Reply to Baker and Holtom

To the Editor—We thank Drs Baker and Holtom [1] for their thoughtful comments on the low number of smear-negative, culture-positive tuberculosis cases in our study [2] and another recent study [3] of the GeneXpert MTB/RIF assay (Xpert). They astutely point out that this may have led us to underestimate the potential benefit of Xpert in low-burden settings. We agree that the incremental sensitivity of Xpert in sputum smear–negative patients is an area of added benefit of Xpert; as noted, multiple studies show that Xpert can detect more than half of all smear-negative tuberculosis patients in low-burden settings [4]. However, a single sputum Xpert will miss some cases of smear-negative tuberculosis, and in another recent study from Montreal, the sensitivity of Xpert was only 28% (95% confidence interval, 10%–56%) in this population [5]. This raises the concern that the spectrum of paucibacillary disease could be well below the threshold of Xpert detection in some settings, such as when those undergoing Xpert are identified through active case finding [6]. We fully agree with Baker and Holtom that the value of a positive result in this setting is high, but to better understand the negative predictive value of Xpert and to better inform revised hospital tuberculosis infection control policies, additional high-quality data are needed on Xpert sensitivity among smear-negative patients, on the number of Xpert tests needed to detect smear-negative tuberculosis, and on the incremental cost-benefit ratio of serial Xpert testing.

In addition, Xpert offers at least 2 other potential clinical benefits in low-burden settings, which we were unable to evaluate because the relevant clinical scenarios did not occur in our population during the study. These include the use of Xpert as an add-on test to exclude tuberculosis among patients testing sputum microscopy positive for acid-fast bacilli due to other pathogens, such as nontuberculosis mycobacteria; and the use of Xpert as a screening test for multidrug-resistant tuberculosis. All of these additional potential benefits, combined with the high accuracy, rapid turnaround time, and cost savings for smear-positive tuberculosis demonstrated in the studies [1, 2, 3, 7], make Xpert a valuable tool in low-burden settings.

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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