

Extensively drug-resistant tuberculosis in South Africa

Keertan Dheda and colleagues (May 22, p 1798)¹ report extremely poor treatment outcomes for patients with extensively drug-resistant (XDR) tuberculosis in South Africa and conclude that prevention of XDR tuberculosis through strengthening of tuberculosis programmes overall should be prioritised.

Most patients diagnosed with XDR tuberculosis in this cohort (72%) had previously been diagnosed with multidrug-resistant (MDR) tuberculosis. Presumably, these patients received treatment for MDR tuberculosis before diagnosis of XDR tuberculosis. The standard treatment available for MDR tuberculosis at the time of the study, as described, is a relatively weak regimen likely to lead to amplification of resistance—patients with strains of *Mycobacterium tuberculosis* already resistant to one of the second-line injectable agents or a fluoroquinolone are likely to develop XDR tuberculosis even with good treatment adherence.

Thus, another important strategy to prevent XDR tuberculosis is to ensure adequate treatment of MDR tuberculosis. A regimen for all cases of MDR tuberculosis that contains moxifloxacin and at least three other drugs that are likely to be effective will no doubt substantially reduce the creation of XDR tuberculosis during treatment. Contrary to what some suggest,² moxifloxacin is well tolerated and unlikely to contribute to additional adverse events.³ Such a regimen needs to balance tolerability against efficacy, both in terms of cure and prevention of further resistance.

The contribution of previous treatment of MDR tuberculosis to poor outcomes in this study is unclear, but might well explain the disparity between this study and the relatively good outcomes reported from Peru in patients treated with more robust

second-line regimens.⁴ Given extensive previous treatment in the South African cohort, outcomes might not be generalisable to patients initially diagnosed with XDR tuberculosis and treated appropriately.

We declare that we have no conflicts of interest.

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- 1 Dheda K, Shean K, Zumla A, et al. Early treatment outcomes and HIV status of patients with extensively drug-resistant tuberculosis in South Africa: a retrospective cohort study. *Lancet* 2010; **375**: 1798–807.
- 2 Migliori GB, Sotgiu G. XDR tuberculosis in South Africa: old questions, new answers. *Lancet* 2010; **375**: 1760–61.
- 3 Dorman SE, Johnson JL, Goldberg S, et al. Substitution of moxifloxacin for isoniazid during intensive phase treatment of pulmonary tuberculosis. *Am J Respir Crit Care Med* 2009; **180**: 273–80.
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Keertan Dheda and colleagues¹ found poor treatment outcomes and high mortality in patients with extensively drug-resistant (XDR) tuberculosis in South Africa. Only 19% of patients showed culture conversion and I am very surprised to see that drugs such as amikacin, kanamycin, and ofloxacin were used in the treatment regimen despite the fact that all the patients with XDR tuberculosis were resistant to them. Ofloxacin was used in 18% of patients and thus might have contributed to poor culture conversion.

The high mortality seen in this study is a matter of great concern. Since the number of deaths was not significantly different in patients with or without HIV infection, Dheda and colleagues should have looked for other important comorbidities such as diabetes mellitus in patients with XDR tuberculosis. Diabetes has been shown to be the most common comorbidity in patients with culture-confirmed tuberculosis.² It is also well known that diabetes has

a negative effect on the outcome of tuberculosis treatment. Diabetes is associated with longer time to culture conversion, treatment failure, and high mortality rate in patients undergoing tuberculosis treatment.^{3–5}

In a setting with a high degree of HIV co-infection, careful considerations must be given to supervised treatment of susceptible and multidrug-resistant tuberculosis with the appropriate regimens along with management of important comorbidities to prevent the emergence of XDR tuberculosis. More such studies are required to provide greater insight into the menace of XDR tuberculosis.

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- 1 Dheda K, Shean K, Zumla A, et al. Early treatment outcomes and HIV status of patients with extensively drug-resistant tuberculosis in South Africa: a retrospective cohort study. *Lancet* 2010; **375**: 1798–807.
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Authors' reply

We agree with Helen Cox and colleagues that, given the poor treatment-related outcomes for extensively drug-resistant (XDR) tuberculosis, and the likelihood of multidrug-resistant (MDR) tuberculosis progressing to XDR tuberculosis, hitting hard with the most potent available drug regimen at first contact with MDR tuberculosis is crucial for prevention of XDR tuberculosis.¹ Thus, it would be rational to use third-generation fluoroquinolones to treat MDR tuberculosis.

The printed journal includes an image merely for illustration