Reply to Chen et al

To the Editor—We thank Chen et al for their interest and response to our brief report and appreciate the opportunity to clarify the most notable findings reported.

We believe that our finding that a complex *Mycobacterium tuberculosis* infection (defined by multiple copy numbers in at least 1 mycobacterial interspersed repetitive units–variable number of tandem repeats [MIRU-VNTR] locus) was independently associated with a nearly 2-fold increase in the odds of a persistently positive sputum culture after 2 months of treatment is the most important novel result we report. While multidrug resistance was indeed the risk factor most strongly independently associated with an increased odds of persistent culture positivity, the relationship between multidrug resistance and poorer treatment response has been well documented by others and is an expected finding.
Although we also appreciate the interest in final treatment outcome, we elected to follow a larger cohort for a shorter time, rather than a smaller cohort for a longer duration; this choice was motivated by both an interest in estimating the prevalence of complex infections with greater precision and previous data from this setting indicating that a substantial fraction of patients have positive sputum culture results after 2 months of treatment. Furthermore, it would not have been possible to select a subset of patients for longer follow-up (as Chen et al suggest could have been done), given the delays in obtaining culture and MIRU-VNTR results.

We emphasize that the drug susceptibility testing that was reported was done using an accepted standardized approach (1% proportion method), and we cannot determine whether any participants were affected by heteroresistance (ie, within-host diversity of isolates with respect to drug susceptibility), which would have required alternative drug susceptibility testing strategies.

We appreciate the authors’ data demonstrating that bacterial populations display a diversity of resistance patterns in China, a fact that has also been previously described in many other settings. However, this is unrelated to the question we were exploring in our study, which focused on the presence of multiple infections within a host. We note that the use of the term ‘heteroresistance’ by Chen et al differs from the commonly accepted one [1], which refers to the presence of within-host resistance diversity, rather than the between-host resistance diversity that they describe.

Notes

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Office of the Director, the National Institute of General Medical Science, or the National Institutes of Health.

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