

Management of Newborns of Mothers with TB Disease

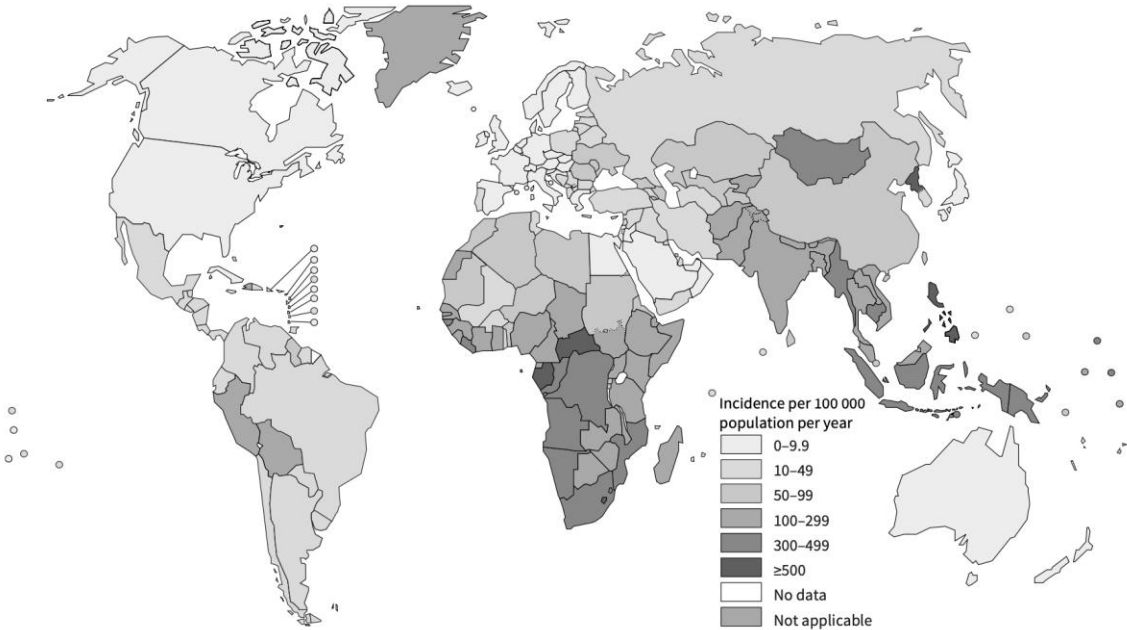
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27 September 2024

Outline

- 1) Burden of TB disease in pregnancy
- 2) Consequences to infant
- 3) Perinatal vs Congenital TB
- 4) Management of infants born to mothers with TB
 - Evaluation
 - Treatment
 - Isolation & breastfeeding

TB Burden in Pregnancy is Likely High but **Unknown**

10.6 Million People with TB in 2022



Males >15 years: 6 million cases



Females >15 years 3.4 million



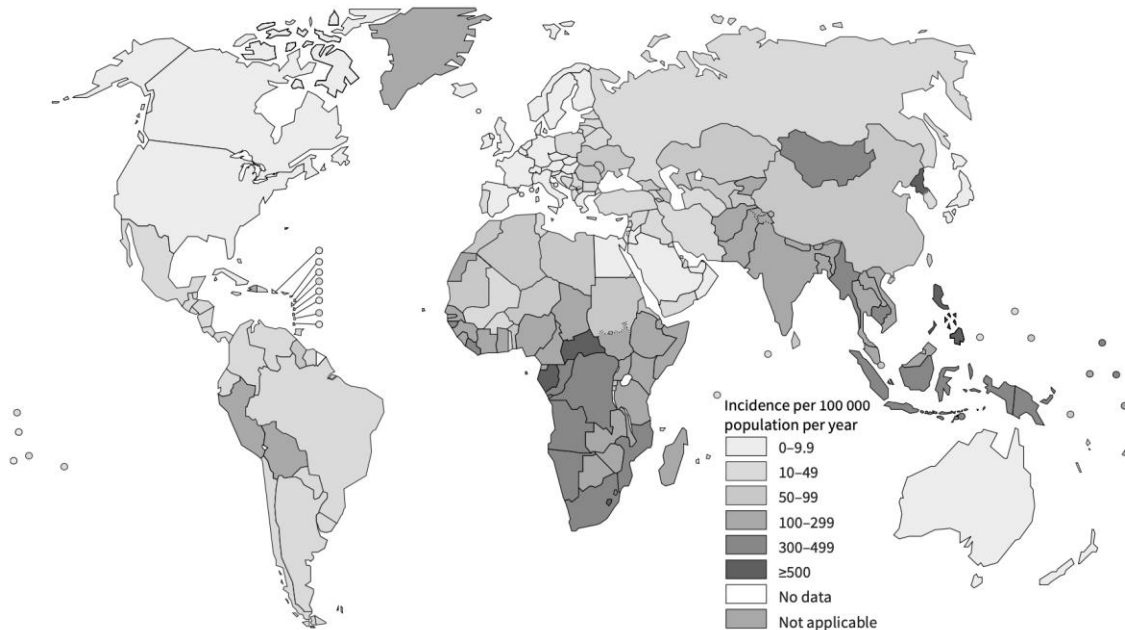
Children < 15 years 1.2 million



Pregnant Women 216,500 ???

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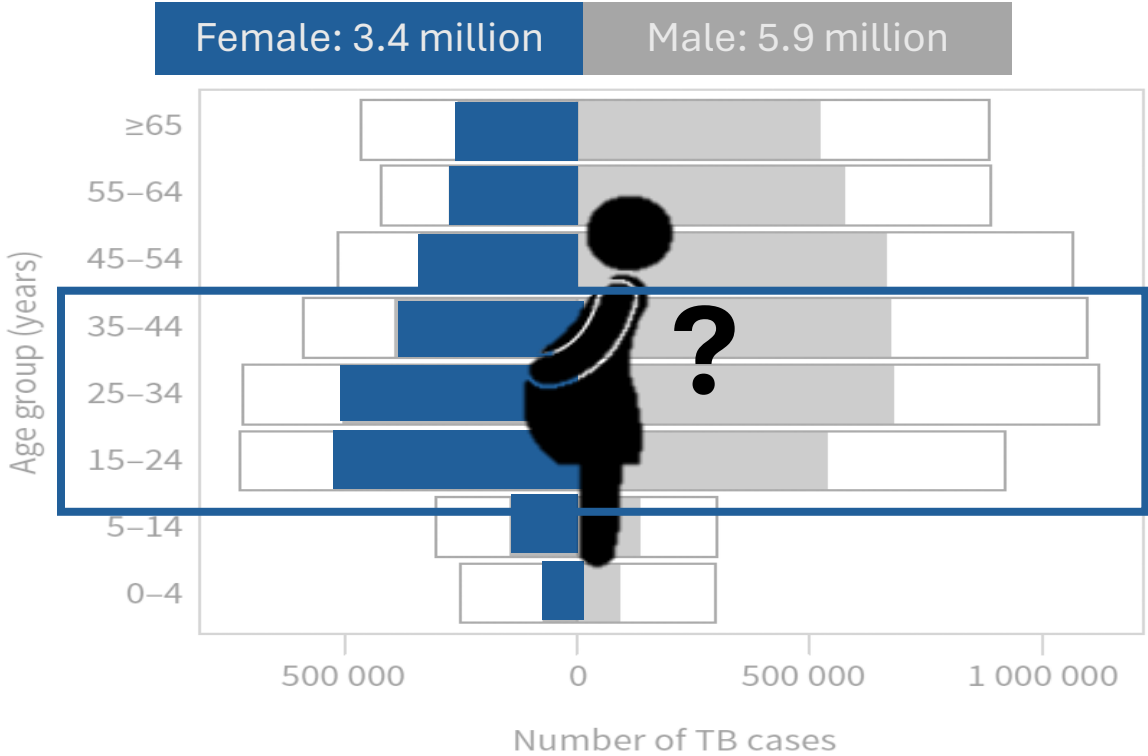
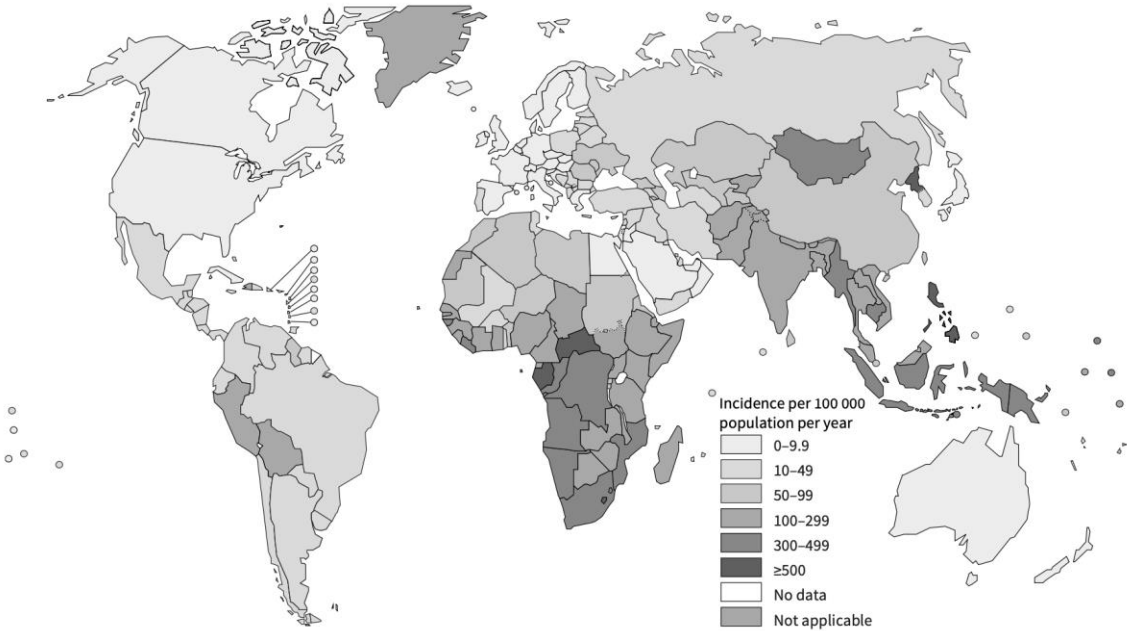


Pregnant Women 216,500 ???

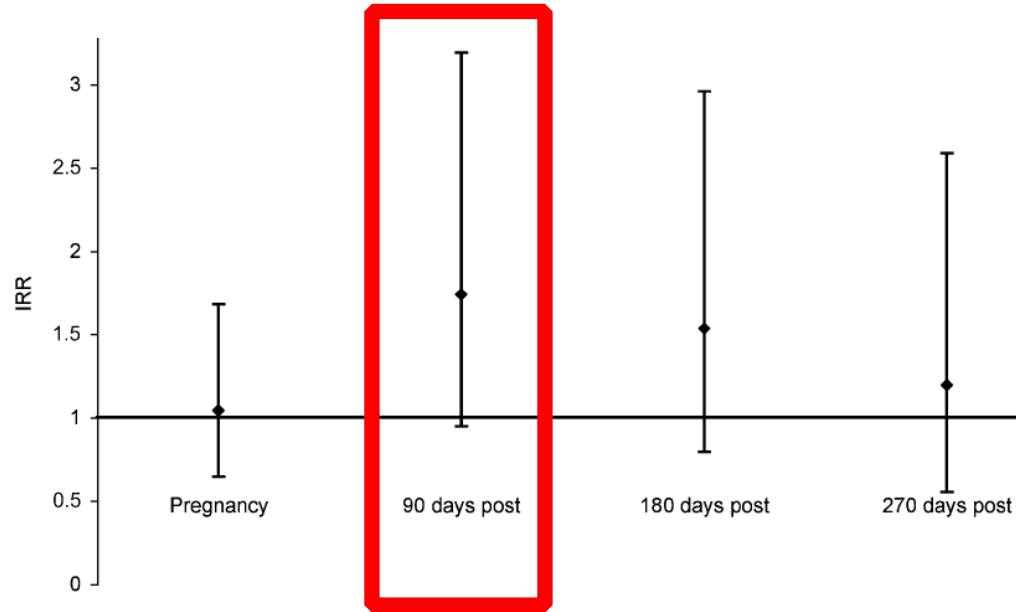
Data on TB & pregnancy is not commonly collected by TB programmes

TB Burden in Pregnancy is Likely High but **Unknown**

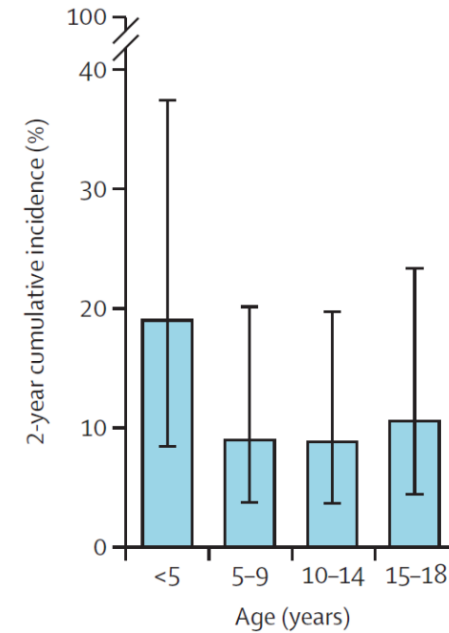
10.6 Million People with TB in 2022



TB Risk in Peripartum Women and Children

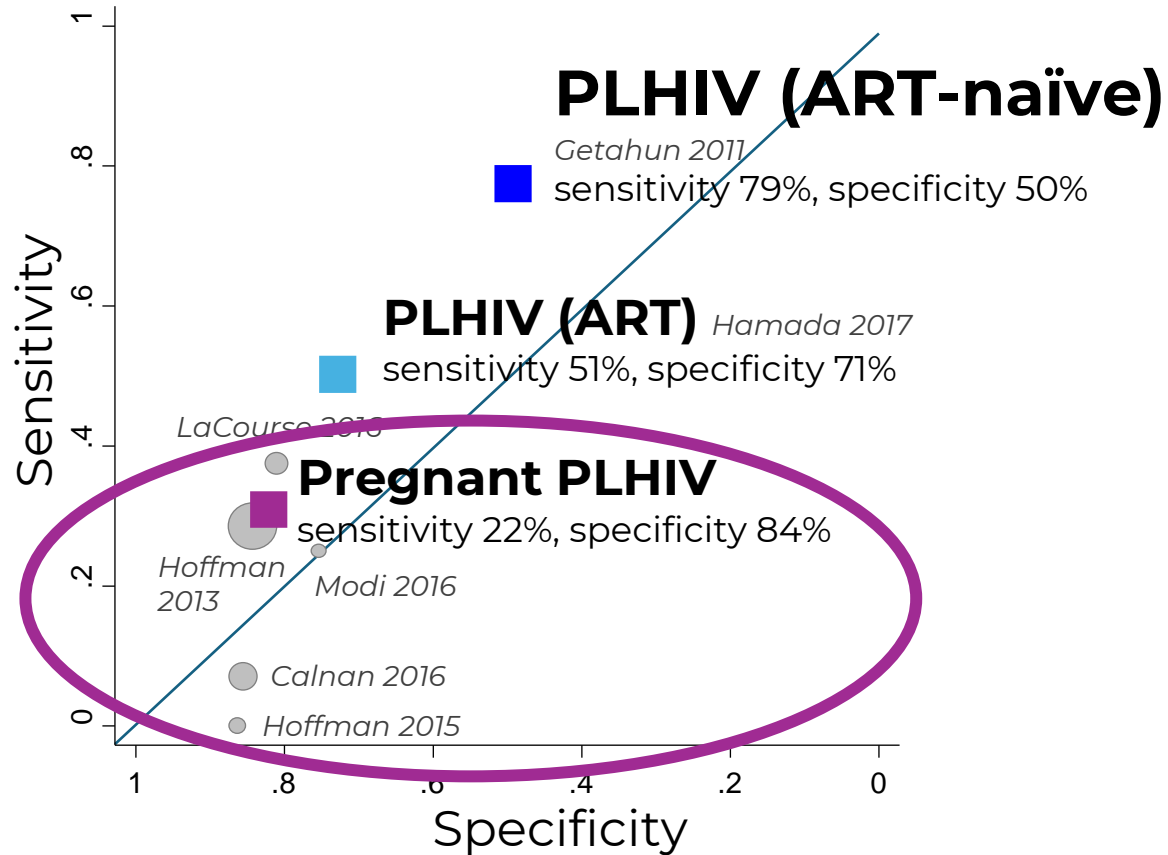


TB incidence is **2x higher** postpartum than non-pregnant/non-postpartum



Other children in the household are also at high risk of disease

Four-symptom WHO TB Screen has Poor Sensitivity in Pregnancy



Additional screening methods may be needed to identify pregnant women with TB/HIV

Increased Identification of TB in PWLHIV through Universal Screening

Methods

- Cluster-randomized trial of **universal vs symptom-based testing** in pregnant PLHIV
- Testing: Xpert only → Xpert + MGIT culture

Conclusions

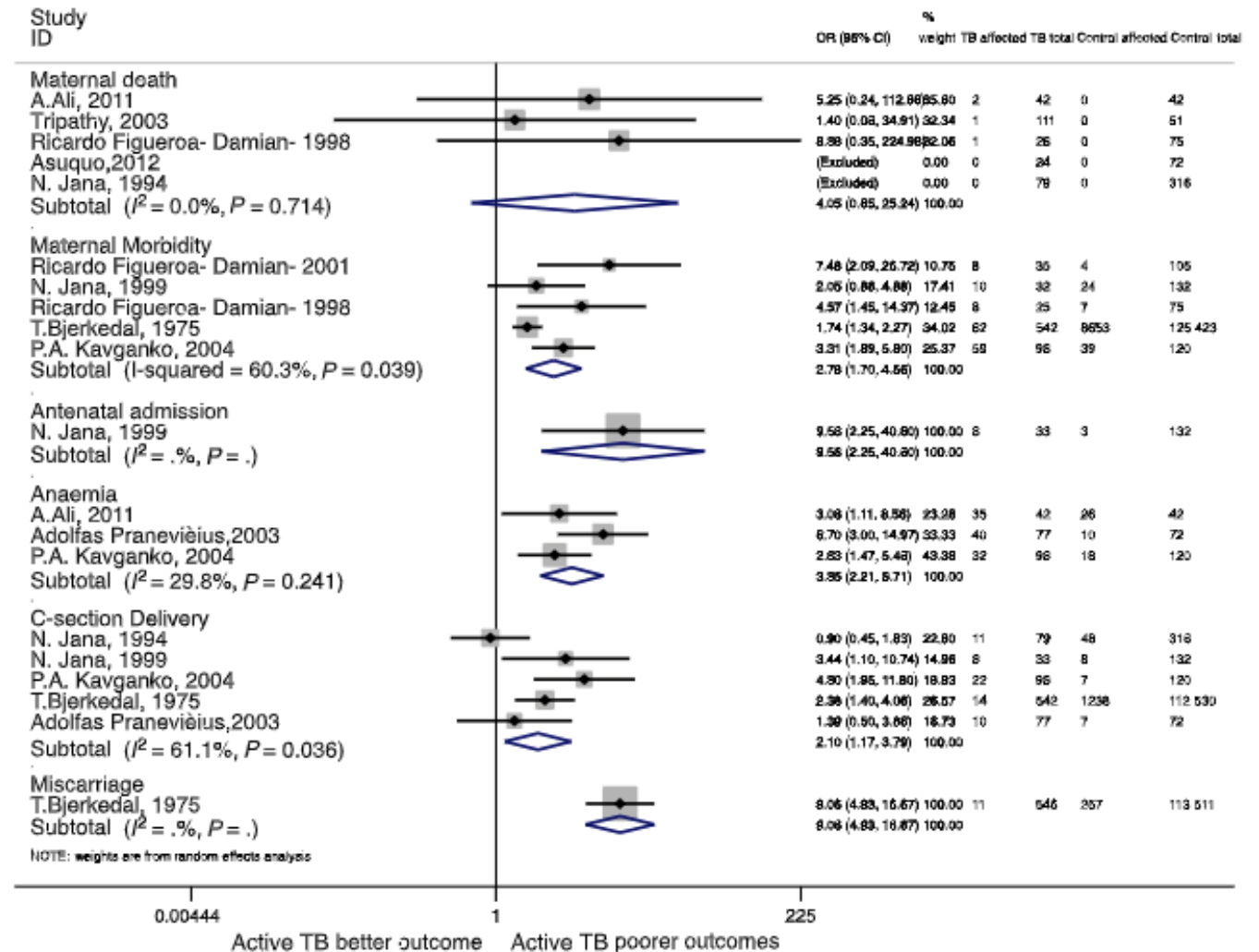
- 10-fold increased detection of TB in universal vs symptom based scrn
- Xpert detects one third the rate of TB compared to MGIT – ?low bacillary load
- Halved infant and maternal deaths (not statistically significant)

Xpert MTB/RIF v MGIT Culture: Universal				
MGIT Mycobacterial Culture				
		Positive	Negative	
Xpert Result	Pos	5 (1.0%)	2 (0.4%)	7 (1.4%)
	Neg	21 (4.1%)	479 (94.5%)	500 (98.6%)
Total		26 (5.1%)	481 (94.9%)	507

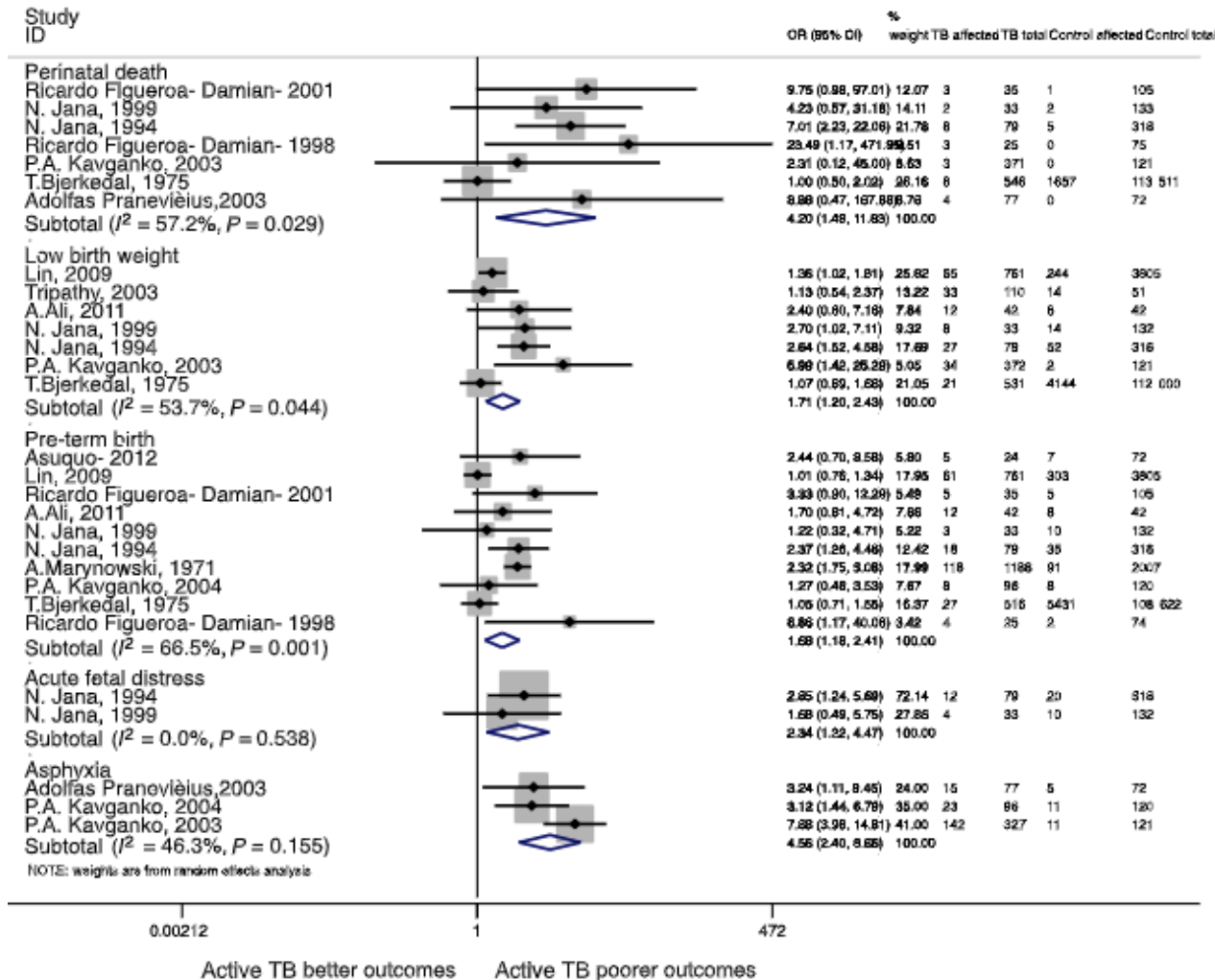
Yield of TB by Arm, by Visit and by Site					
Study Arm	n/N	MTb Yield (95%CI)	Baseline	Matlosana (high burden)	Vhembe (medium burden)
Universal	34/941	3.6% (1.2-6.0)	26/34	4.5%	2.2%
Symptom	4/1100	0.36% (0.0-1.1)	4/4	0%	1.1%

Increased Adverse Maternal and Pregnancy Outcomes

- 4-fold increased **maternal mortality**
- 3-fold increase **morbidity**
- 10-fold increased **hospitalization**
- 4-fold increase **anemia**
- 2-fold increase **cesarean**
- 9-fold increase **miscarriage**



Increased Adverse Infant Outcomes



- 4-fold increased **perinatal death**
- 2-fold increase **LBW**
- 2-fold increased **preterm birth**
- 2-fold increase **acute fetal distress**
- 5-fold increase **birth asphyxia**

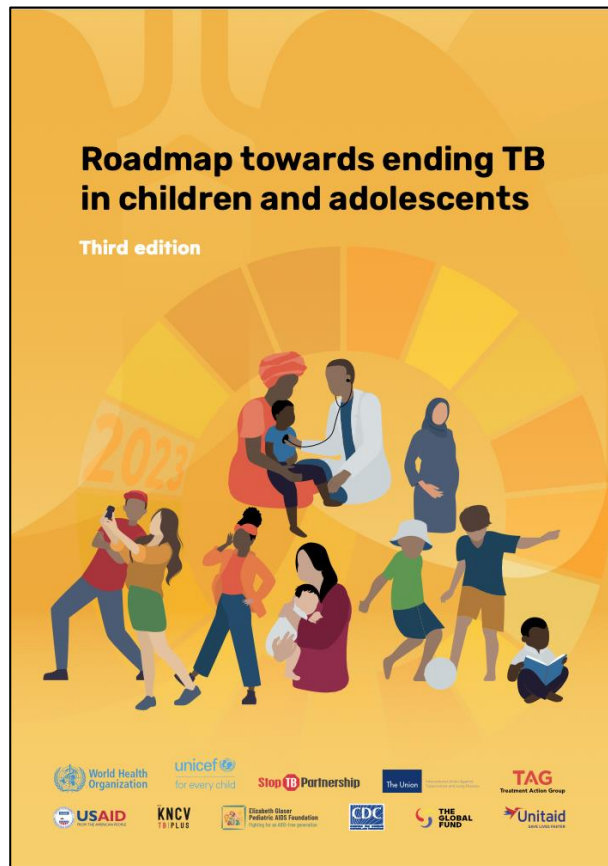
Poor Infant Outcomes Associated with Subclinical TB

Table 2 Obstetric and infant outcomes by TB status

	TB-negative controls (<i>n</i> = 151) <i>n</i> (%)	Unsuspected prevalent TB (<i>n</i> = 7) <i>n</i> (%)	<i>P</i> value (prevalent vs. controls)	TB-positive cases (<i>n</i> = 70) <i>n</i> (%)
Obstetric outcomes				
Outcome of pregnancy			1.0	
Live birth	149* (99)	7 (100)		67 (96)
Spontaneous abortion	0	0		1 (1)
Stillbirth	2 (1)	0		2 (3)
Composite maternal complications outcome [†]	53 (35)	3 (43)	1.0	31 (44)
Infant outcomes	(<i>n</i> = 150)*	(<i>n</i> = 7)		(<i>n</i> = 67)
HIV transmission	2 (1)	0	1.0	3 (4)
Infant TB	0	1 (14)	0.045	8 (12)
Neonatal sepsis	6 (4)	1 (14)	0.3	3 (4)
Infant hospitalization	16 (11)	3 (43)	0.039	11 (16)
Infant death	1 (1)	0	1.0	5 (7)
Composite infant complications outcome [‡]	17 (11)	3 (43)	0.045	16 (24)

Infants of mothers with HIV & subclinical TB had higher risk of adverse infant outcomes (TB & hospitalization) than mothers with HIV alone

Maternal TB integrated into the Child TB Roadmap



Key actions needed for maternal TB:

- 1) Better understanding of the **burden** of TB disease in pregnant women
- 2) Pregnant and post-partum women and their infants should be **protected through and not from research**; urgent need to include pregnant women and their infants in TB drug & vaccine trials
- 3) Rigorous **operational research and surveillance** will enable rapid detection of uncommon adverse maternal, pregnancy and birth outcomes

Perinatal Tuberculosis

Congenital TB

In utero infection of fetus with *M.tb* (*rare*)

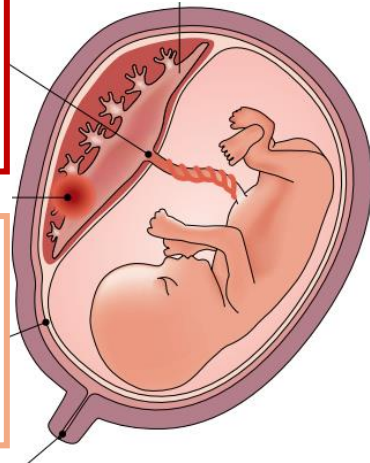
Maternal TB bacillemia (primary or disseminated)
Results in dissemination of infection to placenta, endometrium or genital tract

Transplacental transmission

- Maternal hematogenous spread
- Primary focus in infant liver (fetal circulation)

Aspiration/Ingestion fluid

- Maternal endometritis or placental infection
- Primary focus in lung or GI tract



Postnatal TB

Post natal infection of infant (*common*)

Maternal infectious pulmonary disease
(untreated cavitary disease, etc.)



Airborne transmission

- Maternal infectious pulmonary TB
- Primary focus in lung

Congenital Tuberculosis: Diagnostic Criteria

Cantwell Criteria

Presence of proven tuberculosis disease in the infant with at least one of the following:

- Lesions in the newborn during the first week of life
- Primary hepatic complex or caseating hepatic granuloma
- TB infection of the placenta or maternal genital tract
- Exclusion of possibility of postnatal transmission by investigation of contacts, including hospital staff

Criteria are rather strict, difficult to prove *even* in resource-rich settings

Congenital TB: Signs & Symptoms

Non-specific signs and symptoms

- **Ill neonate** with fever, tachypnea, lethargy, organomegaly, pulmonary infiltrates
- Median time to presentation: 2-3 weeks (range 1-112 days)
- Combined data from 75 cases in 38 case reports/series:

Common (>40%)	Frequent (25-40%)	Infrequent (10-25%)	Rare (< 10%)
<ul style="list-style-type: none">• Respiratory Distress (incl tachypnea)• Hepatosplenomegaly• Fever (often low-grade)• Prematurity/LBW	<ul style="list-style-type: none">• Cough – acute or chronic• Poor feeding• Failure to thrive• Abdominal distension (incl ascites)	<ul style="list-style-type: none">• Irritability• Peripheral LAD• Sepsis syndrome	<ul style="list-style-type: none">• Skin lesions• TB meningitis• Jaundice (obstructive)• Otorrhea/mastoiditis• Wheeze/stridor• Apnea/cyanosis (BRUE)• Facial nerve palsy• Shock

Management of the infant born to a mother with tuberculosis: a systematic review and consensus practice guideline

Nadia Hasan, Clare Nourse, H Simon Schaaf, Adrie Bekker, Marian Loveday, Betina M Alcântara Gabardo, Christopher Coulter, Chishala Chabala, Sushil Kabra, Eilish Moore, Elizabeth Maleche-Obimbo, Nicole Salazar-Austin, Nicole Ritz, Jeffrey R Starke, Andrew P Steenhoff, Rina Triasih, Steven B Welch, Ben J Marais

1) Systematic Review

- MEDLINE, CINAHL & Cochrane Library through December 1, 2022
- 521 published papers → 3 met inclusion criteria → no evidence-based conclusions
- Narrow scope, variable aims, descriptive nature, inconsistent data collection, high attrition rates

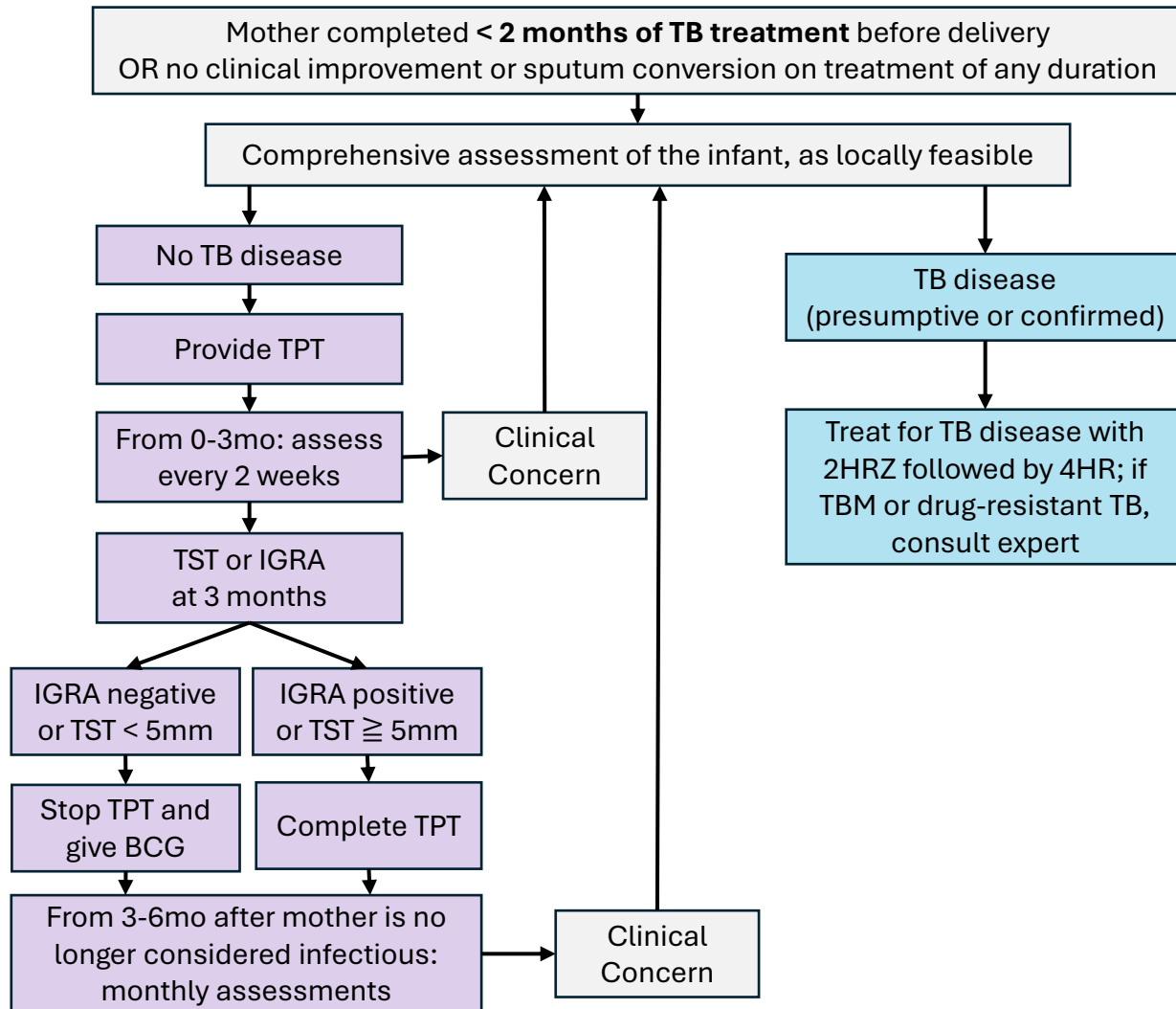
2) Consensus Guideline

- Reviewed 16 international guidelines
- International panel of experts from high/low burden and high/low resource settings
- Developed guidance for mothers who were potentially infectious and non infectious at delivery

Purpose:

- More consistent **clinical management**
- Support the collection of **better data**
- Encourage the **development of more studies** to improve evidence-based care

Management of Infant Born to Mother with Potentially Infectious TB at Delivery



Maintain High Suspicion
Maternal TB may not be diagnosed at the time of infant presentation!

2 months is conservative
Considers:

- Maternal resistance
- Other ill/infectious household members
- Culture/smear conversion may not be documented until 2 months

Maternal disease with increased risk of congenital TB

- Disseminated TB (miliary or TBM)
- Tuberculous pleural effusion (suggestive of recent primary infection)
- Pelvic, genital or placental TB

Comprehensive Clinical Assessment

Routine:

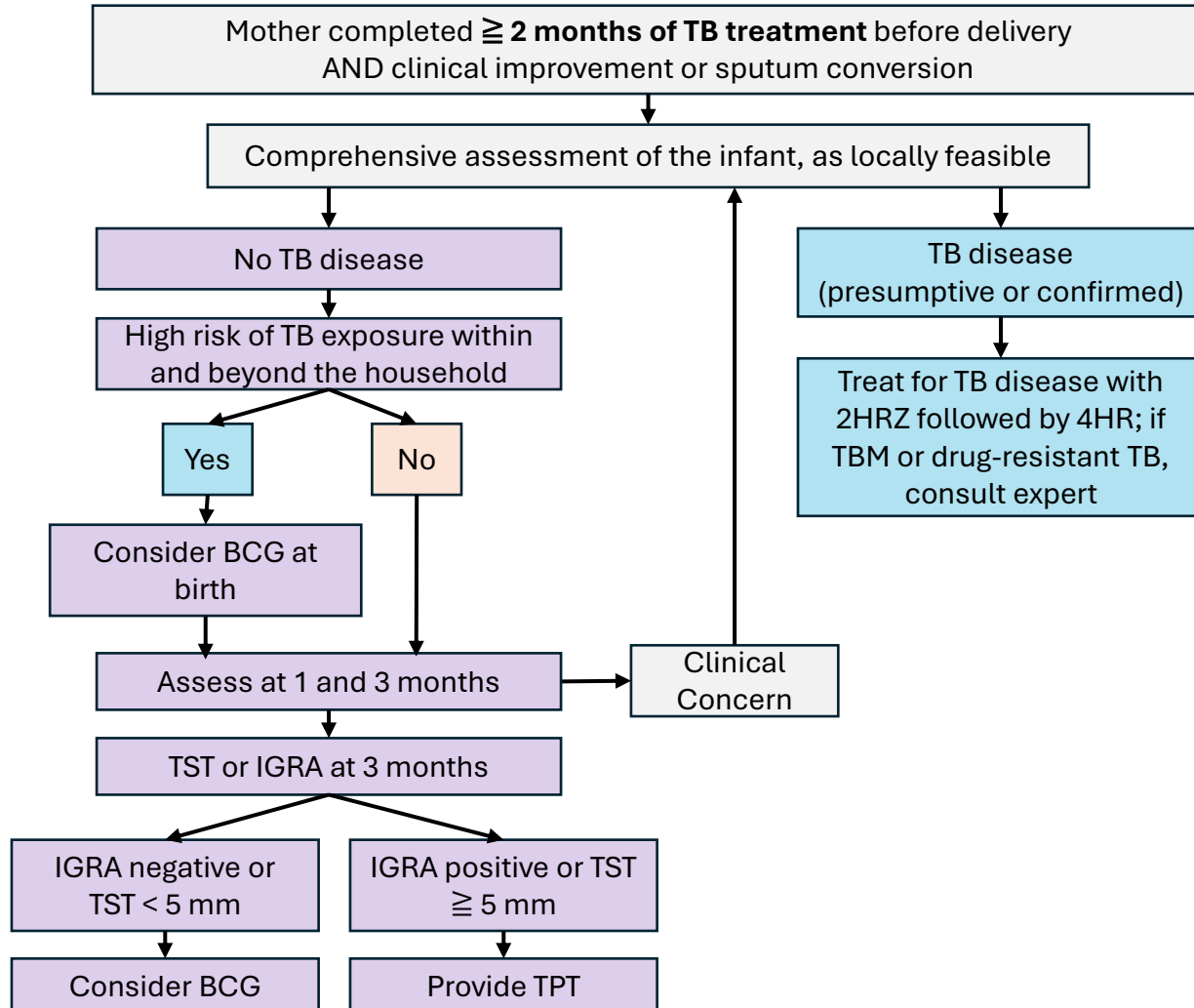
- **Chest X-ray**
- **Abdominal US**
 - Not always available in all settings
 - Especially important when mom is high risk for transplacental transmission

With any signs or symptoms:

- **Abdominal US:** if IUGR, hepatomegaly, and/or ascites
- **Respiratory specimens** for culture and/or NAAT
- **Lumbar Puncture** for cell counts, chemistries, culture, NAAT
- **Fundoscopy** (maternal)
- **Brain imaging** (if signs/symptoms CNS disease)
 - MRI > CT > Head US

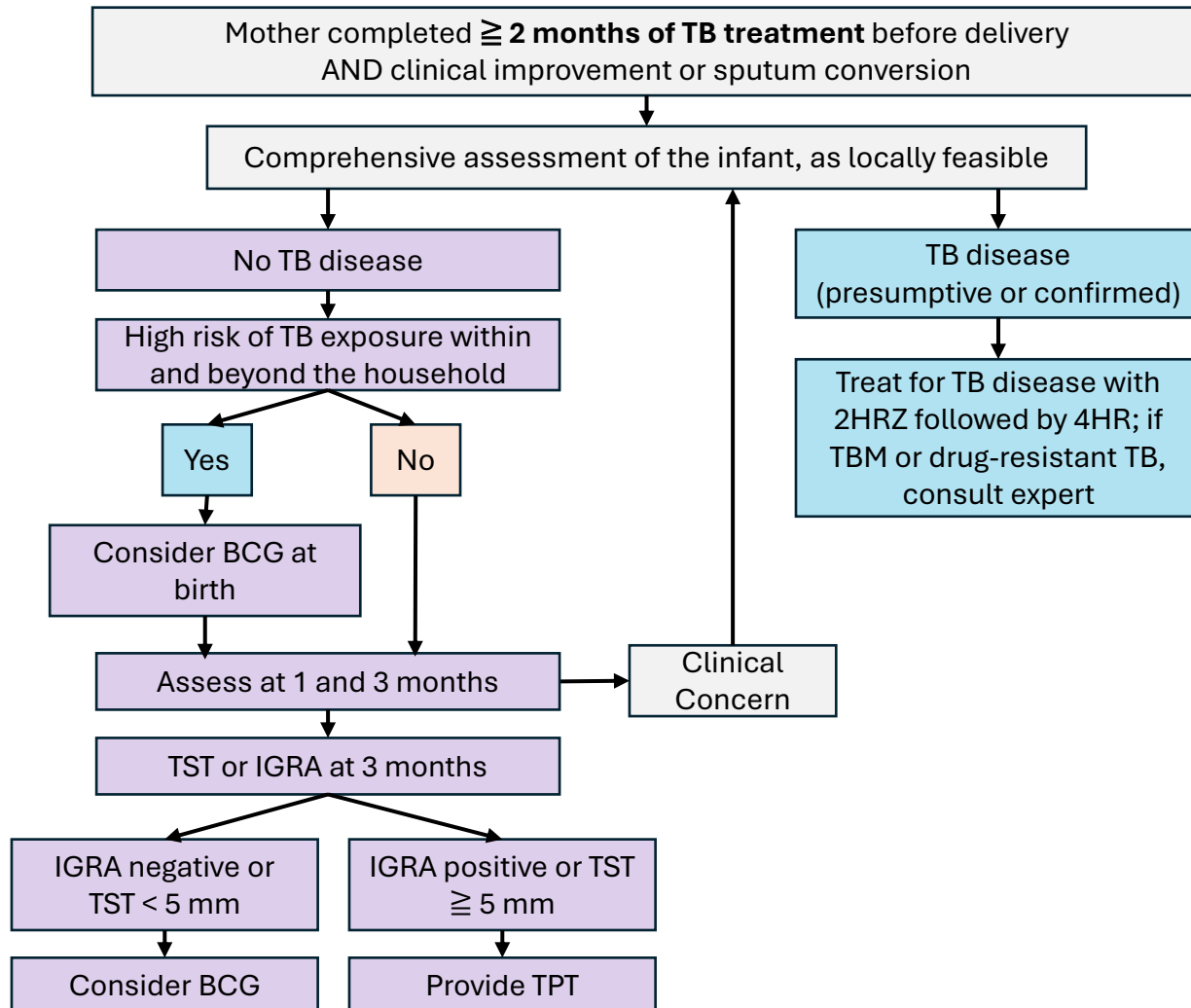
Management of Infant Born to Mother with Non-infectious TB at Delivery

High burden setting

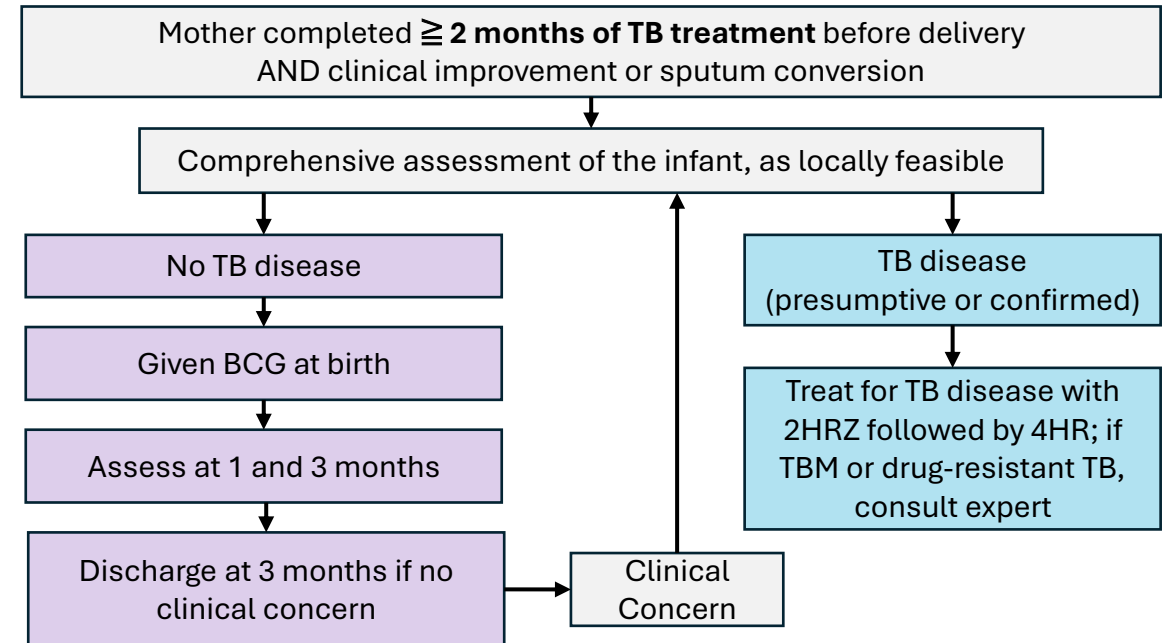


Management of Infant Born to Mother with Non-infectious TB at Delivery

High burden setting



Low burden setting



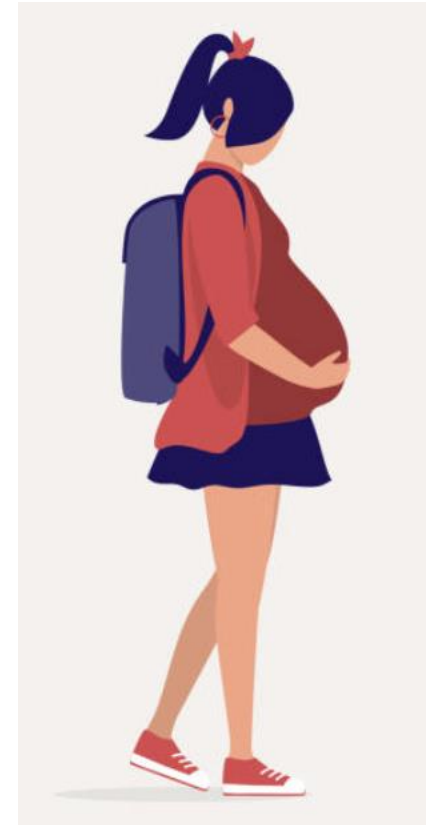
Maternal TB & Breastfeeding



- Breast is best
- Every effort should be made to **facilitate breastfeeding**
- Minimize mother-infant isolation: transmission low once mother on treatment and infant on TPT
 - Surgical mask can be used if mom considered infectious
 - Or no mask if mother has good adherence with treatment response
- Minimal data on TB drugs in breastmilk
 - RHZE – low levels in breastmilk, no direct measures in infants, no known safety concerns
 - Less experience and fewer data with second line medications
 - Lipophilic drugs like BDQ have high BM concentrations in animals and humans and may have therapeutic exposures in infants
 - WHO-led consensus process to encourage the optimal and early inclusion of pregnant women in TB drug and vaccine research

Maternal TB & Adolescents

- Adolescents are at high risk of progression from infection to disease
- Pregnant adolescents may be more likely to experience obstetric & neonatal complications
- High risk of poor adherence resulting in treatment failure, relapse, and resistance with resulting transmission to their infants



Take Home Messages

- Perinatal TB is relatively common; true congenital TB is rare
 - Can be acute and atypical
 - Infants born to mothers with TB can also be exposed by other household members
- High index of suspicion in mothers and infants is required
- Optimal TB screening for mother (particularly if living with HIV) is unknown
- New expert opinion consensus treatment guidelines are available
- Facilitate breastfeeding – transmission low once mother is on treatment and infant is on prophylaxis

Thank you