# TUBERCULOSIS SCREENING AND MANAGEMENT In PREGNANCY

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# **Mycobacterium tuberculosis**



### Estimated TB incidence rates, 2015



#### Percentage of bacteriologically confirmed TB cases tested for RR-TB, 2015



#### Number of patients with laboratory-confirmed XDR-TB started on treatment in 2015



# **Indonesia-Population 2015**

		Rate		
Estimates of TB burden*, 2015	Number (thousands)	(per 100 000 population)		
Mortality (excludes HIV+TB)	100 (67–150)	40 (26–57)		
Mortality (HIV+TB only)	26 (20-34)	10 (7.6–13)		
Incidence (includes HIV+TB)	1 020 (658–1 450)	395 (255–564)		
Incidence (HIV+TB only)	78 (48–116)	30 (18-45)		
Incidence (MDR/RR-TB)**	32 (19–45)	12 (7.4–17)		
TB case notifications, 2015				
Total cases notified		3	333 119	
Total new and relapse		3	331 271	
- % tested with rapid diagnostics at time of diagnosis				
- % with known HIV status			11%	
- % pulmonary			92%	
- % bacteriologically confirmed among (	pulmonary		64%	
TB/HIV care in new and relapse TB patients, 2	2015	Number	(%)	
Patients with known HIV-status who are HIV-positive 352		3 5 2 3	10%	
- on antiretroviral therapy		757	21%	

# **Tuberculosis in pregnancy**

	Mean (95% uncertainty range)	Rate per 1000 pregnant women (95% uncertainty range)	Percentage of global burden
All countries combined	216 500 (192 100 - 247 000)	2-1 (1-8-2-4)	
African Region	89400 (74200-110500)	3.6 (3.0-4.5)	41%
Region of the Americas	4800 (3900–6000)	0.4 (0.3 - 0.5)	2%
Eastern Mediterranean Region	28500 (19700–41900)	2-3 (1-6-3-4)	13%
European Region	4900 (3800–6300)	0.6 (0.5–0.8)	2%
South-East Asia Region	67500 (52000-87100)	2-4 (1-9-3-1)	31%
Western Pacific Region	21 400 (19 400–23 700)	1.1 (1.0 – 1.2)	10%

*Table 2:* Total number of active tuberculosis cases in pregnant women, rate per 1000 pregnant women and percentage of global burden by WHO region and combined

## **TB** as a three-act play



### **IMPACT OF TB ON MATERNAL HEALTH**

TB among mothers is associated with a six-fold increase in perinatal deaths and a two-fold risk of premature birth and low birth-weight.

TB in pregnant women living with HIV increases the risk of maternal and infant mortality by almost 300%.

In Africa, TB rates are up to 10 times higher in pregnant women living with HIV than in pregnant women without HIV infection.

Facility-based studies in a number of high HIVburden settings found TB accounted for 15-34% of indirect causes of obstetric mortality.

Evidence from India has found that TB among mothers living with HIV, is associated with more than double the risk of vertical transmission of HIV to the unborn child.

# Pathogenesis of tuberculosis in the newborn

- Haematogenous spread through the umbilical cord.
- In-utero aspiration or ingestion of infected amniotic fluid.
- Intrapartum aspiration or ingestion of infected amniotic or cervicovaginal secretions.
- Postpartum inhalation or ingestion from an infected source case, usually the mother.

### Breastfeeding does not transmit TB.

### CLINICAL FEATURES OF TUBERCULOSIS IN PREGNANT WOMEN

 similar to those in non-pregnant women
mild cough, fever, and fatigue or haemoptosis and gross weight loss

bronchopneumonia, cavitation,
bronchiectasis, interstitial pneumonitis,
and pleural effusion

Extrapulmonary manifestation

### INVESTIGATIONS OF PREGNANT WOMEN AND MOTHERS WITH TUBERCULOSIS

- microscopical examination of sputum smears for acid-fast bacilli, xpert, culture and DST of sputum,
- other specimens including endometrial samples for M. tuberculosis, histological examination of biopsies from relevant body sites, microscopic, cultur, DST and chest radiography

# **Risk of TB and poor health**

Risk factor	Risk of TB	Health outcomes related to risk factor
Underweight (BMI <18.5)	Pooled relative risk estimate from meta-analysis: 32(95% CI, 3.1–3.3) <sup>78</sup>	Increased risk of death and TB relapse; systematic reviews, no pooled estimate <sup>79,66</sup>
Gastrectomy or jejunoileal bypass	No pooled estimate Gastrectomy: relative risk range, 2–5 Bypass: relative risk range, 27–63 <sup>68,80</sup>	Increased risk of death associated with undernutrition (see "Underweight"), but no published data specifically on gastrectomy or jejunoileal bypass
Diabetes mellitus	Pooled relative risk estimate from systematic review 3.1 (95% Cl, 2.3–4.3) <sup>81</sup>	Pooled relative risk of TB treatment failure or death from systematic review: 1.69 (95% Cl, 1.36–2.12) and relapse: 3.89 (95% Cl, 2.43– 6.23) <sup>82</sup>
Al cohol dependence	Pooled relative risk estimate from systematic review 2.9 (95% Cl, 1.9–4.6) <sup>83</sup>	Higher risk of TB treatment failure and relapse and death during treatment; systematic review, no pooled estimate <sup>84</sup>
Tobacco smoking	Pooled relative risk estimate from systematic review 2.0 (95% Cl, 1.6–2.5) <sup>85</sup>	Increased risk of death; systematic review, no pooled estimate <sup>86</sup>
Chronic renal failure or haemodialysis	No pooled estimate; relative risk range, 10-25 <sup>68,81</sup>	Increased risk of death; systematic review, no pooled estimate <sup>86</sup>

# Risk of TB and poor health outcomes

Risk factor	Risk of TB	Health outcomes related to risk factor
Intravenous drug use	No pooled estimate; <sup>17</sup> increased risk probably due to high prevalence of other risk factors, such as HIV	Increased risk of death; systematic review, no pooled estimate <sup>66</sup>
Solid organ transplantation	No pooled estimate; relative risk range, 20–74 <sup>81</sup>	No published data
Oldage	Not established; prevalence surveys report increased risk with age <sup>27,28</sup>	Increased risk of death; systematic review, no pooled estimate <sup>66</sup>
Previously treated TB	High incidence of TB due to relapse and reinfection; <sup>87,88,89</sup> no systematic review	Retreatment cases have higher risk of poor outcomes and higher risk of MDR-TB
Pregnancy	Not established <sup>90</sup>	Infants of mothers with TB have <u>increased</u> risks of premature birth and perinatal death; <sup>91,9,293</sup> pregnant women with TB are more likely to have complications during pregnancy; initiating TB treatment is associated with better maternal and infant outcomes than late initiation <sup>94,95,96,97,98</sup>

# Weighted mean and range number needed to screen (NNS) to find one case of tuberculosis (TB) in selected risk categories

Population screened (No. of studies)	<b>Low incidence</b> (<30/100,000)	Moderate incidence (30-100/100,000)	Medium incidence (100-300/100,000)	High incidence (>300/100,000)
General population (98)	3922 (137–30865) <sup>a</sup>	669 (15–5594)	603 (25–4286)	100 (16–6355)
Infants in vaccine trial (3)	NS	NS	140 (7–343)	NS
Immigrants (26)	235 (3–1262) <sup>a</sup>	NS	1206 (198–6250)	NS
Refugees (38)	108(6–1630) <sup>a</sup>		120 (57–291)	
Military (6)	1159 (134–492) <sup>a</sup>	NS	1280 (73–1440)	NS
Health-care workers (16)	1613 (30–5550) <sup>a</sup>		506 (25–842) <sup>a</sup>	NS
Miners (8)	48 (–) <sup>b</sup>	154 (–) <sup>b</sup>	NS	36 (21–93)
Other occupations (14)	1565 (47–5235) <sup>a</sup>	NS	109 <b>(4–778)</b>	NS
Homeless people (18)	133 (22–1778)	NS	NS	NS
Prisoners (44)	1180 (4–2945) <sup>a</sup>	155 (19–191)	110 (7–2762)	
General inpatients (4)	NS	NS	795 (6–3364)	
General outpatients (14)	758 (42–30 000)		269 (19–806)	
Nursing homes (7)	120 (68–137) <sup>a</sup>		NS	7 (–) <sup>b</sup>
Psychiatric facilities (3)	1049 (32–1275)		111 (—) <sup>b</sup>	NS
Pregnant women (9)	536 (88–3843) <sup>a</sup>	NS	36 (25-	-143)
People with diabetes (6)	NS	2223 (–) <sup>b</sup>	35 (17–54)	
Drug users (8)	158 (108-252) <sup>a</sup>	5 (_) <sup>b</sup>	20 (8-20)	NS



### Algorithms for screening and diagnosis

**Algorithms 1** This option includes an interview about TB symptoms and HIV status. All people with cough lasting longer than 2 weeks should be investigated for TB

**Algorithms 2** This option includes an interview about TB symptoms and HIV status. Further investigation for TB should be done for persons with any of the following symptoms: cough of any duration, haemoptysis, weight loss, fever or night sweats.

**Algorithms 3** This option includes chest radiography and an interview about HIV status. Persons with an abnormal chest radiograph suggestive of TB should be evaluated for TB

#### Chest X-ray and Xpert MTB/RIF not available



NPV

#### Chest X-ray not available, Xpert MTB/RIF available



NPV

99.7%

99.5%

### Algorithm for TB screening in adults and adolescents living with HIV in HIV-prevalent and resource-constrained settings





# Algorithm 1. Using microscopy, solid or liquid culture, species identification and drug-susceptibility testing to diagnose TB



Algorithm 2. Using the Xpert MTB/RIF assay as an initial diagnostic test for TB followed by drugsusceptibility testing for second-line anti-TB



# Treatment

# Duration of rifampicin in new TB patients

New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE/4HR (Strong recommendation, high grade of evidence)

The use of FDC tablets is recommended over separate drug formulations in the treatment of patients with drug-susceptible TB (Conditional recommendation, low certainty in the evidence)

### **Dosing frequency of TB treatment in new TB patients**

Wherever feasible, the optimal dosing frequency fornew patients with pulmonary TB is daily throughout the course of therapy

(Strong recommendation, high grade of evidence)

# Dosing frequency of TB treatment in persons living with HIV

TB patients with known positive HIV status and TB patients living in HIV-prevalent settings should receive at least 6 months of rifampicin-containing treatment regimen

(Strong recommendation, high quality of evidence).

The optimal dosing frequency is daily during the intensive and continuation phases (Strong recommendation, high quality of evidence).

# Duration of TB treatment for TB patients living with HIV

It is recommended that TB patients who are livingwith HIV should receive at least the same duration of TB treatment as HIVnegative TB patients

(Strong recommendation, high grade of evidence)

Initial regimen in countries with high levels of isoniazid resistance

In populations with known or suspected high levels of isoniazid resistance, new TB patients may receive HRE as therapy in the continuation phase as an acceptable alternative to HR

(Conditional recommendation, insufficient evidence, expert opinion)

### **Treatment of previously treated TB patients**

Specimens for culture and drug-susceptibility testing should be obtained from all previously treated TB patients at or before the start of treatment. Drug-susceptibility testing should beperformed for at least isoniazid and rifampicin

In settings where rapid molecular-based drug susceptibility testing is available, the results should guide the choice of regimen

In patients who require TB retreatment, the category II regimen should no longer be prescribed and drug-susceptibility testing should be conducted to inform the choice of treatment regimen

# Special Consideration Pregnancy and Breastfeeding

- A pregnant woman should be advised that successful treatment of TB with the standard regimen is important for successful outcome of pregnancy. With the exception of streptomycin, the first line anti-TB drugs are safe for use in pregnancy: streptomycin is ototoxic to the fetus and should not be used during pregnancy.
- A breastfeeding woman who has TB should receive a full course of TB treatment. Mother and baby should stay together and the baby should continue to breastfeed.
- After active TB in the baby is ruled out, the baby should be given 6 months of isoniazid preventive therapy, followed by BCG vaccination
- Pyridoxine supplementation is recommended for all pregnant or breastfeeding women taking isoniazid

# Terima kasih