Association of Drug Susceptibility Testing Results for First- and Second-line Drugs With Treatment Outcomes in Patients With Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis

To the Editor—We read the meta-analysis by Bastos et al recently published in Clinical Infectious Diseases [1]. Because of our interest in the association of drug susceptibility testing (DST) results for first- and second-line drugs with treatment outcomes in patients with multidrug-resistant (MDR) tuberculosis and extensively drug-resistant (XDR) tuberculosis, we carefully read the entire article. In this study, the investigators first performed a meta-analysis of 31 cohort studies of patients with MDR and XDR tuberculosis to assess the relationship between treatment outcomes and results of culture-based DST for pyrazinamide, ethambutol, and the second-line drugs. They reached an important conclusion that DST for ethambutol, pyrazinamide, and second-line...
tuberculosis drugs appears to provide clinically useful information to guide selection of treatment regimens for MDR and XDR tuberculosis. It is a valuable study. Nevertheless, there are some comments we would like to raise related to this article.

First, we think that there are some deficiencies in the literature search. Three systematic reviews [2–4] of MDR treatment outcomes were searched by the investigators, all of which were published between 2009 and 2010; we are wondering why the investigators did not search studies after 2010. The incomplete search protocol may be regarded as a drawback of this meta-analysis. We suggest that the investigators search the studies once again and give us a reasonable explanation for the original search protocol to strengthen the credibility of the meta-analysis.

Second, patients who received >1 quinolone or injectable drug were excluded from this analysis. If possible, the investigators should explain this exclusion criterion. Third, the numbers of missing values were imputed for the 5 covariates: age, sex, human immunodeficiency virus infection, extent of disease, and previous history of tuberculosis treatment in multivariable analyses. For imputation, they used the mean from the other members of the same cohort to which the individual belonged if more than half the cohort members had values for that variable, or the mean value from all analyzed individuals. We have doubts as to whether the missing values imputation method is correct.

Fourth, the investigators did not adjust in multivariate analysis for clinical characteristics such as prior treatment, resistance patterns, and concomitant use of other drugs. Meanwhile, they also did not extract data on the medication duration with each individual drug, which might have an influence on the odds of treatment success when assessing DST results. In our opinion, the investigators should add these factors in the multivariate analysis to increase the credibility of the meta-analysis.

Finally, there are differences between laboratories with regard to the DST methods and critical concentrations in all included studies. The differences could affect DST results and make the meta-analysis less credible. If possible, the investigators should analyze the DST method and critical concentrations in all included studies to reduce the influence of this factor.

We thank Bastos et al for their contribution to the assessment of association of DST results for first- and second-line drugs with treatment outcomes in patients with MDR and XDR tuberculosis. However, additional studies are needed to improve, standardize, and validate the laboratory methods and critical concentrations for these tests.

Note

Potential conflict of interest. Both authors: No reported conflicts.

Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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