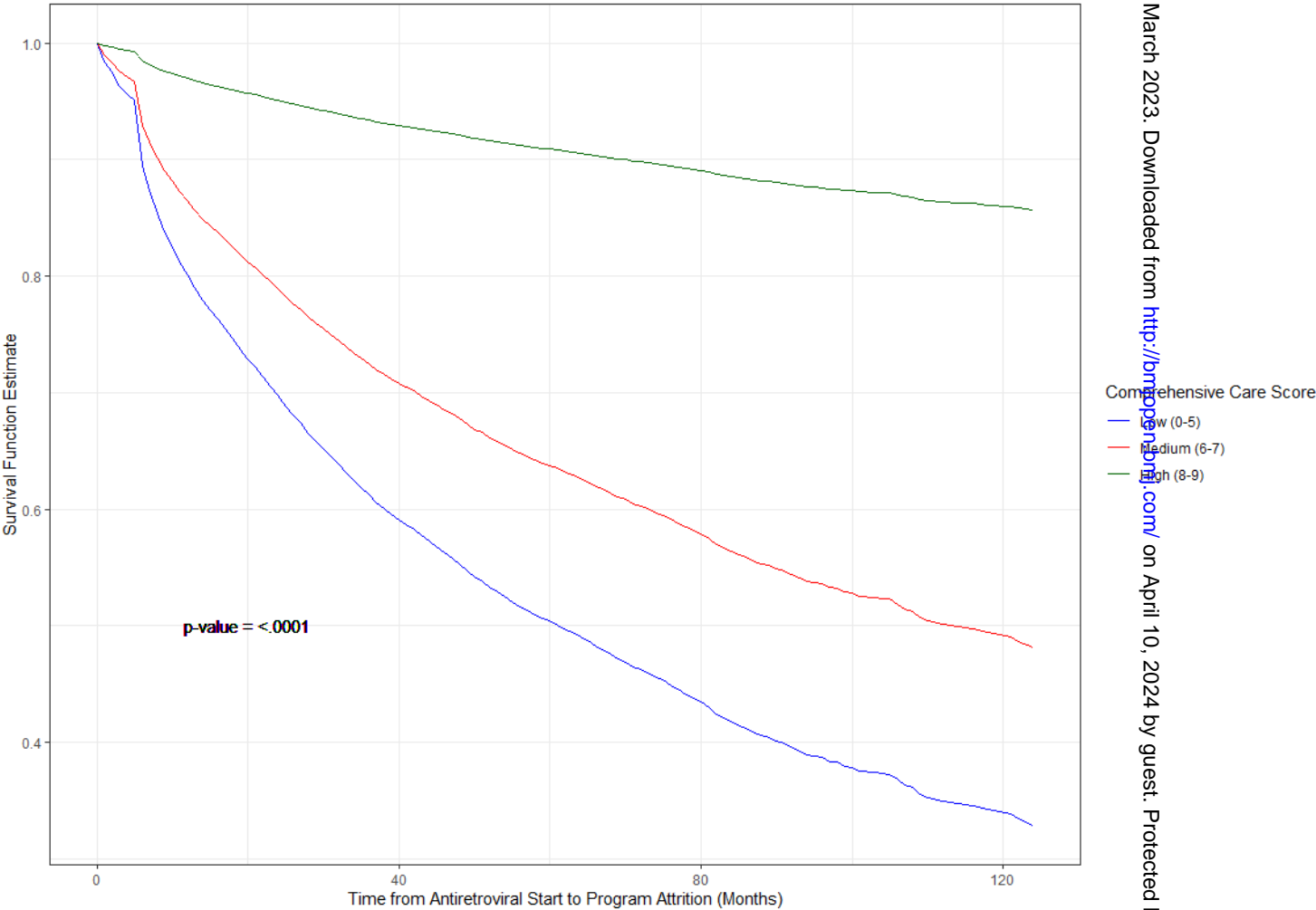


Figure 2. Predicted Survival of Time from Antiretroviral Therapy Initiation to Loss to Follow-up by Site-Level Comprehensive Services among 12,401 Children in East Africa leDEA Enrolled in Care from 2001 to 2014.



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Reporting checklist for quality improvement in health care.

Based on the SQUIRE guidelines.

*Note from the authors: The SQUIRE guidelines/checklist does not perfectly align with our manuscript, but we selected it since it focuses on health service evaluation. This was not an evaluation of a specific intervention and therefore the reporting items do not always apply. We felt this checklist was the most appropriate for our objectives.

	Reporting Item	Page Number
Title	#1 Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	Pg 1 (this manuscript does not seek to improve an initiative, but to understand the current landscape of pediatric health services)
Abstract	#02a Provide adequate information to aid in searching and indexing	Pg. 2
	#02b Summarize all key information from various sections of the text using the abstract format	Pg. 2

1			of the intended publication or a structured	
2			summary such as: background, local	
3			problem, methods, interventions, results,	
4			conclusions	
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11	Introduction			
12				
13	Problem	#3	Nature and significance of the local problem	Pg. 3
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18	Available	#4	Summary of what is currently known about	Pg. 3
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20	knowledge		the problem, including relevant previous	
21			studies	
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26	Rationale	#5	Informal or formal frameworks, models,	Pg. 3 (does not look at a
27			concepts, and / or theories used to explain	specific intervention, but did
28			the problem, any reasons or assumptions	provide rationale for the
29			that were used to develop the	assessment)
30			intervention(s), and reasons why the	
31			intervention(s) was expected to work	
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41	Specific aims	#6	Purpose of the project and of this report	Pg. 3
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44	Methods			
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47	Context	#7	Contextual elements considered important	Pg. 4 (since no intervention,
48			at the outset of introducing the	context is given to how the
49			intervention(s)	assessment was
50				developed)
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Intervention(s)	#08a	Description of the intervention(s) in sufficient detail that others could reproduce it	Pg. 4 (since no intervention, context is given to how the assessment was developed)
Intervention(s)	#08b	Specifics of the team involved in the work	Pg. 4
Study of the Intervention(s)	#09a	Approach chosen for assessing the impact of the intervention(s)	Pg. 4-5
Study of the Intervention(s)	#09b	Approach used to establish whether the observed outcomes were due to the intervention(s)	N/A (no intervention was evaluated)
Measures	#10a	Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	Pg. 4-5
Measures	#10b	Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	Pg. 4-5
Measures	#10c	Methods employed for assessing completeness and accuracy of data	Pg. 5
Analysis	#11a	Qualitative and quantitative methods used to draw inferences from the data	Pg. 5

1	Analysis	#11b	Methods for understanding variation within the data, including the effects of time as a variable	Pg. 5
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8	Ethical considerations	#12	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	Pg. 5
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15	Results	#13a	Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project	N/A (there was no intervention, but does describe when the survey was conducted)
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18		#13b	Details of the process measures and outcome	Pgs 7-10
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20		#13c	Contextual elements that interacted with the intervention(s)	
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22		#13d	Observed associations between outcomes, interventions, and relevant contextual elements	Pg. 9
23				
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25		#13e	Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	N/A (no intervention)
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	#13f	Details about missing data	Pg. 7
Discussion			
Summary	#14a	Key findings, including relevance to the rationale and specific aims	Pg. 10
Summary	#14b	Particular strengths of the project	Pg. 10
Interpretation	#15a	Nature of the association between the intervention(s) and the outcomes	Pg. 10 (described the association between comprehensive score and patient-level outcome)
Interpretation	#15b	Comparison of results with findings from other publications	Pg. 11 (limited similar assessments to compare)
Interpretation	#15c	Impact of the project on people and systems	Pg. 10
Interpretation	#15d	Reasons for any differences between observed and anticipated outcomes, including the influence of context	Pg. 10
Interpretation	#15e	Costs and strategic trade-offs, including opportunity costs	Pg. 10-11
Limitations	#16a	Limits to the generalizability of the work	Pg. 10-11
Limitations	#16b	Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis	Pg. 11

1	Limitations	#16c	Efforts made to minimize and adjust for	Pg. 11
2			limitations	
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6	Conclusion	#17a	Usefulness of the work	Pg. 11
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9	Conclusion	#17b	Sustainability	N/A
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12	Conclusion	#17c	Potential for spread to other contexts	Pg. 11
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15	Conclusion	#17d	Implications for practice and for further	Pg. 11
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19	Conclusion	#17e	Suggested next steps	Pg. 11
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24	Other			
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29	Funding	#18	Sources of funding that supported this work.	Pg. 12
30			Role, if any, of the funding organization in	
31			the design, implementation, interpretation,	
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42 tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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Global HIV prevention, care, and treatment services for children: a cross-sectional survey from the International Epidemiology Databases to Evaluate AIDS (IeDEA) consortium

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Global HIV prevention, care, and treatment services for children: a cross-sectional survey from the International Epidemiology Databases to Evaluate AIDS (IeDEA) consortium

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Abstract

Objectives: To assess access children with HIV have to comprehensive HIV care services, to longitudinally evaluate the implementation and scale-up of services, and to use site services and clinical cohort data to explore whether access to these services influences retention in care.

Methods: A cross-sectional standardized survey was completed in 2014-2015 by sites providing pediatric HIV care across regions of the International Epidemiology Databases to Evaluate AIDS (IeDEA) consortium. We developed a comprehensiveness score based on the World Health Organization (WHO)'s nine categories of essential services to categorize sites as "low" (0-5), "medium" (6-7), or "high" (8-9). When available, comprehensiveness scores were compared with scores from a 2009 survey. We used patient-level data with site services to investigate the relationship between the comprehensiveness of services and retention.

Results: Survey data from 174 IeDEA sites in 32 countries were analyzed. Of the WHO essential services, sites were most likely to offer antiretroviral therapy (ART) provision and counseling (n=173; 99%), co-trimoxazole prophylaxis (168; 97%), prevention of perinatal transmission services (167; 96%), outreach for patient engagement and follow-up (166; 95%), CD4 cell count testing (126; 88%), tuberculosis screening (151; 87%), and select immunization services (126; 72%). Sites were less likely to offer nutrition/food support (97; 56%), viral load testing (99; 69%), and HIV counseling and testing (69; 40%). 10% of sites rated "low," 59% "medium," and 31% "high" in the comprehensiveness score. The mean comprehensiveness of services score increased significantly from 5.6 in 2009 to 7.3 in 2014 ($p<0.001$; $n=30$). Patient level analysis of loss to follow-up after ART initiation estimated the hazard was highest in sites rated "low" and lowest in sites rated "high".

Conclusion: This global assessment suggests the potential care impact of scaling-up and sustaining comprehensive pediatric HIV services. Meeting recommendations for comprehensive HIV services should remain a global priority.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study fills a critical gap in the literature, given the lack of similar assessments of the trend and impact of changes in pediatric HIV care services across a broad global geography.
- Though we had a limited response rate of 53%, this study provides an assessment across the broad range of actual pediatric HIV care practice globally, with comprehensive details.
- A comparison of site-level assessments and patient-level data reveals the clinical impact of a lack of comprehensive services for children living with HIV.
- The data for this study were collected from September 2014 to January 2015 and may not represent the current state of HIV pediatric care; however, these are still some of the only data on this topic available.
- Limitations in the available patient-level data meant that certain analyses were only done for the East Africa region.

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Introduction

In 2020, there were an estimated 1.7 million children with HIV between the ages of 0-15 years.(1) New infections among children declined by 53% from 2010 to 2020, with most new infections occurring in African countries. Access to combination antiretroviral therapy (ART), however, remains an important challenge for this population. In 2020, only 54% of children with HIV globally were accessing ART, which is substantially lower than the percentage of adults with HIV accessing ART (74%).(1) Barriers to scale-up of pediatric treatment include inadequate access to early infant diagnosis, lack of provider experience in delivering pediatric care, limited availability of pediatric antiretroviral formulations, and weak health care infrastructure, but there are few data on the extent to which these specific pediatric HIV services are available globally.(2-5) For children with HIV who are in care, losses to follow-up from care and deaths while in care appear to remain high, though these rates are difficult to accurately report.(6, 7) It is important to document the capacity of HIV care and treatment programs to deliver comprehensive, integrated HIV prevention, care, and treatment services to children across multiple regions in order to identify gaps in services and target resources appropriately.(8-12)

Data on clinical capacity and services are also needed to ensure that pediatric services continue to improve their quality and comprehensiveness, in line with global guidelines for the care of children living with and exposed to HIV. An assessment of global pediatric HIV care capacity at sites of the International Epidemiology Databases Evaluating AIDS (IeDEA) consortium from 2009 revealed that only 38% of sites had capacity for routine viral load monitoring, and that 89% had direct access to infant HIV DNA PCR testing.(13) Over time, the World Health Organization (WHO) has continued to revise its guidelines for the care of children with HIV, including initiation of ART for all children under 5 years of age, initiation of ART for all children >5 years of age with a CD4 cell count <500 cells/μl, routine viral load monitoring for all patients,(14) and then the expansion to recommend treatment of all children and adults with HIV with lifelong ART regardless of immunologic status.(15) The ultimate goal of these guidelines is to improve pediatric morbidity and mortality related to HIV through expanded prevention, treatment, and monitoring services.

Examining whether and how the availability of more comprehensive HIV prevention and treatment services improve patient-level pediatric outcomes are important steps in ensuring that global care services ultimately improve the care of children. Here, we draw on site-level survey assessments administered to a consortium of HIV care programs worldwide to assess the extent to which children with HIV have access to comprehensive HIV care services, to evaluate the implementation and scale-up of these services over time, and to compare these survey findings with clinical cohort data to explore whether access to these services influences the retention in care of children with HIV.

Methods

Population

The IeDEA research consortium was established in 2005 with support from the U.S. National Institute for Allergy and Infectious Diseases to develop a global resource of clinical data from people with HIV (www.iedea.org). IeDEA collects data from seven international regional data

centers: the Asia-Pacific, CCASAnet (encompassing the Caribbean Central and South America), Central Africa, East Africa, NA-ACCORD (encompassing Canada and the U.S.), Southern Africa, and West Africa. Each IeDEA region collaborates with clinical sites to define key variables and harmonize large datasets to address research questions around the impact of the global ART rollout on HIV-related clinical services and outcomes. Pediatric clinical and ART resources across the Africa and Asia-based HIV care sites were previously evaluated in 2009.(13)

Study design and data collection

We surveyed the IeDEA sites that provide HIV treatment and prevention services to children, in any configuration of stand-alone pediatric services or combined care for children and adults. The standardized site assessment tool was adapted from the site assessment survey done in 2009.(13) Study data were collected and managed using a web-based survey on the REDCap (Research Electronic Data Capture) platform (www.project-redcap.org) hosted at the Vanderbilt Institute for Global Health at Vanderbilt University. Site clinical directors or managers were asked to complete the survey, providing information about the sites' physical and clinical characteristics and capacity to deliver WHO-recommended pediatric HIV prevention, care, and treatment services. In 2009, 26 sites in Asia Pacific, 16 sites in Central Africa, 52 sites in East Africa, 19 sites in Southern Africa, and 21 sites in Western Africa were surveyed (N=143). In 2014, an additional 31 sites were surveyed (see Table 1 for regional breakdown). Between 2009 and 2014, 30 sites both 1) provided care for children and/or adolescents with HIV and 2) had consistent site IDs between 2009 and 2014, and therefore these sites' survey findings were used to compare care services.

We created a measure of comprehensiveness of pediatric care services based on the WHO's nine categories of essential services: 1) ART access with psychosocial and adherence counseling; 2) nutrition or food support or counseling; 3) prevention of perinatal transmission services, including medication; 4) CD4 cell count and HIV viral load testing; 5) tuberculosis screening; 6) counseling and testing for HIV; 7) co-trimoxazole prophylaxis; 8) immunization access for select vaccine-preventable diseases (hepatitis B, pneumococcal, influenza vaccine, or yellow fever vaccines); and 9) outreach for patient engagement and follow-up.(16) In calculating the comprehensiveness score, one point was awarded for each service adequately provided by the site, with a total score range between 0 (no services offered) and 9 (all services offered). Sites were then categorized into "low" (0-5), "medium" (6-7), or "high" (8-9) service levels, as was done in prior global site assessment evaluations, from similar site assessment surveys done in 2009.(13)

In order to investigate the relationship between the comprehensiveness of available services and retention in care, patient-level data were also extracted from the IeDEA global cohort database. Patient inclusion criteria were: (1) documented HIV infection; (2) age <16 years of age at enrollment; (3) enrolled into care in 2001 or later at least 6 months prior to site-specific database closure; and (4) either enrolled at a site which completed the 2009 survey or enrolled within six months of the 2014 site assessment survey. Due to high amount of missing data for items from site surveys, only patients seen at sites with missing data for at most 1 item (n=62 sites) were included in the analysis (n=28,378). The sample was further restricted by including only patients

enrolled within six months of the 2014 survey if they were affiliated with sites only completing that round of surveys (n=18,487). Since the resulting de-identified patient-level dataset was overwhelmingly from East Africa (n=17,596 (95.2%)) and less than 5% of the sample consisted of patients from the IeDEA regions of Asia-Pacific, CCASAnet, Central Africa, and West Africa, we selected only sites in East Africa (52 sites) for the patient-level analyses. Then, the dataset was further restricted to patients with non-missing ART start dates (n=12,401 in 35 centers.) See Figure 1.

Statistical analysis

Data were analyzed using SAS (SAS Institute Inc., Cary, NC, U.S.). Descriptive analyses of the 2014 survey were performed, with site characteristics stratified by region. We were able to link data for 30 clinics which responded to both the 2009 and 2014 IeDEA site assessments surveys and analyzed differences in the mean comprehensive of services scores by using paired t-tests.

The analyzed patient-level outcome of interest was time from ART start to loss to program due to either death, transfer, or loss to follow up. Loss to follow-up was defined as no record of death or transfer and no visit between the date of the last clinic visit attended and six months or more of database closure. This was a competing risk model with the two competing events being death and loss to follow-up and being transferred coded as censored. Bivariate Cox proportional hazard models were used to assess the association between comprehensive care category (obtained from the 2014 or earlier 2009 surveys) and loss to program. A multivariable Cox proportional hazards model which included clinically important patient-level variables – age at ART start (categorical, 0 to <5 years, 5 to <10, 10 to <15, 15 to 16); categorical immune status at ART start as defined by the WHO, based on age and CD4 cell count or percentage depending on age, WHO clinical stage at enrollment, and clinic location (urban, mostly urban, mostly rural or rural) – was used to investigate the relationship between level of comprehensiveness of services (low, medium, high) and patient retention in care. Hazards ratios and 95% confidence intervals (CI) were reported. As a sensitivity analysis, the model was refit using data obtained from multiple imputation for missing values for CD4 percentage (24.0%), WHO clinical stage (13.8%), and age at ART start (0.1%) using the Markov Chain Monte Carlo (MCMC) method.(17)

Patient and public involvement

Patients or the public were not involved in the design or conduct of our research. In the East Africa region, briefings on the findings were done in clinics to patients, including both study participants and non-participants.

Results

All 536 sites providing HIV care in the IeDEA global regions received the survey, and 287 (53.5%) sites completed the survey between September 2014 and January 2015. Out of those 287 sites, 174 (61%) provided pediatric care. Site characteristics by IeDEA region are shown in Table 1. Overall, most sites providing pediatric HIV care (82%) saw both children and adult patients, including almost 17,000 children with HIV. The majority of the sites were in African countries, with 88 sites (51%) from Southern Africa, 34 sites (20%) from East Africa, 17 sites

(10%) from Central Africa, 16 sites (9%) from the Asia-Pacific, 12 sites (7%) from West Africa, and 7 sites (4%) from CCASAnet. Most of the care sites were located in urban (39%) or mostly urban (8%) settings, and almost all were public facilities (93%). Overall, the HIV care sites were well distributed across different levels of health care services; 40% were primary care sites, 25% were secondary care sites, and 34% were tertiary care sites. However, the participating sites from the Asia-Pacific, CCASAnet, and Central Africa regions were almost exclusively tertiary facilities.

Table 1. 2014 survey site characteristics by International Epidemiology Databases to Evaluate AIDS (IeDEA) region (n=174 sites)*

		Asia-Pacific (n=16)	CCASAnet (n=7)	Central Africa (n=17)	East Africa (n=34)	Southern Africa (n=88)	West Africa (n=12)	Total (n=174)
Number of Pediatric and Adolescents in Care, 2014		70 (2 sites)	611 (7 sites)	1748 (13 sites)	8165 (33 sites)	3113 (12 sites)	3076 (10 sites)	16783 (77 sites)
Age at Enrollment for Patients in Care in 2014	0 to <5	47 (67.1)	356 (58.3)	567 (32.4)	3519 (43.1)	1934 (62.1)	1666 (54.2)	8089 (48.2)
	5 to <10	17 (24.3)	150 (24.5)	628 (35.9)	2844 (34.8)	685 (22.0)	989 (32.2)	5313 (31.7)
	10 to <15	6 (8.6)	89 (14.6)	461 (26.4)	1514 (18.5)	427 (13.7)	389 (12.6)	2886 (17.2)
	15 to 16	0 (0.0)	16 (2.6)	92 (5.3)	288 (3.5)	67 (2.2)	32 (1.0)	495 (2.9)
Patient Population	Children Only	16 (100.0)	3 (42.9)	0 (0.0)	0 (0.0)	3 (3.4)	10 (83.3)	32 (18.4)
	Both Children and Adults	0 (0.0)	4 (57.1)	17 (100.0)	34 (100.0)	85 (96.6)	2 (16.7)	142 (81.6)
Site Location[^]	Urban	0 (0.0)	7 (100.0)	16 (94.1)	9 (26.5)	32 (36.4)	3 (25.0)	67 (38.5)
	Mostly Urban	0 (0.0)	0 (0.0)	0 (0.0)	8 (23.5)	0 (0.0)	6 (50.0)	14 (8.0)
	Mostly Rural	0 (0.0)	0 (0.0)	0 (0.0)	12 (35.3)	0 (0.0)	0 (0.0)	12 (6.9)
	Rural	0 (0.0)	0 (0.0)	0 (0.0)	5 (14.7)	51 (58.0)	0 (0.0)	56 (32.2)

	Other/Mixed urban-rural	16 (100.0)	0 (0.0)	1 (5.9)	0 (0.0)	5 (5.7)	3 (25.0)	25 (14.4)
Type of Facility	Public	15 (93.8)	6 (85.7)	16 (94.1)	31 (91.2)	83 (94.3)	11 (91.7)	162 (93.1)
	Private	1 (6.3)	1 (14.3)	1 (5.9)	3 (8.8)	5 (5.7)	1 (8.3)	12 (6.9)
Level of Facility	Primary	2 (12.5)	0 (0.0)	0 (0.0)	13 (38.2)	54 (61.4)	1 (8.3)	70 (40.2)
	Secondary	0 (0.0)	0 (0.0)	0 (0.0)	16 (47.1)	25 (28.4)	2 (16.7)	43 (24.7)
	Tertiary	14 (87.5)	7 (100.0)	17 (100.0)	5 (14.7)	9 (10.2)	7 (58.3)	59 (33.9)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)	2 (1.1)
Academic Affiliation	No	4 (25.0)	0 (0.0)	14 (82.4)	22 (64.7)	77 (87.5)	4 (33.3)	121 (69.5)
	Yes	12 (75.0)	7 (100.0)	3 (17.6)	12 (35.3)	10 (11.4)	8 (66.7)	52 (29.9)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.6)
Pediatrician on Site	Available every day clinic open	15 (93.8)	7 (100.0)	6 (35.3)	2 (5.9)	5 (5.7)	10 (83.3)	45 (25.9)
	Available some days	1 (6.3)	0 (0.0)	4 (23.5)	12 (35.3)	7 (8.0)	1 (8.3)	25 (14.4)
	Not available	0 (0.0)	0 (0.0)	7 (41.2)	20 (58.8)	76 (86.4)	1 (8.3)	104 (59.8)

*Findings other than “Pediatric and Adolescents in Care” are listed as n (%).

^Urban= officially designated to be city with city administration and political bodies; mostly urban= big and small towns, peri-urban areas, growth points, mining communities; mostly rural= large and small scale commercial farming areas; rural= subsistence farming areas; other/mixed urban-rural= e.g., small town, peri-urban area, growth points, mining community, etc).

Site-specific characteristics

Most sites (60%) reported that pediatricians were not available, although this varied significantly by region. A majority of sites within the Asia Pacific, CCASAnet, and West Africa regions had a pediatrician either available all days or some days, while most sites in the East and Southern Africa regions (which had the largest pediatric patient populations) reported that a pediatrician was not available on any day.

Out of the nine essential services, we found that sites were most likely to offer ART access (99% of sites), co-trimoxazole prophylaxis (97%), comprehensive prevention of perinatal transmission

services (96%), outreach services for patient follow-up (95%), tuberculosis screening (87%), and immunization services (72%) (Table 2). During this time period, providing either or both CD4 cell count and viral load testing was considered an essential service, and 88% of sites report CD4 cell count testing and 69% reported viral load testing. Sites were less likely to report offering nutrition counseling or food support (56%), and HIV counseling and testing (40%). The median comprehensive care score was 7 (interquartile range [IQR], 6-7). Among the 174 sites, 18 sites (10%) offered a “low” level of services, 103 sites (59%) offered a “medium” level of services, and 53 (31%) offered a “high” level of services. These “high” levels of services or more comprehensive services were clustered at sites in Asia-Pacific (56% of sites in the region), CCASAnet (43%), and East Africa (44%).

Table 2. 2014 survey site capacity and comprehensiveness of services score by IeDEA region (n=174 sites)*

WHO Essential Services		Asia-Pacific (n=16)	CCASAnet (n=7)	Central Africa (n=17)	East Africa (n=34)	Southern Africa (n=88)	West Africa (n=12)	Total (n=174)
ART Access with Counseling		16 (100.0)	6 (85.7)	17 (100.0)	34 (100.0)	88 (100.0)	12 (100.0)	173 (99.4)
Nutrition		12 (75.0)	4 (57.1)	4 (23.5)	25 (73.5)	45 (51.1)	7 (58.3)	97 (55.7)
Prevention of perinatal transmission services		13 (81.3)	7 (100.0)	17 (100.0)	34 (100.0)	87 (98.9)	9 (75.0)	167 (96.0)
CD4 Testing and/or Viral Load Testing	CD4	15 (93.8)	5 (71.4)	13 (81.3)	19 (65.5)	62 (96.9)	12 (100.0)	126 (87.5)
	Viral Load	11 (68.8)	4 (57.1)	12 (75.0)	26 (89.7)	37 (57.8)	9 (75.0)	99 (68.8)
TB screening		16 (100.0)	7 (100.0)	12 (70.6)	32 (94.1)	77 (87.5)	7 (58.3)	151 (86.8)
HIV counseling and testing		11 (68.8)	6 (85.7)	4 (23.5)	16 (47.1)	26 (29.5)	6 (50.0)	69 (39.7)
Co-trimoxazole		16 (100.0)	7 (100.0)	17 (100.0)	31 (91.2)	85 (96.6)	12 (100.0)	168 (96.6)
Immunizations		13 (81.3)	7 (100.0)	12 (70.6)	24 (70.6)	65 (73.9)	5 (41.7)	126 (72.4)
Outreach		14 (87.5)	4 (57.1)	15 (88.2)	34 (100.0)	88 (100.0)	11 (91.7)	166 (95.4)
Comprehensiveness Score	Low (0-5)	0 (0.0)	0 (0.0)	5 (29.4)	2 (5.9)	8 (9.1)	3 (25.0)	18 (10.3)

	Medium (6-7)	7 (43.8)	4 (57.1)	10 (58.8)	17 (50.0)	58 (65.9)	7 (58.3)	103 (59.2)
	High (8-9)	9 (56.3)	3 (42.9)	2 (11.8)	15 (44.1)	22 (25.0)	2 (16.7)	53 (30.5)

*Findings are listed as n (%).

From among pediatric care sites which responded to the 2009 survey (n=143) and 2014 survey (n=714), we were able to link data for 30 sites: East Africa (26 sites), Asia Pacific (3 sites) and Southern Africa (1 site). The mean comprehensiveness of services score increased significantly from 5.6 (standard deviation [SD], 1.4) in 2009 to 7.3 (SD, 1.4) in 2014 ($p<0.001$) (Table 3). A greater proportion of sites reported offering services in the 2014 survey compared to the 2009 survey for each of the nine essential services except for CD4 cell count testing and immunization; 80% of sites reported CD4 cell count testing in 2009 and only 60% reported testing in 2014. Similarly, 80% of sites in 2009 reported offering immunization services, but only 70% of these same sites reported offered immunizations in 2014. From 2009 to 2014, we found that the largest increases were for nutrition services (13% to 80%), viral load testing (7% to 83%), HIV counseling and testing (13% to 43%), and outreach (70% to 100%).

Table 3. Changes in site capacity and comprehensiveness of services from 2009 to 2014 (n=30)

		Site Assessment 1.0 (2009)	Site Assessment 2.0 (2014)
Comprehensiveness score	Mean ± Standard Deviation	5.571 ± 1.372	7.333 ± 1.373*
ART Access with Counseling	N (%)	24 (80.0)	30 (100.0)
Nutrition		4 (13.3)	24 (80.0)
Prevention of perinatal transmission services		26 (86.7)	30 (100.0)
CD4 Testing		24 (80.0)	18 (60.0)
Viral Load Testing		2 (6.7)	25 (83.3)
TB Screening		25 (83.3)	28 (93.3)
HIV Counseling and Testing		4 (13.3)	13 (43.3)
Co-trimoxazole		26 (86.7)	27 (90.0)
Immunizations		24 (80.0)	21 (70.0)
Outreach		21 (70.0)	30 (100.0)

*There was a statistically significant increase in the mean comprehensive care score from 2009 to 2014 among pediatric sites with at most 1 care item missing. Differences in mean comprehensiveness scores were tested by paired t-test.

Patient-level analyses

A total of 12,401 children at 35 sites in the East Africa region were included in the patient-level analysis, of which 192 (1%) were at clinics reporting a “low” level of services, 10,386 (84%) were at clinics reporting a “medium” level of services, and 1,823 (15%) were at clinics reporting a “high” level of services. Care classification was based on either the 2014 or 2009 surveys. Mean age at enrollment was 5.9 years, with median age of 5 years and range from 0 to 16 years. The probability of loss to follow-up after ART initiation was highest in clinics with a “low” level of services and lowest in clinics with a “high” level of services (Figure 2). Hazard ratios from bivariate and multiple regression Cox proportional hazard models are presented in Table 4. In multivariable Cox proportional hazard models, compared with children in care at clinics providing a “low” level of services, children in care at clinics providing “medium” and “high” levels of services had hazard ratios of loss to follow-up of 0.58 (95% CI: 0.47, 0.72) and 0.12 (95% CI: 0.07, 0.23), respectively, adjusting for age at ART start, gender, immunologic status, WHO clinical stage at enrollment, and clinic location. Results from models using imputation of missing covariate data were not substantially different from what is presented here.

Table 4. Hazard ratios from Cox proportional hazard models of time to loss to program

		Bivariate Models				Multiple Regression			
	Level	Hazard Ratio	95% Confidence Interval	Overall Test	p-value	Hazard Ratio	95% Confidence Interval	Overall Test	p-value
Age at ART start	0-<1	1.715	(1.460,2.015)	<.0001	<.0001	2.298	(1.530,3.52)	<.0001	<.0001
	1-<2	1.388	(1.236,1.559)			1.413	(1.139,1.753)		
	2-<5	reference				reference			
	5-<7	0.906	(0.820,1.002)			1.042	(0.907,1.197)		
	7-<10	0.857	(0.780,0.941)			0.989	(0.866,1.130)		
	10-<13	0.941	(0.851,1.040)			1.064	(0.926,1.222)		
	13-<16	1.186	(1.067,1.318)			1.309	(1.132,1.514)		
	16-<23	1.495	(1.258,1.777)			1.716	(1.400,2.103)		
Comprehensive Care Score	(4-5)	reference		<.0001	<.0001	reference		<.0001	<.0001
	(6-7)	0.657	(0.562,0.768)			0.584	(0.472,0.722)		
	(8-9)	0.139	(0.084,0.230)			0.124	(0.066,0.233)		
Gender	Female	1.026	(0.966,1.089)	0.4056	0.4056	1.022	(0.949,1.100)	0.5679	0.5679
	Male	reference				reference			
Immune Status	Not Significant	reference		<.0001	<.0001	reference		<.0001	<.0001
	Advanced immunosuppression	1.026	(0.899,1.172)			0.943	(0.818,1.086)		
	Mild immunosuppression	0.915	(0.781,1.072)			0.901	(0.763,1.064)		
	Severe immunosuppression	1.227	(1.104,1.365)			1.141	(1.019,1.278)		
Facility Location	Mostly rural	0.663	(0.607,0.724)	<.0001	<.0001	0.721	(0.636,0.816)	<.0001	<.0001
	Mostly urban	0.571	(0.524,0.623)			0.575	(0.508,0.650)		

		Bivariate Models				Multiple Regression			
	Level	Hazard Ratio	95% Confidence Interval	Overall Test	p-value	Hazard Ratio	95% Confidence Interval	Overall Test	p-value
WHO/CDC stage at ART start	Rural	0.480	(0.411,0.560)		<.0001	0.440	(0.354,0.546)		<.0001
	Urban	reference				reference			
	1	reference				reference			
	2	1.104	(1.035,1.177)	0.0025	0.0025	1.095	(1.014,1.182)	0.0200	0.0200

Discussion

With only 54% of children with HIV on treatment globally in 2021 and 40% of children with HIV virally suppressed, it is essential that we understand the capacity of global HIV care and treatment sites to provide comprehensive care to children (1). In this evaluation of a broad range of global care sites providing services to children with HIV, we noted significant improvement in the sites' provision of essential HIV care and prevention services for children and pregnant people between assessments done in 2009 and 2014. Access to ART and provision of prevention of perinatal transmission services increased substantially in the 30 sites with both assessments—providing the necessary backdrop to achieving an AIDS-free generation through both prevention and treatment. Moreover, there was a dramatic scale-up in access to routine viral load monitoring (from 6.7% to 83.3%), reflecting success in policy shifts to improve access to viral load monitoring and supporting the global efforts to achieve viral suppression. As routine viral load monitoring increased, these data already showed a parallel drop in CD4 cell count testing services by 2014.

Even though the comprehensiveness of essential pediatric HIV services grew substantially in the five years between the assessments, we can still see critical gaps in access to broader services for children and adolescents. While services such as providing nutrition support and counseling for HIV testing generally increased, these services remained absent from many sites. Perhaps even more concerning from a child health perspective, particularly in the face of the ongoing COVID-19 pandemic, fewer sites reported offering immunizations in the 2014 survey. Addressing potential gaps in access to immunizations for children and adolescents at risk of immune-compromise merits close attention. There is a defined need to catch up on the delayed childhood immunizations missed for 23 million children worldwide related to the COVID-19 pandemic.(18) Moreover, many health systems might consider the potential for these care sites to bolster broader coverage of vaccinations for human papillomavirus to prevent cervical cancer, and to provide SARS-CoV-2 vaccination. The urgency in moving more pediatric care sites globally to provide the full range of essential services is also highlighted by the potential clinical impact. Our findings, from analyses performed in East Africa, one of our constituent regions, suggest that sites providing more comprehensive services also have more children with HIV retained in care, which may in turn result in less HIV-related disease and fewer adverse clinical outcomes. These sites may also be those with the most robust resources or sites where care is more accessible. In considering how to expand the range of services available in a health system, attention must also be given to what specific resources are already available to adapt to care expansion and how access to even more basic levels of care might be improved.

There are several limitations to these data. The data were collected from September 2014 to January 2015 and may not represent the current state of HIV pediatric care. On the other hand, these data do highlight the trajectory of HIV care systems as global pediatric HIV treatment guidelines shift. Moreover, our observations fill a critical gap in the literature, given the lack of similar assessments of the trend and impact of changes in pediatric HIV care services across a broad global geography. We are able to show the age distribution by region (table 1), allowing the comprehensive assessment of services to be compared across the range of pediatric care, including for varying definitions of “child”, whether those less than 15 years or less than 16 years. The response rate to the survey was low, at 53.5%, which may introduce sampling bias

that challenges the representativeness of this sample and thus the generalizability of the findings. Nonetheless, the responses we received to represent a cross-sectional description of services for a range of HIV clinical care sites across a wide swath of resource-limited settings and we believe this still may be one of the most detailed description of the HIV- and related care services available for children and adolescents globally. While we acknowledge the potential lack of generalizability of the East Africa observations to the IeDEA Network, particularly outside of African countries, we are less concerned about the same between IeDEA-affiliated sites and their ambient environment in their respective countries or other similar sites in Africa. For example, in other patient-level analyses from global IeDEA, the East Africa IeDEA cohort demographics have been representative of broader African settings, both within and outside of IeDEA (19-22). Another concern arises due to shifts in the sites participating in the surveys between 2009 and 2014. Because of this shift, we did not have longitudinal data for all sites, in order to assess changes in the services provided over the 5-year period of the study. Nevertheless, a sufficient number of sites did have complete surveys on both occasions. Moreover, the limited response rate indicated by the estimation that only 53% of sites completed the survey is a conservatively low estimate because some of the sites changed their consortium identifiers in the course of the follow-up, making it impossible to pair their data conclusively. Despite the fact that the longitudinal data were only available for 17% of the sites surveyed in 2014, this is still some of the only data on this topic available within these years. The large number of these sites and the consistency of the longitudinal trends in (increasing) comprehensiveness of HIV-related services, provides a broad look at the state of the global pediatric HIV care in these regions during this period.

Conclusions

As global programs work to expand the availability and quality of pediatric HIV treatment and prevention services, understanding the capacity of global sites caring for this population to provide services for children and adolescents with HIV can guide targets for improving care access and quality. This global survey of IeDEA cohort sites demonstrates significant gains in the comprehensiveness of HIV treatment and prevention services available for children between 2009 to 2014, while identifying important remaining gaps. Data from the East Africa region further suggest that sites providing a comprehensive array of HIV-related services experience higher retention in care among their clients, compared to sites offering lower levels of the essential services for HIV treatment and prevention. Achieving global treatment success for children and adolescents with HIV and eliminating perinatal transmission of HIV requires that we continue to prioritize strengthening the healthcare systems available for these populations with HIV worldwide.

Competing interests

The authors declare that they have no competing interests.

Contributors

RCV, CTY, CWW, and KWK designed and provided scientific oversight for the study. Material preparation and data collection were performed by NKNY, CWW, AE, MD, VL, PL, RS, CT, CBM, OOT, and MS. CTY led data analysis in collaboration with SO and SB. The first draft of

the manuscript was written by RCV, NKNY, CWW, AE, MD, VL, PL, RS, CT, CBM, OOT, MS, CTY, KWK, SO, SB, RM, and RCV reviewed and contributed to subsequent versions. All authors read and approved the final manuscript.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author. All data requests must be approved by IeDEA.

Ethical approval

The patient-related data presented here are based on retrospective deidentified information collected on a routine basis in sites participating in the IeDEA consortium. These data were approved for use by the local institutional review boards in each of the IeDEA countries included in the analysis and consent requirements were deferred to the local institutional review boards. As the patient-level data was collected from routine patient care, consent was not required. All sites and IeDEA regional coordinating centres also had Institutional Review Board approvals in place permitting the collection of site-level data for the survey. The Institutional Review Board (IRB) of Indiana University, Indianapolis, IN, USA (approval numbers: 1105005574 and 1105005572) approved this study for the East Africa region, which is the leading and coordinating site for this site assessment.

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Figures

Figure 1. Consort diagram of inclusion criteria for patient level analysis

Figure 2. Predicted survival of time from antiretroviral therapy initiation to loss to follow-up by site-level comprehensiveness of services among 12,401 children in East Africa IeDEA enrolled in care from 2001 to 2014

Figure 1 Consort Diagram of Inclusion Criteria for Patient Level Analysis

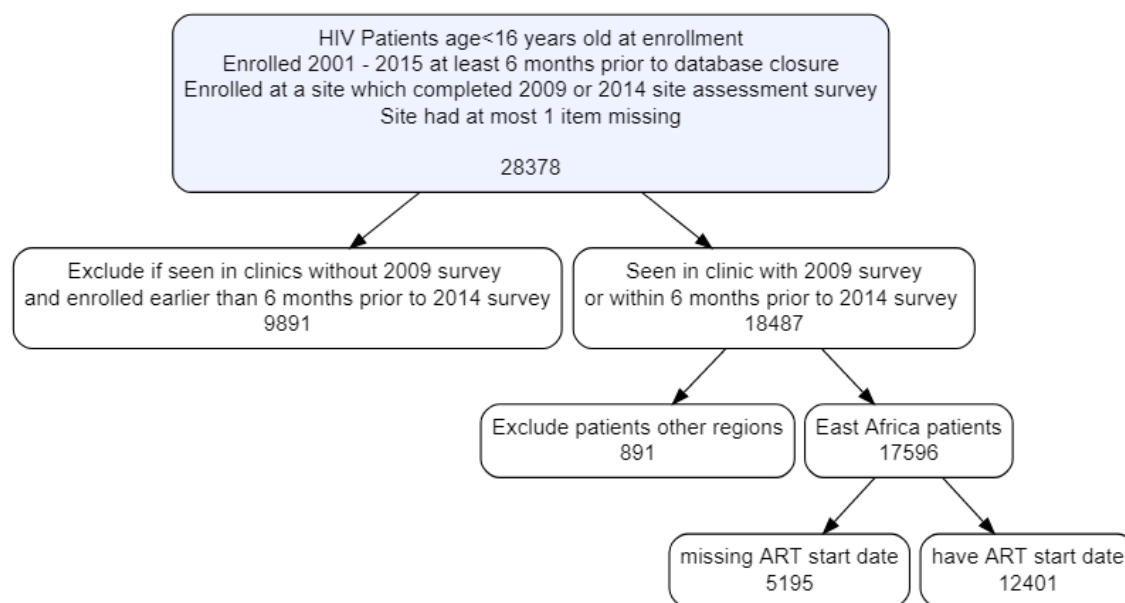
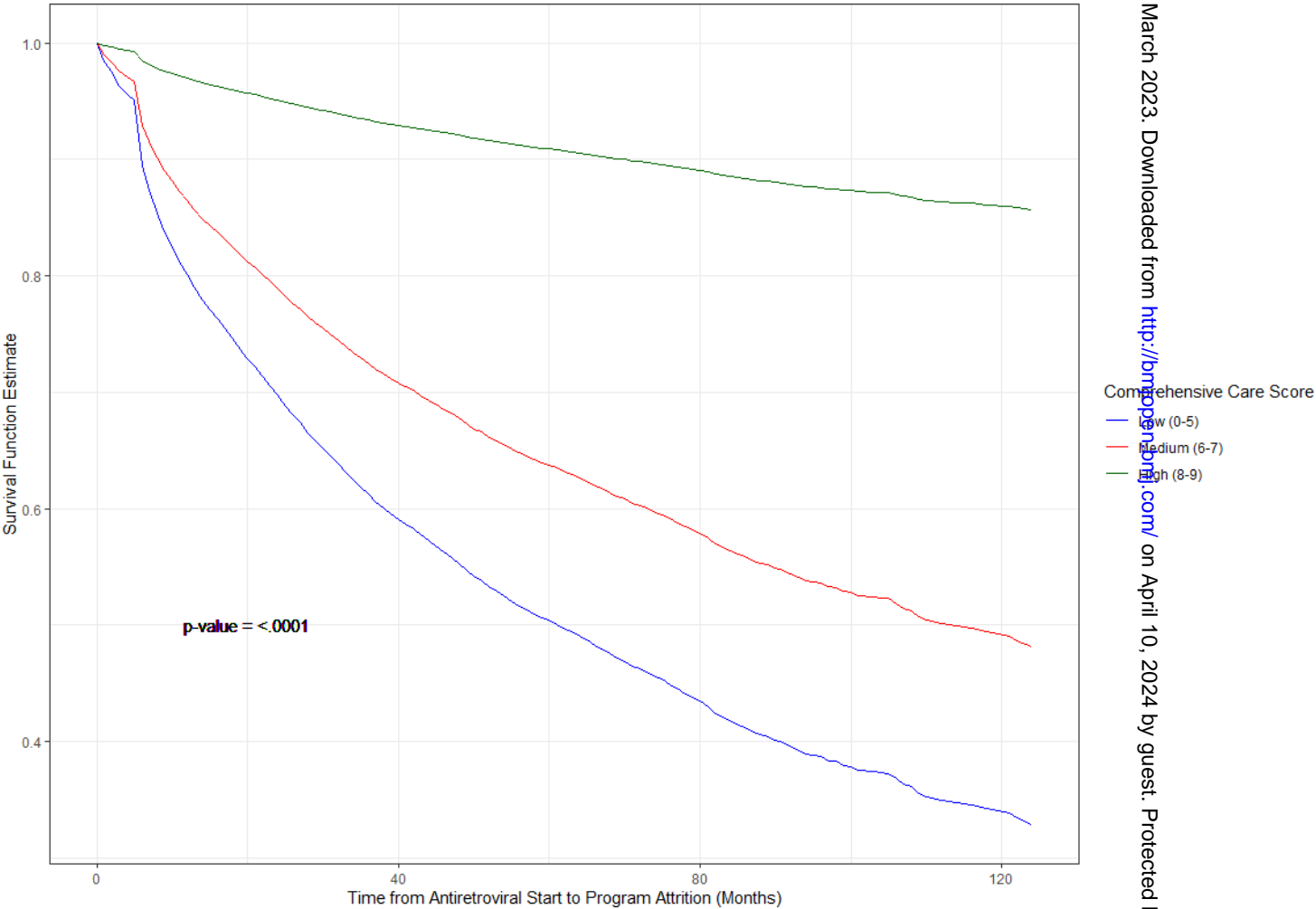


Figure 2. Predicted Survival of Time from Antiretroviral Therapy Initiation to Loss to Follow-up by Site-Level Comprehensive Services among 12,401 Children in East Africa leDEA Enrolled in Care from 2001 to 2014.



Reporting checklist for quality improvement in health care.

Based on the SQUIRE guidelines.

*Note from the authors: The SQUIRE guidelines/checklist does not perfectly align with our manuscript, but we selected it since it focuses on health service evaluation. This was not an evaluation of a specific intervention and therefore the reporting items do not always apply. We felt this checklist was the most appropriate for our objectives.

	Reporting Item	Page Number
Title		
	#1 Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	Pg 1 (this manuscript does not seek to improve an initiative, but to understand the current landscape of pediatric health services)
Abstract		
	#02a Provide adequate information to aid in searching and indexing	Pg. 2
	#02b Summarize all key information from various sections of the text using the abstract format	Pg. 2

of the intended publication or a structured
summary such as: background, local
problem, methods, interventions, results,
conclusions

Introduction

Problem description	#3	Nature and significance of the local problem	Pg. 3
Available knowledge	#4	Summary of what is currently known about the problem, including relevant previous studies	Pg. 3
Rationale	#5	Informal or formal frameworks, models, concepts, and / or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	Pg. 3 (does not look at a specific intervention, but did provide rationale for the assessment)
Specific aims	#6	Purpose of the project and of this report	Pg. 3

Methods

Context	#7	Contextual elements considered important at the outset of introducing the intervention(s)	Pg. 4 (since no intervention, context is given to how the assessment was developed)
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Intervention(s)	#08a	Description of the intervention(s) in sufficient detail that others could reproduce it	Pg. 4 (since no intervention, context is given to how the assessment was developed)
Intervention(s)	#08b	Specifics of the team involved in the work	Pg. 4
Study of the Intervention(s)	#09a	Approach chosen for assessing the impact of the intervention(s)	Pg. 4-5
Study of the Intervention(s)	#09b	Approach used to establish whether the observed outcomes were due to the intervention(s)	N/A (no intervention was evaluated)
Measures	#10a	Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	Pg. 4-5
Measures	#10b	Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	Pg. 4-5
Measures	#10c	Methods employed for assessing completeness and accuracy of data	Pg. 5
Analysis	#11a	Qualitative and quantitative methods used to draw inferences from the data	Pg. 5

1	Analysis	#11b	Methods for understanding variation within the data, including the effects of time as a variable	Pg. 5
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8	Ethical considerations	#12	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	Pg. 5
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15	Results	#13a	Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project	N/A (there was no intervention, but does describe when the survey was conducted)
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22		#13b	Details of the process measures and outcome	Pgs 7-10
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29		#13c	Contextual elements that interacted with the intervention(s)	
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36		#13d	Observed associations between outcomes, interventions, and relevant contextual elements	Pg. 9
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43		#13e	Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	N/A (no intervention)
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	#13f	Details about missing data	Pg. 7
Discussion			
Summary	#14a	Key findings, including relevance to the rationale and specific aims	Pg. 10
Summary	#14b	Particular strengths of the project	Pg. 10
Interpretation	#15a	Nature of the association between the intervention(s) and the outcomes	Pg. 10 (described the association between comprehensive score and patient-level outcome)
Interpretation	#15b	Comparison of results with findings from other publications	Pg. 11 (limited similar assessments to compare)
Interpretation	#15c	Impact of the project on people and systems	Pg. 10
Interpretation	#15d	Reasons for any differences between observed and anticipated outcomes, including the influence of context	Pg. 10
Interpretation	#15e	Costs and strategic trade-offs, including opportunity costs	Pg. 10-11
Limitations	#16a	Limits to the generalizability of the work	Pg. 10-11
Limitations	#16b	Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis	Pg. 11

1	Limitations	#16c	Efforts made to minimize and adjust for	Pg. 11
2			limitations	
3				
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6	Conclusion	#17a	Usefulness of the work	Pg. 11
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9	Conclusion	#17b	Sustainability	N/A
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12	Conclusion	#17c	Potential for spread to other contexts	Pg. 11
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15	Conclusion	#17d	Implications for practice and for further	Pg. 11
16			study in the field	
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19	Conclusion	#17e	Suggested next steps	Pg. 11
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21				
22	Other			
23	information			
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27	Funding	#18	Sources of funding that supported this work.	Pg. 12
28			Role, if any, of the funding organization in	
29			the design, implementation, interpretation,	
30			and reporting	
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39	None The SQUIRE 2.0 checklist is distributed under the terms of the Creative Commons Attribution			
40	License CC BY-NC 4.0. This checklist can be completed online using https://www.goodreports.org/ , a			
41	tool made by the EQUATOR Network in collaboration with Penelope.ai			
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