CrossMark

Tuberculosis: a Persistent Health Challenge for India

Sophie Huddart[1,2] · Vaidehi Nafade[1,2] · Madhukar Pai[1,2,3]

Abstract

Purpose of Review Currently, India accounts for more than a quarter of incident TB cases globally. The Indian government recently announced a new national strategic plan to eliminate TB by 2025, but much is still unknown about the epidemic, in part due to a weakly regulated and highly privatized health sector. In this review, we provide an overview of the current landscape of TB in India, focusing on major challenges to elimination.

Recent Findings Historically, political will and investment in TB care in India have been lacking. To successfully eliminate TB, India will need to broadly improve the quality of care that TB patients receive. Simulated patient studies have shown that the current quality of care is poor, especially in the private sector where drug sales estimate over one million TB patients seek care annually. Cascade of care studies indicate that TB patients are lost at every stage of care-seeking. Access is suboptimal for new diagnostic technologies such as GeneXpert and new drugs such as bedaquiline. Additionally, research in the social determinants of health indicates that factors such as undernutrition, smoking, and diabetes are major driving forces behind the TB epidemic.

Summary India's ambitious plan for TB elimination will require strong political and financial commitment to move forward. In order to effectively tackle TB, the Indian government needs to better engage the private sector and focus on quality: quality of care for patients, quality improvement of TB programs, and overall health quality to address social determinants.

Keywords Tuberculosis · India · Global health · Quality of care · Operational research · Epidemiology

Introduction

Of the 10.4 million new cases of TB in 2016, 2.8 million, more than a quarter, occurred in India. India accounted for 29% of global TB deaths, and 14% of the MDR-TB cases estimated during the same year [1]. TB patients in India often visit multiple providers before being diagnosed [2, 3] with a median of 55 days elapsing between the appearance of symptoms and diagnosis [4•]. Throughout the cascade of care (Fig. 1), many patients are lost from the system with only 53% of prevalent cases being registered for public sector treatment [5••]. Across practitioners, less than a quarter of unconfirmed TB patients are being correctly managed when they contact a health care provider [6••, 7•]. While other emerging economies like China have made impressive progress in curbing their TB epidemic, India has made only minimal gains [1]. In the new Sustainable Development Goals era, as the WHO calls to end TB by 2035 [8], this is the moment for India to fully commit to ending TB.

This year, India's Revised National Tuberculosis Control Program (RNTCP) released an ambitious National Strategic Plan (NSP) for Tuberculosis Elimination with the goal of eliminating TB in India by 2025 [9••]. The decline in TB deaths in India has recently begun to stagnate [10] and TB remains one of the leading causes of death among Indian adults during their most productive years [11]. The tools to turn the tide of the Indian TB epidemic exist, but the Indian TB community needs strong political will, higher investments in health in general and TB control, in particular, sustainable, scaled-up engagement of the private sector, improved quality of care, and interventions targeting the social determinants underlying the TB epidemic [12, 13].

Sophie Huddart and Vaidehi Nafade contributed equally to this work.

This article is part of the Topical Collection on *Infectious Disease Epidemiology*

✉ Madhukar Pai
madhukar.pai@mcgill.ca

1   Department of Epidemiology, Biostatistics and Occupational Health, McGill University, 1020 Pine Ave West, Montreal, QC H3A 1A2, Canada

2   McGill International TB Centre, Montreal, Canada

3   Manipal McGill Centre for Infectious Diseases, Manipal University, Manipal, India

Fig. 1 The cascade of care for all forms of tuberculosis in India's Revised National Tuberculosis Control Program (RNTCP) in India, 2013. Error bars depict 95% confidence intervals. [from reference [5••], https://creativecommons.org/licenses/by/4.0/]
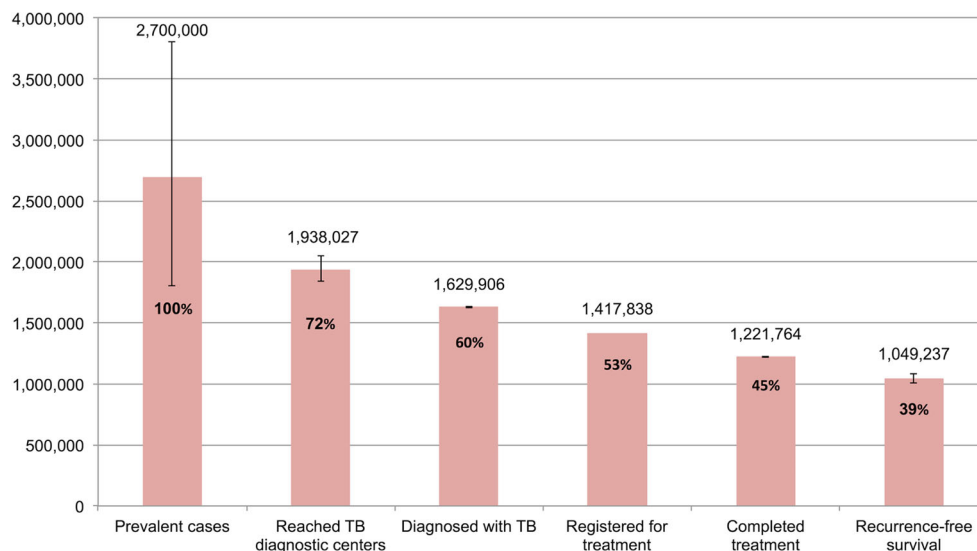
Increase Political Will and Investments in Health

India's current healthcare spending rests at 1.4% of GDP [14], substantially lower than most countries with comparable economies. In fact, all BRICS countries spend more on health than India. This underinvestment has left the public healthcare system struggling to meet the needs of the population, and has pushed people toward private health care that is often expensive and exploitative. Out of 188 countries, India ranks as the 127th in terms of progress toward meeting the health-related Sustainable Development Goals [15].

India's NSP for TB elimination details the RNTCP's intention to increase access to improved diagnostics and treatment support, engage with the private sector, and strengthen the healthcare system and TB surveillance. The total cost of this new effort is estimated at just under US$2.5 billion [9••]. The government has also announced a new National Health Policy which includes a gradual increase in healthcare spending to 2.5% of GDP, a level still lower than most other emerging economies [16] and much lower than the global average of 6%. To fully fund, the NSP would require a much more substantial increase in the government's annual healthcare spending. Involvement of all key stakeholders, including patients, will be necessary to galvanize the political will needed to push this ambitious plan forward.

TB is a highly stigmatized disease in India, which may have contributed to its historical absence from national discourse [17]. Today, more and more patients are speaking out. Patient advocates call for an increased understanding of TB among the general population as well as higher quality and more accessible medical care and support. Groups like Bolo Didi seek to support patients through treatment and organize informal peer-support groups [18]. Amitabh Bachchan, a

Bollywood megastar, has described his battle against TB and appeared in several TB campaigns [19].

While the platform for patient advocacy in India has expanded, raising the profile of TB, major roadblocks still exist. In January of 2017, an 18-year-old patient was forced to sue the government of India for access to bedaquiline, a new anti-TB drug that has provided a glimmer of hope for treating multi- and extensively drug-resistant TB [20]. Bedaquiline is still not routinely available to patients with drug resistance in India [21], despite evidence of its effectiveness [22]. Further, a recent modeling study suggests that withholding bedaquiline from first-line treatment for MDR-TB in India may result in worse patient and public health outcomes [23]. The development of new tools for tackling TB is meaningless if implementation is lacking [24].

The 2017 Global TB Report suggests that India's TB budget has increased in the past few years (US$525 million is the current national TB budget, of which 74% is domestic funding) [1], and this is a promising trend that needs to continue, until the NSP is fully funded and executed.

Effectively Engage the Private Sector

The NSP acknowledges the importance of integrating India's complex and weakly regulated private healthcare sector into the national TB program. Until recently, TB patients treated in the private sector were largely ignored as few private sector physicians were notifying these cases to the national TB program. A 2016 study of anti-TB drug sales in India allowed for the first estimation of the numbers of TB patients treated each year in India's private sector [25••]. As a result, the annual TB burden estimate in India had to be upwardly revised by nearly a million patients [26]. Nearly half of India's TB patients are

treated in the private sector [27•], yet little data are available on outcomes of privately treated patients.

The few studies that investigate the quality of care in the private sector, such as simulated patient (mystery client) studies, have shown that the quality of care in the private sector is poor [6••, 7•]. Private providers have also demonstrated suboptimal knowledge of TB, which can create diagnosis and treatment delays [27•, 28–30]. These delays, as well as nonstandard treatment regimens, increase the risk of patient loss to follow-up and death. However, data on patient outcomes are largely unavailable as there is no national monitoring system for patient outcomes in the private sector.

A promising intervention to improve and integrate private physicians is Private Provider Interface Agencies (PPIAs). These organizations provide incentives and training to private physicians to encourage notification, the use of accurate diagnostics and the prescription of appropriate TB treatment. PPIAs also monitor and support patients during their treatment to promote adherence [31, 32]. In this way, private physicians can retain their patients and provide a higher quality of care while providing important monitoring data to the PPIA and the RNTCP. Additionally, programs like the Initiative for Promoting Affordable & Quality TB Tests (IPAQT) have made GeneXpert, a current gold standard diagnostic, as well as other WHO-endorsed TB tests, available at public sector pricing to private sector laboratories with the requirement that these savings be passed on to patients [33, 34••]. This serves to encourage the use of better TB diagnostics in the private sector where nucleic acid amplification tests were previously prohibitively expensive.

Improve Quality of Care

Globally, the TB community has moved its attention from the traditional focus of achieving coverage of treatment availability to ensuring that the now widely available treatment is of high quality. From simulated patient studies, we see that physicians and pharmacists are failing to recognize TB patients or to manage them appropriately [6••, 7•]. Cascade of care studies have shown that, at every step of care, patients are lost (Fig. 1). In India, only 39% of prevalent cases achieve recurrence-free survival [5••]. Care-seeking, diagnostic, and treatment delays prevent patients from being initiated on anti-TB therapy, without which they may die. Even when patients initiate treatment, poor adherence or loss to follow-up reduces treatment success rates. Additionally, without wide-spread drug sensitivity testing (DST), patients may not even receive effective medication for their TB.

India is one of the countries with the greatest MDR-TB burden, and rates of drug resistance are expected to rise; it has been estimated that MDR-TB will constitute 12.4% of all Indian incident TB cases by 2040 [35]. Widespread access to DST, including access to GeneXpert, can improve patient

outcomes and has the potential to curb the MDR-TB epidemic [36], but only 30% of patients treated under the RNTCP received upfront DST in 2016 [9••].

The directly observed therapy, short course strategy (DOTS) has operated at scale for over a decade in India but quality improvement (QI) has not been routinely integrated into the system. To alter patient outcomes, the RNTCP will need to commit to ongoing assessments of gaps in the patient care cascade using an operational research approach [37]. The RNTCP must evaluate and promote adherence to diagnostic and treatment algorithms among its physicians. Simulated patients offer a window into the real care patients receive as they weave through the healthcare system, and this and other strategies should be implemented broadly to continuously monitor and improve the quality of care. Governments such as South Africa are now building QI into the foundations of their TB treatment programs, but India has not yet moved to systematically evaluate the quality of its TB services.

Address Underlying Social Determinants

Underlying the TB epidemic is a reality of poverty and poor overall health. Historically and across the globe, TB is associated with factors such as low socioeconomic status, malnutrition, tobacco smoke, indoor air pollution, and comorbid health conditions such as HIV and diabetes [38]. Eliminating TB will require a concerted effort to address these risk factors, and improving social determinants of health will bolster the health of the Indian population beyond the TB field as well.

Smoking

Smoking has long been associated with a greater risk of developing TB and suffering worse outcomes [39]. Similarly, TB is a leading cause of death among smokers [40]. According to the most recent estimates of tobacco smoking, 24% of men and 3% of women in India smoke [41]. It is estimated that more than 10% of TB cases in India are attributable to smoking [42]. The NSP recognizes smokers as a high-risk group for TB, and proposes assessing tobacco use in TB patients and linking users to national support programs.

Undernutrition

Undernourished populations have an increased risk of developing TB [43–45]. In India, undernutrition is nothing short of an epidemic itself. Recent State-level Disease Burden Initiative estimates from India show that child and maternal malnutrition are still leading risk factors for premature death and poor health, and that these rates are highest in the poorer states of north India [46••]. Across India, approximately 35% of the adult population aged 15–49 years is undernourished, and up to 55% of the annual

incidence of TB is due to undernutrition [47]. Modeling suggests that nutritional interventions could avert 4.8 million cases and 1.6 million deaths over the next 20 years [48•]. Recognizing this reality, the NSP proposes nutritional assessment and counseling for all TB patients, and the RNTCP now provides guidance on patient nutrition [9••]. Unfortunately, India has made very little progress on the undernutrition-related Sustainable Development Goals [15]. The proposed interventions by the RNTCP are necessary, but due to the extent of undernutrition, widespread implementation will pose a challenge.

Diabetes

As India's economy has grown, its population has begun the epidemiological transition from a health landscape dominated by communicable diseases to one where non-communicable diseases impact large segments of the population [4•, 6••]. Of particular relevance to the TB discussion is the rising rate of diabetes mellitus [49]. The national prevalence in India is approximately 7.3%, but in urban areas, it rises to 11.2% [50]. Diabetes is associated with an increased risk of active TB [51] as well as a greater risk of treatment failure, death, and relapse [52]. Among TB patients in India, diabetes prevalence has been reported between 15 and 25% [53–55]. Nearly 10% of TB cases in India are attributable to diabetes [42], but as diabetes prevalence is projected to increase by 67% by 2035 [56], the burden of TB-diabetes coinfection may increase in the coming years.

Stigma

The highly stigmatized nature of TB in India compounds its complex interactions with other social determinants. TB stigma can prevent patients from seeking care and reduce the support they receive from their families. Unlike the HIV field, the TB community has made little progress in reducing the stigma patients' face [57]. As Daftary and colleagues argue, merely raising awareness about TB stigma is insufficient to mitigate stigma. The TB community needs *consciousness raising*, a form of activism where people with and affected by TB come together to share their experiences, identify common struggles and begin collectively organizing to change harmful practices [57]. Also, common TB policies and practices can be modified to reduce TB stigma, informed by lessons from HIV activism [57]. Efforts to better measure TB stigma and to incorporate its costs into modeling exercises are ongoing [58, 59]. TB stigma negatively correlates with TB knowledge [60] so education campaigns and promoting patient advocate platforms are critical.

Conclusion

The National Strategic Plan for TB Elimination shows that the Indian government and national TB program have stepped up their ambition and are aware of the steps necessary to curb the TB epidemic. The RNTCP recognizes the critical need to engage the private sector, and to assess and improve the quality of care that TB patients receive in every sector they receive it in. It also acknowledges that improvements to the overall quality of care and the underlying social determinants that leave patients vulnerable will ultimately reduce TB mortality, morbidity, and transmission. Additionally, there are early signs of increased funding for TB.

The Indian TB epidemic is large and complex but it is not insurmountable. With strong political leadership and commensurate funding, this could be the beginning of the end of the TB in India and the success of the global effort to end TB depends on it.

Compliance with Ethical Standards

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. World Health Organization. Global tuberculosis report. 2017 Geneva.
2. Kapoor SK, Raman AV, Sachdeva KS, Satyanarayana S. How did the TB patients reach DOTS services in Delhi? A study of patient treatment seeking behavior. PLoS One. 2012;7(8):e42458. https://doi.org/10.1371/journal.pone.0042458.
3. Mistry N, Lobo E, Shah S, Rangan S, Dholakia Y. Pulmonary tuberculosis in Patna, India: durations, delays, and health care seeking behaviour among patients identified through household surveys. J Epidemiol Glob Health. 2017;7(4):241–8. https://doi.org/10.1016/j.jegh.2017.08.001.
4.• 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. **Systematically reviews available literature to show a median patient delay of > 2 weeks and a diagnostic delay of > 1 month for Indian TB patients. Such delays increase transmission and the risk of death.** https://doi.org/10.5588/ijtld.13.0585.
5.•• Subbaraman R, Nathavitharana RR, Satyanarayana S, Pai M, Thomas BE, Chadha VK, et al. The tuberculosis cascade of care in India's public sector: a systematic review and meta-analysis. PLoS Med. 2016;13(10):e1002149. **Systematically reviews**

available literature to characterize the public sector TB patient care cascade. The results show staggering losses at each step of the cascade with nearly half of patients being lost to follow up before treatment initiation. https://doi.org/10.1371/journal.pmed. 1002149.

6.•• 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. **The first application of the standardised patient (SP) methodology to TB. SPs allow for assessment of the real world care patients receive. This work showed that private physicians were failing to correctly manage the majority of TB cases presented to them.** https://doi.org/10.1016/S1473-3099(15)00077-8.

7.• Satyanarayana S, Kwan A, Daniels B, Subbaraman R, McDowell A, Bergkvist S, et al. Use of standardised patients to assess antibiotic dispensing for tuberculosis by pharmacies in urban India: a cross-sectional study. Lancet Infect Dis. 2016;16(11):1261–8. **The same TB SP methodology was applied to Indian pharmacists. This work showed that TB patients were frequently being prescribed non-specific antibiotics but not anti-TB medication.** https://doi.org/10.1016/S1473-3099(16)30215-8.

8. World Health Organization. The end TB strategy: global strategy and targets for tuberculosis prevention, care, and control after 2015. 2015 Geneva.

9.•• Revised National Tuberculosis Control Programme. National strategic plan for tuberculosis elimination 2017–2025. 2017. https:// tbcindia.gov.in/WriteReadData/NSP%20Draft%2020.02.2017% 201.pdf. Accessed 21 Jan 2018. **This NSP outlines the RNTCP's ambitious goal of TB elimination by 2025. It outlines many admirable programs and goalposts but the question remains whether this is enough will and funding to fully execute it.**

10. Registrar General of India, Centre for Global Health Research. A joint report of the registrar General of India and the Centre for Global Health Research: causes of death statistics 2010–2013. 2015. http://www.cghr.org/wordpress/wp-content/uploads/COD-India-Report-2010-2013-Dec-19-2015.pdf. Accessed 21 Jan 2018.

11. Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the global burden of disease study 2015. Lancet. 2016;388(10053):1459–544. https://doi.org/10.1016/S0140-6736(16)31012-1.

12. Pai M, Correa N, Mistry N, Jha P, Piot P, Venkatapuram S. Reducing global tuberculosis deaths-time for India to step up. Lancet. 2017;389(10075):1174–6. https://doi.org/10.1016/S0140-6736(17)30790-0.

13. Pai M, Bhaumik S, Bhuyan SS. India's plan to eliminate tuberculosis by 2025: converting rhetoric into reality. BMJ Glob Heal. 2017;2(2):e000326. https://doi.org/10.1136/bmjgh-2017-000326.

14. The Lancet. Health in India, 2017. Lancet. 2017;389(10065):127. https://doi.org/10.1016/S0140-6736(17)30075-2.

15. Fullman N, Barber RM, Abajobir AA, Abate KH, Abbafati C, Abbas KM, et al. Measuring progress and projecting attainment on the basis of past trends of the health-related sustainable development goals in 188 countries: an analysis from the global burden of disease study 2016. Lancet. 2017;390:1423–59. https://doi.org/10.1016/S0140-6736(17)32336-X.

16. Government of India Cabinet. National Health Policy, 2017 approved by cabinet focus on preventive and promotive health care and universal access to good quality health care services [Press release]. 2017.

17. Chang S-H, Cataldo JK. A systematic review of global cultural variations in knowledge, attitudes and health responses. Int J Tuberc Lung Dis. 2014;18(2):168–73. https://doi.org/10.5588/ijtld.13.0181.

18. Krishnan V. Women survivors who won over TB—The Hindu. The Hindu. 2017.

19. Sherlal J. Amitabh Bachchan: I suffered from TB in 2000. Time India. 2014.

20. Krishnan V. India's refusal to scale up bedaquiline is really the world's problem. The Hindu. 2017.

21. Central TB Division, Government of India. TB India 2017. 2017.

22. Borisov SE, Dheda K, Enwerem M, Romero Leyet R, D'Ambrosio L, Centis R, et al. Effectiveness and safety of bedaquilinecontaining regimens in the treatment of MDR- and XDR-TB: a multicentre study. Eur Respir J. 2017;49(5):1700387. https://doi.org/10.1183/13993003.00387-2017.

23. Mehra M, Kambili C, Potluri R, Rhines A, Singh V, Thomas A. Modeling the impact of bedaquiline treatment strategies on the multidrug-resistant tuberculosis burden in India. Int J Tuberc Lung Dis. 2017;21(8):902–9. https://doi.org/10.5588/ijtld.16.0717.

24. Pai M, Furin J. Tuberculosis innovations mean little if they cannot save lives. Elife. 2017;6 https://doi.org/10.7554/eLife.25956.001.

25.•• Arinaminpathy N, Batra D, Khaparde S, Vualnam T, Maheshwari N, Sharma L, et al. The number of privately treated tuberculosis cases in India: an estimation from drug sales data. Lancet Infect Dis. 2016;16(11):1255–60. **Drug sale data was used, for the first time, to estimate the number of TB patients being treated outside the RNTCP. The estimate caused a large upward revision to the estimated TB burden in India and catalyzed efforts to engage the private sector.** https://doi.org/10.1016/S1473-3099(16)30259-6.

26. World Health Organization. Global tuberculosis report. Geneva. 2016.

27.• Satyanarayana S, Nair SA, Chadha SS, Shivashankar R, Sharma G, Yadav S, et al. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. PLoS One. 2011;6(9):e24160. **This large community-based door-to-door survey estimated that 46% of TB patients were receiving care outside the RNTCP.** https://doi.org/10.1371/journal.pone.0024160.

28. Murrison LB, Ananthakrishnan R, Sukumar S, Augustine S, Krishnan N, Pai M, et al. How do urban Indian private practitioners diagnose and treat tuberculosis? A cross-sectional study in Chennai. PLoS One. 2016;11(2):e0149862. https://doi.org/10.1371/journal.pone.0149862.

29. 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. https://doi.org/10.5588/ijtld.15.0186.

30. Achanta S, Jaju J, Kumar AMV, Nagaraja SB, Shamrao SRM, Bandi SK, et al. Tuberculosis management practices by private practitioners in Andhra Pradesh, India. PLoS One. 2013;8(8): e71119. https://doi.org/10.1371/journal.pone.0071119.

31. How India is moving the needle on TB. In: Bill Melinda Gates Found. 2015 https://www.impatientoptimists.org/Posts/2015/01/How-India-is-moving-the-needle-on-TB#.WfopqBNSxE4. Accessed 1 Nov 2017.

32. Wells WA, Uplekar M, Pai M. Achieving systemic and scalable private sector engagement in tuberculosis care and prevention in Asia. PLoS Med. 2015;12(6):e1001842. https://doi.org/10.1371/journal.pmed.1001842.

33. IPAQT Initiative for Promoting Affordable & Quality TB Tests. http://ipaqt.org/. Accessed 1 Apr 2016.

34.•• Clinton Health Access Initiative. Catalyzing India's private sector market for accurate TB testing. 2016. https://clintonhealthaccess.org/content/uploads/2016/06/Case-Study-India-IPAQT-June-2016.pdf. Accessed 21 Jan 2018. **Clinton Health Access Initiative negotiated with private sector labs and diagnostics companies to provide WHO-endorsed TB diagnostics to the private labs at public sector pricing while enforcing a consumer price ceiling.**

This allowed increased use of high quality diagnostics in the private sector where they have previously been prohibitively expensive.

35. Sharma A, Hill A, Kurbatova E, van der Walt M, Kvasnovsky C, Tupasi TE, et al. Estimating the future burden of multidrug-resistant and extensively drug-resistant tuberculosis in India, the Philippines, Russia, and South Africa: a mathematical modelling study. Lancet Infect Dis. 2017;17(7):707–15. https://doi.org/10.1016/S1473-3099(17)30247-5.

36. 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;10(5):e0126065. https://doi.org/10.1371/journal.pone.0126065.

37. Cazabon D, Alsdurf H, Satyanarayana S, Nathavitharana R, Subbaraman R, Daftary A, et al. Quality of tuberculosis care in high burden countries: the urgent need to address gaps in the care cascade. Int J Infect Dis. 2017;56:111–6. https://doi.org/10.1016/j.ijid.2016.10.016.

38. Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. Soc Sci Med. 2009;68(12):2240–6. https://doi.org/10.1016/j.socscimed.2009.03.041.

39. Lin H-H, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. PLoS Med. 2007;4(1):e20. https://doi.org/10.1371/journal.pmed.0040020.

40. Jha P, Jacob B, Gajalakshmi V, Gupta PC, Dhingra N, Kumar R, et al. A nationally representative case-control study of smoking and death in India. N Engl J Med. 2008;358(11):1137–47. https://doi.org/10.1056/NEJMsa0707719.

41. Mishra S, Joseph RA, Gupta PC, Pezzack B, Ram F, Sinha DN, et al. Trends in bidi and cigarette smoking in India from 1998 to 2015, by age, gender and education. BMJ Glob Heal. 2016;1(1): e000005. https://doi.org/10.1136/bmjgh-2015-000005.

42. Lönnroth K, Castro KG, Chakaya JM, Chauhan LS, Floyd K, Glaziou P, et al. Tuberculosis control and elimination 2010-50: cure, care, and social development. Lancet. 2010;375(9728): 1814–29. https://doi.org/10.1016/S0140-6736(10)60483-7.

43. Lönnroth K, Williams BG, Cegielski P, Dye C. A consistent log-linear relationship between tuberculosis incidence and body mass index. Int J Epidemiol. 2010;39(1):149–55. https://doi.org/10.1093/ije/dyp308.

44. Morán-Mendoza O, Marion SA, Elwood K, Patrick D, FitzGerald JM. Risk factors for developing tuberculosis: a 12-year follow-up of contacts of tuberculosis cases. Int J Tuberc Lung Dis. 2010;14(9): 1112–9.

45. Jubulis J, Kinikar A, Ithape M, Khandave M, Dixit S, Hotalkar S, et al. Modifiable risk factors associated with tuberculosis disease in children in Pune, India. Int J Tuberc Lung Dis. 2014;18(2):198–204. https://doi.org/10.5588/ijtld.13.0314.

46.•• Dandona L, Dandona R, Kumar GA, Shukla DK, Paul VK, Balakrishnan K, et al. Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study. Lancet. 2017;390(10111):2437–60. https://doi.org/10.1016/S0140-6736(17)32804-0. **As a part of the Global Burden of Disease Study, disease burden and risk factor prevelances were estimated for all states in India. This is the first instance of comprehensive, high quality, and granular estimates being available for individual Indian states. The estimates highlight the heterogeneity within India and its progression through the epidemiological transition.**

47. Bhargava A, Benedetti A, Oxlade O, Pai M, Menzies D. Undernutrition and the incidence of tuberculosis in India: national and subnational estimates of the population-attributable fraction related to undernutrition. Natl Med J India. 2014;27(3):128–33.

48.• Oxlade O, Huang CC, Murray M. Estimating the impact of reducing under-nutrition on the tuberculosis epidemic in the central eastern states of India: a dynamic modeling study. PLoS One. 2015;10(6):e0128187. **This modelling study highlighted the drastic impact that ameliorating nutritional status could have on TB rates in India.** https://doi.org/10.1371/journal.pone.0128187.

49. Popkin BM, Horton S, Kim S, Mahal A, Shuigao J. Trends in diet, nutritional status, and diet-related noncommunicable diseases in China and India: the economic costs of the nutrition transition. Nutr Rev. 2001;59(12):379–90.

50. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR–INDIAB population-based cross-sectional study. Lancet Diabetes Endocrinol. 2017;5(8):585–96. https://doi.org/10.1016/S2213-8587(17)30174-2.

51. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med. 2008;5:1091–101.

52. Baker MA, Harries AD, Jeon CY, Hart JE, Kapur A, Lönnroth K, et al. The impact of diabetes on tuberculosis treatment outcomes: a systematic review. BMC Med. 2011;9(1):81. https://doi.org/10.1186/1741-7015-9-81.

53. Viswanathan V, Kumpatla S, Aravindalochanan V, Rajan R, Chinnasamy C, Srinivasan R, et al. Prevalence of diabetes and pre-diabetes and associated risk factors among tuberculosis patients in India. PLoS One. 2012;7(7):e41367. https://doi.org/10.1371/journal.pone.0041367.

54. Agarwal AK, Gupta G, Marskole P, Agarwal A. A study of the patients suffering from tuberculosis and tuberculosis-diabetes comorbidity in Revised National Tuberculosis Control Program Centers of Northern Madhya Pradesh, India. Indian J Endocrinol Metab. 2017;21(4):570–6. https://doi.org/10.4103/ijem.IJEM_89_17.

55. Siddiqui AN, Khayyam KU, Siddiqui N, Sarin R, Sharma M. Diabetes prevalence and its impact on health-related quality of life in tuberculosis patients. Trop Med Int Heal. 2017;22(11):1394–404. https://doi.org/10.1111/tmi.12968.

56. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. 2011;94(3):311–21. https://doi.org/10.1016/j.diabres.2011.10.029.

57. Daftary A, Frick M, Venkatesan N, Pai M. Fighting TB stigma: we need to apply lessons learnt from HIV activism. BMJ Glob Heal. 2017;2(4):e000515. https://doi.org/10.1136/bmjgh-2017-000515.

58. Zwerling A, Dowdy D, von Delft A, Taylor H, Merritt MW. Incorporating social justice and stigma in cost-effectiveness analysis: drug-resistant tuberculosis treatment. Int J Tuberc Lung Dis. 2017;21(11):69–74. https://doi.org/10.5588/ijtld.16.0839.

59. Maleche A, Citro B, Tisile P, Abdullaev T. Measuring TB-related stigma. Int J Tuberc Lung Dis. 2017;21(11):4–5. https://doi.org/10.5588/ijtld.17.0581.

60. Rood EJJ, Mergenthaler C, Bakker MI, Redwood L, Mitchell EMH. Using 15 DHS surveys to study epidemiological correlates of TB courtesy stigma and health-seeking behaviour. Int J Tuberc Lung Dis. 2017;21(11):60–8. https://doi.org/10.5588/ijtld.16.0909.