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## Correlates of suboptimal entry into early infant diagnosis in rural north central Nigeria

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### INTRODUCTION

Despite efforts to halt mother-to-child transmission of HIV, incident pediatric HIV infections continue to occur, especially in sub-Saharan Africa (SSA). In 2011, 90% of the 390,000 new pediatric HIV cases worldwide were in SSA, and nearly all infections were acquired via vertical transmission.<sup>1</sup> The early initiation of HIV-infected infants on antiretroviral therapy (ART) is associated with better clinical and immunological outcomes and improved survival.<sup>3-7</sup> Yet early ART initiation in children is only achievable if HIV-infected infants are identified via Early Infant Diagnosis (EID) testing. This task is proving daunting; in 2012, only a third of HIV-exposed infants across reporting countries underwent EID testing.<sup>2</sup> EID coverage was even worse in SSA, where 6 of 31 countries reported EID testing rates below 10%, resulting in millions of undiagnosed HIV-exposed infants.<sup>2,8</sup> ART coverage among HIV-infected children in 2012 was also approximately half the coverage for adults (34% vs. 64%, respectively).<sup>2</sup>

Nigeria has the second-largest number of persons living with HIV in the world and is a major contributor to the global epidemic of pediatric HIV/AIDS. Despite an estimated 59,000 children being newly infected with HIV in Nigeria in 2012 alone,<sup>2</sup> EID service uptake remains extremely poor.<sup>9</sup> Nigeria national guidelines recommend EID testing at 6

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weeks postpartum, but HIV-1 DNA PCR testing for EID was performed in only 4% of eligible infants by 2 months of age in 2010.<sup>10</sup> ART coverage among HIV-infected Nigerian children in 2010 was also a paltry 12%.<sup>2</sup> Low uptake of EID may be due in part to low uptake of antenatal and postnatal care services by pregnant women,<sup>11</sup> lack of service availability at rural clinical sites,<sup>12</sup> as well as social and educational barriers that limit women's ability to access these services.<sup>13-15</sup> Other contributory factors include: limited number of centralized laboratories with requisite capacity to perform DNA PCR testing, long turn-around times, stock-outs of reagents and consumables, and logistical challenges with getting results back to facilities/healthcare providers. One of the goals of Nigeria's national PMTCT scale-up plan is to provide at least 90% of all HIV-exposed infants with access to EID services by 2015.<sup>16</sup> Accomplishing this goal will require changes to health care delivery that adequately address the mentioned barriers and contributing factors impeding EID uptake in Nigeria.

The Vanderbilt Institute for Global Health (VIGH) was funded from 2008-2013 through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) to assist in provision of comprehensive HIV/AIDS services in the Federal Capital Territory (FCT, Abuja) and rural parts of Kwara and Niger states in north-central Nigeria. Whereas several studies describing experiences with implementation of EID programs in SSA exist,<sup>17-21</sup> there is a dearth of peer-reviewed reports from Nigeria, one of the 22 "Global Plan" focus countries.<sup>22</sup> The aim of this study is to describe the characteristics of pregnant women enrolled in HIV care and treatment in VIGH-supported clinics in rural north central Nigeria, characterize those women who bring their HIV-exposed infants for EID, and to determine the maternal correlates associated with initiation of EID. Lessons learnt from rural Nigeria can help inform EID programming, family and community engagement, and quality improvement efforts in similarly challenging environments.

## METHODS

### Study design and setting

This is an observational study utilizing routinely-collected HIV/AIDS program data from our PEPFAR-supported comprehensive HIV/AIDS program in Niger and Kwara states, described in more detail elsewhere.<sup>23, 24</sup> North-central Nigeria is a region of the country with an adult HIV prevalence of 7.5% compared to the national HIV prevalence of 3.6%.<sup>25</sup> The prevalence of HIV among pregnant women in Niger and Kwara states is estimated to be 4.0% and 2.2%, respectively.<sup>25</sup>

As of October 2013, VIGH/FGH supported HIV/AIDS services in seven secondary level facilities, namely: Sobi Specialist Hospital and Lafiagi General Hospital in Kwara state; Gawu Babangida Rural Hospital, Kuta Rural Hospital, Umaru Yar Adua Memorial Hospital and IBB Hospital in Niger State; and State House Clinic in Abuja. The six clinics in Niger and Kwara states are served by rural HTC/PMTCT feeder sites ('satellite' sites) in a 'hub and spoke' model. HIV care and treatment services commenced at three hospitals in 2009 (Gawu Babangida Rural Hospital, Lafiagi General Hospital and Sobi Specialist Hospital), at two hospitals in 2010 (Umaru Yar Adua Memorial Hospital and Kuta Rural Hospital), and at the State House Clinic in 2011.

## Study population

This analysis uses data collected through September 30, 2013 and includes HIV-infected pregnant patients entering HIV care and treatment at 12 years of age and older. To ensure that mothers had enough time to carry the baby to term and go for EID, only women enrolled into our PMTCT program on or before December 31, 2012 were included in the study.

## Care and treatment protocol

Friends in Global Health, LLC, (FGH), Vanderbilt University's non-governmental affiliate served as the implementing partner for the HIV/AIDS service program run by the states' Ministries of Health. Supported activities were organized around direct technical assistance to government health facilities and human capacity development. Services were supported in the following program areas: adult and pediatric HIV care and treatment, prevention of mother-to-child HIV transmission (PMTCT), HIV testing and counseling (HTC), TB-HIV co-infection, orphans and vulnerable children, pharmaceutical logistics (i.e., procurement and provision of antiretroviral drugs [ARVs]), strengthening of laboratory infrastructure, and improvement of strategic information services.

Nigeria national PMTCT guidelines were followed in all VIGH/FGH supported sites. All pregnant women presenting for ANC were offered opt-out HIV testing with same-day results using the national serial rapid testing algorithm, and those who tested HIV-positive were enrolled into the PMTCT program. All enrolled women received an initial evaluation, including baseline laboratory tests (blood grouping, hematocrit, hemoglobin genotype, VDRL, urinalysis, CD4+ cell count, chemistry), and a full clinical exam by a physician screening for the presence of any opportunistic infections as well as baseline WHO clinical disease staging. Clients received a basic care kit and other services, including adherence counseling, nutritional counseling, palliative care, and home-based care (based on need). Intrapartum HIV testing was provided to all women of unknown HIV status.

Pregnant women who tested HIV positive were offered ARV prophylaxis or treatment, consistent with national guidelines.<sup>25</sup> Pregnant women with CD4+ cell count  $\leq 350/\mu\text{L}$ , irrespective of WHO clinical staging; or WHO clinical stage III or IV disease, regardless of CD4 count were immediately referred to treatment sites for ART initiation. Prophylaxis was provided to HIV-positive pregnant women who did not meet the criteria for ART for their own health, i.e., WHO clinical stage I or II disease with CD4+ cells  $>350/\mu\text{L}$ . Those eligible for prophylaxis received either zidovudine (ZDV) monotherapy or triple drug prophylaxis. The most commonly used ART regimen was a combination of ZDV plus lamivudine (3TC) plus nevirapine (NVP), as per existing national guidelines. Patients requiring second-line ART were placed on two new nucleoside reverse transcriptase inhibitors (NRTIs) plus the boosted protease inhibitor lopinavir/ritonavir (Aluvia<sup>TM</sup>). Women who received NVP at the time of delivery received a 7-day postpartum tail of ZDV. All mothers received counseling and support on safe infant feeding practices regardless of their HIV-infection status. Patients were followed up in clinic every month, or more frequently depending on gestational age. Women were encouraged to return to the facility for childbirth to ensure safe delivery and

appropriate care for the newborn. Home-based care and support teams followed up HIV-infected/exposed mother-infant pairs during the postpartum period.

HIV-exposed infants were prescribed daily NVP from birth to 6 weeks of age. At 6 weeks of life, exposed infants were commenced on cotrimoxazole prophylaxis and recommended for HIV testing via the EID program. Staff at the facilities were trained on the EID process and sample collection of dried blood spots (DBS). The sites were linked to the National EID scale-up plan and to the DBS collection supplies and transport system.

### **Data Source, Collection and Cleaning**

We used routinely collected program data for this analysis. After each clinic day, FGH data clerks entered data from national patient management and monitoring (PMM) forms that had been completed by clinicians, nurses, laboratory, and pharmacy staff into CAREWare™ (JProg®, New Orleans, LA, USA), an electronic medical records system. Routine audits of medical records were performed to ensure that forms were completed accurately and laboratory data were entered correctly. Information from CAREWare™ was cross-checked against our EID register, which includes information on HIV-exposed infant characteristics, infant prophylaxis, date of sample collection, and nutrition/feeding considerations.

Data from four treatment clinics were included in this analysis: Sobi, Lafiagi, Gawu, and Umaru Yar Adua hospitals. Kuta Hospital was excluded because EID records were not kept for that population. Data from IBB hospital was excluded because CAREWare™ data were not routinely collected for that site and linkage with maternal data was not possible.

Data queries were generated for out-of-range and missing data. Each site addressed its data queries; clean data were extracted for the final analyses. The data extraction included all pregnant women enrolled in HIV care and treatment at VIGH/FGH supported sites on or before September 30, 2013. Clinical characteristics collected closest to the date of enrollment up to a 90-day window before or after enrollment were used as enrollment status indicators (e.g., weight, WHO clinical stage, CD4+ cell count). Maternal height was allowed a 365-day window in either direction. In order to ensure that our denominator (pregnant women in HIV care and treatment) was complete, we performed 100% audit of pregnancy status of all women ages 12-55 years against an external database (HIVCare) maintained by FGH personnel for program reporting purposes.

### **Outcomes**

The primary outcome in this study was entry into the EID program. The unit of analysis was a woman documented as pregnant at enrollment or any time following enrollment into HIV care and treatment. The HIV care and treatment database did not include due dates, so the time of delivery could not be ascertained for women who failed to present with their infants for EID. Each woman was credited once for EID entry as long as one or more infants entered the EID program (serial pregnancies in the same woman were not linked).

## Definitions

Pregnant women in study sites who tested HIV-positive, received post-test counseling and had their information recorded in the CAREWare™ database were considered “enrolled into care”. Initiation into EID was based on “enrollment into care” and documentation in the EID register of dried blot sample collection from the infant.

## Statistical analysis

We estimated summary statistics for demographic and clinical characteristics among all pregnant women by EID entry. We modeled the probability of EID initiation using multivariable logistic regression. Covariates identified by the study investigators *a priori* included: age, education, marital status, clinic, body mass index (BMI), functional status, CD4+ cell count, hemoglobin, WHO clinical stage, ART status, and date of enrollment. Linearity assumptions were met for age, BMI, hemoglobin and CD4+ cell count; date of enrollment was included in the model using restricted cubic splines. Multiple imputation was used to account for missing values of covariates and to prevent case-wise deletion of missing data; 180 (25%) patients had complete data for all covariates. Clinic was a covariate of interest; thus we did not account for clustering within clinics. We used predictive mean matching to take random draws from imputation models; 25 imputation data sets were used in the analysis.<sup>26</sup> R-software 3.0.2 ([www.r-project.org](http://www.r-project.org)) was used for data analyses. Analysis scripts are available from the following link: <http://biostat.mc.vanderbilt.edu/ArchivedAnalyses>.

Ethical approval for this study was obtained from the Vanderbilt University Institutional Review Board and the Nigeria Health Research and Ethics Committee.

## RESULTS

We identified 712 HIV-infected pregnant women from a cohort of 2604 (27.3%) HIV-infected women enrolled in HIV care and treatment across the four VIGH/FGH-supported sites during the study period. After an extensive review of the EID database, 357 HIV-infected pregnant women (50.1%) were verified as having enrolled their infants in EID in one of the four study site hospitals (Figure 1). Among those infants enrolled in EID, the median time (interquartile range, IQR) from birth to enrollment was 17 weeks (9-34 weeks), such that 32% of infants were enrolled by 10 weeks of age. Of the 357 women with infants enrolled in EID, 32 infants (9.0%) had a positive DNA PCR result, 258 (77.3%) were negative, and 67 (18.8%) were missing. Excluding missing data, 32 of 290 (11.0%) HIV-exposed infants were confirmed HIV-infected, despite the fact that their mothers were in a HIV care program.

### Sociodemographic and clinical characteristics

Table 1 shows maternal demographics, overall and by EID entry. The majority of study participants were married (89%), unemployed (68%) and enrolled in Umar Yar Adua hospital (43%). The median age (IQR) of enrolled patients was 27 years (24 - 30 years). Women who enrolled their infants in EID and those who did not were similar in age,

occupation, and referral source. The majority of documented referrals came from voluntary HIV counseling and testing settings (63%).

Clinical characteristics of the mothers in the cohort at enrollment into care are shown in Table 2. The median CD4+ cell count of all women at enrollment was 316/ $\mu$ L (IQR: 182 - 494/ $\mu$ L). The values for height, weight, BMI, and selected laboratory indices (CD4+ cell count and hemoglobin) were similar between mothers who enrolled their infants in EID versus those who did not. The proportion of missing maternal laboratory values was substantial across both EID and non-EID groups (Table 2). Advanced HIV disease at enrollment (WHO clinical stage III or IV disease) was noted in 17% of all patients. Mothers who enrolled their infants in EID were more likely to have been placed on combination ART at enrollment than mothers who did not enroll their infants in EID (80% vs. 68% respectively,  $P<0.001$ ).

### Predictors of EID entry

Table 3 shows associations between EID and demographic/clinical characteristics of pregnant women in the study. Clinic of enrollment and date of enrollment were strongly predictive of entry in EID ( $p<0.001$ ). Women enrolled more recently were less likely to bring their infants for EID than those enrolled at the beginning of the project (January 2011 vs. January 2010, OR=0.35 [95%CI: 0.22-0.56]; January 2012 vs. January 2010, OR=0.30 [95%CI: 0.14-0.61]). These odds of EID entry declined steadily with later calendar date of enrollment in care (Figure 2). Women who received care in Umaru Yar Adua hospital were more likely to have their infants enrolled in EID than those who receive care in the three more rural hospitals. This difference was particularly evident in the case of Lafiagi Hospital, where infants of enrolled mothers had 93% lower odds of EID entry compared with infants of mothers enrolled in Umaru Yar Adua Hospital (OR=0.07 [95%CI: 0.03-0.16]). Mothers whose first ART receipt at enrolment was combination ART had a 22% higher odds of infant EID entry than those not placed on triple drug ART (95%CI: 0.77-1.95). We found little evidence of independent associations between EID entry and other maternal demographic and clinical variables (age, marital status, BMI, WHO functional status, and WHO clinical stage).

## DISCUSSION

Only half of all enrolled HIV-positive mothers ever returned with their HIV-exposed infants for EID testing, an indication of ongoing challenges in preserving uninterrupted PMTCT care in our sites. Although this number substantially exceeds the national average of 4% of eligible infants undergoing HIV-1 DNA PCR testing for EID by 2 months of age,<sup>10</sup> it is nevertheless a sobering reminder of the challenges confronting attainment of the national goal of providing at least 90% of all HIV-exposed infants with access to EID services by 2015. The proportion of mothers who failed to bring in their infant for EID testing is similar to rates reported elsewhere in Nigeria<sup>27</sup> and other parts of sub-Saharan Africa.<sup>28-30</sup>

Clients who were enrolled in Umaru Yar Adua Hospital were more likely to bring in their infants for EID testing than mothers who were enrolled in the other 3 study sites. FGH started supporting PMTCT services in Umaru Yar Adua hospital in 2010, and of the four



hospitals in this study it is the closest to Abuja, Nigeria's Federal Capital. Our finding is therefore likely to be a reflection of tracking advantages associated with the relatively more urbanized setting of the hospital and possibly more favorable staffing levels, site-level characteristics that favor closer patient follow-up, including tracking of patients missing clinic visits, more comprehensive counseling of HIV-infected mothers, and/or better informed mothers.

An important finding is that as our treatment program matured, newly enrolled women were less and less likely to bring in their infants for EID. We believe this finding could be due to at least three factors. First, our project underwent a transition in leadership in the second year of the program, reducing the intensity of staff supervision and mentoring as well as logistics coordination. Second, we transitioned experienced FGH clinicians from direct patient care responsibilities to technical assistance in the second year of program implementation, which resulted in less experienced local clinicians taking on direct patient care responsibilities. These changes could have cumulatively affected the quality of services provided, including PMTCT program decision making and postpartum tracking of mothers with missed appointments. Busy clinical facilities and staffing constraints are established factors that could hinder quality of follow-up care for HIV-exposed infants.<sup>8,31</sup> Third, the first mothers to engage HIV-care may have been motivated more than later mothers who were brought into care, affecting the return rate for EID in their newborns.

The strengths of this study include the relatively large sample size and our use of an extensive querying and data cleaning process (e.g., our research assistant performed 100% query for pregnancy status of all CAREWare™ database entries). In addition, our report is based on data generated from real-world, rural Nigeria and reflect the realities of PMTCT program implementation in an otherwise understudied population.

Our study limitations include limited generalizability of findings from these four sites in the north-central region of Nigeria. We also used routinely collected program data whose proportion of missing maternal laboratory values was substantial which required multiple imputation methods to prevent case-wise deletion of 75% of patient records. Routine data had limited sociodemographic, behavioral, and attitudinal data, so causality could not be established for the reasons for non-adherence with EID recommendations. We were unable to establish the outcomes of infants who did not present for EID testing at VIGH/FGH sites. However, we suspect that some of the infants did return to our sites for immunizations, but poor integration of EID services into the maternal and child health clinic may have resulted in missed opportunities for infant testing. Infant death prior to EID receipt would be considered a false negative for EID screening compliance. If our objective were to compare compliers with non-compliers, then there would be some misclassification of those mothers with babies who died prior to EID as non-compliers. We expect this would bias regression results towards the null, if at all. We are unable to assess the full PMTCT continuum of care as we did not have records for HIV-infected women who do not "enroll into care". The design of the EID database does not allow us to distinguish from missing records or test results that were not received or picked up. Since our mothers had been previously identified as HIV-infected and were in HIV care, we think that our EID estimates may overestimate

EID coverage for all HIV-infected women, making this a best-case scenario for the region studied.

This study contributes important lessons from an EID program in Nigeria, a country that contributes significantly to the global burden of mother to child HIV transmission. Strategies that will improve EID uptake and mother-infant retention along the PMTCT cascade are needed urgently. We have shown in rural Mozambique that an enhanced referral process in which mothers were offered direct accompaniment to the site of EID testing for registration prior to discharge and given instructions in the mothers' local native language improved EID uptake to 54.0% compared to 25.6% in the standard care group.<sup>20</sup> Other effective strategies can improve retention and uptake of HIV care along the PMTCT continuum, including: integrating EID services into routine infant care and immunization visits;<sup>32,33</sup> task-shifting to dedicated community health workers;<sup>34</sup> use of mobile technology for reporting EID results<sup>35</sup> and community strategies utilizing individuals or groups for advocacy, support, education, and tracking persons lost to follow-up.<sup>36-40</sup> Different clinics may have different problems in program implementation, such that quality improvement must be tailored for those deficits identified.<sup>41,42</sup> These approaches can be adapted to PMTCT programs in Nigeria. To assure sustainability of the EID program, federal and state governments also need to take on greater fiscal and administrative responsibility for EID programming.

Other recent developments have had a positive impact on Nigerian EID programs. The use of dried blot spots (DBS) technology has enabled decentralization of sample collection to rural settings and has simplified the transport and storage of samples to central laboratories for DNA PCR testing. The development of point-of-care diagnostics and use of mobile technologies to facilitate timely reporting of DBS results will help confront logistics and quality assurance issues in the national EID program. Integrating EID programs with existing well-child visit services (e.g., immunizations), improving client tracking, and increasing family involvement will also help to minimize attrition. An ongoing NIH-funded PMTCT trial in the study area<sup>23</sup> should provide more local context-specific data that will help identify barriers to EID care and refine optimal strategies to eliminating pediatric HIV infections in rural Nigeria and similar settings. It is imperative that quality improvement studies and interventions involve more sites and infants (and their parents) eligible for EID in Nigeria.

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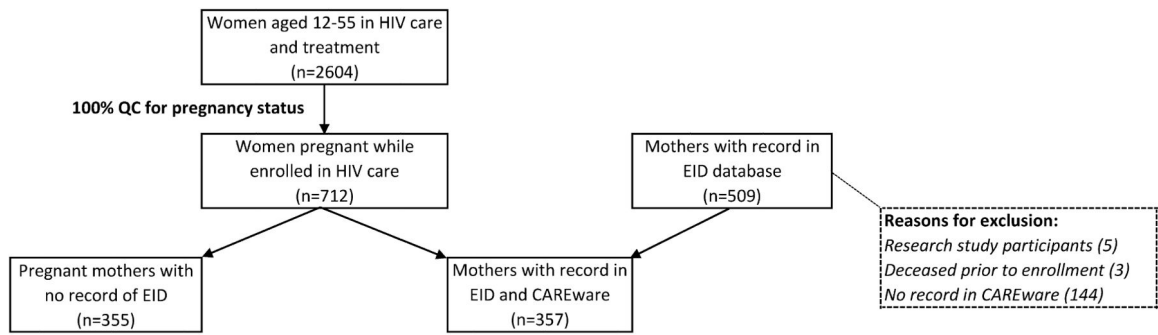


## REFERENCES

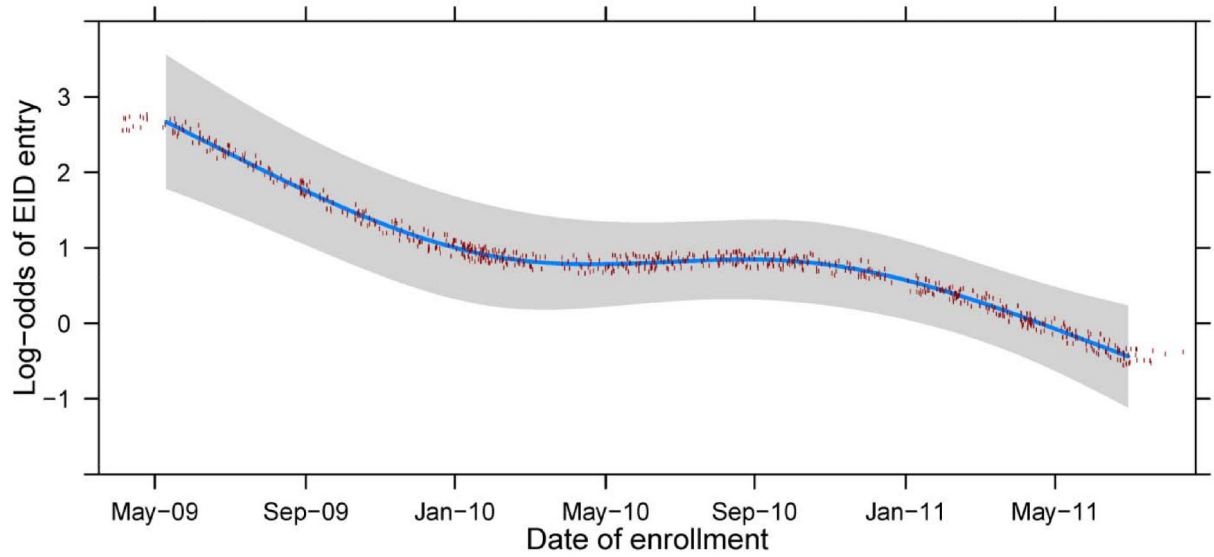
1. UNAIDS. [Accessed December 24, 2013] Global report: UNAIDS report on the global AIDS epidemic 2011. Joint United Nations Programme on HIV/AIDS (UNAIDS). 2012. [http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120\\_unaids\\_global\\_report\\_2012\\_with\\_annexes\\_en.pdf](http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120_unaids_global_report_2012_with_annexes_en.pdf)
2. UNAIDS. Global report: UNAIDS Report on the Global AIDS Epidemic 2013. Joint United Nations Programme on HIV/AIDS (UNAIDS); New York: 2013. [http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS\\_Global\\_Report\\_2013\\_en.pdf](http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf) [Accessed September 24, 2013]
3. Violari A, Cotton MF, Gibb DM, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med*. 2008; 359(21):2233–44. [PubMed: 19020325]
4. Cotton MF, Violari A, Otwombe K, et al. Early time-limited antiretroviral therapy versus deferred therapy in South African infants infected with HIV: results from the children with HIV early antiretroviral (CHER) randomised trial. *Lancet*. 2013; 382(9904):1555–63. [PubMed: 24209829]
5. Newell ML, Coovadia H, Cortina-Borja M, et al. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet*. 2004; 364(9441):1236–43. [PubMed: 15464184]
6. Prendergast A, Mphatswe W, Tudor-Williams G, et al. Early virological suppression with three-class antiretroviral therapy in HIV-infected African infants. *AIDS*. 2008; 22(11):1333–43. [PubMed: 18580613]
7. Penazzato M, Prendergast A, Tierney J, et al. Effectiveness of antiretroviral therapy in HIV-infected children under 2 years of age. *Cochrane Database Syst Rev*. 2012; 7:CD004772. [PubMed: 22786492]
8. Ghadrshenas A, Ben Amor Y, Chang J, et al. Improved access to early infant diagnosis is a critical part of a child-centric prevention of mother-to-child transmission agenda. *AIDS*. 2013; 27(Suppl 2):S197–205. [PubMed: 24361629]
9. National Agency for the Control of AIDS (NACA). Federal Republic of Nigeria Global AIDS Response. Country Progress Report, Nigeria, GARPR 2012; Abuja: 2012. <http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries/Nigeria%202012%20GARPR%20Report%20Revised.pdf> [Accessed September 1, 2012]
10. WHO/UNAIDS/UNICEF. Global HIV/AIDS response: Epidemic update and health services progress toward universal access. Progress report 2011. World Health Organization; Geneva: 2011.
11. National Population Commission (Nigeria) and ICF Macro. Nigeria Demographic and Health Survey. Abuja, Nigeria: 2009.
12. WHO/UNICEF. Co-trimoxazole prophylaxis for HIV-exposed and HIV-infected infants and children: Practical approaches to implementation and scale up. World Health Organization; Geneva: 2009. <http://www.who.int/hiv/pub/paediatric/cotrimoxazole.pdf> [Accessed December 22, 2013]
13. Umeobika JC, Ezebialu IU, Ezenyeaku CT, et al. Knowledge and perception of mother to child transmission of human immunodeficiency virus among South Eastern Nigerian pregnant women. *J HIV Hum Reprod*. 2013; 1:15–9.
14. Olugbenga-Bello A, Adebimpe W, Osundina F, et al. Perception on prevention of mother-to-child-transmission (PMTCT) of HIV among women of reproductive age group in Osogbo, Southwestern Nigeria. *Int J Womens Health*. 2013; 5:399–405. [PubMed: 23874124]
15. Asekun-Olarinmoye E, Asekun-Olarinmoye I, Adebimpe W, et al. Community attitude towards the reproductive rights and sexual life of people living with HIV/AIDS in Olorunda Local Government Area, Osogbo, Nigeria. *HIV AIDS (Auckl)*. 2013; 5:131–6. [PubMed: 23807862]
16. Federal Ministry of Health, Nigeria (FMOH). National guidelines for prevention of mother-to-child transmission of HIV, 2010. Fourth ed.. Abuja, Nigeria: [http://www.emtct-iatt.org/wp-content/uploads/2013/04/Nigeria\\_National-PMTCT-Guidelines\\_2010.pdf](http://www.emtct-iatt.org/wp-content/uploads/2013/04/Nigeria_National-PMTCT-Guidelines_2010.pdf) [Accessed December 15, 2013]

17. Dube Q, Dow A, Chirambo C, et al. Implementing early infant diagnosis of HIV infection at the primary care level: experiences and challenges in Malawi. *Bull World Health Organ.* 2012; 90(9): 699–704. Available from: *Epub.* [PubMed: 22984315]
18. Nuwagaba-Biribonwoha H, Werq-Semo B, Abdallah A, Cunningham A, et al. Introducing a multi-site program for early diagnosis of HIV infection among HIV-exposed infants in Tanzania. *BMC Pediatr.* 2010; 10:44. [PubMed: 20565786]
19. Cook RE, Ciampa PJ, Sidat M, et al. Predictors of successful early infant diagnosis of HIV in a rural district hospital in Zambézia, Mozambique. *J Acquir Immune Defic Syndr.* 2011; 56(4):e104–9. [PubMed: 21266912]
20. Ciampa PJ, Burlison JR, Blevins M, et al. Improving retention in the early infant diagnosis of HIV program in rural Mozambique by better service integration. *J Acquir Immune Defic Syndr.* 2011; 58(1):115–9. [PubMed: 21546845]
21. Ciampa PJ, Tique JA, Jumá N, et al. Addressing poor retention of infants exposed to HIV: a quality improvement study in rural Mozambique. *J Acquir Immune Defic Syndr.* 2012; 60(2):e46–52. [PubMed: 22622077]
22. UNAIDS. Global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive, 2011–2015. Joint United Nations Programme on HIV/AIDS (UNAIDS); New York: 2011.
23. Aliyu MH, Blevins M, Parrish DD, et al. Risk factors for delayed initiation of combination antiretroviral therapy in rural North Central Nigeria. *J Acquir Immune Defic Syndr.* 2013 Epub ahead of print.
24. Parrish DD, Blevins M, Megazzini KM, et al. Haemoglobin recovery among HIV-1 infected patients on zidovudine-based antiretroviral therapy and other regimens in north-central Nigeria. *Int J STD AIDS.* 2014; 25(5):355–9. [PubMed: 24104694]
25. Federal Ministry of Health, Nigeria (FMOH). 2010 National HIV Sero-prevalence Sentinel Survey. Federal Ministry of Health; Abuja: 2010. National AIDS/STI Control Program. Technical Report. Available at: [http://www.nigeria-ids.org/documents/2010\\_National%20HIV%20Sero%20Prevalence%20Sentinel%20Survey.pdf](http://www.nigeria-ids.org/documents/2010_National%20HIV%20Sero%20Prevalence%20Sentinel%20Survey.pdf)
26. Harrell, FE., Jr; Dupont, CT. R Foundation for statistical computing. Vienna, Austria: 2012. Project 'Hmisc'. R: a language and environment for statistical computing.
27. Anoje C, Aiyenigba B, Suzuki C, et al. Reducing mother-to-child transmission of HIV: findings from an early infant diagnosis program in south-south region of Nigeria. *BMC Public Health.* 2012; 12:184. [PubMed: 22410161]
28. Hassan AS, Sakwa EM, Nabwera HM, et al. Dynamics and constraints of early infant diagnosis of HIV infection in Rural Kenya. *AIDS Behav.* 2012; 16(1):5–12. [PubMed: 21213034]
29. Torpey K, Mandala J, Kasonde P, et al. Analysis of HIV early infant diagnosis data to estimate rates of perinatal HIV transmission in Zambia. *PLoS One.* 2012; 7(8):e42859. [PubMed: 22912752]
30. Moon TD, Burlison JR, Sidat M, et al. Lessons Learned while Implementing an HIV/AIDS Care and Treatment Program in Rural Mozambique. *Retrovirology (Auckl).* 2010; 3:1–14. [PubMed: 25097450]
31. Braun M, Kabue MM, McCollum ED, et al. Inadequate coordination of maternal and infant HIV services detrimentally affects early infant diagnosis outcomes in Lilongwe, Malawi. *J Acquir Immune Defic Syndr.* 2011; 56(5):e122–8. [PubMed: 21224736]
32. McCollum ED, Johnson DC, Chasela CS, et al. Superior uptake and outcomes of early infant diagnosis of HIV services at an immunization clinic versus an “under-five” general pediatric clinic in Malawi. *J Acquir Immune Defic Syndr.* 2012; 60(4):e107–10. [PubMed: 22614897]
33. Rollins N, Mzolo S, Moodley T, et al. 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. [PubMed: 19491653]
34. Kim MH, Ahmed S, Buck WC, et al. The Tingathe programme: a pilot intervention using community health workers to create a continuum of care in the prevention of mother to child transmission of HIV (PMTCT) cascade of services in Malawi. *J Int AIDS Soc.* 2012; 15(Suppl 2): 17389. [PubMed: 22789644]

35. Seidenberg P, Nicholson S, Schaefer M, et al. Early infant diagnosis of HIV infection in Zambia through mobile phone texting of blood test results. *Bull World Health Organ.* 2012; 90(5):348–56. [PubMed: 22589568]
36. Marcos Y, Phelps BR, Bachman G. Community strategies that improve care and retention along the prevention of mother-to-child transmission of HIV cascade: a review. *J Int AIDS Soc.* 2012; 15(Suppl 2):17394. [PubMed: 22789647]
37. Teasdale CA, Besser MJ. Enhancing PMTCT programs through psychosocial support and empowerment of women: the Mothers2Mothers model of care. *S Afr J HIV Med.* 2008:60–64. Summer.
38. Farquhar C, Kiarie JN, Richardson BA, et al. Antenatal couple counseling increases uptake of interventions to prevent HIV-1 transmission. *J Acquir Immune Defic Syndr.* 2004; 37(5):1620–6. [PubMed: 15577420]
39. Chandisarewa W, Stranix-Chibanda L, Chirapa E, et al. Routine offer of antenatal HIV testing (“opt-out” approach) to prevent mother-to-child transmission of HIV in urban Zimbabwe. *Bull World Health Organ.* 2007; 85(11):843–50. [PubMed: 18038074]
40. Futterman D, Shea J, Besser M, et al. Mamekhaya: a pilot study combining a cognitive-behavioral intervention and mentor mothers with PMTCT services in South Africa. *AIDS Care.* 2010; 22(9): 1093–100. [PubMed: 20824562]
41. Stringer JS, Sinkala M, Maclean CC, et al. Effectiveness of a city-wide program to prevent mother-to-child HIV transmission in Lusaka, Zambia. *AIDS.* 2005; 19(12):1309–15. [PubMed: 16052086]
42. Stringer EM, Ekouevi DK, Coetzee D, et al. Coverage of nevirapine-based services to prevent mother-to-child HIV transmission in 4 African countries. *JAMA.* 2010; 304(3):293–302. [PubMed: 20639563]



**Figure 1.** Flowchart of steps involved in identifying HIV-infected pregnant women with children enrolled in early infant diagnosis services, northcentral Nigeria, 2009-2012.



**Figure 2.**  
Predicted log-odds of Early Infant Diagnosis (EID) entry by date of enrollment in early infant diagnosis services, north central Nigeria, 2009-2012.

**Table 1**

Summary of maternal demographics by Early Infant Diagnosis (EID) entry, Vanderbilt Institute for Global Health/Friends in Global Health program, Niger and Kwara states, Nigeria, 2009-2012.

	No EID record (n=355)	EID entry (n=357)	Combined (n=712)	P-value <sup>b</sup>
Age, median (IQR)	28 (24 - 30)	27 (24 - 30)	27 (24 - 30)	0.18
Age, range	14-64	14-44	14-64	
Marital status, n (%)				0.02
Missing	100 (28%)	137 (38%)	237 (33%)	
Divorced/Separated	19 (7%)	3 (1%)	22 (5%)	
Married	222 (87%)	203 (92%)	425 (89%)	
Single	7 (3%)	8 (4%)	15 (3%)	
Widowed	7 (3%)	6 (3%)	13 (3%)	
Occupation, n (%)				0.14
Missing	109 (31%)	139 (39%)	248 (35%)	
Employed	44 (18%)	41 (19%)	85 (18%)	
Other	39 (16%)	19 (9%)	58 (12%)	
Student	3 (1%)	3 (1%)	6 (1%)	
Unemployed	160 (65%)	155 (71%)	315 (68%)	
Clinic, n (%)				<0.001
Gawu Babangida Rural Hospital	82 (23%)	92 (26%)	174 (24%)	
Lafiagi General Hospital	79 (22%)	19 (5%)	98 (14%)	
Sobi Specialist Hospital	71 (20%)	62 (17%)	133 (19%)	
Umaru Musa Yar Adua Hospital	123 (35%)	184 (52%)	307 (43%)	
Referral type, n (%)				0.13
Missing	227 (64%)	194 (54%)	421 (59%)	
Outside clinic/provider; TB Clinic, or other	7 (5%)	20 (12%)	27 (9%)	
PMTCT services <sup>c</sup>	38 (30%)	42 (26%)	80 (27%)	
Voluntary Counseling and Testing clinic	83 (65%)	101 (62%)	184 (63%)	

Percentages are computed using the number of patients with a non-missing value.

<sup>a</sup>Continuous variables are reported as medians (interquartile range).

<sup>b</sup>To compare the distribution of study characteristics for participants by sex, we employ chi-square tests. Similarly, we use a Wilcoxon rank sum test for continuous variables by sex.

<sup>c</sup>PMTCT = prevention of mother-to-child transmission of HIV



**Table 2**

Summary of patient clinical characteristics by Early Infant Diagnosis (EID) entry, Niger and Kwara states of Nigeria, 2009-2012.

	No EID record (n=355)	EID entry (n=357)	Combined (n=712)	P-value <sup>b</sup>
Height (cm), median (IQR)	160 (155 - 165)	160 (155 - 164)	160 (155 - 165)	0.78
Missing, n(%)	123 (35%)	81 (23%)	204 (29%)	
Weight (kg) , median (IQR)	55 (49 - 64)	56 (50 - 62)	55 (49 - 63)	0.92
Missing, n(%)	15 (4%)	17 (5%)	32 (4%)	
Body mass index (kg/m <sup>2</sup> ) , median (IQR)	21.7 (19.6 - 24.1)	21.7 (19.7 - 24.6)	21.7 (19.6 - 24.3)	0.812
Missing, n(%)	124 (35%)	90 (25%)	214 (30%)	
Functional status, n(%)				0.04
Missing	8 (2%)	19 (5%)	27 (4%)	
Ambulatory	9 (3%)	21 (6%)	30 (4%)	
Bedridden	1 (<1%)	3 (1%)	4 (1%)	
Working	337 (97%)	314 (93%)	651 (95%)	
CD4+ cell count per $\mu$ L, median (IQR)	306 (175 - 498)	320 (193 - 483)	316 (182 - 494)	0.50
CD4+ cell count category, n(%)				
Missing	49 (14%)	55 (15%)	104 (15%)	
<50 cells/ $\mu$ L	17 (6%)	6 (2%)	23 (4%)	
51-200	77 (25%)	76 (25%)	153 (25%)	
201-350	75 (25%)	87 (29%)	162 (27%)	
>350	137 (45%)	133 (44%)	270 (44%)	
Hemoglobin, median (IQR)	10.4 (9.4 - 11.2)	10.4 (9.2 - 11.3)	10.4 (9.3 - 11.3)	0.80
Missing, n(%)	150 (42%)	131 (37%)	281 (39%)	
WHO clinical stage, n(%)				0.008
Missing	23 (6%)	25 (7%)	48 (7%)	
I	214 (64%)	241 (73%)	455 (69%)	
II	61 (18%)	38 (11%)	99 (15%)	
III	52 (16%)	53 (16%)	105 (16%)	
IV	5 (2%)	0 (0%)	5 (1%)	
First receipt of antiretroviral therapy, n(%)				<0.001
None	63 (18%)	63 (18%)	126 (18%)	
For perinatal prophylaxis	49 (14%)	9 (3%)	58 (8%)	
Combination antiretroviral therapy	243 (68%)	285 (80%)	528 (74%)	

Percentages are computed using the number of patients with a non-missing value.

<sup>a</sup>Continuous variables reported as medians (interquartile range).

<sup>b</sup>To compare the distribution of study characteristics for participants by EID status, we employed chi-square tests. Similarly, we used a Wilcoxon rank sum test for continuous variables by EID status.

<sup>c</sup>Weight, height, functional status, CD4, hemoglobin, creatinine, WHO stage are collected at enrollment. Enrollment data is collected in a window of +/- 90 days from date of enrollment.

**Table 3**

Logistic Regression Model: Maternal factors associated with EID uptake, Niger and Kwara states of north central Nigeria, 2009-2012.

	OR (95% CI)	P-value
Age (per 5 years)	0.95 (0.81, 1.12)	0.53
Education		0.40
None (reference)	1	
Primary	1.11 (0.66, 1.88)	
Secondary	1.37 (0.73, 2.58)	
Post-secondary	2.19 (0.82, 5.83)	
Marital status		0.10
Married (reference)	1	
Divorced/Separated	0.19 (0.05, 0.71)	
Single	0.96 (0.30, 3.09)	
Widowed	0.62 (0.18, 2.16)	
Body mass index per 1 kg/m <sup>2</sup>	1.00 (0.95, 1.05)	0.99
Functional status		0.06
Working (reference)	1	
Ambulatory/Bedridden	2.34 (0.98, 5.57)	
CD4+ cell count per 50 cells/ $\mu$ L	1.02 (0.97, 1.06)	0.47
Hemoglobin per 1 g/dL	0.97 (0.84, 1.13)	0.72
WHO clinical stage		0.10
I (reference)	1	
II	0.59 (0.36, 0.96)	
III or IV	0.90 (0.51, 1.56)	
First receipt of antiretroviral therapy (ART) <sup>a</sup>		<0.001
None (reference)	1	
As Prophylaxis	0.17 (0.07, 0.42)	
Combination ART	1.22 (0.77, 1.95)	
Clinic		<0.001
Umaru Musa Yar Adua Hospital (ref)	1	
Gawu Babangida Rural Hospital	0.38 (0.20, 0.74)	
Lafiagi General Hospital	0.07 (0.03, 0.16)	
Sobi Specialist Hospital	0.37 (0.22, 0.63)	
Date of enrollment		<0.001
January 2010 (reference)	1	
January 2011	0.35 (0.22, 0.56)	
January 2012	0.30 (0.14, 0.61)	

<sup>a</sup>ART = antiretroviral therapy