New technologies for diagnosing active TB: the VANTDET diagnostic accuracy study

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Declared competing interests of authors: Alice Halliday has a patent pending entitled 'A cellular immune signature for risk stratification of latent tuberculosis infection'. Robert Parker reports having the following patents pending: 1719853.2 and 2017904359. Lachlan Coin reports having the following patents pending: WO2014067943A1 and US20150284780A1. In addition, Lachlan Coin has one patent issued: EP2914740B1. Jon Deeks reports grants from National Institute for Health Research (NIHR) during the conduct of the study and receipt of a NIHR Senior Investigator Emeritus award and that he is supported by the NIHR Biomedical Research Centre, University Hospitals Birmingham NHS Foundation Trust and University of Birmingham. Peter White reports grants from the Medical Research Council and the NIHR during the conduct of the study, and grants from Otsuka Pharmaceutical (Tokyo, Japan) outside the submitted work. Onn Min Kon is chairperson of the UK Joint Tuberculosis Committee. Ajit Lalvani reports issued patents underpinning interferon gamma release assays (IGRAs) and next-generation IGRAs, some of which were assigned by the University of Oxford to Oxford Immunotec Global plc (Abingdon, UK), resulting in royalty entitlements for the University of Oxford and Ajit Lalvani. Ajit Lalvani is also inventor of issued and pending unlicensed patents underpinning flow-cytometric diagnosis of tuberculosis.

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Plain English summary

The VANDTET diagnostic accuracy study

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Plain English summary

Globally, tuberculosis (TB) is the most deadly infectious disease, with 10 million cases each year, resulting in 1.3 million deaths. TB is caused by a bacterium that is transmitted from an individual with TB disease of the lungs to another person by coughing. There are several diagnostic tests for TB, most of which detect the presence of the bacteria in clinical samples. However, these tests fail to detect all TB patients, particularly when there is a small number of bacteria present at the site of disease and/or it is difficult to get a sample. This means that some wait a long time for a final diagnosis and incur a delay before starting treatment, or else are given TB treatment without a clear diagnosis. New and improved diagnostic tests that allow for the rapid detection of all active TB cases would greatly improve patient care.

Recently, scientists have found several new approaches to testing for TB disease that use new technologies to measure the immune response in blood samples. In previous studies, these new technologies were able to distinguish between TB and other diseases that appear clinically similar to TB. In this project we aimed to validate these new technologies using samples from patients with the full range of TB disease, including those who test negative on the current tests. Overall, we found that the new technologies worked less well than previously reported. Importantly, they were unable to detect all of the TB patients who tested positive on the current tests. Owing to the poor accuracy for diagnosing all TB patients, and the high cost of these new tests, we found that none of the new tests would be cost-effective for use on all individuals who have suspected TB. However, in the hard-to-diagnose patient groups, for whom there are currently no rapid tests available, some of the new tests may be useful if used alongside existing tests.

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