Reply to Wang and Zhang

TO THE EDITOR—We thank Drs Wang and Zhang for their interest in our manuscript [1, 2]. To clarify the 5 points raised by them:

1. An additional updated literature search had been conducted by the authors (D. Menzies and H. Hussain) to identify additional studies that had been published since the last systematic review and might otherwise have been included in the individual patient data (IPD). Of 523 titles identified, 30 were selected for full text review. Thirteen were additional reports on the cohorts that were already in the IPD data set, and 11 were excluded, leaving 6 studies with a total of 613 patients. However, the characteristics of these 613 patients were very similar to those of the patients included in our analysis, and considering the large data set already included in our study (almost 9000 patients), we are confident that the addition of these studies would not have significantly impacted the current results.

2. The use of >1 quinolone or injectable was a marker of failure—we believed that including these patients in our analysis would have biased our results.

3. We presented the results of the multivariate analysis using mean values from members of the same cohort. In each table where these analyses were presented, we added footnotes with the information of how often the imputation was needed—for all covariables <15% of the data were missing. Also as we stated in the Methods, we performed a sensitivity analysis using probabilistic imputation [3], and the results using this method were virtually identical (estimates and 95% confidence intervals).

4. Although we agree that a major challenge of our study was potential confounding, we did adjust for indicators of

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severity of disease, prior therapy with first-line and second-line drugs, and resistance pattern (as stated in methods and in Tables 2–5). We also looked at whether certain centers were more likely to give drugs when the patients were resistant to that drug—indicating suboptimal availability of other drugs—but no such confounding was detected (Table 6 and Supplementary Tables 4A–E).

5. We have already mentioned in the Discussion section that the lack of standardization of laboratory methods is an important limitation in our study. For this reason we described (in Supplementary Tables 1 and 2), the laboratory methods for first-line and second-line drugs for each cohort included in our manuscript. We also performed and reported secondary analysis to assess these issues. In Table 7 and Supplementary Table 3, we analyzed the association of treatment outcome with different critical cut-points to define susceptibility/resistance. We also stated in results that we found no difference in results with use of solid vs liquid media.

Note

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

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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