

## Stopping the body count: a comprehensive approach to move towards zero tuberculosis deaths



Tuberculosis has been a curable disease since the 1950s. In the more than six decades since then, knowledge has been amassed about how to ameliorate its social causes, prevent its transmission, and treat both its clinical and quiescent forms.<sup>1,2</sup> In many high-income settings, this knowledge has been used with great success. Elsewhere, this is far from the case: more than 4000 people die from this curable and preventable airborne disease each day, mostly in low-income and middle-income settings.<sup>3</sup> Distressed by the status quo, in 2012 more than 500 scientists, policy makers, and advocates from around the world signed the Zero TB Declaration, which called for “a new global attitude” in the fight against tuberculosis, and argued that, with the right set of interventions, the planet could move rapidly towards zero deaths from tuberculosis.<sup>4</sup>

Although tuberculosis incidence has declined over the past 25 years, it has done so at a glacial pace of about 1.65% annually.<sup>5</sup> At this rate, it will take another two centuries to eliminate the disease.<sup>5</sup> This reality reflects the limited set of interventions recommended for, and implemented in, low-income and middle-income settings, a shadow of the comprehensive set of strategies that has brought the tuberculosis epidemic to heel in other places.<sup>1,2</sup> Rather than aggressively finding all cases of tuberculosis, preventing the disease in those at highest risk, and focusing on populations and places of highest transmission, most low-income and middle-income settings have focused narrowly on the diagnosis and treatment of those patients with tuberculosis who manage to access care on their own. An over-reliance on standardised treatment and sputum smear microscopy—a low-sensitivity visual diagnostic test that cannot determine drug resistance—has sidelined not only individuals whose illness is characterised by a lower bacillary load, such as children and individuals with HIV, but also those with extrapulmonary or drug-resistant tuberculosis.<sup>6</sup> Early detection and treatment of both active disease and quiescent (so-called latent) infection, along with efforts to control transmission in health-care and congregate settings, have been belatedly recommended for some groups in limited settings, but have yet to be widely scaled up.<sup>7</sup> Much of the policy

framing to date has been driven by concerns over cost, which has overridden both the scientific and moral imperatives to implement proven interventions that could deflect the global tuberculosis curve more rapidly.<sup>6–8</sup>

Although standardisation of treatment contributed to improved clinical outcomes for some people with tuberculosis, the absence of a comprehensive approach for fighting tuberculosis in high-burden settings has led to predictable and alarming results.<sup>3,9,10</sup> At least 9 million people fall sick from tuberculosis every year, including 1 million children.<sup>3,11</sup> More than 3 million patients with tuberculosis remain undetected and continue to transmit the disease in their families and communities. Appropriate treatment for drug-resistant tuberculosis remains the exception rather than the rule, allowing further transmission of these strains. Most known contacts receive no post-exposure therapy, a standard intervention in most high-income settings. Finally, and most damning of all, almost 1.5 million people still die each year from tuberculosis—a preventable and curable disease.<sup>3</sup>

Ending the tuberculosis epidemic requires the urgent deployment of a comprehensive package of effective, tried and tested interventions in low-income and middle-income settings. This comprehensive approach must happen in tandem with the development of effective point-of-care diagnostics, highly effective and shorter

Published Online  
October 26, 2015  
[http://dx.doi.org/10.1016/S0140-6736\(15\)00320-7](http://dx.doi.org/10.1016/S0140-6736(15)00320-7)  
See [Perspectives](#) page 2247  
See [Series](#) pages 2324, 2334, 2344, and 2354



A mother and child who both have multidrug-resistant tuberculosis at a clinic in Nairobi, Kenya, in March, 2015

Tony Karumbi/Stringer

treatment regimens, and vaccines. The *Lancet Series* on how to eliminate tuberculosis<sup>12–15</sup> reviews a set of proven epidemic-control strategies for combating the disease. Their wider and more systematic application, evidence suggests, will result in quantitatively greater and more rapid progress in tackling the global tuberculosis epidemic.<sup>1,2,16–22</sup> These strategies include: stopping transmission through active identification of sick patients and prompt initiation of the correct therapy; treating infection in close contacts and high-risk individuals; using data from tuberculosis programmes to improve use of current resources and to better target interventions; and addressing some of the social mechanisms that fuel tuberculosis. Each Series paper presents examples of places where these epidemic-control strategies have been successfully used, as well as practical recommendations for implementation. Separately, the effect of these approaches might be modest; in combination, however, global experience and mathematical modelling suggest that they will have a swift and dramatic effect on tuberculosis incidence and mortality.<sup>1,2</sup>

The goals laid out in both the Stop TB Partnership's Global Plan to Stop TB 2016–2020<sup>23</sup> and WHO's End TB Strategy<sup>24</sup> will require “a new global attitude” in the fight against tuberculosis.<sup>4</sup> Part of that shift means moving beyond piecemeal approaches, and deploying a comprehensive epidemic-control strategy that has been shown to work. Beyond courage and vision, the success of this approach will depend on an unwavering commitment to programmatic quality, fidelity, and equity, with all the methods required to stop an airborne epidemic being used at the same time. Moreover, all people who require treatment must be included in this comprehensive approach: children, people with drug-resistant strains, individuals with extrapulmonary disease, those co-infected with HIV, others at high risk of acquiring the disease, and infected contacts. Failure to seize this opportunity now will constitute both a scientific and moral failure. Waiting another two centuries for a curable and preventable disease to disappear is not an option.

\*Salmaan Keshavjee, David Dowdy, Soumya Swaminathan  
 Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA 02115, USA (SK); Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA (DD); and Office of Director General, Indian Council of Medical Research and Department of Health Research, New Delhi, India (SS) salmaan\_keshavjee@hms.harvard.edu

We declare no competing interests. We thank Carly Rodriguez for coordination and research assistance in the preparation of this Comment.

- 1 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**: 2240–46.
- 2 Dye C, Glaziou P, Floyd K, Raviglione M. Prospects for tuberculosis elimination. *Annu Rev Public Health* 2013; **34**: 271–86.
- 3 WHO. Global tuberculosis report 2014. Geneva: World Health Organization, 2014.
- 4 Treatment Action Group. Zero TB declaration. July 22, 2012. <http://www.treatmentactiongroup.org/tb/advocacy/zero-declaration> (accessed July 19, 2015).
- 5 Ortblad KF, Lozano R, Murray CJL. An alternative estimation of tuberculosis incidence from 1980 to 2010: methods from the Global Burden of Disease 2010. *Lancet* 2013; **381**: S104.
- 6 Keshavjee S, Farmer PE. Tuberculosis, drug resistance and the history of modern medicine. *N Engl J Med* 2012; **367**: 931–36.
- 7 McMillan CW. *Discovering tuberculosis: a global history 1900 to the present*. New Haven, CT: Yale University Press, 2015.
- 8 Walsh JA, Warren KS. Selective primary health care: an interim strategy for disease control in developing countries. *N Engl J Med* 1979; **301**: 967–74.
- 9 Obermeyer Z, Abbott-Klafter J, Murray CJL. Has the DOTS strategy improved case finding or treatment success? An empirical assessment. *PLoS One* 2008; **3**: e1721.
- 10 De Cock KM, Chaisson RE. Will DOTS do it? A reappraisal of tuberculosis control in countries with high rates of HIV infection. *Int J Tuberc Lung Dis* 1999; **3**: 457–65.
- 11 Jenkins HE, Tolman AW, Yuen CM, et al. Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. *Lancet* 2014; **383**: 1572–79.
- 12 Theron G, Jenkins HE, Cobelens F, et al. Data for action: collection and use of local data to end tuberculosis. *Lancet* 2015; published online Oct 26. [http://dx.doi.org/10.1016/S0140-6736\(15\)00321-9](http://dx.doi.org/10.1016/S0140-6736(15)00321-9).
- 13 Yuen CM, Amanullah F, Dharmadhikari A, et al. Turning off the tap: stopping tuberculosis transmission through active case-finding and prompt effective treatment. *Lancet* 2015; published online Oct 26. [http://dx.doi.org/10.1016/S0140-6736\(15\)00322-0](http://dx.doi.org/10.1016/S0140-6736(15)00322-0).
- 14 Rangaka MX, Cavalcante SC, Marais BJ, et al. Controlling the seedbeds of tuberculosis: diagnosis and treatment of tuberculosis infection. *Lancet* 2015; published online Oct 26. [http://dx.doi.org/10.1016/S0140-6736\(15\)00323-2](http://dx.doi.org/10.1016/S0140-6736(15)00323-2).
- 15 Ortblad KF, Salomon JA, Bärnighausen T, Atun R. Stopping tuberculosis: a biosocial model for sustainable development. *Lancet* 2015; published online Oct 26. [http://dx.doi.org/10.1016/S0140-6736\(15\)00324-4](http://dx.doi.org/10.1016/S0140-6736(15)00324-4).
- 16 Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City—turning the tide. *N Engl J Med* 1995; **333**: 229–33.
- 17 Cavalcante SC, Durovni B, Barnes GL, et al. Community-randomised trial of enhanced DOTS for tuberculosis control in Rio de Janeiro, Brazil. *Int J Tuberc Lung Dis* 2010; **14**: 203–09.
- 18 Bamrah S, Brostrom R, Dorina F, et al. Treatment for LTBI in contacts of MDR-TB patients, Federated States of Micronesia, 2009–2012. *Int J Tuberc Lung Dis* 2014; **18**: 912–18.
- 19 Graham NM, Galai N, Nelson KE, et al. Effect of isoniazid chemoprophylaxis on HIV-related mycobacterial disease. *Arch Intern Med* 1996; **156**: 889–94.
- 20 Keshavjee S, Gelmanova I, Pasechnikov A, et al. Treating multi-drug resistant tuberculosis in Tomsk, Russia: developing programs that address the linkage between poverty and disease. *Ann N Y Acad Sci* 2008; **1136**: 1–11.
- 21 Rocha C, Montoya R, Zevallos K, et al. The innovative socio-economic interventions against tuberculosis (ISIAT) project: an operational assessment. *Int J Tuberc Lung Dis* 2011; **15**: S50–57.
- 22 Comstock GW. Isoniazid prophylaxis in an underdeveloped area. *Am Rev Respir Dis* 1962; **86**: 810–22.
- 23 Stop TB Partnership. The global plan to stop TB 2016–2020. 2015. <http://www.stoptb.org/global/plan/plan2/> (accessed Sept 11, 2015).
- 24 WHO. *Introducing the End TB Strategy*. Geneva: World Health Organization, 2015.