Journal of Clinical Tuberculosis and Other Mycobacterial Diseases 6 (2017) 14–15

Contents lists available at ScienceDirect

Journal of Clinical Tuberculosis and Other Mycobacterial Diseases

journal homepage: www.elsevier.com/locate/jctube

Editorial

Mind the gap: Time to address implementation gaps in tuberculosis diagnosis and treatment

Tuberculosis (TB) was first identified by Robert Koch in 1882. Sadly, even after a century since Koch's breakthrough discovery, TB continues to kill over 1.5 million people every year [1]. Every year, nearly 9.5 million new cases of TB occur worldwide [1]. Of these, nearly 3 million TB patients are considered 'missing'—they are either not diagnosed, or not reported to TB control programs [1].

In 2014, according to the World Health Organization (WHO), about 80% of reported TB cases occurred in 22 countries [1]. The six countries that stand out as having the largest number of incident cases in 2014 were India, Indonesia, Nigeria, Pakistan, People's Republic of China, and South Africa [1].

In 2014, India alone accounted for nearly 25% of the 9.5 million global TB cases; India also accounted for a third of the three million missing TB cases [1]. TB is a major cause of deaths in India, and the emergence of severe forms of drug-resistant TB in urban areas such as Mumbai is another indication that the TB problem is not under control [2]. There are several likely reasons for India's persistent TB problem, including social determinants and co-morbidities that fuel the TB epidemic, under-investment by the government, weak programme implementation, suboptimal quality of care in the private sector, and insufficient advocacy around TB [3].

In contrast to India, the TB epidemic in sub-Saharan Africa is characterized by high prevalence of HIV and TB co-infection, and a major problem with multidrug-resistant TB (MDR-TB) in countries such as South Africa, which also has the largest number of people living with HIV. The combination of HIV and TB poses immense challenges for TB control in Africa, as both infections work synergistically to cause morbidity and mortality [4].

To curb the TB epidemic, we will need to reach the missing TB patients, diagnose TB without long delays, and make sure they take the full course of anti-tuberculosis therapy. Only then will they stop transmitting the infection to those around them. We also need to make sure all TB-HIV co-infected patients have access to antiretroviral therapy, and interventions of proven value, such as preventive therapy for latent TB infection.

Reaching all the missing patients and ensuring appropriate TB treatment will require doctors and TB control programs to adopt and scale-up the best tools we have today, and modernize TB care. Compared to the situation even a decade ago, we have witnessed big changes in the TB technology landscape. We now have tools such as Xpert MTB/RIF that can rapidly and accurately detect TB, including drug-resistance [5]. With more laboratories offering such rapid tests, there has been a substantial increase in the number of multidrug-resistant (MDR) cases detected [6].

On the new drug front, bedaquiline and delamanid are already on the market in some countries. In addition, trials are underway to evaluate the efficacy of a new TB regimens such as PaMZ (which contains pretomanid, moxifloxacin, and pyrazinamide), and BPaZ (bedaquiline, pretomanid, and pyrazinamide). If these trials succeed, then TB patients might get new, shorter treatments within the next 5 years.

While the product landscape is looking promising, what is worrisome is the implementation gap. A recent report called "Out of Step" by MSF and Stop TB Partnership surveyed 24 high TB burden countries, to see how already existing TB policies and interventions are being implemented [7]. This survey found major implementation gaps. For example, only eight countries surveyed had revised their national policies to include Xpert MTB/RIF as the initial diagnostic test for all adults and children with presumptive TB, replacing smear microscopy. Six countries still recommended intermittent treatment for drug-sensitive TB. Even proven interventions such as fixed dose combinations are not routinely used in all countries.

Other studies have shown similar implementation failures. For example, even though South Africa has scaled-up rapid molecular testing, there are data showing long gaps between sample collection and initiation of TB treatment [8]. Empirical TB management is widespread, even with Xpert roll-out, and health system weaknesses have blunted the impact of new diagnostics [9]. In South Africa, only about half of all patients with TB and HIV are on antiretroviral therapy, and only about 50% of TB patients with MDR are on second-line therapy. These gaps in the TB/HIV treatment cascade underscore the need for better program management.

In India, an average TB patient is diagnosed after a delay of nearly 2 months, and after seeing three providers [10]. At the primary care level, TB testing is rare, even among those with classic TB symptoms, and most patients are managed with repeated cycles of empirical broad-spectrum antibiotic therapies. Indian studies also show major gaps in TB knowledge and self-reported practices of providers, suggesting poor adherence to established standards in the private sector [11]. A recent study, using simulated patients, confirmed the overall low quality of TB care in the private sector, and revealed a substantial gap between what doctors know and what they actually do in their practice [12]. While MDR-TB treatment services have expanded, only 24,073 of the

http://dx.doi.org/10.1016/j.jctube.2016.02.001

estimated 50,000–74,000 MDR-TB cases were initiated on treatment in 2014 [1].

These issues reinforce the message that technologies alone are never enough. Good technologies and interventions need to be effectively implemented for impact to be seen. High-burden countries will need to improve the efficiency of its healthcare delivery system, and ensure better uptake of new technologies, and achieve greater linkages across the TB and HIV care continuum. While we wait for next-generation technologies, national TB programs must scale-up the current best diagnostics. While we wait for shorter drug regimens, doctors and programs can improve the effectiveness of existing treatments by improving treatment adherence. For example, we can and must harness the enormous potential offered by mobile phones to electronically monitor adherence to medications. There are other innovations such as smart pill boxes and fixed-dose combination drugs that can be better exploited.

In summary, it is time for doctors, hospitals, and healthcare programs to embrace and scale-up new TB technologies and address implementation gaps to make sure TB patients get the best care that they deserve. This is absolutely fundamental to reach the goals set out in the End TB Strategy.

Conflicts of interest

None.

Madhukar Pai*
McGill International TB Centre, McGill University, Montreal, QC H3A 1A2, Canada

Zelalem Temesgen
Mayo Clinic Center for Tuberculosis and Division of Infectious Diseases, Mayo Clinic, Rochester, Minnesota, USA

* Corresponding author. Tel.: +1 514 398 5422; fax: +1 514 398 4503.
E-mail address: madhukar.pai@mcgill.ca (M. Pai)

Received 2 February 2016
Accepted 16 February 2016

References

[1] World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015.
[2] Udwadia ZF. MDR, XDR, TDR tuberculosis: ominous progression. Thorax 2012;67(4):286–8.
[3] Pai M, Daftary A, Satyanarayana S. Tuberculosis control: challenges and opportunities for India. Trans Roy Soc Trop Med Hyg 2016;110(3):158–60.
[4] Gilliam BL, Patel D, Talwani R, Temesgen Z. HIV in Africa: challenges and directions for the next decade. Curr Infect Dis Rep 2012;14(1):91–101.
[5] Steingart K, Schiller I, Horne DJ, Pai M, Boehme C, Dendukuri N. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Database Syst Rev 2014 Jan 21;1:CD009593.
[6] Sachdeva KS, Raizada N, Sreenivas A, Van't Hoog AH, van den Hof S, Dewan PK, et al. Use of Xpert MTB/RIF in decentralized public health settings and its effect on pulmonary TB and DR-TB case finding in India. PLoS One 2015 May 21;10(5):e0126065.
[7] Medicins Sans Frontiers and Stop TB Partnership. Out of Step 2015. TB policies in 24 countries. URL: http://www.stoptb.org/assets/documents/news/report_out_of_step_2015_11_pdf_with_interactive_links.pdf2015. (accessed).
[8] Jacobson KR, Theron D, Kendall EA, Franke MF, Barnard M, van Helden PD, et al. Implementation of GenoType(R) MTBDRplus reduces time to multidrug-resistant tuberculosis therapy initiation in South Africa. Clin Infect Dis Feb 2012;56(4):503–8.
[9] Theron G, Zijenah L, Chanda D, Clowes P, Rachow A, Lesosky M, et al. Feasibility, accuracy, and clinical effect of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised, controlled trial. Lancet 2013;383:424–35.
[10] Sreeramareddy CT, Qin ZZ, Satyanarayana S, Subbaraman R, Pai M. Delays in diagnosis and treatment of pulmonary tuberculosis in India: a systematic review. Int J Tuberc Lung Dis 2014;18(3):255–66.
[11] Satyanarayana S, Subbaraman R, Shete P, Gore G, Das J, Cattamanchi A, et al. Quality of tuberculosis care in India: a systematic review. Int J Tuberc Lung Dis 2015;19(7):751–63.
[12] Das J, Kwan A, Daniels B, Satyanarayana S, Subbaraman R, Bergkvist S, et al. Use of standardised patients to assess quality of tuberculosis care: a pilot, cross-sectional study. Lancet Infect Dis 2015;15(11):1305–13.