Cost-optimisation of screening for latent tuberculosis in close contacts

To the Editors:

We read with great interest the article by DIEL *et al.* [1] in a recent issue of the *European Respiratory Journal*. We believe that the authors have been successful in modelling and analysing the cost of alternatives for tuberculosis (TB) contact investigation. Nevertheless, we have some hesitation regarding a simplifying assumption that the authors have made in the follow-up of subjects after a positive screening test.

According to the contact investigation protocol modelled by DIEL *et al.* [1], close contacts with positive initial screening should undergo a chest radiograph, and those who do not receive treatment for latent infection may be followed up with two additional chest radiographs. A probability of 1% was assigned for suspicion of active TB in the follow-up of a positive screening test in all screening strategies. Several studies suggest that the sensitivity of QuantiFERON-TB Gold (QFT-G) in detecting latent or active TB is similar to (if not higher than) that of the tuberculin skin test (TST) [2–4], and its specificity is significantly higher, as QFT-G is not affected by previous bacille Calmette–Guérin (BCG) vaccination [2, 5]. This implies that QFT-G must have a remarkably higher positive predictive value in the presence of a high rate of previous BCG vaccination, and therefore that a higher number of subjects should undergo further work-up for the detection of TB after a positive QFT-G test. In the data provided by the authors, the number of positive TST results is 4.4 times as high as the number of positive QFT-G results (137 *versus* 31). Assuming that QFT-G and TST will result in the same rate of active case detection in the long run (an assumption upon which the cost minimisation analysis is justified), the positive predictive value of QFT-G for detection of active TB must be at least quadruple that of TST. The positive predictive value of the combined tests in other branches of the model should even be higher. This is in contrast with the authors' approach in assigning similar probabilities of suspecting TB in all branches of the decision tree.

Fortunately, since subjects suspected of having tuberculosis exit the model immediately, this is a conservative assumption in favour of the tuberculin skin test. Therefore, the overall conclusion of the study that QuantiFERON-TB Gold is less costly than the tuberculin skin test remains valid. Nevertheless, the calculated level of cost savings and also the rank order of the alternative strategies might be affected.

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From the authors:

I would like to thank M. Sadatsafavi and M. Najafzadeh for raising an interesting concern. First, our cost minimisation analysis [1] was not a cost-effectiveness analysis between the consequences of isoniazid treatment and nontreatment over several decades; it only considered costs that accumulated over the 2 yrs following the last possible moment of exposure of the contact person to the infectious source case.

Secondly, we had to include new tuberculosis (TB) cases that were typically identified in large contact studies in our model. These generally equate to ~1% of the contact persons investigated, and, because they do not result in further investigation costs, must be shown to drop out of the cohort under suspicion. In our model, we distributed this “dropping out” over the entire 2-yr period. The crucial point, however, is simple: previous molecular–epidemiological studies [2–4] have shown that two types of TB cases may be expected in contact investigations of the kind we studied. On the one hand, there are TB cases with no epidemiological connection to the source case in question, *i.e.* they must have been infected by another source case at the same time or even many years prior to their diagnosis. On the other hand, there are secondary cases (re-activations) of infections that are actually acquired from the source case. Only these cases could be directly assigned to contacts that had previously tested positive using the tuberculin skin test or QuantiFERON-gold. Depending on the risk profile of the source case and its contacts, the proportions of the two types will vary and cannot be predicted.

Thus, although we found a number of positive tuberculin skin tests 4.4 times higher than positive QuantiFERON-gold results, we currently do not know whether the positive predictive value of the QuantiFERON-gold is really higher