**Main text**

To understand the potential burden reductions that could arise from new diagnostic tools, it is useful first to understand the distribution of infectious TB in a population, across different stages of the TB care cascade. The upper row of Figure 1 shows results from recent, national prevalence surveys in India and South Africa, highlighting patients with TB that did not report symptoms; patients suffering symptoms who had not sought care; and those that that had sought care, but remained undiagnosed. New diagnostic tools could benefit patients at all stages of this cascade.

First, at the facility level, oral swabs coupled with molecular diagnostics, or future urine-LAM tests, will be more feasible to conduct in decentralised settings, than current sputum-based tests. Such diagnostic strategies could therefore offer new opportunities to expand timely testing for TB at the primary care level. The blue curve shows the potential impact arising from this scenario, averting around 10% and 15% of cumulative TB deaths in India and South Africa, respectively (see table S3, supporting information, for a summary of impacts under all intervention scenarios). In India, the expansion of public-private mix initiatives would have an important role in amplifying this impact, by allowing it to reach more providers, and thus patients: such measures would increase incidence and mortality impact by almost 50%.

Next, to reach symptomatics who have not sought care, oral swabs or urine samples could be collected at the household level, for example facilitated by community healthcare workers who encourage symptomatic individuals to collect self samples. The red curve in both figures shows the potential impact of twice-yearly screening amongst all symptomatics in the community, averting around 17% and 12% of cumulative TB deaths in India and South Africa, respectively.

Finally, to reach those without symptoms, it is likely there will be a need to concentrate on vulnerable populations with a high prevalence of TB. Highly portable screening tools will be required, for example hand-held X-ray combined with artificial intelligence for X-ray reads. The pink curves suggest that screening those with leading risk factors (undernutrition in India, and HIV in South Africa) to identify 10% of subclinical TB would avert 1.8% and 1.7% of cumulative TB deaths in India and South Africa, respectively.

A combination of all of these interventions (green curves) would avert around 25% of cumulative TB deaths in both India and South Africa. Although substantial, these reductions alone are not sufficient to meet the SDG TB goals. Indeed, previous work has shown that, while diagnostics will play a critical role in reducing TB incidence and mortality, meeting the SDG goals will ultimately require the mass prevention of TB (refs).

**Figure caption**

Potential future impact of new diagnostic tools in high-burden countries. Shown are examples of India (left-hand column) and South Africa (right-hand column). The top row shows results from recent prevalence surveys in both countries (refs), highlighting the proportion of prevalence TB that had sought care yet remained undiagnosed (red); that had symptoms but had not sought care (green); and that did not report symptoms, despite being sputum bacteriologically positive (blue). Depending on their characteristics, new diagnostic tools could benefit patients at each stage of this sequence. The lower two rows show cumulative cases and deaths averted under different scenarios for the deployment of new diagnostic tools (see supporting information for incidence and mortality curves relating to each of these scenarios). In these plots, the green curve shows the impact of all interventions implemented in combination, while remaining curves show impacts of interventions implemented individually.

Starting at the right-hand side of the prevalence survey diagram and moving upstream, these interventions are as follows: (i) the blue curve shows a scenario where the probability of diagnosis and treatment initiation per care seeking visit is increased to 90%. Such effects could be achieved, for example, with the use of new tools based on oral swab or urine samples, both of which are easier to collect than sputum. Such tools could help expand the diagnosis of TB in decentralised primary care settings, facilitating early recognition of TB without need for multiple provider visits. (ii) In India, the impact of new diagnostic tools could be amplified if they are made available to all providers managing TB, not just the public sector. The red curve shows a scenario where new diagnostics are implemented as described above, at the same time as 90% of private healthcare providers being successfully engaged with the public programme. This combination increases the cases and deaths averted by over 50%. (iii) For both countries, the purple curves correspond to targeting symptomatics who have not sought care: shown is a scenario where people with symptoms in the general population are tested twice a year for TB, either through programme activities, or by self-testing, similar to COVID-19. Although infeasible with current tools, again the ease-of-implementation of oral swabs and urine samples may facilitate these levels of testing in future. (Iv) In both countries, the pink curves correspond to a scenario where vulnerable populations are tested without symptoms screening, assuming that 10% of subclinical TB in these populations is detected and initiated on treatment each year. Such levels of screening could be achieved with highly-portable screening tools currently in development, such as handheld X-ray combined with AI reads. In India, we assumed the vulnerable population to consist of those with undernutrition while in South Africa, we assumed this group to consist of those with HIV.

See table S1 for calibration data and table S2 for estimated baseline parameters, relevant to these interventions. See also table S3 for overall estimates for cumulative cases and deaths averted by 2030.