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Tuberculosis Screening for People With Chronic Conditions

Rapid Review

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Abbreviations

CD4	cluster of differentiation 4
IGRA	interferon-gamma release assay
NICE	National Institutes for Health and Care Excellence
TB	tuberculosis
TST	tuberculin skin test

Key Messages

- Five guidelines were identified that provide recommendations about screening for tuberculosis in people with chronic conditions. These guidelines cover populations with HIV, psoriasis vulgaris, solid organ and stem transplants, chronic inflammation, and compromised immune systems.
- Three guidelines recommend regularly screening for latent and active tuberculosis in people diagnosed with HIV or those taking medication that suppresses their immune system.
- One guideline for patients with psoriasis recommends using interferon-gamma release assay and a chest X-ray to rule out tuberculosis infection before immunosuppressant treatment is initiated and during treatment.
- Two guidelines recommend using both the interferon-gamma release assay and the tuberculin skin test at the same time to screen for latent tuberculosis infection in people with HIV, people with or who need an organ or stem cell transplant, and in people taking medication that suppresses their immune system.
- One guideline for people living with HIV recommends using a rapid nucleic acid amplification test to confirm clinical suspicions of active tuberculosis in these patients.

Context and Policy Issues

Individuals with medical conditions that compromise their immune system, such as those with organ transplants, have a higher risk of an infection with tuberculosis (TB).[1] These patients are not always screened for TB before treatment, and there is interest in knowing what the recommendations are regarding screening for TB in patients with existing chronic health conditions that compromise the immune system.

In July 2020, CADTH searched the literature for evidence-based guidelines regarding TB screening for populations with existing chronic conditions.[2] This report identified 1 systematic review of guidelines[3] and 6 evidence-based guidelines[4-9] that met the inclusion criteria based on their title and abstract. The purpose of the current report is to review the full texts of these publications, and to summarize and critically appraise the eligible publications.

This report is a component of a larger CADTH Condition Level Review on Tuberculosis. A condition level review is an assessment that incorporates all aspects of a condition, from prevention, detection, treatment of the patient, and management of the disease. For more information on CADTH's Condition Level Review of Tuberculosis, please visit the project page (https://www.cadth.ca/tuberculosis).

Research Question

What are the evidence-based guidelines regarding tuberculosis screening for populations with existing chronic conditions?

Methods

Literature Search Methods

A limited literature search was conducted for a previous CADTH report[2] by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both focused controlled vocabulary (wherein the terms appeared in major subject headings only), such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were tuberculosis, screening, and chronic conditions. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and June 24, 2020. Internet links were provided, where available.

Selection Criteria and Methods

The evidence in this report was identified in a previous CADTH report,[2] where 1 reviewer screened citations and abstracts. For this report, the full-text articles were reviewed by 1 reviewer and the final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published before 2010. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tool as a guide: the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.[10] Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Table 1: Selection Criteria

Criteria	Description
Population	Any person with an existing chronic condition (e.g., diabetes, renal disease, HIV, organ transplant)
Intervention	Screening for tuberculosis infection (active or latent)
Comparator	Not applicable
Outcomes	Recommendations regarding best practices (e.g., when to screen, frequency of screening, which test[s] to use)
Study designs	Health technology assessments, systematic reviews, evidence-based guidelines

Summary of Evidence

Quantity of Research Available

A total of 550 citations were identified in the literature search for the previous CADTH report[2] and 2 potentially relevant publications were retrieved from the grey literature. Seven potentially relevant reports were identified and retrieved for full-text review. Of these potentially relevant articles, 2 publications were excluded (1 systematic review of guidelines[3] did not provide the detailed recommendations from the guidelines, and 1 review did not follow a systematic approach[7]), and 5 evidence-based guidelines[4-6,8,9] met the inclusion criteria and were included in this report.

Summary of Study Characteristics

Five evidence-based guidelines[4-6,8,9] were identified and included in this report, and are summarized below. Additional details regarding the study characteristics are provided in tables in Appendix 1.

One guideline published in 2019 was a joint guideline by the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America (CDC/NIH/HIV MAIDSA)[4]; this guideline is meant to apply to the US . The German guideline for the treatment of psoriasis vulgaris was published in 2018, and is meant to apply to Germany.[8] There were 2 guidelines published in 2016; the guideline by the National Institute for Health Care Excellence (NICE)[5] is meant to apply to the UK, and a joint guideline by the Spanish Society of Infectious Diseases and Clinical Microbiology and the Spanish Society of Respiratory Diseases and Thoracic Surgery (SEIMC/SEPAR)[9] is meant to apply to Spain. A WHO guideline was published in 2013 and is meant to apply globally. One guideline[8] was specific for patients with psoriasis vulgaris. Three guidelines[5,6,9] covered a broader population than the current report (i.e., the general population with or at risk of TB), which included individuals with HIV or other conditions that compromise the immune system (e.g., chronic inflammation). The other guideline[4] was specific to individuals with HIV. The interventions considered within guidelines were broader than the eligible interventions for this report. The interventions that were relevant to this report included screening strategies, the tuberculin skin test (TST), and the interferon-gamma release assay (IGRA).[4-6,8,9]

Summary of Critical Appraisal

The critical appraisal of the included guidelines is summarized below and additional details are provided in.

Two of the guidelines[5,9] in this report were previously included in CADTH reports on guidelines for the treatment of TB[11] or for TB in people with compromised immunity.[12] The detailed critical appraisal of these guidelines can be found in those reports. In brief, both the NICE guideline[5] and the SEIMC/SEPAR guideline[9] used high-quality systematic methods to search for evidence and develop the recommendations.

Overall, the methodology for the CDC/NIH/HIV MAIDSA guideline[4] was poorly reported, reducing the quality of guideline and the certainty in the recommendations. The objective of the guideline, the population of interest, and target users were clearly reported, but the research questions covered by the guideline were not specifically described. While it was

reported that guideline working group members were responsible for searching for evidence using systematic reviews, no other methods were specified. Thus, it is unknown whether systematic approaches were used for searching for, selecting, or evaluating the evidence. In addition, the methods for formulating the recommendations were not reported, nor were specific links between the recommendations and supporting evidence provided. The source of funding was reported, but it was unclear whether the funder influenced the guideline. All members of the guideline development group declared potential conflicts of interest, which were reviewed to determine if members were disqualified from contributing to certain portions of the guideline, thus reducing the risk of bias due to financial or personal conflicts of interest.

The guideline for psoriasis vulgaris[8] included in this report is a shorter version of a longer German guideline, which was not accessible for this report. The guideline reported that certain components, such as the aim of the guideline, detailed methodology, and instructions on using the guideline, are reported in the longer version of the guideline, and as it was not available in English, it is was not possible to assess these aspects. The members of the guideline development, their affiliations, and their roles were reported, and there were patient representatives in the guideline development group, although how the patients contributed was not reported. The methodology used to search for evidence in this guideline varied by topic, and for the section of the guideline that was relevant to this report (i.e., screening for TB), no systematic search for evidence was conducted and the recommendations were generated through consensus among experts, limiting the confidence in these recommendations. The source of funding was reported and it was reported that the funder had no influence on the recommendations. All members of the guideline development group declared their potential conflicts of interest, and specific criteria were used to mitigate these conflicts.

The WHO guideline[6] had a clear description of the scope of the guideline, the health questions covered, the population to whom the guideline was meant to apply, and the target users of the guideline. This guideline used a systematic approach to search for and select the evidence, and the explicit link between the recommendations and supporting evidence were reported. Although the systematic review conducted to address the research questions relevant to the current report did not describe the quality or risk of bias in the included studies, the guideline included an evaluation of the overall quality of the evidence following standard methods (i.e., Grading of Recommendations, Assessment, Development and Evaluations or GRADE), which included an assessment of the study limitations. The methods for developing the recommendations from the evidence were briefly described, and additional details would improve the understanding of how the final decisions were made. In addition, it was not reported whether the views of target population were sought in developing the recommendations. The source of funding was reported, but it was unclear whether the funder influenced the guideline. It was reported that none of the experts declared any conflicts of interest that were judged to significantly affect the development of the recommendations.

Summary of Findings

Additional details regarding the main study findings and authors' conclusions are provided in tables in Appendix 1.

Guidelines Regarding Tuberculosis Screening in Populations with Existing Chronic Conditions

Five evidence-based guidelines[4-6,8,9] included recommendations regarding screening for TB in populations with chronic health conditions.

Screening for Latent Tuberculosis Infection in People with HIV

The CDC/NIH/HIV MAIDSA guideline[4] recommends that all people with HIV should be tested for latent tuberculosis infection (LTBI), at the time of their HIV diagnosis; this is a strong recommendation based on 1 or more well-designed study. The CDC/NIH/HIV MAIDSA guideline[4] also recommends that people with HIV who are at high risk of exposure to TB should receive annual testing for LTBI using TST; this is a strong recommendation based on expert opinion.

For patients with HIV and cluster of differentiation 4 (CD4) counts of fewer than 200 cells/mm^3, the NICE guideline[5] recommends testing for LTBI using an IGRA with a concurrent TST, and if either test is positive to assess for active TB; this recommendation was based off of low- to high-quality evidence, and made with the certainty that for the vast majority of patients this screening approach will do more good than harm.

The SEIMC/SEPAR guideline[9] recommends that people with HIV are screened for LTBI using both the IGRA and the TST; however, in patients with HIV and a CD4 count of fewer than 200 cells/mm^3 this guideline recommends only using IGRA; this is a weak recommendation based on low-quality to very low-quality evidence.

Screening for Active Tuberculosis in People with HIV

The WHO guideline,[6] recommends that people living with HIV be screened for active TB at each visit to a health facility; this is a strong recommendation based on very low-quality evidence.

If a patient with HIV is suspected of having active TB, the NICE guideline[5] recommends using a rapid nucleic acid amplification test for diagnosis; this recommendation is based on very low-quality evidence, but it is made with the certainty that for the vast majority of patients this testing approach will do more good than harm.

Screening for Tuberculosis in People who Require Treatment with a Biologic Therapy

For patients with psoriasis vulgaris, the guideline [8] recommends that IGRA and a chest X-ray are used to screen for TB before initiating treatment with immunosuppressants; this is a strong recommendation based on expert opinion.

For patients with chronic inflammatory disease, the SEIMC/SEPAR guideline[9] recommends screening for LTBI using both the TST and an IGRA before starting biologic therapy; this is a weak recommendation based on low-quality to very low-quality evidence.

The guideline for psoriasis vulgaris[8] also recommends repeating the IGRA and chest X-ray during treatment with biologic therapy, if there is a suspicion that the patient may be infected with TB (i.e., TB reactivation or new infection); this is a strong recommendation based on expert opinion.

Screening for Tuberculosis in People with Other Forms of Compromised Immunity

For patients who will undergo a solid organ or stem cell transplant, the SEIMC/SEPAR guideline[9] recommends that patients are screened for LTBI using both the TST and an IGRA before transplantation; this is a weak recommendation based on very low-quality evidence.

For adults who are severely immunocompromised, such as those who have had a solid organ or stem cell transplant, the NICE guideline[5] recommends testing for LTBI using an IGRA with a concurrent TST, and if either test is positive to assess for active TB; this recommendation was based on low to high-quality evidence, and made with the certainty that for the vast majority of patients this screening approach will do more good than harm.

For adults who are immunocompromised, the NICE guideline[5] recommends testing for LTBI using the IGRA alone or with a concurrent TST, and if either test is positive to further assess the patient for active TB; this recommendation was based off of low- to high-quality evidence and made with the certainty that for most patients this testing strategy will do more good than harm.

Limitations

The findings in this report are limited by the quality of evidence. While 2 guidelines[5,9] used high-quality methods to develop their recommendations, 1 guideline[6] did not report sufficient detail of the methodology used to develop the recommendations and was assessed to be of moderate quality, and the other 2 guidelines did not use systematic methods for searching for evidence and were assessed to be of low quality.[4,8] In addition, the relevant recommendations in the guidelines were based primarily on expert opinion or low-quality evidence, which reduces the certainty of the recommendations summarized in this report.

This report identified recommendations for TB screening in people with HIV, those requiring a biologic therapy (e.g., psoriasis vulgaris), and individuals who have had or who require a solid organ or stem cell transplant but did not identify recommendations for all chronic conditions (e.g., diabetes or end-stage renal disease); and thus, the recommendations regarding screening for TB in populations with those conditions is unknown.

While 1 of the guidelines[6] is meant to apply globally, none of the guidelines are specific to Canada, and it is unknown whether recommendations from guidelines developed outside of Canada are generalizable to the Canadian clinical practice, as there may be geographical differences between countries with regard to access to care for these chronic conditions, and for the availability of screening tests for TB.

Conclusions

This report comprises 5 evidence-based guidelines[4-6,8,9] that included recommendations regarding screening for TB in individuals with chronic health conditions.

With regard to screening strategies for TB, in patients with HIV, 1 guideline[4] recommended that patients are screened for LTBI upon diagnosis of HIV, and annually thereafter. To test for

a LTBI in people with HIV, 1 guideline[9] makes a weak recommendation (based on low-quality to very low-quality evidence) to use both the IGRA and TST tests, unless patients have a CD4 count of fewer than 200 cells/mm^3, in which case only the IGRA is recommended. This is contradicted by a strong recommendation (based on low to high-quality evidence) made by another guideline,[5] which recommends using the IGRA and a concurrent TST to test for LTBI in patients with HIV who have a CD4 count of fewer than 200 cells/mm^3.

It is also recommended that people with HIV are screened for active TB at each health care visit.[6] If a patient with HIV is suspected of having active TB it is recommended that a rapid nucleic acid amplification test is used to diagnosis active TB in this population.[5]

In patients with psoriasis vulgaris, 1 guideline[8] recommends screening for TB using IGRA and a chest X-ray before initiating treatment with immunosuppressants, and during treatment with biologic therapy, if there is a suspicion that the patient may be infected with TB. Screening for LTBI using TST and IGRA before starting biologic therapy was also recommended by 1 guideline[9] for patients with chronic inflammation.

In patients who require or who have received a solid organ or stem cell transplant, screening for LTBI using IGRA with a concurrent TST is recommended, before[9] and after[5] transplantation.

Although the recommendations in this report are associated with a moderate degree of uncertainty due to the quality of reporting in the guidelines and the reliance on expert opinion or low-quality evidence, which should be considered when interpreting the findings of this report, most of the recommendations were strong, and made with the certainty that the interventions would do more good than harm for most patients.

Overall, the recommendations suggest that in populations with chronic conditions that compromise the immune system, patients should be screened for TB upon diagnosis of the condition, before initiating treatment, and regularly throughout their care. In most cases, it is recommended to test for LTBI using the IGRA concurrently with the TST, or the IGRA alone. A chest X-ray is recommended to screen for active TB, and it is recommended that a rapid nucleic acid amplification test is used to confirm clinical suspicions of active TB.

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Appendix 1: Characteristics of Included Publications

Table 2: Characteristics of Included Guidelines

Intended users, target population	Relevant interventions and outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
CDC/NIH/HIV MAIDSA 2019[4]					
Intended users: HIV treatment providers, patients with HIV, and policy-makers **Target population:** Adults and adolescents with HIV	Interventions: IGRA, TST Outcomes: Not reported	Working group panel members are responsible for identifying (via a systematic review) and reviewing relevant literature published since last review of the guideline. The panel members synthesize the available evidence.	Evidence considerations include: study design; quality and appropriateness of methods; number of patients; and effect sizes.	Recommendations are proposed by the working group based on an assessment of the evidence (e.g., quality and impact of the data). Working group and co-editors convene to determine if recommendations will be accepted. Recommendations are rated as follows. Strength of the recommendation: • A = strong • B = moderate • C = optional Quality of supporting evidence: • I = 1 or more RCT with clinical outcomes and/or validated laboratory end points • II = 1 or more well-designed, NRS or observational cohort with long-term clinical outcomes • III = Expert opinion	Before approval and publication all recommendations and supporting evidence are reviewed by the co-editors, office of AIDS research, subject experts at the CDC and HIV MAIDSA.

Intended users, target population	Relevant interventions and outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
Guideline for psoriasis vulgaris, 2018[8]					
Intended users: Not reported **Target population:** Patients with psoriasis vulgaris	**Interventions**: TB screening **Outcomes**: Outcomes were specific to psoriasis (e.g., psoriasis severity index)	Update to the 2012 version of the guideline. Methods reported in a separate document.[13] The guideline included systematic reviews on various topics, but for TB-specific topics, the guideline development group decided to only include consensus-based recommendations.	Only consensus-based recommendations were relevant to this report (i.e., no evidence quality reported for these recommendations).	Recommendations were drafted at a guideline consensus conference using the nominal group technique, where they discussed alternatives and reached a final consensus on the recommendations. The level of consensus reached for each recommendation is reported: • Strong consensus: ≥ 95% of participants • Consensus: 75% to 94% of participants • Simple majority: 51% to 74% of participants • No consensus: ≤ 50% of participants Recommendations were also identified as: • Strongly recommended • Recommended • Can be considered • Not recommended	External review, feedback from professional societies, as well as posting online for stakeholder feedback.

Intended users, target population	Relevant interventions and outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
NICE, 2016[5]					
Intended users: Health care professionals working with TB. Government and public health professionals. People with TB and their care providers. **Target population:** General population, including those with HIV and other forms of compromised immunity.	**Interventions**: IGRA, TST, screening strategies for active TB **Outcomes**: Sensitivity, specificity, concordance between tests	Update to a 2011 version of the guideline. Multiple SRs were conducted for the entire guideline, using comprehensive search strategies. For each SR, detailed eligibility criteria were reported. GRADE evidence profiles were prepared.	NICE methodological checklists were used to critically appraise RCTs and cohort studies. GRADE was used to critically appraise the body of evidence. Criteria considered included risk of bias and inconsistency.	Developed using the NICE manual for developing guidelines.[14] Recommendations balance the benefits and harms, and the quality of the evidence. At the meetings, the results of the meta-analyses, GRADE profiles, and evidence statements were presented and discussed. Specific criteria were used to link evidence to the recommendations, which was used to guide the development of the recommendations. A consensus method was used to formulate the recommendations. The wording used in the recommendations denotes the certainty in the recommendations. The terms used in this guideline are: "Offer — for the vast majority of patients, an intervention will do more good than harm Do not offer — the intervention will not be of benefit for most patients Consider — the benefit is less certain, and an intervention will do more good than harm for most patients. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for an offer recommendation, and so the health care professional should spend more time considering and discussing the options with the patient." (p. 90)	Two formal rounds of stakeholder feedback and public consultation were conducted online before publication. This included responding to each comment and maintaining an audit trial.

Intended users, target population	Relevant interventions and outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
SEIMC/SEPAR, 2016[9]					
Intended users: Clinicians, health care professionals, policy-makers **Target population:** General population, people with HIV, people with chronic inflammatory diseases.	**Interventions**: IGRA, TST **Outcomes**: Predictive values, sensitivity and specificity, concordance of results between tests	A systematic review was conducted to answer the research questions, and outcomes of interested were prioritized. Two panel members from each subgroup (based on their expertise) independently compiled the evidence.	The quality of the evidence was assessed using GRADE. Considerations included: limitations, consistency, availability of direct evidence, precision, and publication bias.	Panel members discussed the evidence and formulated the recommendations based on the evidence for each clinical question. To the strength and direction of the recommendation was based on the quality of the evidence, the balance of harms and benefits, the importance of the outcomes, and the resource implications. When possible, the recommendations were based on the outcomes with the highest level of importance. Recommendations were established by consensus. GRADE categories for the quality of evidence: High = Further research is very unlikely to change our confidence in the estimate of effect Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Very low = Any estimate of effect is very uncertain" (pg. 672).[15]	Guideline was externally reviewed.

Intended users, target population	Relevant interventions and outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
WHO, 2013[6]					
Intended users: Staff at TB programs and public health agencies and those involved in planning, implementing, and monitoring TB. **Target population:** People with suspected active TB in countries with intermediated-to-high burden of TB, including those with HIV.	**Interventions**: Systematic screening for active TB using tests, examinations, and procedures. **Outcomes**: Prevalence or incidence of active TB cases detected through active case-finding	4 systematic reviews were conducted for the whole guideline, covering different aspects of TB screening, each supporting specific research questions and pre-defined eligibility criteria. Guideline meetings were held to review the findings, the decision tables, and the quality of the evidence.	The quality of the evidence was assessed using GRADE. Considerations of the evidence included: study design, limitations, inconsistency, indirectness, imprecision, and the trade-off between the desirable and undesirable effects.	Each decision table and related GRADE tables were discussed separately and used to develop the recommendation (if sufficient evidence existed). Consensus was sought for each recommendation. If consensus was not reached, voting was used. Recommendations are either strong or conditional. "Strong = the desirable effects of adhering to the recommendation are judged to clearly outweigh the undesirable effects, and for which screening is judged to be feasible, acceptable and affordable in all settings Conditional = "the desirable effects of adhering to the recommendation probably outweigh the undesirable effects but the trade-offs, cost-effectiveness, feasibility or affordability, or some combination of these, are uncertain." (p. 10)	Externally peer reviewed by regional, national, and international stakeholders.

CDC = Centers for Disease Control and Prevention; GRADE = Grading of Recommendations, Assessment, Development and Evaluations; IGRA = interferon-gamma release assay; MAIDSA = Medicine Association of the Infectious Diseases Society of America; NICE = National Institute for Health and Care Excellence; NIH = National Institutes of Health; RCT = randomized controlled trial; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Respiratory Diseases and Thoracic Surgery; SR = systematic review; TB = tuberculosis; TST = tuberculin skin test.

Table 3: Strengths and Limitations of Guidelines Using AGREE II[10]

Item	CDC/NIH/HIV MAIDSA 2019[4]	Guideline for psoriasis vulgaris, 2018[8]	NICE, 2016[5]	SEIMC/SEPAR, 2016[9]	WHO, 2013[6]
Domain 1: Scope and purpose					
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	No	Yes	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	No	No	Yes	Yes	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes	Partially	Yes	Yes	Yes
Domain 2: Stakeholder involvement					
4. The guideline development group includes individuals from all relevant professional groups.	Partially	Yes	Yes	Partially	Yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	No	Partially	Yes	Partially	No
6. The target users of the guideline are clearly defined.	Yes	No	Yes	Yes	Yes
Domain 3: Rigour of development					
7. Systematic methods were used to search for evidence.	No	No	Yes	Yes	Yes
8. The criteria for selecting the evidence are clearly described.	No	No	Yes	Yes	Yes
9. The strengths and limitations of the body of evidence are clearly described.	No	No	Yes	Partially	Partially
10. The methods for formulating the recommendations are clearly described.	No	Yes	Yes	Yes	Partially
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	No	No	Yes	Yes	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	No	No	Yes	Yes	Yes
13. The guideline has been externally reviewed by experts before its publication.	No	Yes	Yes	Partially	Yes
14. A procedure for updating the guideline is provided.	Yes	Yes	Yes	Yes	No

Item	CDC/NIH/HIV MAIDSA 2019[4]	Guideline for psoriasis vulgaris, 2018[8]	NICE, 2016[5]	SEIMC/SEPAR, 2016[9]	WHO, 2013[6]
Domain 4: Clarity of presentation					
15. The recommendations are specific and unambiguous.	Yes	Yes	Yes	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes	Not applicable	Yes	Not applicable	Not applicable
17. Key recommendations are easily identifiable.	Partially	Yes	Yes	Yes	Yes
Domain 5: Applicability					
18. The guideline describes facilitators and barriers to its application.	No	No	No	Partially	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No	Yes	Partially	No	No
20. The potential resource implications of applying the recommendations have been considered.	No	No	Yes	Partially	No
21. The guideline presents monitoring and/or auditing criteria.	No	Yes	Yes	No	No
Domain 6: Editorial independence					
22. The views of the funding body have not influenced the content of the guideline.	Partially	Yes	Partially	Yes	Partially
23. Competing interests of guideline development group members have been recorded and addressed.	Yes	Yes	Yes	Yes	Yes

AGREE = Appraisal of Guidelines for Research and Evaluation; CDC = Centers for Disease Control and Prevention; MAIDSA = Medicine Association of the Infectious Diseases Society of America; NICE = National Institute for Health and Care Excellence; NIH = National Institutes of Health; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Respiratory Diseases and Thoracic Surgery.

Table 4: Summary of Recommendations in Included Guidelines

Recommendations and supporting evidence	Strength of recommendations and quality of evidence
CDC/NIH/HIV MAIDSA, 2019[4]	
Recommendation 1: "All persons with HIV should be tested for LTBI at the time of HIV diagnosis, regardless of their epidemiological risk of TB exposure." (p. 226) Evidence summary not provided. Recommendation 2: "Annual testing for LTBI using TST is recommended for persons with HIV who are at high risk for repeated or ongoing exposure to persons with active TB disease." (p. 226) Based on expert opinion.	Recommendation 1: AII (i.e., strong recommendation, with evidence from 1 or more well-designed non-randomized or observational study) Recommendation 2: AII (i.e., strong recommendation, based on expert opinion)

Recommendations and supporting evidence	Strength of recommendations and quality of evidence
Guideline for psoriasis vulgaris, 2018[8]	
Recommendation 1: "Ruling out TB using IGRA and chest X-ray is recommended before initiating treatment with immunosuppressants (methotrexate [MTX], TNF-alpha antagonists, ustekinumab, secukinumab)." (p. 808) Recommendation 2: "If there is justified suspicion of TB reactivation or new infection during biologic therapy, repeating the IGRA and chest X-ray is recommended." (p.808)	Recommendation 1: strongly recommended; clinical consensus point (strong consensus) Recommendation 2: strongly recommended; clinical consensus point (strong consensus)
NICE, 2016[5]	
Recommendation 1: "For adults who are severely immunocompromised, such as those with HIV and CD4 counts of fewer than 200 cells/mm^3, or after solid organ or allogeneic stem cell transplant, offer an interferon-gamma release assay and a concurrent Mantoux test. • If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB. • If this assessment is negative, offer them treatment for latent TB infection." (p. 16) Recommendation 2: "For other adults who are immunocompromised, consider an interferon-gamma release assay alone or an interferon-gamma release assay with a concurrent Mantoux test. • If either test is positive (for Mantoux, this is an induration of 5 mm or larger, regardless of BCG history), assess for active TB. • If this assessment is negative, offer them treatment for latent TB infection." (p. 17) For recommendations 1 and 2, low to high-quality evidence found that the percent concordance between the IGRA and TST tests varied by population: HIV (75% to 96%), post-kidney transplant (80%), immune-mediated inflammatory diseases before biologic therapy (60% to 93%). Recommendation 3: Request rapid diagnostic nucleic acid amplification tests for the*M. tuberculosis*complex (*M. tuberculosis*, M. bovis, M. africanum) on primary specimens if there is clinical suspicion of TB disease, and the person has HIV" (p. 25) Very low quality evidence from 16 cross-sectional studies in adults with HIV informed this recommendation (pooled sensitivity of 80.9%, and pooled specificity of 98.8%)	The wording of the recommendations reflects the certainty in the recommendation. Recommendation 1: Offer = for the vast majority of patients, the intervention will do more good than harm Recommendation 2: Consider = the benefit is less certain, and an intervention will do more good than harm for most patients. Recommendation 3: Request = for the vast majority of patients, the intervention will do more good than harm

Recommendations and supporting evidence	Strength of recommendations and quality of evidence
SEIMC/SEPAR, 2016[9]	
Recommendation 1: "The panel suggests using both the TST and an IGRA to screen for TB infection in people with HIV infection. In people with HIV and a CD4-cell count < 200/mL, the panel suggests using only an IGRA." (p. 4) Evidence from 5 observational studies (4 prospective and 1 retrospective) conducted on people with HIV infection from low-prevalence countries contributed to this recommendation. In this population, the positive predictive value of IGRA ranged from 5.9% to 25%, and the negative predictive value ranged from 98.8% to 100%. Recommendation 2: "The panel suggests using both the TST and an IGRA to screen for TB infection in patients with chronic inflammatory disease before starting biological therapy." (p. 4) Evidence from 8 observational studies (7 prospective and 1 retrospective) that assessed the predictive value of IGRA to screen for TB infection in patients with biologic therapies in low-prevalence countries was used to form this recommendation. In this population, the positive predictive value of IGRA ranged from 0% to 1.9%, and the negative predictive value ranged from 97% to 100%. Recommendation 3: "The panel suggests using both the TST and an IGRA to screen for TB infection in patients due to undergo solid organ or allogeneic hematopoietic stem cell transplantation." (p. 4) Evidence from 6 observational studies (4prospective and 2 retrospective) that assessed the predictive values of IGRAs for the development of TB in patients undergoing transplantation. In this population, the positive predictive value of IGRA ranged from 0% to 6%, and the negative predictive value ranged from 95% to 100%.	Recommendation 1: weak recommendation, low to very low-quality evidence Recommendation 2: weak recommendation, low to very low=quality evidence Recommendation 3: weak recommendation, very low-quality evidence
WHO, 2013[6]	
"People living with HIV should be systematically screened for active TB at each visit to a health facility." (p. 19) Evidence from 74 studies that included people with HIV was considered in developing this recommendation. Although the quality of the direct evidence is very low, the guideline development group placed high value on ensuring that TB is diagnosed early in this high-risk group due to the high risk of poor health outcomes in the absence of early diagnosis and treatment.	Strong recommendation, very low-quality evidence

BCG = bacillus Calmette–Guérin; CD4 = cluster of differentiation 4; CDC = Centers for Disease Control and Prevention; IGRA = interferon-gamma release assay; LTBI = latent tuberculosis infection; MAIDSA = Medicine Association of the Infectious Diseases Society of America; NICE = National Institute for Health and Care Excellence; NIH = National Institutes of Health; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Respiratory Diseases and Thoracic Surgery; TB = tuberculosis; TST = tuberculin skin test.