VAN LEEUWEN *et al.* [1] mention that speed to rule out TB is of great importance in terms of infection-control measures. However, with the exception of immunosuppressed individuals or young children in whom immediate clinical work-up is mandatory, IGRA tests and TST take 6–8 weeks to convert after infection: no large-scale contact-tracing procedure is warranted for the first 2 months following diagnosis and treatment of the index case.

Sensitivity, likelihood ratio in the event of a negative test and pre-test probability are of major importance to rule out active disease. Furthermore, sensitivity varies according to the IGRA test used and according to the population tested. FERRARA *et al.* [7] studied both IGRA tests in routine clinical practice and reported a 16–25% false-negative rate (a sensitivity of 75–84%) in 24 subjects with active TB, using both IGRA tests available. Sensitivity reported for T-SPOT^{TM}.*TB* is 83–100% and is 64–97% for QuantiFERON-TB GOLD (Cellestis, Carnegie, Victoria, Australia); this is on average slightly lower than that of T-SPOT^{TM}.*TB* [8–10].

The Centers for Disease Control and Prevention 2005 guidelines state that, for reasons of suboptimal sensitivity, a negative QuantiFERON-TB GOLD test cannot be used to exclude the diagnosis of active TB [11]. Although the sensitivity of the T-SPOT^{TM}.*TB* is probably better on average than that of the QuantiFERON-TB GOLD, there are too many clinical situations, such as all forms of immunosuppression, severe comorbidity, HIV infection, older subjects, in which its sensitivity is probably decreased and thus Centers for Disease Control and Prevention guidelines appear reasonable for both IGRA tests. T-SPOT^{TM}.*TB* may at the very best reasonably rule out *Mycobacterium tuberculosis* infection in immunocompetent individuals, without any risk factor for exposure to TB, and with a low clinical pre-test probability of *Mycobacterium tuberculosis* infection (<0.25).

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STATEMENT OF INTEREST

None declared.

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From the authors:

We would like to thank J-P. Janssens for his interest and comments on our recent paper [1]. We fully agree that the decision to use the T-SPOT^{TM}.*TB* (Oxford, Immunotec, Oxford, UK) to exclude active tuberculosis (TB) infection should not be taken lightly. We appreciate the opportunity to make some comments in reply to his letter.

First, he calculates the risk of suffering from active TB to be intermediate (0.25–0.75) in the patients described. His criteria for this risk estimation are not mentioned and could be arbitrary.

Secondly, because acid-fast bacteria were initially identified in all patients, one could easily say that the risk of active TB is high (>0.75). However, research in the Netherlands in 2005 demonstrated that ~600 (38%) out of 1,600 cultured isolates were Mycobacteria other than TB [2]. This would decrease the *a priori* likelihood for *M. tuberculosis* (MTB) infection considerably.

Thirdly, in our case study we described four patients with a relatively high probability for active MTB infection (condition A) and the use of a test to confirm or exclude active MTB infection (condition B). As we noted in the paper, the sensitivity of the T-SPOT^{TM}.*TB* test in our hospital, with our patient population, was 100%. To date, we have identified 33 patients with active TB. One patient had an indeterminate test result and the remaining 32 patients were all T-SPOT^{TM}.*TB* positive. Thus, condition B has a probability of 1 and Bayes theorem should not be used if one of the conditional probabilities is 1 [3].

J-P. Janssens correctly mentioned that the sensitivity of T-SPOT^{TM}.*TB* for detecting active TB is not 100% in different studies. Therefore, we were cautious in our paper not to use this approach in severely immunocompromised patients and, furthermore, not to incorrectly interpret indeterminate results as negative. Case B was immunocompromised based on the use

of steroids and azathioprine. However, steroids are not associated with indeterminate elispot results [4], and a positive elispot result has been demonstrated in a patient with chronic azathioprine treatment [5]. We suggest each clinic must establish its own test performance before the T-SPOT^{TM}.*TB* can be used to rule out active TB disease. Even then, we are reluctant to fully rely on negative T-SPOT^{TM}.*TB* test results. Withholding therapy while awaiting culture results can only be justified if the patient's condition is closely monitored and precautions to avoid further spreading of Mycobacteria are made.

Case A has been under observation for nearly 2 yrs and to date has not shown any signs of TB disease. In the other three cases atypical Mycobacteria (*M. genavense*, *M. avium* and *M. malmoense*) were cultured and treated.

Exclusion of active TB will not be feasible in countries with a high incidence of latent TB infection because the background T-SPOT^{TM}.*TB* positive test results will be high and, as a consequence, the specificity to prove active disease will be low.

Infection control measures will always be undertaken the moment a patient is suspected to suffer from active pulmonary TB. In a hospital setting the patient will most likely be isolated from other patients, in an outpatient setting the patient will be told to stay at home and to not visit places with high numbers of people, such as pubs and bars, supermarkets or sport clubs. Furthermore, the stigma of suffering from TB is a real problem even in the 21st century. Emotional distress for the patient and their close contacts is not to be dismissed. In the Netherlands, the Municipal Health Authority will be notified when there is suspicion of active TB. The Authority will not wait for another 6–10 weeks before starting contact tracing. The first circle of contacts (household members and close friends) will be screened as soon as possible to identify a possible source patient or to diagnose other patients with active TB disease.

In conclusion, we underscore the general point made by J-P. Janssens that an interferon-γ release assay should not be used lightly to exclude active tuberculosis. However, in a setting with: 1) low endemicity; 2) the possibility to follow the patient; 3) a proven track record of the facilitating laboratory; and 4) including the T-cell stimulation control test to detect non-responsive (indeterminate) patients, such an approach is feasible.

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STATEMENT OF INTEREST

None declared.

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The effect of gas standardisation on exhaled breath condensate pH and PCO_2

To the Editors:

We read with interest the recent article by KULLMANN *et al.* [1] reporting the effect of gas standardisation on exhaled breath condensate (EBC) pH. pH can be determined immediately upon sampling, without gas standardisation [2], or following EBC gas standardisation in case of delayed analysis [3–5]. The influence of ambient air and analytical sample preparation pose a major problem for pH and carbon dioxide tension (P_{CO_2}) determination in EBC. In gas standardisation (argon bubbling or CO_2-free gas), CO_2 is removed from the sample, thus reducing the effect of CO_2 on pH determination. KULLMANN *et al.* [1] even proposed CO_2 standardisation at a P_{CO_2} of 5.33 kPa, physiological alveolar P_{CO_2}. Based on the experience with gas determination in blood, which should not be exposed to ambient air, the aim of our study was to determine P_{CO_2} and pH in argon-overlined EBC immediately upon sampling. To our knowledge, it was the first analysis of argon-overlined EBC.

EBC was collected from a total of 53 children (18 children with gastro-oesophageal reflux (GER), 22 asthmatics and 13 healthy controls), aged 5–16 yrs. All asthmatics received their regular anti-asthmatic treatment with inhaled corticosteroids (ICS) or ICS plus long-acting β_2-agonists for 4 weeks. Chronic cough due to GER was diagnosed by 24-h oesophageal pH monitoring. The