

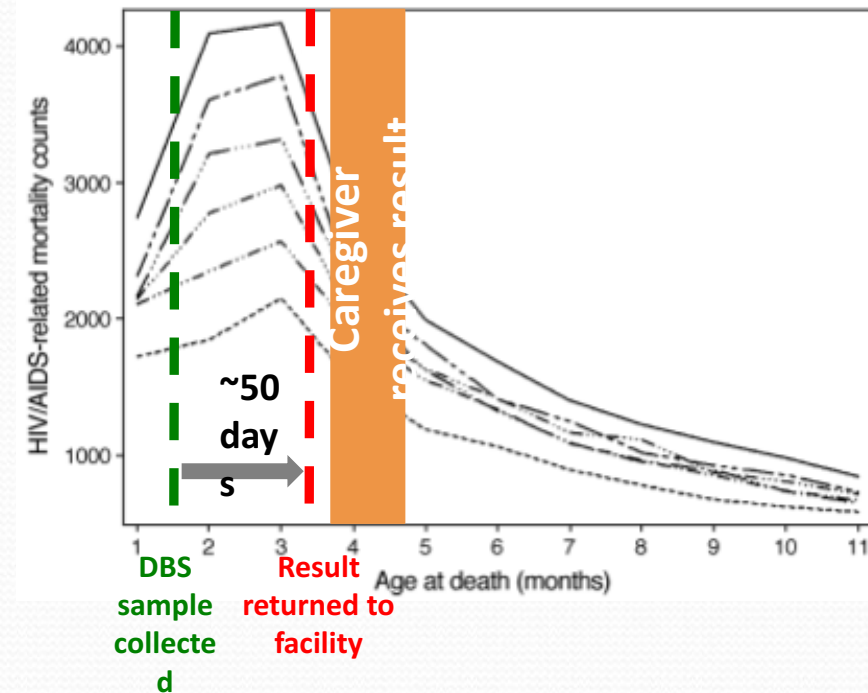
Performance of point-of-care birth HIV testing in primary health care clinics: an observational cohort study

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Background

- Laboratory capacity for early infant diagnosis of HIV has expanded, but health systems struggle with long test turn-around times associated with centralized testing
- Only 51% of infants born to women living with HIV received a virological test within the first two months of life (2015)
- High rates of loss to follow-up before initiation of ART remains a public health problem and contributes to HIV-related infant mortality
- WHO recently prequalified two point-of-care technologies for early infant diagnosis



WHO recommends adding NAT at Birth to the EID strategy

Box 1 Adding NAT at birth to the existing EID strategy

As EID programmes are further scaled up, every effort should be made to improve uptake of NAT at 4–6 weeks, strengthen retention along the testing-to-treatment cascade, ensure confirmation of NAT positive results with a second sample and ensure that infants who test negative by NAT are retained in care until a final diagnosis is made.

To add NAT at birth, effective linkage to maternal HIV screening at the time of delivery should be ensured and the following steps taken:

- collection of data on performance and feasibility of birth testing during implementation;
- improvement of uptake and retention in the testing-to-treatment cascade;
- active tracking of infants with negative NAT at birth to ensure that they return at six weeks for retesting and cotrimoxazole initiation, and
- retesting of infants who test positive at birth with collection of a second specimen as soon as possible. ART should be started immediately after the first positive test and can be stopped if the second specimen tests negative.

Objectives

General objective:

The overall aim of this study was to evaluate the performance and benefit of POC EID testing of HIV-exposed newborns at birth in maternities.

Specific objectives:

- **Specific Objective 1: Determine the sensitivity, specificity and predictive values of POC EID at birth compared with laboratory-based EID testing at birth.**
- **Specific Objective 2: Determine the proportion of HIV infected infants diagnosed by testing at birth and four to six weeks compared by testing only at four to six weeks.**



Methods-General

- **Study Design:** prospective observation study
- **Study sites** were 7 maternity wards and respective PMTC clinics.
- **Conventional:** Roche CAP/CTM 96 HIV-1 Qualitative Test v2 (Roche Molecular Diagnostics, Branchburg NJ, USA).
- **POC:** Alere q HIV-1/2 Detect system (Alere Inc, Waltham, Massachusetts, USA)
- **Both POC and SOC EID** were performed by nurses at maternity wards using whole blood collected from infants < 24 hours of age.
- **A total of 2,350 infants** were enrolled in the study from November 2014 to July 2016.

Methods-Study Design

Maternity
Wards : <24 h



Follow-up

Child At Risk
Consultation: >4-6 weeks



- Informed Consent/Inclusion
- Demographic data collection
- Sample collection and testing on POC

Active tracing
and reminders

- Demographic Table
- Sample collection and testing on PÔC

Methods- Eligibility Criteria

- **Inclusion Criteria:**

- HIV-exposed infants born of HIV-positive pregnant women over 18 years of age, regardless of their PMTCT history.
- Less than 24 hours of age.
- Whose mothers or guardians provide informed consent

- **Exclusion Criteria:**

- Older than 24 hours of age when being tested at birth.
- Serious medical conditions, like hemophilia, idiopathic thrombocytopenic purpura and hemolytic disease of the newborn which would make testing harmful for the infant, or disrupt the accuracy of normal laboratory analysis and its interpretation.
- Mothers given a delivery by Cesarean or with any delivery complications.

Results (1)- Flow Diagram at birth

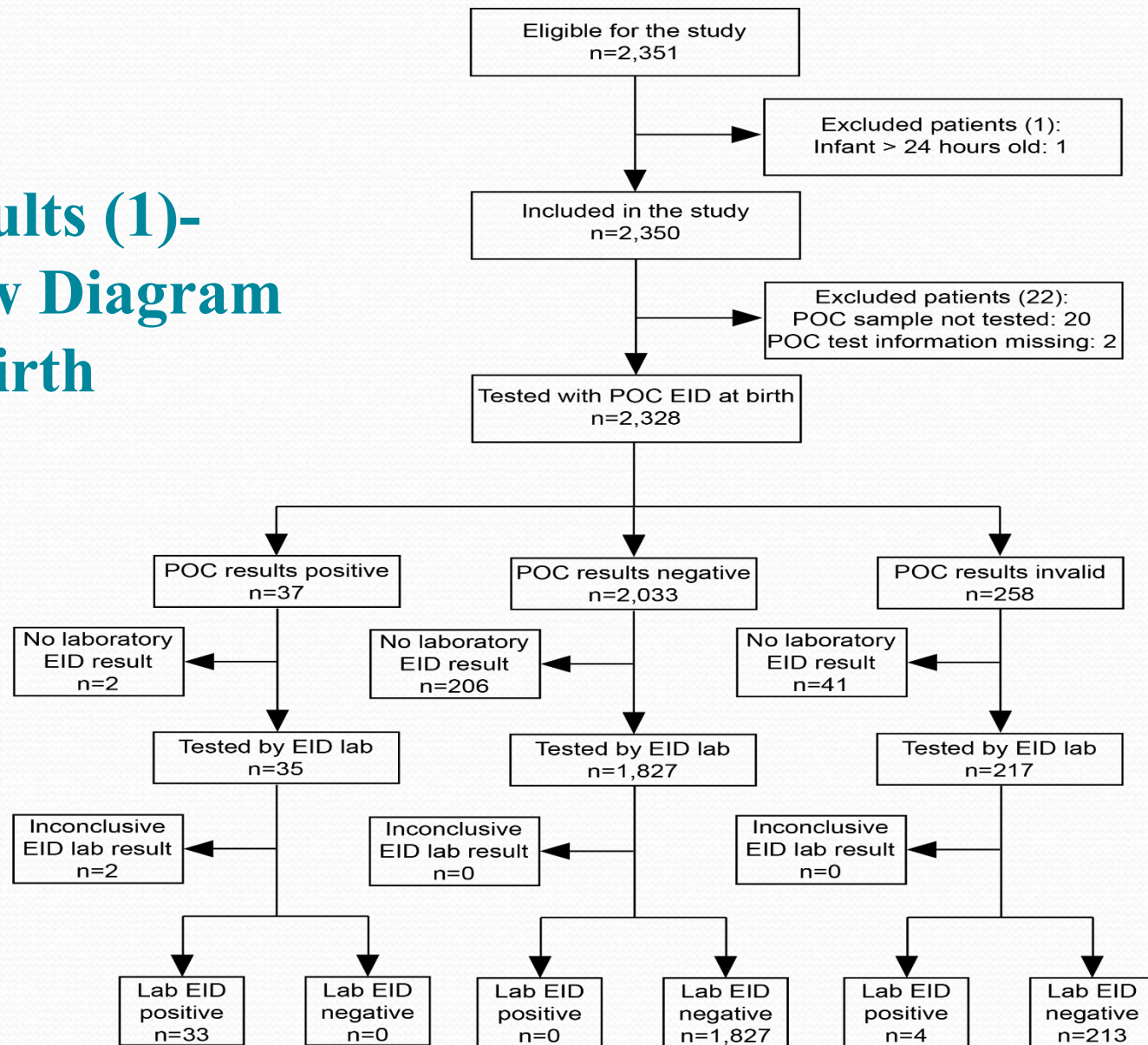


Figure 1. Flow diagram of study participants at birth.

POC results invalid correspond to reported testing errors.

No laboratory EID result correspond to dried blood spot specimens that were rejected from testing or results not reported.

Results (2)- Patient characteristics

Birth laboratory Test									
		Total		Negative		Positive		Invalid	
		n	%	n	%	n	%	n	%
Total		2350	100.0%	2051	87.3%	37	1.6%	262	11.1%
Sex	Female	1185	50.4%	1024	86.4%	24	2.0%	137	11.6%
	Male	1141	48.6%	1005	88.1%	12	1.1%	124	10.9%
	Data not available	24	1.0%	22	91.7%	1	4.2%	1	4.2%
Mother regimen	None	13	0.6%	10	76.9%	2	15.4%	1	7.7%
	Option A	11	0.5%	10	90.9%	1	9.1%	0	0.0%
	ART	1981	84.3%	1733	87.5%	29	1.5%	219	11.1%
	Data not available	345	14.7%	298	86.4%	5	1.4%	42	12.2%
Routine laboratory Early Infant Diagnosis Test									
Total		2350	100%	1501	63.9%	59	2.5%	790	33.6%
Sex	Female	1185	50.4%	746	63.0%	30	2.5%	409	34.5%
	Male	1141	48.6%	742	65.0%	28	2.5%	371	32.5%
	Data not available	24	1.0%	13	54.2%	1	4.2%	10	41.7%
Age	≤2 months	1597	68.0%	1326	83.0%	45	2.8%	226	14.2%
	2 - 6 months	130	5.5%	97	74.6%	9	6.9%	24	18.5%
	6 - 12 months	8	0.3%	5	62.5%	2	25.0%	1	12.5%
	Data not available	615	26.2%	73	11.9%	3	0.5%	539	87.6%
Mother regimen	None	13	0.6%	9	69.2%	1	7.7%	3	23.1%
	Option A	11	0.5%	4	36.4%	2	18.2%	5	45.5%
	ART	1981	84.3%	1427	72.0%	54	2.7%	500	25.2%
	Data not available	345	14.7%	61	17.7%	2	0.6%	282	81.7%
Infant regimen	None	9	0.4%	6	66.7%	2	22.2%	1	11.1%
	NVP	1442	61.4%	1220	84.6%	51	3.5%	171	11.9%
	AZT	24	1.0%	18	75.0%	0	0.0%	6	25.0%
	Data not available	875	37.2%	257	29.4%	6	0.7%	612	69.9%
Infant breastfeeding	No	41	1.7%	26	63.4%	2	4.9%	13	31.7%
	Yes	1174	50.0%	974	83.0%	41	3.5%	159	13.5%
	Data not available	1135	48.3%	501	44.1%	16	1.4%	618	54.4%

Option A=WHO recommended prophylaxis which includes: ante-partum AZT starting as early as 14 weeks gestation; intra-partum single-dose NVP and first dose of AZT/3TC at onset of labour; post-partum daily AZT/3TC for 7 days. NVP=Nevirapine. AZT=Zidovudine. ART=antiretroviral therapy. Invalid=Results not available or DBS sample rejected due to poor quality

Resultados (3)- Performance of Alere a at Birth

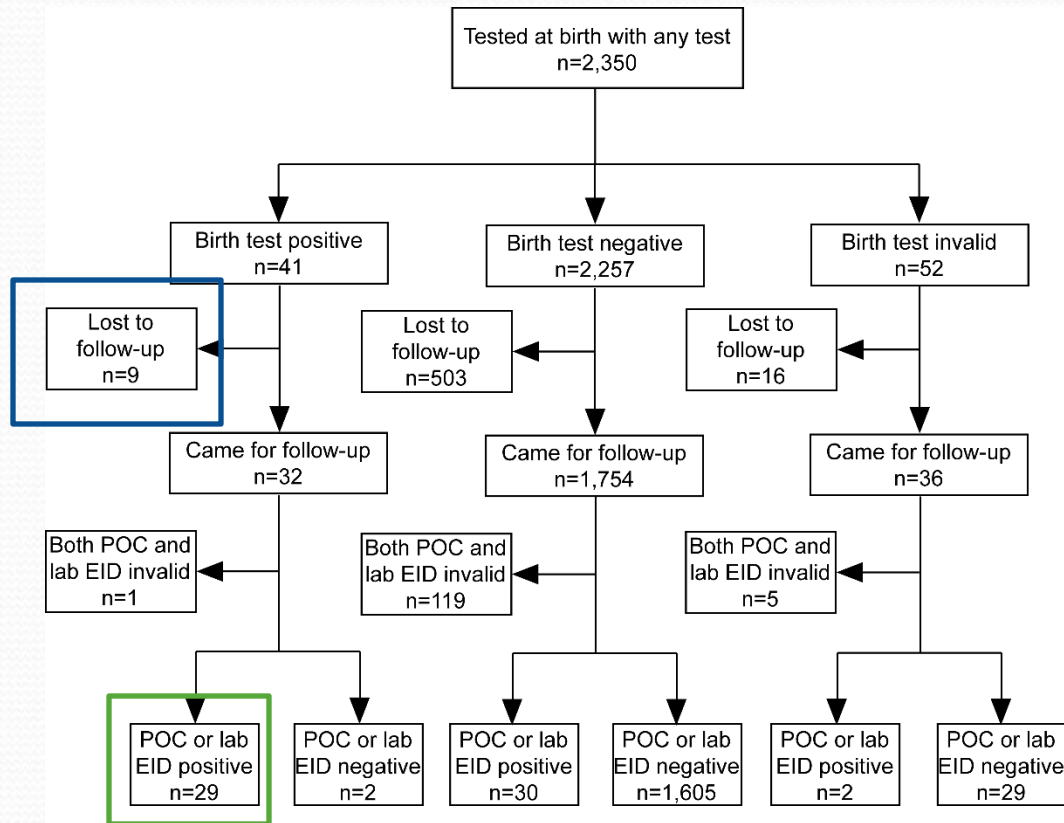
Table 1: Results of at birth point-of-care testing with the Alere q HIV-1/2 Detect system vs reference birth laboratory testing using the Roche CAP/CTM Qualitative HIV-1 assay.

		Point-of-Care Early Infant Diagnosis			Total
		Positive	Negative	Invalid	
Laboratory Early Infant Diagnoses	Positive	33	0	4	37
	Negative	0	1827	224	2051
	Invalid	4	206	52	262
	Total	37	2033	280	2350

Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value(95% CI)	Negative Predictive Value (95% CI)
100% (89,4-100)	100% (99,8-100)	100% (89,4-100)	100% (99,8-100)

Table 2: Performance of Alere q a birth

Results (4)- Flow Diagram at birth vs routine EID test at 4-6 weeks



Around 50% were already positive at Birth (29/61)

Increase of 16,4% of patient yield if birth testing is added (71 vs 61)

Figure 2. Flow diagram of study participants at birth and at routine EID testing time point
Lost to follow-up=patients tested at birth but who did not attend routine early infant diagnosis time point.
POC=point-of-care test. EID=early infant diagnosis. Lab=laboratory test.

Results (5)- Patients with discordant test results between birth and after four weeks.

	At Birth Testing						≥4 Weeks		≥4 Weeks (repeat)			
	Mother Prophylaxis	Infant Prophylaxis	Infant Breast-feeding	POC	Lab	Age (Days)	POC	Lab	Age (Days)	POC	Lab	Age (days)
Patient 1	ART	NVP	Yes	Pos	Pos	1	Neg	DBS Rejected	31	Pos	Pos	142
Patient 2	ART	NVP	No	Pos	Pos	1	Not Processed	Neg	51	Pos	Pos	123
Patient 3	ART	NVP	Yes	Pos	Inv	1	Neg	DBS Rejected	32	Not Processed	Neg	127
Patient 4	None	NVP	Yes	Pos	Inv	1	Neg	DBS Rejected	29	Neg	Neg	63

POC=Point-of-Care test. LAB=laboratory test ART=antiretroviral therapy. NVP=Nevirapine. Pos=Positive. Neg=Negative. Inv=Invalid.

Conclusions

- In conclusion, we have demonstrated that POC HIV EID at birth is feasible and accurate when conducted by nurses in primary health care clinics in low-resource settings, and may be an important tool to expand access to birth testing.
- We also highlighted that birth testing in combination with routine 4-6 weeks screening may increase access to EID.
- However, implementing POC EID at birth will need confirmatory testing of positives and supportive health systems to ensure reliable testing and retention of infants after birth.
- Nevertheless, POC testing may improve opportunities for newborns to access ART especially in decentralised and task-shifted low-resource settings.

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