Birth Weight and Preterm Delivery Outcomes of Perinatally vs. Non-Perinatally HIV-infected Pregnant Women in the U.S.: Results from the PHACS SMARTT Study and IMPAACT P1025 Protocol

Jennifer Jao, Deborah Kacanek, Paige Williams, Mitchell Geffner, Elizabeth G. Livingston, Rhoda Sperling, Kunjal Patel, Arlene D. Bardeguez, Sandra K. Burchett, Nahida Chakhtoura, Gwendolyn B. Scott, Russell Van Dyke, MD, and Elaine J. Abrams, for the Pediatric HIV/AIDS Cohort Study (PHACS) and the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1025 Protocol

BACKGROUND

- Increasing numbers of perinatally HIV-infected (PHIV) youth reaching reproductive age

- Pregnancy and neonatal outcomes in PHIV women not well documented

- Low Birth Weight (LBW) and Small-for-Gestational-Age (SGA) outcomes

Kapogiannis BG et al. *CID.* 2011
Jao J et al. *AIDS.* 2012
Williams SF et al. *Am J Obstet Gynecol.* 2009
Cruz ML et al. *AIDS.* 2010

OBJECTIVE

- To assess whether:

Maternal Perinatal HIV Infection (PHIV) → **Adverse Birth Weight and Preterm Delivery Outcomes**

METHODS

- **Study population**
  - HIV-infected pregnant women and their infants enrolled in either:
    - SMARTT: Pediatric HIV/AIDS Cohort Study (PHACS) Surveillance Monitoring for ART Toxicities (SMARTT) study of HIV-uninfected children born to HIV-infected women
    - P1025: International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Perinatal Core Protocol P1025
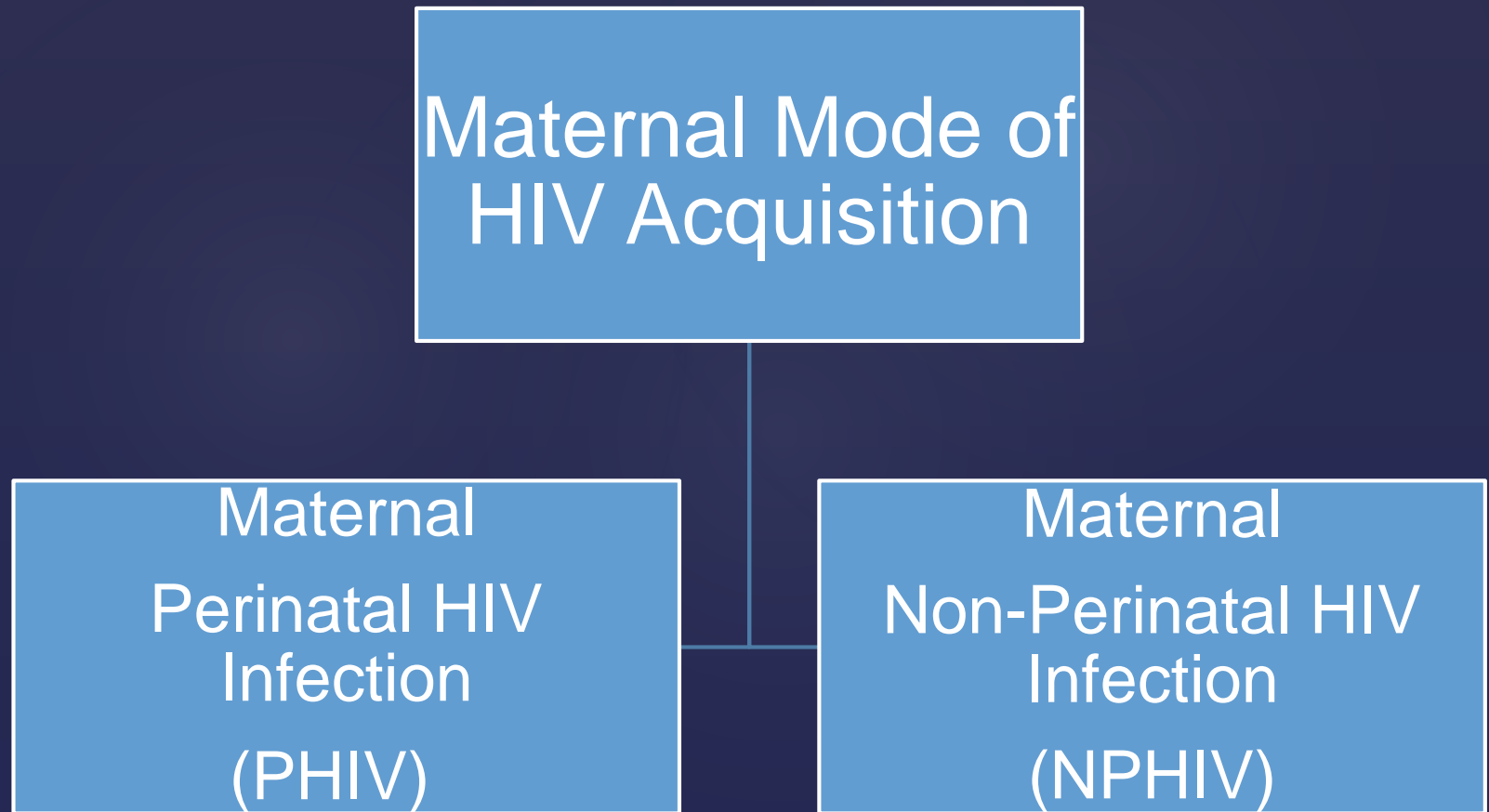- **Inclusion Criteria**
  - HIV-infected pregnant women ages 13-30 years
  - Singleton live births
  - Birth weight, gestational age, maternal mode of HIV acquisition information were available
- **Exclusion Criteria**
  - HIV-infected infants

METHODS

Exposure

METHODS

- Outcomes
  - Birth Weight (BW) measured in the following manners:
    - BW z scores (BWZ)*
    - Small-for-Gestational-Age (SGA) <10th percentile*
    - Low Birth Weight (LBW) < 2500 g
  - Preterm Delivery at <37 weeks GA

*Olsen IE et al. *Pediatrics.* 2010

METHODS
Statistical Analyses

- For dichotomous outcomes (SGA, LBW, Preterm Delivery)
  - *Log binomial models using GEE to obtain relative risks (RR)*

- For continuous outcomes (BWZ)
  - *Linear mixed effects models for mean BWZ*

Characteristics of Pregnant Women

Characteristic	PHIV (n=235)	NPHIV (n=2035)	Total (n=2270)	*p* value
Age, years	21 (19, 23)	25 (22, 28)	25 (22, 28)	<0.01
Race				
White/Other	91 (39%)	535 (26%)	626 (28%)	<0.01
Black	129 (55%)	1,360 (67%)	1,489 (66%)	
Unknown/ Declined	15 (6%)	140 (7%)	155 (6%)	
Hispanic Ethnicity	85 (36%)	545 (27%)	630 (28%)	<0.01
Year of Delivery				
1996-2005	16 (7%)	670 (33%)	686 (30%)	<0.01
2006-2009	80 (34%)	717 (35%)	797 (35%)	
2010-2013	138 (59%)	647 (32%)	785 (35%)	
Pre-pregnancy BMI, kg/m²				
<18.5	15 (6%)	54 (3%)	69 (3%)	<0.01
18.5-24.9	86 (37%)	485 (24%)	571 (25%)	
25.0-29.9	35 (15%)	333 (16%)	368 (16%)	
$\geq$30	40 (17%)	521 (25%)	561 (24%)	
Tobacco Use in Pregnancy	32 (14%)	397 (20%)	429 (19%)	0.01

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Characteristics of Pregnant Women

Characteristic	PHIV (n=235)	NPHIV (n=2035)	Total (n=2270)	p value
CD4 at enrollment, cells/mm^3				
<200	44 (19%)	228 (11%)	272 (12%)	0.01
200-500	107 (46%)	943 (46%)	1,050 (46%)	
>500	81 (34%)	774 (38%)	855 (38%)	
HIV RNA level at delivery, copies/mL				
≤400	164 (70%)	1,572 (77%)	1,736 (76%)	<0.01
>400-1000	12 (5%)	86 (4%)	98 (4%)	
>1000-10000	34 (14%)	158 (8%)	192 (8%)	
>10000	20 (9%)	105 (5%)	125 (6%)	
ART during pregnancy				
≥3 classes	54 (23%)	50 (2%)	104 (5%)	<0.01
INSTI-based	3 (1%)	18 (1%)	21 (1%)	
PI-based	159 (68%)	1,422 (70%)	1,581 (70%)	
NNRTI-based	3 (1%)	158 (8%)	161 (7%)	
NRTI-based	11 (5%)	233 (11%)	244 (11%)	
Non-combination ART regimen	2 (1%)	82 (4%)	84 (4%)	
No ARVs/Unknown	3 (1%)	72 (4%)	75 (4%)	

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Characteristics of Infants

	PHIV (n=270)	NPHIV (n=2422)	TOTAL (n=2692)	*p* value
GA (weeks)	38.1 (1.9)	38.2 (2.0)	38.2 (2.0)	0.56
Preterm Delivery (<37 weeks)	388 (16%)	41 (15%)	429 (16%)	0.67
SGA	265 (11%)	32 (12%)	297 (11%)	0.73
LBW (<2500 g)	350 (14%)	48 (18%)	398 (15%)	0.19
BWZ	-0.44 (0.75)	-0.33 (0.84)	-0.34 (0.83)	0.06

All continuous variables shown as mean (SD) and dichotomous variables as n (%); BWZ=Birth Weight Z score; GA=Gestational Age; LBW=Low Birth Weight; SGA=Small-for-Gestational-Age

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Preterm Delivery (<37 weeks)	388 (16%)	41 (15%)	429 (16%)	0.67
SGA	265 (11%)	32 (12%)	297 (11%)	0.73
LBW (<2500 g)	350 (14%)	48 (18%)	398 (15%)	0.19
BWZ	-0.44 (0.75)	-0.33 (0.84)	-0.34 (0.83)	0.06

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Unadjusted and Adjusted Models for LBW, SGA, and Preterm Delivery Outcomes Comparing PHIV vs NPHIV

LBW		SGA		Preterm Delivery	
RR (95% CI)	*p* value	RR (95% CI)	*p* value	RR (95% CI)	*p* value
Unadjusted:					
1.22 (0.92,1.62)	0.17	1.06 (0.76,1.49)	0.72	0.94 (0.70,1.27)	0.69
Adjusted:*					
1.19 (0.88,1.61)	0.25	1.03 (0.71,1.49)	0.86	0.90 (0.65,1.25)	0.53

Models adjusted for age, race/ethnicity, pre-pregnancy BMI, tobacco use, substance use, CD4, and maternal ART.

Mixed Model for Mean BWZ Outcome Comparing PHIV vs. NPHIV

Unadjusted Difference		Adjusted* Difference	
Mean (95% CI)	p value	Mean (95% CI)	p value
-0.11 (-0.22,-0.01)	0.03	-0.13 (-0.24, -0.01)	0.03

*Models adjusted for age, race/ethnicity, pre-pregnancy BMI, tobacco use, substance use, CD4, and maternal ART.

Mixed Model for Mean BWZ Outcome Comparing PHIV vs. NPHIV

Unadjusted Difference		Adjusted* Difference	
Mean (95% CI)	*p* value	Mean (95% CI)	*p* value
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Models adjusted for age, race/ethnicity, pre-pregnancy BMI, tobacco use, substance use, CD4, and maternal ART.

Strengths/ Limitations

- **Strengths**
  - **Novel data**
  - **Largest cohort of PHIV pregnant women to date**
- **Limitations**
  - **Heterogeneity of *in utero* ARVs**
  - **Potential for misclassification bias**
  - **No distinction between spontaneous vs. non-spontaneous preterm birth**

CONCLUSIONS

- Infants of PHIV women do not appear to be at increased risk for LBW, SGA, or preterm birth.

- Although the absolute difference was small, infants of PHIV women may be at greater risk for lower birth weight compared to those of NPHIV women.

- Future studies are warranted to understand mechanisms by which the intrauterine environment of PHIV women may affect fetal growth.

ACKNOWLEDGMENTS

PHACS SMARTT and IMPAACT 1025 are funded by: