

# Two interferon gamma release assays for predicting active tuberculosis: the UK PREDICT TB prognostic test study

Ibrahim Abubakar,<sup>1\*</sup> Ajit Lalvani,<sup>2</sup>  
Jo Southern,<sup>3</sup> Alice Sitch,<sup>4</sup> Charlotte Jackson,<sup>1</sup>  
Oluchukwu Onyimadu,<sup>5</sup> Marc Lipman,<sup>6</sup>  
Jonathan J Deeks,<sup>4</sup> Chris Griffiths,<sup>7</sup>  
Graham Bothamley,<sup>8</sup> Onn Min Kon,<sup>9</sup>  
Andrew Hayward,<sup>10</sup> Joanne Lord<sup>5</sup> and  
Francis Drobniowski<sup>2</sup> on behalf of the PREDICT  
study team

<sup>1</sup>Institute for Global Health, University College London, London, UK

<sup>2</sup>Tuberculosis Research Centre, National Heart and Lung Institute, Imperial College London, London, UK

<sup>3</sup>National Infection Service, Public Health England, London, UK

<sup>4</sup>Institute of Applied Health Research, University of Birmingham, Birmingham, UK

<sup>5</sup>Southampton Health Technology Assessment Centre, University of Southampton, Southampton, UK

<sup>6</sup>Respiratory Medicine, University College London, London, UK

<sup>7</sup>Blizard Institute, Queen Mary University of London, London, UK

<sup>8</sup>Homerton University Hospital, London, UK

<sup>9</sup>Imperial College Healthcare NHS Trust, London, UK

<sup>10</sup>Institute of Epidemiology and Health Care, University College London, London, UK

\*Corresponding author [i.abubakar@ucl.ac.uk](mailto:i.abubakar@ucl.ac.uk)

**Declared competing interests of authors:** Ibrahim Abubakar is a member of the Health Technology Assessment (HTA) Commissioning Board. Ajit Lalvani is a named inventor on several patents underpinning the T-SPOT.TB test assigned by the University of Oxford to Oxford Immunotec Ltd and has royalty entitlements from the University of Oxford. He was the scientific founder of Oxford Immunotec Ltd and ceased to be a director 10 years ago. He is a member of the National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation Board. Charlotte Jackson was funded by NIHR, during the conduct of the study, and reports personal fees from Otsuka Pharmaceutical, outside the submitted work. Chris Griffiths is involved in NIHR-funded clinical trials units. Jonathan J Deeks is Chairperson of the NIHR HTA Efficient Studies Themed Board, Chairperson of the NIHR HTA Multimorbidities in Older People Themed Board, Deputy Chairperson of the NIHR HTA Commissioning Board, Chairperson of the NIHR HTA Monitoring Strategy Group, a member of the NIHR HTA Methods Group for Diagnostic, Technologies & Screening, a member of the NIHR HTA Methods Group for Elective & Emergency Specialist Care, a member of the NIHR HTA Programme Commissioning Strategy Group and a member of the NIHR HTA Strategy and Oversight Group. The other authors have no competing interests to declare.

Published October 2018

DOI: 10.3310/hta22560

## Plain English summary

### Interferon gamma release assays for predicting active tuberculosis

Health Technology Assessment 2018; Vol. 22: No. 56

DOI: 10.3310/hta22560

NIHR Journals Library [www.journalslibrary.nihr.ac.uk](http://www.journalslibrary.nihr.ac.uk)

## Plain English summary

People can be infected with the bacteria that cause tuberculosis (TB) without having symptoms. They are then said to have latent TB infection (LTBI). For a small proportion of people, the bacteria can later 'reactivate' to cause TB disease. To avoid reactivation, people with LTBI may be offered treatment to clear the infection before they become ill. Ideally, treatment would be given only to people who are at the highest risk of progressing to active disease. However, at the moment, we cannot accurately predict people's risk of progressing.

This study was designed to determine how well new blood tests, called interferon gamma release assays (IGRAs), can predict who will develop active TB compared with an older test [tuberculin skin test (TST)]. It also assessed how cost-effective the new tests are on their own or in combination with other tests.

The study recruited 6386 participants who had a test result for all three LTBI tests (the TST and two different IGRAs), of whom 97 developed TB disease. When we compared the three different tests and combinations of these tests, none appeared to be better than the others for predicting who would develop TB disease. The approach with the best value from a health systems perspective is to combine the skin test with either of the blood tests. However, there were only small differences in cost-effectiveness between the different testing strategies.

This study concluded that no particular test or combination of tests was statistically superior to other approaches at predicting who would develop TB disease. However, a two-step approach that combined the skin test with either of the blood tests and took into account people's previous vaccination against TB provided the most benefit, taking into account the cost. Skin testing that did not account for previous vaccination was worse than other test options.



ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.513

*Health Technology Assessment* is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) ([www.publicationethics.org/](http://www.publicationethics.org/)).

Editorial contact: [journals.library@nhr.ac.uk](mailto:journals.library@nhr.ac.uk)

The full HTA archive is freely available to view online at [www.journalslibrary.nhr.ac.uk/hta](http://www.journalslibrary.nhr.ac.uk/hta). Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: [www.journalslibrary.nhr.ac.uk](http://www.journalslibrary.nhr.ac.uk)

## Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

## HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: <http://www.nets.nhr.ac.uk/programmes/hta>

## This report

The research reported in this issue of the journal was funded by the HTA programme as project number 08/68/01. The contractual start date was in May 2010. The draft report began editorial review in August 2017 and was accepted for publication in January 2018. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.

© Queen's Printer and Controller of HMSO 2018. This work was produced by Abubakar *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library ([www.journalslibrary.nhr.ac.uk](http://www.journalslibrary.nhr.ac.uk)), produced by Prepress Projects Ltd, Perth, Scotland ([www.prepress-projects.co.uk](http://www.prepress-projects.co.uk)).

## NIHR Journals Library Editor-in-Chief

**Professor Tom Walley** Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

## NIHR Journals Library Editors

**Professor Ken Stein** Chair of HTA and EME Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

**Professor Andrée Le May** Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals)

**Dr Martin Ashton-Key** Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

**Professor Matthias Beck** Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

**Dr Tessa Crilly** Director, Crystal Blue Consulting Ltd, UK

**Dr Eugenia Cronin** Senior Scientific Advisor, Wessex Institute, UK

**Dr Peter Davidson** Consultant Advisor, Wessex Institute, University of Southampton, UK

**Ms Tara Lamont** Scientific Advisor, NETSCC, UK

**Dr Catriona McDaid** Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

**Professor William McGuire** Professor of Child Health, Hull York Medical School, University of York, UK

**Professor Geoffrey Meads** Professor of Wellbeing Research, University of Winchester, UK

**Professor John Norrie** Chair in Medical Statistics, University of Edinburgh, UK

**Professor John Powell** Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK

**Professor James Raftery** Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

**Dr Rob Riemsma** Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

**Professor Helen Roberts** Professor of Child Health Research, UCL Great Ormond Street Institute of Child Health, UK

**Professor Jonathan Ross** Professor of Sexual Health and HIV, University Hospital Birmingham, UK

**Professor Helen Snooks** Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

**Professor Jim Thornton** Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

**Professor Martin Underwood** Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of editors: [www.journalslibrary.nihr.ac.uk/about/editors](http://www.journalslibrary.nihr.ac.uk/about/editors)

**Editorial contact:** [journals.library@nihr.ac.uk](mailto:journals.library@nihr.ac.uk)