Thinking in three dimensions: a web-based algorithm to aid the interpretation of tuberculin skin test results

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SUMMARY

BACKGROUND: The tuberculin skin test (TST) is the most widely used test for detecting tuberculosis (TB) infection. Accurate interpretation of TST requires consideration of three dimensions—the size of the skin reaction, the positive predictive value (PPV) and risk of disease.

METHODS: We developed a web-based algorithm incorporating epidemiological, medical and radiographic risk factors to help in the interpretation of positive TST results in adults (http://www.meakins.mcgill.ca/meakins/NEW TST Calculator/homeE.htm). We used summary estimates from published reviews on the prevalence of latent TB infection, the likelihood of false-positive TST and risk of active TB disease.

RESULTS: The algorithm calculations show that the most important determinants of risk of active disease are the presence of medical and radiographic risk factors, while the size of the reaction is of modest importance. In persons who have received bacille Calmette-Guérin vaccination after infancy, the algorithm calculations show that the PPV will be low. In such persons, the risk of disease is predicted to be very low, unless there are medical or radiographic risk factors that increase the risk of reactivation.

CONCLUSIONS: Our web-based algorithm can generate clinically useful estimates of the annual and cumulative lifetime risk of developing TB in adults with a positive TST.

KEY WORDS: tuberculin skin test; latent TB infection; prediction rules; clinical decision aids; software
systematic review and meta-analysis of false-positive TST reactions due to BCG vaccination and NTM, which has been published elsewhere.\textsuperscript{9} We also used information from a second literature review regarding the relative risk (RR) of reactivation associated with various medical and radiological risk factors.\textsuperscript{10} This published information was then integrated into a predictive algorithm.

**METHODS**

**Overview of the development of the algorithm**

The algorithm was designed to calculate the predictive value of a positive TST based on size of reaction, the likelihood of false-positive reactions from exposure to NTM or BCG vaccination and the likelihood of true LTBI. The annual risk of development of active disease is then estimated, based on the annual incidence of disease in healthy general population samples and the RR of disease with various medical and radiographic risk factors. The annual risk of disease, multiplied by the positive predictive value (PPV) and then multiplied by the number of years of anticipated survival, provides a final calculated cumulative lifetime risk of TB disease.

**Calculating the positive predictive value**

The likelihood that a positive TST represents true TB infection:

\[
\text{Positive predictive value (PPV)} = \frac{\text{TP} (\text{prevalence of LTBI})}{\text{TP} + \text{FP} (\text{FP-TST}_{\text{BCG}} + \text{FP-TST}_{\text{NTM}})}
\]

The rates of true positive (TP) TST from LTBI and false-positive (FP) TST from BCG and NTM were calculated as follows (and are summarised in Table 1).

**Calculating the prevalence of LTBI**

\[
l_{\text{LTBI}} = 1 - \frac{(1 - c)(1 - \text{ARI})^{\text{age}}}{100}
\]

where \( l_{\text{LTBI}} \) = prevalence of LTBI, \( c \) = prevalence of TB infection in contacts, and \( \text{ARI} \) = annual risk of infection in the general population.

As suggested by Styblo,\textsuperscript{11} the ARI in the general population was calculated as the incidence of smear-positive pulmonary TB per 100 000 population divided by 49. The incidence of smear-positive TB was taken from World Health Organization (WHO) estimates.\textsuperscript{12} The expected prevalence of infection among contacts was taken from published literature and a recent review.\textsuperscript{13–18} If the person tested is not a contact, then \( c = 0 \). This results in the above equation being simplified to:

\[
l_{\text{LTBI}} = 1 - (1 - \text{ARI})^{\text{age}}
\]

**Calculating the effect of BCG on TST reactions**

In our previous review and meta-analysis,\textsuperscript{9} the major determinant of the effect of BCG vaccination on TST reactions was age when vaccinated. We accordingly estimated the effect separately for subjects who were vaccinated in infancy (age 0–1 year), or after the age of 1 year (in practical terms this is usually in primary school, i.e., age 5–7 years). We compared the proportion of BCG-vaccinated and non-vaccinated individuals with TST reactions of 10–14 mm and \( \geq 15 \) mm. For each TST size category, the difference between vaccinated and non-vaccinated was assumed to represent the percentage with false TST due to BCG (FP-TST\textsubscript{BCG}). We estimated the average effect separately as a weighted average of all studies of individuals vaccinated in infancy, or vaccinated in older age.

**Calculating the effect of NTM on TST reactions**

In our previous review,\textsuperscript{9} we identified 12 studies that performed dual testing with antigen from *Mycobacterium tuberculosis* (purified protein derivative) and from NTM. In these studies, if the reaction to one antigen was larger than the other, the smaller reaction was considered a cross-reaction\textsuperscript{19–21} and hence considered a false-positive reaction. When the TST was 10–14 mm

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Estimates</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of true-positive TST</td>
<td>( [1 - (1 - \text{ARI}^{\text{age}})]^{100} )</td>
<td>11</td>
</tr>
<tr>
<td>General population (country-specific)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contacts, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Close</td>
<td>40</td>
<td>13–18</td>
</tr>
<tr>
<td>Casual</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Prevalence of false-positive TST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From BCG vaccination (by age last vaccinated), %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infancy (age 0–1 years)</td>
<td>8.5</td>
<td>9</td>
</tr>
<tr>
<td>Older (age ( \geq 2 ) years)</td>
<td>41.8</td>
<td>9</td>
</tr>
<tr>
<td>From NTM sensitivity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TST=10–14 mm, % false-positive if NTM-sensitive</td>
<td>2.7</td>
<td>Calculated</td>
</tr>
<tr>
<td>Prevalence NTM sensitivity, country-specific, %</td>
<td>2–58</td>
<td></td>
</tr>
<tr>
<td>Prevalence false positive TST\textsubscript{NTM}, country-specific, %</td>
<td>0.1–1.6</td>
<td>(from 9)</td>
</tr>
</tbody>
</table>

TST = tuberculin skin test; ARI = annual risk of infection; TB = tuberculosis; BCG = bacille Calmette-Guérin; NTM = non-tuberculous mycobacteria.
and the simultaneous NTM reaction was larger (dominant), then the TST reaction was considered a cross-reaction due to NTM sensitivity\textsuperscript{19,21} and the TST was considered false-positive (FP-TST\textsubscript{NTM}). However, if the TST was $\geq 15$ mm, the subject was considered to have LTBI (true positive) regardless of the size of the NTM reaction.\textsuperscript{19,20}

Using the 12 studies with dual testing, we estimated the rate of FP-TST\textsubscript{NTM} this rate was multiplied times the prevalence of NTM in different countries to estimate the absolute rate of false-positive TST related to NTM in different countries or world regions.

**Calculating the risk of disease**

Annual rate of disease (ARD) = $[PPV \times (\text{baseline annual rate of disease if no risk factors are present}) \times (\text{relative risk of disease, given the presence of specific risk factors})].$

The baseline annual risk of TB disease was taken from a large cohort of healthy TST-positive US military recruits followed up for 4 years.\textsuperscript{22} The risks of disease relative to such healthy persons, associated with radiographic abnormalities or medical risk factors, are summarised in Table 2.

- At age = $n$, up to age of 80:
  - Cumulative risk of disease = ARD $\times (80 - n)$ years.

For computational simplicity, subjects were assumed to live to the age of 80.

**Table 2** Summary of input parameters for algorithm calculation of relative and annual risks of active tuberculosis disease (adapted from Ref 23)

<table>
<thead>
<tr>
<th>Medical or radiographic risk factor</th>
<th>RR</th>
<th>References</th>
<th>Annual risk, % per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>None (healthy or ‘low-risk reactor’$^*$)</td>
<td>1</td>
<td>22</td>
<td>0.1</td>
</tr>
<tr>
<td>Abnormal chest X-ray, granuloma</td>
<td>2</td>
<td>24, 25</td>
<td>0.2</td>
</tr>
<tr>
<td>Cigarette smoker ($\geq 1$ pack/day)</td>
<td>3</td>
<td>26</td>
<td>0.3</td>
</tr>
<tr>
<td>Underweight ($&lt;90%$ ideal body weight)</td>
<td>3</td>
<td>27</td>
<td>0.3</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3.6</td>
<td>28–31</td>
<td>0.36</td>
</tr>
<tr>
<td>Infliximab (TNF-(\alpha) inhibitor therapy)</td>
<td>4</td>
<td>32</td>
<td>0.4</td>
</tr>
<tr>
<td>Abnormal chest X-ray, fibronodular disease$^*$</td>
<td>6</td>
<td>25, 33, 34</td>
<td>0.6</td>
</tr>
<tr>
<td>Recent TB infection ($\leq 2$ years)$^*$</td>
<td>15</td>
<td>35, 36</td>
<td>1.5</td>
</tr>
<tr>
<td>Close contact</td>
<td>15</td>
<td>35, 36</td>
<td>1.5</td>
</tr>
<tr>
<td>Carcinoma of head and neck</td>
<td>16</td>
<td>37</td>
<td>1.6</td>
</tr>
<tr>
<td>Chronic renal failure (requiring hemodialysis)</td>
<td>25.3</td>
<td>38–41</td>
<td>2.5</td>
</tr>
<tr>
<td>Pulmonary silicosis</td>
<td>30</td>
<td>42, 43</td>
<td>3.0</td>
</tr>
<tr>
<td>HIV infection (all stages)</td>
<td>50</td>
<td>44–47</td>
<td>5.0</td>
</tr>
<tr>
<td>Transplantation (requiring immune-suppressant therapy)</td>
<td>74</td>
<td>48–51</td>
<td>7.4</td>
</tr>
</tbody>
</table>

$^*$ Lower estimate from Nolan of RR = 6.0,\textsuperscript{13} and not the higher estimate of RR = 19 from Grzybowski.\textsuperscript{34}

$^*$ Risk of disease elevated for first 2 years after infection, then falls to annual risk of 0.1% thereafter (close contacts should be considered to have recent infection in algorithm).

RR = relative risk; TNF-\(\alpha\) = tumour necrosis factor-alpha; TB = tuberculosis; HIV = human immunodeficiency virus.

As this study did not directly involve human subjects, ethics approval was not needed.

**RESULTS**

In 24 studies involving 240,203 subjects who were BCG-vaccinated in infancy (age 0–1 year), 20,406 (8.5\%) had a TST of $\geq 10$ mm attributable to BCG, although only 56 of 5639 (1\%) were TST-positive if tested $\geq 10$ years after BCG. In 12 studies of 12,728 subjects vaccinated after their first birthday, 5314 (41.8\%) had a false-positive TST of $\geq 10$ mm and 191 of 898 (21.2\%) had a false-positive TST after $\geq 10$ years. Based on the 12 studies of 11,691,05 persons who underwent dual TST and NTM testing, for every 100 persons sensitised to NTM, 2.0 persons would have a false-positive TST of 10–14 mm. Using the five studies with 12,984 persons with detailed data, the rate of FP-TST\textsubscript{NTM} (of 10–14 mm) was 2.7 per 100 NTM sensitised persons. When this higher estimate of FP-TST\textsubscript{NTM} was multiplied by the prevalence of NTM sensitisation in 18 published surveys, the prevalence of FP-TST\textsubscript{NTM} fanged from 0.1\% in Canada or France, to a maximum of 1.6\% in India.\textsuperscript{9}

The algorithm$^*$ estimates the PPV using the TST reaction size, country of origin (and state of birth if US-born), current age and age at immigration (in the case of migrants), BCG vaccination status and history of contact with TB. The annual and cumulative risk (to the age of 80) of disease is then calculated based on radiographic findings and medical history. See Figure 1 for an example screenshot of the parameters to be entered. Once all the relevant input parameters are entered, the algorithm computes the predictive value of a positive TST, as well as the annual and cumulative lifetime risk of disease. See example screen shot of algorithm output in Figure 2.

As seen in Table 3, the calculated cumulative risk of disease up to the age of 80 for a 35-year-old adult varies widely. The most critical determinants of risk of disease are country of origin, BCG vaccination and medical risk factors. The effect of TST size is relatively small, except in populations where the prevalence of NTM sensitivity is high and LTBI is uncommon—such as occurs in Southern USA. BCG vaccination has an important effect of reducing PPV and hence risk of disease, when expected prevalence of LTBI is low and BCG was routinely given to school-age children or

$*$ The algorithm is accessible at: http://www.meakins.mcgill.ca/meakins/NEW TST Calculator/homeE.htm. The screen should appear as Figure 1. Simply enter the demographic and clinical parameters, including TST size, for the patient, then ‘Submit’. Results will appear as shown in Figure 2. Close that screen to re-enter new values for a different patient, etc. Software submitted, but not intended for direct publication, nor included in transfer of copyright to the IJTLD. Available freely as shared software upon request, or directly on website of authors.
adolescents. This was the practice in many European countries such as the UK, France and throughout Eastern Europe until quite recently.

DISCUSSION

Interpretation of a TST should take multiple factors into account. It is best to interpret the TST in three distinct stages or dimensions—size, PPV and risk of development of disease. To facilitate interpretation, we have developed a simple, web-accessible tool to calculate the likelihood that a TST is true-positive and the risk of active disease. These calculations are based on numerous studies published over the past 40 years—an important advantage of the TST. As demonstrated by the examples generated from this web-based programme, the cumulative risk of disease will be substantial in adults with important medical risk factors, particularly if the PPV of the test is >50%. These predictions are supported by a recent modelling study that emphasised the importance of medical conditions in determining the lifetime risk of TB. However, in healthy low-risk adults, the cumulative risk of disease is low, even if the TST is almost certainly true-positive. This
reinforces the recommendation\textsuperscript{10,53} to test only individuals who are at increased risk of disease in whom potential causes of false-positive TST can be ignored. This computerised algorithm has a number of potential limitations. First, the current estimates of prevalence of true infection are based on currently available estimates of incidence of smear-positive TB from the WHO data. In some low-income countries, these estimates may be inaccurate due to limited case finding. However, as incidence tends to be very high in these countries, even if the actual incidence is 25\% higher or lower than published estimates, this will have a relatively small impact on the estimated PPV as the estimated prevalence of true infection in adults will be high with all estimates. Furthermore, to estimate the annual risk of infection, the algorithm incorporates the Styblo formula. This formula has been criticised as it ignores the potential effect of transmission from smear-negative cases, which may account for 20–25\% of all transmission,\textsuperscript{54} thus potentially underestimating infection risk. However, Styblo based his formula on observed rates of disease and infection in countries that had, at the time, little or no capacity for diagnosis of smear-negative disease.\textsuperscript{11} Hence the observed infection risk did account for all cases in the community at that time. The formula would be invalid now if the proportion of smear-negative to -positive cases had changed over the last two decades. This could have happened in countries with high human immunodeficiency virus (HIV) seroprevalence, as HIV-co-infected cases are more often smear-negative.\textsuperscript{55} However, use of this formula is justified because it has

\begin{table}[h]
\centering
\caption{Illustration of the algorithm calculations: cumulative risk (to the age of 80) of developing tuberculosis in 35-year-old adults with TST reactions of 10–14 or >15 mm}
\begin{tabular}{|c|c|c|c|c|c|}
\hline
Country of origin & History of BCG vaccination & \multicolumn{2}{|c|}{PPV} & \multicolumn{2}{|c|}{Cumulative risk of active TB disease} \\
 & & TST 10–14 mm & TST >15 mm & TST 10–14 mm & TST >15 mm \\
\hline
Healthy—no risk factor, normal chest X-ray & & & & & \\
Florida, USA & None* & 50 & 100 & 2.3 & 4.5 \\
Canada & None & 93 & 100 & 4.2 & 4.5 \\
 & Infancy & 18 & 19 & 0.8 & 0.8 \\
 & Older & 3 & 3 & 0.1 & 0.1 \\
Russia* & None & 99.6 & 100 & 4.5 & 4.5 \\
 & Older* & 41 & 41 & 1.8 & 1.8 \\
Haiti* & None & 99.5 & 100 & 4.4 & 4.5 \\
 & Infancy* & 90 & 91 & 4.0 & 4.5 \\
Diabetes & & & & & \\
Florida, USA & None & 50 & 100 & 8.1 & 16.2 \\
Canada & None & 93 & 100 & 16.2 & 16.2 \\
 & Older & 41 & 41 & 7 & 7 \\
Russia† & Infancy & 90 & 91 & 14.5 & 15.1 \\
Granuloma on chest X-ray and underweight & & & & & \\
Florida, USA & None & 50 & 100 & 11.3 & 22.5 \\
Canada & None & 93 & 100 & 21 & 22.5 \\
 & Older & 41 & 41 & 9.1 & 9.1 \\
Haiti & Infancy & 90 & 91 & 20.6 & 20.8 \\
Healthy but recent contact with active TB & & & & & \\
Florida, USA & None & 99 & 100 & 8.9 & 9.0 \\
Canada & None & 100 & 100 & 9.0 & 9.0 \\
Russia† & Older & 71 & 71 & 6.8 & 6.8 \\
Haiti & Infancy & 94 & 95 & 8.4 & 8.4 \\
\hline
\end{tabular}
\end{table}

* Values of BCG vaccination most likely indicate BCG status in persons from that country.
† Immigrated to Canada at age 32.
TST = tuberculin skin test; TB = tuberculosis; BCG = bacille Calmette-Guérin; PPV = positive predictive value.
been validated, albeit many years ago, and there is no other formula available that does account for these factors and yet is simple enough to be incorporated into the algorithm.

A second limitation is that our NTM prevalence estimates for many countries were extrapolated from results in nearby countries with a similar climate. However, the estimated effect of NTM is small (even if somewhat greater than originally estimated), so even moderate imprecision in these extrapolated estimates would have a trivial effect on the estimated PPVs.

Other limitations include that the algorithm will not identify false-negative tests, as it is designed only to assist the interpretation of a positive TST. The effects on TST reactions of BCG and NTM are derived from studies in non-HIV-infected persons, so may not be accurate in HIV-infected persons. However, because the risk of active TB is so high with HIV infection, imprecision regarding false-positive rates should have little impact on the estimated risk of disease, and current guidelines recommend that possible causes of false-positive TST, such as BCG, should be ignored in HIV-infected persons. The values incorporated for each parameter were based on a thorough review of the literature, but there is no published information regarding how combinations of factors interact to affect likelihood of disease. The assumption that the presence of more than one risk factor will further increase risk is not based on published observations. It would be very difficult to validate the algorithm predictions in such patients, because such high-risk patients should receive treatment for LTBI. One can thus only check whether the resultant estimates, such as those shown in Table 3, are clinically reasonable.

Finally, the current algorithm does not estimate PPV or risk of disease for TST reactions of 5–9 mm. This is because there is much less published information regarding prevalence of infection, relative risk and PPV in persons with TST reactions of this size. The algorithm also does not estimate risk for results of serial testing—again because there is less and inconsistent information regarding the occurrence and interpretation of serial TST testing in different populations. We acknowledge that this algorithm, like all software programmes, is work in progress. Readers and users are therefore invited to send comments or corrections to the authors. We hope to develop updated versions with calculations for TST of 5–9 mm and for serial testing. Another possible development would be to adapt this for interpretation of the results of the newer interferon-gamma release assays (IGRAs). The algorithm would be simpler, as the PPV of IGRA should be uniformly high given that false-positive reactions are much less common. There are, however, no published cohort studies of the follow-up of untreated populations with positive IGRA results. Estimates of risk of disease would therefore have to be based on older cohorts who were followed up after TST testing.

A key question is whether busy clinicians will use this tool. On the first occasion that colleagues in our institute tried the algorithm, they required about half a minute to launch the programme and another 15–20 seconds to input the data. If installed on a palm pilot, this could be even quicker and more accessible.

In conclusion, we believe that many of the limitations of TST interpretation can be overcome with this computer-based decision tool. A busy clinician can input a number of variables and estimate the risk of disease for patients in less than a minute. As demonstrated in our examples, individuals with medical risk factors for active TB or abnormal chest X-rays will have a high risk of developing active disease, even after accounting for potential false-positive tests. This reinforces an important advantage of the TST—the validity for prediction of disease risk. These findings also underscore the importance of performing the TST only in adults at increased risk to develop disease if infected, as they will benefit most from treatment of LTBI.

Acknowledgements

The authors thank I Sesartic for programming the web-based prediction algorithm and L Zolpy for assistance in review of the literature.

Authors’ contributions: DM conceived the idea, participated in the literature review and in the development of the software, drafted text and made final corrections. GG had input in the design of the algorithm and made critical revisions to the text. MF conducted the first literature review, contributed to the design and development of the web-based algorithm and made critical revisions to the text. CG contributed to the literature review, development of the web-based algorithm and made critical revisions to the text. MP contributed to the revisions of the web-based algorithm and made critical revisions to the manuscript.

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**RÉSUMÉ**

**CONTEXTE :** Le test cutané tuberculinique (TST) est le test le plus largement utilisé pour la détection de l’infection tuberculeuse. Une interprétation précise du TST exige la prise en compte de trois éléments : la dimension de la réaction cutanée, la valeur prédictive positive (PPV) et le risque de maladie.

**MÉTHODES :** Nous avons élaboré un algorithme basé sur le web et incorporant les facteurs de risque épidémiologiques, médicaux et radiologiques afin d’aider à l’interprétation d’un résultat positif du TST chez un adulte. Nous avons utilisé des estimations résumées dans des revues publiées sur la prévalence de l’infection TB latente dans diverses populations, sur la vraisemblance d’un test TST faussement positif provenant d’une vaccination par le bacille Calmette-Guérin (BCG) ou d’infections mycobactériennes non-tuberculeuses ainsi que le risque de tuberculose (TB) active lié à différents facteurs de risque médicaux et radiologiques.

**RÉSULTATS :** Les calculs de l’algorithme montrent que les déterminants les plus importants du risque de maladie active sont la présence de facteurs de risque médicaux ou radiologiques, alors que la taille de la réaction n’a qu’une importance modeste. Chez les personnes ayant reçu la vaccination par le BCG après la petite enfance, les calculs de l’algorithme montrent que la PPV d’un test positif sera faible particulièrement lorsque la probabilité d’une infection authentique est basse. Chez ces personnes, on peut prédire un risque très faible de maladie sauf s’il existe des facteurs de risque médicaux ou radiologiques qui augmentent le risque de réactivation.

**CONCLUSIONS :** Notre algorithme basé sur le web aide à clarifier les relations complexes entre la TB latente et la TB active et à le potentiel pour générer des estimations cliniquement utiles sur les risques annuels et les risques cumulatifs de développement d’une TB après un TST positif sur l’ensemble de la vie.

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**RESUMEN**

**MARCO DE REFERENCIA :** La reacción cutánea a la tuberculina (TST) es la prueba más ampliamente utilizada en el diagnóstico de la infección tuberculosa. La interpretación exacta de la prueba precisa la consideración de tres aspectos: el tamaño de la reacción cutánea, el valor positivo de predicción (PPV) y el riesgo de enfermedad.

**MÉTODOS :** Se concibió un algoritmo con base en la web, que incorpora factores de riesgo epidemiológicos, médicos y radiográficos cuyo propósito es ayudar en la interpretación de un resultado positivo de la TST en el adulto. Se emplearon las estimaciones finales provenientes de reseñas publicadas sobre la prevalencia de infección tuberculosa latente en diversas poblaciones, la probabilidad de resultados positivos falsos debidos a la vacuna antituberculosa (BCG) o a infecciones por micobacterias diferentes a *Mycobacterium tuberculosis* y el riesgo de tuberculosis (TB) activa asociada con diversos factores de riesgo médicos y radiográficos.

**RESULTADOS :** Los cálculos con el algoritmo ponen en evidencia que los mayores determinantes del riesgo de enfermedad activa son la presencia de factores de riesgo médicos o radiográficos y que el tamaño de la reacción cutánea tiene escaso valor. En personas con antecedente de BCG después de la infancia, estos cálculos muestran que el PPV es bajo sobre todo cuando la probabilidad real de una infección es baja. En tales personas, se predice que el riesgo de enfermedad es muy bajo, a menos que existan factores de riesgo médicos o radiográficos que aumenten la probabilidad de reactivación.

**CONCLUSIÓN :** El algoritmo concebido con base en la web ayuda a aclarar la relación compleja entre TB latente y TB activa y puede contribuir a generar estimaciones con interés clínico sobre el riesgo anual y el riesgo acumulado durante la vida de presentar enfermedad tuberculosa tras un resultado positivo a la TST.