OPEN

The Cascade of Care From Routine Point-of-Care HIV Testing at Birth: Results From an 18-Months Pilot Program in Eswatini

Philisiwe Ntombenhle Khumalo, PGDipPH,[a] Emma Sacks, PhD,[b] Caspian Chouraya, MBChB, MSc,[c] Bhekisisa Tsabedze, MPH,[a] Thembie Masuku, MSc,[d] Gcinile Nyoni, BSN,[d] Tandzile Zikalala, BMLT,[d] Bonisile Nhlabatsi, MPH,[e] Nobuhle Mthethwa, MCUR,[f] and Jennifer Cohn, MD, MPH[g]

Background: HIV testing at birth may improve early treatment, but concerns remain about feasibility and retention of infants in care. In 2017, point-of-care (POC) HIV birth testing was introduced into routine care at 3 high-volume maternity health facilities in Eswatini.

Methods: POC birth testing was offered to HIV-exposed infants (HEI) born at, or presenting to, 3 maternities within 3 days of birth. Data were collected from a project-specific EID test request form and routine registers on all tests conducted from August 1, 2017 to November 30, 2018, including retesting at 6–8 weeks for infants testing negative at birth and six-month retention in HIV care and viral load suppression among infants testing HIV-positive at birth.

Results: Of 4322 eligible HEI, 3311 (76.6%) were tested. Twenty-six HIV-infected infants were identified (positivity rate 0.8%) and 25 initiated on antiretroviral therapy (ART) (96.1%). The median time from sample collection to ART initiation was 20.50 days (IQR 14–45). Twenty-one (84%) ART-initiated infants were on ART at 6 months after initiation. Nineteen infants (90.5%) had viral load test information at 6 months and 16 (84.2%) were virally suppressed. Of 3126 HEI testing negative at birth, 3004 (96.1%) were linked to laboratory databases and 2744 (91.3%) were retested at 6–8 weeks, with 9 (0.3%) additional infants testing HIV-positive.

Conclusions: Uptake of POC birth testing was high in Eswatini with low HIV positivity. Almost all infants identified HIV-positive at birth were initiated on ART, with high retention in care and viral suppression. Birth testing did not seem to significantly reduce subsequent 6–8-week testing.

From the [a]Research and Public Health Evaluation, Elizabeth Glaser Pediatric AIDS Foundation, Mbabane, Eswatini; [b]Department of Global Health, Milken Institute School of Public Health, The George Washington University, Washington, DC; [c]Executive Leadership & Senior Management Teams, Elizabeth Glaser Pediatric AIDS Foundation, Mbabane, Eswatini; [d]Innovations/Unitaid, Elizabeth Glaser Pediatric AIDS Foundation, Mbabane, Eswatini; [e]Eswatini National AIDS Program, Ministry of Health, Mbabane, Eswatini; [f]Sexual Reproductive Heath Unit, Ministry of Health, Mbabane, Eswatini; and [g]Innovation and New Technology, Elizabeth Glaser Pediatric AIDS Foundation, Washington, DC.

Funded and supported by Unitaid [EB21/R08], Unitaid, Geneva, Switzerland.
The authors have no conflicts of interest to disclose.

Correspondence to: Philisiwe Khumalo, Elizabeth Glaser Pediatric AIDS Foundation, Mbabane, Eswatini H100 (e-mail: pkhumalo@pedaids.org).

Key Words: HIV/AIDS, PMTCT, EID, POC, birth testing, MNCH, newborn health, observational study

(*J Acquir Immune Defic Syndr* 2020;84:S22–S27)

BACKGROUND

Globally, approximately 160,000 children aged 0–14 years became newly infected with HIV in 2018.[1,2] Pediatric HIV is associated with high rates of morbidity and mortality,[3,4] and early initiation of antiretroviral therapy (ART) is critical for reducing mortality risk.[5–7] Early infant diagnosis of HIV (EID), including at birth, can help in early identification of in utero HIV infection among infants and ART initiation.

Eswatini has one of the highest HIV prevalence rates in the world, with an adult prevalence rate over 27% (adults aged 15–49 years), and over 13,000 children (aged 0–14 years) living with HIV.[8] Approximately 35% of pregnant women in Eswatini are HIV-infected, and over 9000 HIV-exposed infants (HEI) are born in the country each year,[9,10] with 6–8 weeks mother to child HIV transmission (MTCT) rates of 1% in 2018.[9] The Government of the Kingdom of Eswatini has made the prevention of MTCT (PMTCT) of HIV, and identification and treatment for infected infants, through new diagnostic and treatment innovations, a top priority.[2]

Currently, the Eswatini 2018 Integrated HIV Management Guidelines recommend HIV nucleic acid testing (NAT) of HEI at 6 weeks of age to identify both in utero and intrapartum HIV-infected infants.[11] This timing was conveniently scheduled at the same time as the recommended six-week expanded programme for immunization visit. The 2016 WHO guidelines recommend that countries with strong six-week testing programmes consider the addition of NAT at birth to existing EID testing approaches to identify in utero HIV infection in HEI.[12] This change was intended to facilitate earlier diagnosis of the in utero infected infants and initiate them on life-saving treatment before clinical deterioration.[13,14] Among infants infected in utero or intrapartum, studies suggest that mortality begins to increase at about 3–4 weeks of age compared to uninfected infants, and is as high as 10% by 2 months of age, reaching a peak of 30%–40% between 8 and 12 weeks of age.[3,5,15] From a public health approach, the addition of birth testing to the EID schedule could result in more HIV-infected infants identified and starting ART early.[16,17] Early

ART initiation could also result in a reduced HIV reservoir and promote normal immune and brain development.[7,15,18]

A few other countries are implementing (Thailand, South Africa, Zimbabwe) or planning/piloting (Kenya, Zambia) birth testing for infant diagnosis of HIV, but no country outside of South Africa has scaled-up birth testing to a large percentage of their population, thus there is limited experience with birth testing in low- and middle-income countries. National guidelines in South Africa changed in June 2015 to include routine birth polymerase chain reaction testing for all HEI and repeat testing at 10 weeks for those with a negative test at birth.[19] A modeling study using data from South Africa concluded that testing once at 6 weeks would be clinically and economically superior to either birth testing or 10 weeks testing alone, but testing twice, at birth and at 10 weeks, would improve outcomes and was cost-effective, compared to 6 weeks' testing alone.[20] The study recommended that programmes with incomplete six-week EID coverage could focus on scaling-up 6-week programmes before adding birth testing; however, those with strong 6-week testing programmes could consider the addition of birth testing.[20] As Eswatini has a 94.0% testing coverage for exposed infants at 6 weeks,[9] and 87.7% of infants are born in health facilities,[2] it is a prime candidate for the introduction and scale-up of facility-based HIV birth testing.

Point-of-care (POC) EID has been shown to dramatically decrease time to result return to caregivers, improve the percentage of results returned, and increase the percentage of HIV-infected infants initiated on ART in several studies.[21,22]

In 2017, birth testing was introduced in Eswatini in 5 maternity units within 5 health facilities, 3 of which provided POC EID and 2 offered conventional EID. The goal of introducing birth testing in few pilot facilities was to better learn how it can be implemented before national guidelines were amended. This is the first study of HIV testing at birth in Eswatini and one of the first studies on POC testing at birth. The aim of the study is to describe the uptake, testing, and treatment cascade of birth testing using POC NAT in maternity settings in Eswatini.

METHODS

Three maternities (Mbabane Government Referral Hospital in Hhohho region, Hlathikhulu Government Hospital in Shiselweni region, and Good Shepherd Hospital in Lubombo region) were included in this evaluation of POC EID birth testing. These facilities were high-volume maternities representing 37% of annual births in the country.[9] Basic maternity services in the 3 POC EID sites are free, but additional services may have a fee. One of the maternities charged a fee for extra inpatient days. The 3 maternities were offering EID services for the first time through the birth testing pilot programme. However, the hospitals offered six-week EID services in other departments such as in-patient wards, tuberculosis wards, and public health units (PHUs).

Two of the maternities piloting POC birth testing had a fully dedicated POC platform, whereas one maternity shared a platform with a PHU attached to the hospital and consequently the POC platform was also used for EID testing at 6 weeks at the PHU. All 3 POC EID facilities received training on the use of POC testing, continuous supervision visits by clinical and laboratory mentors, regular POC platform maintenance, and data quality monitoring. Three phlebotomists were hired and placed in the maternities to support nurses with running tests due to general shortages in the maternities.

With the aim to detect in utero HIV infection and with recommendation from the Ministry of Health in Eswatini, POC birth testing was offered to HEI born at, or presenting to, the maternities within 3 days of birth. Blood draws were conducted by nurses, physicians, and phlebotomists who were trained on capillary blood draws. POC tests were primarily run by phlebotomists. Nurses were also trained to run POC tests and would occasionally run POC tests particularly on evenings and weekends or other times when phlebotomists were not on site. Standard patient identifying information was included for all samples according to national guidelines and practices.

The POC assay in use for birth testing was the Abbot mPIMA (formerly Alere) Q HIV-1/2 Detect, which has received WHO prequalification,[23] CE marking (European diagnostic device approval), and in-country approval. The health worker performing the test transferred at least 25 mL of capillary blood into the cartridge, snapped into place the cartridge cap to prevent sample spillage or contamination of the instrument, and inserted the closed cartridge into the mPIMA Analyser. The test took approximately 52 minutes to run. Tests were conducted onsite for the 2 maternities with a dedicated POC platform and at the PHU for the site sharing a platform (results were sent to the maternity through an SMS printer). If a valid result (positive or negative) was produced, the infant's caregiver was approached to relay the results and for further counseling, following Eswatini national protocols. If an error or other invalid test result was obtained, the infant's caregiver was approached for repeat sample collection. All tests at birth were documented in a Ministry of Health-approved POC EID Form.

For infants testing HIV-negative, caregivers were counseled on the interpretation of the result and requested to return for another HIV test at 6 weeks. Infants testing HIV-positive had a second sample run for POC EID. If the second test was reactive, the infant was referred for HIV treatment at the ART unit in the same health facility providing birth testing or to other health facilities in the country depending on where the caregiver preferred to receive child welfare and HIV services. The Eswatini 2018 Integrated HIV Management Guidelines recommend to start HIV-infected infants identified at birth on an NVP-based three-drug ART within the first 2 weeks of life and to switch the infant from NVP to lopinavir/ritonavir (LPV/r)-based regimen at 14 days of life.[11] If the second test was nonreactive, a confirmatory dried blood spot was obtained and sent for testing at the Eswatini National Referral Laboratory (SNRL). In the case of discrepant tests, in the absence of clinical symptoms, clinicians were recommended to wait for laboratory confirmation before initiating treatment.

Prospective data were collected on all POC birth tests occurring from 1 August 2017–30 November 2018 using a POC EID Testing Form, which was approved by the Ministry of Health.[21] Data on retesting at 6–8 weeks of infants testing negative at birth, retention in care six months after ART initiation for HIV-positive infants either at birth or at 6 weeks, and viral load (VL) testing were abstracted from routine data sources and registers. All data were entered in MS Excel and uploaded into Power BI to link records across

databases. Study records were assigned a unique identification number and patient identifying information was coded to maintain confidentiality. Data were analyzed using SPSS version 21. For continuous variables, mean values and SDs or medians and interquartile ranges were used, and for categorical variables, frequencies and proportions were used.

This study received approval from the US-based Advarra (formerly Chesapeake) IRB on 20 July 2016 and the National Health Research Review Board (NHRRB) of the Eswatini Ministry of Health on 18 November 2016. A waiver of informed consent was approved by the IRBs, and the study was deemed to present no more than minimal risk of harm to patients whose records were abstracted and involved no procedures for which written consent is normally required outside of the research context.

Findings

Sociodemographic Characteristics

During the pilot program, 3311 infants received a test for HIV through POC; 49.0% (n = 1624) of the infants tested at birth were females (Table 1). The mean age of infants tested at birth was 0 days (IQR: 0–1). 98.2% (n = 3251) of the infants received prophylaxis at birth. Of infants who received prophylaxis, 95.3% (n = 3098) received NVP only and 4.7% (n = 152) received AZT + NVP. All caregivers were HIV-positive and 96.2% (n = 3184) were on ART. Among caregivers on ART, 67.3% (n = 2144) started ART before the pregnancy, 32.2% (n = 1025) started ART during pregnancy, and 0.3% (n = 8) started during labor and delivery. Of the caregivers on ART, 89.2% (n = 2840) were on TDF + 3 × TC + EFV. Only one caregiver was on second-line ART regimen (AZT + 3 × TC + LPV/r).

Testing and Results Uptake

Among the 4322 infants born to HIV-infected mothers in the 3 maternities, 76.6% (n = 3311) received a HIV test at birth (Table 2). Of the 3311 infants tested at birth, 8.6% (n = 284) tests were performed by nurses and 91.4% (n = 3027) by phlebotomists (Table 1). The 2 maternities that had a dedicated platform tested 85.2% and 83.6% of eligible infants identified in each health facility and the site that was sharing a platform with the attached PHU tested 55.7% of eligible infants identified in the health facility (Table 2). 95.2% (n = 3152) obtained a positive or negative result of which 98.1% (n = 3091) of the results reached caregivers. For 159 (4.8%) infants, the POC platform produced an error and required further testing at a later date. Of the results reaching the caregiver, 95.4% (n = 2948) reached the caregiver on the same day as testing. All HIV-positive results (100%) were received by caregivers. The median turnaround time from sample collection to caregiver receipt was 0 days (IQR 0–0).

HIV Positivity and ART Initiation

Twenty-six HIV-infected infants were identified (positivity rate = 0.8%), and 25 (96.2%) were initiated on antiretroviral treatment (Table 2). Two HIV-infected infants were initiated by day 14 of life, 13 were initiated at 14–30 days, 6 were initiated at 30–60 days, and 4 were initiated after 60 days. One infant died after diagnosis, but before ART initiation. The median time from sample collection to caregiver receipt for HIV-positive infants was 0 days (IQR 0–0), and from result reception by caregiver to ART initiation was 20.50 days (IQR 14–45). Of the children initiated on treatment, 96.0% (n = 24) were initiated on (ABC + 3 × TC + LPV/r and 4.0% (n = 1) on AZT + 3 × TC + NVP.

TABLE 1. Sociodemographic Characteristics of Infants Tested at Birth for HIV: Eswatini 2017–2018

	Infant Received Positive/ Negative HIV Result		
	Yes (n = 3152)	No (n = 159)	Total (n = 3311)
Demographic Characteristics	**n (%)**	**n (%)**	**n (%)**
Age (d)			
	Mean = 0.11 SD = 0.096	Mean = 0.12 SD = 0.096	Mean = 0.11 SD = 0.096
Sex			
Female	1544 (49.0)	78 (49.1)	1622 (49.0)
Male	1608 (51.0)	81 (50.9)	1689 (51.0)
Results received by caregiver			
Yes	3091 (98.1)	137 (86.2)	3228 (97.5)
No	61 (1.9)	22 (13.8)	83 (2.5)
Test performed by:			
Phlebotomist	2878 (91.3)	149 (93.7)	3027 (91.4)
Nurse	274 (8.7)	10 (6.3)	284 (8.6)
Infant received prophylaxis			
Yes	3094 (98.2)	157 (98.7)	3251 (98.2)
No	35 (1.1)	1 (0.6)	36 (1.1)
Unknown	23 (0.7)	1 (0.6)	24 (0.7)
Prophylaxis received			
AZT + NVP	124 (4.0)	28 (17.8)	152 (4.7)
NVP	2969 (96.0)	129 (82.2)	3098 (95.3)
None	1 (<1)	0 (0.0)	1 (<1)
Infant breast feeding after delivery			
Yes	3114 (98.8)	159 (100.0)	3273 (98.9)
No	36 (1.1)	0 (0.0)	36 (1.1)
Unknown	2 (0.1)	0 (0.0)	2 (0.1)
Mother's HIV status			
Positive	3152 (100.0)	159 (100.0)	3311 (100.0)
Mother on ART			
Yes	3029 (96.1)	155 (97.5)	3184 (96.2)
No	122 (3.9)	4 (2.5)	126 (3.8)
Unknown	1 (<1)	0 (0.0)	1 (<1)
Period mother started ART			
Before pregnancy	2030 (67.0)	114 (73.5)	2144 (67.3)
During pregnancy	987 (32.6)	38 (24.5)	1025 (32.2)
During labor and delivery	5 (0.2)	3 (1.9)	8 (0.3)
After delivery	5 (0.2)	0 (0.0)	5 (0.2)
Unknown	2 (<1)	0 (0.0)	2 (<1)
Mother's ART regimen			
TDF/3 TC/EFV	2696 (89.0)	144 (92.9)	2840 (89.2)
TDF/3 TC/DTG	182 (6.0)	3 (1.9)	185 (5.8)
Other regimen	151 (5.0)	8 (5.2)	159 (5.0)

TABLE 2. POC HIV NAT of Eligible Infants, Positivity, ART Initiation, Retention in Care, and Retesting at 6 Weeks by Facility: Eswatini 2017–2018

	Facility 1	Facility 2 (Additional Charge for Extra Inpatient d)	Facility 3 (Shared Platform)	Overall
	n (%)	n (%)	n (%)	n (%)
Number of infants eligible for HIV testing at birth	1688	1448	1186	4322
Eligible infants tested for HIV at birth (≤3 days)	1439 (85.2)	1211 (83.6)	661 (55.7)	3311 (76.6)
Tested infants obtaining positive/negative result	1377 (95.7)	1172 (96.8)	603 (91.2)	3152 (95.2)
Positive/negative result received by caregivers	1338 (97.2)	1170 (99.8)	583 (96.7)	3091 (98.1)
Positive/negative result reaching caregivers within 1 d	1333 (99.6)	1037 (88.6)	578 (99.1)	2948 (95.4)
Positive/negative result reaching caregivers after 1 d	5 (0.4)	133 (11.4)	5 (0.9)	143 (4.6)
Infants testing HIV-positive at birth (≤3 days) (yield)	13 (0.9)	7 (0.6)	6 (0.9)	26 (0.8)
HIV-infected infants initiated on ART	13 (100)	6 (85.7)	6 (100.0)	25 (96.2)
Died before ART initiation	0 (0.0)	1 (14.3)	0 (0.0)	1 (3.8)
Infants retained in ART 6 months after initiation	12 (91.8)	4 (66.7)	5 (83.3)	21 (84.0)
On ART 3 months after initiation	12 (91.7)	4 (66.7)	5 (83.3)	21 (84.0)
Died after ART initiation	1 (8.3)	1 (16.7)	1 (16.7)	3 (12.0)
Lost to follow-up (LTFU)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.0)
HIV ART-initiated infants with viral test information	11 (91.7)	4 (100.0)	4 (80.0)	19 (90.5)
VL undetectable 6 months after ART initiation	6 (54.5)	3 (75.0)	2 (50.0)	11 (57.9)
VL suppressed 6 months after ART initiation	3 (27.3)	1 (25.0)	1 (25.0)	5 (26.3)
VL unsuppressed 6 months after ART initiation	2 (18.2)	0 (0.0)	1 (25.0)	3 (15.8)
Infants testing HIV-negative at birth (≤3 days)	1364	1165	597	3126
Linked to laboratory database*	1336 (97.9)	1126 (96.7)	542 (90.8)	3004 (96.1)
HIV negative infants retesting at 6–8 wk	1217 (91.1)	1036 (92.0)	491 (90.6)	2744 (91.3)
Yield (positivity) at 6–8 wk	4 (0.3)	2 (0.2)	3 (0.6)	9 (0.3)
Infants retesting HIV-positive at 6–8 weeks initiated on ART	2 (50.0)	1 (50.0)	3 (100.0)	6 (66.7)
Died before ART initiation	1 (25.0)	0 (0.0)	0 (0.0)	1 (11.1)
Unknown if initiated on ART†	1 (25.0)	1 (50.0)	0 (0.0)	2 (22.2)
On ART 3 months after initiation	2 (100.0)	1 (100.0)	2 (66.7)	5 (83.3)
On ART 6 months after initiation	2 (100.0)	0 (0.0)	2 (66.7)	4 (66.7)
Died after ART initiation	0 (0.0)	0 (0.0)	1 (33.3)	1 (16.7)
Lost to follow-up (LTFU)	0 (0.0)	1 (100.0)	0 (0.0)	1 (16.7)
Infants retesting HIV-positive at 6–8 weeks with documented VL information 6 months after ART initiation	1 (50.0)	0 (0.0)	2 (100.0)	3 (50.0)
VL undetectable 6 months after ART initiation	1 (100.0)	0 (0.0)	2 (100.0)	3 (100.0)

*Records for 122 infants testing HIV-negative at birth could not be linked to laboratory databases to ascertain retesting at 6–8 wk.
†Records could not be found in either APMR or CMIS to ascertain ART initiation.

Retention in Care and Viral Load Suppression

Eighty-four percent (n = 21) of infants initiated on ART were still alive and on treatment 6 months after initiating treatment (Table 2). Of the 4 (16%) infants out of care, all were out of care within the first 3 months of ART initiation with one of the infants lost to follow-up and 3 had died. Nineteen (90.5%) of the 21 infants still in care 6 months after initiation had VL test information; and 11 (57.9%) had VL less than 20 copies/mL, 5 (26.3%) had VL 20–1000 copies/mL, and 3 (15.8%) had VL above 1000 copies/mL.

Retesting of HIV-Negative Infants at Six Weeks

Out of 3126 HEI testing negative at birth, 96.1% (3004) were linked to EID records at the national laboratory and 91.3% (n = 2744) had a documented retest for HIV at 6–8 weeks. Nine (0.3%) of the 2744 children retesting at 6–8 weeks tested HIV-positive. Of the 9 HIV-infected children, 6 (66.7%) were confirmed to have initiated ART, whereas one (11.1%) died before initiation and 2 (22.2%) could not be confirmed. Of the children initiated on ART, 5 (83.3%) were still in HIV care 3 months after initiation and 4 (66.7%) were still in care at 6 months after initiation. One (16.7%) child died after initiation and one (16.7%) was lost to follow-up after 3 months. The median time from HIV diagnosis to ART initiation was 8 days (IQR 6–22). Three of the 5 children in HIV care at 6 months after initiation had documented VL information and all 3 (100.0%) had undetectable VL (VL < 20c/mL). The 6 children on ART were initiated on ABC + 3 × TC + LPV/r.

DISCUSSION

The uptake of birth testing was fairly high with 76.6% of eligible HEI tested for HIV using POC NAT HIV test.

Other studies have demonstrated that it is possible to achieve universal coverage of birth testing irrespective of where the test is provided (within maternity or outside maternity) and the method of EID (POC or conventional).[17,24,25] In a retrospective cohort study conducted in a health center in South Africa using polymerase chain reaction, HIV testing uptake of birth testing was 87.6%[24] and it was 98.6% in a prospective study also conducted in South Africa.[17] A high proportion of the children who were not tested for HIV at birth were from the site that shared a platform with a PHU. This may have led to longer wait times and resulted in fewer HEI being tested. Infants in the 3 maternities may also have missed birth testing due to over-reliance on phlebotomists to draw blood, perform tests, and record results in health facility-based logs and registers, yet these phlebotomists were not working during weekends and holidays. Uptake for birth testing in Eswatini could be strengthened by increasing staffing and training additional staff to operate the POC machine.

HIV positivity both at birth and among infants who were negative at birth but received a 6–8-week test was low at 0.8% and 0.3%, respectively. Overall, 1% of children in Eswatini were found to be HIV-infected at the 6-week test in 2018.[1] Thus, in this sample, a majority of infants testing positive by 6 weeks of age were identified at birth. Although overall ART uptake for HIV-infected infants was high, only 2 infants were initiated within 14 days of life. This study did not systematically assess the reasons for this delay from diagnosis to treatment initiation. Programmatic experience suggests that most mothers wanted to confirm with their partners or other family members (especially male partners) before beginning treatment. It will be critical for programmes supporting birth testing in Eswatini and elsewhere to institute quality improvement initiatives to investigate the reasons for delayed ART initiation and work toward rapid ART initiation. Studies conducted in South Africa, Zimbabwe, and Kenya showed that with rigorous follow-up activities by health care workers and engagement for caregivers, it is possible to reduce time to ART initiation.[26]

The six-month retention in HIV care of infants identified positive at birth was high with 84% still on ART at 6 months after initiation, although 3 of the infants out of care had died soon after initiation on ART. Retention in this cohort was better than overall retention of children less than 15 years in Eswatini, which was 75% by 6 months in 2018 from programmatic data.[9] Of the 19 children with VL results, 16 (84.2%) were virally suppressed (VL $<$ 1,000c/mL) and this is comparable to the VL suppression rates of 85% noted for children $<$1 year in Eswatini in 2018.[9]

Avoiding loss to follow-up after birth testing for infants who test negative is critical. Modeled data from South Africa suggested that if $>$37% of infants with a negative birth test fail to return at 6 weeks, the clinical benefits of adding birth testing are lost.[20] Unlike in studies conducted in South Africa[24,27] that found that retesting was low at 6–8 weeks or subsequent testing points for infants identified HIV-negative at birth, our study shows high uptake of retesting of 91.3% at 6–8 weeks. The return for testing at 6–8 weeks can be mixed and needs further investigation. It is possible that our estimate of the number of birth-tested infants who underwent retesting at 6–8 weeks was an underestimate because some of the children who re-tested were not in the systems we searched. In addition, there were inconsistencies with the use of birth testing codes to identify and link infants, which may also lead to underestimation.

The POC birth testing pilot program had several programmatic challenges. The program was implemented in busy maternity units, which are generally understaffed. Phlebotomists who were supporting testing of infants for HIV did not work at nights or on weekends. One of the maternities was also sharing a platform with a PHU that was offering testing for children at 6 weeks. In addition, the women tended to leave as soon they were discharged after delivery. This may have contributed to eligible infants missed for testing and retesting in case there was an error while processing the specimen. One of the maternities charged an extra fee for additional inpatient days and this may have contributed to some caregivers leaving without a repeat test for tests producing errors or receiving results for infants. The maternities were also not initiating ART, leading to delays in initiating HIV-positive infants.

This study also had a number of limitations. There were challenges with tracking of infants after they received birth testing. Tracking infants for ART initiation, retention in HIV care, and VL testing was difficult because a few children moved out of the pilot sites and regions and they could not be located for follow-up. The study also relied on routine program and national laboratory systems data that have gaps and may have led to potential underestimation or misreporting of some of the indicators. There are also no data from low-volume facilities to inform scale-up of the program. This is a possible area for research in the future. In addition, there was no randomization either of facilities or patient, and there was no comparison group, which may limit the generalizability of the findings from the study. The study did not formally assess the reasons why eligible infants did not receive birth testing, nor did we follow those who were not tested at birth to determine whether they eventually tested at 6–8 weeks or at other subsequent testing points. Finally, most previous data on routine birth testing are from the South African experience. Although these data from Eswatini provide the experience of birth testing in another context, because this was a single country study, the generalizability of the findings may still be limited.

More research may be required on population impacts of birth testing when programmes are scaled-up further. Qualitative research to assess acceptability of and satisfaction with POC birth testing is being conducted to provide more insights on the feasibility of birth testing in Eswatini. In addition, conducting a cost analysis for providing birth testing would valuable.

CONCLUSIONS

Uptake of POC birth testing was high in Eswatini. Almost all infants identified HIV-positive at birth were initiated on ART and more than 80% were virally suppressed at 6 months after ART initiation. However, HIV positivity at birth and 6–8 weeks was low. The cost-benefit of birth testing must be considered in light of PMTCT coverage and in utero transmission rates.[28] Depending on these factors, the success of other key HIV interventions and the resources available for

overall HIV programming, birth testing may or may not be a priority in a given country. As programmes roll out birth testing, additional information to inform feasibility should be collected, such as qualitative assessments and ensuring outcomes obtained in this pilot will be maintained at scale. Further cost-effectiveness modeling would be useful to define the cost-effectiveness and timing of EID testing, including at birth, for a population with a strong PMTCT program such as Eswatini. This study shows that birth testing can be considered as a useful tool for countries to improve early identification and treatment of HIV-infected infants and, with appropriate systems, may not negatively affect subsequent EID testing.

Acknowledge

The authors thank the EGPAF POC EID team (Jeff Lamaire, Flavia Bianci, Shannon Viana, Stephanie Bruno, Dr Lydia Mpango, Thabile Dlamini, Khulekani Simelane, Njabuliso Zondi, Bongani Zwane, Nomsimelelo Shongwe, and Dr Christopher Makwindi) for their work on the day-to-day implementation of the POC EID project including, but not limited to, ensuring the collection of complete and high-quality data. The authors thank the ministry of health and healthcare workers in pilot sites for their collaboration and support for the project. The authors thank the infants and caregivers involved in this project evaluation.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). *Start Free Stay Free AIDS Free 2019 Progress Report*. Gevena, Switzerland: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2019.
2. World Health Organization. Preventing mother-to-child transmission of HIV in Eswatini. World Health Organization, 2019. Available at: https://www.who.int/features/2012/pmtct_swaziland/en/. Accessed January 6, 2019.
3. Newell ML, Coovadia H, Cortina-Borja M, et al. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet.* 2004;364:1236–1243.
4. Mayaux MJ, Burgard M, Teglas JP, et al. Neonatal characteristics in rapidly progressive perinatally acquired HIV-1 disease. The French Pediatric HIV Infection Study Group. *JAMA.* 1996;275:606–610.
5. Desmonde S, Coffie P, Aka E, et al. Severe morbidity and mortality in untreated HIV-infected children in a paediatric care programme in Abidjan, Côte d'Ivoire, 2004-2009. *BMC Infect Dis.* 2011;11:182.
6. Davies MA, Gibb D, Turkova A. Survival of HIV-1 vertically infected children. *Curr Opin HIV AIDS.* 2016;11:455–464.
7. Violari A, Cotton MF, Gibb DM, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med.* 2008;359:2233–2244.
8. Avert-Global information and education on HIV and AIDS. HIV and AIDS in Eswatini. Avert-Global information and education on HIV and AIDS, 2019. Available at: https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/swaziland. Accessed January 6, 2019.
9. The Government of the Kingdom of Eswatini-Ministry of Health. *HIV Annual Program Report 2018*. Mbabane, Swaziland: Ministry of Health.
10. The Government of the Kingdom of Eswatini-Ministry of Health. *National Strategic Plan for Ending AIDS and Syphilis in Children (2018–2022)*. Mbabane, Swaziland: Ministry of Health; 2018.
11. The Government of the Kingdom of Eswatini-Ministry of Health. *2018 Integrated HIV Managemnet Guidelines*. Mbabane, Swaziland: he Governemnt Kingdom of Eswatini; 2018.
12. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection Recommendations for a Public Health Approach*. 2nd ed. Geneva, Switzerland: WHO Press; 2016.
13. Essajee S, Vojnov L, Penazzato M, et al. Reducing mortality in HIV-infected infants and achieving the 90-90-90 target through innovative diagnosis approaches. *J Int AIDS Soc.* 2015;18(suppl 6):20299.
14. Davies M-A, Pinto J. Targeting 90-90-90—don't leave children and adolescents behind. *J Int AIDS Soc.* 2015;18(suppl 6):20745.
15. Goulder PJ, Lewin SR, Leitman EM. Paediatric HIV infection: the potential for cure. *Nat Rev Immunol.* 2016;16:259–271.
16. Lilian RR, Kalk E, Bhowan K, et al. Early diagnosis of in utero and intrapartum HIV infection in infants prior to 6 weeks of age. *J Clin Microbiol.* 2012;50:2373–2377.
17. Technau K-G, Kuhn L, Coovadia A, et al. Improving early identification of HIV-infected neonates with birth PCR testing in a large urban hospital in Johannesburg, South Africa: successes and challenges. *J Int AIDS Soc.* 2017;20:21436.
18. Laughton B, Cornell M, Grove D, et al. Early antiretroviral therapy improves neurodevelopmental outcomes in infants. *AIDS.* 2012;26:1685–1690.
19. Republic of South Africa-National Department of Health. *National Consolidated Guidelines: For the Prevention of Mother-To-Child Transmission of HIV (PMTCT) and the Management of HIV in Children, Adolescents and Adults*. Pretoria, Republic of South Africa: National Department of Health; 2015.
20. Francke JA, Penazzato M, Hou T, et al. Clinical impact and cost-effectiveness of diagnosing HIV infection during early infancy in South Africa: test timing and frequency. *J Infect Dis.* 2016;214:1319–1328.
21. Bianchi F, Cohn J, Sacks E, et al. Evaluation of a routine point-of-care intervention for early infant diagnosis of HIV: an observational study in eight African countries. *Lancet HIV.* 2019;6:e373–e381.
22. Jani IV, Meggi B, Loquiha O, et al. Effect of point-of-care early infant diagnosis on antiretroviral therapy initiation and retention of patients. *AIDS.* 2018;32:1453–1463.
23. World Health Organization. *WHO Prequalification of in Vitro Diagnostics m-PIMA HIV-1/2 Detect*. Geneva, Switzerland: World Health Organization; 2019.
24. Bisschoff C, Coulon J. HIV testing at birth: are we getting it right? *South Afr J HIV Med.* 2019;20:951.
25. Meggi B, Vojnov L, Mabunda N, et al. Performance of point-of-care birth HIV testing in primary health care clinics: an observational cohort study. *PLoS One.* 2018;13:e0198344.
26. World Health Organization. *HIV Diagnosis and ARV USE in HIV Exposed Infants: A Programmatic Update*. Geneva, Switzerland: World Health Organization; 2018.
27. Maritz J, Hsiao NY, Preiser W, et al. Low uptake of routine infant diagnostic testing following HIV PCR testing at birth. Conference on Retroviruses and Opportunistic Infections (CROI); February 22–25, 2016; Boston, MA.
28. Tchuenche M, Gill MM, Bollinger L, et al. Estimating the cost of diagnosing HIV at birth in Lesotho. *PLoS One.* 2018;13:e0202420.