India should speed up access to bedaquiline-based all-oral regimens, not procrastinate further

We read with concern the Editorial by Jain[1] suggesting that India is moving too quickly when it comes to rolling out bedaquiline (BDQ)-based, all-oral regimens for drug-resistant forms of tuberculosis (DR-TB). India is home to the largest population of people living with DR-TB in the world,[2] and improving access to innovative diagnostic and therapeutic approaches is the only way the country will be able to move beyond its crippling TB problem. We would disagree with several of the authors' claims and argue that India hasten to adopt all oral MDR regimes if it is to keep its pledge of eliminating TB by 2025.

Touting the efficacy of the so-called "Bangladesh" regimen, no mention is made however of the high rates of failure of this regimen if used in multidrug-resistant tuberculosis (MDR)-TB "hotspots" with high rates of additional resistance. Our study in Mumbai, where fluoroquinolone resistance is commonly encountered, showed that <5% of 559 patients were actually sensitive to all the drugs in the Bangladesh regimen when complete genotypic and phenotypic drug susceptibility tests were checked.[3] The paper also fails to mention more recent publications showing high rates of treatment success with new all-oral regimens. Indeed, a recent study by Khan *et al*. showed culture conversion rates of 83.8% (526/628) in patients receiving all oral BDQ or delamanid-based regimens in the end-TB observational study conducted in 15 high-burden countries across the globe.[4]

Oral regimens may also serve to dramatically shorten treatment of MDR-TB to just 6 months as in the on-going TB-PRACTECAL trial, the world's first new all-oral trial. This study has stopped enrolling patients after initial clinical data showed the superiority of a regimen of bedaquiline, pretomanid, linezolid, and moxifloxacin over current care.[5] The trial data have been shared with the World Health Organization (WHO), and such regimens could not only save thousands of lives but also vastly improve the quality of these lives.

The editorial by Jain[1] also glosses over the unacceptable rates of serious adverse events – including permanent hearing loss – as well as the trauma associated with injectable therapy use. Given that monitoring for hearing loss is virtually nonexistent in most parts of India, the use of injectable agents is far more dangerous than that of the new oral drugs, whose safety has been clearly demonstrated at all age groups and even when given in combination.[6]

Finally, the author relies on tired and ill-informed arguments regarding cost, which only take into account the up-front costs of medications. Conveniently ignored are the rights and perspectives of the affected community, who have stated a clear preference for injectable-free DR-TB treatment regimens.[7] The vast majority of practicing physicians would clearly choose BDQ (oral, WHO Group A) over amikacin (injectable, WHO Group C) if they were afflicted with DR-TB. Why then should we accept anything less for our patients?

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Conflicts of interest
Zarir F Udwadia was invited by WHO to be on their DR-TB guidelines group.

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