Maternal ART and Hospitalization or Death among HIV-Exposed Uninfected Infants

Scott Dryden-Peterson,[1,2,3] Tatiana Ramos[4], Roger Shapiro[1,3], Shahin Lockman[1,2,3]

[1]Botswana Harvard AIDS Inst., Gaborone; [2]Brigham and Women's Hosp, Boston; [3]Harvard T.H. Chan Sch. of Pub. Health, Boston; [4]Mass. Gen Hosp, Boston

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Background:

Excess deaths from HIV-exposed uninfected infants are a major contributor to under-5 mortality in Africa

Antenatal maternal ART nearly eliminates mother-to-child transmission, but impact on health outcomes on HIV-uninfected infants is unknown

- Improved maternal health on ART could yield immunologic and other benefits to their infants
- Increased risk of prematurity and low birthweight associated with maternal ART could increase infant risk

Objective:

We sought to simulate a randomized experiment to examine the effect of maternal ART on the risk of HIV-uninfected infant hospitalization and/or death by 6 months of age

Methods:

Botswana Mother-Infant Cohort

- Pooled data from 2 randomized trials (Mashi, Mma Bana) and 2 observational studies (CTX Safety, Tshipidi), 2001 to 2012
- Studies conducted in overlapping clinical sites
- Utilized harmonized covariate and endpoint assessments

Antiretroviral exposure

- Mothers off ART received antenatal zidovudine (3rd trimester) and their infants 4 weeks of zidovudine
- ART regimens varied, but most common regimens were ZDV/3TC/NVP, ZDV/3TC/LPV/r, ABC/3TC/ZDV

Analytic approach

- Used inverse probability weighting (IPW) to generate maternal population where ART receipt was no longer linked to maternal age, antenatal CD4, SES, year of delivery, or participation in RCT/observational
- Estimated effect of maternal ART in the IPW population using Cox MSM including feeding method at birth
- Evaluated for difference in ART effect by feeding method

Results:

	Maternal ART Status		
	On ART (N = 1460)	Not on ART (N = 1205)	p-value
Maternal Characteristics			
Age, median (IQR)	28.7 (25-33)	27.0 (23-31)	<0.001
Low income (<$50/mo), no. (%)	702 (48.4)	682 (57.4)	<0.001
Primary school or less, no. (%)	236 (23.3)	316 (26.6)	0.076
Own toilet or latrine, no. (%)	1237 (85.3)	1039 (87.8)	0.059
Rural Resident, no. (%)	631 (43.2)	657 (54.5)	<0.001
Delivery year, median (IQR)	2009 (2008-11)	2003 (2002-04)	<0.001
Enrolled in clinical trial, no. (%)	759 (52.0)	1028 (85.3)	<0.001
CD4 cell count (cells/μL), median (IQR)	354 (219-497)	390 (279-538)	<0.001
ART start before pregnancy, no. (%)	211 (14.5)	—	—
Infant Characteristics			
Gestational age birth, median (IQR)	39 (38-40)	39 (38-40)	0.002
Premature (<37 weeks), no. (%)	182 (18.0)	154 (13.0)	0.002
Birthweight (kg), median (IQR)	2.9 (2.6-3.2)	3.1 (2.8-3.4)	<0.001
Small for gestational age, no. (%)	180 (17.8)	101 (8.5)	<0.001
Breastfed, no. (%)	1152 (79.1)	512 (42.5)	<0.001

Table 1: Maternal and infant characteristics.

Endpoints

- 291 (10.9%) infants hospitalized or died, 152 (10.4%) in maternal ART and 139 (10.9%) in no maternal ART
- 98 (3.7%) infant deaths, 52 (3.6%) in maternal ART and 46 (3.8%) in no maternal ART

Effect of maternal ART

- No significant effect seen for either combined hospitalization and death (P=0.97), or death (P=0.95)
- Suggestion of divergent impact of ART on infant mortality by feeding method (interaction P=0.075)
- Breastfeeding protective for infant (HR 1.23, 95%CI 0.50-3.00), but not exposed to maternal ART, but not for ART-exposed infants (HR 1.23, 95%CI 0.50-3.00)

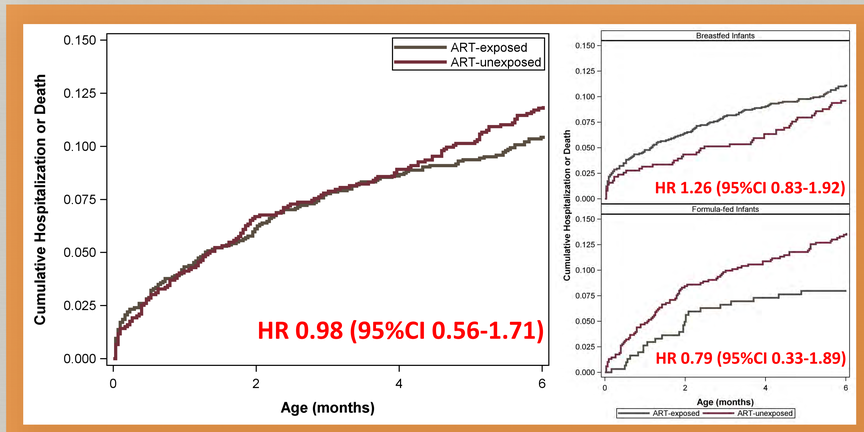

Figure 1: Cumulative incidence of hospitalization or death by maternal ART (and feeding method. No significant effect modification detected in ART effect by feeding method (P=0.34).

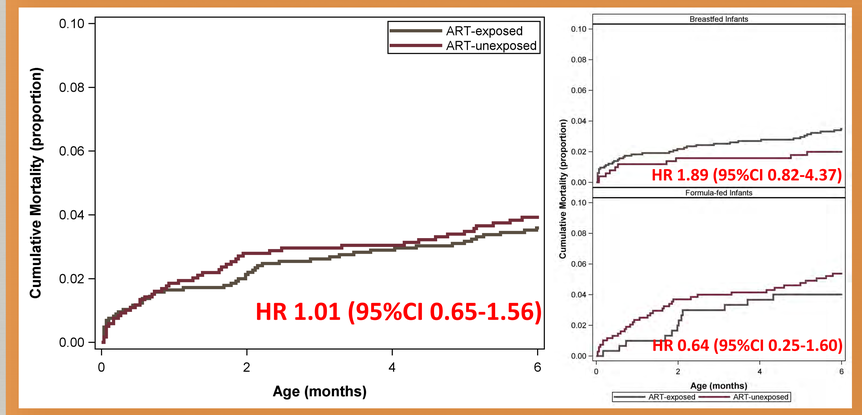

Figure 2: Cumulative mortality by maternal ART (and feeding method). Possible effect modification in ART effect by feeding method (P=0.075).

Limitations:

- Despite adjusting for several key predictors, residual confounding possible
- Does not currently account for possible differential effect for different maternal ART regimens
- Analysis does not currently account for changes to infant feeding method after discharge from maternity ward

Conclusions:

- Expanding ART for prevention of MTCT is not expected to improve excess mortality in HEU infants
- Possible explanations for the differential effect of ART by feeding method should be explored
- New strategies are urgently needed to mitigate mortality among the large vulnerable group of HIV-exposed uninfected infants

BOTSWANA HARVARD AIDS INSTITUTE PARTNERSHIP FOR HIV RESEARCH AND EDUCATION

BRIGHAM AND WOMEN'S HOSPITAL

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

Poster 805

For more information contact:
Scott Dryden-Peterson, MD
scott_peterson@post.harvard.edu
Harvard T.H. Chan School Public Health
François-Xavier Bagnoud 401
651 Huntington Avenue
Boston, MA 02115