

Controlling extensively drug-resistant tuberculosis

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Recent successes in the fight against tuberculosis¹ rely on short-course chemotherapy with our two most powerful drugs, isoniazid and rifampicin.² Unfortunately, not only do hundreds of thousands of people or more still die every year of curable tuberculosis,¹ but inadequate treatment has also contributed to the origination of strains of tuberculosis resistant to these two drugs, (ie, multidrug-resistant [MDR] tuberculosis).³ MDR tuberculosis can then spread from person to person, and needs expensive treatment regimens lasting 2 years or more. Further inadequate treatment can lead to resistance to crucial second-line drugs and the advent of extensively drug-resistant (XDR) tuberculosis, which is even more dangerous and expensive to treat.⁴

Nosocomial transmission of XDR strains seems to have contributed to a major outbreak in HIV-positive individuals in Tugela Ferry, South Africa.⁵ To better understand how to control XDR tuberculosis, today's *Lancet* presents a report of a new mathematical model, developed by Sanjay Basu and colleagues, of the transmission of tuberculosis in this region.⁶

Their model builds on previous tuberculosis models, and was corroborated by independently collected epidemiological data for the area. Such mathematical models of tuberculosis can be useful instruments for policymaking because they incorporate a representation of the natural history and transmission of infection and disease, and are the only way to rigorously explore the effects of policies before they are field-tested.

Basu and co-workers conclude that the interventions they analysed (ie, use of masks, reduced time as an inpatient, improved ventilation, rapid resistance testing, HIV treatment, and tuberculosis isolation facilities) have a substantial and synergistic effect, averting about half the expected cases of XDR tuberculosis by 2012. The analysis supports urgent implementation of the aforementioned control measures when possible, and suggests that the XDR problem will only get worse if nothing is done. However, their model also implies that XDR tuberculosis cannot be successfully halted without interventions beyond those studied, and therefore further implies that funding must be found for such interventions.

But what other control measures are available? Basu and co-workers show that the enforcement of involuntary detention of patients with confirmed XDR tuberculosis who refuse therapy, without isolation facilities for them, will worsen the epidemic by needlessly exposing further patients to infection. Tuberculosis control depends on patients with symptomatic active tuberculosis presenting for treatment. Thus, although not included in their model, such presentation could be jeopardised by the loss of community trust that large-scale detention might engender. When isolation facilities are sufficient, detention can only be regarded as a last resort for protection of the community when all other methods for ensuring patients' compliance with therapy have failed.⁷

Even the most complex epidemiological models make many simplifying assumptions. Basu and colleagues assumed, for instance, that fitness costs of resistance affected transmission rates, but not other virulence parameters related to the natural history. They additionally used the standard, but occasionally eschewed,^{8,9} assumption that transmission rates in

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A patient with tuberculosis in KwaZulu Natal

the community are homogeneous. The authors also assume that their single rural site in South Africa is typical. Although models must be intuitively plausible and qualitatively accurate, model validation does not necessarily follow from a good fit to the available data, because many complex models can fit limited data quite well.

Many people in the developed world have forgotten the horror of tuberculosis in the age before antibiotics, a time in which only the wealthy could retreat to sanatoria, as in Thomas Mann's *The Magic Mountain*,¹⁰ and the poor were threatened with stigma and fear, as portrayed in Victoria Spivey's *TB Blues*: "TB's all right to have, but your friends treat you so low down."¹¹ Now, as then, tuberculosis is associated with poverty. The same absence of resources that contributes to extensive drug resistance makes treatment of MDR and XDR tuberculosis impossible for many. Multidrug and extensive drug resistance are monsters of our own creation. They might be with us longer than we think and might need us to spend more than governments or institutions are willing or able to pay. Although scientific warnings are often ignored until too late, effective interventions^{2,12} for the control of XDR tuberculosis in Africa are national and international responsibilities, and the world community ignores this message¹³ at great peril.

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We thank Spivey Records for permission to reproduce lyrics from the song *TB Blues*. We declare that we have no conflict of interest.

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Burma and the challenge of humanitarian assistance

Burma's "Saffron Revolution", and the brutal military crackdown which followed it, brought the world's attention to this closed and troubled country. The Buddhist monks and nuns who led the movement have called for dialogue, democracy, and human rights. But they also called on the junta to address the initial spark of the uprising: the five-fold increase in the cost of gas, the doubling of diesel prices, and the two-thirds increases in petrol costs imposed by the junta on Aug 19, 2007. Burma's people were already in desperate straights before these price hikes. In 2000, Burma's health-care system was ranked 190th out of 191 nations by WHO.¹ UNICEF estimates that close to a third of children nationwide were malnourished in 2006, real wages were

being devoured by inflation, and HIV/AIDS, tuberculosis, malaria, and a range of other health threats were taking terrible tolls on ordinary Burmese.² UNICEF reported that Government spending on health care in Burma amounted to US\$0.40 per citizen per year in 2005, compared with \$61 in neighbouring Thailand.² Childhood (aged under 5 years) mortality was 106 per 1000 livebirths in 2006, compared with 21 per 1000 in Thailand.² The price increases were especially inflammatory for two reasons. First, they affected an already impoverished majority. One estimate is that for an average worker in Rangoon, 50–75% of daily wages would now be spent on travel alone—and fuel-price increases immediately raised the cost of basic commodities, including food.^{3,4}