MATERIALS AND METHODS (Supplementary materials)

Statistical analysis.

Development and validation of multi-variable risk prediction model

We developed a risk prediction model for active TB disease by using multi-variable logistic regression analyses. First, we used a bootstrap backward selection algorithm, with all the selected candidate predictors except the IGRA test, to assess the importance and consistency of each candidate predictor of active TB disease. The procedure provided the number of times each candidate predictor was selected out of the total number of bootstrap replications, which we used as an indicator of the degree of importance and consistency of each candidate predictor. The higher the number of appearance, the more important and consistent the candidate predictor is. We used 1000 bootstrap replications and a significance level of 10% ($p<0.1$) for removing a candidate predictor from the model in the backward selection method.

We then fitted multi-variable logistic regression models starting with all the candidate predictors, arranged in decreasing order of number of times each candidate predictor was selected in the 1000 bootstrap repetitions. We progressively eliminated the least important/consistent candidate predictor one at a time regardless of the p-value, using Likelihood Ratio Test (LRT) after each removal to assess whether the model without the least important/consistent candidate predictor fits the data as good as the model including that candidate predictor at 5% level of significance. A candidate predictor was then discarded based on its degree of importance, consistency as well as the LRT. The model selection procedure was repeated until we obtained the most parsimonious clinical prediction model.

The selected clinical prediction model was then extended with the addition of IGRA test to assess the incremental effect of a positive IFN-ɣ response on predicting active TB disease. Calibration of the models was assessed using Hosmer-Lemeshow goodness-of-fit test. The

ability of the prediction models to discriminate between active TB disease and OD was assessed by calculating the area under the receiver operating characteristic curve (AUC). Finally, internal validation of the clinical prediction model was carried out using bootstrapping techniques with 1000 bootstrap repetitions in a macro to assess the stability of the adjusted odds-ratio (AOR) and the AUC through their normal-based 95% confidence intervals.

All statistical analyses were carried out using STATA software version 13 (StataCorp, College Station, TX, USA).