

# MATERNAL TB AND NEONATAL IMPLICATIONS

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# CASE

- Cc: fever
- HPI: 8 day old male born in Taiwan at 37 weeks gest.
  - Fever for 2 days
  - No respiratory or GI symptoms
  - No known sick contacts
- Exam: T 39C, other vitals stable
  - Clear lungs, no HSM
- Labs:
  - WBC 17,500/uL
  - CRP 7.3 mg/dL
  - CSF and all cultures negative
- A/P: Sepsis -> Cefotaxime/ampicillin

# HOSPITAL COURSE: 4 DAYS LATER

- Exam: still febrile
  - Abdominal distention
- Labs:
  - HSV, EBV, CMV, H
  - CRP 14.4 mg/dL
- CXR:



- Plan: Change abx to Vanc/Ceftazidime

# HOSPITAL COURSE: CONT'D

- Day 6: CT with R pleural effusion
  - Parents refused drainage
- Day 11: Parents allow gastric lavage -> 1/3 with few AFB
- Day 15: CT c/a/p with patchy consolidation in RUL, multiple bilateral pulmonary nodules, splenic and hepatic nodules
  - Treatment: INH, RIF, PZA
  - Cultures ultimately grow DS TB

Delay in diagnosis:

- ✓ Reluctance for invasive procedures
- ✓ Symptoms overlap with sepsis

# CONGENITAL TB

Signs & Symptoms <sup>2</sup>	%
Fever	64%
Resp. distress	64%
Hepatosplenomegaly	65%
Lethargy/irritable	40%
Poor feeding	39%
Cough	35%
Failure to thrive	25%
Pale	25%
Abd. Distention	22%
Lymphadenopathy	20%

- Diagnostic criteria for congenital<sup>1</sup>: Proven TB lesions with...
  - In the first week of life, OR
  - Primary hepatic complex or caseating granulomas in the liver, OR
  - TB infection in placenta or maternal genital tract, OR
  - Contact investigation excludes postnatal transmission
- Published cases in English: <350
  - 80% in Asia

# NEONATAL TB DIAGNOSIS

- 80% have abnormal chest imaging<sup>1</sup>
  - 50% miliary or nodular
- AFB/culture/PCR
  - 75% yield if from early AM gastric aspirate<sup>2</sup>
- Mortality remains HIGH<sup>1</sup>
  - 53% before 1994
  - 34% post 1994



# NEONATES GET TB FROM THEIR MOMS

Characteristic	Results
Average onset age (days)	20.7 ± 20.2
Median	15
Maternal TB	157 (92%)
Prepartum	36 (22%)
Postpartum	121 (77%)
Maternal TB type	
Miliary	53
Genital or placenta	45
TB pleurisy	22
TB meningitis	12
Infiltrative pulmonary TB	22
Unknown/Other	8

- 75% of mothers who transmit TB to their babies DON'T KNOW IT<sup>1</sup>
- Mortality of infants born to mothers with TB was 2.2x higher if mothers were asymptomatic<sup>2</sup>

# BACK TO THE CASE...

- Mother developed dry cough at 1 week postpartum, weakness
- Day 24 postpartum: altered mental status
  - *AFTER* baby was diagnosed!
- Labs:
  - HIV neg
  - Renal failure
  - Liver failure
  - AFB+, PCR for MTB+
- Treatment: RIPE
  - Died 3 days later





# IMMUNE CHANGES MASK SYMPTOMS

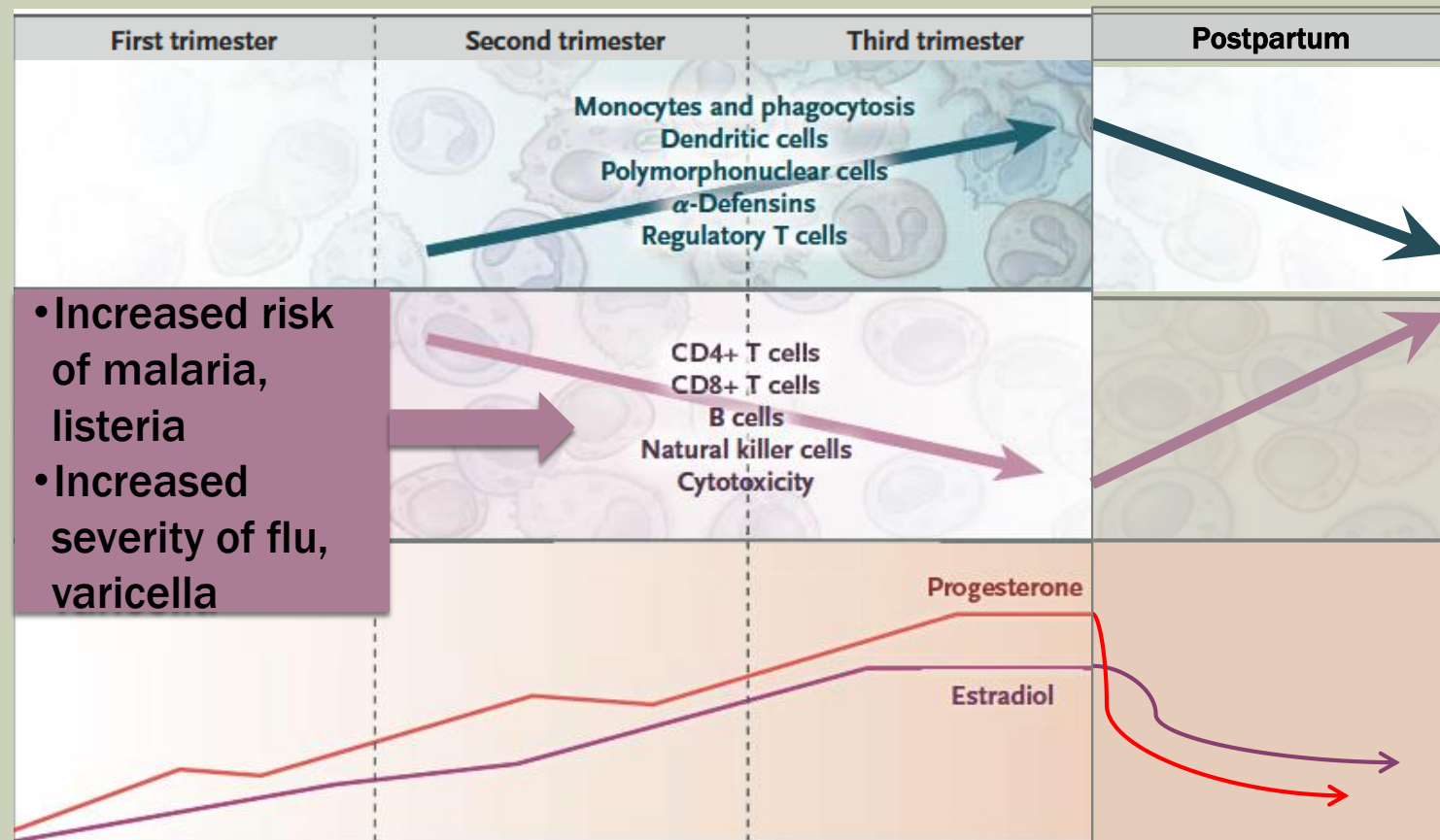


Figure adapted from Kourtis NEJM 2014

# PREGNANCY AND INFANT OUTCOMES

## Pregnancy

- Pre-eclampsia & eclampsia (2 fold)
- Vaginal bleeding (2 fold)
- Hospitalization (12 fold)
- Miscarriage (10 fold)
- **Mortality**
  - **25 fold for HIV-uninfected**
  - **37 fold for HIV-infected**



## Infant

- Low birth weight (2 fold)
- Lower Apgar scores
- Prematurity (2 fold)
- Small for gestational age (2 fold)
- Infant HIV (2 fold)
- Congenital TB (rare)
- **Infant mortality (3.4 fold)**

# TREATMENT OF PULMONARY TB IN PREGNANCY

	HIV negative	HIV positive
Low Burden <sup>1</sup>	INH 5mg/kg/d x 9 mo RIF 10mg/kg/d x 9mo EMB wt-based x 2 mo B6 25mg/d x 9 mo	INH 5 mg/kg/d × 6 mo RIF 10 mg/kg/d × 6 mo EMB 15mg/kg/d x 2 mo PZA 25mg/kg/d x 2 mo B6 10-25mg/d x 6 mo
High Burden <sup>2</sup>	INH 300 mg/d × 6 mo RIF 600 mg/d × 6 mo EMB wt-based x 2mo PZA wt-based × 2 mo B6 25mg/d x 6 mo	INH 5 mg/kg/d × 6 mo RIF 10 mg/kg/d × 6 mo EMB 15mg/kg/d x 2 mo PZA 25mg/kg/d x 2 mo B6 10-25mg/d x 6 mo

**DIFFERENCE IN PZA guidance**

**NO MDR-TB guidelines**

<sup>1</sup> CDC, ATS, IDSA guidelines; <sup>2</sup> WHO, British thoracic Society, RNTCP and IUATLD guidelines

# BREASTFEEDING?

- Breast feeding allowed if on 1<sup>st</sup> line
  - NOT recommended with rifabutin or fluoroquinolones
  - No evidence for other DR medications
- If mother suspected of having TB, separate from infant<sup>1</sup>
  - Can resume when smear negative (after 2-3 weeks of treatment), or infant started on TB treatment
  - Baby should get INH (3-6 months) + BCG

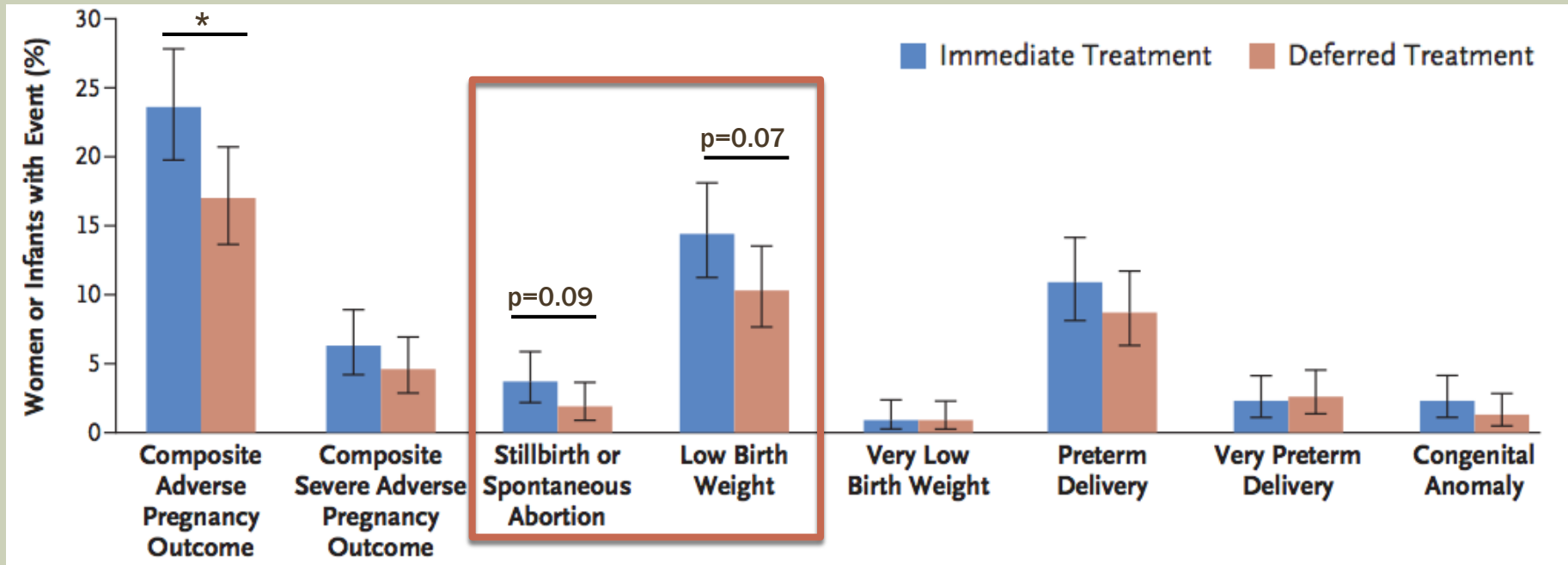


# TREATMENT OF LTBI IN PREGNANCY

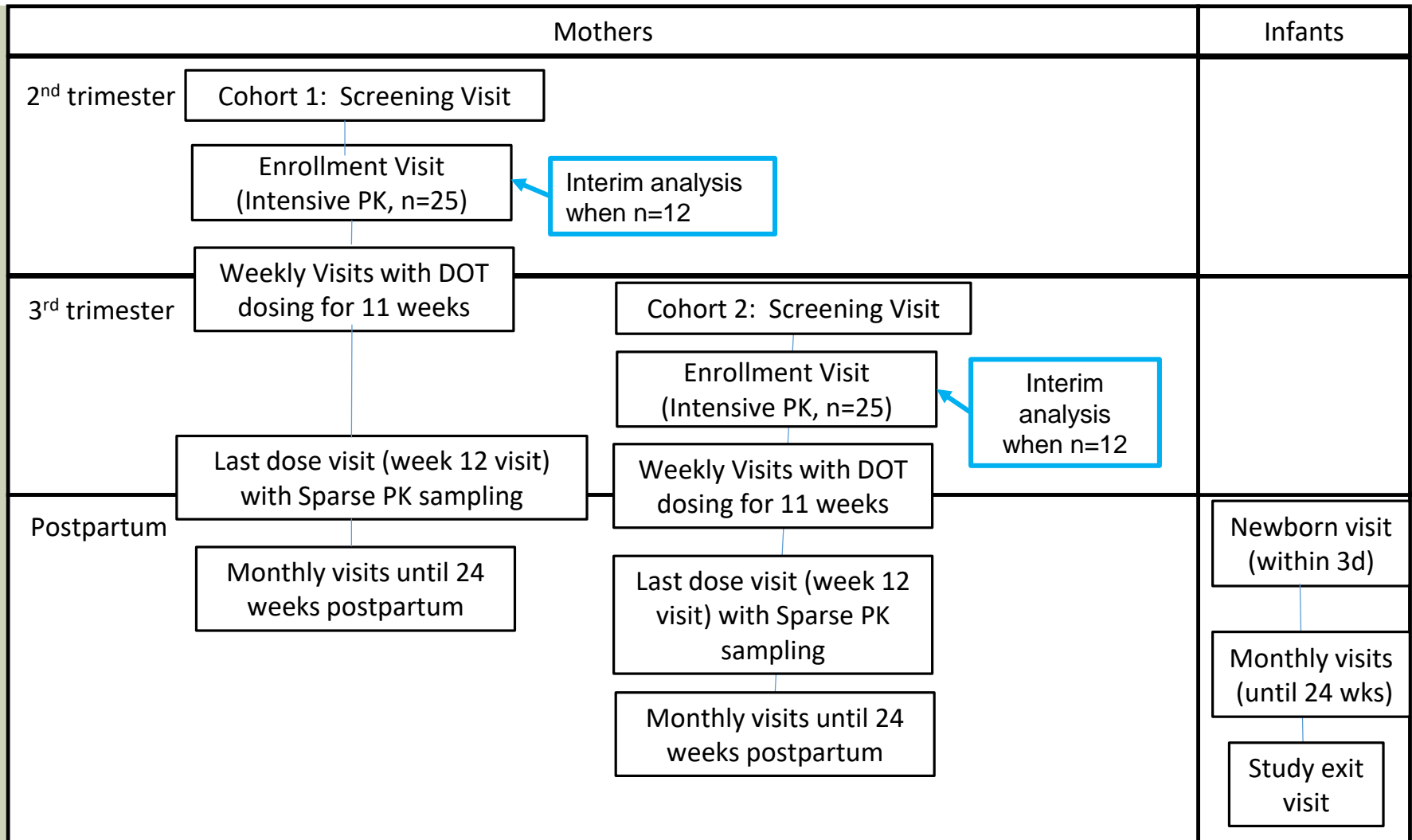
	<b>HIV negative</b>	<b>HIV positive</b>
<b>Low burden</b>	Defer until postpartum, unless recent household contact	INH 300mg + Vit B6 (10-25mg) daily for 6-9 mos <sup>1,2</sup>
<b>High burden</b>	No official guidance	INH 300mg + Vit B6 (10-25mg) daily for 6-9 mos <sup>1,2</sup>

# P1078: RISK OF IPT IN PREGNANCY

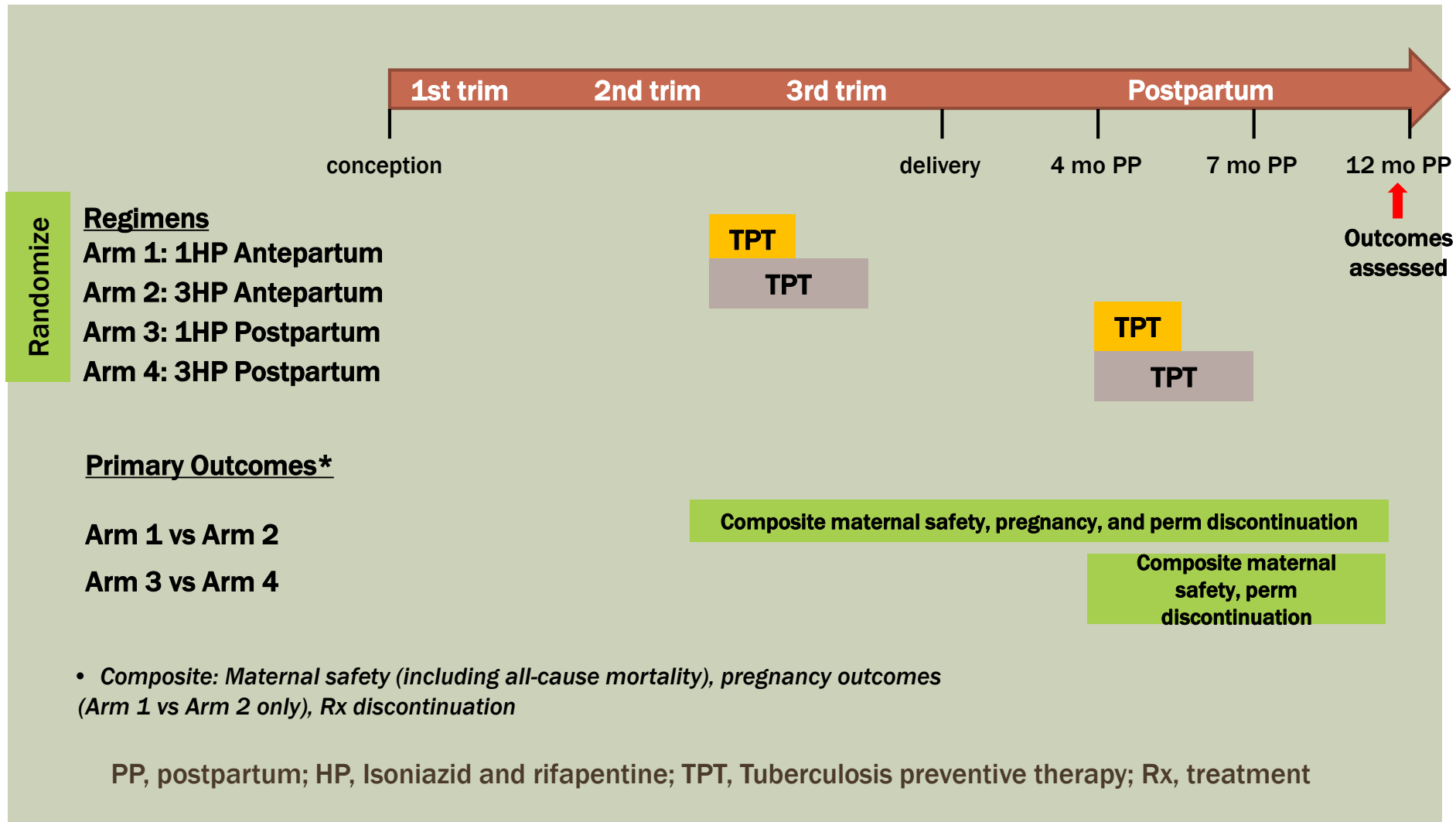
- 956 HIV+ pregnant women from 8 countries
  - Randomized to immediate versus deferred (12 wk PP) IPT



# P2001: 3HP IN PREGNANT/ POSTPARTUM WOMEN



# IMPAACT 2025: 1HP VS. 3HP IN PREGNANT VS. POSTPARTUM WOMEN





# WHAT WE NEED

## Neonatal

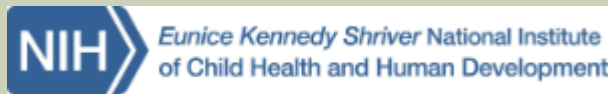
- Better screening guidelines
- Diagnostics (POC)
- Evidence-based treatment guidelines (DS and DR)

PK studies from breast milk

## Maternal

- Better screening guidelines
- Diagnostics- POC and improved sensitivity
- Evidence-based treatment guidelines (DR, PZA)

# THANK YOU



Weill Cornell Medicine  
CENTER FOR GLOBAL HEALTH



NIAID: K23AI129854

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NCATS: KL2 TR00458 of the CTSC at Weill Cornell Medical College

Foundations: Ujala, Wyncote, Gilead

Indian Dept. of Biotechnology (DBT) and Council of Medical Research (ICMR)

# WANT TO HEAR MORE?

## Maternal and child lung health working group

- Thursday, October 31 @ 7:45am
- Room: MR G.03 &G.04

## Other sessions:

- Friday, November 1
  - TB preventive therapy: Is it safe and how should we implement it?
    - 10:30-12: Room: MR G01 & G02
  - TB in pregnancy: optimising diagnosis and treatment
    - 12:15-1:15, Eposter area 2
- Saturday, November 2
  - Confronting the crisis: emerging research in maternal-child TB
    - 10:30-12, Room G05&G06
  - Meet the Expert, IPT in Mothers and children: Yael Hirsch-Moverman, Jyoti Mathad
    - 12:15-1:15, MR 2.03&2.04