

# Time to DNA-PCR Positivity in Non-Breastfed HIV-Infected Infants (Primarily B HIV Subtype)

An analysis of data from the Perinatal AIDS Collaborative Transmission Study (PACTS) and the Women and Infants Transmission Study (WITS)

November 16, 2020

# Goals

- Estimate the time to DNA PCR test positivity in non-breastfed, HIV infected infants
- Evaluate differences in DNA PCR test positivity according to exposure to maternal/infant HIV regimen
- Combine data from the Perinatal AIDS Collaborative Transmission Study (PACTS) and the Women and Infants Transmission Study (WITS)

# Background

- Accurate diagnostic tests to detect HIV infection in infants are critical to ensure early treatment.
- HIV DNA-PCR tests have imperfect sensitivity when given soon after birth.
- Our previous work in infants infected with non-B subtype HIV showed that time to HIV test positivity may be longer in infants exposed to combination therapy, but data are limited.
  - Balasubramanian, R., Fowler, M.G., Dominguez, K., Lockman, S., Tookey, P. A., Huong, N. N. G., Nesheim, S., Hughes, M. D., Lallemand, M., Toswill, J., Shaffer, N., Sherman, G., Palumbo, P., Shapiro, D. E. (2017): Time To First Positive HIV-1 DNA PCR May Differ With Antiretroviral Regimen In Infants Infected With Non-B Subtype HIV-1, *AIDS*, 31 (18), pp. 2465-2474. PMID: PMC5710822.

# Cohorts

- **Pediatric AIDS Collaborative Transmission Study (PACTS)**
  - A multicenter, prospective cohort study (1986-1999) of HIV-infected pregnant women and their newborns conducted in 4 US cities to monitor the incidence of mother-to-child HIV transmission and to describe the natural course of pediatric HIV disease progression.
- **Women and Infants Transmission Study (WITS)**
  - WITS is a prospective epidemiologic study (1999-2007) of the natural history of HIV infection in pregnant women and their infants carried out at obstetric/gynecologic and pediatric clinics in Boston, Chicago, Manhattan, Brooklyn, San Juan, and Houston.

# Inclusion/exclusion criteria

- Inclusion Criteria:

- HIV infection status: Infant HIV-infected or indeterminate; AND
- Infant has at least one DNA-PCR test before age 3 months

- Exclusion Criteria:

- DNA PCR tests with missing result or missing age at time of blood draw
- Excluded infants whose mother's ARV exposure was unknown

# Summary of participant characteristics

## **WITS:**

- Number of HIV positive infants: 129
- Number of HIV positive mothers: 126

## **PACTS:**

- Number of HIV positive infants: 299
- Number of HIV positive mothers: 298

# Classifying Maternal and Infant ARV Regimen

## Maternal ARV :

- Most complex ARV received in the 3<sup>rd</sup> trimester and at the time of labor/delivery.

## Infant ARV :

- Prophylactic regimen with a start date prior to 45 days after birth.

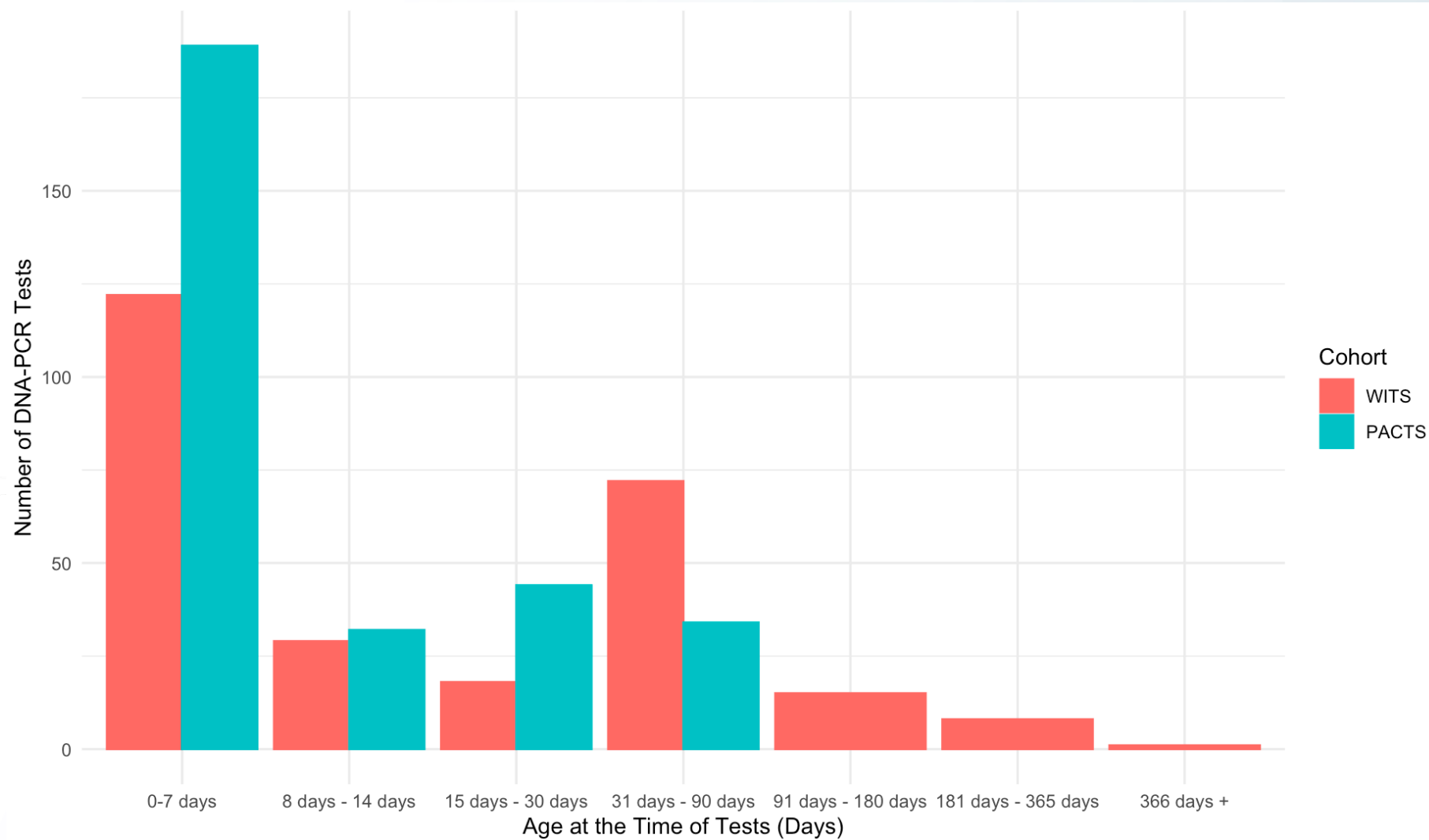


# Maternal ARV by Infant ARV

Maternal ARV	Infant ARV		
	None	ZDV	Other
<b>A: no ARV</b>	193	5	0
<b>B: Single NRTI</b>	54	35	0
<b>C: 2-3 NRTIs</b>	9	2	0
<b>D: 2-3 NRTIs with sdNVP</b>	6	2	0
<b>E/F: E (3 or more ARVs, with NNRTIs, no PI) + F (3 or more ARVs, with PI)</b>	80	23	3
<b>G: sdNVP only</b>	5	1	0
<b>H: ZDV + sdNVP</b>	8	2	0



# Timing of DNA PCR tests



# Participant characteristics

Maternal ARV	Maternal CD4 closest to delivery	Maternal viral load closest to delivery	Gestational age	Delivery Type		
				Vaginal	CS no labor/ROM	CS with labor/ROM
<b>A: no ARV</b>	530 [282 - 775]	11250 [1,125 - 41,250]	39 [35 - 40]	81	3	16
<b>B: Single NRTI</b>	400 [287 - 617]	8,000 [9 - 42,000]	37 [35 - 40]	82	7	11
<b>C: 2-3 NRTIs</b>	249 [65 - 536]	9 [0 - 37,714]	38 [36 - 40]	78	11	11
<b>D: 2-3 NRTIs with sdNVP</b>	455 [300 - 552]	1,183 [906 - 2,830]	38 [36 - 40]	67	0	33
<b>E/F: 3 or more ARVs, with NNRTIs or PI)</b>	459 [298 - 738]	0 [0 - 2,380]	38 [36 - 39]	44	38	18
<b>G: sdNVP only</b>	300 [97 - 473]	52,873 [10,441 - 106,879]	37 [31 - 38]	67	33	0
<b>H: ZDV + sdNVP</b>	471 [364 - 704]	3,553 [0 - 66,666]	37 [35 - 38]	50	30	20

# Statistical methods

- Used methods for interval-censored data
  - Time to DNA PCR test positivity is uncertain; in interval between last negative and first positive DNA-PCR test
- Regression modeling to adjust for potential confounders
  - Parametric Weibull proportional hazards models

# Cumulative Probability of Positive DNA-PCR

Maternal ARV	Number of Infants	Birth - 1 day	≤ 14 days	≤ 30 days	≤ 90 days
<b>A</b> [No ARV]	198	<b>0.29 [0.22-0.38]</b>	<b>0.58 [0.5-0.66]</b>	<b>0.68 [0.58-0.77]</b>	<b>0.81 [0.68-0.91]</b>
<b>B</b> [Single NRTI]	89	<b>0.25 [0.17-0.35]</b>	<b>0.51 [0.39-0.65]</b>	<b>0.60 [0.46-0.76]</b>	<b>0.74 [0.56-0.89]</b>
<b>C</b> [2-3 NRTIs]	11	0.04 [0.01-0.26]	0.1 [0.01-0.52]	0.13 [0.02-0.62]	0.18 [0.03-0.76]
<b>D</b> [2-3 NRTI + sdNVP]	8	0.09 [0.02-0.34]	0.21 [0.06-0.62]	0.27 [0.08-0.72]	0.37 [0.11-0.84]
<b>E/F</b> [3+ ARVs]	106	<b>0.05 [0.02-0.09]</b>	<b>0.11 [0.06-0.18]</b>	<b>0.14 [0.08-0.23]</b>	<b>0.2 [0.12-0.32]</b>
<b>G</b> [sdNVP only]	6	0.28 [0.1-0.66]	0.57 [0.23-0.93]	0.66 [0.29-0.97]	0.8 [0.39-0.99]
<b>H</b> [ZDV + sdNPV]	10	0.11 [0.03-0.32]	0.25 [0.09-0.59]	0.31 [0.11-0.69]	0.42 [0.16-0.82]

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# Effect of Maternal ARV on time to test positivity

(Weibull PH model; HR>1 Means Earlier Detection of HIV)

Maternal ARV Groups	Unadjusted Hazard Ratio [95% CI]	Adjusted Hazard Ratio [95% CI]
<b>A</b> [No ARV]	<b>7.5</b> [4.06-13.8]	<b>5.8</b> [2.6-12.8]
<b>B</b> [Single NRTI]	<b>6.2</b> [3.1-12.4]	<b>4.7</b> [2.0-11.1]
<b>C</b> [2-3 NRTIs]	0.9 [0.1-6.9]	1.8 [0.2-14.7]
<b>D</b> [2-3 NRTI + sdNVP]	2.1 [0.5-9.3]	2.0 [0.4-10.5]
<b>E/F</b> [3+ ARVs]	<b>1</b>	<b>1</b>
<b>G</b> [sdNVP only]	7.2 [2.0-25.6]	3.5 [0.8-14.5]
<b>H</b> [ZDV + sdNPV]	2.5 [0.7-8.7]	2.5 [0.7-9.3]
<b>P value for ARV Group</b>	<b>1.28e-12</b>	<b>5.95e-4</b>



# Time to test positivity by infant ARV

(Weibull PH model; HR>1 Means Earlier Positive)

<b>Infant ARV</b>	<b>Unadjusted Hazard Ratio [95% CI]</b>	<b>Adjusted Hazard Ratio [95% CI]</b>
<b>None</b>	1.0 [0.6-1.5]	0.68 [0.39-1.19]
<b>ZDV</b>	1.0	1.0
<b>Other</b>	0.65 [0.09-4.87]	0.51 [0.06-4.31]
<b>P value for infant ARV</b>	0.90	0.38

# Summary

- **Time to DNA-PCR test positivity was later with receipt of  $\geq 3$  ARVs than with no ARV or single NRTI**
- **Differences in test positivity rates were observed at birth and remained at 3 months after birth.**
- **Adjusting for maternal/infant characteristics did not attenuate the findings.**

# Study team/Acknowledgements

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