



## Location, location, location: tuberculosis services in highest burden countries

Early diagnosis of tuberculosis and rapid treatment initiation are crucial for tuberculosis care and for interrupting transmission<sup>1</sup> and require delivery of tuberculosis care services where most patients seek initial care. In most countries, National Tuberculosis Programs (NTPs) are expected to have basic tuberculosis diagnosis by use of smear microscopy available at the primary care level, via a network of microscopy centres.<sup>2</sup> However, there is little published information on where latent tuberculosis and multi-drug resistant tuberculosis (MDR-TB) diagnostic and treatment services are exactly available in the highest tuberculosis burden countries.

We addressed this gap by surveying 14 countries that have been identified by WHO as having the highest burden of tuberculosis cases, MDR-TB, and co-infection of HIV and tuberculosis.<sup>3</sup> These countries are Angola, China, DR Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Papua New Guinea, South Africa, Thailand, and Zimbabwe.<sup>3</sup>

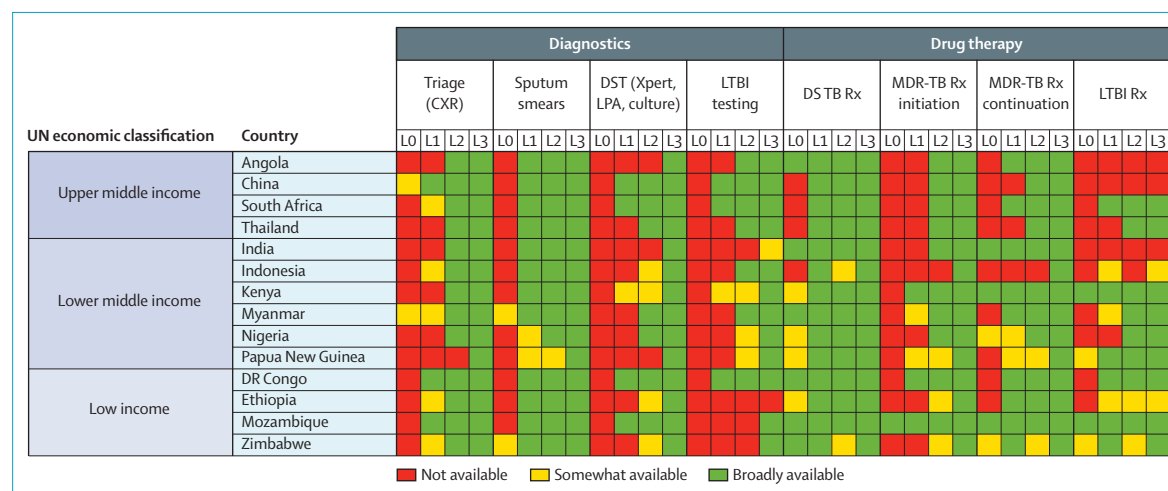
We contacted tuberculosis experts in these 14 countries between June and August, 2016, and asked them about diagnosis and treatment availability in their countries at each level of health care (from the most decentralised to the tertiary level). Health-care levels were defined as L0, which included care by community or village health workers or at local health posts; L1, which included microscopy centres or primary health centres; L2, district hospitals or community health centres; and L3, reference or tertiary hospitals. For ten (71%) of 14 countries, at least two completed surveys were obtained. Among the respondents were NTP and National Reference Laboratory staff, tuberculosis researchers, and members of international agencies (eg, WHO, Foundation for Innovative New Diagnostics).

Regarding diagnosis, we asked about availability of screening or triage tests (eg, chest radiographs), tests for active tuberculosis (eg, smear microscopy), tests for latent tuberculosis infection (eg, tuberculin skin test, interferon-gamma release assays), and drug-susceptibility testing (eg, cultures, Xpert MTB/RIF, and line probe assays). Concerning drug therapy, we asked about availability of treatment for drug-sensitive tuberculosis (standard

four-drug regimen), MDR-TB (second-line therapy), and latent tuberculosis infection (isoniazid preventive therapy). For tuberculosis treatment, we asked at what level therapy can be initiated, and at what level such therapy can be continued.

In general, very few countries have any tuberculosis diagnostic or treatment services available at the most decentralised L0 level (figure). Most countries have chest radiography available only at the L2 (13 of 14, 93%) or L3 level (14 of 14, 100%), while smear microscopy is available, starting at the L1 level (14 of 14, 100%). Drug susceptibility testing is mainly available at the tertiary or referral (L3) level, with the majority of countries having at least some capacity at L2 (11 of 14, 79%). Latent tuberculosis testing capacity is mainly available at L2 (ten of 14, 71%) and L3 levels (13 of 14, 93%).

Treatment for drug-sensitive disease is available in all countries at the L1 level, and ten (71%) of 14 countries are able to continue therapy at the L0 level. By contrast, most countries (eight of 14, 57%) are only able to initiate MDR-TB treatment at L2 and L3 levels. Some countries are able to continue MDR-TB therapy at the L1 level, and very few can continue MDR-TB therapy



**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.

at the L0 level (five of 14, 36%). About half the surveyed countries have isoniazid preventative therapy available at L1 centres, while three countries reported no infrastructure for treatment of latent tuberculosis infection at any level. As shown in the figure, diagnostics and treatment availability were not strongly related to country income level or geographic region. However, our analysis is limited because it focused on availability of services, rather than access or quality.

The End TB Strategy calls for early diagnosis of tuberculosis including universal drug susceptibility testing, and systematic screening of contacts and high-risk groups.<sup>1</sup> Mathematical models suggest that broad access to new methods early in the patient pathways can offer the best impact in terms of reducing tuberculosis incidence.<sup>4-6</sup>

Our analysis shows that although most countries have invested in basic tuberculosis diagnosis (ie, smears) and drug-sensitive tuberculosis treatment services at the L1 level and higher, availability of triage testing, testing for MDR and latent tuberculosis infection, and therapy is quite limited at the decentralised L0/L1 levels. This limitation means that patients or samples are being referred, which results in losses. Indeed, analyses of cascades of tuberculosis care show major gaps in the continuum of care, and might explain the persistently high incidence of tuberculosis in some countries.<sup>7,8</sup>

Our data also suggest that services for tuberculosis care in many countries might not be fully integrated into general health-care services. As countries work towards universal health coverage, it is crucial to not only strengthen tuberculosis services, but also ensure greater integration with primary health care. In parallel, we need to develop simpler methods (eg, non-sputum based biomarker tests) and drug regimens (eg, a universal drug regimen that does not require extensive drug-sensitive testing) that can be implemented closer to patients.

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- 1 World Health Organization. The End TB Strategy. Global strategy and targets for tuberculosis prevention, care and control after 2015. URL: [http://www.who.int/tb/post2015\\_TBstrategy.pdf?ua=1](http://www.who.int/tb/post2015_TBstrategy.pdf?ua=1) (accessed April 7, 2015).
- 2 Kik SV, Denkinger CM, Chedore P, Pai M. Replacing smear microscopy for the diagnosis of tuberculosis: what is the market potential? *Eur Respir J* 2014; **43**: 1793-96.
- 3 World Health Organization. Use of high burden country lists for TB by WHO in the post-2015 era: Summary. Geneva: World Health Organization, 2015. [http://www.who.int/tb/publications/global\\_report/high\\_tb\\_burdencountrylists2016-2020summary.pdf?ua=1](http://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020summary.pdf?ua=1) (accessed Aug 15, 2016).
- 4 Sun AY, Pai M, Salje H, Satyanarayana S, Deo S, Dowdy DW. Modeling the impact of alternative strategies for rapid molecular diagnosis of tuberculosis in Southeast Asia. *Am J Epidemiol* 2013; **178**: 1740-49.
- 5 Salje H, Andrews JR, Deo S, et al. The importance of implementation strategy in scaling up Xpert MTB/RIF for diagnosis of tuberculosis in the Indian health-care system: a transmission model. *PLoS Med* 2014; **11**: e1001674.
- 6 Arinaminpathy N, Dowdy D. Understanding the incremental value of novel diagnostic tests for tuberculosis. *Nature* 2015; **528**: S60-67.
- 7 Alsdurf H, Hill PC, Matteelli A, Getahun H, Menzies D. The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. *Lancet Infect Dis* 2016; **16**: 1269-78.
- 8 Subbaraman R, Nathavitharana RR, Satyanarayana S, et al. The tuberculosis cascade of care in India's public sector: a systematic review and meta-analysis. *PLoS Med* 2016; **13**: e1002149.