

## Multidrug-resistant tuberculosis in India: looking back, thinking ahead



With an estimated 480 000 new cases developing every year,<sup>1</sup> multidrug-resistant tuberculosis is one of the greatest public health challenges worldwide. Multidrug-resistant tuberculosis is much more common in patients who have previously been treated for tuberculosis,<sup>1</sup> and public health efforts have typically focused on high-quality treatment of drug-susceptible tuberculosis to prevent acquisition of resistance while on therapy.<sup>2</sup> However, a substantial proportion of patients with multidrug-resistant tuberculosis might have transmitted drug resistance (ie, present before treatment begins), and drug resistance is therefore often the cause of treatment failure, not the result. Several studies have illustrated how, as multidrug-resistant tuberculosis epidemics take hold in populations, most multidrug-resistant tuberculosis cases can shift from being acquired during treatment to primarily transmitted.<sup>3</sup> At least one modelling analysis suggests that this transition has already taken place in many countries throughout the world.<sup>4</sup> Such transitions have important implications for public health efforts: once multidrug-resistant tuberculosis becomes a primarily transmitted disease, improving the effectiveness of drug-susceptible tuberculosis treatment can no longer contain the spread of resistance, and public health efforts must shift to diagnosis and treatment of multidrug-resistant tuberculosis. As the cost of multidrug-resistant tuberculosis treatment can exceed that of first-line tuberculosis therapy by a factor of ten or more,<sup>1</sup> the resource implications of this epidemiological shift are profound.

In *The Lancet Public Health*, Stephanie Law and colleagues<sup>5</sup> extend this literature with a dynamic model of the tuberculosis epidemic in India, which they use to estimate the incidence of drug-susceptible tuberculosis and multidrug-resistant tuberculosis over the next 20 years. Their approach is novel in that they explicitly model the contributions to resistance from India's burgeoning private sector. The authors project that—if current practices continue—the incidence of multidrug-resistant tuberculosis could increase substantially from 3.9 cases per 100 000 population (95% uncertainty range [UR] 2.7–5.4) to 14.1 cases

per 100 000 population (95% UR 11.2–16.0) between 2012 and 2032. They estimate that the fraction of multidrug-resistant tuberculosis incidence resulting from primary transmission (versus acquisition during treatment) will rise from 15% to 85% during this time—a substantially faster transition than previously projected.<sup>3</sup> The authors further explore the effects of correcting treatment errors or shifting more treatment to the public sector; none of these potential changes has a large effect on the projected incidence of multidrug-resistant tuberculosis, consistent with an epidemic driven primarily by transmission rather than acquisition of resistance during treatment.

A substantial increase, such as has been estimated here, in multidrug-resistant tuberculosis incidence has never before been seen on a scale this large. China, for example, has an estimated multidrug-resistant tuberculosis prevalence nearly twice the global average,<sup>6</sup> but this has been seen on a regional level for many years, with no clear evidence of a recent increase.<sup>7</sup> India—with its strong private sector involvement—might have epidemiological reasons to experience a larger increase in multidrug-resistant tuberculosis over the coming 20 years. But such a substantial shift has not yet occurred despite decades of treating tuberculosis with rifampin and isoniazid, and would be unprecedented outside the prison system of the former Soviet Union.<sup>8</sup> In assessing whether India is likely to experience such an explosion of drug resistance, certain limitations of the study need to be understood. As the authors point out, robust national estimates of drug resistance in India are lacking; the baseline estimates of multidrug-resistant tuberculosis incidence and of primary multidrug-resistant tuberculosis transmission used here are lower than in other models,<sup>3,4</sup> which might make subsequent increases seem larger. Additionally, the model is not calibrated to previous trends of multidrug-resistant tuberculosis incidence in India; those trends might in reality be more stable than projected. These factors—reflecting insufficient data rather than any inherent flaw in model design—could produce overly pessimistic projections of India's future multidrug-resistant tuberculosis epidemic. A nationwide tripling of

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multidrug-resistant tuberculosis incidence in 20 years is certainly far from inevitable.

In the end, however, the exact magnitude of these projections matters less than the recognition that the apparent stability of India's multidrug-resistant tuberculosis epidemic in the past does not necessarily portend a constant epidemic in the future. As multidrug-resistant tuberculosis transitions from an acquired condition to a primarily transmitted disease, the possibility for a sharp upswing in incidence still exists—an upswing that could be prevented with a well-crafted public health response. For example, following a rise in tuberculosis and multidrug-resistant tuberculosis in New York City in the 1980s, swift public health action caused multidrug-resistant tuberculosis incidence to drop precipitously and more rapidly than drug-susceptible tuberculosis,<sup>9</sup> a trend that has been replicated in other settings.<sup>10</sup> As the authors' results suggest, such an effective response to multidrug-resistant tuberculosis cannot focus on treating drug-susceptible tuberculosis alone but must include strong surveillance systems, drug susceptibility testing for all patients with tuberculosis, rapid linkage to effective treatment, and patient-centered care throughout the treatment course. Ultimately, we cannot afford to be complacent in the public health response to multidrug-resistant tuberculosis; past epidemic stability is no assurance of an optimistic future.

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