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Tuberculosis in People with Compromised Immunity: A Review of Guidelines

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Abbreviations

AEDV	Spanish Academy of Dermatology and Venereology
AGREE II	Appraisal of Guidelines for Research & Evaluation 2
AOCC	Asian Organization for Crohn's and Colitis
APAGE	Asia Pacific Association of Gastroenterology;
ATS	American Thoracic Society
BCG	Bacillus Calmette-Guérin
BHIVA	British HIV Association
CDC	Centers for Disease Control and Prevention
ECDC	European Centre for Disease Prevention and Control
ERS	European Respiratory Society
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
IGRA	Interferon-gamma release assay
LF-LAM	Lateral flow urine lipoarabinomannan assay
LTBI	Latent tuberculosis infection
NICE	National Institute for Health and Care Excellence
NTAC	National Tuberculosis Advisory Committee
PHAC	Public Health Agency of Canada
SEIMC	Spanish Society of Infectious Diseases and Clinical Microbiology
SEPAR	Spanish Society of Pulmonology and Thoracic Surgery
SEPD	Spanish Society of Digestive Diseases
SER	Spanish Society of Rheumatology
TB	Tuberculosis
TNF	Tumour necrosis factor
TST	Tuberculin skin test
WHO	World Health Organization

Context and Policy Issues

Tuberculosis (TB) is an infectious disease caused by the bacteria Mycobacterium tuberculosis and is transmitted through the air by those who are infected with the bacteria (i.e., coughing). There are two distinct categories of TB, latent TB infection (LTBI)and active TB disease (also known as active TB).[1,2] A person with LTBI is not contagious as they cannot spread the bacteria to others and do not possess any visible symptoms.[1] However, persons with LTBI can develop active TB if the infection is left untreated or the treatment regimen is not followed.[1] Active TB occurs when an individual's immune system is compromised and the bacteria begins to multiply leading to an active infection. Unlike LTBI, an individual with active TB is contagious and can spread the M. tuberculosis bacteria to others. Common symptoms associated with active TB include excessive coughing, chest pain, weight loss, fever, and fatigue.[1]

Canada has one of the lowest rates of active TB disease in the world,[3] however, annual rates of TB in Canada have remained the same since the 1980's rather than declining.[3] Certain risk factors can increase the risk of TB, and these include increased exposure to the TB bacteria (e.g., close contact with someone with TB, or birth in an area with a high incidence of TB) as well as impaired immunity.[4] Impaired or compromised immunity can result from diseases that compromise the immune system (e.g., HIV infection, autoimmune disease, cancer), or from treatments that cause immunosuppression (e.g., anti-rejection

drugs for transplant recipients, or tumor necrosis factor (TNF) inhibitors).[3,4] Patients with compromised immunity have a higher risk of LTBI infection, and developing active TB disease.[4] For instance, people with HIV have a higher risk of developing active TB disease compared to HIV-uninfected people due to their compromised immune system and the inability to adequately fight off infection.[5]

Given the complexity of some of these conditions that compromise the immune system, there may be additional considerations for the prevention, identification, and treatment of TB in these patients. For instance, when identifying TB in patients with compromised immunity, the underlying condition (e.g., HIV infection) may alter the response to a TB diagnostic test. In addition, when treating TB, it may be necessary to consider whether the TB drugs will interact with the other therapies that patients are currently receiving (e.g., anti-TNF or antiretroviral therapies).[5] Moreover, patients on immunomodulators (e.g., anti-TNF) have an increased risk of reactivating TB infection due to the suppression of the individual's immune response, making it difficult to suppress TB infection.[6] Consequently, patients with compromised immunity may require alternative preventive, diagnostic, and treatment strategies for TB compared to the general population.

There are numerous guidelines published regarding the prevention, identification, and treatment of TB. Some guidelines focus on TB in patients with compromised immunity, while other guidelines cover a broad spectrum of populations at risk of TB. These guidelines vary by the populations and topics covered, and the quality of the report, which may make it difficult for health care professionals to select the best guidance on TB in patients with compromised immunity.[7] The purpose of this report is to review and critically appraise the evidence-based guidelines regarding the prevention, identification, and treatment of TB for patients with compromised immunity.

This report is part of series of evidence reviews on TB guidelines and can serve as a guidance document to identify which guidelines include recommendations for TB in patients with compromised immunity and the strength of the guidelines. This report covers recommendations regarding the prevention, identification, and treatment of TB in people with HIV or other conditions that compromise the immune system.

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

Research Question

What are the evidence-based guidelines for the prevention, identification, or treatment of tuberculosis in people with compromised immunity?

Key Findings

Twenty evidence-based guidelines for the prevention, identification, or treatment of TB were identified and included in this report.

Four guidelines made recommendations regarding the prevention of TB in patients with compromised immunity. Twelve guidelines made recommendations regarding the identification of LTBI and nine guidelines made recommendations regarding the identification of active TB disease in patients with compromised immunity. For the treatment

of TB in patients with compromised immunity, ten guidelines made recommendations regarding the treatment of LTBI and ten guidelines made recommendations regarding the treatment of active TB disease.

Overall, there are seven high-quality, one moderate-quality, and twelve low-quality guidelines that include between one and 47 recommendations on TB in patients with compromised immunity. The recommendations vary in strength and the quality of the evidence, as well as the population of interest. The population and topic of interest may determine which guideline(s) and which recommendation(s) are of interest.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was tuberculosis. Search filters were applied to limit retrieval to guidelines. The search was also limited to English language documents published between Jan 1, 2014 and Nov 7, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1. Evidence-based guidelines including recommendations regarding the prevention, identification, or treatment of TB in people who are immunocompromised were considered eligible.

Table 1: Selection Criteria

Population	People with compromised immunity who may have been exposed to pulmonary tuberculosis, who are suspected of having pulmonary tuberculosis, or who have been diagnosed with pulmonary tuberculosis
Intervention	Any intervention for the prevention, identification, or treatment of tuberculosis
Comparator	Any other intervention for the prevention, identification, or treatment of tuberculosis
Outcomes	Recommendations regarding the prevention, identification, or treatment of TB in patients who are immunocompromised
Study Designs	Evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included guidelines were assessed with the AGREE II instrument.[8] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included guideline were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 446 citations were identified in the literature search. Following screening of titles and abstracts, 377 citations were excluded and 69 potentially relevant reports from the electronic search were retrieved for full-text review. 6 potentially relevant publications were retrieved from the grey literature search for full text review. Of these potentially relevant articles, 55 publications were excluded for various reasons, and 20 evidence-based guidelines met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA[9] flowchart of the study selection.

Additional publications that did not meet the inclusion criteria for an evidence-based guideline, but may be of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Twenty evidence-based guidelines were identified and included in this report.[10-29] Detailed characteristics of the guidelines are available in Appendix 2, Table 2.

For 13 of the guidelines[10-12,14,15,18,20,21,24-28] in this report, the population covered by the guideline is broader than the population of this report, and these guidelines are also included in other CADTH reports, as part of the series of evidence reviews on TB guidelines. The detailed methods of these 13 guidelines can be found in the other reports. Specifically, the methods of eight guidelines[11,12,14,15,24,26-28] can be found in the report on guidelines for TB treatment;[30] the methods of three guidelines[10,18,21] can be found in the report on guidelines for TB identification;[31] and methods of two guidelines[20,25] can be found in the report on guidelines for TB prevention.[32] Detailed methods for the other seven guidelines[13,16,17,19,22,23,29] unique to this report are available in Appendix 2,Table 3.

Study Design

Four guidelines were developed by the World Health Organization (WHO); one was published in 2019,[16] two were published in 2018[15,25] and one was published in 2017.[11] Three guidelines were developed by the Italian Pediatric TB Study Group in 2016.[18-20] A two part guideline was published in 2018 by the Asian Organization for Crohn's and Colitis (AOCC) and the Asia Pacific Association of Gastroenterology (APAGE).[22,23] Two guidelines were developed by the Public Health Agency of Canada (PHAC) and published in 2014.[12,13] These guidelines represent two chapters from a larger report by PHAC: the 7th edition of the Canadian Tuberculosis Standards.[33] A guideline by the British HIV Association (BHIVA) was published in 2019.[29] Two other guidelines were published in 2018; these were developed by the Centers for Disease Control and Prevention (CDC),[26] and the European Respiratory Society (ERS) and European Centre for Disease (ECDC).[28] One guideline by the Australian National Tuberculosis Advisory Committee (NTAC) was published in 2017.[10] Five guidelines were published in 2016 by the following organizations; the Singapore Ministry of Health,[14] the National Institute for Health Care Excellence (NICE),[24] a joint guideline by the American Thoracic Society (ATS), CDC, and Infectious Diseases Society

of America (IDSA),[27] 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),[21] and a joint guideline by SEPAR, the Spanish Academy of Dermatology and Venereology (AEDV), the Spanish Society of Digestive Diseases (SEPD), the Spanish Society of Rheumatology (SER) and SEIMC.[17]

Nine guidelines followed standardized methodology for guideline development that is available online.[11,15,16,22-25,27,29] The three guidelines produced by the Italian Pediatric Study Group (i.e., the guidelines for preventing TB, for diagnosing TB, and for immunocompromised patients) reported following the 'Consensus Conference Method' to develop the recommendations, but did not report a reference for this guidance document.[18-20] The other eight guidelines included brief details of the development process, but did not cite published methodology.[10,12-14,17,21,26,28] Nine guidelines reported methods for critically appraising the evidence, and reported ratings of the quality of evidence and the strength of the recommendations.[11,15,16,21-24,27,29] Six guidelines provided ratings of the quality of evidence and strength of the recommendations, but did not provide the methods for evaluating the evidence.[12-14,18-20] Five guidelines did not rate of the quality of evidence or the strength of the recommendations.[10,17,25,26,28] Decisions about the recommendations were reached through consensus in 14 guidelines.[10,11,14-16,18-21,24,25,27-29] For the two AOCC/APAGE guidelines [22,23] a recommendation was accepted if at least 75% of the participants voted in favor. In the other guidelines, the methods for reaching consensus on the recommendations were unclear or not reported.[12,13,17,26]

Country of Origin

Two PHAC guidelines are meant to apply to Canada.[12,13] Four guidelines from the WHO are meant to apply globally.[11,15,16,25] One guideline by the ERS/ECDC[28] is meant to apply to all of Europe, while other guidelines are specific to the United Kingdom[24,29], Italy[18-20] and Spain[17,21]. Two guidelines are meant to apply to the United States[26,27] and two guidelines are specific to Korea[22,23]. One guideline was developed for Singapore[14] and one was specific to Australia.[10]

Patient Population

The main populations covered by the guidelines were adults with HIV,[10-16,19-21,24-29] children with HIV,[12,13,15,16,19,20,25,26] adults with other conditions that compromise immunity (e.g., receiving anti-TNF therapy, chronic inflammatory diseases),[10,17,21-25,28] and children with other conditions that compromise immunity (e.g., T lymphocyte immunodepression).[12,17-20,24,25]

The intended users for 11 guidelines were health care workers and other key TB stakeholders.[11-16,18,21,24-26] For six guidelines, the intended users were health care professionals.[17,19,22,23,28,29] For two guidelines, the intended users were key TB stakeholders.[10,27] The intended users of one guideline were not specified.[20]

Interventions

Four guidelines include recommendations regarding prevention strategies for TB[13,20,25,29] Twelve guidelines included recommendations regarding the identification of LTBI[10,13-15,17-19,21,22,24,28,29] and nine guidelines[10,13,15,16,18,19,22,28,29] include recommendations regarding the identification of active TB. Ten guidelines include recommendations regarding the treatment of LTBI[10,12,13,15,17,23,24,26,28,29] and ten guidelines[11,13,14,17,19,23,24,27-29] include recommendations regarding the treatment for active TB disease.

Outcomes

The number of recommendations regarding the prevention, identification, and treatment of TB for patients with compromised immunity ranges from one to 47 recommendations across guidelines.[10-15,17-29] Seventeen guidelines contain twelve or fewer recommendations.[10-12,14-18,20-28].The BHIVA guideline[29] has 47 recommendations; the PHAC HIV guideline[13] has 45 recommendations; and the Italian Pediatric immunocompromised guideline[19] has 23 recommendations.

Nine of the guidelines reported which outcomes were considered in the systematic reviews that were used for developing the recommendations.[11,15,16,21,24-27,29] The other eleven guidelines[10,12-14,17-20,22,23,28] did not specify which outcomes were considered when developing the recommendations.

Summary of Critical Appraisal

This report includes seven high-quality guidelines,[11,15,16,21,24,27,29] one moderate-quality guideline,[25] and 12 low-quality guidelines.[10,12-14,17-20,22,23,26,28] Additional details regarding the strengths and limitations of the included guidelines are provided in Appendix 3, in Table 4, Table 5, and Table 6.

Thirteen of the guidelines[10-12,14,15,18,20,21,24-28] included in this report are included in the other CADTH reports on TB guidelines, and the detailed critical appraisal of these guidelines can be found in those reports. Specifically, the critical appraisal of eight guidelines[11,12,14,15,24,26-28] can be found in the report on guidelines for TB treatment;[30] the critical appraisal of three guidelines[10,18,21] can be found in the report on guidelines for TB identification;[31] and the critical appraisal of two guidelines[20,25] can be found in the report on guidelines for TB prevention.[32] In brief, of the 13 guidelines covered by the other CADTH TB guideline reports, five guidelines (i.e., the WHO consolidated LTBI guidelines,[15] the WHO guideline for drug-susceptible TB,[11] the ATS/CDC/IDSA treatment guideline,[27] the SEIMC/SEPAR guideline,[21] and the NICE Guideline[24]) followed a detailed process for developing the recommendations, and were assessed to be high-quality. The WHO Position Paper on the BCG vaccine[25] followed standard guideline methodology, but did not grade the strength of the recommendation or the quality of the evidence, and was assessed to be moderate-quality. Four guidelines (i.e., Italian Pediatric guidelines for diagnosis[18] and prevention,[20] the Singapore Guideline,[14] and the PHAC LTBI Treatment guideline[12]) were assessed to be low-quality as they did not report sufficient methods for developing the recommendations. Another three guidelines (i.e., the CDC treatment guideline,[26] the ERS/ECDC Standards,[28] and the NTAC Position Statement[10]) had limited methodological detail and did not evaluate the strength of the recommendations or the quality of the evidence, and the guideline was assessed to be a low-quality.

Seven guidelines[13,16,17,19,22,23,29] are unique to this report of TB guidelines for patients with compromised immunity.

The BHIVA guideline[29] and the WHO LF-LAM guideline[16] are high-quality guidelines. These guidelines have clear, unambiguous recommendations, and the overall objective and health questions covered by these guidelines were well described. The population and subgroups to whom the recommendations apply to are clearly outlined within each recommendation, and in the WHO LF-LAM guideline[16] the target users of the guideline are described. Both guidelines include a list of all members of the guideline development group; in the WHO LF-LAM guideline[16] the specific roles or expertise of each member were described, and the

BHIVA guideline[29] did not outline the specific roles and expertise of each member, thus it is unclear who was responsible for what components of the guideline development. These guidelines used high-quality, systematic methods for developing the recommendations: systematic reviews with transparent search methodology and eligibility criteria, the quality of the evidence was evaluated and well described; and the process for formulating the recommendations was clear. Both guidelines underwent external peer review. For the BHIVA guideline,[29] the competing interests of the members were recorded, but the guideline did not address how these potential conflicts were handled, and it was not reported whether this guideline was funded or sponsored by another organization. For the WHO LF-LAM guideline,[16] the conflicts of interest were stated and were in line with the WHO guidelines for conflicts of interest, and it was acknowledged that the funder did not influence the content of the guidelines.

Five guidelines were assessed to be low-quality due to the lack of reporting of methods, creating uncertainty in the recommendations.[13,17,19,22,23]

For the AOCC/APAGE guidelines Part 1[22] and Part 2,[23] the guidelines had clear descriptions of the scope, the target users, and populations to whom the recommendations were relevant, but they did not state what the health questions were, thus it is unknown what guided the development of the recommendations. The members of the guideline development group were reported, but it is unclear what their roles were, or whether any members of the target population were involved in developing the guideline. It was reported that a structured process was followed to develop the recommendations, however, there was limited detail reported on the process. The authors reported that they conducted a systematic literature search, but did not provide the search strategy or eligibility criteria, nor did they report the critical appraisal of the primary studies. Narrative descriptions of the evidence were provided for each topic, detailing the risks and benefits, but the guideline does not provide evidence-to-decision tables, and there is no explicit link from the evidence to the recommendations. The strength of the recommendations and quality of the evidence were reported, but no methods were provided and it is unclear how the individual components were scored. The authors declared no conflicts of interest, but it was not reported whether the funding agency had any influence on the guideline.

The Italian Pediatric immunocompromised guideline [19] has a clear description of the scope of the guideline, and the health questions covered by the guideline, however, there is uncertainty in the recommendations due to a lack of details on the process of developing of the recommendations. The guideline development group included numerous experts from relevant disciplines, and the roles of the members were clear, although it was not stated whether the panel sought public opinion or considered the affected communities. The authors conducted a systematic literature search, with high quality search methods but did not describe the eligibility criteria, nor did they report the quality of the primary studies (although they reported using Scottish Intercollegiate Guidelines Network to assess the quality of the primary studies). It was reported that the ‘consensus conference method’ was used to develop the recommendations, however, the method was not described. The Delphi method was used to reach a consensus among the panel members when the evidence did not provide consistent and unambiguous recommendations. A narrative summary of the evidence is provided for each health question, but it is unclear how the recommendations were formulated from the evidence. The authors declared no conflicts of interest, but it was not reported whether the funding agency had any influence on the guideline.

The SEPAR/AEDV/SEPD/SER/SEIMC guideline[17] has clear, specific recommendations, but lacked methodological detail on the development process for the recommendations, contributing to uncertainty in the guideline. The overall scope of the guideline and the populations to who the recommendations apply were well described. The health questions that guided the development of the guideline were not reported, and it was not reported whether the views of the target population were sought. This guideline acknowledged the various members involved in the development of the guideline, including the authors of the writing committee, the coordinating authors, and the steering committee. This guideline did not provide any methods with regards to the search for evidence, thus the quality of the search strategy and eligibility criteria for selecting the evidence is unknown. This guideline reports the strength of the recommendation and the quality of evidence for each recommendation, and it includes an explanation of how these scores can be interpreted, however, no there are no methods to explain how these criteria were applied. It is unknown how the quality of the primary studies was evaluated, and no evidence tables were provided, thus the strengths and limitations of the evidence are unclear. It was reported that an external review occurred, but it is unclear what the process was for the external review. The funding body was not disclosed and there is no explicit statement that the views of the funding body have influenced the guideline. COIs were disclosed for some authors, but it was not reported how they were addressed. The other authors declared no conflicts.

The PHAC HIV guideline[13] has clear and specific recommendations that are easy to identify, however, limited detail on the process for developing the recommendations was provided, creating a lack of certainty in the recommendations. The overall scope and the population to whom the guideline applies were not explicitly stated, but could be inferred from the content of the guideline. The health questions that guided the development of the recommendations were not reported. This guideline listed a small number of authors (i.e., two authors) and their institutions, but their specific roles were unclear. It was not reported whether a larger guideline development group was involved in the process, thus is unknown if individuals from all relevant professional groups were involved or whether the views of the target population were sought. The quality of the search strategy and eligibility criteria for selecting the evidence is unknown, as the guideline did not report any methods regarding the search for evidence. The strength of the recommendation and the quality of evidence for each recommendation was reported, and the scores are explained in the preface document,[34] however, it is unclear how these criteria were applied. It is unknown how the quality of the primary studies were evaluated, and no evidence tables are provided, thus the strengths and limitations of the evidence are unclear, and no methods for formulating the recommendations were reported. A list of external reviewers was reported for the whole set of PHAC TB Standards, but it was unclear who reviewed these recommendations, or what the process was for the external review. The funding body was disclosed for the PHAC guidelines, but there is no explicit statement that the views of the funding body have not influenced the guideline, and the authors did not disclose whether they had any conflicts, thus it is unclear whether there were any conflicts of interest from the funder or the authors.

Summary of Findings

Guidelines

Twenty evidence-based guidelines were identified that made recommendations regarding the prevention, identification, or treatment of TB in patients with compromised immunity.[10-29] Four guidelines made recommendations regarding the prevention of TB patients with compromised immunity.[13,20,25,29] Twelve guidelines made recommendations regarding the

identification of LTBI.[10,13-15,17-19,21,22,24,28,29] Nine guidelines made recommendations regarding the identification of active TB disease in patients with compromised immunity.[10,13,15,16,18,19,23,28,29] For the treatment of TB in patients with compromised immunity, ten guidelines made recommendations regarding the treatment of LTBI[10,12,13,15,17,23,24,26,28,29] and ten guidelines made recommendations regarding the treatment of active TB disease.[11,13,14,17,19,23,24,27-29]

Recommendations Regarding the Prevention of TB

The high-quality BHIVA guideline[29] made a strong recommendation, based on moderate quality evidence regarding a TB infection control plan for hospitals treating patients with HIV.

The recommendations in the moderate-quality WHO Position Paper on the BCG vaccine[25] covered BCG vaccination in neonates with HIV or born to mothers with HIV, as well as BCG vaccination in people with other immunodeficiency conditions. These recommendations were not graded, and the quality of the evidence from which the recommendations are based is unknown.

The low-quality Italian Pediatric Guideline on prevention[20] includes strong recommendations based on evidence from observational studies, regarding BCG vaccination in neonates with a family history of HIV or other immunodeficiencies.

The low-quality PHAC HIV guideline[13] covered TB infection control plans for hospitals treating patients with HIV, and BCG vaccination in patients or neonates with HIV or other immunodeficiency, or a family history of these conditions. This guideline includes conditional and strong recommendations, based on weak to strong.

Recommendations Regarding the Identification of LTBI

Four of the guidelines that made recommendations regarding the identification of LTBI in patients with compromised immunity were high-quality guidelines.[15,21,24,29]

The high-quality BHIVA guideline[29] includes strong and weak recommendations, based on very low- to high-quality evidence, as well as some ‘good practice points’ (i.e., suggested best practices based on clinical judgement and experience when no evidence is available; see grading system in Table 3) regarding who should be tested for LTBI, including contact tracing, excluding active TB prior to LTBI testing, and which test to use for LTBI testing (i.e., tuberculin skin test (TST) or interferon gamma release assay (IGRA)).

The high-quality WHO consolidated LTBI guideline[15] includes conditional and strong recommendations, based on very low to strong quality evidence, regarding LTBI testing prior to preventive TB treatment in patients with HIV, as well as screening for LTBI in people who are candidates for biological treatments (e.g., anti-TNF therapy).

The high-quality SEIMC/SEPAR Guideline[21] made weak recommendations, based on low to very low quality evidence regarding screening for LTBI in people who are candidates for biological treatments, and which test to use for LTBI testing in patients with HIV or other immunocompromised conditions.

The high-quality NICE Guideline[24] covered which test to use for LTBI testing in patients with HIV or other immunocompromised conditions, TB risk assessments for adults who are anticipated to be immunocompromised, and referrals to specialists for pediatric patients

who are immunocompromised. In this guideline, the certainty of the recommendation is reflected in the wording, and the strength of the evidence differs across recommendations.

There were six low-quality guidelines that made recommendations regarding the identification of LTBI in patients who are immunocompromised.[13,14,17-19,22] The strength of the recommendations varied across and within the guidelines, ranging from very weak to strong recommendations, and the recommendations were based on evidence ranging from very low- to high-quality evidence.

The AOCC/APAGE guideline Part 1[22] made recommendations regarding screening for LTBI in patients receiving anti-TNF therapy, such as who to screen, the use of chest radiographs, and using the TST or IGRA.

The Italian Pediatric guideline for diagnosing TB[18] and the Italian Pediatric guideline for immunocompromised patients[19] both included recommendations regarding the use of the TST or IGRA for pediatric patients with T lymphocyte immunodepression.

The SEPAR/AEDV/SEPD/SER/SEIMC guideline[17] made recommendations regarding screening for LTBI in candidates for anti-TNF therapy, as well as the use of the TST or IGRA for immunocompromised patients.

The Singapore Guideline[14] includes a recommendation regarding the use of the TST or IGRA for patients with HIV.

The PHAC HIV guideline[13] includes recommendations regarding who should be tested for TB, and the use of the TST or IGRA in patients with HIV.

The ERS/ECDC Standards[28] and the NTAC Position Statement[10] also included recommendations for the identification of LTBI, however, these low-quality guidelines did not report the strength of the recommendations or the quality of evidence. The ERS/ECDC Standards[28] included a recommendation for TB contact tracing in patients with HIV, and the NTAC Position Statement[10] included recommendations regarding testing for TB in patients with HIV, and different diagnostic tests for LTBI (e.g., TST, IGRA, chest radiographs) in patients with other immunocompromised conditions (e.g., receiving anti-TNF therapy, organ transplant recipients).

Recommendations Regarding the Identification of Active TB Disease

Three of the guidelines that made recommendations regarding the identification of active TB disease in patients with compromised immunity were high-quality guidelines.[15,16,29]

The high-quality BHIVA guideline[29] includes recommendations regarding identifying active TB in patients with HIV using various diagnostic tools, including recognizing the signs and symptoms of TB, the use of the TST or IGRA, microscopy, rapid molecular tests, and drug susceptibility testing. This guideline includes strong and weak recommendations, based on very low- to high-quality evidence, as well as some ‘good practice points’.

The high-quality WHO LF-LAM guideline [16] includes conditional and strong recommendations regarding the use of lateral flow urine lipoarabinomannan assay (LF-LAM) in patients with HIV to diagnose TB, based on very low- to moderate-quality evidence.

The WHO consolidated LTBI guideline[15] includes conditional and strong recommendations based on very low to strong evidence regarding the diagnosis of active TB in patients with

HIV, such as who should be evaluated for TB, the signs and symptoms, and chest radiography.

There were four low-quality guidelines that made recommendations regarding the identification of LTBI in patients who are immunocompromised.[13,18,19,23] The strength of the recommendations varied across and within these low-quality guidelines, ranging from very weak to strong recommendations, and the recommendations were based on evidence ranging from very low- to high-quality evidence.

The AOCC/APAGE guidelines, Part 2[23] includes a recommendation regarding monitoring for the development of active TB after treatment for LTBI in patients receiving anti-TNF therapy.

The Italian Pediatric guideline for diagnosing TB[18] and the Italian Pediatric guideline for immunocompromised patients[19] both include recommendations regarding diagnosing active TB disease in pediatric patients with T lymphocyte immunodepression.

The PHAC HIV guideline[13] makes recommendations regarding who should be evaluated for active TB disease.

The ERS/ECDC Standards[28] and the NTAC Position Statement[10] also included recommendations for the identification of active TB disease, however, these low-quality guidelines did not report the strength of the recommendations or the quality of evidence. The ERS/ECDC Standards[28] includes a recommendation regarding expediting diagnostic evaluations for TB in people with immune-compromising conditions. The NTAC Position Statement[10] makes recommendations regarding the use of chest radiography and sputum specimens for diagnosing active TB in patients with HIV.

Recommendations Regarding the Treatment of LTBI

There are three high-quality guidelines that made recommendations regarding the treatment of LTBI in patients with compromised immunity.[15,24,29]

The high-quality BHIVA guideline[29] includes recommendations regarding treating patients with HIV for LTBI, including who should be treated and the treatment regimen. The recommendations in this guideline vary in strength and quality of evidence.

The high-quality WHO consolidated LTBI guideline[15] includes conditional and strong recommendations for the treatment regimen for LTBI for patients with HIV, as well as preventive LTBI treatment in patients with HIV.

The high-quality NICE Guideline[24] covered LTBI treatment regimens for patients with HIV. The certainty of the recommendation is reflected in the wording, and in this case suggests that for the majority of patients, the intervention will do more good than harm. The strength of the evidence differs across recommendations within this guideline.

There are four low-quality guidelines that include recommendations regarding the treatment of LTBI in patients with HIV and other conditions that compromise the immune system.[12,13,17,23] These low-quality guidelines include a mix of conditional and strong recommendations, based on evidence ranging from very low- to high-quality evidence.

The AOCC/APAGE guideline, part 2[23] has recommendations regarding the treatment of LTBI in patients prior to and currently receiving anti-TNF therapy.

The SEPAR/AEDV/SEPD/SER/SEIMC guideline[17] has a recommendation regarding LTBI treatment prior to anti-TNF therapy.

The PHAC HIV guideline[13] includes recommendations regarding LTBI treatment regimens for patients with HIV, including preventive LTBI treatment, and LTBI treatment for patients who are pregnant or breastfeeding, as well as recommendations concerning antiretroviral therapy for people with LTBI, and directly observed therapy in this population.

The PHAC LTBI Treatment guideline[12] includes recommendations concerning LTBI treatment regimens for patients with HIV, including those who are pregnant or breastfeeding.

Three additional low-quality guidelines include recommendations regarding the treatment of LTBI, however, the strength of the recommendation and the quality of evidence were not reported in these guidelines.[10,26,28] The CDC treatment guideline[26] includes a recommendation regarding a specific treatment for LTBI (i.e., once-weekly isoniazid-rifapentine for 12 weeks, also known as 3HP) for patients with HIV. The ERS/ECDC Standards[28] and the NTAC Position Statement[10] both make a recommendation regarding preventive LTBI treatment in patients with HIV.

Recommendations Regarding the Treatment of Active TB Disease

Recommendations regarding the treatment of active TB disease in patients with compromised immunity were included in four high-quality guidelines.[11,24,27,29]

The high-quality BHIVA guideline,[29] includes mostly strong recommendations, with some weak recommendations and 'good practice points', regarding treating active TB disease in patients with HIV, covering topics such as treatment regimens, treating drug-resistant TB, directly observed therapy, managing the treatment, and treatment during pregnancy.

Two high-quality guidelines, the WHO guideline for drug-susceptible TB[11] and the ATS/CDC/IDSA treatment guideline,[27] both include one conditional recommendation, with very low certainty in the evidence regarding the treatment regimen for active TB in patients with HIV. These two guidelines also include two strong recommendations with high certainty in the evidence regarding the provision of antiretroviral treatment in people with HIV and TB.[11,27]

The high-quality NICE Guideline[24] also includes recommendations regarding treatment regimens for active TB in patients with HIV, as well as the use of multidisciplinary teams to manage patients who have TB and HIV. For this guideline, the certainty of the recommendations is reflected in the wording of the recommendations.

Recommendations concerning the treatment of active TB disease in patients who are immunocompromised were also made in five low-quality guidelines.[13,14,17,19,23] The strength of the recommendations in these low-quality guidelines varies from weak to strong, and the evidence ranges from expert opinion to high-quality evidence, depending on the topic and the guideline.

The AOCC/APAGE guideline, part 2[23] and the SEPAR/AEDV/SEPD/SER/SEIMC guideline[17] includes recommendations regarding the treatment of active TB in patients who are receiving anti-TNF therapy.

The Italian Pediatric guideline for immunocompromised patients[19] includes recommendations for treating active TB disease in pediatric patients who are receiving anti-

TNF therapy or immunosuppressive treatment, or pediatric patients who are undergoing treatment for cancer or who have received an organ transplant.

The Singapore Guideline[14] includes recommendations regarding the treatment regimen for active TB in patients with HIV.

The PHAC HIV guideline[13] includes recommendations concerning the treatment of active TB in patients with HIV, including the treatment regimen, the provision of antiretroviral therapy, the use of a multidisciplinary team, and monitoring treatment response.

The low-quality ERS/ECDC Standards[28] also included recommendations regarding HIV screening in patients newly diagnosed with TB and antiretroviral therapy in patients with HIV and TB, however, the strength of the recommendations or the quality of evidence were not reported in this guideline.

Limitations

There are limitations associated with the evidence in this report on guidelines for the prevention, identification, and treatment of TB in patients with compromised immunity.

The evidence may be limited by the availability of recommendations for specific populations. In this report, the topics covered by the recommendations were divided by recommendations for patients with HIV and recommendations for patients with other immune compromising conditions (e.g., T lymphocyte immunodepression, chronic inflammatory conditions, cancer, transplant recipients, and patients receiving anti-TNF therapy). Overall, there were more topics relating to patients with HIV (i.e., 39 topics) compared to topics relating to all the other immune compromising conditions combined (i.e., 20 topics). This suggests that there may be a gap in the evidence with regards to evidence-based guidelines for TB in patients with certain immune compromising conditions other than HIV.

Some of the topics covered by the recommendations in this report may also be limited by the quality of the guidelines. This report includes one moderate-quality guideline,[25] and 12 low-quality guidelines,[10,12-14,17-20,22,23,26,28] and four of these guidelines[10,25,26,28] did not grade the strength of the recommendations or the quality of the evidence. Twenty two of the 58 topics covered by the recommendations were only covered in one or more moderate- or low-quality guideline, and the recommendations associated with these topics may have reduced reliability. With regard to prevention, recommendations for BCG vaccination in patients with compromised immunity (either HIV or other conditions) were not covered in any of the high-quality guidelines. Other topics that were only covered in the low-quality guidelines include the identification of latent and active TB in non-HIV immune compromising conditions and the treatment of LTBI and active TB disease in patients receiving anti-TNF therapy or other immunosuppressive treatments.

This report may also be limited in its generalizability to the Canadian context. Two of the guidelines by PHAC[12,13] were developed for Canada, and four other guidelines[11,15,16,25] are intended for global use, while the 15 other guidelines were developed for other regions, including Europe, the United States, Australia, Singapore, and Korea. It is unknown if the guidelines developed outside of Canada are generalizable to the Canadian context, as there may geographical differences the populations with compromised immunity, as well as differences in resources and practices used for the prevention, identification and treatment of TB compared to Canada.

This report is also limited by the large volume of recommendations concerning TB in patients with compromised immunity. The guidelines included in this report have between one and 47 relevant recommendations covering multiple different topics (i.e., prevention, and identification and treatment of LTBI and active TB), and it was not possible to compare the recommendations. Thus, it is unclear whether any of the recommendations contradict each other or whether there is agreement in the evidence across guidelines.

Conclusions and Implications for Decision or Policy Making

This report was comprised of 20 guidelines covering the prevention, identification, and treatment of TB in patients with compromised immunity.[10-29]

Four guidelines covered the prevention of TB in patients with compromised immunity.[13,20,25,29] This includes one high-quality guideline[29] that made a recommendation regarding a TB infection control plans for hospitals treating patients with HIV. A moderate-quality guideline[25] that did not grade the evidence included recommendations regarding BCG vaccination in patients with compromised immunity. Two low-quality guidelines also have recommendations regarding BCG vaccination; one was specific to Italian pediatric patients with compromised immunity,[20] and one was a Canadian guideline specific to patients with HIV.[13]

Twelve guidelines include recommendations regarding the identification of LTBI.[10,13-15,17-19,21,22,24,28,29] There were four high-quality guidelines that made recommendations regarding the identification of LTBI in patients with compromised immunity,[15,21,24,29] which included both weak and strong recommendations. The recommendations in these high-quality guidelines covered topics such as which test to use for patients with HIV or other immune compromising conditions,[21,24,29] and who should be tested for LTBI.[29] There were eight low-quality guidelines that made recommendations regarding the identification of LTBI in patients with compromised immunity,[10,13,14,17-19,22,28] including two guidelines[10,28] that did not grade the recommendations. The recommendations in these low-quality guidelines covered topics such as which screening test to use for LTBI in patients with compromised immunity,[10,13,14,17-19,22] and contact tracing.[28]

Three high-quality guidelines[15,16,29] and six low-quality[10,13,18,19,23,28] made recommendations regarding the identification of active TB disease in patients with compromised immunity. The high-quality guidelines include a mix of weak and strong recommendations covering various diagnostic tests for active TB in patients with HIV (e.g., microscopy, chest radiography, molecular tests),[15,29] the use of LF-LAM in patients with HIV,[16] and who should be evaluated for TB.[15] The low-quality guidelines include recommendations covering topics such as diagnosing active TB in p pediatric patients with T lymphocyte immunodepression,[18,19] who should be evaluated for TB,[13] expediting diagnostic tests for active TB in patients with compromised immunity,[28] and diagnostic tests in patients with HIV.[10]

Ten guidelines made recommendations regarding the treatment of LTBI in patients with compromised immunity.[10,12,13,15,17,23,24,26,28,29] Three high-quality guidelines covered treating LTBI in patients with HIV, including treatment regimens, who should be treated, and preventive therapy.[15,24,29] The seven low-quality guidelines.[10,12,13,17,23,26,28] including three guidelines that did not grade the quality of the evidence,[10,26,28] include recommendations regarding treatment regimens for patients with compromised immunity.[10,12,13,17,23,26,28] The Canadian guidelines also include recommendations regarding LTBI treatment in patients

with HIV who are also pregnant or breastfeeding,[12,13] and directly observed therapy for LTBI in patients with HIV.[13]

Four high-quality guidelines[11,24,27,29] and six low-quality guidelines[13,14,17,19,23,28] include recommendations regarding the treatment of active TB disease in patients with compromised immunity. The high-quality guidelines made very weak to strong recommendations regarding treatment regimens for active TB in patients with HIV,[11,24,27,29] treating drug-resistant TB in patients with HIV,[29] and the provision of antiretroviral treatment in people with HIV and TB.[11,27] The low-quality guidelines include recommendations regarding the treatment of active TB in patients who are receiving anti-TNF therapy,[17,23] treating active TB in pediatric patients with compromised immunity,[19] the treatment regimen for active TB in patients with HIV,[13,14] and antiretroviral therapy in patients with HIV and TB.[28]

Overall, this report identified seven high-quality guidelines[11,15,16,21,24,27,29] that include recommendations regarding the prevention, identification, and treatment of latent and active TB in patients with compromised immunity. This report also identified one moderate-quality guideline[25] and 12 low-quality guidelines[10,12-14,17-20,22,23,26,28] that may provide additional guidance on TB in patients with compromised immunity, however, there is uncertainty associated with these low-quality guidelines and the recommendations should be interpreted with caution.

References

1. The Difference Between Latent TB Infection and TB Disease Atlanta: Centers for Disease Control and Prevention; 2014: https://www.cdc.gov/tb/publications/factsheets/general/ltbiandactivetb.htm. Accessed 2020 Jan 8.
2. Global Tuberculosis Report 2019. Geneva: World Health Organization; 2019: https://www.who.int/tb/publications/global_report/en/. Accessed 2020 Jan 8.
3. Public Health Agency of Canada. Tuberculosis: Monitoring Ottawa: Public Health Agency of Canada; 2019: https://www.canada.ca/en/public-health/services/diseases/tuberculosis/surveillance.html. Accessed 2020 Jan 8.
4. Horsburgh CR, Jr. Epidemiology of tuberculosis. Waltham (MA): UpToDate; 2019: www.uptodate.com.
5. Menzies D. Treatment of latent tuberculosis infection in nonpregnant adults with HIV infection. Waltham (MA): UpToDate; 2019: www.uptodate.com.
6. Anastasopoulou A, Ziogas DC, Samarkos M, Kirkwood JM, Gogas H. Reactivation of tuberculosis in cancer patients following administration of immune checkpoint inhibitors: current evidence and clinical practice recommendations. *J Immunother Cancer.* 2019;7(1):239.
7. Tuberculosis: Guidelines, reviews, statements, recommendations, standards. Geneva: Geneva Foundation for Medical Education and Research 2020: https://www.gfmer.ch/Guidelines/Tuberculosis/Tuberculosis_mt.htm Accessed 2020 Jan 9.
8. Agree Next Steps Consortium. The AGREE II Instrument. [Hamilton, ON]: AGREE Enterprise; 2017: https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf. Accessed 2019 Jul 10.
9. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol.* 2009;62(10):e1-e34.
10. Bastian I, Coulter C, National Tuberculosis Advisory Committee. Position statement on interferon-γ release assays for the detection of latent tuberculosis infection. *Commun Dis Intell Q Rep.* 2017;41(4):E322-E336.
11. World Health Organization. Guidelines for treatment of drug-susceptible tuberculosis and patient care (2017 update). Geneva: World Health Organization; 2017: https://www.who.int/tb/publications/2017/dstb_guidance_2017/en/. Accessed 2020 Feb 21.
12. Menzies D, Alvarez GG, Khan K. Canadian Tuberculosis Standards, Chapter 6 - Treatment of Latent Tuberculosis Infection. Ottawa: Public Health Agency of Canada; 2014: https://www.canada.ca/en/public-health/services/infectious-diseases/canadian-tuberculosis-standards-7th-edition/edition-18.html. Accessed 2020 Feb 21.
13. Houston SW, T;. Canadian Tuberculosis Standards, Chapter 10 - Tuberculosis and Human Immunodeficiency Virus. 2014: https://www.canada.ca/en/public-health/services/infectious-diseases/canadian-tuberculosis-standards-7th-edition/edition-6.html.
14. Prevention, Diagnosis and Management of Tuberculosis. Singapore: Ministry of Health; 2016: https://www.moh.gov.sg/docs/librariesprovider4/guidelines/moh-tb-cpg-full-version-for-website.pdf. Accessed 2019 Nov 7.
15. World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva: World Health Organization; 2018: https://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/. Accessed 2020 Feb 21.
16. World Health O. Lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis of active tuberculosis in people living with HIV, 2019 Update. 2019: https://www.who.int/tb/publications/2019/diagnose_tb_hiv/en/. Accessed Nov 1 2019.
17. Mir Viladrich I, Dauden Tello E, Solano-Lopez G, et al. Consensus Document on Prevention and Treatment of Tuberculosis in Patients for Biological Treatment. *Arch Bronconeumol.* 2016;52(1):36-45.
18. Chiappini E, Lo Vecchio A, Garazzino S, et al. Recommendations for the diagnosis of pediatric tuberculosis. *Eur J Clin Microbiol Infect Dis.* 2016;35(1):1-18.
19. Lancella L, Galli L, Chiappini E, et al. Recommendations Concerning the Therapeutic Approach to Immunocompromised Children With Tuberculosis. *Clin Ther.* 2016;38(1):180-190.
20. Montagnani C, Esposito S, Galli L, et al. Recommendations for pediatric tuberculosis vaccination in Italy. *Hum Vaccin Immunother.* 2016;12(3):644-650.
21. Santin M, Garcia-Garcia JM, Dominguez J, et al. Guidelines for the use of interferon-gamma release assays in the diagnosis of tuberculosis infection. *Enferm Infecc Microbiol Clin.* 2016;34(5):303.e301-313.
22. Park DI, Hisamatsu T, Chen M, et al. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 1: risk assessment. *Intestinal Res.* 2018;16(1):4-16.
23. Park DI, Hisamatsu T, Chen M, et al. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 2: management. *Intestinal Res.* 2018;16(1):17-25.
24. Turnbull L, Bell C, Child F. Tuberculosis (NICE clinical guideline 33). *Archives of Disease in Childhood Education & Practice,.* 2017;102(3):136-142.
25. World Health O. BCG vaccine: WHO position paper, February 2018 - Recommendations. *Vaccine.* 2018;36(24):3408-3410.
26. Borisov AS, Bamrah Morris S, Njie GJ, et al. Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent Mycobacterium tuberculosis Infection. *MMWR Morb Mortal Wkly Rep.* 2018;67(25):723-726.

27. Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. *Clin Infect Dis.* 2016;63(7):e147-e195.

28. Migliori GB, Sotgiu G, Rosales-Klintz S, et al. ERS/ECDC Statement: European Union standards for tuberculosis care, 2017 update. *Eur Respir J.* 2018;51(5):05.

29. Anonymous. British HIV Association guidelines for the management of tuberculosis in adults living with HIV 2019. *HIV Med.* 2019;20 Suppl 6:s2-s83.

30. Brett K, Dulong C, Severn M. Treatment of tuberculosis: a review of guidelines. *(CADTH rapid response report: summary with critical appraisal)*. Ottawa: CADTH; 2020.

31. Brett K, Dulong C, Severn M. Identification of tuberculosis: a review of the guidelines. *(CADTH rapid response report: summary with critical appraisal)*. Ottawa: CADTH; 2020.

32. Brett K, Dulong C, Severn M. Prevention of tuberculosis: a review of guidelines. *(CADTH rapid response report: summary with critical appraisal)*. Ottawa: CADTH; 2020.

33. Canadian Tuberculosis Standards. 7th ed. Ottawa: Public Health Agency of Canada; 2014: https://www.canada.ca/en/public-health/services/infectious-diseases/canadian-tuberculosis-standards-7th-edition.html. Accessed 2019 Dec 1.

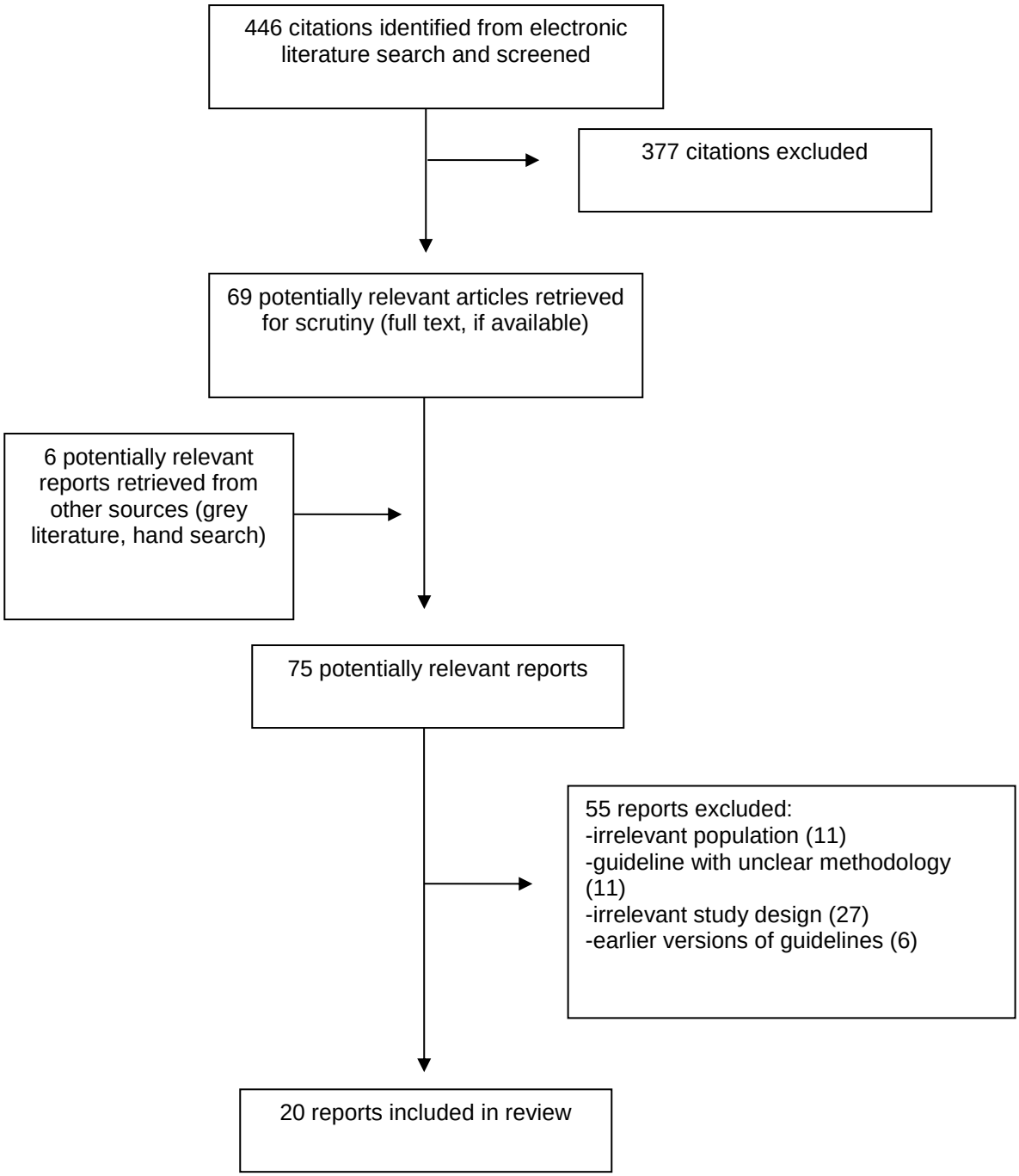
34. Canadian Tuberculosis Standards, Preface. Ottawa: Public Health Agency of Canada; 2014: https://www.canada.ca/en/public-health/services/infectious-diseases/canadian-tuberculosis-standards-7th-edition/edition-22.html. Accessed 2020 Jan 8.

35. British HIV Association (BHIVA) Guideline Development Manual. Letchworth (GB): British HIV Association (BHIVA); 2014: https://www.bhiva.org/GuidelineDevelopmentManual. Accessed 2020 Mar 10.

36. World Health Organization. WHO handbook for guideline development. Geneva: World Health Organization; 2014: http://apps.who.int/medicinedocs/documents/s22083en/s22083en.pdf. Accessed 2020 Jan 8.

37. Public Health Agency of Canada. Canadian Tuberculosis Standards 7th Edition. Ottawa: Public Health Agency of Canada; 2014: https://www.canada.ca/en/public-health/services/infectious-diseases/canadian-tuberculosis-standards-7th-edition.html. Accessed 2020 Feb 21.

Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of the Guidelines

Guideline and year	Country, Funding body, Developer	Scope or Objective	Target Users	Health Technologies, total # of recommendations	Populations covered by the recommendations
British HIV Association guidelines for the management of tuberculosis in adults living with HIV, BHIVA[29] 2019	**Country**: United Kingdom **Funding**: Not Specified **Developing institution:** British HIV Association (BHIVA))	To help physicians manage adults with TB/HIV co-infection. Recommendations for the treatment of TB in HIV-positive adults are similar to those in HIV-negative adults.	**Primary users:** Physicians, health care professionals	**Technologies**: -prevention of TB -Identification of LTBI -Identification of active TB - Treatment of LTBI -Treatment of active TB **Total # of Recommendations:** 47	**Main population:** Adults living with HIV **Subgroups**: -Those suspected of DR-TB - Those with drug resistant TB -Pregnant or breastfeeding
Lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis of active tuberculosis in people living with HIV WHO, LF-LAM[16] 2019	**Country:** Global **Funding:** United States Agency for International Development (USAID) **Developing institution:** World Health Organization	Review the accuracy, clinical effectiveness, cost-effectiveness, feasibility, acceptability and equity of the LF-LAM for diagnosis of active TB in adults, adolescents and children who are HIV-positive	Policy-makers, doctors, health care staff, HIV and TB program managers, technical agencies, and partners supporting the use of TB diagnostics in resource-limited settings.	**Technologies**: Identification of active TB - lateral flow urine lipoarabinomannan assay (LF-LAM) **Total # of Recommendations:** 8	**Main population:** HIV-positive adults, adolescents and children **Subgroups**: inpatient and outpatient settings
Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent Mycobacterium tuberculosis Infection CDC treatment guideline[26] 2018	**Country:** United States **Funding:** United States Centers for Disease Control and Prevention **Developing institution:** Not specified	CDC Work Group conducted a systematic review and meta-analyses of the 3HP regimen using methods adapted from the Guide to Community Preventive Services	**Primary users:** Clinicians and health care professionals, public health departments **Other users:** Patients with LTBI	**Technologies**: Treatment of LTBI **Total # of Recommendations: 1**	**Subgroup:** Persons with HIV infection

Guideline and year	Country, Funding body, Developer	Scope or Objective	Target Users	Health Technologies, total # of recommendations	Populations covered by the recommendations
ERS/ECDC Statement: European Union standards for tuberculosis care, 2017 update ERS/ECDC Standards[28] 2018	**Country:** Europe **Funding:** European Respiratory Society (ERS) **Developing institution:** ERS and European Centre for Disease Prevention and Control (ECDC)	Incorporate the new scientific evidence that has become available since the publication of the European Union Standards for Tuberculosis Care in 2012.	Clinicians; health care professionals	Technologies: - culture-based techniques, species identification) -HIV testing and treatment - contact tracing - preventive treatment **Total # of Recommendations:** 5	**Subgroups**: Individuals with HIV or immune compromising decisions
Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 1: risk assessment AOCC/APAGE, Part 1[22] 2018	**Country:** Korea **Funding:** supported by a grant from the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea **Developing institution**: Asian Organization for Crohn's and Colitis and the Asia Pacific Association of Gastroenterology (AOCC/ APAGE)	*"Developed a set of consensus statements on the risk assessment, detection and prevention of LTBI, and management of active TB infection in patients with IBD receiving anti-TNF treatment. These recommendations will help clinicians optimize patient outcomes by reducing the morbidity and mortality associated with TB infection."* (p. 2)	**Primary users:** clinicians and health care professionals	**Technologies**: Identification of latent TB: - TST - IGRA Identification of active TB **Total # of Recommendations: 11**	**Main population:** Individuals with IBD and receiving anti-TNF treatment (and on immunosuppressive agents) and who are at risk of TB
Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 2: management	**Country:** Korea **Funding:** Supported by a grant from the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea **Developing institution**: Asian Organization for Crohn's and Colitis and the Asia Pacific Association of	"*Developed a set of consensus statements on the risk assessment, detection and prevention of LTBI, and management of active TB infection in patients with IBD receiving anti-TNF treatment. These recommendations will help clinicians optimize patient outcomes by*	**Primary users:** clinicians and health care professionals	**Technologies**: Treatment for LTBI - treatment recommendations - monitoring for active TB Treatment of active TB - duration of treatment - monitoring anti-TNF therapy	**Main population:** Individuals with IBD and receiving anti-TNF treatment (and on immunosuppressive agents)

Guideline and year	Country, Funding body, Developer	Scope or Objective	Target Users	Health Technologies, total # of recommendations	Populations covered by the recommendations
AOCC/APAGE, Part 2 [23] 2018	Gastroenterology (AOCC/ APAGE)	*reducing the morbidity and mortality associated with TB infection*" (p. 2)		**Total # of Recommendations: 12**	
BCG vaccines: WHO position paper WHO BCG[25] 2018	**Country**: Global **Funding**: **Developing institution:** World Health Organization	Guidance on the BCG vaccine for children, including those infected with HIV	**Primary users:** National public health officials and managers of immunization programs **Other users**: international funding agencies, healthcare providers and researchers, vaccine advisory groups and manufacturers.	**Technologies**: Prevention of TB - BCG vaccine **Total # of Recommendations:** 6	**Subgroups**: Immunocompromised and HIV infected adults and children
Latent tuberculosis infection Updated and consolidated guidelines for programmatic management WHO LTBI[15] 201	**Country:** Global **Funding**: The US CDC, US Agency for International Development, and the Ministry of Health of the Republic of Korea **Developing institution:** World Health Organization	Six previous WHO guidelines were consolidated and updated to provide a recent and comprehensive set of recommendations for the management of LTBI. Can be adapted to the national and local epidemiology of TB, and the availability of resources.	**Primary users**: National TB and HIV control programs, ministries of health, and policy-makers working on TB and HIV. **Other users**: Health officials in other areas including prison services, social services, immigration, and clinicians and public health practitioners working on TB or HIV.	**Technologies**: - identification of LTBI - identification of active TB - Treatment of LTBI - preventive treatment **Total # of Recommendations:** 11	**Subgroups**: Patients with HIV
Position statement on interferon-gamma release assays for the detection of latent tuberculosis infection NTAC[10] 2017	**Country:** Australia **Funding:** Not specified **Developing institution:** The National Tuberculosis Advisory Committee	The use of TST and IGRA for the investigation of LTBI	TB community, Communicable Diseases Network Australia, Department of Health (Australian Government)	**Technologies**: -Identification of LTBI -Identification of active TB - preventive treatment	**Subgroups**: -Patients with HIV - Immunocompromised patients (e.g., receiving anti-TNF therapy)

Guideline and year	Country, Funding body, Developer	Scope or Objective	Target Users	Health Technologies, total # of recommendations	Populations covered by the recommendations
				Total # of Recommendations: 12	
Guidelines for treatment of drug-susceptible tuberculosis and patient care (2017 update) WHO drug susceptible[11] 2017	**Country:** Global **Funding:** United States Agency for International Development (USAID) **Developing institution:** World Health Organization	The objective of the guideline is to provide updated recommendations for the treatment of drug-susceptible TB based on new evidence	**Users:** All health professionals (e.g., doctors, nurses) who treat patients with TB, and key TB policy-makers	**Technologies**: - treatment of active TB - antiretroviral therapy **Total # of Recommendations:** 3	**Subgroups**: TB patients living with HIV
Recommendations for the diagnosis of pediatric tuberculosis The Italian Pediatric guideline for diagnosis[18] 2016	**Country:** Italy **Funding:** Italian Ministry of Health **Developing institution:** Italian Pediatric TB Study Group	Recommendation for diagnosing TB in pediatric patients in Italy	**Primary users**: Clinicians and health care professionals and policy-makers	**Technologies**: Identification of latent TB (TST, IGRA) Identification of active TB **Total # of Recommendations:** 3	**Subgroups**: Children with T lymphocyte immunodepression
Recommendations Concerning the Therapeutic Approach to Immunocompromised Children With Tuberculosis The Italian Pediatric Immunocompromised [19] 2016	**Country**: Italy **Funding**: a grant from the Italian Ministry of Health and the Italian Society for Pediatric Infectious Diseases **Developing institution:** Italian Pediatric TB Study Groups	Recommendations for diagnosing and treating TB in pediatric patients who are immunocompromised	**Primary users:** Those who care for pediatric patients who are immunocompromised, with or without TB	**Technologies**: -Identification of LTBI -Identification of active TB -Treatment of active TB **Total # of Recommendations:** 23	**Main population**: Immunocompromised children **Subgroups**: - T lymphocyte immunodepression - patients undergoing immunosuppression - oncologic or transplantation patients - those receiving anti-TNF therapy - patients with HIV
Recommendations for pediatric tuberculosis vaccination in Italy	**Country:** Italy **Funding:** supported by a grant from the Italian Society	Recommendations on the use of the BCG vaccine in pediatric patients in Italy	Not specified	**Technologies**: Prevention of TB - BCG vaccine	**Subgroups**: Infants with a possible HIV infection or immunodeficiency

Guideline and year	Country, Funding body, Developer	Scope or Objective	Target Users	Health Technologies, total # of recommendations	Populations covered by the recommendations
The Italian Pediatric prevention guideline[20] 2016	for Pediatric Infectious Diseases **Developing institution:** Italian Pediatric TB Study Group			**Total # of Recommendations:** 2	
Consensus Document on Prevention and Treatment of Tuberculosis in Patients for Biological Treatment SEPAR/AEDV/SEPD/SER/ SEIMC[17] 2016	**Country: Spain** **Funding:** Not reported **Developing institution:** Spanish Society of Pulmonology and Thoracic Surgery (SEPAR), Spanish Academy of Dermatology and Venereology (AEDV), Spanish Society of Digestive Diseases (SEPD), Spanish Society of Rheumatology (SER) and Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC).	Summarize the current knowledge and expert opinion of biologic therapies, including TNF-blocking treatments. It provides recommendations for the diagnosis of LTBI and for preventive therapy in these patients.	Clinicians; health care professionals	Technologies: - identification of LTBI - preventive therapy **Total # recommendations: 10**	**Main population:** Patients who are candidates for biological treatment or who are being treated for immune mediated inflammatory diseases
Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis ATS/CDC/IDSA treatment guidelines[27] 2016	**Country:** United States **Funding:** The American Thoracic Society, Centers for Disease Control and Prevention, and Infectious Diseases Society of America **Developing institution:** American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America**,** European Respiratory Society, and US	Recommendations on the clinical and public health management of drug-susceptible TB in children and adults in settings in which mycobacterial cultures, molecular and phenotypic drug susceptibility tests, and radiographic studies, among other diagnostic tools, are available on a routine basis.	**Primary users**: National TB programs, or their equivalents in ministries of health, and for other policy-makers working on TB	**Technologies**: Treatment of active TB - regimen, dosing, drug-drug interactions **Total # of Recommendations: 3**	**Sub-group:** Patients with HIV

Guideline and year	Country, Funding body, Developer	Scope or Objective	Target Users	Health Technologies, total # of recommendations	Populations covered by the recommendations
	National Tuberculosis Controllers Association				
Guidelines for the use of interferon-y release assays in the diagnosis of tuberculosis infection SEIMC/SEPAR Guideline[21] 2016	**Country:** Spain **Funding:** Spanish Society of Respiratory Diseases and Thoracic Surgery and the Spanish Society of Infectious Diseases and Clinical Micro-biology **Developing institution:** Spanish Society of Respiratory Diseases and Thoracic Surgery and the Spanish Society of Infectious Diseases and Clinical Micro-biology	Recommendation on the use of IGRAs for diagnosing TB infection and to minimize the uncertainty and variability in the diagnosis of TB infection by the IGRAs.	**Primary users**: Clinicians and health care professionals and policy-makers	**Technologies**: Identification of LTBI -TST -IGRA **Total # of Recommendations: 3**	**Sub-groups:** - People with HIV - People with chronic inflammatory diseases - Patients requiring transplant
Prevention, Diagnosis and Management of Tuberculosis Ministry of Health Singapore[14] 2016	**Country:** Singapore **Funding:** Not specified **Developing institution:** Ministry of Health, Singapore	Diagnosis and treatment of active and latent TB, and public health actions required by physicians treating patients with TB	**Primary users**: All healthcare practitioners in Singapore **Other users**: Public health service providers who treat patients with TB.	**Technologies**: Identification of LTBI Treatment of active TB **Total # of Recommendations:** 4	**Subgroups**: Patients with HIV
Tuberculosis NICE[24] 2016	**Country:** United Kingdom **Funding:** Not specified **Developing institution:** National Institute for Health and Care Excellence	Preventing, identifying and managing latent and active TB in children and adults	Healthcare professionals and TB multidisciplinary teams. Substance misuse services, prisons and immigration removal centers. Local government, TB control boards, directors of public health, volunteers, people with TB and their care givers.	**Technologies**: -Identification of LTBI -Treatment of LTBI -Treating active TB **Total # of Recommendations:** 7	**Subgroups**: - Immunocompromised adults and children - Patients with HIV

Guideline and year	Country, Funding body, Developer	Scope or Objective	Target Users	Health Technologies, total # of recommendations	Populations covered by the recommendations
Canadian Tuberculosis Standards Chapter 10: Tuberculosis and Human Immunodeficiency Virus PHAC HIV[13] 2014	**Country:** Canada **Funding:** Jointly funded by the Canadian Thoracic Society of the Canadian Lung Association, and the Public Health Agency of Canada **Developing institution:** Jointly produced by the Canadian Thoracic Society of the Canadian Lung Association, and the Public Health Agency of Canada	Identification and treatment of latent and active TB in patients with HIV	Public health and clinical professionals	Technologies: -BCG vaccine - infection control - identification of LTBI - identification of active TB -treatment of LTBI - treatment of active TB **Total # of Recommendations**: 45	**Main population:** Patients with HIV
Canadian Tuberculosis Standards Chapter 6: Treatment of Latent Tuberculosis Infection PHAC Treatment LTBI[12] 2014	**Country:** Canada **Funding:** Jointly funded by the Canadian Thoracic Society of the Canadian Lung Association, and the Public Health Agency of Canada **Developing institution:** Jointly produced by the Canadian Thoracic Society of the Canadian Lung Association, and the Public Health Agency of Canada	Treatment of LTBI	Public health and clinical professionals	Technologies: - drug regimen and dosing **Total # of Recommendations**: 3	**Subgroups**: - patients with HIV - patients with HIV who are pregnant or breastfeeding

AEDV = Spanish Academy of Dermatology and Venereology; AOCC = Asian Organization for Crohn's and Colitis; APAGE = Asia Pacific Association of Gastroenterology; ATS = American Thoracic Society; BCG = Bacillus Calmette-Guérin; BHIVA = British HIV Association; CDC = Centers for Disease Control and Prevention; ECDC = European Centre for Disease; ERS = European Respiratory Society; HIV = human immunodeficiency virus; IBD = inflammatory bowel disease; IDSA = Infectious Diseases Society of America; IGRA = interferon gamma release assay; LF-LAM = lateral flow urine lipoarabinomannan assay; LTBI = latent tuberculosis; NICE = National Institute for Health and Care Excellence; NTAC = National Tuberculosis Advisory Committee; PHAC = Public Health Agency of Canada; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Pulmonology and Thoracic Surgery; SEPD = Spanish Society of Digestive Diseases; SER = Spanish Society of Rheumatology; TB = tuberculosis; TNF = tumour necrosis factor; TST= tuberculin skin test; WHO= World Health Organization.

Table 3: Methods used in the Guidelines

Guideline and year	Development Process	Evidence Collection and Critical Appraisal	Recommendation formulation and validation	Grading system	External review, Process for updating
British HIV Association guidelines for the management of tuberculosis in adults living with HIV, BHIVA[29] 2019	Development of the guidelines followed the process outlined in the BHIVA Guideline Development Manual[35] A writing group agreed upon the scope, purpose and topics of the guideline. A systematic search was conducted for each topic in the guideline and the working group.	A systematic search of the literature was conducted for each selection criteria and topic. Nine different searches were conducted, and each PICO criteria was outlined every search. The writing group members identified and evaluated the available literature for each of the nine searches. The modified GRADE approach was used to assess the quality of the body of evidence and the strength of the recommendations for each PICO question. The modified GRADE system provides an informative and transparent summary.	The strength of the recommendation not only looked at the quality of the defined outcomes of the intervention but also the difference between desirable and undesirable effects, values and preferences or resource use. Based upon the GRADE instrument the authors aimed to reach a consensus on the strength of recommendation and level of supporting evidence.	The quality of evidence was graded into four categories: A = true effect lies close to the estimate effect supported by high quality evidence B = moderate quality evidence with consistent effects and exclusion of most potential sources of bias. C = low quality evidence with a variety of limitations including the effects and potential bias. D = evidence only based on case studies or expert opinion leading to little confidence in the effect estimate. The evidence was graded into: Grade 1(A, B, C and D) = strong recommendation Grade 2 (A, B, C and D) = weaker or conditional recommendation Good practice points = recommendations based on the clinical judgement and experience of the group where there is not, or unlikely to be, sufficient evidence. They are regarded as sound clinical practice, but do not replace evidence-based recommendations.	The guidelines were externally-peer reviewed and published online for public consultation. The guidelines will be fully updated and revised in 2021. In the interim, the working group will continually me to assess new information to inform best clinical practice.
Lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis of active tuberculosis	Guideline development group convened a meeting to review the evidence for the use of LF-LAM.	The SR team conducted a SR to review the current literature and to address the seven PICO questions developed for this guideline on LF-LAM. Details of the	The development of the recommendations were based upon the direction and strength of the recommendations by using	Four levels of evidence quality:[36] High: Very confident that the true effect lies close to that of the estimate of the effect. Moderate: Moderately confident that the true effect is likely to be	The current guidelines will be updated if new evidence arises with an average time

Guideline and year	Development Process	Evidence Collection and Critical Appraisal	Recommendation formulation and validation	Grading system	External review, Process for updating
in people living with HIV WHO, LF-LAM[16] 2019	Recommendations were based on consensus from this committee. The guideline development group also reviewed data on the use of the technology and its initial results. The evidence review group reviewed the draft of the guideline before it was finalized to make sure any revisions were necessary or content was unclear. The Steering Group prepared an initial list of relevant outcomes (e.g., benefits and harms) for consideration when drafting the outcomes.	databases searched, selection of studies and data synthesis were outlined in the supplemental material. The quality of the included studies in the systematic review were appraised using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. This tool assesses risk of bias and applicability in four domains: patient selection, index test, reference standard, and flow and timing. No studies were available on the feasibility acceptability, price, cost and cost-effectiveness of the LF-LAM. GRADE evidence-to-decision tables were created from the systematic review evidence to guide the development of the recommendations. The evidence that contributed to the recommendations was also summarized narratively in the guideline.	evidence-to-decision tables. The Steering Group helped the guideline development group formulate recommendations based on the evidence. Decisions were based on consensus.	close to the estimate of the effect, but there is a possibility that it is substantially different. Low: Our confidence in the effect estimate is limited: the true effect may be substantially different. Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different. Two levels of strength of the recommendation: Strong: the guideline development group was confident that the desirable effects of adherence would outweigh the undesirable effects. Could be either in favour of or against an intervention. Conditional: the guideline development group concluded that the desirable effects of adherence would probably outweigh the undesirable effects, but the guideline development group was not confident about the trade-off. Reasons for lack of confidence included: absence of high-quality evidence; imprecise estimates of benefit or harm; uncertainty or variation in the value of the outcomes for different individuals; and small benefits or benefits that might not be worth the cost.	frame of three to five years.
Asian Organization for Crohn's and	Development of the guidelines followed the process outlined	A systematic search of the literature was conducted. The search strategy or	The GRADE system was used to classify the	Level of agreement: 1 = Strongly agree 2 = Agree	External review and process for updating

Guideline and year	Development Process	Evidence Collection and Critical Appraisal	Recommendation formulation and validation	Grading system	External review, Process for updating
Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory bowel disease receiving anti-tumor necrosis factor treatment. Part 1: risk assessment AOCC/APAGE, Part 1[22] 2018	in the WHO Handbook for Guideline Development.[36] One individual from the committee collected and interpreted the data while another individual planned and conducted the studies and the rest of the collected and interpreted the evidence and data.	selection criteria for the evidence was not described. Did not report critical appraisal of primary studies. The GRADE approach was used to assess the confidence in the certainty of the evidence that supports the recommendations. The quality of was graded by several factors including study limitations, inconsistency of results, indirectness of evidence, imprecision, reporting bias, the magnitude of the treatment effect.	strength of the recommendation. The recommendation was classified by four key factors: quality of evidence, balance of desirable benefits and undesirable harm, values and preferences of client and health care providers and resource implications. Web-based consensus voting was performed by 211 IBD specialists from 9 Asian countries concerning each statement. A consensus statement was accepted if at least 75% of the participants voted. If a statement was not accepted, the wording of the statement was discussed and revised, and then re-voting was conducted	3 = Uncertain 4 = Disagree 5 = Strongly Disagree The strength of a recommendation was categorized as either strong or weak.	the guideline not indicated
Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology consensus on tuberculosis infection in patients with inflammatory	The methodology was stated in the first part of the guideline[22] Development of the guidelines followed the process outlined in the WHO Handbook for Guideline Development.[36]	A systematic search of the literature was conducted. The search strategy or selection criteria for the evidence was not described. Did not report critical appraisal of primary studies.	The GRADE system was used to classify the strength of the recommendation. The recommendation was classified by four key factors: quality of evidence, balance of desirable benefits and undesirable harm, values and preferences of client and	Level of agreement: 1 = Strongly agree 2 = Agree 3 = Uncertain 4 = Disagree 5 = Strongly Disagree The strength of a recommendation was categorized as either strong or weak.	External review and process for updating the guideline not indicated

Guideline and year	Development Process	Evidence Collection and Critical Appraisal	Recommendation formulation and validation	Grading system	External review, Process for updating
bowel disease receiving anti-tumor necrosis factor treatment. Part 2: management AOCC/APAGE, Part 2 [23] 2018	One individual from the committee collected and interpreted the data while another individual planned and conducted the studies and the rest of the collected and interpreted the evidence and data.	The GRADE approach was used to assess the confidence in the certainty of the evidence that supports the recommendations. The quality of was graded by several factors including study limitations, inconsistency of results, indirectness of evidence, imprecision, reporting bias, the magnitude of the treatment effect.	health care providers and resource implications. Web-based consensus voting was performed by 211 IBD specialists from 9 Asian countries concerning each statement. A consensus statement was accepted if at least 75% of the participants voted. If a statement was not accepted, the wording of the statement was discussed and revised, and then re-voting was conducted		
Recommendations Concerning the Therapeutic Approach to Immunocompromised Children With Tuberculosis The Italian Pediatric Immunocompromised [19] 2016	The Working Group agreed on a list of clinical problems concerning the therapeutic management of TB immunocompromised patient. Topics and evidence were presented at the committee meeting. The panel included clinicians and experts in evidence-based medicine with the help of participating societies.	A systematic review was conducted, and evidence was identified in MEDLINE and the Cochrane Database of Systematic Reviews until December 31, 2014. The search focused on patients aged 0 to 18 years of age and included section-specific targeted searches. The literature was appraised using the Scottish Intercollegiate Guidelines Network (SIGN) methodologic checklists and categorized the	The Delphi method was used to reach a consensus when the evidence did not provide an overall conclusion to make a recommendation.	Quality of evidence: I = evidence from at least one well designed RCT or SR II = evidence from one well designed RCT III = evidence from cohort studies or meta-analysis IV = evidence from retrospective case-control studies or meta-analysis V = evidence from case series without a control group VI = evidence from expert opinion or clinical experience Strength of recommendations: A = strongly support recommendation B = moderately support recommendation	The guideline did not indicate if it will be updated or the process of an update. The guideline did not indicate if it was externally reviewed.

Guideline and year	Development Process	Evidence Collection and Critical Appraisal	Recommendation formulation and validation	Grading system	External review, Process for updating
		evidence into six different levels.		C = marginally support recommendation	
Consensus Document on Prevention and Treatment of Tuberculosis in Patients for Biological Treatment SEPAR/AEDV/SEPD/SER/SEIMC[17] 2016	The guideline included a team of experts designated by various scientific societies.	The evidence collection process was not described The guideline did not state if the evidence was critically appraised by experts or committee members.	Recommendations have been formulated based on the classification of the American Society of Infectious Diseases	Recommendations According to Category of Strength *I: Good evidence to support recommendation* *II: Moderate evidence to support recommendation* *III: Poor evidence to support recommendation* Recommendations According to Scientific Quality *Grade I: Recommendation on at least one well-designed RCT study* *Grade II: Recommendation is based on one at least well designed NRS* *Grade III: Recommendation based on expert opinion, descriptive studies or clinical experience*	Not specified
Canadian Tuberculosis Standards Chapter 10: Tuberculosis and Human Immunodeficiency Virus PHAC HIV[13] 2014	This 7th edition of the Canadian Tuberculosis Standards builds off previous versions and has been revised to include new information. Each chapter is written by experts from across Canada.	The authors synthesized and rated the evidence. No other details provided	Not reported	"Quality of Evidence Strong = Evidence from multiple randomized controlled trials (RCTs – for therapeutic evidence), or cohort studies (etiologic evidence) with strong designs and consistent results. Moderate = Evidence from only one RCT or RCTs with an inadequate number participants or inconsistent results, or multiple observational studies of strong design providing consistent results. Weak = Evidence from observational analytic studies that had weak designs, weak effect	Process for external review not reported. Process for updating the guidelines not reported.

Guideline and year	Development Process	Evidence Collection and Critical Appraisal	Recommendation formulation and validation	Grading system	External review, Process for updating
				estimates or inconsistent results, or generalization from a randomized trial that involved one type of patients to a different group of patients. Very weak = Evidence from published case series and/or opinion of the authors and other experts Strength of Recommendations Strong = The recommendation implies that the desirable effects clearly outweigh undesirable effects, was based on strong/moderate evidence and was considered unlikely to change with additional published evidence. Conditional = The recommendation implies that the desirable effects are closely balanced with undesirable effects, and/or was based on moderate/weak/very weak evidence and was considered likely to change with additional published evidence." (p. 3-4, from Preface[37])	

AEDV = Spanish Academy of Dermatology and Venereology; AOCC = Asian Organization for Crohn's and Colitis; APAGE = Asia Pacific Association of Gastroenterology; BHIVA = British HIV Association; GRADE = Grading of Recommendations Assessment, Development and Evaluation; HIV = human immunodeficiency virus; LF-LAM = lateral flow urine lipoarabinomannan assay; PHAC = Public Health Agency of Canada; PICO = population, intervention, comparator, outcome; RCT = randomized controlled trial; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Pulmonology and Thoracic Surgery; SEPD = Spanish Society of Digestive Diseases; SER = Spanish Society of Rheumatology; SR = systematic review; TB = tuberculosis; WHO= World Health Organization.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of the first six Guidelines using AGREE II[8]

Item	Guideline					
	BHIVA[29]	WHO, LF-LAM[16]	CDC treatment guideline[26]	ERS/ECDC Standards[28]	AOCC/ APAGE, Part 1[22]	AOCC/ APAGE, Part 2 [23]
Domain 1: Scope and Purpose						
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	Yes	Partially	Yes	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes	Yes	No	No	No	No
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes	Yes	Partially	Yes	Yes	Yes
Domain 2: Stakeholder Involvement						
4. The guideline development group includes individuals from all relevant professional groups.	Yes	Yes	Partially	Partially	Partially	Partially
5. The views and preferences of the target population (patients, public, etc.) have been sought.	Yes	Yes	Partially	No	No	No
6. The target users of the guideline are clearly defined.	Partially	Yes	Partially	Partially	Yes	Yes
Domain 3: Rigour of Development						
7. Systematic methods were used to search for evidence.	Yes	Yes	Yes	Partially	No	No
8. The criteria for selecting the evidence are clearly described.	Yes	Yes	Yes	No	No	No
9. The strengths and limitations of the body of evidence are clearly described.	Yes	Yes	Partially	No	Partially	Partially
10. The methods for formulating the recommendations are clearly described.	Yes	Yes	No	No	Partially	Partially
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Partially	Yes		No	Partially	Partially

Item	Guideline					
	BHIVA[29]	WHO, LF-LAM[16]	CDC treatment guideline[26]	ERS/ECDC Standards[28]	AOCC/ APAGE, Part 1[22]	AOCC/ APAGE, Part 2 [23]
12. There is an explicit link between the recommendations and the supporting evidence.	Yes	Yes	Partially	Yes	Partially	Partially
13. The guideline has been externally reviewed by experts prior to its publication.	Yes	Yes	Partially	Yes	No	No
14. A procedure for updating the guideline is provided.	Yes	Yes	No	No	No	No
Domain 4: Clarity of Presentation						
15. The recommendations are specific and unambiguous.	Yes	Yes	Yes	Yes	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes	Yes	not applicable	Partially	Yes	Yes
17. Key recommendations are easily identifiable.	Yes	Partially	Yes	Yes	Yes	Yes
Domain 5: Applicability						
18. The guideline describes facilitators and barriers to its application.	Yes	Yes	No	No	Partially	Partially
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	Partially	Yes	No	No	No	No
20. The potential resource implications of applying the recommendations have been considered.	Partially	Yes	No	No	No	No
21. The guideline presents monitoring and/or auditing criteria.	No	Yes	No	No	No	No
Domain 6: Editorial Independence						
22. The views of the funding body have not influenced the content of the guideline.	Yes	Yes	No	Partially	Yes	Yes
23. Competing interests of guideline development group members have been recorded and addressed.	Yes	Yes	Yes	Partially	Yes	Yes

AOCC = Asian Organization for Crohn's and Colitis; APAGE = Asia Pacific Association of Gastroenterology; BHIVA = British HIV Association; CDC = Centers for Disease Control and Prevention; ECDC = European Centre for Disease; ERS = European Respiratory Society; LF-LAM = lateral flow urine lipoarabinomannan assay; WHO = World Health Organization.

Table 5: Strengths and Limitations of the next seven Guidelines using AGREE II[8]

Item	Guideline						
	WHO, BCG[25]	WHO LTBI[15]	NTAC[10]	WHO drug-susceptible TB[11]	Italian Pediatric diagnosis[18]	Italian Pediatric Immunocompromised [19]	Italian Pediatric Prevention[20]
Domain 1: Scope and Purpose							
1. The overall objective(s) of the guideline is (are) specifically described.	Partially	Yes	Partially	Yes	Yes	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes	Yes	Partially	Yes	Yes	Yes	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Partially	Yes	Partially	Partially	Partially	Yes	Partially
Domain 2: Stakeholder Involvement							
4. The guideline development group includes individuals from all relevant professional groups.	Partially	Partially	No	Yes	Partially	Yes	Partially
5. The views and preferences of the target population (patients, public, etc.) have been sought.	No	Yes	No	Partially	No	No	No
6. The target users of the guideline are clearly defined.	Yes	Yes	No	Yes	No	Partially	No
Domain 3: Rigour of Development							
7. Systematic methods were used to search for evidence.	Partially	Yes	No	Yes	Yes	Yes	Yes
8. The criteria for selecting the evidence are clearly described.	Partially	Yes	No	Yes	No	No	No
9. The strengths and limitations of the body of evidence are clearly described.	Partially	Yes	No	Yes	No	No	No
10. The methods for formulating the recommendations are clearly described.	Partially	Yes	Partially	Yes	Partially	Partially	Partially
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Partially	Yes	No	Yes	Partially	Partially	Partially

Item	Guideline						
	WHO, BCG[25]	WHO LTBI[15]	NTAC[10]	WHO drug-susceptible TB[11]	Italian Pediatric diagnosis[18]	Italian Pediatric Immunocompromised [19]	Italian Pediatric Prevention[20]
12. There is an explicit link between the recommendations and the supporting evidence.	Partially	Yes	Partially	Yes	Partially	Partially	Partially
13. The guideline has been externally reviewed by experts prior to its publication.	Partially	Yes	No	Yes	No	No	Partially
14. A procedure for updating the guideline is provided.	Yes	Yes	Partially	Yes	No	No	No
Domain 4: Clarity of Presentation							
15. The recommendations are specific and unambiguous.	Yes	Yes	Partially	Yes	Partially	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Not applicable	Yes	not applicable	Yes	Yes	Yes	NA
17. Key recommendations are easily identifiable.	Partially	Yes	Partially	Yes	Yes	Yes	Yes
Domain 5: Applicability							
18. The guideline describes facilitators and barriers to its application.	Yes	Yes	No	Partially	No	Yes	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No	Partially	No	Yes	No	Partially	No
20. The potential resource implications of applying the recommendations have been considered.	Partially	Partially	Partially	Partially	No	Partially	No
21. The guideline presents monitoring and/or auditing criteria.	yes	Yes	No	Yes	No	No	No
Domain 6: Editorial Independence							
22. The views of the funding body have not influenced the content of the guideline.	Yes	Partially	No	Yes	Partially	Partially	Partially
23. Competing interests of guideline development group members have been recorded and addressed.	Yes	Yes	Partially	Yes	Yes	Yes	Yes

BCG = Bacillus Calmette-Guérin; NTAC = National Tuberculosis Advisory Committee; LTBI = latent tuberculosis infection; TB = tuberculosis; WHO = World Health Organization.

Table 6: Strengths and Limitations of the last seven Guidelines using AGREE II[8]

Item	Guideline						
	SEPAR/ AEDV/SEPD/ SER/SEIMC[17]	ATS/CDC/ IDSA treatment guidelines[27]	SEIMC/SE PAR Guideline[21]	Singapore[14]	NICE[24]	PHAC HIV[13]	PHAC Treatment LTBI[12]
Domain 1: Scope and Purpose							
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	Yes	Yes	Yes	Yes	No	No
2. The health question(s) covered by the guideline is (are) specifically described.	No	Yes	Yes	No	Yes	No	No
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes	Yes	Yes	Partially	Yes	Partially	Yes
Domain 2: Stakeholder Involvement							
4. The guideline development group includes individuals from all relevant professional groups.	Partially	Yes	Partially	Partially	Yes	Partially	Partially
5. The views and preferences of the target population (patients, public, etc.) have been sought.	No	No	Partially	No	Yes	No	No
6. The target users of the guideline are clearly defined.	No	Yes	Yes	Yes	Yes	Partially	Partially
Domain 3: Rigour of Development							
7. Systematic methods were used to search for evidence.	No	Yes	Yes	No	Yes	No	No
8. The criteria for selecting the evidence are clearly described.	No	Yes	Yes	No	Yes	No	No
9. The strengths and limitations of the body of evidence are clearly described.	Partially	Yes	Partially	Partially	Yes	No	No
10. The methods for formulating the recommendations are clearly described.	No	Yes	Yes	No	Yes	No	No
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	No	Yes	Yes	No	Yes	Partially	Partially
12. There is an explicit link between the recommendations and the supporting evidence.	No	Yes	Yes	Partially	Yes	No	No

Item	Guideline						
	SEPAR/ AEDV/SEPD/ SER/SEIMC[17]	ATS/CDC/ IDSA treatment guidelines[27]	SEIMC/SE PAR Guideline[21]	Singapore[14]	NICE[24]	PHAC HIV[13]	PHAC Treatment LTBI[12]
13. The guideline has been externally reviewed by experts prior to its publication.	No	Yes	Partially	No	Yes	Partially	Partially
14. A procedure for updating the guideline is provided.	No	No	Yes	Yes	Yes	No	No
Domain 4: Clarity of Presentation							
15. The recommendations are specific and unambiguous.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes	Yes	not applicable	Yes	Yes	Yes	Yes
17. Key recommendations are easily identifiable.	Partially	Yes	Yes	Yes	Yes	Yes	Yes
Domain 5: Applicability							
18. The guideline describes facilitators and barriers to its application.	Partially	No	Partially	No	No	No	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No	Partially	No	No	Partially	No	No
20. The potential resource implications of applying the recommendations have been considered.	Partially	Partially	Partially	No	Yes	No	No
21. The guideline presents monitoring and/or auditing criteria.	No	No	No	Partially	Yes	No	Partially
Domain 6: Editorial Independence							
22. The views of the funding body have not influenced the content of the guideline.	Yes	Yes	Yes	No	Partially	Partially	Partially
23. Competing interests of guideline development group members have been recorded and addressed.	Partially	Yes	Yes	No	Yes	No	No

AEDV = Spanish Academy of Dermatology and Venereology; ATS = American Thoracic Society; CDC = Centers for Disease Control and Prevention; HIV = human immunodeficiency virus; IDSA = Infectious Diseases Society of America; LTBI = latent tuberculosis infection; NICE = National Institute for Health and Care Excellence; PHAC = Public Health Agency of Canada; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Pulmonology and Thoracic Surgery; SEPD = Spanish Society of Digestive Diseases; SER = Spanish Society of Rheumatology; WHO = World Health Organization.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 7: Summary of the topics regarding the Prevention of TB

Topics Covered by the recommendation	BHIVA[29]	WHO, BCG [25]	Italian Pediatric prevention [20]	PHAC HIV[13]
TB Infection control plan for hospital for patients with HIV	X			X
BCG vaccination in patients with HIV or other immunodeficiency syndromes		X		X
BCG vaccination in neonates born to women of known or unknown HIV status		X	X	X
BCG vaccination in neonates with HIV infection		X		X
BCG vaccination in neonates with family history of immunodeficiency			X	

BCG = Bacillus Calmette-Guérin; BHIVA = British HIV Association; HIV = human immunodeficiency virus; PHAC = Public Health Agency of Canada; TB = tuberculosis; WHO= World Health Organization.

Note: X = the guideline made a recommendation on this topic.

Table 8: Summary of the topics regarding the Identification of LTBI

Topics Covered by the Recommendations	BHIVA[29]	ERS/ ECDC [28]	AOCC /APAGE, Part 1[22]	WHO, LTBI [15]	NTAC [10]	Italian Pediatric diagnosis[18]	Italian Pediatric Immunocompromised [19]	SEPAR/ AEDV/SEPD/ SER/ SEIMC[17]	SEIMC/ SEPAR Guideline[21]	Singapore[14]	NICE [24]	PHAC HIV[13]
Specific to patients with HIV												
Contact tracing	X	X										
Who should be tested for LTBI	X				X							X
Excluding active TB prior to LTBI testing	X											
LTBI testing prior to preventive treatment				X								
Use of IGRA or TST to identify LTBI	X				X				X	X	X	X
Other Immunocompromised conditions												
Screening for LTBI in candidates for biological treatments (e.g., anti-TNF therapy)			X	X				X	X			
How to diagnose LTBI patients receiving anti-TNF therapy			X									
Chest radiographs, patients receiving anti-TNF therapy			X		X							

Topics Covered by the Recommendations	BHIVA[29]	ERS/ ECDC [28]	AOCC /APAGE, Part 1[22]	WHO, LTBI [15]	NTAC [10]	Italian Pediatric diagnosis[18]	Italian Pediatric Immunocompromised [19]	SEPAR/ AEDV/SEPD/ SER/ SEIMC[17]	SEIMC/ SEPAR Guideline[21]	Singapore[14]	NICE [24]	PHAC HIV[13]
Chest radiographs, immunocompromised patients (e.g., organ transplant)					X							
Use of IGRA or TST for identifying LTBI, patients receiving anti-TNF therapy			X		X							
Use of IGRA or TST for identifying LTBI, immunocompromised patients (e.g., organ transplant)					X			X	X		X	
TST or IGRA in pediatric patients with T lymphocyte immunodepression						X	X					
Risk assessments for adults who are or are anticipated to be immunocompromised											X	
Referral to specialists for immunocompromised pediatric patients											X	

AEDV = Spanish Academy of Dermatology and Venereology; AOCC = Asian Organization for Crohn's and Colitis; APAGE = Asia Pacific Association of Gastroenterology; BHIVA = British HIV Association; CDC = Centers for Disease Control and Prevention; ECDC = European Centre for Disease; ERS = European Respiratory Society; HIV = human immunodeficiency virus;; IGRA = interferon gamma release assay; LTBI = latent tuberculosis; NICE = National Institute for Health and Care Excellence; NTAC = National Tuberculosis Advisory Committee; PHAC = Public Health Agency of Canada; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Pulmonology and Thoracic Surgery; SEPD = Spanish Society of Digestive Diseases; SER = Spanish Society of Rheumatology; TB = tuberculosis; TNF = tumour necrosis factor; TST= tuberculin skin test; WHO= World Health Organization.

Note: X = the guideline made a recommendation on this topic.

Table 9: Summary of the topics regarding the Identification of Active TB disease

Topics Covered by the Recommendations	BHIVA[29]	WHO, LF-LAM[16]	ERS/ ECDC [28]	AOCC/ APAGE, Part 2 [23]	WHO, LTBI [15]	NTAC [10]	Italian Pediatric diagnosis[18]	Italian Pediatric Immunocompromised [19]	PHAC HIV[13]
Specific to patients with HIV									
Who should be evaluated for active TB					X				X
Signs and symptoms of TB	X				X				
Use of TST or IGRA to diagnose active TB	X								
Chest radiography					X	X			
Use of sputum specimens						X			
Use of acid-fast bacilli smear microscopy	X								
Nucleic Acid Amplification Tests (NAAT) or Rapid molecular test	X								
Drug sensitivity testing	X								
Phenotypic drug susceptibility testing (for potential drug-resistant TB)	X								
Lateral flow urine lipoarabinomannan assay (LF-LAM)		X							
Expediting the diagnostic evaluation for people with immune-compromising conditions			X						
Other Immunocompromised conditions									
Monitoring for the development of active TB after treatment for LTBI in patients receiving anti-TNF therapy				X					
Diagnosing active TB in pediatric patients with T lymphocyte immunodepression							X	X	

AOCC = Asian Organization for Crohn's and Colitis; APAGE = Asia Pacific Association of Gastroenterology; BHIVA = British HIV Association; ECDC = European Centre for Disease; ERS = European Respiratory Society; HIV = human immunodeficiency virus; LF-LAM = lateral flow urine lipoarabinomannan assay; LTBI = latent tuberculosis; NTAC = National Tuberculosis Advisory Committee; PHAC = Public Health Agency of Canada; TB = tuberculosis; TNF = tumour necrosis factor; TST= tuberculin skin test; WHO= World Health Organization.

Note: X = the guideline made a recommendation on this topic.

Table 10: Summary of the topics regarding the Treatment of LTBI

Topics Covered by the Recommendations	BHIVA[29]	CDC treatment [26]	ERS/ ECDC [28]	AOCC/ APAGE, Part 2 [23]	WHO, LTBI [15]	NTAC [10]	SEPAR/ AEDV/ SEPD/SER /SEIMC[17]	NICE [24]	PHAC HIV[13]	PHAC Treatment LTBI[12]
Specific to patients with HIV										
Who should be treated for LTBI	X									
Treatment regimen for LTBI	X				X			X	X	X
Use of 3HP therapy		X								
Preventive LTBI treatment for patients with HIV			X		X	X			X	
Treatment of LTBI in HIV infected patients who are pregnant or breast feeding									X	X
Antiretroviral treatment for people with LTBI and HIV									X	
Directly observed therapy									X	
Other Immunocompromised conditions										
LTBI treatment in candidates for biological therapies (e.g., anti-TNF) prior to anti-TNF therapy				X			X			
LTBI treatment for patients previously treated for TB receiving anti-TNF therapy				X						
Treatment regimens for patients with LTBI receiving anti-TNF therapy				X						

3HP = once-weekly isoniazid-rifapentine for 12 weeks; AEDV = Spanish Academy of Dermatology and Venereology; AOCC = Asian Organization for Crohn's and Colitis; APAGE = Asia Pacific Association of Gastroenterology; BHIVA = British HIV Association; CDC = Centers for Disease Control and Prevention; ECDC = European Centre for Disease; ERS = European Respiratory Society; HIV = human immunodeficiency virus; LTBI = latent tuberculosis; NICE = National Institute for Health and Care Excellence; NTAC = National Tuberculosis Advisory Committee; PHAC = Public Health Agency of Canada; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Pulmonology and Thoracic Surgery; SEPD = Spanish Society of Digestive Diseases; SER = Spanish Society of Rheumatology; TB = tuberculosis; TNF = tumour necrosis factor; WHO= World Health Organization.

Note: X = the guideline made a recommendation on this topic.

Table 11: Summary of the topics regarding the Treatment of Active TB

Topics Covered by the Recommendations	BHIVA[29]	ERS/ ECDC [28]	AOCC/A PAGE, Part 2 [23]	WHO drug-susceptible[11]	Italian Pediatric Immunocompromised [19]	SEPAR/AEDV /SEPD/ SER/SEIMC[17]	ATS/CDC/ IDSA treatment guidelines[27]	Singapore[14]	NICE [24]	PHAC HIV[13]
Specific to patients with HIV										
Treatment regimen for active TB	X			X			X	X	X	X
Treatment regimen for active TB in pediatric patients with HIV					X					
Treatment regimen for drug-resistant TB	X									
Management of treatment failure or relapse	X									
Directly observed therapy	X									
Antiretroviral treatment for people with TB and HIV	X	X		X			X			X
Medication reconciliation prior to starting treatment for TB or HIV	X									
Managing immune reconstitution inflammatory syndrome	X									
Treatment during pregnancy and breastfeeding	X									
Use of a multidisciplinary team to manage TB and HIV									X	X
HIV screening for patients with newly diagnosed TB		X								X
Monitoring treatment										X
Other Immunocompromised conditions										
Treatment of active TB in patients receiving anti-TNF therapy			X			X				
Treatment of active TB in pediatric patients receiving anti-TNF therapy					X					
Treatment of pediatric patients undergoing immunosuppressive treatment					X					

Topics Covered by the Recommendations	BHIVA[29]	ERS/ ECDC [28]	AOCC/A PAGE, Part 2 [23]	WHO drug-susceptible[11]	Italian Pediatric Immunocompromised [19]	SEPAR/AEDV /SEPD/ SER/SEIMC[17]	ATS/CDC/ IDSA treatment guidelines[27]	Singapore[14]	NICE [24]	PHAC HIV[13]
Treatment of pediatric oncologic or transplantation patients (drug regimen)					X					

AEDV = Spanish Academy of Dermatology and Venereology; AOCC = Asian Organization for Crohn's and Colitis; APAGE = Asia Pacific Association of Gastroenterology; ATS = American Thoracic Society; BHIVA = British HIV Association; ECDC = European Centre for Disease; ERS = European Respiratory Society; HIV = human immunodeficiency virus; IDSA = Infectious Diseases Society of America; NICE = National Institute for Health and Care Excellence; PHAC = Public Health Agency of Canada; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology; SEPAR = Spanish Society of Pulmonology and Thoracic Surgery; SEPD = Spanish Society of Digestive Diseases; SER = Spanish Society of Rheumatology; TB = tuberculosis; TNF = tumour necrosis factor; WHO= World Health Organization.

Note: X = the guideline made a recommendation on this topic.

Appendix 5: Additional References of Potential Interest

Guidelines with Unclear Methodology

Bamford A, Turkova A, Lyall H, et al. Paediatric European Network for Treatment of AIDS (PENTA) guidelines for treatment of paediatric HIV-1 infection 2015: optimizing health in preparation for adult life. HIV Med. 2018;19(1):e1-e42.

Group AS. Executive summary of the GESIDA/National AIDS Plan consensus document on antiretroviral therapy in adults infected by the human immunodeficiency virus (updated January 2016). Enferm Infecc Microbiol Clin. 2016;34(7):439-451.

Navas C, Torres-Duque CA, Munoz-Ceron J, et al. Diagnosis and treatment of latent tuberculosis in patients with multiple sclerosis, expert consensus. On behalf of the Colombian Association of Neurology, Committee of Multiple Sclerosis. Mult. 2018;4(1):2055217317752202.

Ooi CJ, Hilmi I, Banerjee R, et al. Best practices on immunomodulators and biologic agents for ulcerative colitis and Crohn's disease in Asia. J Gastroenterol Hepatol. 2019;34(8):1296-1315.