

Can we overcome barriers to latent TB testing in LMICs?

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Sunil Kaparde, RNTCP India

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Ingrid Schoeman, TB Proof

Andrea Tattersall, Oxford Immunotec

Moderator: Ruvandhi Nathavitharana, Harvard

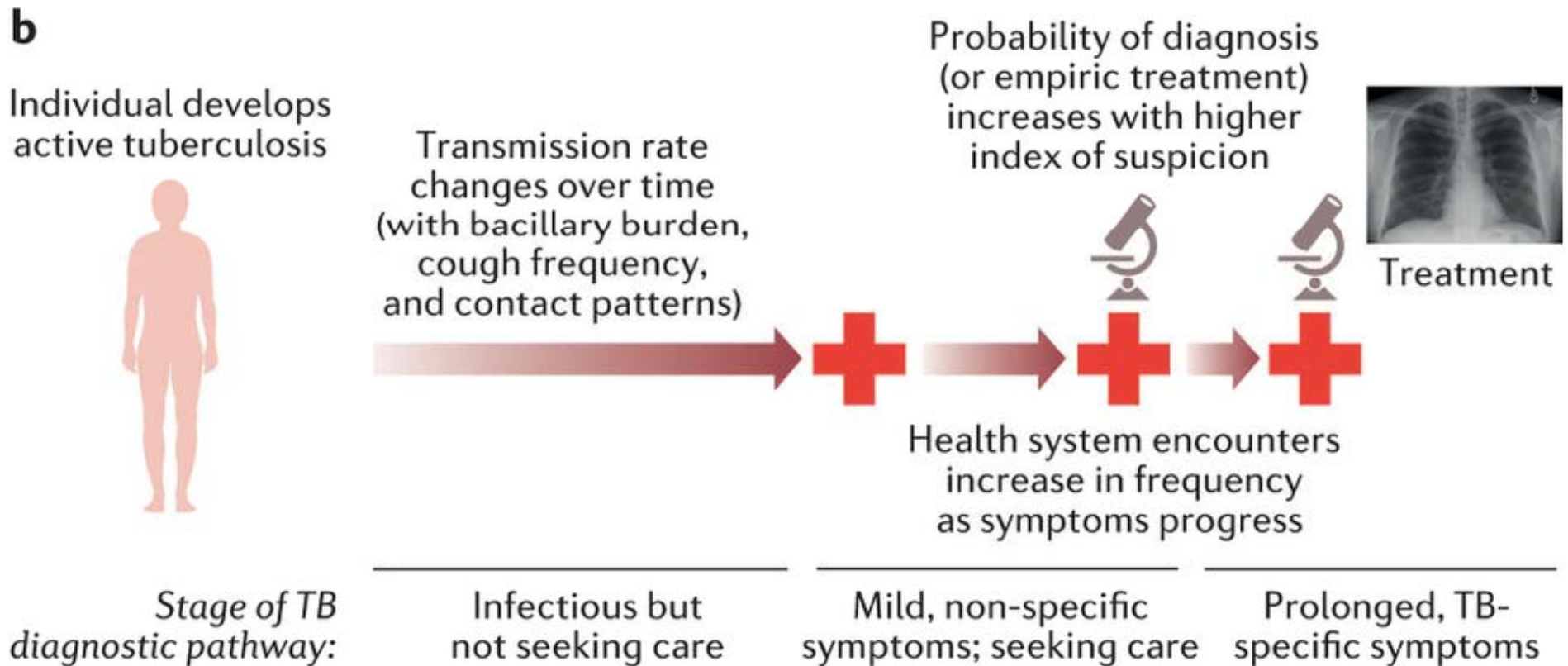


**Beth Israel Deaconess
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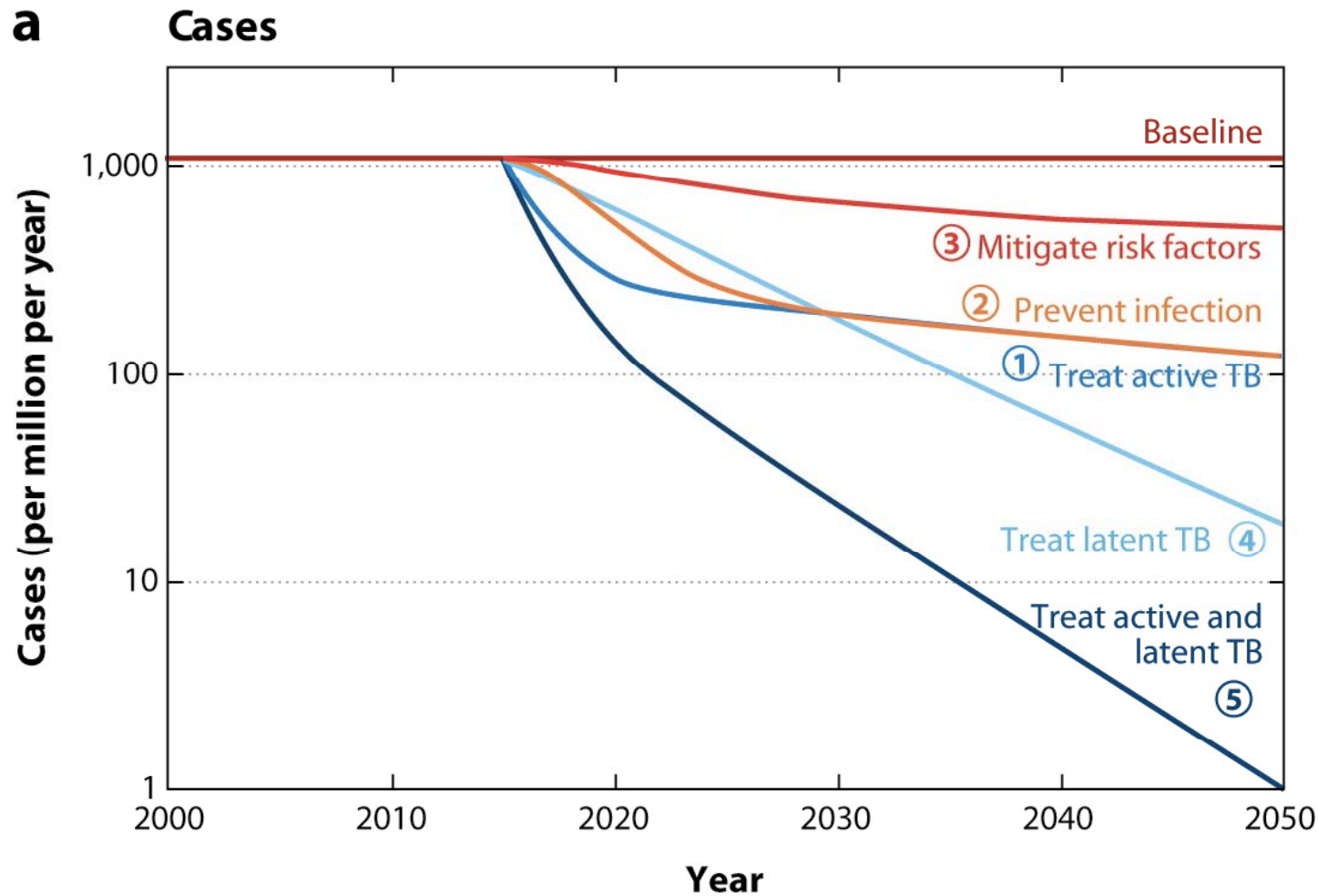


**HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL**

Trying to intercept TB transmission



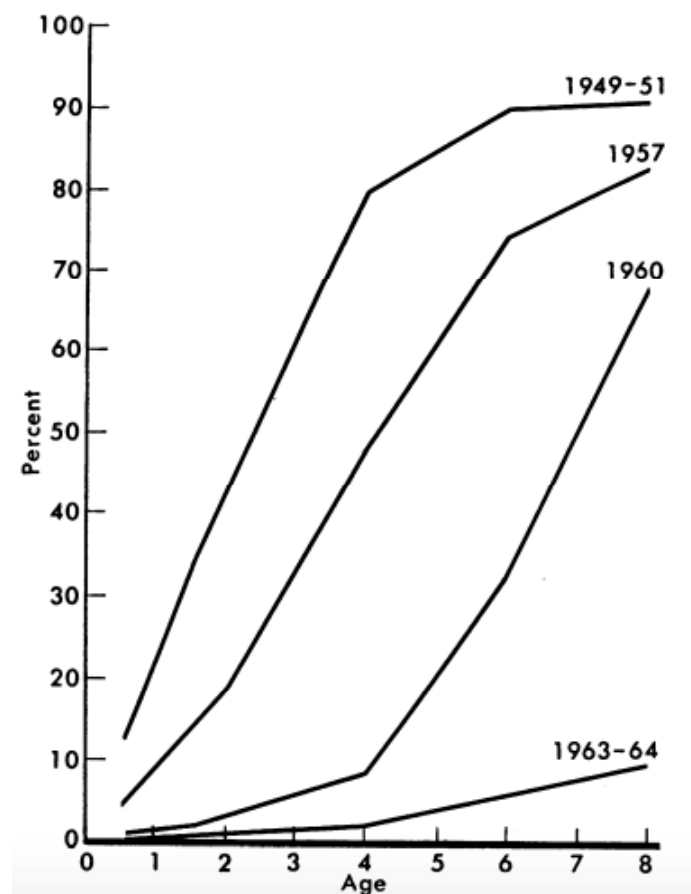
Impact of Addressing Latent TB infection



Preventive (LTBI) Therapy

- Bethel Alaska 2000/100 000
- 1957 RCT: after community-wide screening, people without TB disease were randomized to INH or placebo
- 68% reduction in TB attributable to INH prophylaxis, reduced risk of TB demonstrated over the next 19 yrs

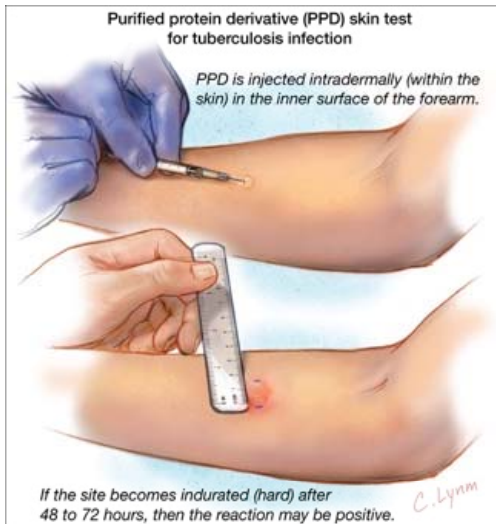
Figure 2. Prevalence of tuberculin sensitivity among Eskimo children 0–9 years from the Yukon-Kuskokwim Delta of Alaska in four successive surveys



Porter and Comstock 1962
Comstock 1979

Tests for Latent TB

-Interferon Gamma Release Assay (IGRA) & Tuberculin Skin Test (TST)



- Sensitivity 77 – 92% (lower in PLHIV), Specificity 93-98%
- IGRA antigens are not cross-reactive with BCG strain
- **Poor predictive ability** (1-3% develop active TB in 2 yrs)
- Different implementation challenges, test reversions

Preventive Therapy for TB Infection

- LTBI Rx is effective in preventing TB reactivation but durability of effect at risk in high transmission settings
- Regimens: INH 9m, INH 6m, RIF 4m, INH/RPT 3m
- WHO 2018: LTBI Dx/Rx in PLHIV and ALL contacts
- CROI 2018: 1HP non-inferior to 9H in multi-site phase 3 open-label RCT of PLHIV >13 years, fewer adverse effects and higher Rx completion rates
- WHIP3 trial: annual 3HP in all PLHIV, annual 1HP
- MDR-LTBI trials: TB-CHAMP, V-QUIN, PHOENIX

Implementation Gap- Prevention

- TB reactivation risk 5-15%/yr in PLHIV
- PT for PLHIV recommended by WHO since 1998!
- **32% reduced risk, 62% if TST +**
- 1.3 million PLHIV started PT in 2016
- 18/30 HBCs did not report PT

TABLE 12. PREVENTIVE THERAPY IN COUNTRIES SURVEYED (2015)¹

Country and classification	Coverage, by percent, of TB preventive therapy among HIV-positive people newly enrolled in care
Bangladesh (■ ▲)	Not reported
Cambodia (■)	25%
Ethiopia (■ ● ▲)	47%
Indonesia (■ ● ▲)	2%
Kenya (■ ● ▲)	33%
Mozambique (■ ● ▲)	45%
Myanmar (■ ● ▲)	10%
Nigeria (■ ● ▲)	20%
Philippines (■ ▲)	43%
South Africa (■ ● ▲)	38%
Viet Nam (■ ▲)	Not reported
Zimbabwe (■ ● ▲)	31%

WHO classified high-burden countries: ■ TB, ● TB/HIV, ▲ MDR-TB

Panel:

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Preventive Mexico**

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Biology, CAMS, China**

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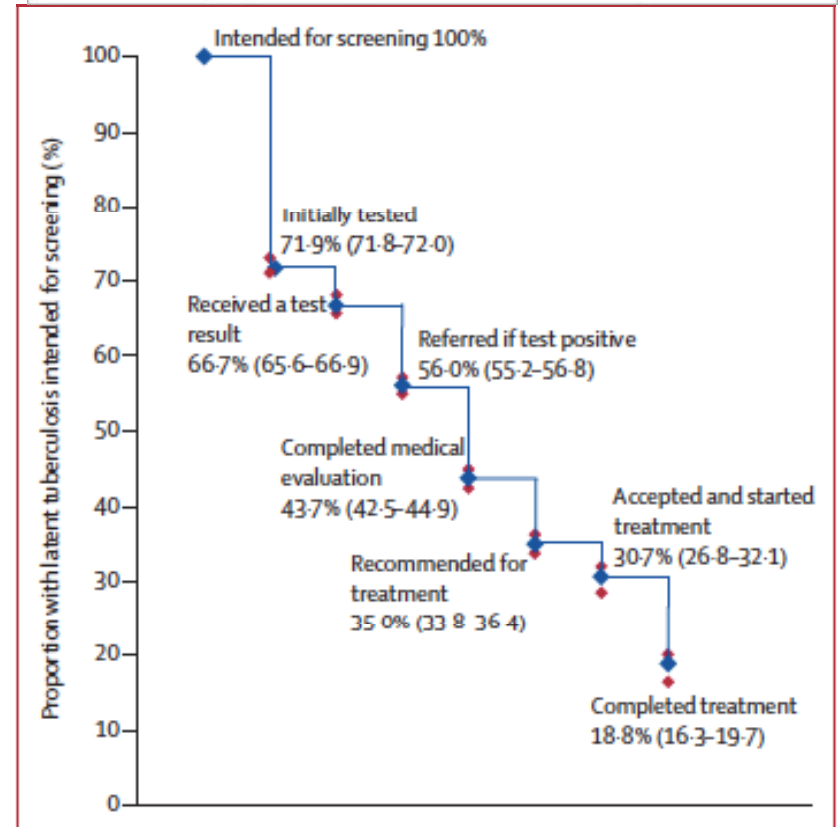
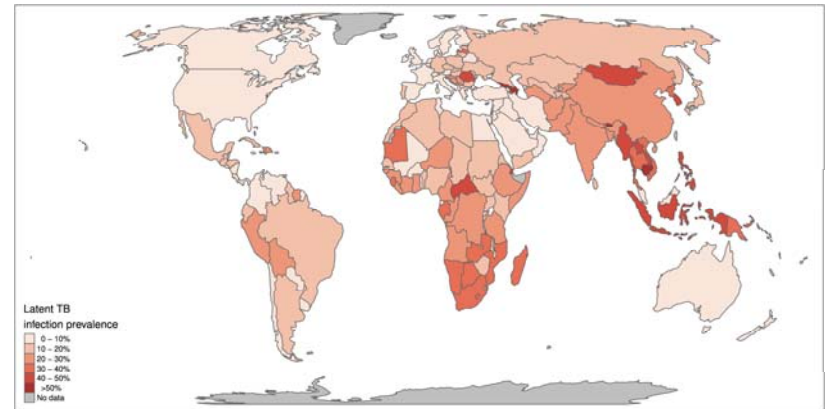
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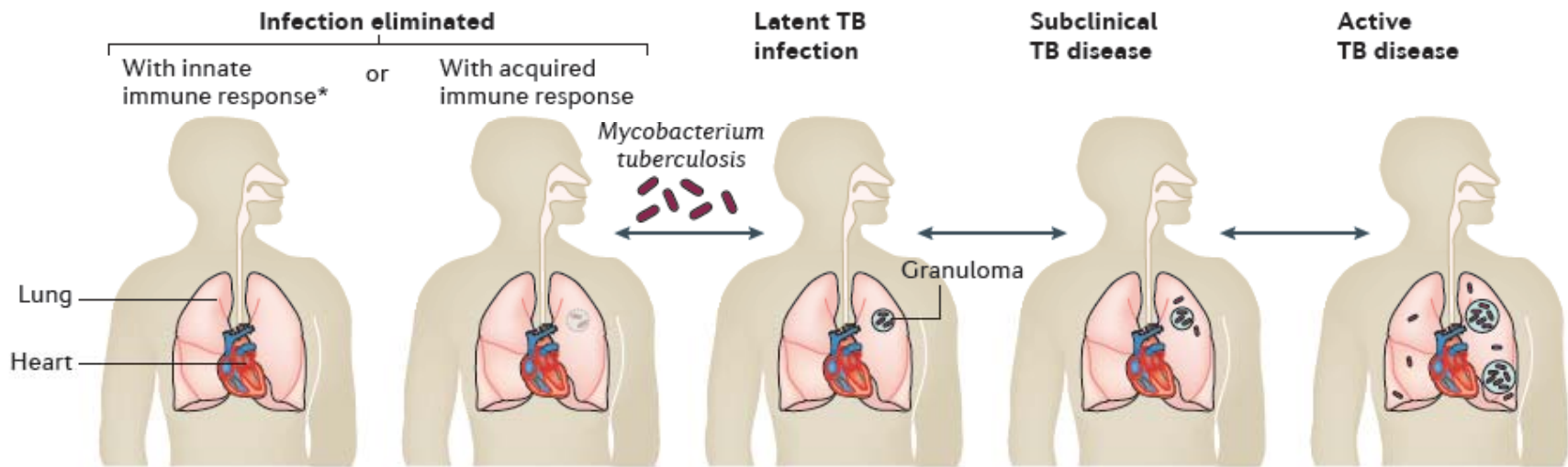
**Andrea Tattersall, Oxford
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TB spectrum of disease



	Infection eliminated With innate immune response*	Infection eliminated With acquired immune response	Latent TB infection	Subclinical TB disease	Active TB disease
TST	Negative	Positive	Positive	Positive	Usually positive
IGRA	Negative	Positive	Positive	Positive	Usually positive
Culture	Negative	Negative	Negative	Intermittently positive	Positive
Sputum smear	Negative	Negative	Negative	Usually negative	Positive or negative
Infectious	No	No	No	Sporadically	Yes
Symptoms	None	None	None	Mild or none	Mild to severe
Preferred treatment	None	None	Preventive therapy	Multidrug therapy	Multidrug therapy

Location, Location, Location: where are TB services in HBCs?

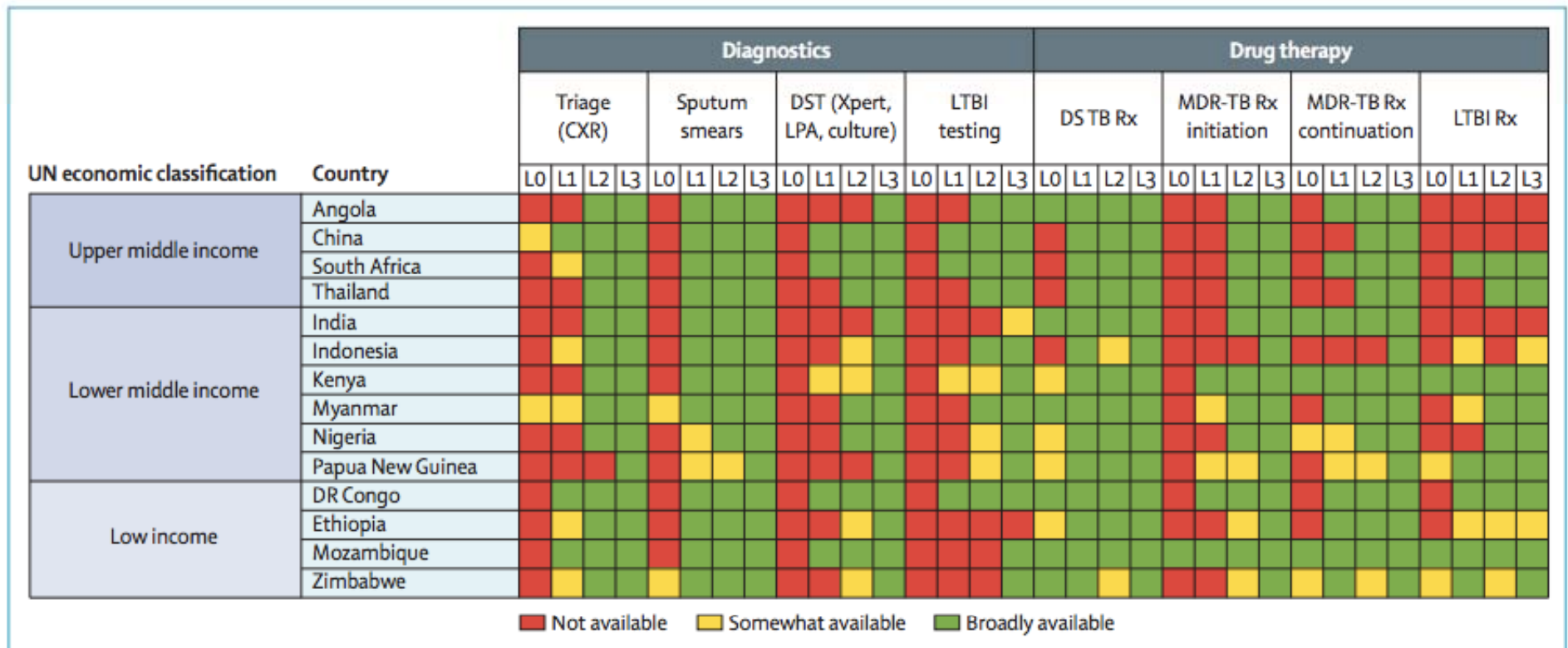


Figure 1: Availability of tuberculosis diagnostic and treatment services across various health-care levels in 14 highest burden countries
 CXR=chest radiography. LTBI=latent tuberculosis infection. DS=drug sensitive. DST=drug sensitivity testing. MDR-TB=multidrug-resistant TB. L0=care by community or village health workers or at health posts. L1=microscopy centres or primary health centres. L2=district hospitals or community health centres. L3=reference or tertiary hospitals. TB=tuberculosis.