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## The way forward for drug-resistant tuberculosis in the Philippines

Dean and colleagues<sup>1</sup> highlighted the effect of the COVID-19 pandemic on the diagnosis and treatment of drug-resistant tuberculosis, resulting in reduced case notification rates and number of patients receiving treatment for drug-resistant tuberculosis. In the Philippines, a lower-middle-income country in southeast Asia where around a million individuals have tuberculosis, disruptions in health services due to the pandemic have severely affected the incidence notification of drug-resistant tuberculosis—the Philippines is one of ten countries accounting for 70% of the gap between the estimated global incidence of drug-resistant tuberculosis and the number of people enrolled in treatment.<sup>2</sup> Nationally, only 57% of newly diagnosed tuberculosis cases have drug susceptibility testing results.<sup>3</sup>

Early detection with the Xpert MTB/XDR assay was recently integrated into the Philippines' drug-resistant tuberculosis diagnostic algorithm due to its low complexity, enabling decentralisation and scaled-up screening in peripheral laboratories.<sup>3</sup> However, the implementation of these tests is hampered by insufficient digital surveillance systems that link patients and their clinical data and allow referral to subsequent health facilities for treatment.<sup>1</sup> Furthermore, the lack of Xpert cartridges and long turnaround times have resulted in high rates of loss to follow-up, especially in community-based initiatives. Support for patients with interrupted treatment has not been established, contributing to the prevalence of drug-resistant tuberculosis.<sup>2</sup>

Filipino patients face substantial barriers to drug-resistant tuberculosis care in terms of health financing, infrastructure, and workforce. The National Tuberculosis Program is crucially underfunded, with available

resources amounting to only 37% of the actual need.<sup>4</sup> Notably, the national health insurance does not cover drug-resistant tuberculosis treatment, Xpert, or culture.<sup>4</sup> The health-care system is also understaffed, with most health-care workers stationed in private tertiary hospitals. Drug-resistant tuberculosis hotspots, particularly in geographically isolated areas and prisons, face greater challenges in accessing drug-resistant tuberculosis health-care services.<sup>5</sup> Only a small proportion of high-risk and vulnerable groups are being reached with current drug-resistant tuberculosis screening and testing services.

We agree with Dean and colleagues<sup>1</sup> that timely and accurate epidemiological surveillance is central to addressing drug-resistant tuberculosis. Locally, there is a need to build sentinel surveillance systems and integrate next-generation sequencing into the national anti-drug-resistant tuberculosis surveys to document local resistance patterns. Transitioning from paper-based recording to case-based digital surveillance systems will allow real-time data aggregation and analysis. Active case-finding initiatives through predictive analytics and hotspot mapping will greatly improve case detection. Lastly, strengthening patient referral systems and emphasising adherence to treatment are crucial to minimising the emergence of resistance to new drugs for drug-resistant tuberculosis.

We declare no competing interests.

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1 Dean AS, Tosas August O, Glaziou P, et al. 25 years of surveillance of drug-resistant tuberculosis: achievements, challenges, and way forward. *Lancet Infect Dis* 2022; published online March 3. [https://doi.org/10.1016/S1473-3099\(21\)00808-2](https://doi.org/10.1016/S1473-3099(21)00808-2).

2 WHO. Global tuberculosis report 2021. Geneva: World Health Organization, 2021.

3 Philippines Department of Health. National tuberculosis control program: manual of procedures 6th edition. Manila: Republic of the Philippines Department of Health, 2020.

4 Philippines Department of Health. Joint program review 2019 report. Manila: Republic of the Philippines Department of Health, 2019.

5 Phelan JE, Lim DR, Mitarai S, et al. *Mycobacterium tuberculosis* whole genome sequencing provides insights into the Manila strain and drug-resistance mutations in the Philippines. *Sci Rep* 2019; **9**: 9305.

## Effect of novel antimalarial ZY-19489 on *Plasmodium falciparum* viability in a volunteer infection study

Bridget E Barber and colleagues<sup>1</sup> published a first-in-human study of the antimalarial activity of ZY-19489, a novel triaminopyrimidine, in healthy volunteers. In this study, rapid initial parasite clearance, with a half-life of approximately 7 h, occurred in all 15 participants after administration of a single dose of either 200 mg, 300 mg, or 900 mg, with the rate of initial clearance being dose-independent. This observation suggests that the maximal killing rate might saturate at doses as low as 200 mg. However, we have previously shown that parasite clearance, as measured by quantitative PCR (qPCR), might not fully capture the parasite killing activity of antimalarial drugs.<sup>2</sup> Previously, we developed a method to assess parasite viability after in-vivo exposure to an antimalarial drug,<sup>2</sup> which was used to compare total circulating parasite number (traditionally measured by microscopy or PCR) with viable parasite number (measured by an ex-vivo viability assay) in another volunteer infection study.<sup>3</sup> Our analysis revealed that parasites are rendered non-viable by artesunate more rapidly than previously thought,<sup>2</sup> suggesting that measuring circulating parasite