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Drug-resistant tuberculosis in Mumbai, India: An agenda for operations research

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ABSTRACT

Operations research (OR) is well established in India and is also a prominent feature of the global and local agendas for tuberculosis (TB) control. India accounts for a quarter of the global burden of TB and of new cases. Multidrug-resistant TB is a significant problem in Mumbai, India's most populous city, and there have been recent reports of totally resistant TB. Much thought has been given to the role of OR in addressing programmatic challenges, by both international partnerships and India's Revised National TB Control Programme. We attempt to summarize the major challenges to TB control in Mumbai, with an emphasis on drug resistance. Specific challenges include diagnosis of TB and defining cure, detecting drug resistant TB, multiple sources of health care in the private, public and informal sectors, co-infection with human immunodeficiency virus (HIV) and a concurrent epidemic of non-communicable diseases, suboptimal prescribing practices, and infection control. We propose a local agenda for OR: modeling the effects of newer technologies, active case detection, and changes in timing of activities, and mapping hotspots and contact networks; modeling the effects of drug control, changing the balance of ambulatory and inpatient care, and adverse drug reactions; modeling the effects of integration of TB and HIV diagnosis and management, and preventive drug therapy; and modeling the effects of initiatives to improve infection control.

1. Introduction

Operations research, India, and tuberculosis

India has operations research (OR) history. Established in 1957 and affiliated with the International Federation of Operational Research Societies (IFORS), the Operational Research Society of India was the first in the South, and hosted the first international conference on OR for Development, in Ahmedabad in 1992 (ORSI: www.orsi.in). Nevertheless, OR on public health has been limited, and in this India is no exception [1,2]. In a recent discussion, Royston suggests that OR has a rather broader interpretation in global health than in management science [3]. Health initiatives have tended to use group methods of qualitative character (brainstorming, behavioral simulation, scenario analysis, system mapping), rather than quantitative exercises such as mathematical modeling and system dynamics. We think this is true, but understandable. Proponents of OR for global health – and for TB control in particular – see it as research "intended to provide managers, administrators, and policy makers with the information that they need to improve service delivery activities and plan future ones" [4]; or, "research into strategies, interventions, tools or knowledge that can enhance the quality, coverage, effectiveness or performance of the health system or programmes in which the research is being conducted" [5,6]. This sort of language is less intimidating than "an interdisciplinary branch of applied mathematics or formal science that uses advanced analytic methods to make better decisions or research that provides optimal solutions to complex decision-making" (http://www.scienceofbetter.org/what/index.htm).

It turns out that OR for health in low-income countries has been championed by people involved in tuberculosis (TB) control, from making the case for OR [5,7–9] to more tightly specified agendas [10,11]. The sort of OR that might be described as implementation science is crucial to the success of TB programmes [12,13], and guided the development of current approaches based on Directly Observed Therapy Short-course (DOTS) [11]. Substantial efforts have been made to support OR for TB control through funding, training and guidelines, but it is not always clear that it has delivered [11]. Commentaries call for greater coordination — for activity to be more programme-driven than researcher-driven — [9] and for a clear sequence of steps from research to implementation [8].

The current WHO Stop TB Strategy has six concerns: (i) high-quality management of TB through DOTS, (ii) co-infection with TB and human immunodeficiency virus (TB-HIV), multidrug-resistant

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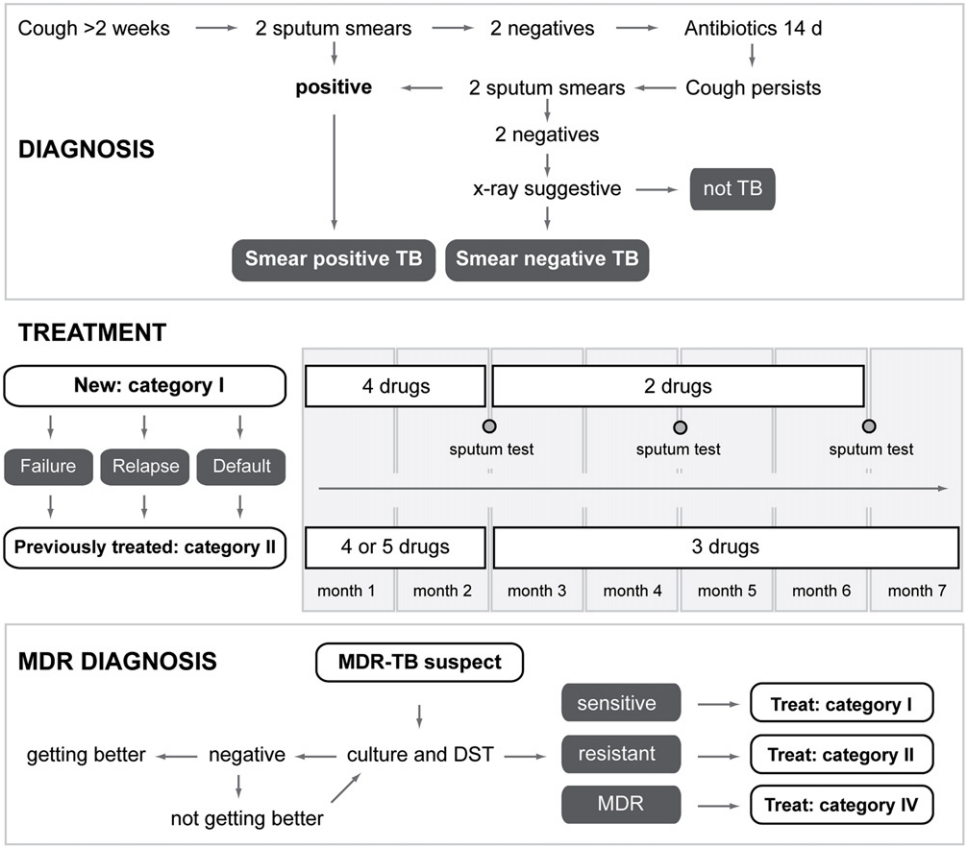

Fig. 1. Schematic overview of key tuberculosis control activities in India's Revised National Tuberculosis Control Programme.

TB (MDR-TB) and the needs of poor and vulnerable populations, (iii) health systems, (iv) multiple providers of health care, and (v) partnerships with people with TB [14]. The sixth concern is the need for research, and the Global Plan to Stop TB 2011–2015 is unusual in emphasizing OR (http://www.stoptb.org) [15].

Tuberculosis in India

Nowhere is the OR agenda more pressing than in India, which accounts for 25% of the global burden of TB and 29% of global TB mortality [16]. TB causes an estimated 320 000 annual deaths in India: 17.6% of communicable disease deaths and 3.5% of all-cause mortality [17]. While the incidence has fallen from 216 to 185 per 100 000 over the last decade, notifications reached 1.5 million in 2010. 1.2 million of these were new cases. India contributed 23% of new diagnoses of TB globally, but 43% of individuals who required retreatment. The primary notional provider of care is the Revised National TB Control Programme (RNTCP): Fig. 1 is an overview of major activities.

Mumbai

If one wanted to design an environment conducive to the spread of TB, failure of treatment, and emergence of resistance, Mumbai would fit the remit. A land-starved megacity in which a resident population of 12.5 million are compressed into 437 km^2 [18], Mumbai combines extreme population density with inadequate water, sanitation, and solid waste management, indoor and outdoor air pollution, an unbridled multiplicity of healthcare providers, inequalities startling in their visibility and proximity, and an epidemic of predisposing malnutrition and illness. The city has a mean population density of 49 000 per km^2 [19], over half of whom live in the informal settlements, *zopadpattis, bastis* and *chawls* loosely described as slums [18]. TB is a disease of poverty and marginality [20], and the UN-HABITAT definition of a slum could double as a pro-tuberculotic checklist: overcrowding, inadequate safe water and sanitation, poor housing fabric, and insecurity of tenure [21]. Coupled with this are epidemics of non-communicable disease: 34% of women have low body mass index, and 44% are anaemic, and 46% of children in the poorest quartile are underweight [22]. Tobacco and alcohol use are common, and diabetes — which affects an estimated 40 million Indians [23] — has a prevalence of 1900 per 100 000 in slum-dwelling men and 1170 in women.

Mumbai houses 12% of the population of Maharashtra state, but accounts for 22% of notified cases of TB and — significantly in terms of potential drug resistance — 50% of people undergoing retreatment after relapse (SHRC, unpublished data). TB treatment is estimated at 600 per 100 000 in slum areas and 458 in non-slum areas [19,22]. The RNTCP registered ∼30 000 people for treatment in 2010, of whom ∼15 000 were smear-positive and ∼2000 (9%) were children. Given that 50%–70% of people seeking treatment do so in the private sector [24], the incidence of TB in Mumbai is likely to be at least 60 000 cases annually; half of them documented in terms of type, treatment, and outcome.

The emergence of drug-resistant TB in Mumbai is a prospect so alarming that the paucity of available evidence may be a case of 'out of sight, out of mind'. What reports there are have consistently shown higher levels of MDR-TB (resistant to the 2 first-line drugs rifampicin and isoniazid) than in other parts of India, at 24%–30% of new cases [25,26] and 11%–67% of treated cases [25–27] (the corresponding figures from other parts of the country are 1%–13% and 12%–40%, respectively [28–35]). Extensively drug-resistant (XDR) TB (MDR-TB that is also resistant to both a fluoroquinolone and a second-line injectable agent) was detected in Mumbai in 2005 [36], but the most nightmarish of scenarios has been evoked by a recent report of totally drug resistant (TDR) TB [37].

In the fallout from the TDR-TB findings, which came from Hinduja Hospital and were widely reported [38], the local