People with tuberculosis falling through the cracks

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SUMMARY

Subbaraman *et al*. present a cascade of care for tuberculosis (TB) in India's public sector for the year 2013. Drawing from the World Health Organization (WHO) Global TB Reports, the Revised National TB Control Programme (RNTCP) of the Government of India annual reports as well as three systematic reviews conducted by the authors, this study provides estimates of the number of patients with TB in India who reach each step along the pathway from care-seeking to cure. Although prior research has characterized barriers to specific stages of care[1] or components of the cascade in subnational samples,[2] this study is considered to be the first to describe a national-level TB care cascade.[3]

The authors conceptualize the pathway of public sector TB care to include six separate steps and the corresponding gaps: (i) total prevalent active TB cases; (ii) evaluation for TB in public sector facilities; (iii) successful diagnosis with TB; (iv) treatment registration through RNTCP; (v) treatment completion or cure; and (vi) 1-year recurrence-free survival. Starting with the WHO figure of 2.7 million individuals with active TB in India in 2013, it was estimated that only 39% of patients with TB successfully reached the final cascade step. Overall, the largest gap in the cascade was access to care with 28% of all prevalent TB cases not reaching public sector TB diagnostic facilities. The attrition between each of the remaining steps in the care cascade was similar, ranging from 13% to 16%.

As individuals with different forms of TB may face disparate barriers to care, separate public sector care cascades were also constructed for different categories of TB: new smear-positive, new smear-negative, retreatment smear-positive, retreatment smear-negative, extrapulmonary and multidrug-resistant (MDR)-TB. Notably, the gaps in public sector care were different for different categories of TB. For example, new and retreatment smear-positive patients had high levels of pre-treatment loss to follow-up (i.e. diagnosed with TB but not initiating treatment; 15% attrition), poor treatment outcomes (i.e. treatment loss to follow-up, treatment failure or death; 12% new, 29% retreatment) and recurrence or death within 1 year of treatment completion (16% new, 27% retreatment). In contrast, reaching public sector diagnostic facilities but not being successfully diagnosed was the largest gap for extrapulmonary (20% attrition), MDR (59%) and both categories of smear-negative TB (38% new, 29% retreatment). MDR-TB patients also experienced high levels of poor treatment outcomes (54%).

COMMENT

India accounts for approximately one-quarter of the estimated global burden of TB and MDR-TB.[4] Achieving the 2015 WHO End TB Strategy[5] and the latest Government of India target of TB elimination by 2025[6] will require substantial efforts and funding to continue to improve TB care in India. The present research identifies major gaps in both the measurement and implementation of India's public sector TB programme with implications to inform the programme's activities and to guide future research.

The cascade of care model, more frequently used in other fields, such as HIV[7] and maternal and child health,[8] is a useful framework that defines all or part of the pathway from care-seeking to a specific health outcome. However, a linear cascade model is unable to account for the complex dynamics of care-seeking and transfers that have been documented with TB[9] as well

as HIV.[10] For example, there is the potential to conflate loss to follow-up from the public sector programme with an individual being undiagnosed or off treatment entirely. In reality, individuals lost to follow-up at any stage along the cascade may be linked into alternative care programmes (e.g. private sector providers or non-governmental organizations) or have silently transferred to another public sector facility.[11] Furthermore, the completion of steps along this pathway is necessary but does not guarantee timely, high-quality TB care. Indicators of care without a time element for example may inadequately capture crucial barrier information.[12] Being evaluated for TB at a public sector facility within 2 weeks of symptom onset versus within 6 months of onset have profoundly different implications to both patients and public health programmes.

To their credit, the authors discuss many of these caveats as well as several other specific limitations in the available data and their analysis, including: uncertainty in the WHO estimate of prevalent active TB in India, assumption that all TB patients in the private sector were undiagnosed or not on treatment, inability to control for small numbers of duplicate patient records, misdiagnoses of TB and misclassification of TB categories, availability of only composite treatment outcome data, among others. One of the greatest strengths of this laudable work is the extensive documentation of the research methodology, including explicit descriptions of the assumptions underlying and sources of uncertainty in the estimation of each step and gap along the cascade of TB care. Sensitivity analyses could have been useful though to assess the impact of conservative assumptions that were made where limited data were available (e.g. 1-year recurrence for MDR-TB and pre-treatment loss to follow-up for smear-negative patients).[13]

A key contribution of this work is in clearly describing what is known about India's public sector TB cascade of care and laying the groundwork for future research aiming to improve these estimates. Beyond the steps included in the present cascade model, future refinements could include a variety of other patient-centred aspects of care from early HIV screening and adequate TB counselling to community reintegration or palliative care.[14] Characterizing the temporal[13] and spatial[15] variation in the TB care cascade could also provide more nuanced information to evaluate programme changes and geographically target programme activities. Important differences in the cascade by gender, HIV status, socioeconomic status and other variables may also be crucial to evaluate to ensure equitable care. Some of these knowledge gaps may be addressed through the utilization of more detailed existing programmatic data not currently reported at the state or national levels, such as duration of delays, timing of loss to follow-up from treatment and disaggregated outcome data. Despite implementation challenges,[16] Nikshay, an online governmental platform for the notification and monitoring of TB patients in India's public and private sectors,[17] shows promise in facilitating patient reporting, data standardization and timely data availability.[18]

Subbaraman *et al*. provide compelling evidence of the utility of programmatic data and focused systematic reviews to inform interventions and future research on TB care in India. Their estimation of the extent of attrition along the public sector TB care pathway provides considerable opportunities to direct interventions to specific gaps to maximize the impact of available resources. However, focusing on single stages of the cascade may 'shift attrition downstream'[19] due to weak linkages, additional barriers to care and operational challenges.[20] Integrated and patient-centred

approaches to addressing access, implementation and quality barriers along the entire cascade have the greatest potential to improve patient outcomes and reduce transmission.[13,21,22] The latest RNTCP policy changes have attempted to address several identified gaps in care. Successful pilot projects in India have shown the potential of scaling-up molecular diagnostics,[23] public–private partnerships[24] and alternative treatment models such as directly observed therapy by family members.[25] The ongoing roll-out of daily treatment regimens for drug-susceptible TB, fixed-dose combination drugs and the latest recommendation of a 2-year follow-up of all TB patients after treatment[26] is likely to improve treatment outcomes and reduce relapse. Continued political commitment, increased funding and leadership at all levels[27] will, however, be essential for demonstration projects to be brought to scale and for effective policy implementation.

Conflicts of interest. None

REFERENCES

1 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:**255–66.

2 Dandona R, Dandona L, Mishra A, Dhingra S, Venkatagopalakrishna K, Chauhan LS. Utilization of and barriers to public sector tuberculosis services in India. *Natl Med J India* 2004;**17:**292–9.

3 Pai M. India needs to address gaps in the TB care cascade. Available at *www.naturemicrobiologycommunity.nature.com/users/20892-madhukar-pai/posts/13007-india-needs-to-address-gaps-in-the-tb-care-cascade* (accessed on 16 Dec 2016).

4 World Health Organization. *Global Tuberculosis Report 2016.* Geneva:WHO; 2016. Available at *www.who.int/tb/publications/global_report/en/* (accessed on 20 Feb 2017).

5 World Health Organization. *The end TB strategy.* Geneva:WHO; 2015. Available at *www.who.int/tb/post2015_strategy/en/* (accessed on 10 Dec 2016).

6 Ministry of Finance. *Key features of budget 2017–2018.* New Delhi:Ministry of Finance, Government of India; 2017. Available at *www.indiabudget.nic.in/ub2017-18/bh/bh1.pdf* (accessed on 16 Feb 2017).

7 Medland NA, McMahon JH, Chow EP, Elliott JH, Hoy JF, Fairley CK. The HIV care cascade: A systematic review of data sources, methodology and comparability. *J Int AIDS Soc* 2015;**18:**20634. doi: 10.7448/IAS.18.1.20634. eCollection 2015.

8 Kerber KJ, de Graft-Johnson JE, Bhutta ZA, Okong P, Starrs A, Lawn JE. Continuum of care for maternal, newborn, and child health: From slogan to service delivery. *Lancet* 2007;**370:**1358–69.

9 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:**e42458.

10 Nsanzimana S, Kanters S, Remera E, Forrest JI, Binagwaho A, Condo J, *et al.* HIV care continuum in Rwanda: A cross-sectional analysis of the national programme. *Lancet HIV* 2015;**2:**e208–15.

11 Geng EH, Odeny TA, Lyamuya R, Nakiwogga-Muwanga A, Diero L, Bwana M, *et al.* Retention in care and patient-reported reasons for undocumented transfer or stopping care among HIV-infected patients on antiretroviral therapy in Eastern Africa: Application of a sampling-based approach. *Clin Infect Dis* 2016;**62:**935–44.

12 Perlman DC, Jordan AE, Nash D. Conceptualizing care continua: Lessons from HIV, hepatitis C virus, tuberculosis and implications for the development of improved care and prevention continua. *Front Public Health* 2017;**4:**296.

13 O'Donnell MR, Daftary A, Frick M, Hirsch-Moverman Y, Amico KR, Senthilingam M, *et al.* Re-inventing adherence: Toward a patient-centered model of care for drug-resistant tuberculosis and HIV. *Int J Tuberc Lung Dis* 2016;**20:**430–4.

14 Nosyk B, Montaner JS, Colley G, Lima VD, Chan K, Heath K, *et al.* The cascade of HIV care in British Columbia, Canada, 1996–2011: A population-based retrospective cohort study. *Lancet Infect Dis* 2014;**14:**40–9.

15 Goswami ND, Schmitz MM, Sanchez T, Dasgupta S, Sullivan P, Cooper H, *et al.* Understanding local spatial variation along the care continuum: The potential impact of transportation vulnerability on HIV linkage to care and viral suppression in high-poverty areas, Atlanta, Georgia. *J Acquir Immune Defic Syndr* 2016;**72:**65–72.

16 Chadha SS, Nagaraja SB, Trivedi A, Satapathy S, Devendrappa NM, Sagili KD. Mandatory TB notification in Mysore city, India: Have we heard the private practitioner's plea? *BMC Health Serv Res* 2017;**17:**1.

17 Jitendra R. 'NIKSHAY'–Harnessing information technology for delivery of enhanced TB care. *NTI Bull* 2012;**48:**1–4.

18 Kundu D, Chopra K, Khanna A, Babbar N, Padmini TJ. Accelerating TB notification from the private health sector in Delhi, India. *Indian J Tuberc* 2016;**63:**8–12.

19 Fox MP. Are we shifting attrition downstream in the HIV cascade? *Lancet HIV* 2016;**3:**e554–5.

20 Chawla KS, Kanyama C, Mbewe A, Matoga M, Hoffman I, Ngoma J, *et al.* Policy to practice: Impact of GeneXpert MTB/RIF implementation on the TB spectrum of care in Lilongwe, Malawi. *Trans R Soc Trop Med Hyg* 2016;**110:**305–11.

21 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:**111–16.

22 Graham WJ, Varghese B. Quality, quality, quality: Gaps in the continuum of care. *Lancet* 2012;**379:**e5–e6.

23 Raizada N, Sachdeva KS, Swaminathan S, Kulsange S, Khaparde SD, Nair SA, *et al.* Piloting upfront Xpert MTB/RIF testing on various specimens under programmatic conditions for diagnosis of TB and DR-TB in paediatric population. *PLoS One* 2015;**10:**e0140375.

24 Wells WA, Uplekar M, Pai M. Achieving systemic and scalable private sector engagement in tuberculosis care and prevention in Asia. *PLoS Med* 2015;**12:**e1001842.

25 Dave PV, Shah AN, Nimavat PB, Modi BB, Pujara KR, Patel P, *et al.* Direct observation of treatment provided by a family member as compared to non-family member among children with new tuberculosis: A pragmatic, non-inferiority, cluster-randomized trial in Gujarat, India. *PLoS One* 2016;**11:**e0148488.

26 Revised National TB Control Programme (RNTCP). *Technical and operational guidelines for tuberculosis control in India 2016.* New Delhi:Central TB Division, Ministry of Health and Family Welfare, Government of India; 2016. Available at *www.tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=4573&lid=3177* (accessed on 20 Feb 2017).

27 Pai M, Arinaminpathy N. How can India overcome tuberculosis? *BMJ Opin* Available at *www.blogs.bmj.com/bmj/2016/10/03/how-can-india-overcome-tuberculosis/* (accessed 20 Feb 2017).

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