NICE National Institute for Health and Care Excellence

2018 surveillance (exceptional review) of tuberculosis (NICE guideline NG33)

Surveillance report

Published: 31 October 2018

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Contents

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Surveillance decision

We will plan a partial update of tuberculosis. This update will focus on diagnosing latent tuberculosis (TB) in adults.

Reason for the decision

Assessing the evidence

The purpose of this exceptional review was to examine any impact on NICE's guideline on TB following the publication of a National Institute for Health Research funded trial: the UK PREDICT TB prognostic test study. Alongside this, the August 2018 update to Tuberculosis: the green book, chapter 32 was considered for impact on the guideline. No additional evidence published since the publication of NICE's guideline on tuberculosis in May 2016 was considered by the exceptional review.

Methods

The PREDICT study is a prospective cohort study that assessed the prognostic value of 2 interferon gamma release assays (IGRAs) compared with the standard tuberculin skin test (TST) for predicting active TB. The study recruited individuals aged ≥16 years who were:

- close contacts of patients with active TB or
- new entrants to the UK arriving in the last 5 years from high-incidence countries.

At the time of the study, treatment of latent TB infection (LTBI) was recommended only for individuals aged under 35 years so recruitment was prioritised to patients aged over 35 years (who were not eligible for chemoprophylaxis) in order to estimate and compare the ability of the TST and IGRAs to predict natural progression to active disease in the absence of treatment.

Participants were tested with 2 IGRAs: ELISA (QFT-GIT) and ELISPOT assay (T-SPOT.TB) and then with a Mantoux test (TST). Three TST thresholds were considered:

- TST-5: a skin induration of ≥5 mm

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- TST-10: a skin induration of ≥10 mm
- TST-15: a skin induration of ≥15 mm for those known to have had a Bacillus Calmette-Guérin (BCG) vaccination.

Follow-up was from recruitment to the development of TB or censoring at data cutoff (24 months).

The primary outcome was the development of active TB, with the prognostic values of tests quantified as incidence rate ratios (IRRs), comparing those with positive results and those with negative results, among contacts and new entrants to the UK. Individuals were considered to have progressed to active TB if they had culture-confirmed TB or were clinically diagnosed with radiological or histological evidence of TB and a clinician had decided to treat the individual with a full course of anti-TB disease treatment.

Results

The PREDICT study recruited 10,045 participants from 54 different NHS centres and community settings located in London, Leicester and Birmingham between May 2010 and July 2015. Of these participants, 175 were identified as having TB at baseline (diagnosed or treated less than 21 days after being recruited) and an additional 260 participants received treatment for LTBI during the study. Removing these participants left 9,610:

- 4,861 (50.6%) had contact with someone with TB
- 4,749 (49.4%) were new entrants to the UK from a high-incidence country.

The results of the study indicated that 97 individuals (1%) developed active TB (per protocol population was 77 individuals [1.2%]):

- A positive T-SPOT.TB result was a significantly better predictor of progression to active TB than all other tests
- A positive result for TST-5 was a significantly worse predictor of progression to active TB than positive results for any of the other tests
    - However, TST-5 identified a higher proportion of people (64 out of 77 tested [83%]) progressing to active TB compared with all other tests and TST thresholds

The authors concluded that the most suitable TB screening strategies among high-risk groups were IGRA-based or BCG-stratified TST strategies.

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Guideline development

The evidence review of close contacts of a person with TB conducted for NICE guideline NG33 identified low quality evidence (11 studies; n=1,844 participants) showing that positive IGRAs were more strongly associated with increasing TB exposure than positive Mantoux tests. Economic modelling was undertaken with various strategies from no action to a 2-step strategy with either a Mantoux test followed by interferon-gamma testing, or serial IGRAs. Of these options, the model provided most support, on grounds of cost-effectiveness, for a 2-step approach with an initial Mantoux test, followed by an IGRA to confirm positivity. The guideline committee also supported this because of clinical utility and feasibility. The committee felt that although IGRAs seemed better from ratio of diagnostic odds ratios, the evidence was of poor quality and that recommendations should ideally be based on longitudinal studies that aimed to determine positive and negative predictive values of a person developing active TB.

In terms of the recently arrived population considered in NICE guideline NG33, the TST (≥5mm) alone strategy was less costly and more effective than TST (≥5mm) positive followed by QFT-GIT, T-SPOT.TB and QFT-GIT alone testing strategies. In both cases, a single cut-off point for a positive TST test regardless of BCG vaccination status was recommended.

Policy landscape

Public Health England (PHE) is responsible for a TB screening programme in England, which covers population screening for TB including active case finding and screening for LTBI. The current programme screens new migrants aged 16–35 who have been in the UK for less than 5 years and have come from a country with more than 150 per 100,000 incidence. Testing involves a 1-step IGRA and no TST. If the IGRA is inconclusive a second IGRA is offered. This approach differs from the recommended approach in NICE guideline NG33. Feedback from PHE indicated that there is variable application of NICE guidance outside of the screening programme. Some services use TST, some IGRAs and some both, depending on local policies and preferences indicating NICE guidance is not being applied in a standard way across the country.

TB immunisation information for health professionals is provided by PHE's Tuberculosis: the green book, chapter 32. The green book recommendations around BCG vaccination of healthcare workers and laboratory staff that were available when NICE guideline NG33 was developed were broadly aligned. However, chapter 32 of the green book was updated

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in August 2018 and the updated recommendations are much more restrictive in terms of when healthcare workers or laboratory staff should be vaccinated with BCG.

Research landscape

The National Institute for Health Research currently has a funding opportunity for a modelling grant on screening options for TB. This is likely to influence screening strategies in the future.

Views of topic experts

In this exceptional review we engaged with topic experts who were either members of the guideline committee involved in the development of NICE guideline NG33 or were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. We received feedback from 6 topic experts with all agreeing that the guideline should be updated to take account of the PREDICT study.

In terms of TB immunisation information for health professionals, topic experts noted that in practice the advice in the green book is followed rather than the guideline.

Impact

PREDICT study

The results of the PREDICT study indicated that an IGRA is a significantly better predictor of progression to active TB than all other tests in individuals aged ≥16 years who were:

- close contacts of patients with active TB or
- new entrants to the UK arriving in the last 5 years from high-incidence countries.

The results of this study are not in line with current guidance in NICE guideline NG33 which recommends Mantoux testing as the first option in these populations.

Regarding strengths and limitations of PREDICT, it was a large UK-based study directly relevant to recommendations in the NICE guideline. However, a lower incidence threshold (40 per 100,000) was used compared with the PHE TB screening programme meaning the overall incidence of TB (and pre-test probability) was lower than would be in practice.

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Additionally, a different service delivery model was used meaning some of the assumptions were not in line with current practice.

Since the guideline was developed, policy in this area has moved on. There is a new migrant LTBI programme funded by NHS England as part of their commitment to the Collaborative TB Strategy for England, which focuses on 59 high-burden Clinical Commissioning Groups with very clear criteria and instructions for screening. Additionally, the cost-effectiveness model in which the NICE guideline recommendations are based is out of date, in part due to the substantial reduction in the cost of IGRAs that came with the national new migrant LTBI programme.

Following consideration of the results published in PREDICT, as well as topic expert feedback, the new evidence may have an impact on the current recommendations on diagnosing latent TB in close contacts of patients with active TB or new entrants to the UK from high-incidence countries.

Tuberculosis green book

Chapter 32 of the green book was updated in August 2018 and the updated recommendations are much more restrictive compared to the previous version in terms of when healthcare workers or laboratory staff should be vaccinated with BCG. NICE guideline NG33 currently recommends that BCG vaccination should be offered to healthcare workers and other NHS employees who have contact with patients or clinical specimens, irrespective of age, who were previously unvaccinated and Mantoux negative. This differs from the updated green book, which now recommends BCG vaccination only for healthcare workers or laboratory workers, who have either direct contact with TB patients or with potentially infectious clinical materials or derived isolates. Feedback from topic experts indicated that they defer to the green book for recommendations on BCG vaccination for healthcare workers rather than following recommendations in the NICE guideline. Therefore, it is proposed to refresh recommendation 1.1.3.16 in the guideline to state:

- 1.1.3.16 Offer BCG vaccination to healthcare workers and other NHS employees as advised in the Green Book.

Other clinical areas

This exceptional surveillance review did not search for new evidence relating to other

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clinical areas in the guideline.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

See how we made the decision for further information.

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How we made the decision

Exceptionally, significant new evidence may mean an update of a guideline is agreed before the next scheduled check of the need for an update. The evidence might be a single piece of evidence, an accumulation of evidence or other published NICE guidance.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence

This surveillance report provides an overview of 1 study published since the end of the search period for the guideline (December 2014). The results of this study were considered in detail to determine if there is an impact on guideline recommendations.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline.

Views of stakeholders

Because this was an exceptional surveillance review we did not consult on the decision.

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The NICE project team would like to thank the topic experts who participated in the surveillance process.

ISBN: 978-1-4731-3153-8

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