Increasing pediatric HIV testing positivity rates through focused testing in high-yield points of service in health facilities—Nigeria, 2016-2017

Abstract

Background

In 2017, UNAIDS estimated that 140,000 children aged 0–14 years are living with HIV in Nigeria, but only 35% have been diagnosed and are receiving antiretroviral therapy. Children are tested primarily in outpatient clinics, which show low HIV-positive rates. To demonstrate efficient facility-based HIV testing among children aged 0–14 years, we evaluated pediatric HIV-positivity rates in points of service in select health facilities in Nigeria.

Methods

We conducted a retrospective analysis of HIV testing and case identification among children aged 0–14 years at all points of service at nine purposively sampled hospitals (November 2016–March 2017). Points of service included family index testing, pediatric outpatient department (POPD), tuberculosis (TB) clinics, immunization clinics, and pediatric inpatient ward. Eligibility for testing at POPD was done using a screening tool while all children with unknown status were eligible for HIV test at other points of service. The main outcome was HIV positivity rates stratified by the testing point of service and by age group. Predictors of an HIV-positive result were assessed using logistic regression. All analyses were done using Stata 15 statistical software.

Results

Of 2,180 children seen at all facility points of service with unknown HIV status, 1,822 (83.6%) were tested for HIV, of whom 43 (2.4%) tested HIV positive. The numbers of children tested by age group were <1 year=230 (12.6%); 1-4 years =752 (41.3%); 5-9 years= 520 (28.5%); and 10-14 years= 320 (17.6%). The number of children tested by point of service were POPD=906 (49.7%); family index testing=693 (38.0%); pediatric inpatient ward=192 (10.5%); immunization clinic=16 (0.9%); and TB clinic=15 (0.8%). HIV positivity rates by point of service were TB clinic= 6.7% (95% Confidence Interval (CI): 0.9-35.2%); pediatric inpatient ward=4.7% (95%CI: 2.5-8.8%); family index testing=3.5% (95%CI: 2.3-5.1%); immunization clinic=16 (0.9%); and TB clinic=15 (0.8%). HIV-positivity rates by point of service were TB clinic= 6.7% (95% Confidence Interval (CI): 0.9-35.2%); pediatric inpatient ward=4.7% (95%CI: 2.5-8.8%); family index testing=3.5% (95%CI: 2.3-5.1%); immunization clinic=16 (0.9%); and TB clinic=15 (0.8%).

Conclusion

In Nigeria, to improve facility-based HIV positivity rates among children aged 0–14 years, an increased focus on HIV testing among children seeking care in pediatric inpatient wards, through family index testing, and perhaps TB clinics is appropriate.
Reviewers: The authors have adequately addressed my comments raised in a previous version but for reference #10 which is not well cited in line 288. Here is the correct reference: https://doi.org/10.1371/journal.pone.0214251. Please note that even though this article is from the same author (Yumo et al.), it’s different from reference #10 well cited for example in line 271. Please, amend this reference number and the references list as well.

Authors’ response: We have made the required changes to the reference. Please review the lines 298 and 442 to 445 of the Tracked version of the revised manuscript. The journal is now correctly cited as reference #30 in line 298 and correctly referenced in lines 442 to 445.

Question: Financial Disclosure

Response: This work was supported by the President’s Emergency Plan for AIDS Relief (PEPFAR) through Centers for Disease Control and Prevention (CDC) under the terms of GH002097, GH002098, GH002099 and GH002100.
Unfunded studies
Enter: The author(s) received no specific funding for this work.

Funded studies
Enter a statement with the following details:
• Initials of the authors who received each award
• Grant numbers awarded to each author
• The full name of each funder
• URL of each funder website
• Did the sponsors or funders play any role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript?
• NO - Include this sentence at the end of your statement: The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.
• YES - Specify the role(s) played.

Competing Interests
Use the instructions below to enter a competing interest statement for this submission. On behalf of all authors, disclose any competing interests that could be perceived to bias this work—acknowledging all financial support and any other relevant financial or non-financial competing interests.

This statement will appear in the published article if the submission is accepted. Please make sure it is accurate. View published research articles from PLOS ONE for specific examples.

The authors have declared that no competing interests exist.
NO authors have competing interests

Enter: The authors have declared that no competing interests exist.

Authors with competing interests

Enter competing interest details beginning with this statement:

I have read the journal's policy and the authors of this manuscript have the following competing interests: [insert competing interests here]

* typeset

Ethics Statement

Enter an ethics statement for this submission. This statement is required if the study involved:

- Human participants
- Human specimens or tissue
- Vertebrate animals or cephalopods
- Vertebrate embryos or tissues
- Field research

Write "N/A" if the submission does not require an ethics statement.

General guidance is provided below. Consult the submission guidelines for detailed instructions. Make sure that all information entered here is included in the Methods section of the manuscript.

The study protocol was reviewed and approved by National Health Research Ethics Committee of Nigeria. This activity was also reviewed and approved in accordance with the Centers for Disease Control and Prevention (CDC) human research protection procedures.
Format for specific study types

Human Subject Research (involving human participants and/or tissue)
- Give the name of the institutional review board or ethics committee that approved the study
- Include the approval number and/or a statement indicating approval of this research
- Indicate the form of consent obtained (written/oral) or the reason that consent was not obtained (e.g. the data were analyzed anonymously)

Animal Research (involving vertebrate animals, embryos or tissues)
- Provide the name of the Institutional Animal Care and Use Committee (IACUC) or other relevant ethics board that reviewed the study protocol, and indicate whether they approved this research or granted a formal waiver of ethical approval
- Include an approval number if one was obtained
- If the study involved non-human primates, add additional details about animal welfare and steps taken to ameliorate suffering
- If anesthesia, euthanasia, or any kind of animal sacrifice is part of the study, include briefly which substances and/or methods were applied

Field Research

Include the following details if this study involves the collection of plant, animal, or other materials from a natural setting:
- Field permit number
- Name of the institution or relevant body that granted permission

Data Availability

Authors are required to make all data underlying the findings described fully available, without restriction, and from the time of publication. PLOS allows rare exceptions to address legal and ethical concerns. See the PLOS Data Policy and FAQ for detailed information.

Yes - all data are fully available without restriction
A Data Availability Statement describing where the data can be found is required at submission. Your answers to this question constitute the Data Availability Statement and will be published in the article, if accepted.

**Important:** Stating ‘data available on request from the author’ is not sufficient. If your data are only available upon request, select ‘No’ for the first question and explain your exceptional situation in the text box.

Do the authors confirm that all data underlying the findings described in their manuscript are fully available without restriction?

**Describe where the data may be found in full sentences. If you are copying our sample text, replace any instances of XXX with the appropriate details.**

- If the data are **held or will be held in a public repository**, include URLs, accession numbers or DOIs. If this information will only be available after acceptance, indicate this by ticking the box below. For example: *All XXX files are available from the XXX database (accession number(s) XXX, XXX).*

- If the data are all contained **within the manuscript and/or Supporting Information files**, enter the following: *All relevant data are within the manuscript and its Supporting Information files.*

- If neither of these applies but you are able to provide **details of access elsewhere**, with or without limitations, please do so. For example:

  *Data cannot be shared publicly because of [XXX]. Data are available from the XXX Institutional Data Access / Ethics Committee (contact via XXX) for researchers who meet the criteria for access to confidential data.*

  *The data underlying the results presented in the study are available from [include the name of the third party]*
and contact information or URL).

- This text is appropriate if the data are owned by a third party and authors do not have permission to share the data.

* typeset

Additional data availability information:
Increasing pediatric HIV testing positivity rates through focused testing in high-yield points of service in health facilities—Nigeria, 2016-2017

Solomon Odafe¹, Dennis Onotu¹, Johnson Omodele Fagbamigbe¹, Uzoma Ene¹, Emilia Rivadeneira², Deborah Carpenter², Austin I. Omoigberale³, Yakubu Adamu⁴, Ismaila Lawal⁴, Ezekiel James⁵, Andrew T. Boyd⁶, Emilio Dirlikov², Mahesh Swaminathan¹

1. Division of Global HIV and Tuberculosis, Center for Global Health, Centers for Disease Control and Prevention, Abuja, Nigeria
2. Division of Global HIV and Tuberculosis, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA
3. Department of Pediatrics, University of Benin Teaching Hospital, Benin City, Nigeria
4. Walter Reed Army Institute of Research – Military HIV Research Program, Abuja, Nigeria
5. HIV/AIDS Care and Treatment, United States Agency for International Development

Background
In 2017, UNAIDS estimated that 140,000 children aged 0–14 years are living with HIV in Nigeria, but only 35% have been diagnosed and are receiving antiretroviral therapy. Children are tested primarily in outpatient clinics, which show low HIV-positive rates. To demonstrate efficient facility-based HIV testing among children aged 0–14 years, we evaluated pediatric HIV-positivity rates in points of service in select health facilities in Nigeria.

Methods
We conducted a retrospective analysis of HIV testing and case identification among children aged 0–14 years at all points of service at nine purposively sampled hospitals (November 2016–March 2017). Points of service included family index testing, pediatric outpatient department (POPD), tuberculosis (TB) clinics, immunization clinics, and pediatric inpatient ward. Eligibility for testing at POPD was done using a screening tool while all children with unknown status were eligible for HIV test at other points of service. The main outcome was HIV positivity rates stratified by the testing point of service and by age group. Predictors of an HIV-positive result were assessed using logistic regression. All analyses were done using Stata 15 statistical software.

Results
Of 2,180 children seen at all facility points of service with unknown HIV status, 1,822 (83.6%) were tested for HIV, of whom 43 (2.4%) tested HIV positive. The numbers of children tested by age group were <1 years=230 (12.6%); 1-4 years =752 (41.3%); 5-9 years= 520 (28.5%); and 10-14 years= 320 (17.6%). The number of children tested by point of service were POPD=906 (49.7%); family index testing=693 (38.0%); pediatric inpatient ward=192 (10.5%); immunization clinic=16 (0.9%); and TB clinic=15 (0.8%). HIV positivity rates by point of service were TB clinic= 6.7% (95% Confidence Interval (CI): 0.9-35.2%); pediatric inpatient ward=4.7% (95%CI: 2.5-8.8%); family index testing=3.5% (95%CI: 2.3-5.1%); POPD= 1.0% (95%CI: 0.5-1.9%); and immunization clinic=0%. The percentage contribution to total HIV positive children found by point of services was: family index testing= 55.8% (95%CI: 40.9-69.8%);
POPD=20.9% (95%CI: 11.3-35.6%); inpatient ward=20.9 (95%CI: 11.3-35.6%) and TB Clinic=2.3% (95%CI: 0.3-14.8%). Compared with the POPD, the adjusted odds ratio (95% CI) for finding an HIV positive child by point of service were TB clinic=7.2 (95% CI: 0.9-60.9); pediatric inpatient ward=4.9 (95% CI: 1.9-12.8); and family index testing= 3.7 (95% CI: 1.5-8.8). HIV-positivity rates did not significantly differ by age group.

**Conclusion**
In Nigeria, to improve facility-based HIV positivity rates among children aged 0–14 years, an increased focus on HIV testing among children seeking care in pediatric inpatient wards, through family index testing, and perhaps TB clinics is appropriate.
Background

HIV/AIDS has significantly impacted the health of children globally since the beginning of the pandemic [1]. There are about 1.7 million children aged 14 years and below living with HIV worldwide in 2018, and about 54% of them are receiving lifesaving antiretroviral treatment (ART)[2]. In 2018, the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that they were 140,000 children living with HIV in Nigeria[3]. However, compared with global achievements, there have been relatively slower progress in Nigeria with only 35% of HIV infected children receiving ART in 2018 [3].

Government of Nigeria (GON) first commenced the national HIV treatment program in 2002, and with support from the United States (US) government through US President’s Emergency Plan for AIDS Relief (PEPFAR) has significantly expanded HIV care and treatment services in the country [4-6]. The initiation of people living with HIV (PLHIV) on ART in Nigeria was initially restricted to tertiary health centers due to weak health systems in other levels of care. In 2004, following rapid scale-up of ART services and infrastructural upgrades, secondary hospitals began providing ART services to children in Nigeria. However, pediatric HIV treatment coverage in Nigeria lags behind adult HIV treatment coverage [7]. To improve treatment coverage in children, GON adopted the use of family index testing as a key strategy for improving case finding in its accelerated plan for scaling up access to pediatric HIV treatment services between 2016 and 2018 [8]. However, progress with implementation has been slow. A trend analysis of national data indicated that pediatric ART coverage (based on CD4 cell count eligibility criterion of <350 cells/µL) from 2010-2014 improved marginally from 10.2% to 20.7% while the adult ART program reached nearly half of all adults requiring ART in 2014 [7]. The UNAIDS 2018 estimates showed a disproportionately lower treatment coverage in children aged 0-14 years (35%) and in adult males aged 15 years and over (37%) compared with adult females aged 15 years and older (68%)[3]. Major reasons for the disproportionately lower coverage among children include among others, lower HIV testing positivity rates, indicating poorly-targeted HIV testing, and lower linkage to treatment among children.

In 2016, PEPFAR adopted a program strategy geared towards working with GON and other partners to refocus efforts in a small number of prioritized high-burden Local Government Areas (LGAs), designated as “scale-up LGAs”, to achieve HIV epidemic control by the end of the fiscal year 2018 (FY18). This is in line with the ambitious UNAIDS 90-90-90 targets of having 90 percent of PLHIV diagnosed, 90 percent of those diagnosed on ART, and 90 percent of those on ART virally suppressed by 2020. Achieving these targets also demands dramatic progress in closing the treatment gap for children [9], and this requires finding children living with HIV as a first step.

A blanket approach to HIV testing has not worked well for pediatric HIV case identification in HIV programs in Africa [10-12]. In Nigeria, blanket testing has not worked even in high-burden LGAs. As of June 2016, program monitoring results from PEPFAR-supported facilities in scale-up LGAs showed an overall HIV-positivity rate of 1.1% for children aged 0-14 years. The overall HIV-positivity rate for children and adolescents aged 0-19 years tested between October 2015 and September 2016 at all PEPFAR–supported LGAs was 0.8% with a 71% linkage to treatment rate for those who tested positive during this period.
However, published reports from similar setting suggests that a more targeted approach to test may improve testing yield \[13\]. These statistics are indicative of a need for more effective targeted testing strategies in order to improve testing efficiency, by increasing testing yield, and efficacy, by linking more HIV-positive children to care and treatment.

To address the issues of low HIV testing yield and linkage among children, we piloted a pediatric intensive case-finding (PICF) approach at selected health facilities in Nigeria to identify efficient HIV testing points to identify children living with HIV for early ART initiation and to develop effective strategies for scale-up of pediatric HIV case finding and linkage in Nigeria.

Methods

Study Design

This is a retrospective analysis of available program data collected during a PICF pilot in Nigeria.

Study population

Data from all children aged less than 15 years seeking care in selected points of service (POS) in selected secondary level hospitals during the PICF pilot were included in the analysis.

The major outcome measures

The HIV positivity rate among children tested, linkage rate to treatment among children tested positive, HIV results by age group and point of services, the proportion of total positive by point of service, and predictors of HIV positive result among children tested in pilot sites were the main outcome measures. Patients factors included in the model for odds ratio were age group and HIV testing point of service.

Description of sites and process of site selection for pilot

In October 2016, a pediatric program gap analysis was conducted across ART sites in Nigeria by comparing the proportion of HIV positive children on ART with those of adults on ART. The review team looked at the total clients on ART at each site to determine the ratio of children <15 on ART compared to that of adults currently on ART. It was expected that 6% of individuals on ART within each facility should be <15 years, based on the national proportion of children living with HIV among all PLHIV at the time of review (220,000 of 3,400,000 total estimated PLHIV) \[14\]. The pediatric ART gap for each site was calculated by estimating the additional number of children needed to be put on ART to make the ratio up to 6% of total clients currently on ART. The PICF pilot was conducted from November 15, 2016, to March 31, 2017, in selected treatment sites supported by PEPFAR in Nigeria. The selection was guided by the pediatric HIV program gap analysis. Nine secondary level hospitals with the widest gap were selected from the over four hundred treatment sites supported by PEPFAR to participate in the pilot.
Strategies implemented during PICF pilot

Strategies for improving pediatric HIV case identification were implemented at all points of service (POS) for pediatric care seekers at the nine selected hospitals between November 15, 2016, to March 31, 2017. The POS were family index testing, pediatric outpatient department (POPD), tuberculosis (TB) clinics, immunization clinics, and pediatric inpatient ward. The family index testing POS identified new cases through a previously identified case, i.e. children of an HIV positive mother or siblings of an index child. HIV positive mothers were identified during counseling, at the ART clinic, ante-natal clinic, post-natal clinic or outpatient clinics and encouraged to return to the clinic with their children for HIV test. Additionally, parents of a previously identified HIV positive child were also encouraged to bring other children with unknown HIV status for HIV tests. At the TB clinic and pediatric inpatient ward, HIV testing was offered to all children whose parents reported that the child’s HIV status was unknown. Targeted testing in immunization clinics was introduced, based on maternal HIV status; specifically, only infants whose mothers had unknown HIV status or were previously identified as HIV positive were eligible for testing. Finally, at the POPD children were screened to determine their eligibility for an HIV test using the Bandason screening tool. The Bandason screening tool consists of four questions: “Has the child been admitted before?” “Does the child have recurring skin problems?” “Are one or both parents of the child deceased?” and “Has the child had poor health in the last 3 months?” An answer of yes to any of the four screening questions made the child eligible for an HIV test. The health workers at the selected sites were trained on the use of the Bandason screening tool. Advocacy about the PICF pilot was conducted to the leadership and staff of the selected sites and to the host state and local governments where these sites were located. These PICF strategies were piloted at the TB clinics, pediatric inpatient medical wards, adult outpatient clinics among families of identified index cases, POPDs, and the immunization clinics in the selected sites. All children less than 18 months of age were tested using HIV DNA PCR while children greater than 18 months of age were tested using a rapid diagnostic test, in accordance with World Health Organization testing guidelines. The strategy for improving the linkage of newly-diagnosed to ART initiation was accompanied, immediate referral using volunteers to the ART clinic.

Data Analysis

The proportions of children tested and testing HIV positive were analyzed by age group, and percent contributions of each age group to total testing and total identified HIV-positive children were reported with 95% confidence intervals (CI). The proportions of children tested and testing HIV positive were then analyzed by POS. Additionally, the HIV-positivity rates from family index testing, POPD, inpatient ward, and TB clinics at pilot hospitals were reported with 95% CIs. To examine testing efficiency at the POS, we compared the contribution of each POS to the total children tested and total identified HIV-positive children at the sites. To determine the linkage rate we compared the number of children testing HIV positive at the POS of interest, with the number of HIV-positive children started on treatment from that POS. Furthermore, we calculated unadjusted and adjusted (adjusting for testing POS when comparing age
group and for age group when comparing the testing POS) odds ratios for identification of pediatric HIV case by covariates of age group and POS. To account for the clustered design (i.e., design effect of the nine sites for combined analysis), we used a weighted analysis accounting for clustering by site. All analysis was done using Stata 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LP). We accounted for the complex survey design (i.e., clustering and weighting) using svyset and svy procedures in Stata during data analysis.

**Ethics statement**

The study protocol was reviewed and approved by the National Health Research Ethics Committee of Nigeria (NHREC). The protocol received a non-research determination from the US Centers for Disease Control and Prevention (CDC) Atlanta. Patient informed consent was not required as only routine, anonymous, operational monitoring data were collected and analyzed.

**Results**

**HIV testing outputs from all POS by age group**

Information on outputs from the HIV testing service by age group from all POS from the nine pilot sites are summarized in Table 1. A total of 6,747 children who visited the participating secondary level sites during the pilot period were enumerated. Overall, a total of 2,180 (32.3%) of the enumerated children had unknown HIV status. Of those with unknown HIV status, 2,021 (92.7%) had parents or guardians who consented to have them tested for HIV, and among those with consent provided, 1,822 (90.2%) were tested for HIV. Among those tested, 43 (2.4%) of the children were found to be HIV positive. Children in the age group 1 to 4 years contributed the largest proportion (41.3%, [95% CI 39.0-43.6%]) of the total number of children tested. Among those tested, 43 (2.4%) of the children were found to be HIV positive. Children in the age group 1 to 4 years contributed the largest proportion (41.3%, [95% CI 39.0-43.6%]) of the total number of children tested. Among those tested, 43 (2.4%) of the children were found to be HIV positive. Of note, all 43 HIV-positive children identified were linked to ART initiation.

**HIV testing acceptance for all age groups by POS**

The results from the HIV testing service by POS for all age groups and all pilot sites are summarized in Table 2. Of the 2,180 children with unknown HIV status seen at all POS, parents or guardians of 2,021 children (92.7%) accepted that their children be tested for HIV. In family index testing, 807 out of 890 parents (90.7%) gave consent for their children to be tested. Acceptance rates for HIV testing was 76.4%, 95.3%, 99.5% and 100% for immunization clinic, POPD, pediatric inpatient ward and TB clinic respectively.

**HIV testing outputs from all sites by POS**

HIV positivity rates by point of service were TB clinic= 6.7% (95% Confidence Interval (CI): 0.9-35.2%); pediatric inpatient ward=4.7% (95%CI: 2.5-8.8%); family index testing=3.5% (95%CI: 2.3-5.1%); POPD= 1.0% (95%CI: 0.5-1.9%); and immunization clinic=0%. The largest proportion of children tested were from the POPD (49.7% [95%CI: 47.4-52.0%]), followed by family index testing POS (38.0% [35.8-40.3%]).
However, the largest proportion of the total number of HIV-positive children identified were from the family index testing POS (55.8% [95%CI: 40.9-69.8%]), followed by POPD (20.9% [95%CI: 11.3-35.6%]) and the inpatient ward, accounting for 20.9% (95%CI: 11.3-35.6%) of the total number of children testing HIV positive. The TB clinic POS had the highest yield, at 6.7% (0.9-35.2%), but contributed only 2.3% (0.3-14.8%) of the total number of children testing HIV positive.

In examining odds ratios of pediatric HIV case detection by age group, after adjusting for POS, using age group <1 year of age as the control, there was no significant difference in adjusted odds of HIV positivity rate by age group (Table 3). However, in examining odds ratios of pediatric HIV case detection by POS, after adjusting for age, compared with the POPD, the inpatient ward (Adjusted Odds Ratio (AOR) 4.9 (95% CI: 1.9-12.8)) and family index testing POS (AOR: 3.7 (95% CI: 1.5-8.8)) had significantly higher odds for finding a HIV positive child (Table 3). The AOR for TB clinic did not achieve statistical significance, but the magnitude of the effect was large and probably statistical significance was not achieved due to the small number of patients in the TB clinic.

Discussion

Our study found that the pediatric inpatient wards and family index testing POS provided the highest number of HIV-positive children, while still maintaining high HIV positivity rates compared with other POS. The pediatric inpatient ward and family index testing modality also contributed a disproportionately higher amount of total identified HIV-positive children than their contributions to the total HIV testing, a fact supported by significantly higher odds ratios of finding HIV-positive children in these POS compared with that of the POPD. While there were as many children living with HIV identified in the POPD as in the inpatient ward, this result was coupled with a significantly lower yield. Even with the use of the HIV risk screening tool in the POPD, this POS gave a low yield of 1.0%. TB clinics had the highest yield, but TB clinics had fewer absolute numbers of pediatric HIV cases found because there were few pediatric clients seen in that POS. These findings suggest that a focus on pediatric inpatient and family index testing POS as pediatric HIV testing points might be the most efficient approach for HIV testing among children in Nigeria.

The entry point for HIV testing in children influences the proportion of cases found [16-18]. A study by Wagner et al. conducted in Nairobi, Kenya, where HIV-infected adults were encouraged to bring their children for HIV testing (family index testing), found that the rate of pediatric HIV testing increased 3.8-fold from 3.5% to 13.6% [16]. A similar study by Lewis Kulzer et al. conducted in the Nyanza province in Kenya reported that HIV testing through the family index approach increased case detection among children[17]. Both study findings suggest that scaling up family index testing has the potential of improving HIV case detection among children. We also found that the family index testing modality was the most efficient POS for all sites, accounting for about 38% of total children tested but contributing more than half (55.8%) of all the positives identified.

One of the key recommendations of the national acceleration plan for improving pediatric case finding in Nigeria was the use of family index testing[8]. The findings from our study give credence to the
recommended approach in the national acceleration plan. Furthermore, a study conducted in Cameroon that compared case detection in biological children of HIV-positive parents (targeted testing) and other children at the POPD (blanket testing), reported a higher HIV positivity rate of 3.5% in the targeted group compared with 1.6% in the blanket group[10]. The HIV positivity rate of 3.5% among children identified through family index testing in our study was similar to the HIV-positive rate found in biological children of HIV-positive parents in the study in Cameroon[10].

Our study found a relatively high HIV positivity yield of 4.7% among children in the inpatient ward. A study conducted in Zambia among hospitalized children reported a high HIV positivity rate of 29.2% and concluded that the inpatient ward has a huge potential for identifying children with HIV[19]. The differences in HIV positivity rates in our study and the Zambian study was the population HIV prevalence. Whereas Nigeria’s adult population HIV prevalence was 1.5% [14] that for Zambia was 11.3%[20]. Nonetheless, there was a consistently high HIV case finding among children in the inpatient ward in both studies.

PEPFAR program guidance suggests that testing children not only in pediatric wards, and but also in POPDs among children screening as high risk may increase the case detection of HIV-infected children [21]. Our findings suggest that the pediatric inpatient ward was an efficient POS for finding children living with HIV. Although the contribution of inpatient (20.9%) to case finding was similar to POPD (20.9%), a lot more tests had to be done at POPD to find the same number of patients as the inpatient ward. The observed HIV positivity yield of 1% at POPD in our study using the Bandason tool was much lower than the reported HIV positivity yield of 4% at POPD by Yumo et al using a symptoms-based testing strategy in Cameroon[10]. The differences in HIV positivity rates were due to differences in general population HIV prevalence, the adult HIV prevalence in Cameroon is much higher, 3.6% compared with 1.5% in Nigeria[3, 22, 23]. In both studies, the HIV test results at POPD was similar to the population HIV prevalence. However, considering the relatively large number of children that needed to be tested to find a positive case at the POPD despite the use of a screening tool in our study, there is a need to re-assess the validity of the Bandason screening tool in low HIV prevalence settings like Nigeria and among children, less than six years since the Bandason tool was only tested for children above six years[12].

Additionally, we found the highest HIV positivity rate (6.7%) and the highest adjusted odds ratio for finding a positive result among children at the TB clinic. In a much larger study among children infected with TB conducted by Tilahun et al in Ethiopia, 291 children were tested for HIV and 28.2% of them were HIV positive[24]. Our findings suggest all children in TB clinic should be tested for HIV, but TB clinic cannot be counted on to provide high absolute numbers of children living with HIV.

In our study we observed that all the children identified through the POS were also initiated on treatment, giving a linkage to treatment rate of 100%. The sites employed a strategy of accompanied referral, which used volunteers to immediately accompany parents or guardians and newly diagnosed children to ART POS to ensure all children identified HIV positive were linked to treatment. The
approach assisted parents/guardians to quickly navigate the ART clinic and obtain care for their children. The excellent linkage rate observed in our study was comparable to those reported for a South African ART program that utilized escort services to facilitate linkage to treatment among HIV positive adults, and scale-up of this approach in the Nigeria HIV program will ensure that identified HIV-positive children are offered ART [25].

We found HIV testing acceptance rates of 76.4%, 90.7%, 95.3%, 99.5% and 100% for parents/guardians at immunization clinic, family index testing, POPD, inpatient ward and TB clinic respectively. A systematic review of several studies conducted mainly in Kenya and Uganda by Govindasamy et al reported the highest acceptance of HIV testing (86.3%) by parents/guardians at inpatient wards and lowest acceptance (51.7%) in the family index modality [26]. Compared with reports by Govindasamy et al, with the exception of the immunization clinic, our study found a much higher HIV testing acceptance rate among all the provider-initiated testing and counseling POS. The finding suggests that the pre-test counseling provided for families of at-risk pediatric patients at our study sites was effective. Furthermore, a study conducted in Cameroon by Yumo et al reported high HIV testing acceptance rates for children among both HIV-positive parents (99.7%) and other guardians/parents at POPD (98.8%). In our study, HIV acceptance rates were comparable to those reported by Yumo et al for Cameroon[10].

However, even with this high acceptance by guardians to have at-risk pediatric patients tested for HIV, we found that there were missed opportunities for testing at the immunization clinic and at the family index testing POS. We found that 76.4% of mothers accepted the HIV test for their babies but only 16.5% of children with unknown status at the immunization clinic were eventually tested for HIV. A systematic review examining HIV testing in immunization clinics in children reported an acceptance rate of 89.5 to 100%. However, in that systematic review, only about 56.8% to 86.0% of the children were eventually tested [27]. While the acceptance of HIV testing in the immunization clinic in our study was only slightly lower than that in the systematic review, the percentage of children tested at immunization clinics in our study was much lower than those previously reported. While previous studies have reported that immunization clinic may be a promising area for identifying and testing HIV exposed children in high HIV prevalence settings [28, 29], the low HIV positivity rate among children tested at the immunization clinics in our study suggests that scaling up testing at immunization clinic as it is currently done may not be an efficient way to find pediatric HIV cases.

There were also missed opportunities at the family index testing POS. About 24% of children with unknown status identified through the family index POS were not tested for HIV. However, the percentage of children with unknown status that was not tested (24%) in our study was much lower than the 43.3% reported by Yumo et al for neighboring Cameroon[30]. A major reason for the missed opportunity was that at this POS, the method for getting these children tested was simply to ask parents to return to the clinic with the children, and parents often did not return with their children for HIV testing as scheduled. A similar factor played a role in the high missed opportunity in the study in Cameroun[10]. The researchers insinuated that the reason for the high missed opportunity in their study was because parents initially came for their own care and did not have their children with them at
the time of accepting to test their children and eventually failed to follow through[10]. Our study did not investigate the reasons for the failure of parents or guardians to return with their children. However, a previous study in Nigeria found that HIV infection among family income earners adversely affects families socioeconomically and impacts on parents’ ability to continue to seek health services for their children, including for family index testing [28]. This suggests that a home-based HIV testing and counseling approach for children of consenting parents/guardian, or health outreach workers going to the home to conduct testing of children, may be required for the successful implementation of the family index testing.

In examining the pediatric HIV testing cascade by age group in our study, it is noteworthy that although the age group <1 year had the most children accessing care, it also had the lowest proportion of children with unknown HIV status, and lowest percentage testing HIV positive. This may be because all sites involved in our study had a PMTCT program. Studies have demonstrated that PMTCT programs increase HIV test rates during ante-natal care in pregnant women, promote uptake of antiretroviral drugs during pregnancy and promote HIV testing among HIV exposed infants [31-34]. We found that the percentage of contributions by age group to total children tested were closely aligned to the proportions contributed to total HIV positive found. This finding was further supported by no statistically significant difference in odds ratios for finding an HIV-positive child by age group. Thus, our findings do not support program emphasis on a specific age group. That said, because of a greater proportion of children with an unknown HIV status among 1-4-year-olds, the largest number of HIV cases were found among this age group. This indicates the need for health providers to consider HIV risk stratification for all children irrespective of age if no HIV status is documented when they present at a health facility.

The strength of our study is the data from a large number of samples of children analyzed in the study. However, the purposive nature of site selection limits the generability of the findings from our analysis. Additionally, other POS with the potential to give high positivity yields, such as malnutrition clinics, were not thoroughly assessed in our study. Nonetheless, the findings provide important insights into how HIV positivity rates and testing efficiency can be improved by focusing on testing and ensuring linkage, in targeted POS in health facilities.

**Conclusion**

The pilot of pediatric intensified case finding demonstrated that the family index testing POS, followed by pediatric inpatient testing, was the most efficient testing streams for HIV testing among children. Specifically, these modalities identified high numbers of children living with HIV while maintaining high HIV positivity rates. Furthermore, while the POPD was an important testing point for identifying high numbers of HIV positive children, yield was poor, even with the application of a validated screening tool for identifying children at risk for having HIV. Testing among children attending TB clinic gives high yield but low absolute numbers. The study findings suggested that to improve facility-based HIV positivity rates among children aged 0–14 years in Nigeria, an increased focus on offering and ensuring HIV testing through family index testing, offering testing to all children in pediatric inpatient wards who do
not know status, testing in POPD only if targeted using a validated screening tool tailored to the population, and among all children attending TB clinics is appropriate. This focus, coupled with the continuation of the 100% linkage to ART initiation among these children in the study, will allow Nigeria to make progress in closing the pediatric ART treatment gap.

Acknowledgment

This work was supported by the President’s Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control and Prevention (CDC) under the terms of GH002097, GH002098, GH002099 and GH002100.

Disclaimer

The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the views of the United States (U.S.) Centers for Disease Control and Prevention. The use of trade names is for identification only and does not imply endorsement by the U.S. Centers for Disease Control and Prevention or the U.S. Department of Health and Human Services.
References

1. Abrams EJ, Simonds RJ, Modi S, Rivadeneira E, Vaz P, Kankasa C, et al. PEPFAR scale-up of pediatric HIV services: innovations, achievements, and challenges. J Acquir Immune Defic Syndr. 2012;60 Suppl 3:S105-12. doi:10.1097/QAI.0b013e31825cf4f5. PubMed PMID: 22797731; PubMed Central PMCID: PMCPMC4941954.
2. UNICEF. Paediatric care and treatment New York: UNICEF; 2019 [cited 2020 January 8]. Available from: https://data.unicef.org/topic/hivaids/paediatric-treatment-and-care/.
3. UNAIDS. Country factsheets: Nigeria Geneva: UNAIDS; 2019 [cited 2020 January 8]. Available from: https://www.unaids.org/en/regionscountries/countries/nigeria.
4. Dalhatu I, Onotu D, Odae S, Abiri O, Debem H, Agolory S, et al. Correction: Outcomes of Nigeria's HIV/AIDS Treatment Program for Patients Initiated on Antiretroviral Treatment between 2004-2012. PloS one. 2017;12(1):e0170912. doi: 10.1371/journal.pone.0170912. PubMed PMID: 28114385; PubMed Central PMCID: PMC5256961.
5. Auld AF, Shiraishi RW, Oboho I, Ross C, Bateganya M, Pelletier V, et al. Trends in Prevalence of Advanced HIV Disease at Antiretroviral Therapy Enrollment - 10 Countries, 2004-2015. MMWR Morbidity and mortality weekly report. 2017;66(21):558-63. doi: 10.15585/mmwr.mm6621a3. PubMed PMID: 28570507; PubMed Central PMCID: PMC5657820.
6. Odae S, Idoko O, Badru T, Aiyenigba B, Suzuki C, Khamofu H, et al. Patients' demographic and clinical characteristics and level of care associated with lost to follow-up and mortality in adult patients on first-line ART in Nigerian hospitals. Journal of the International AIDS Society. 2012;15(2):17424. doi: 10.7448/IAS.15.2.17424. PubMed PMID: 23010378; PubMed Central PMCID: PMC3494164.
7. FMoH. National Acceleration Plan for Paediatric HIV Treatment and Care 2016-2018. In: Division HA, editor. Abuja: FMOH; 2016.
8. Federal Ministry of Health. National Accelerated Plan for Paediatric HIV Treatment and Care. In: National AIDS and Sexually Transmitted Disease Control Programme, editor. Abuja: Federal Ministry of Health, ; 2016.
9. UNAIDS. 90-90-90.An Ambitious Treatment Target to Help End the AIDS Epidemic. Geneva: UNAIDS; 2014 [cited 2017 March, 31st]. Available from: http://www.unaids.org/en/resources/documents/2014/90-90-90.
10. Yumo HA, Kuaban C, Ajeh RA, Nji AM, Nash D, Kathryn A, et al. Active case finding: comparison of the acceptability, feasibility and effectiveness of targeted versus blanket provider-initiated-testing and counseling of HIV among children and adolescents in Cameroon. BMC Pediatr. 2018;18(1):309. Epub 2018/09/27. doi: 10.1186/s12887-018-1276-7. PubMed PMID: 30253758; PubMed Central PMCID: PMCPMC6156944.
11. Ahmed S, Kim MH, Sugandhi N, Phelps BR, Sabelli R, Diallo MO, et al. Beyond early infant diagnosis: case finding strategies for identification of HIV-infected infants and children. Aids. 2013;27 Suppl 2:S235-45. doi: 10.1097/QAD.0000000000000099. PubMed PMID: 24361633; PubMed Central PMCID: PMC4122794.
12. Bandason T, McHugh G, Dauya E, Munafua S, Munyati SM, Weiss HA, et al. Validation of a screening tool to identify older children living with HIV in primary care facilities in high HIV prevalence settings. AIDS. 2016;30(5):779-85. Epub 2015/11/21. doi: 10.1097/QAD.0000000000000959. PubMed PMID: 26588175; PubMed Central PMCID: PMCPMC4937807.
13. Moucheraud C, Chasweka D, Nyirenda M, Schooley A, Doval K, Hoffman RM. Simple Screening Tool to Help Identify High-Risk Children for Targeted HIV Testing in Malawian Inpatient Wards. Journal of acquired immune deficiency syndromes. 2018;79(3):352-7. Epub 2018/07/12. doi: 10.1097/QAI.0000000000001804. PubMed PMID: 29995704.
14. UNAIDS. Country factsheets Nigeria Geneva: UNAIDS; 2019 [cited 2019 21st January]. Available from: http://www.unaids.org/en/regionscountries/countries/nigeria.
15. World Health Organization. HIV Testing Services: 5Cs: Consent, Confidentiality, Counseling, Correct Results and Connection. Geneva: WHO; 2015. p. 91-110.
16. Wagner AD, Mugo C, Nguguna IN, Maleche-Obimbo E, Sherr K, Inwani IW, et al. Implementation and Operational Research: Active Referral of Children of HIV-Positive Adults Reveals High Prevalence of Undiagnosed HIV. J Acquir Immune Defic Synrd. 2016;73(5):e83-9. Epub 2016/11/16. doi: 10.1097/QAI.0000000000001184. PubMed PMID: 27846074; PubMed Central PMCID: PMCPMC5175406.
17. Lewis Kulzer J, Penner JA, Marima R, Oyaro P, Oyanga AO, Shade SB, et al. Family model of HIV care and treatment: a retrospective study in Kenya. J Int AIDS Soc. 2012;15(1):8. Epub 2012/02/23. doi: 10.1186/1758-2652-15-8. PubMed PMID: 22335553; PubMed Central PMCID: PMCPMC3298805.

18. Luyirika E, Twomey MS, Achan J, Muhangi J, Senyimba C, Lule F, et al. Scaling up paediatric HIV care with an integrated, family-centred approach: an observational case study from Uganda. PLoS One. 2013;8(8):e69548. doi: 10.1371/journal.pone.0069548. PubMed PMID: 23936337; PubMed Central PMCID: PMCPMC3735564.

19. Kankasa C, Carter RJ, Briggs N, Bulterys M, Chama E, Cooper ER, et al. Routine offering of HIV testing to hospitalized pediatric patients at university teaching hospital, Lusaka, Zambia: acceptability and feasibility. J Acquir Immune Defic Syndr. 2009;51(2):202-8. Epub 2009/06/09. doi: 10.1097/qai.0b013e31819c173f. PubMed PMID: 19504732; PubMed Central PMCID: PMCPMC5117627.

20. UNAIDS. HIV and AIDS Estimates Geneva: UNAIDS; 2019 [cited 2020 January 20.]. Available from: https://www.unaids.org/en/regionscountries/countries/zambia.

21. (CDC) CfDCaP. Strategies for identifying and linking HIV-infected Infants, Children, and Adolescents to HIV Care and Treatment. In: Health CfG, editor. Atlanta PEPFAR; 2015. p. 4-5.

22. UNAIDS. Country HIV Factsheet: Cameroon Geneva: UNAIDS; 2019 [cited January 29, 2020]. Available from: https://www.unaids.org/en/regionscountries/countries/cameroon.

23. UNICEF. Key demographic indicators: Cameroon New York: UNICEF; 2020 [cited 2020 January 29]. Available from: https://data.unicef.org/country/cmr/.

24. Tilahun G, Gebre-Selassie S. Treatment outcomes of childhood tuberculosis in Addis Ababa: a five-year retrospective analysis. BMC Public Health. 2016;16:612. Epub 2016/07/23. doi: 10.1186/s12889-016-3193-8. PubMed PMID: 27443308; PubMed Central PMCID: PMCPMC4957362.

25. Shamu S, Slabbert J, Guloba G, Blom D, Khupakonke S, Masihleho N, et al. Linkage to care of HIV positive clients in a community based HIV counselling and testing programme: A success story of non-governmental organisations in a South African district. PLoS one. 2019;14(1):e0210826. Epub 2019/01/23. doi: 10.1371/journal.pone.0210826. PubMed PMID: 30668598; PubMed Central PMCID: PMCPMC6342293.

26. Govindasamy D, Ferrand RA, Wilmore SM, Ford N, Ahmed S, Afnan-Holmes H, et al. Uptake and yield of HIV testing and counselling among children and adolescents in sub-Saharan Africa: a systematic review. Journal of the International AIDS Society. 2015;18:20182. doi: 10.7448/IAS.18.1.20182. PubMed PMID: 26471265; PubMed Central PMCID: PMC4607700.

27. Chamla D, Luo C, Adjorlolo-Johnson G, Vandelaer J, Young M, Costales MO, et al. Integration of HIV infant testing into immunization programmes: a systematic review. Paediatrics and international child health. 2015;35(4):298-304. doi: 10.1080/20469047.2015.1109233. PubMed PMID: 26744153.

28. Oluwagbemiga AE. HIV/AIDS and family support systems: A situation analysis of people living with HIV/AIDS in Lagos State. SAHARA J : journal of Social Aspects of HIV/AIDS Research Alliance. 2007;4(3):668-77. PubMed PMID: 18185894.

29. Rollins N, Mzolo S, Moodley T, Esterhuizen T, Rooyen Hv. Universal HIV testing of infants at immunization clinics: an acceptable and feasible approach for early infant diagnosis in high HIV prevalence settings. Aids. 2009;23(14):1851-7. Epub 2009/09/10. doi: 10.1097/QAD.0b013e32832d84fd.

30. Yumo HA, Ajeah RA, Beissner M, Ndenkeh JN, Jr., Sieleunou I, Jordan MR, et al. Effectiveness of symptom-based diagnostic HIV testing versus targeted and blanket provider-initiated testing and counseling among children and adolescents in Cameroon. PLoS One. 2019;14(5):e0214251. Epub 2019/05/07. doi: 10.1371/journal.pone.0214251. PubMed PMID: 31059507; PubMed Central PMCID: PMCPMC6502453.

31. Vrazo AC, Sullivan D, Ryan Phelps B. Eliminating Mother-to-Child Transmission of HIV by 2030: 5 Strategies to Ensure Continued Progress. Glob Health Sci Pract. 2018;6(2):249-56. Epub 2018/07/01. doi: 10.9745/GHSP-D-17-00097. PubMed PMID: 29959270; PubMed Central PMCID: PMCPMC6024627.

32. Sau MS, Balamane M, Lurie M, Harwell J, Welle E, Mean C, et al. Assessment of Prevention of Mother-to-Child Transmission HIV Services in the Bantry Meanchey Province in Cambodia. J Int Assoc Provid AIDS Care. 2016;15(4):345-9. Epub 2015/09/05. doi: 10.1177/2325957415599208. PubMed PMID: 26337679; PubMed Central PMCID: PMCPMC4828308.
33. Thorne C, Aebi-Popp K. Beyond prevention of mother-to-child HIV transmission. Lancet HIV. 2016;3(1):e5-6. Epub 2016/01/15. doi: 10.1016/S2352-3018(15)00243-X. PubMed PMID: 26762994.

34. van Lettow M, Landes M, van Oosterhout JJ, Schouten E, Phiri H, Nkhoma E, et al. Prevention of mother-to-child transmission of HIV: a cross-sectional study in Malawi. Bull World Health Organ. 2018;96(4):256-65. Epub 2018/04/27. doi: 10.2471/BLT.17.203265. PubMed PMID: 29695882; PubMed Central PMCID: PMCPMC5872011.
### Table 1: HIV testing pediatric cascade by age group across all PICF pilot sites

| Indicator                                                                 | Age Group in Years | <1 year | 1-4 yrs. | 5-9 yrs. | 10-14 yrs. | Total   |
|---------------------------------------------------------------------------|---------------------|---------|----------|----------|------------|---------|
| Number children enumerated (N)                                            |                     | 3,164   | 1,400    | 1,254    | 929        | 6,747   |
| Number children with Unknown HIV status and eligible for HIV test (n [col %]) |                     | 382 (12.1%) | 851 (60.8%) | 575 (45.9%) | 372 (40.0%) | 2,180 (32.3%) |
| Number children with Unknown HIV status whose guardian consented for HIV test (n [col %]) |                     | 332 (86.9%) | 833 (97.9%) | 521 (90.6%) | 335 (90.1%) | 2,021 (92.7%) |
| # Tested (n [col %])                                                      |                     | 230 (69.3%) | 752 (90.3%) | 520 (99.8%) | 320 (95.5%) | 1,822 (90.2%) |
| # Tested HIV+ (n [col %])                                                 |                     | 4 (1.7%)   | 19 (2.5%)  | 12 (2.3%)  | 8 (2.5%)    | 43 (2.4%)  |
| # Initiated on ART (n [col %])                                            |                     | 4 (100%)    | 19 (100%)  | 12 (100%)  | 8 (100%)    | 43 (100%)  |
| Testing yield (%[95%CI])                                                  |                     | 1.7% (0.7-4.6) | 2.5% (1.6-3.9) | 2.3% (1.3-4.0) | 2.5% (1.3-4.9) | 2.4% (1.8-3.2) |
| Age group percent contribution to total HIV testing (%[95%CI])            |                     | 12.6% (11.2-14.2) | 41.3% (39.0-43.6) | 28.5% (26.5-30.7) | 17.6% (15.9-19.4) | 100%     |
| Age group percent contribution to total HIV+                              |                     | 9.3% (3.5-22.3)  | 44.2% (30.2-59.1) | 27.9% (16.6-43.0) | 18.6% (9.6-33.0) | 100%     |
Table 2: HIV testing pediatric cascade by points of service across all PICF pilot sites

| Indicator                                                                 | Family index modality | POPD | TB clinic | Immunization clinic | Inpatient ward | Total       |
|---------------------------------------------------------------------------|-----------------------|------|-----------|---------------------|----------------|-------------|
| Number children enumerated (N)                                            | 2,509                 | 1,098| 44        | 2,835               | 257            | 6,743*      |
| Number children with Unknown HIV status and eligible for HIV test (n [col %]) | 890 (35.5%)           | 955 (87.0%) | 15 (34.1%) | 127 (4.5%)          | 193 (75.1%)    | 2,180 (32.3%) |
| Number children with Unknown HIV status whose guardian consented for HIV test (n [col %]) | 807 (90.7%)          | 910 (95.3%) | 15 (100%)  | 97 (76.4%)          | 192 (99.5%)    | 2,021 (92.7%) |
| # Tested (n [col %])                                                      | 693 (85.9%)           | 906 (99.6%) | 15 (100%)  | 16 (16.0%)          | 192 (100%)     | 1,822 (90.2%) |
| # Tested HIV+ (n [col %])                                                 | 24 (3.5%)             | 9 (1.0%)   | 1 (6.7%)   | 0 (0%)              | 9 (4.7%)       | 43 (2.4%)   |
| # Initiated on ART (n [col %])                                            | 24 (100%)             | 9 (100%)   | 1 (100%)   | 0 (0%)              | 9 (100%)       | 43 (100%)   |
| Testing yield (%[95%CI])                                                  | 3.5% (2.3-5.1)        | 1.0% (0.5-1.9) | 6.7% (0.9-35.2) | 0 (0%) | 4.7% (2.5-8.8) | 2.4% (1.8-3.2) |
| Point of service percent contribution to total HIV testing (%[95%CI])     | 38.0% (35.8-40.3)     | 49.7% (47.4-52.0) | 0.8% (0.27-3.1) | 0.9% (0.5-1.4) | 10.5% (9.2-12.0) | 100%        |
| Point of service percent contribution to total HIV+ (%[95%CI])            | 55.8% (40.9-69.8)     | 20.9% (11.3-35.6) | 2.3% (0.3-14.8) | 0 (0%)              | 20.9% (11.3-35.6) | 100%        |

*Four patients enumerated in malnutrition clinic but not tested were not included in the table*
Table 3: Unadjusted and adjusted odds ratios of pediatric HIV case detection by patient age group and POS

| Patient Characteristics | Unadjusted Odds ratio (95%CI) | Adjusted Odds ratio (95%CI) |
|-------------------------|-------------------------------|-----------------------------|
| **Age group**           |                               |                             |
| <1 year                 | 1                             | 1                           |
| 1-4 years               | 1.5 (0.5 - 4.3)               | 1.2 (0.3 – 4.1)             |
| 5-9 years               | 1.3 (0.4 - 4.2)               | 1.1 (0.3 – 4.3)             |
| 10-14 years             | 1.4 (0.4 - 4.9)               | 0.9 (0.2 – 4.4)             |
| **POS**                 |                               |                             |
| POPD                    | 1                             | 1                           |
| Family index            | 3.6 (1.7 - 7.7)               | 3.7 (1.5 – 8.8)             |
| Inpatient ward          | 4.9 (1.9 - 12.5)              | 4.9 (1.9 – 12.8)            |
| TB clinic               | 7.1 (0.8 - 60.2)              | 7.2 (0.9 – 60.9)            |
Click here to access/download
**Supporting Information**
PICF minimal dataset.xls
Increasing pediatric HIV testing positivity rates through focused testing in high-yield points of service in health facilities—Nigeria, 2016-2017

Solomon Odafe, Dennis Onotu, Johnson Omodele Fagbamigbe, Uzoma Ene, Emilia Rivadeneira, Deborah Carpenter, Austin I. Omoigberale, Yakubu Adamu, Ismaila Lawal, Ezekiel James, Andrew T. Boyd, Emilio Dirlikov, Mahesh Swaminathan

1. Division of Global HIV and Tuberculosis, Center for Global Health, Centers for Disease Control and Prevention, Abuja, Nigeria
2. Division of Global HIV and Tuberculosis, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA
3. Department of Pediatrics, University of Benin Teaching Hospital, Benin City, Nigeria
4. Walter Reed Army Institute of Research – Military HIV Research Program, Abuja, Nigeria
5. HIV/AIDS Care and Treatment, United States Agency for International Development

Background

In 2017, UNAIDS estimated that 140,000 children aged 0–14 years are living with HIV in Nigeria, but only 35% have been diagnosed and are receiving antiretroviral therapy. Children are tested primarily in outpatient clinics, which show low HIV-positive rates. To demonstrate efficient facility-based HIV testing among children aged 0–14 years, we evaluated pediatric HIV-positivity rates in points of service in select health facilities in Nigeria.

Methods

We conducted a retrospective analysis of HIV testing and case identification among children aged 0–14 years at all points of service at nine purposively sampled hospitals (November 2016–March 2017). Points of service included family index testing, pediatric outpatient department (POPD), tuberculosis (TB) clinics, immunization clinics, and pediatric inpatient ward. Eligibility for testing at POPD was done using a screening tool while all children with unknown status were eligible for HIV test at other points of service. The main outcome was HIV positivity rates stratified by the testing point of service and by age group. Predictors of an HIV-positive result were assessed using logistic regression. All analyses were done using Stata 15 statistical software.

Results

Of 2,180 children seen at all facility points of service with unknown HIV status, 1,822 (83.6%) were tested for HIV, of whom 43 (2.4%) tested HIV positive. The numbers of children tested by age group were <1 years = 230 (12.6%); 1-4 years = 752 (41.3%); 5-9 years = 520 (28.5%); and 10-14 years = 320 (17.6%). The number of children tested by point of service were POPD = 906 (49.7%); family index testing = 693 (38.0%); pediatric inpatient ward = 192 (10.5%); immunization clinic = 16 (0.9%); and TB clinic = 15 (0.8%). HIV positivity rates by point of service were TB clinic = 6.7% (95% Confidence Interval (CI): 0.9–35.2%); pediatric inpatient ward = 4.7% (95%CI: 2.5–8.8%); family index testing = 3.5% (95%CI: 2.3–5.1%); POPD = 1.0% (95%CI: 0.5–1.9%); and immunization clinic = 0%. The percentage contribution to total HIV positive children found by point of services was: family index testing = 55.8% (95%CI: 40.9–69.8%);
POPD=20.9% (95%CI: 11.3-35.6%); inpatient ward=20.9 (95%CI: 11.3-35.6%) and TB Clinic=2.3% (95%CI: 0.3-14.8%). Compared with the POPD, the adjusted odds ratio (95% CI) for finding an HIV positive child by point of service were TB clinic=7.2 (95% CI: 0.9-60.9); pediatric inpatient ward=4.9 (95% CI: 1.9-12.8); and family index testing= 3.7 (95% CI: 1.5-8.8). HIV-positivity rates did not significantly differ by age group.

**Conclusion**
In Nigeria, to improve facility-based HIV positivity rates among children aged 0–14 years, an increased focus on HIV testing among children seeking care in pediatric inpatient wards, through family index testing, and perhaps TB clinics is appropriate.
Background

HIV/AIDS has significantly impacted the health of children globally since the beginning of the pandemic [1]. There are about 1.7 million children aged 14 years and below living with HIV worldwide in 2018, and about 54% of them are receiving lifesaving antiretroviral treatment (ART)[2]. In 2018, the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that they were 140,000 children living with HIV in Nigeria[3]. However, compared with global achievements, there have been relatively slower progress in Nigeria with only 35% of HIV infected children receiving ART in 2018 [3].

Government of Nigeria (GON) first commenced the national HIV treatment program in 2002, and with support from the United States (US) government through US President’s Emergency Plan for AIDS Relief (PEPFAR) has significantly expanded HIV care and treatment services in the country [4-6]. The initiation of people living with HIV (PLHIV) on ART in Nigeria was initially restricted to tertiary health centers due to weak health systems in other levels of care. In 2004, following rapid scale-up of ART services and infrastructural upgrades, secondary hospitals began providing ART services to children in Nigeria. However, pediatric HIV treatment coverage in Nigeria lags behind adult HIV treatment coverage [7]. To improve treatment coverage in children, GON adopted the use of family index testing as a key strategy for improving case finding in its accelerated plan for scaling up access to pediatric HIV treatment services between 2016 and 2018 [8]. However, progress with implementation has been slow. A trend analysis of national data indicated that pediatric ART coverage (based on CD4 cell count eligibility criterion of <350 cells/µL) from 2010-2014 improved marginally from 10.2% to 20.7% while the adult ART program reached nearly half of all adults requiring ART in 2014 [7]. The UNAIDS 2018 estimates showed a disproportionately lower treatment coverage in children aged 0-14 years (35%) and in adult males aged 15 years and over (37%) compared with adult females aged 15 years and older (68%)[3]. Major reasons for the disproportionately lower coverage among children include among others, lower HIV testing positivity rates, indicating poorly-targeted HIV testing, and lower linkage to treatment among children.

In 2016, PEPFAR adopted a program strategy geared towards working with GON and other partners to refocus efforts in a small number of prioritized high–burden Local Government Areas (LGAs), designated as “scale-up LGAs”, to achieve HIV epidemic control by the end of the fiscal year 2018 (FY18). This is in line with the ambitious UNAIDS 90-90-90 targets of having 90 percent of PLHIV diagnosed, 90 percent of those diagnosed on ART, and 90 percent of those on ART virally suppressed by 2020. Achieving these targets also demands dramatic progress in closing the treatment gap for children [9], and this requires finding children living with HIV as a first step.

A blanket approach to HIV testing has not worked well for pediatric HIV case identification in HIV programs in Africa [10-12]. In Nigeria, blanket testing has not worked even in high-burden LGAs. As of June 2016, program monitoring results from PEPFAR-supported facilities in scale-up LGAs showed an overall HIV-positivity rate of 1.1% for children aged 0-14 years. The overall HIV-positivity rate for children and adolescents aged 0-19 years tested between October 2015 and September 2016 at all PEPFAR–supported LGAs was 0.8% with a 71% linkage to treatment rate for those who tested positive during this period.
However, published reports from similar setting suggests that a more targeted approach to test may improve testing yield [13]. These statistics are indicative of a need for more effective targeted testing strategies in order to improve testing efficiency, by increasing testing yield, and efficacy, by linking more HIV-positive children to care and treatment.

To address the issues of low HIV testing yield and linkage among children, we piloted a pediatric intensive case-finding (PICF) approach at selected health facilities in Nigeria to identify efficient HIV testing points to identify children living with HIV for early ART initiation and to develop effective strategies for scale-up of pediatric HIV case finding and linkage in Nigeria.

**Methods**

**Study Design**

This is a retrospective analysis of available program data collected during a PICF pilot in Nigeria.

**Study population**

Data from all children aged less than 15 years seeking care in selected points of service (POS) in selected secondary level hospitals during the PICF pilot were included in the analysis.

**The major outcome measures**

The HIV positivity rate among children tested, linkage rate to treatment among children tested positive, HIV results by age group and point of services, the proportion of total positive by point of service, and predictors of HIV positive result among children tested in pilot sites were the main outcome measures. Patients factors included in the model for odds ratio were age group and HIV testing point of service.

**Description of sites and process of site selection for pilot**

In October 2016, a pediatric program gap analysis was conducted across ART sites in Nigeria by comparing the proportion of HIV positive children on ART with those of adults on ART. The review team looked at the total clients on ART at each site to determine the ratio of children <15 on ART compared to that of adults currently on ART. It was expected that 6% of individuals on ART within each facility should be <15 years, based on the national proportion of children living with HIV among all PLHIV at the time of review (220,000 of 3,400,000 total estimated PLHIV) [14]. The pediatric ART gap for each site was calculated by estimating the additional number of children needed to be put on ART to make the ratio up to 6% of total clients currently on ART. The PICF pilot was conducted from November 15, 2016, to March 31, 2017, in selected treatment sites supported by PEPFAR in Nigeria. The selection was guided by the pediatric HIV program gap analysis. Nine secondary level hospitals with the widest gap were selected from the over four hundred treatment sites supported by PEPFAR to participate in the pilot.
Strategies implemented during PICF pilot

Strategies for improving pediatric HIV case identification were implemented at all points of service (POS) for pediatric care seekers at the nine selected hospitals between November 15, 2016, to March 31, 2017. The POS were family index testing, pediatric outpatient department (POPD), tuberculosis (TB) clinics, immunization clinics, and pediatric inpatient ward. The family index testing POS identified new cases through a previously identified case, i.e. children of an HIV positive mother or siblings of an index child. HIV positive mothers were identified during counseling, at the ART clinic, ante-natal clinic, post-natal clinic or outpatient clinics and encouraged to return to the clinic with their children for HIV test. Additionally, parents of a previously identified HIV positive child were also encouraged to bring other children with unknown HIV status for HIV tests. At the TB clinic and pediatric inpatient ward, HIV testing was offered to all children whose parents reported that the child’s HIV status was unknown. Targeted testing in immunization clinics was introduced, based on maternal HIV status; specifically, only infants whose mothers had unknown HIV status or were previously identified as HIV positive were eligible for testing. Finally, at the POPD children were screened to determine their eligibility for an HIV test using the Bandason screening tool [12]. The Bandason screening tool consists of four questions [12]: “Has the child been admitted before?” “Does the child have recurring skin problems?” “Are one or both parents of the child deceased?” and “Has the child had poor health in the last 3 months?” An answer of yes to any of the four screening questions made the child eligible for an HIV test. The health workers at the selected sites were trained on the use of the Bandason screening tool. Advocacy about the PICF pilot was conducted to the leadership and staff of the selected sites and to the host state and local governments where these sites were located. These PICF strategies were piloted at the TB clinics, pediatric inpatient medical wards, adult outpatient clinics among families of identified index cases, POPDs, and the immunization clinics in the selected sites. All children less than 18 months of age were tested using HIV DNA PCR while children greater than 18 months of age were tested using a rapid diagnostic test, in accordance with World Health Organization testing guidelines [15]. The strategy for improving the linkage of newly-diagnosed to ART initiation was accompanied, immediate referral using volunteers to the ART clinic.

Data Analysis

The proportions of children tested and testing HIV positive were analyzed by age group, and percent contributions of each age group to total testing and total identified HIV-positive children were reported with 95% confidence intervals (CI). The proportions of children tested and testing HIV positive were then analyzed by POS. Additionally, the HIV-positivity rates from family index testing, POPD, inpatient ward, and TB clinics at pilot hospitals were reported with 95% CIs. To examine testing efficiency at the POS, we compared the contribution of each POS to the total children tested and total identified HIV-positive children at the sites. To determine the linkage rate we compared the number of children testing HIV positive at the POS of interest, with the number of HIV-positive children started on treatment from that POS. Furthermore, we calculated unadjusted and adjusted (adjusting for testing POS when comparing age
group and for age group when comparing the testing POS) odds ratios for identification of pediatric HIV case by covariates of age group and POS. To account for the clustered design (i.e., design effect of the nine sites for combined analysis), we used a weighted analysis accounting for clustering by site. All analysis was done using Stata 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LP). We accounted for the complex survey design (i.e., clustering and weighting) using svyset and svy procedures in Stata during data analysis.

**Ethics statement**

The study protocol was reviewed and approved by the National Health Research Ethics Committee of Nigeria (NHREC). The protocol received a non-research determination from the US Centers for Disease Control and Prevention (CDC) Atlanta. Patient informed consent was not required as only routine, anonymous, operational monitoring data were collected and analyzed.

**Results**

**HIV testing outputs from all POS by age group**

Information on outputs from the HIV testing service by age group from all POS from the nine pilot sites are summarized in Table 1. A total of 6,747 children who visited the participating secondary level sites during the pilot period were enumerated. Overall, a total of 2,180 (32.3%) of the enumerated children had unknown HIV status. Of those with unknown HIV status, 2,021 (92.7%) had parents or guardians who consented to have them tested for HIV, and among those with consent provided, 1,822 (90.2%) were tested for HIV. Among those tested, 43 (2.4%) of the children were found to be HIV positive. Children in the age group 1 to 4 years contributed the largest proportion (41.3%, [95% CI 39.0-43.6%]) of the total number of children tested, followed by children in the age group 5 to 9 years (28.5%, [26.5-30.7%]). Similarly, children in the age groups 1 to 4 years and 5 to 9 years contributed 44.2% (30.2-59.1%) and 27.9% (16.6-43.0%) of the total number of children that tested HIV positive. Of note, all 43 HIV-positive children identified were linked to ART initiation.

**HIV testing acceptance for all age groups by POS**

The results from the HIV testing service by POS for all age groups and all pilot sites are summarized in Table 2. Of the 2,180 children with unknown HIV status seen at all POS, parents or guardians of 2,021 children (92.7%) accepted that their children be tested for HIV. In family index testing, 807 out of 890 parents (90.7%) gave consent for their children to be tested. Acceptance rates for HIV testing was 76.4%, 95.3%, 99.5% and 100% for immunization clinic, POPD, pediatric inpatient ward and TB clinic respectively.

**HIV testing outputs from all sites by POS**

HIV positivity rates by point of service were TB clinic= 6.7% (95% Confidence Interval (CI): 0.9-35.2%); pediatric inpatient ward=4.7% (95%CI: 2.5-8.8%); family index testing=3.5% (95%CI: 2.3-5.1%); POPD=1.0% (95%CI: 0.5-1.9%); and immunization clinic=0%. The largest proportion of children tested were from the POPD (49.7% [95%CI: 47.4-52.0%]), followed by family index testing POS (38.0% [35.8-40.3%]).
However, the largest proportion of the total number of HIV-positive children identified were from the family index testing POS (55.8% [95%CI: 40.9-69.8%]), followed by POPD (20.9% [95%CI: 11.3-35.6%]) and the inpatient ward, accounting for 20.9% (95%CI: 11.3-35.6%) of the total number of children testing HIV positive. The TB clinic POS had the highest yield, at 6.7% (0.9-35.2%), but contributed only 2.3% (0.3-14.8%) of the total number of children testing HIV positive.

In examining odds ratios of pediatric HIV case detection by age group, after adjusting for POS, using age group <1 year of age as the control, there was no significant difference in adjusted odds of HIV positivity rate by age group (Table 3). However, in examining odds ratios of pediatric HIV case detection by POS, after adjusting for age, compared with the POPD, the inpatient ward (Adjusted Odds Ratio (AOR) 4.9 (95% CI: 1.9-12.8)) and family index testing POS (AOR: 3.7 (95% CI: 1.5-8.8)) had significantly higher odds for finding a HIV positive child (Table 3). The AOR for TB clinic did not achieve statistical significance, but the magnitude of the effect was large and probably statistical significance was not achieved due to the small number of patients in the TB clinic.

Discussion

Our study found that the pediatric inpatient wards and family index testing POS provided the highest number of HIV-positive children, while still maintaining high HIV positivity rates compared with other POS. The pediatric inpatient ward and family index testing modality also contributed a disproportionately higher amount of total identified HIV-positive children than their contributions to the total HIV testing, a fact supported by significantly higher odds ratios of finding HIV-positive children in these POS compared with that of the POPD. While there were as many children living with HIV identified in the POPD as in the inpatient ward, this result was coupled with a significantly lower yield. Even with the use of the HIV risk screening tool in the POPD, this POS gave a low yield of 1.0%. TB clinics had the highest yield, but TB clinics had fewer absolute numbers of pediatric HIV cases found because there were few pediatric clients seen in that POS. These findings suggest that a focus on pediatric inpatient and family index testing POS as pediatric HIV testing points might be the most efficient approach for HIV testing among children in Nigeria.

The entry point for HIV testing in children influences the proportion of cases found [16-18]. A study by Wagner et al. conducted in Nairobi, Kenya, where HIV-infected adults were encouraged to bring their children for HIV testing (family index testing), found that the rate of pediatric HIV testing increased 3.8-fold from 3.5% to 13.6% [16]. A similar study by Lewis Kulzer et al. conducted in the Nyanza province in Kenya reported that HIV testing through the family index approach increased case detection among children[17]. Both study findings suggest that scaling up family index testing has the potential of improving HIV case detection among children. We also found that the family index testing modality was the most efficient POS for all sites, accounting for about 38% of total children tested but contributing more than half (55.8%) of all the positives identified.

One of the key recommendations of the national acceleration plan for improving pediatric case finding in Nigeria was the use of family index testing[8]. The findings from our study give credence to the
recommended approach in the national acceleration plan. Furthermore, a study conducted in Cameroon that compared case detection in biological children of HIV-positive parents (targeted testing) and other children at the POPD (blanket testing), reported a higher HIV positivity rate of 3.5% in the targeted group compared with 1.6% in the blanket group[10]. The HIV positivity rate of 3.5% among children identified through family index testing in our study was similar to the HIV-positive rate found in biological children of HIV-positive parents in the study in Cameroon[10].

Our study found a relatively high HIV positivity yield of 4.7% among children in the inpatient ward. A study conducted in Zambia among hospitalized children reported a high HIV positivity rate of 29.2% and concluded that the inpatient ward has a huge potential for identifying children with HIV[19]. The differences in HIV positivity rates in our study and the Zambian study was the population HIV prevalence. Whereas Nigeria’s adult population HIV prevalence was 1.5% [14] that for Zambia was 11.3%[20]. Nonetheless, there was a consistently high HIV case finding among children in the inpatient ward in both studies.

PEPFAR program guidance suggests that testing children not only in pediatric wards, and but also in POPDs among children screening as high risk may increase the case detection of HIV-infected children [21]. Our findings suggest that the pediatric inpatient ward was an efficient POS for finding children living with HIV. Although the contribution of inpatient (20.9%) to case finding was similar to POPD (20.9%), a lot more tests had to be done at POPD to find the same number of patients as the inpatient ward. The observed HIV positivity yield of 1% at POPD in our study using the Bandason tool was much lower than the reported HIV positivity yield of 4% at POPD by Yumo et al using a symptoms-based testing strategy in Cameroon[10]. The differences in HIV positivity rates were due to differences in general population HIV prevalence, the adult HIV prevalence in Cameroon is much higher, 3.6% compared with 1.5% in Nigeria[3, 22, 23]. In both studies, the HIV test results at POPD was similar to the population HIV prevalence. However, considering the relatively large number of children that needed to be tested to find a positive case at the POPD despite the use of a screening tool in our study, there is a need to re-assess the validity of the Bandason screening tool in low HIV prevalence settings like Nigeria and among children, less than six years since the Bandason tool was only tested for children above six years[12].

Additionally, we found the highest HIV positivity rate (6.7%) and the highest adjusted odds ratio for finding a positive result among children at the TB clinic. In a much larger study among children infected with TB conducted by Tilahun et al in Ethiopia, 291 children were tested for HIV and 28.2% of them were HIV positive[24]. Our findings suggest all children in TB clinic should be tested for HIV, but TB clinic cannot be counted on to provide high absolute numbers of children living with HIV.

In our study we observed that all the children identified through the POS were also initiated on treatment, giving a linkage to treatment rate of 100%. The sites employed a strategy of accompanied referral, which used volunteers to immediately accompany parents or guardians and newly diagnosed children to ART POS to ensure all children identified HIV positive were linked to treatment. The
approach assisted parents/guardians to quickly navigate the ART clinic and obtain care for their children.

The excellent linkage rate observed in our study was comparable to those reported for a South African ART program that utilized escort services to facilitate linkage to treatment among HIV positive adults, and scale-up of this approach in the Nigeria HIV program will ensure that identified HIV-positive children are offered ART [25].

We found HIV testing acceptance rates of 76.4%, 90.7%, 95.3%, 99.5% and 100% for parents/guardians at immunization clinic, family index testing, POPD, inpatient ward and TB clinic respectively. A systematic review of several studies conducted mainly in Kenya and Uganda by Govindasamy et al reported the highest acceptance of HIV testing (86.3%) by parents/guardians at inpatient wards and lowest acceptance (51.7%) in the family index modality [26]. Compared with reports by Govindasamy et al, with the exception of the immunization clinic, our study found a much higher HIV testing acceptance rate among all the provider-initiated testing and counseling POS. The finding suggests that the pre-test counseling provided for families of at-risk pediatric patients at our study sites was effective.

Furthermore, a study conducted in Camerooun by Yumo et al reported high HIV testing acceptance rates for children among both HIV-positive parents (99.7%) and other guardians/parents at POPD (98.8%). In our study, HIV acceptance rates were comparable to those reported by Yumo et al for Camerooun[10].

However, even with this high acceptance by guardians to have at-risk pediatric patients tested for HIV, we found that there were missed opportunities for testing at the immunization clinic and at the family index testing POS. We found that 76.4% of mothers accepted the HIV test for their babies but only 16.5% of children with unknown status at the immunization clinic were eventually tested for HIV. A systematic review examining HIV testing in immunization clinics in children reported an acceptance rate of 89.5 to 100%. However, in that systematic review, only about 56.8% to 86.0% of the children were eventually tested [27]. While the acceptance of HIV testing in the immunization clinic in our study was only slightly lower than that in the systematic review, the percentage of children tested at immunization clinics in our study was much lower than those previously reported. While previous studies have reported that immunization clinic may be a promising area for identifying and testing HIV exposed children in high HIV prevalence settings [28, 29], the low HIV positivity rate among children tested at the immunization clinics in our study suggests that scaling up testing at immunization clinic as it is currently done may not be an efficient way to find pediatric HIV cases.

There were also missed opportunities at the family index testing POS. About 24% of children with unknown status identified through the family index POS were not tested for HIV. However, the percentage of children with unknown status that was not tested (24%) in our study was much lower than the 43.3% reported by Yumo et al for neighboring Camerooun[30]. A major reason for the missed opportunity was that at this POS, the method for getting these children tested was simply to ask parents to return to the clinic with the children, and parents often did not return with their children for HIV testing as scheduled. A similar factor played a role in the high missed opportunity in the study in Camerooun[10]. The researchers insinuated that the reason for the high missed opportunity in their study was because parents initially came for their own care and did not have their children with them at
the time of accepting to test their children and eventually failed to follow through[10]. Our study did not investigate the reasons for the failure of parents or guardians to return with their children. However, a previous study in Nigeria found that HIV infection among family income earners adversely affects families socioeconomically and impacts on parents’ ability to continue to seek health services for their children, including for family index testing [28]. This suggests that a home-based HIV testing and counseling approach for children of consenting parents/guardian, or health outreach workers going to the home to conduct testing of children, may be required for the successful implementation of the family index testing.

In examining the pediatric HIV testing cascade by age group in our study, it is noteworthy that although the age group <1 year had the most children accessing care, it also had the lowest proportion of children with unknown HIV status, and lowest percentage testing HIV positive. This may be because all sites involved in our study had a PMTCT program. Studies have demonstrated that PMTCT programs increase HIV test rates during ante-natal care in pregnant women, promote uptake of antiretroviral drugs during pregnancy and promote HIV testing among HIV exposed infants[31-34]. We found that the percentage of contributions by age group to total children tested were closely aligned to the proportions contributed to total HIV positive found. This finding was further supported by no statistically significant difference in odds ratios for finding an HIV-positive child by age group. Thus, our findings do not support program emphasis on a specific age group. That said, because of a greater proportion of children with an unknown HIV status among 1-4-year-olds, the largest number of HIV cases were found among this age group. This indicates the need for health providers to consider HIV risk stratification for all children irrespective of age if no HIV status is documented when they present at a health facility.

The strength of our study is the data from a large number of samples of children analyzed in the study. However, the purposive nature of site selection limits the generability of the findings from our analysis. Additionally, other POS with the potential to give high positivity yields, such as malnutrition clinics, were not thoroughly assessed in our study. Nonetheless, the findings provide important insights into how HIV positivity rates and testing efficiency can be improved by focusing on testing and ensuring linkage, in targeted POS in health facilities.

**Conclusion**

The pilot of pediatric intensified case finding demonstrated that the family index testing POS, followed by pediatric inpatient testing, was the most efficient testing streams for HIV testing among children. Specifically, these modalities identified high numbers of children living with HIV while maintaining high HIV positivity rates. Furthermore, while the POPD was an important testing point for identifying high numbers of HIV positive children, yield was poor, even with the application of a validated screening tool for identifying children at risk for having HIV. Testing among children attending TB clinic gives high yield but low absolute numbers. The study findings suggested that to improve facility-based HIV positivity rates among children aged 0–14 years in Nigeria, an increased focus on offering and ensuring HIV testing through family index testing, offering testing to all children in pediatric inpatient wards who do
not know status, testing in POPD only if targeted using a validated screening tool tailored to the population, and among all children attending TB clinics is appropriate. This focus, coupled with the continuation of the 100% linkage to ART initiation among these children in the study, will allow Nigeria to make progress in closing the pediatric ART treatment gap.

**Acknowledgment**

This work was supported by the President’s Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control and Prevention (CDC) under the terms of GH002097, GH002098, GH002099 and GH002100.

**Disclaimer**

The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the views of the United States (U.S.) Centers for Disease Control and Prevention. The use of trade names is for identification only and does not imply endorsement by the U.S. Centers for Disease Control and Prevention or the U.S. Department of Health and Human Services.
References

1. Abrams EJ, Simonds RJ, Modi S, Rivadeneira E, Vaz P, Kankasa C, et al. PEPFAR scale-up of pediatric HIV services: innovations, achievements, and challenges. J Acquir Immune Defic Syndr. 2012;60 Suppl 3:S105-12. doi: 10.1097/QAI.0b013e31825cf4f5. PubMed PMID: 22797731; PubMed Central PMCID: PMCPMC4941954.

2. UNICEF. Paediatric care and treatment New York: UNICEF; 2019 [cited 2020 January 8]. Available from: https://data.unicef.org/topic/hiv/aids/paediatric-treatment-and-care/.

3. UNAIDS. Country factsheets Nigeria Geneva: UNAIDS; 2019 [cited 2020 January 8]. Available from: https://www.unaids.org/en/regionscountries/countries/nigeria.

4. Dalhatu I, Onotu D, Odafe S, Abiri O, Debem H, Agolory S, et al. Correction: Outcomes of Nigeria’s HIV/AIDS Treatment Program for Patients Initiated on Antiretroviral Treatment between 2004-2012. PloS one. 2017;12(1):e0170912. doi: 10.1371/journal.pone.0170912. PubMed PMID: 28114385; PubMed Central PMCID: PMCS256961.

5. Auld AF, Shiraishi RW, Oboho I, Ross C, Bateganya M, Pelletier V, et al. Trends in Prevalence of Advanced HIV Disease at Antiretroviral Therapy Enrollment - 10 Countries, 2004-2015. MMWR Morbidity and mortality weekly report. 2017;66(21):558-63. doi: 10.15585/mmwr.mm6621a3. PubMed PMID: 28570507; PubMed Central PMCID: PMCP567820.

6. Odafe S, Idoko O, Badru T, Aiyenigba B, Suzuki C, Khamofu H, et al. Patients’ demographic and clinical characteristics and level of care associated with lost to follow-up and mortality in adult patients on first-line ART in Nigerian hospitals. Journal of the International AIDS Society. 2012;15(2):17424. doi: 10.7448/IAS.15.2.17424. PubMed PMID: 23010378; PubMed Central PMCID: PMCS494164.

7. FMOH. National Acceleration Plan for Paediatric HIV Treatment and Care 2016-2018. In: Division HA, editor. Abuja: FMOH; 2016.

8. Federal Ministry of Health. National Accelerated Plan for Paediatric HIV Treatment and Care. In: National AIDS and Sexually Transmitted Disease Control Programme, editor. Abuja: Federal Ministry of Health, ; 2016.

9. UNAIDS. 90-90-90.An Ambitious Treatment Target to Help End the AIDS Epidemic. Geneva: UNAIDS; 2014 [cited 2017 March, 31st]. Available from: http://www.unaids.org/en/resources/documents/2014/90-90-90.

10. Yumo HA, Kuaban C, Ajeh RA, Nji AM, Nash D, Kathryn A, et al. Active case finding: comparison of the acceptability, feasibility and effectiveness of targeted versus blanket provider-initiated-testing and counseling of HIV among children and adolescents in Cameroon. BMC Pediatr. 2018;18(1):309. Epub 2018/09/27. doi: 10.1186/s12887-018-1276-7. PubMed PMID: 30253758; PubMed Central PMCID: PMCPMC6156944.

11. Ahmed S, Kim MH, Sugandhi N, Phelps BR, Sabelli R, Diało MO, et al. Beyond early infant diagnosis: case finding strategies for identification of HIV-infected infants and children. AIDS. 2013;27 Suppl 2:S235-45. doi: 10.1097/QAD.0000000000000099. PubMed PMID: 24361633; PubMed Central PMCID: PMC4122794.

12. Bandason T, McHugh G, Dauya E, Mungofa S, Munyati SM, Weiss HA, et al. Validation of a screening tool to identify older children living with HIV in primary care facilities in high HIV prevalence settings. AIDS. 2016;30(5):779-85. Epub 2015/11/21. doi: 10.1097/QAD.0000000000000959. PubMed PMID: 26588175; PubMed Central PMCID: PMCPMC4937807.

13. Moucheraud C, Chasweka D, Nyirenda M, Schooley A, Dovel K, Hoffman RM. Simple Screening Tool to Help Identify High-Risk Children for Targeted HIV Testing in Malawian Inpatient Wards. Journal of acquired immune deficiency syndromes. 2018;79(3):352-7. Epub 2018/07/12. doi: 10.1097/QAI.0000000000001804. PubMed PMID: 29995704.

14. UNAIDS. Country factsheets Nigeria Geneva: UNAIDS; 2019 [cited 2020 January 8]. Available from: http://www.unaids.org/en/regionscountries/countries/nigeria.

15. World Health Organization. HIV Testing Services: 5Cs: Consent, Confidentiality, Counseling, Correct Results and Connection. Geneva: WHO; 2015. p. 91-110.

16. Wagner AD, Mugo C, Njuguna IN, Maleche-Obimbo E, Sherr K, Inwani IW, et al. Implementation and Operational Research: Active Referral of Children of HIV-Positive Adults Reveals High Prevalence of Undiagnosed HIV. J Acquir Immune Defic Syndr. 2016;73(5):e83-e9. Epub 2016/11/16. doi: 10.1097/QAI.0000000000001184. PubMed PMID: 27846074; PubMed Central PMCID: PMCPMC5175406.
17. Lewis Kulzer J, Penner JA, Marima R, Oyaro P, Oyang AO, Shade SB, et al. Family model of HIV care and treatment: a retrospective study in Kenya. J Int AIDS Soc. 2012;15(1):8. Epub 2012/02/23. doi: 10.1186/1758-2652-15-8. PubMed PMID: 22353553; PubMed Central PMCID: PMCPMC3298805.

18. Luyirika E, Twole MS, Achan J, Muhangi J, Senyimba C, Lule F, et al. Scaling up paediatric HIV care with an integrated, family-centred approach: an observational case study from Uganda. PLoS One. 2013;8(8):e69548. doi: 10.1371/journal.pone.0069548. PubMed PMID: 23936337; PubMed Central PMCID: PMCPMC3735564.

19. Kankasa C, Carter RJ, Briggs N, Bulterys M, Chama E, Cooper ER, et al. Routine offering of HIV testing to hospitalized pediatric patients at university teaching hospital, Lusaka, Zambia: acceptability and feasibility. J Acquir Immune Defic Syndr. 2009;51(2):202-8. Epub 2009/06/09. doi: 10.1097/qai.0b013e31819c173f. PubMed PMID: 19504732; PubMed Central PMCID: PMCPMC5117627.

20. UNAIDS. HIV and AIDS Estimates Geneva: UNAIDS; 2019 [cited 2020 January 20]. Available from: https://www.unaids.org/en/regionscountries/countries/zambia.

21. (CDC) CfDCaP. Strategies for identifying and linking HIV-infected Infants, Children, and Adolescents to HIV Care and Treatment. In: Health CfG, editor. Atlanta PEPFAR; 2015. p. 4-5.

22. UNAIDS. Country HIV Factsheet: Cameroon Geneva: UNAIDS; 2019 [cited January 29, 2020]. Available from: https://www.unaids.org/en/regionscountries/countries/cameroun.

23. UNICEF. Key demographic indicators: Cameroon New York: UNICEF; 2020 [cited 2020 January 29]. Available from: https://data.unicef.org/country/cmr/.

24. Tilahun G, Gebre-Selassie S. Treatment outcomes of childhood tuberculosis in Addis Ababa: a five-year retrospective analysis. BMC Public Health. 2016;16:612. Epub 2016/07/23. doi: 10.1186/s12889-016-3193-8. PubMed PMID: 27443308; PubMed Central PMCID: PMCPMC4957362.

25. Shamu S, Slabbert J, Guloba G, Blom D, Khupakonke S, Masihleho N, et al. Linkage to care of HIV positive clients in a community based HIV counselling and testing programme: A success story of non-governmental organisations in a South African district. PLoS one. 2019;14(1):e0210826. Epub 2019/01/23. doi: 10.1371/journal.pone.0210826. PubMed PMID: 30668598; PubMed Central PMCID: PMCPMC6342293.

26. Govindasamy D, Ferrand RA, Wilmore SM, Ford N, Ahmed S, Afnan-Holmes H, et al. Uptake and yield of HIV testing and counselling among children and adolescents in sub-Saharan Africa: a systematic review. Journal of the International AIDS Society. 2015;18:20182. doi: 10.7448/IAS.18.1.20182. PubMed PMID: 26471265; PubMed Central PMCID: PMCPMC4607700.

27. Chamla D, Luo C, Adjorlolo-Johnson G, Vandelaaer J, Young M, Costales MO, et al. Integration of HIV infant testing into immunization programmes: a systematic review. Paediatrics and international child health. 2015;35(4):298-304. doi: 10.1080/20469047.2015.1109233. PubMed PMID: 26744153.

28. Oluwagbemiga AE. HIV/AIDS and family support systems: A situation analysis of people living with HIV/AIDS in Lagos State. SAHARA J : journal of d international child health. 2007;4(3):668-77. PubMed PMID: 18185894.

29. Rollins N, Mzolo S, Moodley T, Esterhuizen T, Rooyen Hv. Universal HIV testing of infants at immunization clinics: an acceptable and feasible approach for early infant diagnosis in high HIV prevalence settings. Aids. 2009;23(14):1851-7. Epub 2009/09/10. doi: 10.1097/QAD.0b013e32832d84fd

30. Yumo HA, Ajeh RA, Beissner M, Ndenkeh JN, Jr., Sieleunou I, Jordan MR, et al. Effectiveness of symptom-based diagnostic HIV testing versus targeted and blanket provider-initiated testing and counseling among children and adolescents in Cameroon. PLoS One. 2019;14(5):e0214251. Epub 2019/05/07. doi: 10.1371/journal.pone.0214251. PubMed PMID: 31059507; PubMed Central PMCID: PMCPMC6502453.

31. Vrazo AC, Sullivan D, Ryan Phelps B. Eliminating Mother-to-Child Transmission of HIV by 2030: 5 Strategies to Ensure Continued Progress. Glob Health Sci Pract. 2018;6(2):249-56. Epub 2018/07/01. doi: 10.9745/GHSP-D-17-00097. PubMed PMID: 29959270; PubMed Central PMCID: PMCPMC6024627.

32. Sau MS, Balamane M, Lurie M, Harwell J, Welle E, Mean C, et al. Assessment of Prevention of Mother-to-Child Transmission HIV Services in the Bantey Meanchey Province in Cambodia. J Int Assoc Provid AIDS Care. 2016;15(4):345-9. Epub 2015/09/05. doi: 10.1177/2325957415599208. PubMed PMID: 26337679; PubMed Central PMCID: PMCPMC4828308.
33. Thorne C, Aebi-Popp K. Beyond prevention of mother-to-child HIV transmission. Lancet HIV. 2016;3(1):e5-6. Epub 2016/01/15. doi: 10.1016/S2352-3018(15)00243-X. PubMed PMID: 26762994.

34. van Lettow M, Landes M, van Oosterhout JJ, Schouten E, Phiri H, Nkhoma E, et al. Prevention of mother-to-child transmission of HIV: a cross-sectional study in Malawi. Bull World Health Organ. 2018;96(4):256-65. Epub 2018/04/27. doi: 10.2471/BLT.17.203265. PubMed PMID: 29695882; PubMed Central PMCID: PMCPMC5872011.
Table 1: HIV testing pediatric cascade by age group across all PICF pilot sites

| Indicator                                                                 | Age Group in Years | <1 year | 1-4 yrs. | 5-9 yrs. | 10-14 yrs. | Total   |
|---------------------------------------------------------------------------|--------------------|---------|----------|----------|------------|---------|
| Number children enumerated (N)                                           |                    | 3,164   | 1,400    | 1,254    | 929        | 6,747   |
| Number children with Unknown HIV status and eligible for HIV test (n [col %]) |                    | 382 (12.1%) | 851 (60.8%) | 575 (45.9%) | 372 (40.0%) | 2,180 (32.3%) |
| Number children with Unknown HIV status whose guardian consented for HIV test (n [col %]) |                    | 332 (86.9%) | 833 (97.9%) | 521 (90.6%) | 335 (90.1%) | 2,021 (92.7%) |
| # Tested (n [col %])                                                      |                    | 230 (69.3%) | 752 (90.3%) | 520 (99.8%) | 320 (95.5%) | 1,822 (90.2%) |
| # Tested HIV+ (n [col %])                                                |                    | 4 (1.7%)   | 19 (2.5%)  | 12 (2.3%)  | 8 (2.5%)    | 43 (2.4%)  |
| # Initiated on ART (n [col %])                                           |                    | 4 (100%)   | 19 (100%)  | 12 (100%)  | 8 (100%)    | 43 (100%)  |
| Testing yield (%[95%CI])                                                 |                    | 1.7% (0.7-4.6) | 2.5% (1.6-3.9) | 2.3% (1.3-4.0) | 2.5% (1.3-4.9) | 2.4% (1.8-3.2) |
| Age group percent contribution to total HIV testing (%[95%CI])           |                    | 12.6% (11.2-14.2) | 41.3% (39.0-43.6) | 28.5% (26.5-30.7) | 17.6% (15.9-19.4) | 100%    |
| Age group percent contribution to total HIV+                              |                    | 9.3% (3.5-22.3) | 44.2% (30.2-59.1) | 27.9% (16.6-43.0) | 18.6% (9.6-33.0) | 100%    |
### Table 2: HIV testing pediatric cascade by points of service across all PICF pilot sites

| Indicator                                                                 | Family index modality | POPD | TB clinic | Immunization clinic | Inpatient ward | Total      |
|---------------------------------------------------------------------------|-----------------------|------|-----------|--------------------|----------------|------------|
| Number children enumerated (N)                                            | 2,509                 | 1,098| 44        | 2,835              | 257            | 6,743*     |
| Number children with Unknown HIV status and eligible for HIV test (n [col %]) | 890 (35.5%)            | 955 (87.0%)     | 15 (34.1%)  | 127 (4.5%)         | 193 (75.1%)    | 2,180 (32.3%) |
| Number children with Unknown HIV status whose guardian consented for HIV test (n [col %]) | 807 (90.7%)          | 910 (95.3%)      | 15 (100%)   | 97 (76.4%)         | 192 (99.5%)    | 2,021 (92.7%) |
| # Tested (n [col %])                                                     | 693 (85.9%)            | 906 (99.6%)    | 15 (100%)   | 16 (16.0%)         | 192 (100%)     | 1,822 (90.2%) |
| # Tested HIV+ (n [col %])                                                | 24 (3.5%)              | 9 (1.0%)       | 1 (6.7%)    | 0 (0%)             | 9 (4.7%)       | 43 (2.4%)   |
| # Initiated on ART (n [col %])                                           | 24 (100%)             | 9 (100%)      | 1 (100%)    | 0 (0%)             | 9 (100%)       | 43 (100%)   |
| Testing yield (%[95%CI])                                                 | 3.5% (2.3-5.1)        | 1.0% (0.5-1.9) | 6.7% (0.9-35.2) | 0 (0%) | 4.7% (2.5-8.8) | 2.4% (1.8-3.2) |
| Point of service percent contribution to total HIV testing (%[95%CI])    | 38.0% (35.8-40.3)     | 49.7% (47.4-52.0) | 0.8% (0.27-3.1) | 0.9% (0.5-1.4) | 10.5% (9.2-12.0) | 100% |
| Point of service percent contribution to total HIV+ (%[95%CI])           | 55.8% (40.9-69.8)     | 20.9% (11.3-35.6) | 2.3% (0.3-14.8) | 0 (0%)           | 20.9% (11.3-35.6) | 100% |

*Four patients enumerated in malnutrition clinic but not tested were not included in the table*
| Patient Characteristics | Unadjusted Odds ratio (95%CI) | Adjusted Odds ratio (95%CI) |
|-------------------------|------------------------------|-----------------------------|
| **Age group**           |                              |                             |
| <1 year                 | 1                            | 1                           |
| 1-4 years               | 1.5 (0.5 - 4.3)              | 1.2 (0.3 – 4.1)             |
| 5-9 years               | 1.3 (0.4 - 4.2)              | 1.1 (0.3 – 4.3)             |
| 10-14 years             | 1.4 (0.4 - 4.9)              | 0.9 (0.2 – 4.4)             |
| **POS**                 |                              |                             |
| POPD                    | 1                            | 1                           |
| Family index            | 3.6 (1.7 - 7.7)              | 3.7 (1.5 – 8.8)             |
| Inpatient ward          | 4.9 (1.9 - 12.5)             | 4.9 (1.9 – 12.8)            |
| TB clinic               | 7.1 (0.8 - 60.2)             | 7.2 (0.9 – 60.9)            |
Response to Reviewers’ Comments

Reviewer 3 Comments and Authors’ responses:

Reviewer #3: The authors have adequately addressed my comments raised in a previous version but for reference #10 which is not well cited in line 288. Here is the correct reference: https://doi.org/10.1371/journal.pone.0214251. Please, note that even though this article is from the same author (Yumo et al.), it’s different from reference #10 well cited for example in line 271. Please, amend this reference number and the references list as well.

Authors’ response:
We have made the required changes to the reference. Please review the lines 298 and 442 to 445 of the Tracked version of the revised manuscript. The journal is now correctly cited as reference #30 in line 298 and correctly referenced in lines 442 to 445.