# Would pan-tuberculosis treatment regimens be cost-effective?

There is an urgent need for shorter, more effective treatments for tuberculosis. A simple 6 month oral regimen, composed of three new and repurposed drugs, showed encouraging results in the treatment of extensively drug-resistant tuberculosis.[1] As a recent Comment in *The Lancet Respiratory Medicine* discussed, better tolerated analogues could allow regimens with activity against the most drug-resistant forms of tuberculosis to rival the effectiveness and tolerability of the current first-line therapy for rifampicin-susceptible (RS) tuberculosis.[2,3] Novel regimens have potential to improve drug-resistant tuberculosis outcomes; using the same novel regimen for RS tuberculosis (ie, as a pan-tuberculosis regimen) could benefit the many patients with undetected drug resistance. A pan-tuberculosis regimen might also improve programmatic efficiency, consolidate the market for tuberculosis regimens, and potentially improve RS tuberculosis treatment.

Among the uncertainties in developing and implementing pan-tuberculosis regimens, one important need is for an economic case that accounts for budgetary and epidemiological effects. To help evaluate this economic perspective, we adapted an existing transmission model[4] to estimate the affordability and cost-effectiveness of introducing a novel regimen with pan-tuberculosis potential, in a hypothetical setting representative of high-burden settings globally.

We modelled a novel regimen's health effect in a setting with tuberculosis prevalence of 300 per 100 000, HIV coprevalence of 10%, rifampicin-resistant (RR; inclusive of multidrug-resistant [MDR]) tuberculosis in 4% of new tuberculosis cases, and rifampicin susceptibility testing provided to 24% of new and 53% of retreatment patients (increasing linearly over time), reflecting averages among high tuberculosis burden countries. We assumed the regimen[4] had equivalent efficacy, duration, and tolerability to current RS tuberculosis therapy but offered the same high efficacy against RR tuberculosis. For simplicity, we assumed the regimen had a high barrier to resistance and initially required no adjustments for individual patient characteristics.

We estimated the total health system cost (measured in 2015 US$) by combining estimated health system spending (median drug and non-drug costs, stratified by RR notification status, among 30 high-burden countries)[5] with model estimates of the patients receiving each regimen. Calculations incorporated regimen prices, savings on RR tuberculosis patient management, and reductions in future tuberculosis incidence. We evaluated effectiveness (disability adjusted life-years [DALYs] saved)

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| | Effect on overall tuberculosis incidence* | | Effect on RR tuberculosis incidence | | Budget-neutral price per patient† | Incremental cost-effectiveness, per DALY averted, at specified price point‡ | | |
|---|---|---|---|---|---|---|---|---|
| | Cases averted (over 10 years, per 100 000) | Percent reduction (at 10 years) | RR cases averted (over 10 years, per 100 000) | Percent reduction (at 10 years) | | $200 per patient | $1000 per patient | $10 000 per patient |
| **Relative to no use of regimen** | | | | | | | | |
| Use of regimen for diagnosed RR tuberculosis only | 15 (8–30) | 1·2% (0·7–2·6) | 16 (8–32) | 33% (22–47) | $5600 (4300–7000) | Cost-saving | Cost-saving | $1200 (600–2100) |
| Use of regimen for all tuberculosis | 25 (13–49) | 1·8% (0·7–3·9) | 36 (23–65) | 67% (54–79) | $290 (210–430) | Cost-saving | $3900 (1800–8300) | $53 000 (27 000–110 000) |
| **Relative to use for diagnosed RR tuberculosis only (incremental adoption)** | | | | | | | | |
| Use of regimen for all tuberculosis, incremental epidemiological effect | 11 (3–24) | 0·6%§ (0–1·5) | 20 (13–35) | 33%§ (24–42) | .. | .. | .. | .. |
| Use of regimen for all tuberculosis, incremental cost-effectiveness | .. | .. | .. | .. | $128 (100–170) | $900 (200–3200) | $12 000 (4600–33 000) | $130 000 (55 000–360 000) |

MDR =multidrug-resistant. RR=rifampicin-resistant; inclusive of multidrug-resistant. DALY=disability-adjusted life-year. *All results expressed as median (95% uncertainty range) of 476 model simulations. †Price-per-patient of the novel regimen that results in net-neutral health system tuberculosis expenditure over 10 years. We assumed that the novel regimen reduced non-drug spending per RR tuberculosis patient (including costs of diagnosis and treatment monitoring) to the midpoint between the current non-drug costs of MDR tuberculosis and drug-susceptible tuberculosis. ‡Cost-effectiveness is calculated over 10 years after the introduction of the novel regimen, with costs and DALYs discounted 3% per year, and reported in 2015 US dollars. §Reductions in tuberculosis and RR incidence are calculated relative to the incidence projected at 10 years with no use of the novel regimen. Relative to the incidence projected when the novel regimen is used for RR tuberculosis only, the projected incidence with a pan-tuberculosis regimen represents 0·6% (0–1·6) and 50% (38–64) relative reductions in tuberculosis and RR tuberculosis incidence, respectively.

***Table:*** **Cost-effectiveness of a potential pan-tuberculosis regimen in a high-tuberculosis-burden setting by indication for use**

by coupling estimates of disability and years of life lost[6] with 10-year projections of tuberculosis prevalence and mortality using 3% per year discounting.

When used only for RR tuberculosis patients, the regimen was estimated to reduce RR tuberculosis incidence by 33% (95% uncertainty range 22–47) in 10 years. The cost-effectiveness case was also compelling: this new regimen was budget-neutral (ie, achieving positive epidemiological outcomes at zero net health system cost) at $5000 per patient, and could be highly cost-effective in a low-income setting (<$1200 per DALY saved) at a price as high as $10 000 per patient (table).

Using the novel regimen for both RR and RS tuberculosis doubled its estimated 10 year effect on RR tuberculosis incidence, yet this broader indication reduced cost-effectiveness. Because current RS tuberculosis treatment is inexpensive, the additional cost of treating this disease with the novel regimen must be recovered in other ways.[5] For example, the estimated cost-effectiveness of a $10 000 per patient novel regimen was $1200 per DALY saved when used for RR tuberculosis alone but $53 000 per DALY saved if used universally. A much lower regimen price (around $1000 per patient, similar to the currently recommended 9–12 month MDR-tuberculosis regimen[7]) would be needed to bring this cost-effectiveness ratio down to $3900 per DALY saved, below the per-capita gross national income of many middle-income countries (table).

The adoption of a pan-tuberculosis regimen is likely to occur incrementally, with indications increasing as experience with the regimen accrues. Once already in use for RR tuberculosis, the regimen would have to reach an even lower price point for incremental expansion to RS tuberculosis to be cost-effective (table), and only at a price point approaching $200 per patient would it fall below a $1200 per DALY-saved threshold. However, the economic outlook for new regimens is enhanced by the potential for market growth and accompanying price efficiencies as clinical performance becomes well established.

Other factors (not considered here) could also strengthen the economic case for a pan-tuberculosis regimen. If novel pan-tuberculosis regimens improve upon the current standard of care for RS tuberculosis, health gains from superior effectiveness[4] or cost reductions from shorter treatment durations[8] could improve cost-effectiveness. Improvements in programmatic efficiency, for example, reducing the need for specialised centres to manage RR tuberculosis, could yield additional cost savings. Additionally, consolidating the RR tuberculosis and RS tuberculosis regimens with a unified regimen could ease challenges of volume and forecasting faced by drug manufacturers[9] and enable economies of scale and market competition to improve access and affordability. Lastly, a highly efficacious, easy to deliver pan-tuberculosis regimen would improve patient experience and costs, by speeding time to appropriate treatment for patients with RR tuberculosis who often have a long duration of illness and substantial difficulties in initiating adequate care.

However, developing an economic case for a pan-tuberculosis regimen should not detract from the need to strengthen diagnostic infrastructure. Gaps in detection of tuberculosis drug resistance are likely to be more efficiently addressed by scaling up suitable point-of-care diagnostics[10] than by expanding a novel drug regimen. Furthermore, no regimen can remain a pan-tuberculosis regimen forever; resistance will eventually develop and require diagnostic capacity and treatment alternatives.[11] Further, as we better understand patient-level determinants of successful treatment,[12] customising regimen duration or composition to individual patients might become a preferred strategy.

In summary, new, shorter, simpler regimens with the potential to treat all forms of tuberculosis could have a transformative effect on RR tuberculosis epidemics, but using such regimens universally would be less economically favourable. To make the strongest cost-effectiveness case for universal use, novel regimens will need to hit price points approaching $200 per patient, be more effective than current RS tuberculosis treatment, offer major benefits to patient care, and show durable gains in programmatic or market efficiency.

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