Testing Times for TB

Background

Covid 19 reversed years of gain in detection, notification and treatment of tuberculosis (TB), which is the second leading cause of infectious deaths after Covid 19. But what is alarming is that data shows that while acquired drug resistance remains a constant (attributable to the evolutionary cycle of drug resistance in the context of TB treatment mismanagement), it is person-to-person contact transmission that is now the driving force of the global drug-resistant TB burden. TB is by no means an outlier as far as drug resistance goes. The WHO has identified antimicrobial resistance as a top ten global health threat. But the airborne and contagious disease remains a major contributor to deaths related to antimicrobial resistance. What it means is that the bacteria causing TB have become resistant to the treatment for it leading to forms such as multi-drug resistant tuberculosis and extensively-drug resistant tuberculosis. According to the 2022 WHO Global Report, the treatment success rate for drug-resistant tuberculosis, at 60% globally, remains low. Detecting it quickly therefore becomes critical to check its spread and treat it in time.

Rapid molecular platforms for TB diagnosis enable detection of both dug-susceptible tuberculosis as well as drug-resistant tuberculosis without requiring costly laboratory set-ups. Getting the test results within the same day and even under an hour instead of the weeks it would take earlier, also means an early diagnosis, which provides a headstart for TB treatment enabling better retention in care and treatment outcomes. Till recently, Cepheid's GeneXpert platform offering high-quality testing for drug-sensitive tuberculosis remained the sole low-complexity rapid molecular platform for TB diagnosis approved by the WHO. An alternative emerged with Truenat manufactured by Molbio Diagnostics in India, which is portable and does not require an airconditioned environment to work, for instance. Contrary to the global trend, India saw a rise in TB notifications, which in 2022 even exceeded pre-pandemic levels. One of the tools facilitating this was Truenat, which besides testing and diagnosing for drug-susceptible tuberculosis

could also detect more drug-resistant TB strains than GeneXpert could and Covid 19 among other diseases. Having since earned WHO prequalification it will be adopted worldwide.

Pricing it Right

During Covid 19 , the vaccines, diagnostics and treatments largely financed with public money remained out of reach because of unaffordable pricing or lack of equitable access. Disappointingly, The Political Declaration to end TB by 2030 still had no explicit commitment to ensure public spending was tied to access conditionalities. Hence, pricing the Truenat device is critical to ensuring that if taken to scale, it reaches those who need it where they need it without going out of pocket.

A partnership between the Global Fund, USAID and Stop TB Partnership with manufacturer Molbio Diagnostics will reduce the price of the Truenat cartridge, from $9 to $7.90, to offer more affordable access to it across the globe. The low price is also due to the learning from the GeneXpert experience. The Global Fund found that the initial high price of the GeneXpert cartridge led to countries choosing to ration its use to prioritized groups or only used it after initial diagnosis by other tests like smear microscopy, X-ray, among others. Once the pricing went down from $9.98 to $7.97, to match the market alternative, countries used the substantial savings to reinvest in increased procurement of the cartridges expanding the use of the rapid molecular diagnostic test. Additionally, manufacturers of both platforms assured enhanced commitments to expand access to comprehensive global service and maintenance standards.

Challenges

Speaking at a 2023 Global Antibiotic Research and Development Partnership (GARDP) webinar Hema Srinivasan, Senior Advisor, MedAccess pointed out that market shaping remains largely focused on the supply side without considering the complementary demand side of the market in all its nuance and importance. Why? because it's simpler to talk about price, funding, revenue and volume guarantees. But the critical part to ensure adoption of the test also includes product evaluations and training as well as supply planning. This holds true for the rapid diagnostic tests as well. The Truenat, for instance, is semi-automatic and staff need to be trained in the manual steps required. GeneXpert requires annual refitting and recalibration. The challenge of also ensuring sustainability in domestic financing of molecular diagnostics for TB had been pointed out by the Office of the Inspector General in an audit of the Global Fund related to GeneXpert.

According to a 2021 presentation by Brenda Waning, Chief of the Global Drug Facility, Stop TB Partnership, the proportionate share of diagnostics across the board in Global Fund 2021 Procurement Estimates of $260 million to 122 countries for 2021, was higher than it was in the Grant Cycle 2017-2019 period and in 2020 of the next cycle as well. However, the 37th Stop TB Board meeting held in February 2024, noted with concern that unfunded country requests under the Global Fund's Grant Cycle 7 totalled USD 1.2 billion and these included funding for essential commodities, especially rapid molecular

diagnostics. While appreciating the collaborative partnerships by global funders and manufacturers in molecular diagnostics, the Stop TB Board admitted that below-par TB budget allocations have caused national TB programs to either scale back on the actual rollout of the molecular diagnostic platforms and/or adopt algorithms that embed restrictions in their use. Countries like India and Indonesia have benefitted from innovative combinations of blended loan and grant financing backed by the World Bank and Global Fund, and the Stop TB Board called for such arrangements to be extended to other TB high burden countries.

With the rapid advances in treatment, molecular diagnostic tests must be able to keep pace to detect resistance to the newer/repurposed drugs under the evolving WHO approved treatment regimen. But whether the required recurring investments into the multiple diagnostic tools that will emerge in the market will be available and whether these tests will remain affordable and accessible will reflect the seriousness with which global health initiatives and countries take the threat of tuberculosis.

The immeasurable benefits of ending TB

The collaborative partnerships in diagnostics for TB are not restricted to TB alone but also benefit the health sector as they detect other diseases as well and the learning can be used in other health interventions. Averting cases of tuberculosis and averting deaths due to it also has wider social implications. It will reduce the stigma around people and families who live with the threat of the disease who are more likely to be from already marginalized communities and with low socio-economic status living in low- and middle-income countries. In the words of a TB survivor in India who was unable to share his tuberculosis status with his own brother and got through only because of the tremendous support from his parents and doctor: “No matter how educated the other person the reaction to a disease like TB will always be disturbing. Recently, one of the patients at the hospital I work died not because of the disease or treatment but the social stigma. She committed suicide and died. We usually ignore the underlying NCDs associated with communicable diseases like TB.” Hence, while putting a price on ending TB the world needs to also prize health equity and realise that there are many benefits of ending tuberculosis that do not get quantified as was pointed out by a 2023 cost-benefit analysis of increased spending to do so that drew on the Global Plan 2023-2030 to end tuberculosis.

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