the failure rate turned out to be higher than 10%. A third concern was that the results based on the per-protocol analysis were overemphasised in the conclusion. We respectfully disagree with this comment. We suggested, rather than concluded, that linezolid might have a role in treating drug-susceptible tuberculosis based on the per-protocol analysis.

According to another suggestion, we did an additional subgroup analysis of patients with tuberculosis who showed cavitation on chest x-ray. However, no difference was found in culture conversion at 2 months or in the times to culture conversion in these patients in the modified intention-to-treat analysis. Negative cultures in liquid media at 8 weeks of treatment were observed in 39 (71%) of 55 patients in the control group, 35 (73%; p=0·82) of 48 patients in the linezolid 2 weeks group, and 41 (76%; p=0·55) of 54 patients in the linezolid 4 weeks groups. The median time to culture conversion from randomisation in liquid media was 56 days (IQR 32–58) in the control group, 32 days (28–54; p=0·06) in the linezolid 2 weeks group, and 30 days (14–56; p=0·12) in the linezolid 4 weeks group.

Finally, a concern was raised regarding the use of linezolid, a potentially toxic drug, for pulmonary tuberculosis without any resistance. We believe that any physician who has seen the substantial effects of linezolid for patients with multidrug-resistant tuberculosis[4] wonders whether this drug can be safely used to improve the treatment outcome in patients with drug-susceptible pulmonary tuberculosis. The results of our trial[3] show that use of linezolid for up to 4 weeks is safe and potentially effective for pulmonary tuberculosis without the development of resistance.

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Zika's passage to India

Kriangsak Ruchusatsawat and colleagues[1] reported an observational study of individuals with suspected Zika virus infection in Thailand between January, 2016, and December, 2017. Phylogenetic analysis suggested persistent circulation of Zika virus in Thailand since at least 2002. This finding is important because it suggests that Zika virus has the potential for endemic transmission. Although comparable data for other Asian countries are not available, concern exists about possible epidemic transmission elsewhere in Asia, particularly in India.[2] Four Zika cases were reported in India in 2016–17, which were probably due to local transmission because the individuals did not report any travel history in the past several months.[3] But travellers are also a potential source of Zika virus in India, particularly individuals from Malaysia and Singapore, where Zika cases have been reported in the past 3 years.[4]

The more recent outbreaks of Zika virus in India are a major cause for concern. In late 2018, 159 cases of Zika virus infection were reported in Rajasthan[5] and 127 in Madhya Pradesh.[6] Since most Zika virus infections are mild or asymptomatic, the extent of these outbreaks is probably underestimated, and the consequences could be severe if the pattern continues into 2019. As many as 465·7 million people in India could become infected if a major Zika virus outbreak was to occur.[7] On Dec 13, 2018, the US Centre for Disease Control and Prevention issued a level 2 alert for travellers to India, recommending enhanced precautions against Zika virus infection and advising pregnant women not to travel to affected areas.

Numerous parallels exist between India, Thailand, and the most affected countries in South America, particularly the similar climates, distribution of mosquito species, and prevalence of other arboviruses such as chikungunya and dengue. The widespread poverty and large population in India make uncontrolled spread of Zika virus likely.[8] Ruchusatsawat and colleagues[1] suggested that Zika virus in Thailand has found a so-called middle ground, with transmission levels high enough to maintain the virus but not high enough for widespread immunity to develop; perhaps a similar dynamic has been established in India.

130 pregnant women in Thailand had Zika virus infection between January, 2016, and August, 2018, of whom 119 gave birth, with four babies having microcephaly.[1,9] During this period, 285 cases of microcephaly were reported in Thailand with no maternal history of Zika virus infection. Three of these cases were identified as congenital Zika virus syndrome. No similar data exist for India, but mechanisms need to be put in place to identify Zika congenital syndrome or other serious disease manifestations in the country. We note with some concern the advisory note of the Indian Ministry of Health and Family Welfare titled *Zika virus strain that causes microcephaly not found in Rajasthan*, the content and title of which seem to imply the Zika

For the **advisory note from the Government of India** see http://pib.nic.in/newsite/PrintRelease.aspx?relid=184586

virus strains in India do not cause microcephaly. This conclusion is based on the absence in Zika viruses isolated in Rajasthan of a single mutation[5] that has been associated with neurovirulence in vitro and in mice.[10] No genetic or epidemiological data exist to support this claim, which we consider to be dangerously simplistic.

We believe that data for India similar to that reported by Ruchusatsawat and colleagues for Thailand are urgently needed, allowing Indian authorities to adopt the most appropriate public health strategies to deal with the risk of a major Zika outbreak.

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Bedaquiline and delamanid in combination for treatment of drug-resistant tuberculosis

Here we report on the final outcomes for the cohort of 28 patients from Armenia, India, and South Africa who initiated regimens containing the combination of bedaquiline and delamanid from January to August, 2016, for the treatment of multidrug-resistant tuberculosis in our cohort study.[1] The median duration on combination treatment was 12 months (interquartile range [IQR] 5·9–20·0); 17 (61%) of 28 patients received the combination for more than 6 months.

Overall, 13 (46%) patients were cured or completed treatment, five (18%) died, five (18%) were lost to follow-up, four (14%) had treatment failure, and one (4%) was transferred-out. There were no significant differences on the basis of HIV status. One death was previously reported as probably due to immune reconstitution inflammatory syndrome;[1] four additional deaths were considered to be a result of meningitis in advanced HIV (in two patients), disease progression and treatment failure (in one patient), or cardiopulmonary failure (in one patient). Median time to loss to follow-up was 6·7 months (IQR 6·2–14·9). Of four cases of treatment failure, two never had sputum culture conversion and two had sputum culture conversion by month 6 but reconverted to positive.

In total, there were 26 serious adverse events (SAEs) encountered by ten (36%) patients; an overall incidence of 6·22 SAEs per 100 person treatment months. One instance of QT corrected by means of the Fredericia prolongation greater than 500 msec at month 7 was reported.

In light of WHO recommendations,[2] our data constitute a meaningful contribution to the evidence base, which has a paucity of programmatic data on the use of bedaquiline and delamanid in combination.[3] Given the complex resistant strains of multidrug-resistant tuberculosis observed among this cohort (86% with fluoroquinolone resistance) and the severity of the cases, a treatment success rate of 46% is not surprising in light of the poor prognosis anticipated.[4] Additionally, our data support the safety of using bedaquiline and delamanid in combination, with a reassuring cardiotoxicity profile and relatively few SAEs directly attributed to the combination.[5] Earlier initiation of effective regimens would improve the chance of cure for patients with few therapeutic options. Concomitant use of effective drugs should be ensured for such patients, while awaiting the findings from ongoing clinical trials.

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