Electronic Drug Monitoring of Infant Adherence to Antiretroviral Therapy Prophylaxis

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Conflict of Interest Disclosure

No conflicts of interest to disclose

PMTCT

- Prevention of Maternal to Child Transmission of HIV (PMTCT) is a public health success story:
  - Rates of maternal to child transmission of HIV: ~40% to < 3%.[1]
- Option B+ is the WHO-recommended PMTCT policy:
  - Lifelong antiretroviral therapy (ART) for all HIV-positive pregnant women.
  - 6 weeks of postnatal ART prophylaxis for exposed infants and early infant diagnosis (EID) at 6 weeks of life
- Poor retention of mother-infant dyads in Option B+ but overall limited knowledge about adherence to infant ART prophylaxis during the infant's first six weeks of life

Background

- HIV in Uganda:
  - High burden country: 8% prevalence in pregnant women
  - Rapid scale-up of WHO's Option B+
  - >95% of HIV+ pregnant women on ART by 2015
  - Only 38% of HIV-exposed infants received prophylactic ART postnatally
  - Only 50% of infants were tested for HIV by 6 weeks of life

Electronic Drug Monitoring

- Prior studies in sub-Saharan Africa have used electronic drug monitoring (EDM) devices to measure adherence to pediatric antiretroviral regimens.[10-11]
- The use of EDM devices in measuring adherence to antiretroviral **prophylaxis** in HIV-exposed infants has not been investigated.

This pilot study examined the acceptability and feasibility of an EDM device affixed to a bottle containing the standard NVP suspension provided to HIV-exposed infants.

The Uganda Wise Infant Study

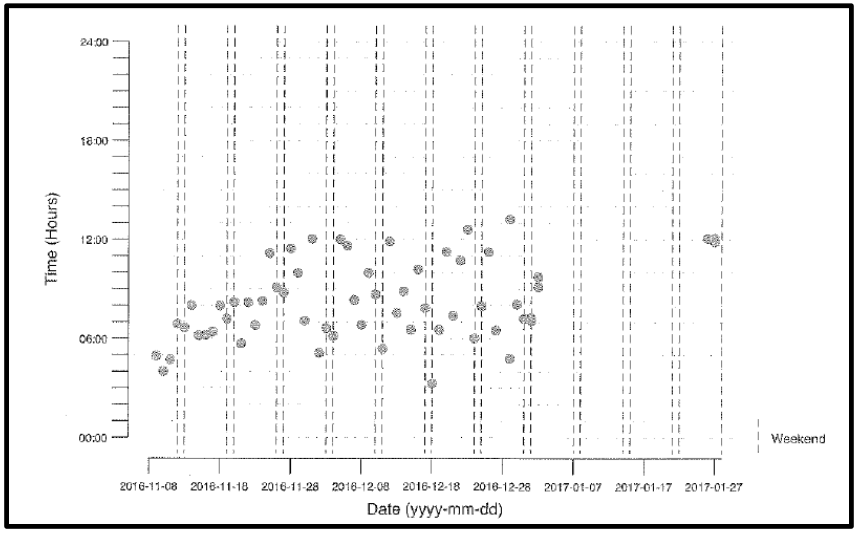
- Routine care in Uganda: HIV-exposed infants receive daily nevirapine (NVP) for ART prophylaxis postnatally to 6 weeks of age.
- The EDM bottles provided to mothers had caps, which contained a microchip that records the date and time of each bottle opening and stores this data until downloaded using a specialized cap reader.
- No real-time feedback regarding the EDM usage was given to participants or the study team.
- We used the EDM-generated data as a proxy for adherence to NVP prophylaxis, based on evidence that EDM data are a reliable measure of medication adherence.[11-15]

Methods: Enrollment

- Mityana District Hospital in Central Uganda from July to December 2016
- Eligibility: HIV-positive pregnant women with estimated gestational age greater >24 weeks
- Inclusion criteria also included the intent to deliver at Mityana District Hospital.

Data Collection and Analysis

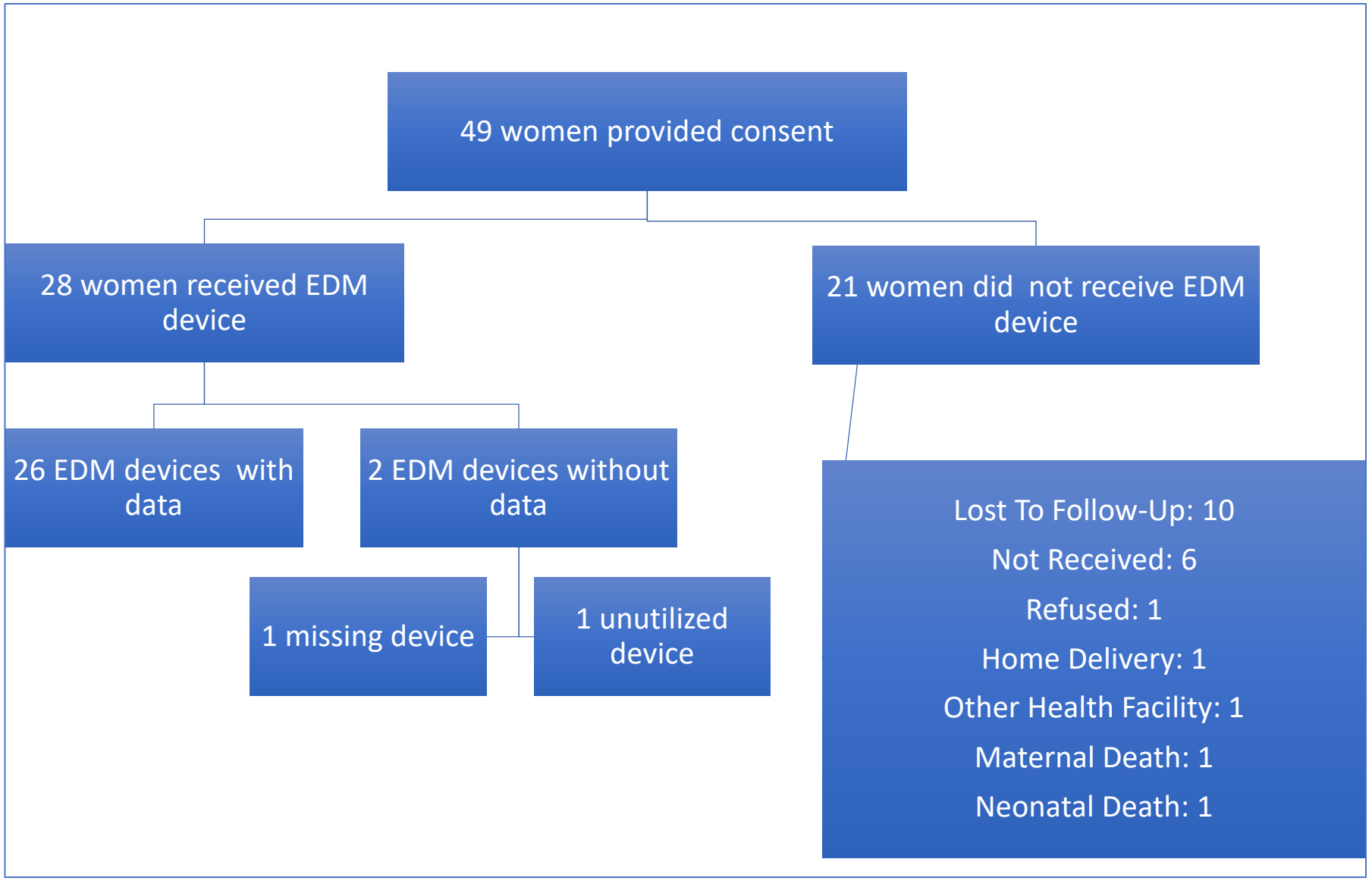
- At enrollment, we administered a survey questionnaire to collect quantitative data on sociodemographic characteristics of the mothers.
  - Maternal age, ethnicity, education, employment, time since maternal HIV diagnosis, reproductive health history, and maternal self-reported ART adherence.
- NVP adherence data were collected via the EDM device after return of the EDM bottle, regardless of how long the EDM bottle was in the possession of the mother.



Methods: Measures

- We estimated adherence to ART prophylaxis by calculating:
  - Proportion of daily doses administered within the first 42 days of EDM possession
  - Proportion of daily doses administered during the entirety of EDM possession, respectively.
- High adherence was defined as having > 90% adherence to NVP.
- Bivariate analyses using Fisher's exact test and Wilcoxon rank sum test, SAS version 9.4 (SAS Institute).

Results


49 women provided consent
28 women received EDM device
21 women did not receive EDM device
26 EDM devices with data
2 EDM devices without data
1 missing device
1 unutilized device
Lost To Follow-Up: 10
Not Received: 6
Refused: 1
Home Delivery: 1
Other Health Facility: 1
Maternal Death: 1
Neonatal Death: 1

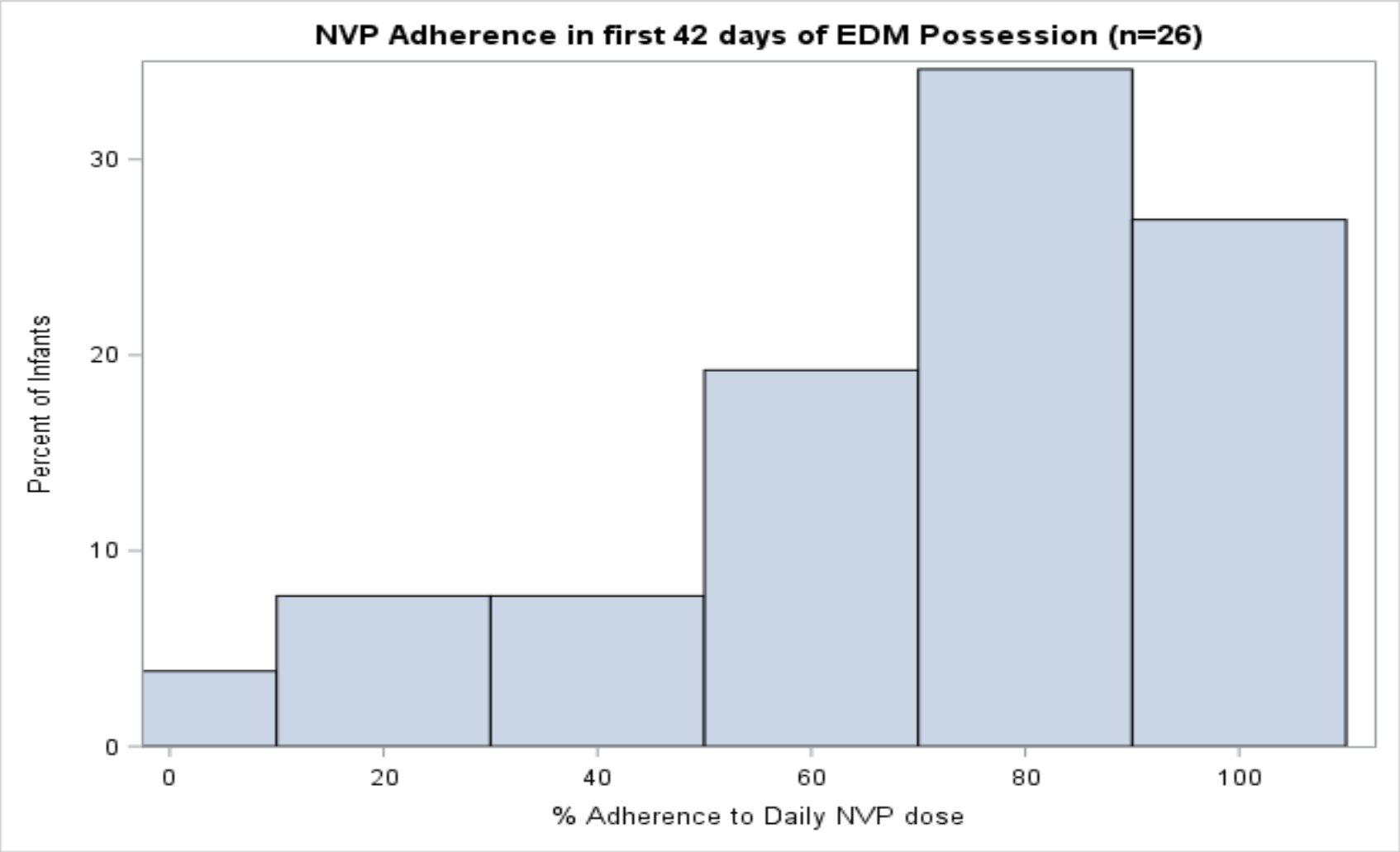
Baseline Maternal Characteristics (n=26)

Characteristic	N (%) or Mean (SD)
Age (years)	26.6 (4.6)
Parity	1.8 (1.5)
Maternal ART duration (years)	2.4 (1.9)
Household size	3.4 (1.4)
Education	
None	4 (15.4)
Primary	14 (53.9)
Secondary	8 (30.8)
Employment	
Housewife	13 (50.0)
Employed outside home	13 (50.0)

Results

Variable	N = 26
Duration of EDM possession, days, median (range)	45 (34 – 85)
Infants who missed at least one dose in first 42 days, n (%)	24 (92.3)
Missed doses in first 42 days, median (range)	10 (2 – 40)
Infants who missed at least one dose during EDM possession, n (%)	25 (96.2)
Missed doses during EDM possession, median (range)	11 (2 – 51)
Infants with double or more openings of EDM device, n (%)	14 (53.9)
Days with double or more openings of EDM device, mean (sd)	3.4 (2.3)
Percent adherence in first 42 days, mean (sd)	69.9 (26.4)
Percent adherence during EDM possession, mean (sd)	63.6 (27.8)
Adherence in first 42 days, n (%) High adherence (≥ 90%) Low adherence (< 90%)	 7 (26.9) 19 (73.1)

Results


NVP Adherence in first 42 days of EDM Possession (n=26)
Percent of Infants
30
20
10
0
0
20
40
60
80
100
% Adherence to Daily NVP dose

Infant Adherence by Maternal Characteristics

Variable	High adherence (n = 7)	Low adherence (n = 19)	p-value
Age, median (IQR)	25 (22 – 28)	27 (24 – 30)	0.557
Parity, median (IQR)	1 (0 – 1)	2 (1 – 3)	0.121
Maternal ART, median (IQR)	1 (0.3 – 2.0)	2 (1.5 – 5.0)	0.106
Household size, median (IQR)	3 (2 – 4)	4 (2 – 5)	0.409
Education, n (%) None Primary Secondary	 2 (50.0) 3 (21.4) 2 (25.0)	 2 (50.0) 11 (78.6) 6 (75.0)	0.608
Employment, n (%) Housewife Employed outside home	 4 (30.8) 3 (23.1)	 9 (69.2) 10 (76.9)	1.000

Feasible and Acceptable?

- To our knowledge, this pilot study evaluating the feasibility of EDM in measuring adherence to ART prophylaxis among HIV-exposed infants in Uganda is the first to utilize EDM devices in assessing adherence to PMTCT in HIV-exposed infants.
- Nearly half of enrolled women did not get the device as intended
  - Study site?
  - More intensive formative work needed?
- Qualitative data regarding acceptability still being analyzed

Take-home results

- Utilization of the EDM devices varied among the participants.
  - Median time of EDM possession: 45 days (range: 34 – 85 days).
  - Almost all infants (92.3%) missed at least one dose of ART prophylaxis in the first 42 days of therapy
  - Median number of missed doses of NVP was 10 (range: 2 – 40).
  - The mean infant adherence in the first 42 days of therapy was 69.9% and only 26.9% of infants were at least 90% adherent.
- More than half of the infants had double openings of the cap (or more frequent) during EDM possession.
  - May be attributed to EDM devices not being the standard of practice accustomed to the mothers for infant prophylaxis,
  - May indicate that NVP was inappropriately being given.

Limitations

- Pilot study
- Small sample size
  - Cannot determine significant associations.
  - Only EDM data, used here as a proxy for ART adherence, but no other measures of infant adherence, such as serum NVP levels for the exposed infants.
  - No ‘real-time’ data regarding the usage of the device.
  - EDM data not captured before conducting in-depth interviews to facilitate more informative discussions with the mothers.

Conclusions

- Revealed low adherence levels to ART prophylaxis among HIV-exposed infants: < 1/3 of infants demonstrated high (>90%) adherence.
- HIV-exposed infants are a special population: require high adherence to a single daily dose of ART for a relatively short period of time.
- Methods of ensuring good adherence to ART prophylactic regimens for exposed infants remain important for PMTCT efforts.
- Demonstrated the potential feasibility of using an EDM device to measure adherence to ART prophylaxis.
- This study is the first study to utilize EDM technology in this population, with potential for EDM to possibly be used as an intervention to ensure adequate adherence for HIV-exposed infants.

Wise Infant Study Team and Acknowledgments

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