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Differentiated community-based point-of-care early infant diagnosis to improve HIV diagnosis and ART initiation among infants and young children in Zambia: a quasi-experimental cohort study

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ABSTRACT

Introduction An estimated 800 000 children (<15 years) globally living with HIV remain undiagnosed. To reach these children with timely HIV testing services during infancy, we implemented a community-based differentiated care model using mobile point-of-care (POC) technology for early infant diagnosis (EID) of HIV, and assessed its effects on EID positivity, antiretroviral therapy (ART) initiation and 3-month retention in care.

Methods Between 1 June 2019 and 31 May 2020 at six health facilities in Lusaka, Zambia, we enrolled mother-infant pairs (MIPs) at high risk for vertical transmission of HIV based on missing or late infant EID testing or other maternal risk factors. We offered these MIPs community POC EID testing (post-intervention), and compared their outcomes to historical high-risk controls at the same sites (1 June 2017–31 May 2018; pre-intervention). We used propensity score matched weighting and mixed effects regression modelling to estimate outcome differences pre-intervention and post-intervention, and to identify MIP characteristics predictive of vertical transmission of HIV.

Results 2577 MIPs were included in the analysis: 1763 and 814 high-risk MIPs from the pre-intervention and post-intervention periods, respectively. Infant HIV positivity was significantly higher in the post-intervention (2.2%) vs pre-intervention (1.1%) period (p=0.038), however this difference was attenuated (0.83%, 95% CI: −0.50%, 2.15%) after adjusting for differences in maternal age, maternal antenatal care visits, infant birth month and facility. During the post-intervention period, MIPs where the mother disengaged from care were 12.97 (95% CI: 2.41, 69.98) times as likely to have an infant diagnosed with HIV vs those in which the infant received late EID testing without maternal care disengagement. Among 18 infants diagnosed with HIV by the intervention, 16 (88.9%) initiated same-day ART and all continued ART at 3-month follow-up.

Conclusion Community-based differentiated care employing POC EID technology increased testing positivity in unadjusted analyses, and resulted in high ART initiation and early care retention, suggesting it may be a promising approach for reaching infants and young children living with HIV being missed by current facility-based approaches.

Trial registration number This trial is registered under the following Clinicaltrials.gov Identifier: NCT03133728

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Sub-Saharan Africa accounts for 90% of all new paediatric HIV infections globally, of which up to 50% remain undiagnosed largely from challenges with early infant diagnosis (EID) of HIV, resulting in a widening paediatric HIV treatment gap. While recent trials and large-scale evaluations have shown that new point-of-care (POC) EID diagnostic technologies result in increased rates of EID testing among infants with perinatal HIV exposure, shorter result turnaround times and greater receipt of antiretroviral therapy among infants and young children (IYCs) living with HIV, no studies have evaluated deployment of this technology in community settings to reach mother-infant pairs (MIPs) missed by traditional prevention of vertical transmission of HIV programming.

WHAT THIS STUDY ADDS

⇒ Although several studies have demonstrated the value of POC EID testing in health facilities, none have examined the impact of using this technology in community settings. We showed that our differentiated community-based model is a promising approach for identifying and linking to HIV care IYCs living with HIV missed by more traditional facility-based approaches so they can access life-saving treatment in a timely fashion.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings potentially add a new strategy to global efforts to identify, reach, test and treat IYCs who have disengaged from prevention of vertical transmission of HIV and EID programming in high HIV burden settings. Moving EID testing out of facilities, and into the community, for high-risk MIPs in a client-centred way that uses POC EID technology may reach IYCs living with HIV badly in need of treatment and reorient HIV programmes to go the last mile necessary to eliminate vertical transmission of HIV.

INTRODUCTION

Despite steady declines in incident paediatric HIV infection and remarkable progress toward the elimination of vertical transmission of HIV, an estimated 160 000 newborns still acquire HIV each year.[1] Sub-Saharan Africa accounts for 90% of these new paediatric infections, of which up to 50% were undiagnosed in 2021, resulting in many infants and young children (IYC) being unable to access life-saving antiretroviral therapy (ART).[2 3] Women living with HIV in Sub-Saharan Africa (SSA) have long faced unique barriers to accessing HIV testing, treatment and care for themselves and their IYC.[4 5] This has been due, in part, to standard of care HIV exposure screening and case-finding approaches typically being limited to health facilities where inadequate laboratory capacity can limit access to timely early infant diagnosis (EID) of HIV testing and subsequent clinical action. This contributes to delays in the timely return of test results, which may lead to losses to follow-up, failed or delayed ART initiation, and death.[4–8]

In Zambia, an estimated 66 000 children are living with HIV.[9] In 2021, only 71% of infants HIV-exposed received EID testing, and, of those who tested positive, only 67% initiated ART compared with 92% of their adult counterparts.[9 10] Although the Zambia Ministry of Health (MOH) recommends universal HIV exposure screening and EID testing in all paediatric service access points, IYCs living with HIV are often missed at health facilities. Based on recent UNAIDS data, at least 30% of Zambian infants who are HIV-exposed miss EID testing within 2 months of birth.[11] Because ART clinics and Maternal, Newborn, and Child Health (MNCH) departments have been the main entry points for EID testing in Zambia, and because mother-infant pairs (MIPs) at higher risk for poor HIV outcomes often only present when the child is sick, many IYCs living with HIV do not receive EID testing until symptoms of advanced HIV disease become apparent.[12 13]

In 2016, the m-PIMA HIV-1/2 Detect point-of-care (POC) platform ('m-PIMA'), a fully automated nucleic acid amplification testing (NAAT) platform, developed by Alere Healthcare (now Abbott Laboratories) was prequalified by the WHO for EID testing in resource-limited settings.[14] Extensive field evaluations of m-PIMA for EID have been done in health facilities in SSA that consistently demonstrate its effects on increasing EID testing uptake, shortening testing times (to about 52 min), expediting HIV diagnosis, and increasing rates of early ART initiation for infants who are HIV-infected.[15–17] However, despite the favourable impact of this assay, there are no studies from SSA describing its effects when used in community or household settings as part of a differentiated testing approach to diagnose paediatric HIV.[18 19] We developed a community-based model to reach MIPs missed by facility-based approaches and offer them timely EID testing using the m-PIMA coupled with linkage to care and ART initiation for IYCs found to be living with HIV. Our objective in this paper is to describe our community-based POC EID differentiated care model (ie, 'the community POC model') and estimate its effectiveness according to metrics of EID testing positivity, and ART initiation and 3-month retention in care for IYCs living with HIV in Lusaka, Zambia.

METHODS

Study setting and design

We conducted a quasi-experimental pre-post study examining the effects of the community POC model at six health facilities and their surrounding communities (ie, 'sites') in Lusaka, Zambia. The study sites were selected based on their comparable urban demography, catchment areas and patient populations. All sites had similarly high annual volumes of pregnant and breastfeeding women (PBFW) living with HIV and infants who are HIV-exposed accessing prevention of vertical transmission of HIV services and infants living with HIV accessing ART. Each site is staffed by government healthcare workers, including nurses, clinicians and laboratory technicians, and provides antenatal care (ANC), labour and delivery, dried blood spot (DBS)-based EID testing, ART, and other services for the prevention of vertical transmission of HIV. We delivered the community POC model during the 'post-intervention period' from 1 June 2019 to 31 May 2020 during which time MIPs were actively enrolled, followed and received the intervention. For a comparison group, we defined an analogous pre-intervention period from 1 June 2017 to 31 May 2018, and reviewed existing routine medical records at the same study sites for all PBFW living with HIV with an infant born during this period and followed their records through 30 November 2019 to ascertain a testing outcome.

Participants

For the pre-intervention and post-intervention periods, we reviewed routine MOH paper and electronic records at the six study sites to identify 'potential high-risk' MIPs. In this paper, we defined MIPs as potentially high risk for an adverse HIV outcome if they included a PBFW ≥18 years and an infant or young child who was: 0 days to 17 months old during the pre-periods or post-periods, had probable or known HIV exposure based on history of a missing or positive maternal or positive infant rapid antibody test, and/or missing or late (by >4 weeks) latest age-appropriate EID testing milestone (ie, from age 6 weeks,

6 months, and/or from 6 weeks post-cessation of breastfeeding per the standard of care (SOC) below). For the post-intervention period, we traced by phone or in person potential high-risk MIPs who also had one or more of the following: a. attended ≥1 ANC visits without receiving HIV testing; b. delivered at home and did not return for post-natal care at a health facility (ie, child not tested for HIV); c. were documented as being HIV-positive but never initiated ART; or d. experienced treatment interruption or otherwise disengaged from HIV care. MIPs who met the aforementioned criteria, confirming them as high risk, and who provided written informed consent to receive the intervention were enrolled in the post-intervention cohort. For the pre-intervention period, we were granted a waiver of informed consent for the review of existing, de-identified routine data. For this period, we included records for all potential high-risk MIPs with a non-missing EID testing record. MIPs in which the infant had evidence of receiving all EID testing milestones and the mother was documented to have been initiated and retained on ART were excluded from the study.

Standard of care

Under the SOC during the pre-intervention period, infants exposed to HIV were followed at the clinic from birth until cessation of breastfeeding or age 18 months, whichever occurred first. Infants and young children received facility-based EID testing by DNA PCR (done off-site at a specialised referral laboratory) from age 6 weeks, 6 months, and at 9 months or from 6 weeks after breastfeeding cessation by rapid antibody testing (with DNA PCR confirmation). Nevirapine plus zidovudine (AZT) prophylaxis was prescribed to all infants who were HIV-exposed for 6 weeks after birth, with extension of prophylaxis to 12+ weeks for infants born to women with selected high-risk criteria per national guidelines (ie, women with established HIV infection and not on ART or having received <12 weeks of ART at the time of delivery, or women with viral load (VL) >1000 copies/mL within the 4 weeks before delivery when VL available).[20] All PBFW and children living with HIV were eligible for immediate, lifelong ART regardless of CD4+ count or WHO stage. Prevention of vertical transmission of HIV and EID services largely involved passive ascertainment of maternal HIV exposure status and HIV testing of infants who are HIV-exposed and present for care in ANC, ART, Under 5, outpatient malnutrition and post-natal care clinics.

Community-based active case-finding model

Our community POC model has been described previously.[18] Briefly, it incorporated the following core components: (1) review of site-level routine MOH records to identify high-risk MIPs; (2) a dedicated team, fully integrated within the national prevention of vertical transmission of HIV and EID programme (known as the 'PMTCT programme'), to conduct POC EID testing in the home, community or the nearest convenient location (including health facilities) based on maternal preference; and (3) mobile use of the m-PIMA platform. Six dedicated study teams, assigned to one study site each, partnered with MOH staff from the MNCH departments at the sites to deliver the model, and were comprised of a nurse study coordinator, one data coordinator, two data associates, six research assistants (RAs) and six peer educators.

We trained study and site MOH staff on the community POC model and mobile use of the m-PIMA. RAs were trained to review routine medical records to identify potential high-risk MIPs who met the study inclusion criteria as outlined above. On identifying a potential high-risk MIP, RAs would use routinely available locator information to contact the mother or caregiver by phone or, failing that, by home visit to ask if they might be interested in study participation. If interested, RAs verified participants' study eligibility, consented them for the study, confirmed their high-risk criteria and offered them the community POC model. Consenting parents or guardians were asked for their preferred site for HIV testing in the community (eg, their home, a friend or relative's home, community health post, etc) or the nearest health facility. If the parent/guardian chose to test their child outside the home, the study team accompanied them to their preferred site in the community or at the facility. RAs had experience as lay HIV counsellors and were trained on DBS sample collection and EID testing using the m-PIMA. Study peer educators, who had backgrounds as community health workers from study communities, supported MIP home visits and community follow-ups. MOH nurse midwives were available at each study site to perform confirmatory EID testing using the m-PIMA in cases of a first positive test in the community.

Study procedures

Pre-post cohort construction

For the post-intervention period, we constructed a cohort of high-risk MIPs whose infants were born 1 June 2019–31 May 2020 and who met study eligibility criteria using a two-step process. In the first step, trained RAs reviewed the following routine records to identify potential high-risk MIPs: the national SmartCare HIV electronic medical record (EMR), CIDRZ Central Laboratory Information Management System (LIMS), and routine MOH registers from the ANC, prevention of vertical transmission of HIV, Under 5, and HIV Testing Services (HTS) departments. MIPs potentially at high risk based on review of these routine records had their data entered into a secure, electronic study log. For mothers with documented HIV infection, we reviewed the SmartCare EMR and ART clinic records for any evidence of missed ART initiation, ART treatment interruption, or other disengagement from HIV care to further define their risk status. In the second step, we contacted MIPs in the study log by phone or in person in the community, confirmed their high-risk status in person and offered them study participation and the community POC model as described above.

For the pre-intervention period, we reviewed all available medical records at the study sites and constructed a cohort of all MIPs who met study eligibility criteria and received the SOC between 1 June 2017 and 31 May 2018. Individual-level clinical and demographic data were abstracted from available records through 30 November 2019, to allow at least 18 months of observation time.

Eid testing and linkage to care procedures

RAs collected ~400 µL of blood by heel or finger prick from infants. Approximately 350 µL (70 µL × 5 spots) was collected onto a DBS card while 25 µL was collected directly into a capillary tube and tested on location using the m-PIMA. m-PIMA results were made available to the parent/guardian within 1 hour, while DBS samples were sent to the central laboratory for confirmatory DNA PCR testing. If the m-PIMA test result returned positive, the study team escorted the parent/guardian to the nearest health facility for repeat testing using the same m-PIMA platform and to immediately initiate ART. If the m-PIMA test result returned negative, the parent/guardian was asked to return to the clinic within 4 weeks to receive the results of confirmatory DBS DNA PCR testing, at which time the infant exited the study if this was negative. Parents/guardians of infants testing positive on m-PIMA also were required to return to the health facility to collect results of confirmatory DBS DNA PCR testing. Infants confirmed to have HIV infection remained on ART. Concordant and discordant results were managed per national guidelines.[20 21]

Data collection

All MIPs had the following routine data abstracted from their medical records: demographic information, maternal HIV status, infant HIV testing history, maternal ART history, infant ART history (if relevant) and follow-up visit dates. MIPs in the post-intervention cohort underwent study-specific data collection at enrolment and follow-up on HIV, obstetric, and infant clinical histories, EID testing history, and maternal and infant medication histories. All data were entered into a study database in Microsoft Excel (Redmond, WA, USA) for the pre-intervention period and OpenClinica for all data collected during the post-intervention period.

Study follow-up

Infants who tested as being HIV-positive through the study were followed for 12 weeks past enrolment to observe 3-month retention on ART and to complete a one-time study follow-up visit.

Outcomes

The primary outcome was HIV positivity, a metric of the efficiency of EID testing and overall risk status of the mother-infant pair, defined as the percent of exposed infants with a documented positive EID test result. The numerator was the number of eligible exposed infants with a documented positive EID test result from age 6 weeks and the denominator as the number of infants with a documented EID test result. For IYCs living with HIV, the primary outcome was ART uptake, and 3-month survival and retention in care. Secondary outcomes included median infant age at time of first documented EID test result, time from sample collection to return of results to the caregiver (ie, total turnaround time), time from specimen collection to ART initiation, and median age at ART initiation.

Statistical analysis

We used descriptive statistics to characterise the pre-intervention and post-intervention populations assessing significant differences between the two using the t-test for continuous variables and χ^2 test for categorical variables. The pre-post analysis used propensity score matched weighting to account for unmeasured secular trends and unbalanced differences between the pre-intervention and post-intervention populations. Propensity score matching included maternal age, facility and infant birth month. Infant birth month was included to account for unmeasured secular trends in peripartum MIP migration (eg, to be with family support networks) that might influence access to health services.[22] Next, we conducted a propensity score-weighted mixed effects regression analysis to estimate the difference in the primary outcome measure, HIV positivity, between the pre-intervention and post-intervention populations adjusting for fixed effects of age, birth month, and health facility, and allowing for random effects at the facility level. For the post-intervention period analysis of factors associated with vertical transmission of HIV, we used mixed effects regression allowing for random effects at the facility level. For this analysis, we examined maternal risk factors from our intervention eligibility criteria, including women who did not initiate ART or had any record of treatment interruption.[23] Finally, we created marginal probability plots with 95% CIs to identify characteristics predictive of mother-infant pairs with the highest risk for vertical transmission of HIV. All analyses were conducted using Stata 17 (StataCorp, 2021, College Station, TX, StataCorp LLC).

Patient involvement

Patients were involved in the conduct, reporting and dissemination of this research. During the feasibility stage, in-depth interviews were conducted to determine the feasibility and acceptability of the intervention (findings have been published). Once the trial is published, findings will be disseminated through existing technical working groups, community structures and Zambia annual national health conference.

Role of funding source

The study funder assisted with the study design, results interpretation, and writing of the report, but had no role in the data collection process or the decision to publish the data.

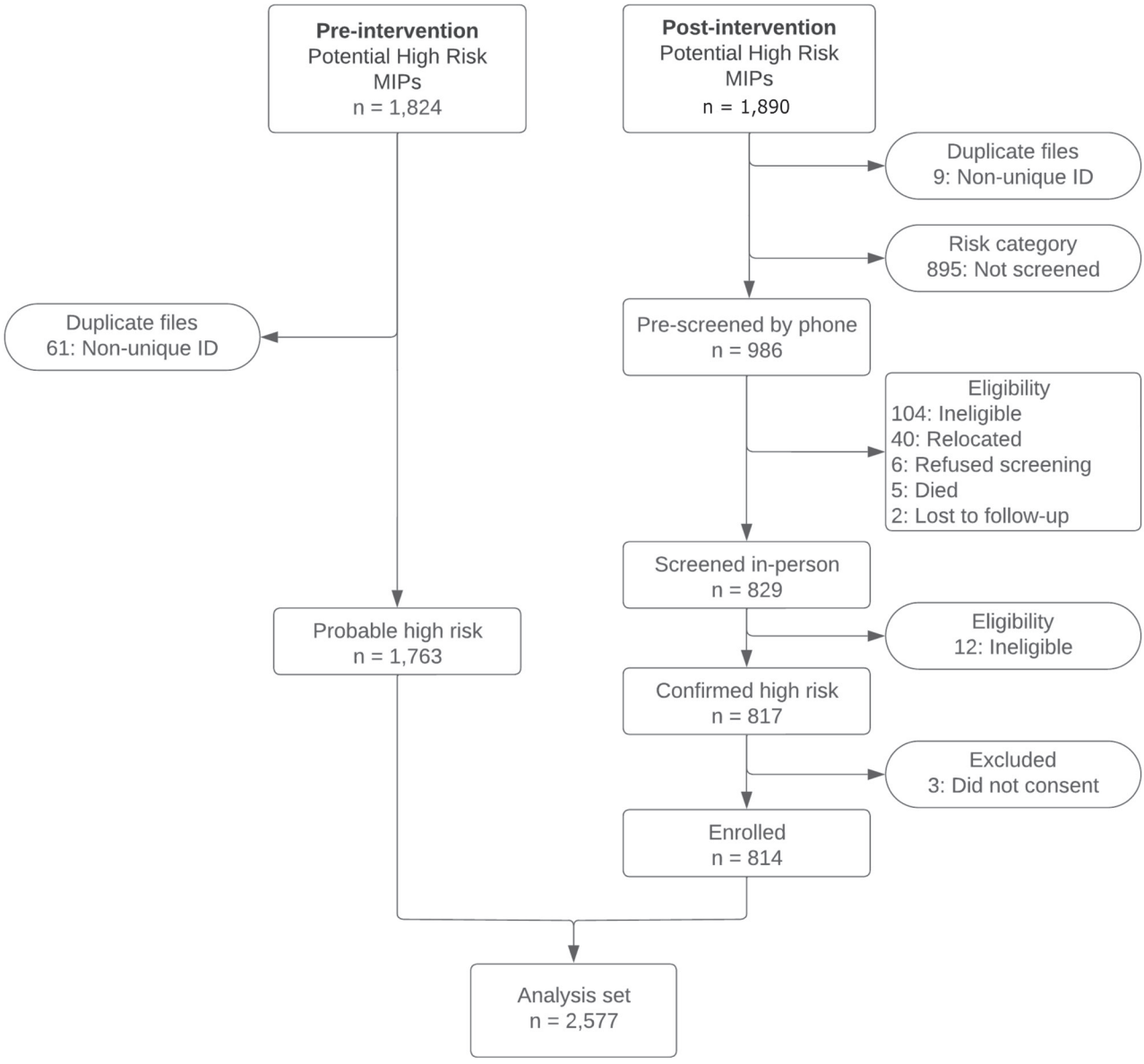


Figure 1 Study population flow diagram by intervention period.

RESULTS

We reviewed 2824 medical records from the pre-intervention period and 3435 from the post-intervention period and identified 1824 (64.6%) and 1890 (55.0%) MIPs in each period, respectively, who were potential high risk. Of these, 1763 (96.7%) in the pre-intervention and 814 (43.1%) in the post-intervention period were included, giving a total of 2577 MIPs in the final analysis (figure 1). The overall median maternal age was 29 years (IQR: 25–34 years), with the pre-intervention median being 29 years (IQR: 25–34 years) and the post-intervention median 30 years (IQR: 25–35 years).

The pre-intervention and post-intervention study populations differed by maternal age, the number of ANC visits recorded, MIP high-risk category, study site distribution and the month of infant birth (table 1). As expected, the two populations also differed in the location of EID testing, with home and other community-based testing being more common in the post-intervention cohort.

Overall, we found a significantly higher proportion of infants had a positive EID test result in the post-intervention period (2.2%, 18/814) compared with infants in the pre-intervention group (1.1%, 20/1743) (p=0.038). After adjustment for maternal age, number of ANC visit, infant birth month and health facility, the testing positivity in the intervention population was 0.83% (95% CI: −0.50%, 2.15%) higher compared with the pre-intervention population, which was not statistically significant. When examining our primary outcome using logistic regression modelling, we estimated that MIPs

Table 1 Population characteristics by intervention status (n=2577)

Factor	Level	Pre-intervention N (%)	Post-intervention N (%)
N		1763	814
Age category	18–24 years	176 (10.0)	160 (19.7)
	25–29 years	422 (23.9)	239 (29.4)
	30–34 years	467 (26.5)	201 (24.7)
	35+ years	404 (22.9)	206 (25.3)
	Not recorded	294 (16.7)	8 (1.0)
Location of EID testing	Facility	1763 (100.0)	389 (47.8)
	Home	0 (0.0)	391 (48.0)
	Community venue*	0 (0.0)	34 (4.2)
Number of ANC visits	0 visit	114 (6.5)	2 (0.2)
	1 visit	124 (7.0)	18 (2.2)
	2 visits	203 (11.5)	52 (6.4)
	3 visits	340 (19.3)	158 (19.4)
	4 visits	270 (15.3)	274 (33.7)
	5+ visits	96 (5.4)	295 (36.2)
	Not recorded	616 (34.9)	15 (1.8)
High-risk category	Late for 6-week test	9 (0.5)	710 (87.2)
	No testing at ≥6 months	524 (29.7)	42 (5.2)
	No testing after cessation of breastfeeding	818 (46.4)	35 (4.3)
	Maternal HIV care disengagement†	412 (23.4)	27 (3.3)
Study site	George	259 (14.7)	154 (18.9)
	Kalingalinga	187 (10.6)	128 (15.7)
	Kamwala	352 (20.0)	139 (17.1)
	Makeni	245 (13.9)	104 (12.8)
	Martero	373 (21.2)	133 (16.3)
	N'gombe	347 (19.7)	156 (19.2)
Infant birth month	January	120 (6.8)	98 (12.0)
	February	155 (8.8)	78 (9.6)
	March	172 (9.8)	74 (9.1)
	April	174 (9.9)	90 (11.1)
	May	129 (7.3)	72 (8.8)
	June	171 (9.7)	58 (7.1)
	July	142 (8.1)	42 (5.2)
	August	147 (8.3)	30 (3.7)
	September	134 (7.6)	39 (4.8)
	October	140 (7.9)	87 (10.7)
	November	140 (7.9)	66 (8.1)
	December	138 (7.8)	80 (9.8)
	Not recorded	1 (0.1)	0 (0.0)

*Community venue: included locations that were not at home and included participant-identified testing venues like churches, community health posts and schools.
†Maternal HIV care disengagement: women who did not initiate ART or had any record of treatment interruption during the pre-intervention or post-intervention periods.
ANC, antenatal care; EID, early infant diagnosis.

Table 2 Adjusted regression results for infant testing HIV positive (n=2577)

Study population	Unadjusted			Adjusted		
	OR	95% CI	P value	aOR	95% CI	P value
Pre-intervention	1.00 (ref)	ref	ref	1.00 (ref)	ref	ref
Post-intervention	1.97	(1.04, 3.75)	0.038	2.03	(0.69, 5.99)	0.197

*Adjustment set includes age, birth month, and number of antenatal visits with random effect at facility level
aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

receiving our community POC model were 2.03 times more likely (95% CI: 0.69, 5.99) to have an infant diagnosed with HIV after adjusting for potential confounders but non-significantly so (table 2).

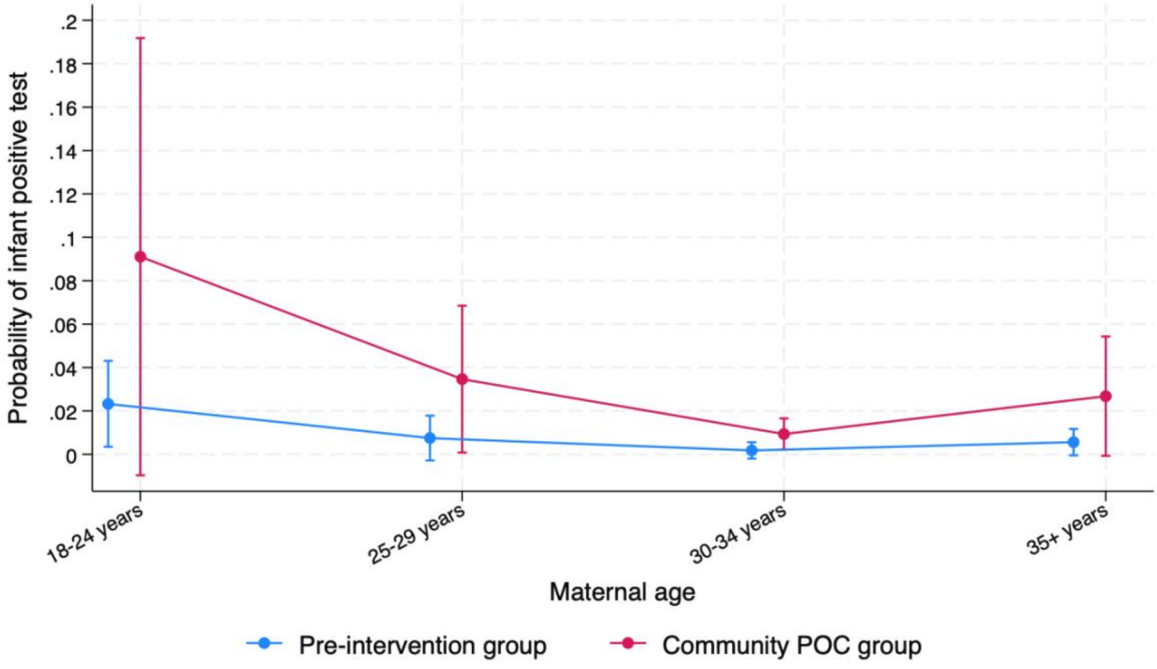
In the post-intervention period, we identified significant associations between infant HIV positivity and maternal characteristics after adjusting for select covariates, including maternal risk category, maternal age, timing of maternal HIV diagnosis and place of infant HIV testing (table 3). Young mothers 18–24 years old had 7.38 (95% CI: 2.55, 21.33) times the odds of having an infant test HIV-positive compared with older mothers aged ≥35 years. PBFW who received an HIV diagnosis during the post-natal period had 43.10 (95% CI: 16.26, 114.27) times the odds of having an infant test HIV-positive compared with women diagnosed pre-conception. MIPs who received EID testing in the home had a 71% decreased likelihood (aOR 0.29, 95% CI: 0.10, 0.83) of testing positive compared with MIPs who received EID testing following accompaniment to a health facility as the last step in the community POC model. Finally, MIPs who experienced disengagement from HIV care (ie, who experienced treatment interruption or loss to follow-up) had 12.97 (95% CI: 2.41, 69.98) times the adjusted odds of having an infant diagnosed with HIV compared with those who had no documented evidence of care disengagement.

Though not quite significantly different in our marginal probability model, younger mothers, aged 18–24 years, had the highest point estimate probability at

Table 3 Crude and adjusted estimates for odds of HIV-positivity among infant participants

Covariate	Level	Crude		Adjusted	
		OR	95% CI	aOR	95% CI
Maternal age	18–24 years	6.91	(2.62, 18.21)	7.38	(2.55, 21.33)
	25–29 years	2.17	(0.32, 14.90)	2.17	(0.31, 15.44)
	30–34 years	0.51	(0.12, 2.17)	0.54	(0.12, 2.40)
	35+ years	ref	–	ref	–
Number of ANC visits	≤2 visits	ref	–	ref	–
	3 visits	1.37	(0.17, 11.07)	1.33	(0.16, 11.31)
	4 visits	0.92	(0.10, 8.59)	0.92	(0.09, 9.44)
	5+ visits	0.36	(0.03, 4.61)	0.34	(0.02, 5.30)
High-risk category	Late for 6-week test	ref	–	ref	–
	No testing at ≥6 months	3.49	(0.6, 20.2)	2.59	(0.31, 21.37)
	No testing after cessation of breastfeeding	2.05	(0.93, 4.55)	2.20	(0.35, 13.93)
	Maternal HIV care disengagement*	15.86	(4.71, 53.38)	12.97	(2.41, 69.98)
Timing of maternal HIV diagnosis	Pre-conception	ref	–	ref	–
	Antenatal	3.10	(0.91, 10.5)	1.97	(0.59, 6.57)
	Post-natal	40.96	(13.03, 128.74)	43.10	(16.26, 114.27)
Location of EID testing	Facility	ref	–	ref	–
	Home	0.40	(0.14, 1.13)	0.29	(0.10, 0.83)
	Community venue†	0.96	(0.31, 2.96)	0.58	(0.32, 1.03)

Adjustment for age, number of antenatal visits and location of EID testing.
*Maternal HIV care disengagement: women who did not initiate ART or had any record of treatment interruption during the pre-intervention or post-intervention periods.
†Community venue: included locations that were not at home and included participant-identified testing venues like churches, community health posts and schools.
ANC, antenatal care; EID, early infant diagnosis.



Note: Adjusted for health facility and month of infant birth

Figure 2 Adjusted marginal probability plot of participant mother-infant pairs with a positive HIV test result by maternal age and intervention status with accompanying 95% CIs.

9.11% (95% CI: −0.01, 19.18%) of having an infant test positive for HIV while older mothers, aged 30–34 years, had the lowest point estimate probability at 0.50% (95% CI: −0.48, 1.48%) (figure 2).

The median time from birth to first HIV test in the pre-intervention period was 46 days (IQR: 43–55 days) while the median time among those in the community POC model was 213 days (IQR: 120–243 days). A total of 18 infants were diagnosed with HIV through the community POC model, with a median age of 219.5 days (IQR: 140–313 days), and, of these, 16 (88.9%) initiated ART. The median time to ART was 0 days for these 16 infants (IQR: 0–0.5 days) demonstrating same-day ART initiation. At 3 months of follow-up, of those who initiated ART, 16 (100.0%) infants were retained and continuing on ART. The 2 (11.1%) infants who were not documented to have initiated ART were considered lost to follow-up.

DISCUSSION

While several studies have demonstrated the benefits of providing facility-based POC EID testing for infants exposed to HIV, this is the first study, to our knowledge, that describes the effects of deploying this technology at community level as part of a novel differentiated care model for high-risk MIPs.[17 19] We previously demonstrated the acceptability, feasibility and appropriateness of this model when integrated into the national HIV treatment programme at community level.[18] The results presented in this paper extend those previous findings, and suggest that our model reaches MIPs who have experienced a gap along the continuum of care for the prevention of vertical transmission of HIV, and offers their infants needed EID testing and access to same-day ART.

Our study described identifying infants exposed to HIV with numerically higher HIV test positivity after introducing our community POC model despite declining paediatric HIV incidence in Zambia over the study period, suggesting that the model preferentially reached MIPs at greater risk for vertical transmission of HIV. Infants in the post-intervention period had a substantially longer time to first EID test result, reflecting the care disengagement in the intervention population. In most SSA countries, diagnosing HIV in infants who are HIV-exposed involves passive case-finding approaches deployed routinely in ART clinics and maternal and child health service access points, and requires EID testing using specialised equipment at central laboratories. Even with central laboratories in all provinces of Zambia, and national guidelines advocating for testing from birth up to 6 weeks post-cessation of breastfeeding, many infants who are HIV-exposed either do not get tested at all, miss one or more DBS collections for DNA PCR testing, or never receive the test result.[24 25] Differentiated, mobile deployment of the m-PIMA provided the opportunity to overcome some of these barriers for infants at highest risk for HIV acquisition. Indeed, despite being initially missed by health facilities, infants diagnosed through the community POC model initiated ART on the same day as HIV diagnosis, on average, and had high retention in care at 3 months.

We provided EID testing to over half of the intervention population at home or in another convenient

community-based location based on MIPs' stated preference for testing venue. While offering MIPs choice in where to undergo EID testing may have enhanced the client-centeredness of our model, concerns surrounding privacy with EID testing in the community may have influenced their decision.[18] Interestingly, testing at home was associated with significantly lower odds of infant HIV-positivity. In so far as women who opted for EID testing at home had disclosed their HIV status to other members of the household, including their partners, this finding may reflect the protective effects of HIV status disclosure on vertical transmission of HIV, with women who had not disclosed their status and, therefore, at higher risk for vertical transmission of HIV potentially preferring accompaniment to the nearest facility to preserve confidentiality.[26 27]

Infants and young children newly diagnosed with HIV through our model were more likely to have a mother who was younger, had their HIV identified postnatally, and to have experienced HIV care disengagement, all of which are known risk factors for vertical transmission of HIV.[23 28 29] Thus, our study points to an emerging 'risk profile' of PBFW in Zambia who might benefit from differentiated prevention of vertical transmission of HIV support. The finding that women with an infant who tested HIV-positive through our community POC model had specific risk factors fits with evidence from Zambia and the region showing pregnant and breastfeeding adolescent girls and young women to be a particularly vulnerable population in need of tailored and evidence-based strategies for HIV testing, treatment and prevention of vertical transmission of HIV.[30 31] Studies have found lower uptake of ART among pregnant adolescents and higher rates of vertical transmission of HIV among adolescent girls compared with their adult counterparts.[32–36] The extent to which other vulnerable populations may have comprised high-risk MIPs in our study is unknown, but we suspect we enrolled women facing particularly high barriers to prevention of vertical transmission of HIV and EID services, such as PBFW who received HIV testing late or women engaged in sex work. In Malawi, for example, PBFW living with HIV who had a positive HIV test postpartum (either confirming a new HIV diagnosis or prior diagnosis following return to care) were nearly seven times as likely to experience vertical transmission of HIV as PBFW with a positive test during pregnancy, and late identification of HIV positivity was associated with living far from the nearest health facility.[29] Other studies have documented the barriers faced by female sex workers (FSWs). In one study, 70% of FSWs reported that none of their children had been offered HIV testing in the last 5 years despite high rates of maternal HIV infection in this population.[30] Thus, additional research is required to further adapt our community POC model for adolescent girls and young women and FSWs living with HIV, and to estimate its impact on vertical transmission of HIV and EID outcomes for these vulnerable and key populations. With further study and investment, our model may have the potential to better reach these underserved communities and at-risk populations with timely prevention of vertical transmission of HIV and EID services.[18]

Several implementation issues with our model should be considered by governments and implementing partners before translating our findings into policy and practice to strengthen prevention of vertical transmission of HIV programmes. First, identification of high-risk MIPs from paper-based records is a time-consuming process and one that should be automated using available routine electronic data systems, such as EMRs, which can be assisted by emerging machine learning technologies. Second, in our study, a dedicated mobile team implemented tracing, POC EID testing in the community, MIP accompaniment to health facilities, and immediate linkage to care for infants who tested positive for HIV. Given prevailing health worker shortages in many SSA settings, scale-up of a community POC model will require task-shifting to community health workers and integration within existing community-based service delivery platforms to be feasible. As such, further study and investment should focus on how best to leverage existing PEPFAR commodities, human resources and differentiated service delivery models to provide community-based EID testing services that reach the most vulnerable MIPs in the community. Third, several operational issues with the m-PIMA platform call for further investment in strengthening laboratory health system building blocks for EID services. Notably, laboratory diagnostic networks and quality assurance and control structures must extend their remit beyond specialised central laboratories to address the following issues for optimal mPIMA operability: (a) the platform's battery life supports up to 6 tests between charges, often necessitating keeping a backup battery on hand to extend the duration of community activities; (b) the platform is relatively lightweight but requires transportation to safely use it in community venues; (c) minimising error rates requires stable platform operating temperatures and quality control measures to prevent unnecessary re-testing; (d) embedding the platform within an existing laboratory quality management system is key to establish and monitor operator competence, perform analyser maintenance and calibration, and conduct regular proficiency testing; and (e) supply chain management systems must be robust to ensure an uninterrupted supply of testing cartridges.

Although our implementation research approach likely provided results relevant to routine prevention of vertical transmission of HIV programme settings, our study had several limitations. First, the pre-intervention phase relied exclusively on existing routinely collected MOH data, and, by necessity, on including infants with a documented EID test result, which may have resulted in potential selection bias. However, based on our programmatic experience in Zambia, EID test results that return negative are more likely to go unreported in MOH registers. In so far as infants who underwent sample collection but did not have an EID test result recorded were

more likely to be HIV-negative than HIV-positive, it is possible that our findings underestimate the true effect size of the intervention. Second, a lower than expected proportion of high-risk MIPs from the post-intervention period were included in the study due to the inability to reach many MIPs by phone or home visit to complete the pre-screening process. Missing locator information routinely collected at health facilities, including phone numbers and addresses, limited our ability to reach potential participants to pre-screen them for study enrolment and provision of the study intervention. Third, due to the pragmatic nature of our study, we were only able to follow-up on study participants living with HIV for 3 months to document linkage to care, ART initiation and short-term care retention. Future work should examine longer-term outcomes to estimate effects on retention in care, viral suppression and survival at 1 year and beyond. Fourth, while we previously demonstrated the acceptability, feasibility and appropriateness of the community POC model, we did not collect other implementation outcomes data, such as costing data. Lastly, while this study enrolled women facing particularly high barriers to prevention of vertical transmission of HIV and EID services, findings may not be generalisable to rural populations or other settings outside Southern Africa.

In conclusion, the implementation of a differentiated community-based model employing novel POC EID technology may be a promising approach to achieve the following benefits: (1) reaching MIPs at higher risk for vertical transmission of HIV; (2) identifying IYCs living with HIV missed by traditional facility-based approaches; and (3) starting IYCs living with HIV who experienced diagnostic delay on same-day ART. Further study of the model in hybrid effectiveness-implementation pragmatic trials could help establish the effects of the model on longer-term infant clinical outcomes, elucidate how best to scale this approach alongside complementary facility-based EID approaches and reveal the impact on implementation metrics like reach among all high-risk MIPs, cost per new paediatric HIV case identified, or incremental cost-effectiveness. Prevention of vertical transmission of HIV programmes serving large populations of adolescent and young PBFW, women who belong to key population groups, or those with higher rates of care disengagement during the peripartum period might especially benefit from the implementation of the community POC model for early identification and linkage to care of IYCs living with HIV missing from their programme.

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