

PK of FTC, TFV and 3TC in Ugandan and Nigerian Breastfeeding Mother-Infant Pairs

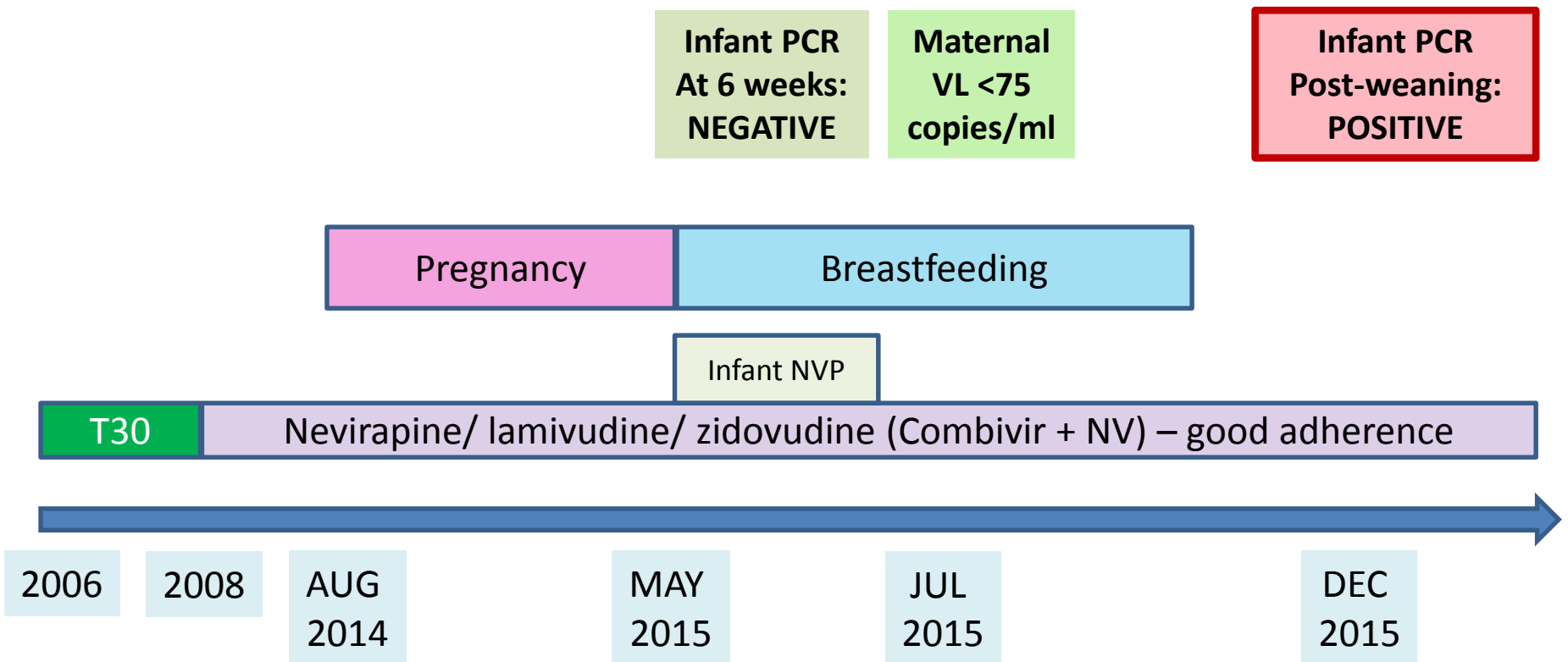
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Case: 35 year old female



Universal access doesn't eliminate HIV transmission risk

- Estimated 1.5 million pregnant HIV+ women per year
- Exclusive breastfeeding recommended to 6 months in low resource settings
- HIV transmission through breastfeeding whilst on ART remains at 1-3%
- Infants infected via breastfeeding have high rates (~75%) of drug resistance*
- Exposure to maternal ARVs may also cause toxicities

*Zeh C *PLoS Med* 2011; **8**(3): e1000430.

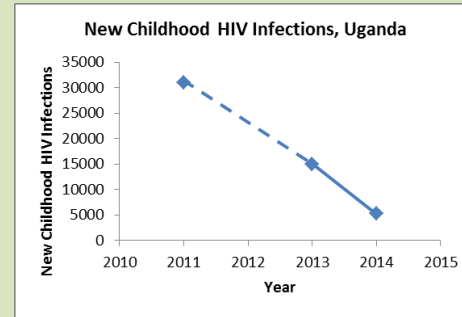
Fogel J *Clin Infect Dis* 2011; **52**(8): 1069-76.

Marked reduction in new infections among children;

31,000 in 2011

15,000 in 2013

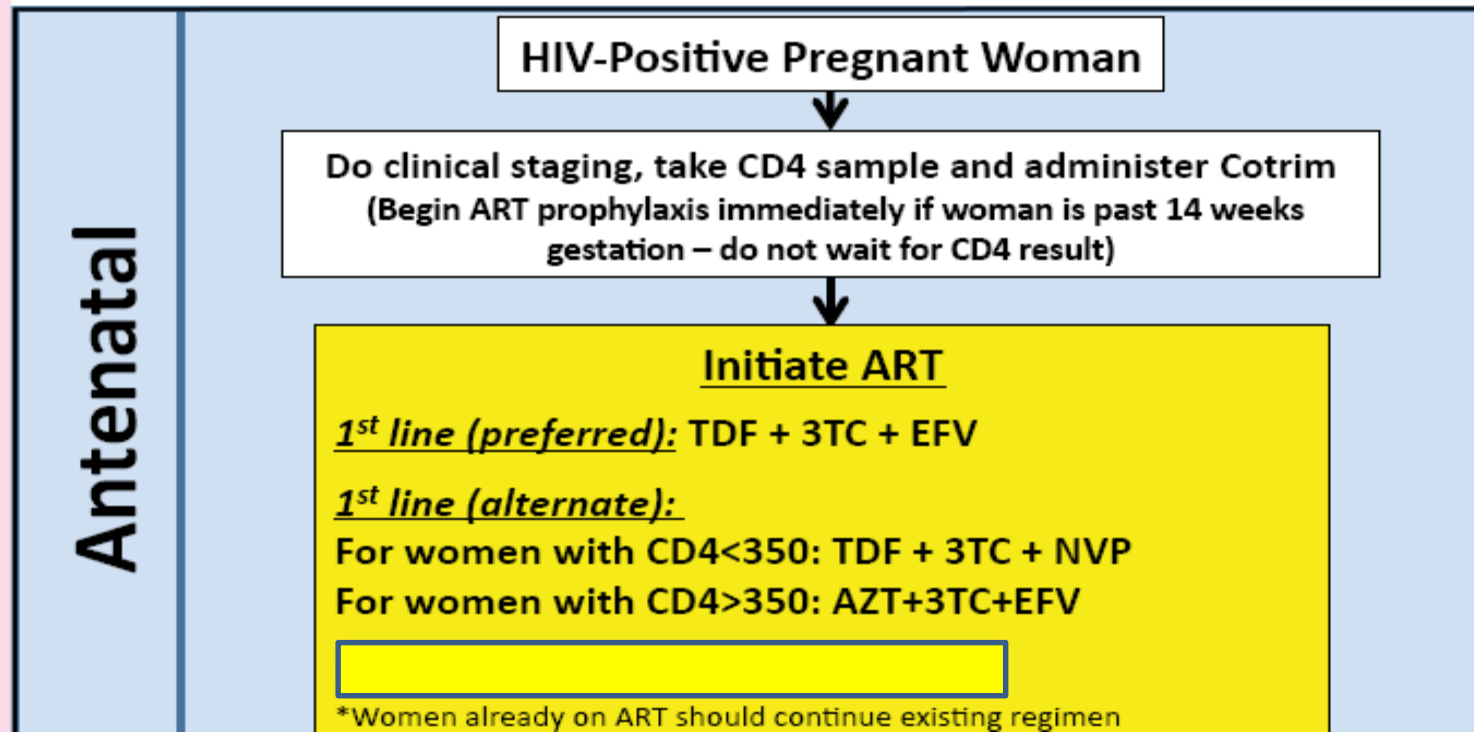
5,200 in 2014



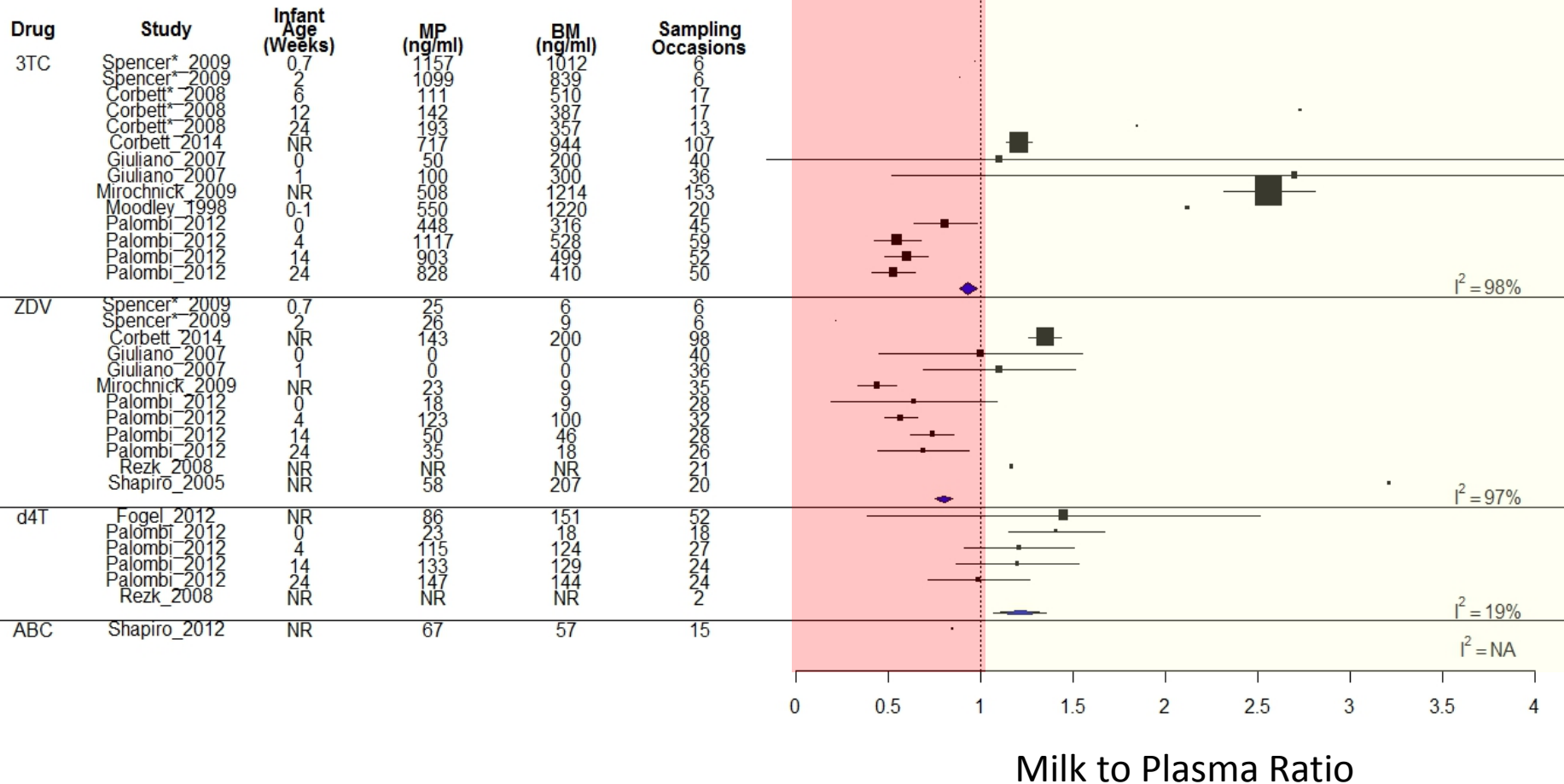
National PMTCT Programme

Option B-Plus ARVs for PMTCT:

Providing lifelong ART for pregnant mothers



Milk to Plasma Ratio: NRTIs



Aim

To obtain rich PK data from breast feeding mother-infant pairs of orally administered TDF/3TC/FTC containing ART.

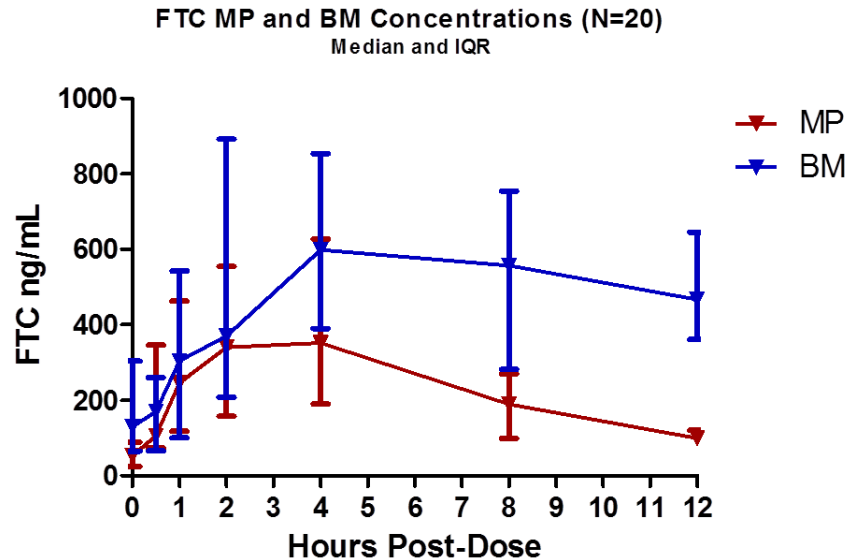
Methods

- **Design:** Non-randomized, open-label, two-group, cross-sectional PK study
- **Sample size:** 48
 - 21- Uganda
 - 27- Nigeria
- **Sampling:** Serial paired dried blood spots and dried breast milk spots (0-12 hr)
- **Assays:** NRTIs quantified by LC-MS/MS
- **Data analysis:**
 - Non-compartmental PK
 - Milk-to-plasma (M:P) ratios

Results

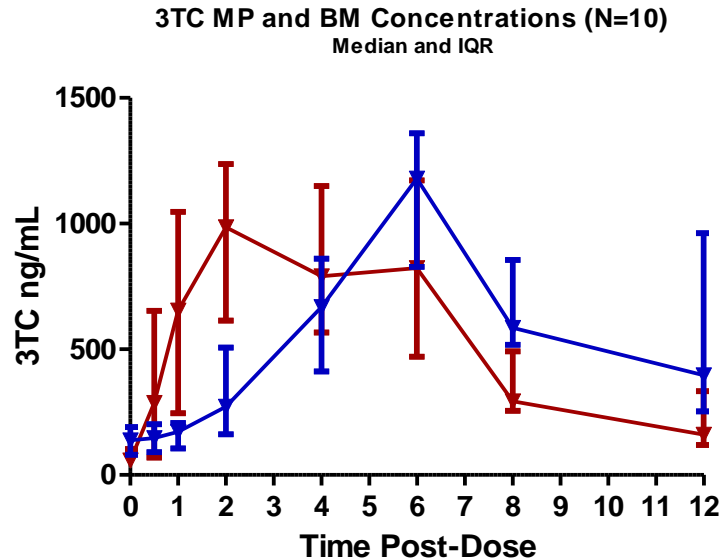
Variable	Uganda	Nigeria
Number of participants	21	27
Maternal weight (Kg; mean, range)	61 (43-87)	59 (46-79)
Infant age (Days; mean, range)	101 (81-146)	143 (80-215)
Infant weight (Kg; mean, range)	5.9 (4.0-6.8)	6.2 (3.0 – 10.0)

Results: FTC Data (Nigeria Only)



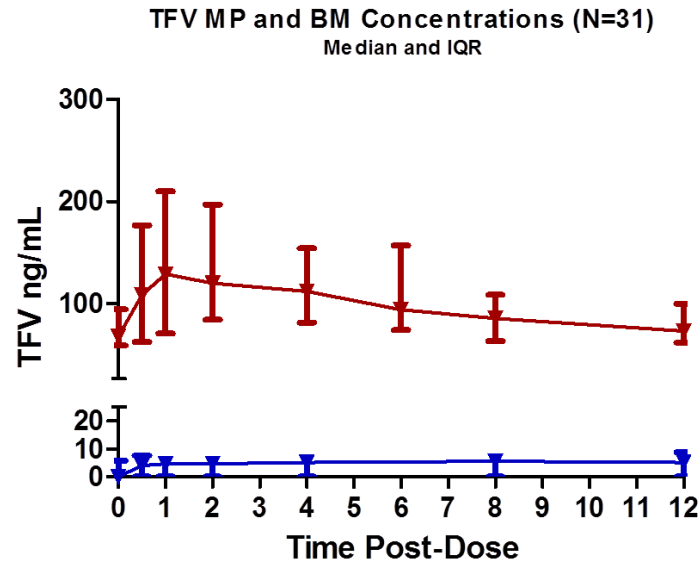
- High levels reached in BM with M:P ratio of 2.13 (SD 1.77)
- Detectable in 19% of infants with median 18.5 (SD 3.4) ng/mL
- Novel data-set

Results: 3TC Data



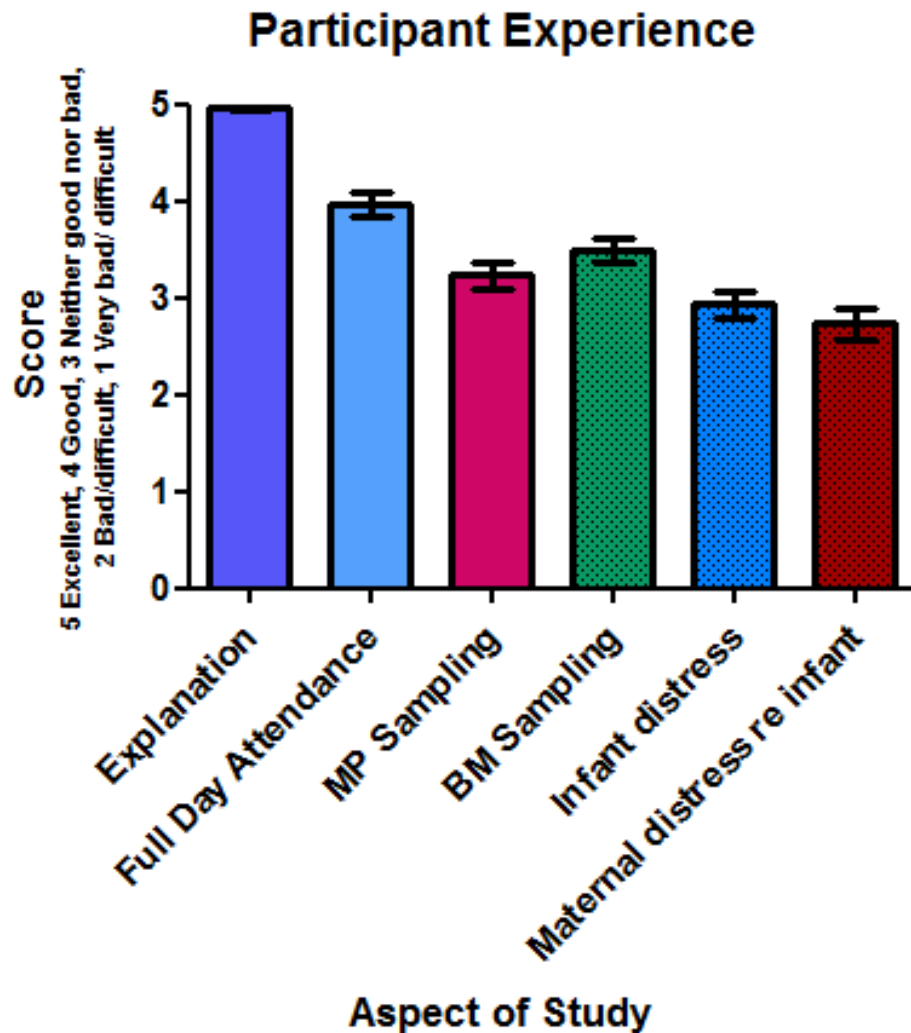
- M:P ratio of 1.02 (SD 0.79)
- 3TC detectable in 41% infants with median concentration 16.4 (SD 8.5) ng/mL
- Consistent between Uganda and Nigeria, and in keeping with previous data

Results: TDF Data



- Detectable in BM in most women but M:P ratio low at 0.034 (SD 0.09) ng/mL
- No infant had detectable TFV (LLQ 16.6)
- Consistent between Uganda and Nigeria
- Novel data set

Is it acceptable to do PK work in breastfeeding mothers and their babies?



- Simple Likert method (5=Excellent, 4=Good, 3=Neutral, 2=Bad/difficult, 1=Very bad/difficult)
- The full day of PK sampling was not seen as a great inconvenience
- Sampling blood, milk and infant blood was considered acceptable
- No additional challenges reported by study team
- Enables further, more detailed work to be undertaken

Summary and conclusions

Key Findings

- 3TC is equivalent in BM and blood, measurable in 40% infants
- FTC accumulates in BM, measurable in 19% of infants
- TDF measurable in BM, but not detectable in infants

Conclusions

NRTI transfer through BM from mother to infant occurs for FTC and 3TC but not TDF

Ongoing work will explore the clinical significance of these PK findings

Acknowledgements

- Study participants
- Study teams



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