EVALUATING STAKEHOLDER ACCESSIBILITY OF GUIDELINES

EVALUATING AND IMPROVING STAKEHOLDER ACCESSIBILITY OF THE WORLD HEALTH ORGANIZATION'S TUBERCULOSIS GUIDELINES

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LAY ABSTRACT

Tuberculosis (TB) is a leading cause of death worldwide. The World Health Organization's (WHO) Global TB (GTB) Programme offers guidelines with recommendations to help decision-makers use evidence on TB prevention, diagnosis, treatment, and care. With the goals of improving the accessibility and use of these recommendations, the WHO and McMaster University have worked together to develop the WHO eTB catalogue of recommendations. This catalogue allows decision-makers to search, filter, and view WHO TB recommendations. This thesis contributed to this work by exploring feedback from decision-makers to identify whether the goals of the WHO eTB catalogue were achieved. The work included creating and leading a randomized controlled trial that compared the WHO eTB catalogue to the earlier way of accessing these recommendations using the WHO publications website. This thesis also explored ways that this feedback could be used to improve the WHO eTB catalogue in the future.

ABSTRACT

Background: Tuberculosis (TB) is the leading cause of death from a single infectious agent worldwide. The World Health Organization's (WHO) Global Tuberculosis (GTB) Programme issues evidence-informed guidelines with recommendations on TB. In an effort to improve the accessibility and use of these guidelines, we developed a new digitized WHO eTB catalogue of recommendations.

Objective: The objective of this thesis was to explore stakeholder engagement with WHO TB recommendations. We sought to compare the accessibility of the WHO eTB catalogue to the conventional method of accessing WHO TB recommendations, and to explore the ways in which stakeholder feedback could be incorporated into quality improvement frameworks.

Methods: We conducted a two-arm superiority randomized controlled trial through a survey among stakeholders who were past or planned future users of TB guidelines, recommendations, or policy advice. Using a 1:1 ratio, we randomly assigned participants to complete an activity using WHO eTB or the conventional website. We compared outcomes of accessibility, understanding, satisfaction and preference between groups. We incorporated qualitative feedback from free-text boxes into a quality improvement framework.

Results: From February 26th to March 24th, 2021, we received 188 survey responses, 110 participants were randomized, and 102 were included in the interim analysis. On average, participants rated the WHO eTB catalogue as more accessible across four domains when compared to the WHO TB website. There was no difference in participant understanding of recommendation strength and certainty, but the ability to locate evidence to decision tables favored WHO eTB. We also received 75 qualitative responses, 47 of which yielded five themes: purpose, navigation, presentation, organization, and outreach.

Conclusions: The WHO eTB catalogue of recommendations improved the accessibility of WHO TB recommendations and supporting evidence for stakeholders of interest. Our findings support the continued use, promotion, and quality improvement of the WHO eTB catalogue in the future.

This thesis has been written as a "sandwich thesis". It contains four chapters, including the introduction, manuscript, quality improvement, and conclusion sections. There is some overlap in the content between introduction and manuscript sections. However, the introduction describes background concepts in greater detail, whereas the manuscript describes the methods in greater detail. The manuscript will be submitted to an academic journal for publication. The structure is as follows:

Chapter 1: Introduction

Chapter 2: Manuscript titled "Comparing the Accessibility of the World Health Organization's Conventional Tuberculosis Guidelines to the eTB Catalogue of Recommendations: A Two-Arm Superiority Randomized Controlled Trial"

Chapter 3: Quality Improvement

Chapter 4: Conclusion

At the time of thesis submission, this manuscript has not yet been submitted for publication.

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ABBREVIATIONS AND SYMBOLS

AMR: Antimicrobial Resistance
CIHR: Canadian Institutes of Health Research
CONSORT: Consolidated Standards of Reporting Trials
DR-TB: Drug resistant Tuberculosis
EBDM: Evidence-Based Decision Making
EIPH: Evidence-Informed Public Health
EtD: Evidence to Decision
GDG: Guideline Development Group
G-I-N: Guidelines International Network
GRADE: Grading of Recommendations Assessment, Development and Evaluation
HEI: Department of Health Research Methods, Evidence, and Impact
HIC: High-Income Country
KT: Knowledge Translation
LMIC: Low- and Middle- Income Country
MDGs: Millennium Development Goals
MDR-TB: Multidrug Resistant Tuberculosis
MuSE: Multi Stakeholder Engagement Consortium
NICE: National Institute for Health and Care Excellence
PDSA: Plan-Do-Study-Act
PICO: Population, Intervention, Comparison, Outcome
QI: Quality Improvement
RCT: Randomized Controlled Trial
SoF: Summary of Findings
TB: Tuberculosis
UN: United Nations
UX: User Experience
WHO: World Health Organization
WHO eTB: World Health Organization eTB Catalogue of Recommendations
WHO GTB: World Health Organization Global Tuberculosis Programme
XDR-TB: Extensively Drug Resistant Tuberculosis

DECLARATION OF ACADEMIC ACHIEVEMENT

I, Micayla Matthews, declare that this thesis has been composed solely by myself. It has not been submitted, in whole or in part, in any previous application for a degree. This work is entirely my own, except where it states otherwise by reference or acknowledgement. Part of this document may be submitted for publication later.

My supervisor, Dr. Holger Schünemann, and members of my supervisory committee (Dr. Mark Loeb, Dr. Dominik Mertz, and Dr. Nancy Santesso), have provided feedback and guidance on this work. Furthermore, Dr. Tamara Lotfi (project coordinator), and team members at the WHO and Evidence Prime Inc. have provided feedback on the survey and manuscript. Their guidance assisted me in the review of relevant background literature, design of study methods, data analysis, and interpretation of the results.

CHAPTER 1: INTRODUCTION

1.1 Background

1.1.1 Tuberculosis

Tuberculosis (TB) is the leading cause of death from a single infectious agent worldwide, with an estimated 10 million new cases in 2019.[1] It is a communicable disease that is caused by the bacillus *Mycobacterium tuberculosis*, which currently infects approximately 1.7 billion people, or one quarter of the world's population.[1] It is estimated that about 5-10% of those infected with *M. tuberculosis* will develop active TB disease during their lifetime.[1] Tuberculosis primarily affects the lungs, which is known as pulmonary TB, but it can also affect several other body sites, known as extrapulmonary TB.[2] It is primarily transmitted person to person by breathing in the aerosolized droplets of an individual with active TB.[2]

The majority of TB disease is both preventable and curable. Prompt diagnosis and treatment with first-line antibiotics (isoniazid, rifampicin, ethambutol and pyrazinamide) for six months can cure most TB cases.[1] Furthermore, TB disease may be prevented by addressing risk factors such as poverty, poor housing quality, malnutrition, smoking, and diabetes.[1] However, the emergence of drug-resistant TB (DR-TB) has led to additional treatment complexities.

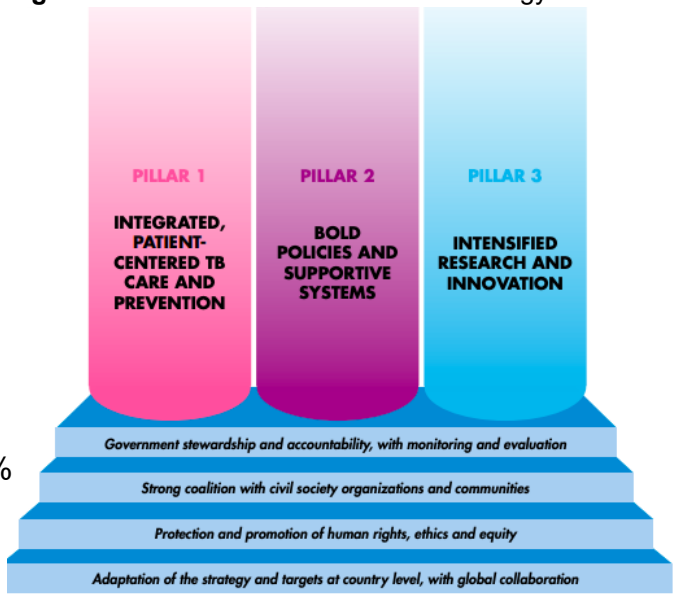
Drug-resistant TB is defined as resistance to one of the first-line antibiotics,

which is most often rifampicin resistance (RR-TB). *M. tuberculosis* that develops RR-TB often also develops resistance to isoniazid, resulting in multidrug-resistant TB (MDR-TB).[3] In 2018, 3.4% of new TB cases, and 18% of previously treated TB cases developed RR or MDR-TB.[1] Furthermore, extensively drug-resistant TB (XDR-TB) is defined as *M. tuberculosis* that is resistant to any fluoroquinolone and to at least one injectable agent used to treat MDR-TB.[3] In 2018, 6.2% (95% CI: 4.4-8.2%) of MDR-TB cases were identified as XDR-TB.[1]

1.1.2 WHO End TB Strategy

In 1993, the World Health Organization (WHO) declared TB a global public health emergency.[4] In 2014, the WHO and the United Nations (UN) unanimously endorsed the WHO End TB Strategy with a goal of ending the global TB epidemic by 2035.[4] This is considered an ambitious but attainable goal, which includes the targets of a 90% reduction in TB incidence, and a 95% reduction in TB deaths (<10 per 100,000 population).[4] These

Figure 1. Pillars of the WHO End TB Strategy



targets are equivalent to TB rates in low incidence regions, such as North America and Western Europe.[4]

The WHO End TB strategy is supported by three comprehensive pillars: integrated, patient-centered care and prevention, bold policies and supportive systems, and intensified research and innovation (see Figure 1).[4] These pillars include the key actions of early diagnosis, access to treatment, prevention, community engagement, political commitment, and development and implementation of new tools.[4]

The attention to TB and strategies developed by the WHO and its partners has led to many advancements in TB care. Between 2000 and 2017, these interventions have resulted in a 33% decrease in TB deaths and an estimated 54 million lives saved.[4] Nevertheless, there is still much work to be done. The majority of high-burden TB countries were not on schedule to meet the 2020 milestones, which included a 20% reduction in TB incidence and a 35% reduction in TB deaths.[4] Thus, they must sustain and intensify their public health efforts in order to meet the 2035 goal.

1.1.3 WHO Tuberculosis Guidelines

The WHO's core mandate includes offering guidance on TB prevention, diagnosis, treatment, and care.[4,5] Accordingly, the WHO Global TB Programme (GTB) has issued guidelines containing recommendations on TB since 1997.[5]

Since 2009, these guidelines have been structured using the WHO Handbook for Guideline Development. This handbook includes the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method, which is considered to be a transparent, evidence-based framework for recommendation development.[5] GRADE assists guideline panel members in question prioritization, quality assessments, balancing benefits and risks, and considering equity and feasibility in context.[6] Furthermore, it provides a framework for the reporting of these decisions using evidence to decision (EtD) tables and evidence summaries, such as summary of findings (SoF) tables.[6]

WHO TB recommendations are located in many discrete documents on the WHO publications website. These recommendations may be found in standard guidelines, consolidated guidelines, interim guidelines, and guidelines produced in response to an emergency or urgent need. Furthermore, there are recommendations contained in non-guideline documents including secretariat reports, operational manuals, and implementation tools. Given the large number and variety of publications, ways to enhance their connectivity and accessibility for stakeholders should be explored.

1.1.4 WHO and McMaster TB Quality Improvement Project

In 2019, the WHO partnered with researchers in the McMaster University Department of Health Research Methods, Evidence and Impact (HEI), and an

information technology team from Evidence Prime Inc., to propose the project titled "Revisiting the Development of Tuberculosis Recommendations: A Quality Improvement Project". This two-year project seeks to enhance connectivity and accessibility of WHO TB recommendations for stakeholders of interest. This project comprises of three areas: (1) the mapping and organization of WHO TB recommendations, (2) easing the adolopment (adoption, adaptation, or de novo development)[7] of recommendations in a rapid learning health system, and (3) tailoring outputs to stakeholders.

This quality improvement project strives to compliment all three pillars of the WHO End TB Strategy by improving access to guidance on TB care in order to promote evidence-informed clinical, public health, and policy decisions (see Figure 1). Most notably, this work strives to complement pillar three by engaging in intensified research and innovation through the optimization of available tools, development of new tools, and encouragement of discovery.[4]

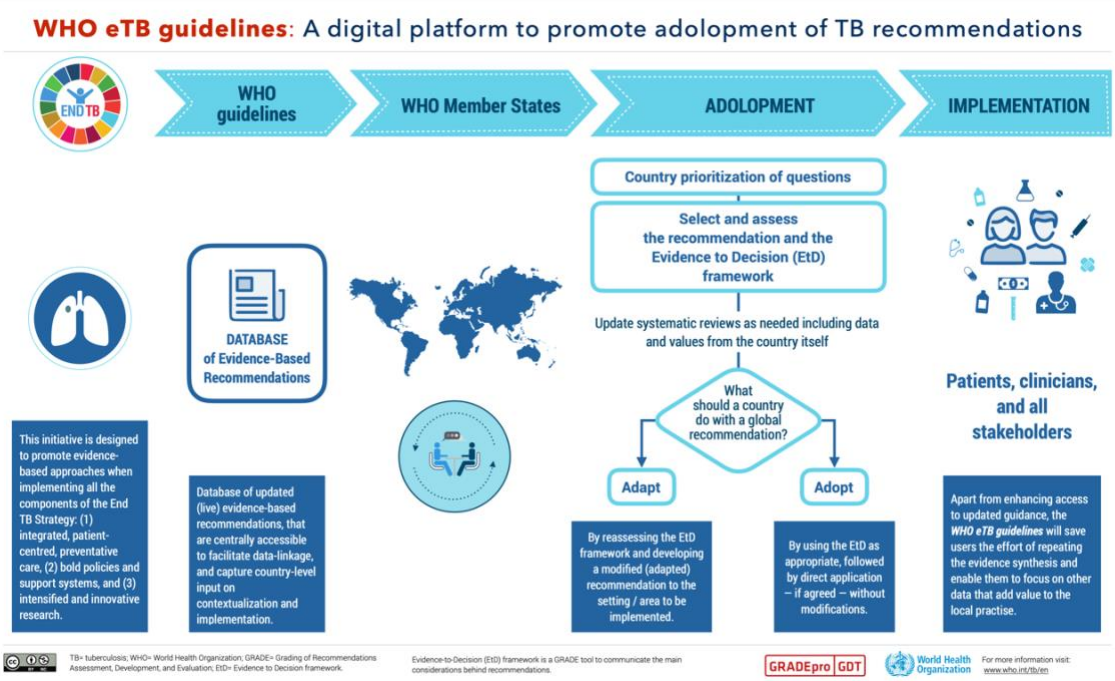
In area one of this project, a mixed-methods study by Hajizadeh, et al.[8] suggested that key stakeholders, including members of the WHO-GTB guideline development group (GDG), desire direct access to WHO TB recommendations and supplementary information. Surveys and semi-structured interviews were conducted with 21 stakeholders, many of which had been involved in TB-focused work for over ten years. These stakeholders identified the potential benefits of consolidating recommendations

in one place and increasing access to evidence to decision (EtD) tables and evidence profiles for decision-making.[8]

1.1.5 WHO eTB Catalogue of Recommendations

In an effort to consolidate and optimize the presentation of WHO TB recommendations as part of the WHO and McMaster Quality Improvement Project, we developed a digitized eTB catalogue of recommendations available at tuberculosis.evidenceprime.com.[9] This catalogue is anticipated to increase accessibility of the most up-to-date and relevant WHO TB recommendations for stakeholders based on their questions of interest (see Figure 2).[8,9] It identifies, lists, and maps WHO TB recommendations using novel

Figure 2. WHO eTB Guidelines



recommendation mapping methods. Recommendation mapping is defined as an "online repository of recommendations from several guidelines on a condition, providing links to the underlying evidence and expert judgements that inform them, allowing users to filter and cross-tabulate the search results." (p. 2)[8] The presentation of the WHO eTB catalogue allows stakeholders to search for recommendations by patient care cascade, keywords, publication date, or by the population and intervention that the recommendation addresses. See Figures 3-5 for images of the WHO eTB catalogue from this open-access website.[9]

Figure 3. WHO eTB Home Page

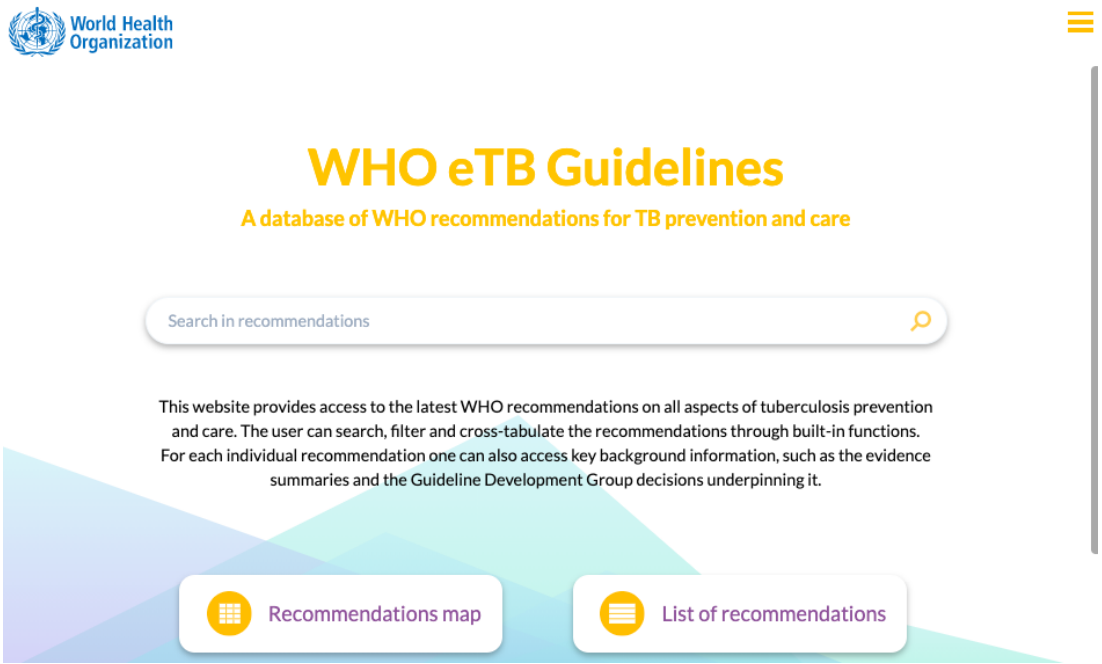


Figure 4. WHO eTB Recommendations List

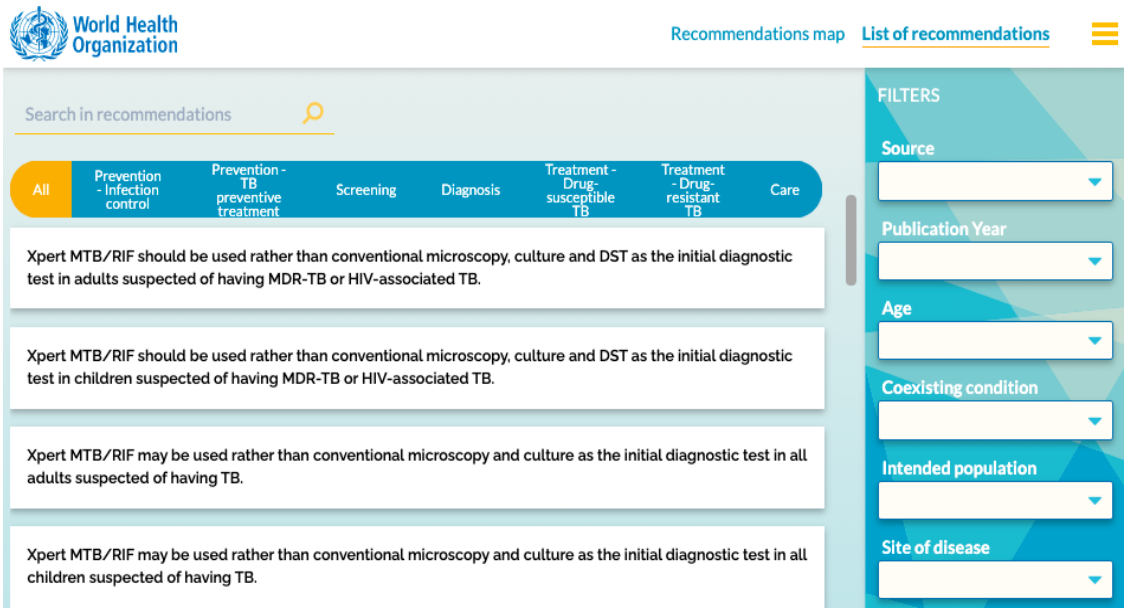


Figure 5. WHO eTB Recommendations Map

The WHO eTB catalogue will also be connected with the GRADEpro Guideline Implementation Tool to facilitate adolopment (adoption, adaptation, or de novo development) of recommendations.[7] The adolopment process will allow stakeholders to contextualize WHO TB recommendations to their specific

country and setting (see Figure 2).

1.1.6 Stakeholder Engagement

Public health and healthcare literature define a stakeholder as a person accountable for, or influenced by, health decisions informed by research evidence.[10] Additionally, engagement is defined as the bi-directional relationship between stakeholders and researchers or guideline developers.[10] The WHO recognizes that stakeholder engagement at all levels of organizations and communities is fundamental to ending the TB epidemic.[4] Furthermore, the National Institute for Health and Care Excellence (NICE), and the Guidelines International Network (G-I-N) endorse stakeholder consultation and engagement in guideline development, dissemination, and implementation processes.[11–13]

Stakeholder engagement has the ability to prevent controversy and uncertainty in the guideline development process by ensuring that guideline products are feasible and acceptable to end-users.[13–15] The Multi Stakeholder Engagement (MuSE) Consortium, which is an international team that has developed practical guidance on stakeholder engagement in guideline development, has stated that "involving stakeholders may make study questions more relevant, methods and approaches more transparent, findings more useful, and evidence more likely to be used in practice" (p. 459).[10] Thus,

stakeholder engagement is an essential consideration in the restructuring of WHO TB guidelines, recommendations, and policy advice.

With the number and variety of individuals and groups who may be accountable for, or influenced by WHO TB recommendations, a framework should be used to ensure that stakeholders are comprehensively identified. The 10 Ps Framework is a recognized tool in the process of stakeholder identification.[16] Each "P" represents a stakeholder group, such as patients and the public, providers of healthcare, purchasers and payers of health services, policymakers, program managers, product makers, principal investigators, and peer review editors.[16] These categories are not mutually exclusive, and all groups may not have a stake in every question. Nevertheless, this framework helps to ensure comprehensiveness in the identification process. Descriptions of each of the 10 P categories are available in Table 1.

Table 1. 10 Ps Framework

Group	**Description**[16]
Patients	Current and potential consumers of healthcare, caregivers, families, patient and consumer advocacy groups.
The Public	Current and potential consumers of population-focused public health and advocacy groups.
Providers	Healthcare professionals (e.g., nurses, physicians, allied health professionals, etc.), health centers, or community organizations that provide care to patients and populations.
Purchasers	Employers, the self-insured, government, and other entities responsible for underwriting the costs of healthcare.
Payers	Insurers, insurance exchanges, individuals with deductibles, or others responsible for reimbursement for healthcare.
Policy makers	Government, departments of health, professional associations, intermediaries, other policy-making groups.

Program managers	Program managers of organizations in member countries.
Product makers	Drug and device manufacturers.
Principal investigators	Researchers, academics, research teams, and their funders.
Peer review editors	Peer reviewers of journals or guidelines.

Once identified, it is important to develop methods to involve stakeholders in the guideline development, dissemination, and implementation processes. The G-I-N offers a public toolkit with several strategies for patient and public involvement (PPI) in guideline development. This toolkit suggests consultation through surveys and interviews that gather perspectives on needs, experiences and expectations.[13] These strategies should be considered in the restructuring and dissemination of WHO TB guideline recommendations.

1.1.7 Knowledge Translation and Evidence-Informed Public Health

The Canadian Institutes of Health Research (CIHR) defines knowledge translation (KT) as a "dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge".[17] Preferably, this knowledge is synthesized high-quality research evidence accompanying other important clinical, public health, and context-specific considerations. Use of the GRADE method in guideline development facilitates the KT process by incorporating such comprehensive considerations in recommendations.[6,7] Thus, stakeholder use of guidelines developed in accordance with the GRADE method may facilitate evidence-based decision

making (EBDM) and evidence-informed public health (EIPH), which is the process of integrating science-based interventions with community preferences to improve population health.[18]

The WHO eTB catalogue is anticipated to bridge potential gaps between the evidence available in WHO TB recommendations, and clinical, public health and policy practice. We anticipate that it will accomplish this by increasing stakeholder accessibility and use of WHO TB recommendations. In order to promote KT of WHO TB recommendations, it is important to consider the factors that influence stakeholder decisions to use evidence and guidelines. Health policy frameworks have identified that an individual's decision to use evidence may be influenced by their beliefs and values, as well as their social networks.[19–21] Furthermore, qualitative studies have identified that a stakeholder's decision to engage with guidelines may be influenced by guideline presentation, stakeholder awareness of their existence, and perceptions of their relevance.[22–24]

1.1.8 User Experience

The WHO eTB catalogue of recommendations is a digitalized platform. Therefore, it is also important to consider the factors that influence a stakeholder's decision to engage with technology. User experience (UX) is a field of research that seeks to identify the factors that influence user

engagement with a product, system or service.[25] UX theory is often used in the field of information technology to evaluate stakeholder experiences with novel technological platforms. Scholars of UX theory have identified that a user's decision to engage with technology may be influenced by perceived pragmatic or ergonomic quality (perspicuity, efficiency, dependability), hedonic quality (stimulation, novelty), and overall attractiveness.[25,26] Pragmatic or ergonomic quality may be described as the ability to reach goals with efficiency and effectiveness, and hedonic quality may be described as non-task oriented visual quality and originality of the interface.[25] These user experiences are subsequently combined to determine the overall attractiveness of the system.[25] The factors identified in UX theory should also be considered when seeking to improve the accessibility of WHO TB recommendations through the use of a digitalized WHO eTB catalogue.

1.1.9 Experimental Studies on Methods

The WHO eTB catalogue of recommendations, which involves novel recommendation mapping methods, was developed to organize, streamline and enhance the accessibility of WHO TB recommendations for stakeholders of interest.[8] These new methods may now be compared to existing methods through the application of an experimental study. Experimental studies on methods is a field of research that seeks to compare new to conventional

methods, with the unit of analysis being the participant who is applying these methods.[27]

In order to ensure that the WHO eTB catalogue satisfies its objective of improving the accessibility and use of WHO TB recommendations for stakeholders, it should be compared to the conventional method of accessing TB recommendations using the WHO website. Experimental studies on methods have been used to investigate similar comparisons between new and current formats of GRADE SoF tables, which present evidence on systematic reviews to facilitate interpretation by decision-makers.[28] These SoF tables have been strategically designed using stakeholder feedback collected from randomized controlled trials (RCTs) administered using online questionnaires.[29–32] The investigators of these RCTs have explored the outcomes of understanding, accessibility of information, satisfaction, and preference, which were measured using multiple choice and Likert-scale questions.

1.1.10 Quality Improvement

Quality Improvement (QI) is a methodology that seeks to optimize and streamline systems and processes. In the context of public health, QI has been described as the use of a deliberate and defined improvement process, such as the Plan-Do-Study-Act (PDSA) cycle (see Table 2), in order to achieve

measurable improvements in several outcomes including efficiency, effectiveness, and performance.[33] The basic principles of QI include strong leadership, system approach to management, continual improvement, consumer focus, and mutually beneficial relationships.[34] Although QI is often described as separate from research, some scholars have recognized that complementary research-QI efforts may strengthen both research findings and QI outputs.[35]

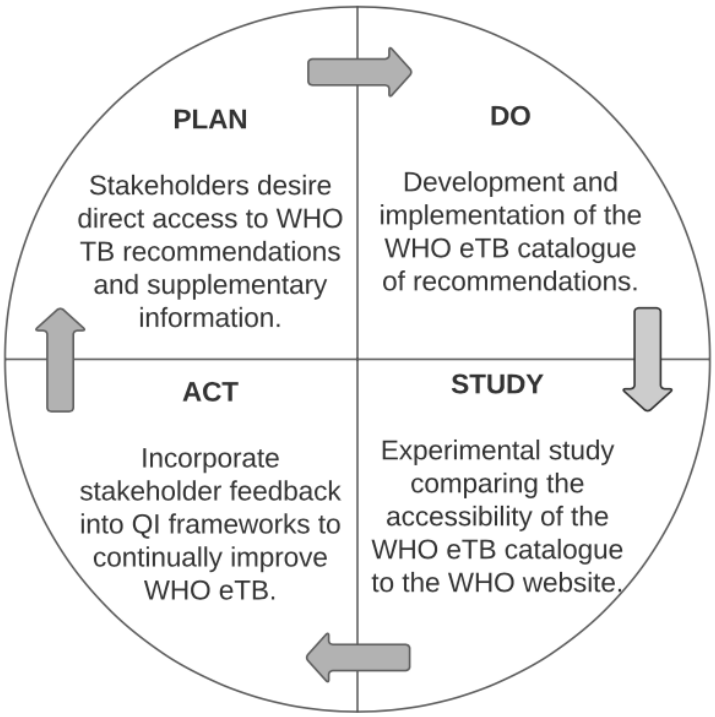
Table 2. Plan-Do-Study-Act (PDSA) Process[33,36]

Plan	• Investigate the current situation. • Collect and analyze baseline data. • Attempt to identify and understand nature of the problem and root causes.
Do	• Implement new solutions or interventions.
Study	• Compare solutions or interventions to baseline. • Determine whether improvement was achieved.
Act	• Act upon what has been learned. • Adopt, adapt, and re-test.

The WHO has recognized that a lack of robust QI is a barrier to reaching the Millennium Development Goals (MDGs) concerning several health issues, including TB.[37] This is because gaps or breakdowns in the health system may prevent access to timely and efficient resources including evidence-based standards.[37] The mixed-methods study by Hajizadeh, et al. (2021) accompanying the development of the WHO eTB catalogue identified that stakeholders desire direct access to WHO TB recommendations and supplementary information, such as EtD and SoF tables.[8] The identification of

this need through research, and the succeeding development of the WHO eTB catalogue may be recognized as the "Plan" and "Do" sections of a PDSA cycle (see Figure 6). The "Study" section, during which interventions are compared to the baseline, may be addressed using an objective RCT in which stakeholder experiences are compared between the conventional WHO TB guidelines and the new WHO eTB catalogue of recommendations. Finally, it is important to "Act" on this feedback through additional frameworks that aim to continually improve accessibility and use of WHO TB recommendations in the future.

Figure 6. WHO eTB Plan-Do-Study-Act (PDSA) Cycle



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CHAPTER 2: MANUSCRIPT

Comparing the Accessibility of the World Health Organization's Conventional Tuberculosis Guidelines to the eTB Catalogue of Recommendations:
A Two-Arm Superiority Randomized Controlled Trial

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2.1 Abstract

Objective: In an effort to improve the accessibility and use of tuberculosis (TB) guidelines issued by the World Health Organization (WHO), we developed a new electronic catalogue of TB recommendations (eTB). The objective of this study was to compare the accessibility of the new catalogue to the conventional method of accessing recommendations using the WHO website, in order to demonstrate whether WHO eTB is superior.

Study Design: We conducted a two-arm superiority randomized controlled trial among stakeholders who were past or planned future users of TB guidelines. Using a 1:1 ratio, we randomly assigned participants to complete an activity using the WHO eTB catalogue or conventional website. We compared the outcomes of accessibility, understanding, satisfaction and preference between groups.

Results: This manuscript describes the results of the pre-planned interim analysis. From February 26 to March 24, 2021, we received 188 responses, 110 were randomized, and 102 were included for analysis. Participants rated WHO eTB as more accessible across four domains when compared to the conventional website. There was no difference in participant understanding of recommendation strength and certainty, but the ability to locate evidence to decision (EtD) tables favored WHO eTB.

Conclusion: The WHO eTB catalogue improved the accessibility of WHO TB recommendations and supporting evidence for stakeholders of interest.

Keywords: Guideline; Recommendation; Tuberculosis; GRADE;

Evidence-Based Practice; Evidence to Decision Table

Trial Registration: This trial is registered with ClinicalTrials.gov (NCT04745897).

Funding: The development of the eTB catalogue was funded by the WHO. This trial was not funded by the WHO, and the WHO was not involved in the collection or analysis of study findings.

Consent to Participate: The study questionnaire included a consent statement that described the study purpose, confidentiality, risks, and voluntary participation.

Data Protection and Confidentiality: Anonymized survey data were stored in SurveyMonkey® password-protected software. Participant names collected for follow-up were stored in a separate document on a secure password-protected computer. Only the research team have access to these data.

Availability of Data and Materials: Anonymous survey data are available from the authors upon request.

Disclaimers: The authors of this manuscript are responsible for its content.

Declaration of Interests: HJS' institution received funding and fees from the World Health Organization for research on WHO tuberculosis guideline development and related educational activities; including for the eTB catalogue of recommendations. This trial was not funded by the WHO.

Ethics Approval: Hamilton Integrated Research Ethics Board (HiREB)

Abbreviations

EtD: Evidence to Decision

GDG: Guideline Development Group

G-I-N: Guidelines International Network

GRADE: Grading of Recommendations Assessment, Development and Evaluation

HIC: high-income country

LMIC: low- and middle-income country

NICE: National Institute for Health and Care Excellence

RCT: Randomized Controlled Trial

SoF: Summary of Findings

TB: Tuberculosis

UN: United Nations

WHO: World Health Organization

WHO eTB: World Health Organization eTB Catalogue of Recommendations

WHO GTB: WHO Global TB Programme

Highlights: What is new?

Key Findings:

- The new World Health Organization (WHO) eTB catalogue improves the accessibility of tuberculosis (TB) recommendations for stakeholders across four domains when compared to the conventional method.
- The eTB catalogue also improves the ability of stakeholders to access supporting evidence and decisions underpinning recommendations.

What this adds to what is known:

- Our findings suggest that the eTB catalogue improves accessibility, understanding, and satisfaction, which are surrogates for the correct implementation of evidence in practice.
- This study also demonstrates that randomized controlled trials (RCTs) may be used to compare stakeholder feedback on guideline platforms.

What is the implication, what should change now:

- Our findings support the continued use, promotion, and quality improvement of the WHO eTB catalogue of recommendations.
- Researchers should consider the use of RCTs to evaluate stakeholder feedback on guideline presentation.

2.2. Background

Tuberculosis (TB) is the leading cause of death from a single infectious agent worldwide, with an estimated 10 million new cases in 2019.[1] In a concerted effort to end the TB epidemic, the WHO Global TB Programme (WHO-GTB) has issued guidelines with recommendations on TB prevention, diagnosis, treatment, and care.[2,3] Since 2009, these guidelines have been developed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method[3], which is a transparent, evidence-based framework for the assessment of the certainty in a body of evidence and recommendation development.[4] Specifically, GRADE assists guideline developers in question prioritization, certainty assessments, balancing benefits and risks, and considering cost, equity, acceptability, and feasibility in context.[4,5]

WHO TB recommendations are located in many discrete publications on the WHO website, including standard, consolidated, interim, and emergency guidelines. Given the large number and variety of publications, ways to enhance their connectivity and accessibility should be explored like for guidelines in other fields. A mixed-methods study by Hajizadeh, et al.[6] suggested that stakeholders, including members of the WHO-GTB guideline development group (GDG), desire direct access to WHO TB recommendations and supplementary information, such as evidence to decision (EtD) tables and

evidence profiles.[6]

In an effort to improve accessibility and use of WHO TB recommendations, we developed a WHO eTB recommendation map in a collaboration between the Michael G DeGroote Cochrane Canada Centre and the WHO-GTB.[6,7] This catalogue identifies, lists, and maps WHO TB recommendations using recommendation mapping methodology, which is a tool to visually organize recommendations in order to identify clusters and gaps.[6] Furthermore, it is anticipated to facilitate the adoption, adaptation, or de novo development of recommendations in a variety of countries and settings.[8]

In order to ensure that this new WHO eTB catalogue improves the accessibility and use of information for stakeholders, it should be compared to the conventional method of accessing WHO TB recommendations. In this randomized controlled trial, we sought to determine whether the WHO eTB catalogue of recommendations, compared to the conventional publication of WHO TB guidelines, improved the accessibility and understanding of these recommendations in relevant stakeholders.

2.3. Methods

This study was reported in accordance with the most recent guidance from the Consolidated Standards of Reporting Trials (CONSORT).[9] The CONSORT reporting checklist for this trial is available in Appendix A. The trial protocol was

registered with ClinicalTrials.gov (trial registration: NCT04745897).

2.3.1 Study Setting

This study was a two-arm randomized controlled superiority trial to compare the accessibility of the WHO eTB catalogue (WHO eTB) to the conventional method of accessing TB recommendations through the WHO publications website (WHO TB). It was administered using a SurveyMonkey® questionnaire, accessible through a link shared via email (see Appendix B). Participants responded to demographic questions and were subsequently randomized using 1:1 allocation to access a recommendation using either WHO eTB or WHO TB (platforms). Randomization was stratified by participant background (e.g. patient, healthcare provider, policy maker) in order to ensure balance between groups. Participants completed Likert-scale and multiple-choice questions about the platform which they were allocated. After completing the key portion of the trial, they received information about the alternative platform to respond to a question on their preference.

2.3.2. Participants

2.3.2.1. Eligibility Criteria

Stakeholders who considered themselves to be users or potential users of TB guidelines, recommendations, and policy advice were eligible. For the

purposes of this trial, we defined a user as someone who responded "yes" to the question "have you ever accessed TB guidelines, recommendations or policy advice in the past?". A potential user was someone who responded "yes" to the question "do you plan on accessing TB guidelines, recommendations or policy advice in the future?". Eligible participants could be part of any group with a stake in TB, including the public, healthcare providers, policy makers, and researchers, and there were no restrictions on country of origin, level of education, or prior TB work experience. Individuals who were involved in WHO eTB development were not eligible to participate.

2.3.2.2. Recruitment

We used a targeted snowball recruitment strategy by emailing survey links to WHO TB Guideline Development Group (GDG) members and other stakeholders involved in the process of using and applying TB guideline recommendations. We requested that these members disseminate the survey within their networks, which may include healthcare providers, policy makers, researchers, and people living with TB. We also shared the survey invitation on social media.

2.3.3. Intervention and Comparison

In this randomized controlled superiority trial, the intervention was the new

WHO eTB catalogue of recommendations (WHO eTB), and the comparison was the conventional method of accessing TB recommendations using the WHO website (WHO TB). We asked survey participants to complete an activity in searching for the same recommendation using the one platform which they had been randomly allocated. Instructions and questions for both arms were worded as similarly as possible. See Table 1 for an overview of the differences between WHO eTB and WHO TB.

Table 1. Description of differences between WHO TB and WHO eTB

	WHO TB	**WHO eTB**
Website	WHO website	WHO eTB website
Search	PDF documents	Search bar and filters
Strength and certainty defining the recommendation	Often near recommendation	Always near recommendation
EtD tables	Separate appendix	Link to page in appendix
Recommendation mapping	No	Yes

Abbreviations: WHO TB, accessing World Health Organization tuberculosis recommendations via the World Health Organization's website; eTB, the new eTB catalogue of recommendations; PDF, portable document format; EtD, evidence to decision tables

2.3.4. Outcomes

This trial used several of the same outcomes that have been validated in the evaluation of GRADE Summary of Findings (SoF) tables.[10–13]

2.3.4.1. Primary Outcome

Accessibility of Information

The primary outcome of interest was the accessibility of information available

on WHO eTB compared to WHO TB. We defined accessibility as the ability to access and use the presented information. This outcome considered the four following domains: (1) how easy it was to find the information (2) how easy it was to understand the information (3) whether the presentation facilitated decision-making (4) whether the website was easy to navigate.

2.3.4.2. Secondary Outcomes

Understanding

We defined understanding as the correct comprehension of findings. This outcome was measured using three multiple-choice questions with five choices and one correct answer. The questions were: 'what is the recommendation strength?', 'what is the certainty of the evidence?' and 'on which page does the EtD table for this recommendation start?'. Appendix C describes these questions and correct responses.

Satisfaction

We defined satisfaction as a stakeholder's impression of platform presentation. This outcome considered the presentation of three domains: (1) home page (2) recommendation list (3) individual recommendation.

Preference

We defined preference as a greater liking of one platform over the other. All participants were provided with a short demonstration of both platforms (see Appendix D). They were subsequently asked 'between the WHO Tuberculosis Guidelines (current website), and the WHO eTB Guidelines (alternative website), which do you prefer?'.

2.3.5. Outcomes Measurement

We used the original Likert-scale to obtain responses for the outcomes of accessibility and satisfaction. We measured preference using a Likert-type scale to express the degree of preference with seven answer options (1 = strongly prefer WHO TB, 2 = prefer WHO TB, 3 = somewhat prefer WHO TB, 4 = same preference for WHO TB and eTB, 5 = somewhat prefer WHO eTB, 6 = prefer WHO eTB, 7 = strongly prefer WHO eTB).

2.3.6. Sample Size Calculation

Sample size was calculated using the primary outcome of accessibility in WINPEPI® (PEPI-for-Windows) version 11.65. For this two-sided ($\alpha = 0.05$) superiority analysis, these computations were made based on a t-test with the null hypothesis that there is no difference between the WHO eTB and WHO TB in the accessibility of information.

H_0: *WHO eTB = WHO TB*

H_1: *WHO eTB ≠ WHO TB*

With sample sizes of 122 per arm (244 total) we would achieve 80% power to detect a difference on the Likert-scale of 0.5 (effect size) with a standard deviation of 1.0 between intervention and control groups. We applied the effect size and standard deviation from previous studies on GRADE SoF tables.[10–13] We assumed that 15% would not complete the survey, but we did not factor stratifying participants by stakeholder group into the calculation, as the aim of stratification was to balance participants rather than be sufficiently powered to detect subgroup effects.

2.3.7. Randomization

Participant response to a question on their role as a participant in this study was used for stratification into one of four categories described in Figure 1. Participants within each of these categories were randomly assigned in a 1:1 ratio to the WHO eTB or WHO TB arms.

Participants were randomly assigned to access one of two recommendations in a 1:1 ratio. The same two recommendations were presented for both arms, selected because they contain mostly plain language and, thus make them more accessible to non-clinical participants (see Appendix C).

2.3.8. Allocation Concealment

The allocation sequence was concealed through the use of SurveyMonkey® software based on a commercial, but unknown algorithm without a pre-identified sequence.

2.3.9. Blinding

Participants were not aware of their random allocation to WHO eTB or WHO TB until disclosure (see Figure 1). Thus, participants were blinded for all outcomes except the secondary outcome of preference. Neutral language was used in both trial arms to prevent promotion of the intervention or comparison.

2.3.10. Consultation and Pilot Testing

We performed a pilot test for survey length, question relevance, and question clarity from February 9 to 14, 2021. Participants (n = 20) were researchers and information technology developers affiliated with McMaster University. Minor revisions were made to the questionnaire using pilot test feedback.

2.3.11. Statistical Analysis

This was a pre-planned interim analysis on March 24, 2021 based on the thesis defence date of the first author (MM). The interim analysis was not used to stop the study or draw final conclusions. We conducted the analyses of this

two-arm superiority, randomized controlled trial in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement[9] using IBM SPSS® (Statistical Package for Social Sciences) version 23.

2.3.11.1. Descriptive Analysis

We summarized participant baseline characteristics and outcomes using descriptive statistics, including means and standard deviations (SD) for continuous variables, and proportions for categorical variables.

2.3.11.2. Inferential Analysis

We performed a primary analysis including all randomized participants except for those who completed the survey in less than five minutes. We determined this cut-off a priori because user testing deemed it impossible to complete the work in that time. We conducted a second per-protocol analysis excluding participants who were flagged by SurveyMonkey® software (see below). For the outcomes of accessibility and satisfaction, we used t-tests and mean differences with 95% confidence intervals (95% CIs) to compare the means and standard deviations (SDs) between the intervention and control groups. For the outcome of understanding, we used χ^2 tests and risk difference (RD) with 95% CIs to compare the proportion of correct responses between groups. Finally, for preference, we presented preference as mean (SD)

overall and for both trial arms. Skewness, Shapiro-Wilk tests, and Histograms were used to evaluate whether the distribution was shifted toward the same preference in both groups. Levene's test of equal variances was used for all t-tests, with degrees of freedom adjusted for $p < 0.05$. We reported all p-values to three decimal places, with values less than 0.001 reported as < 0.001. Additional details on the analyses are available in Appendix E, which includes the planned analyses when the full trial data are available.

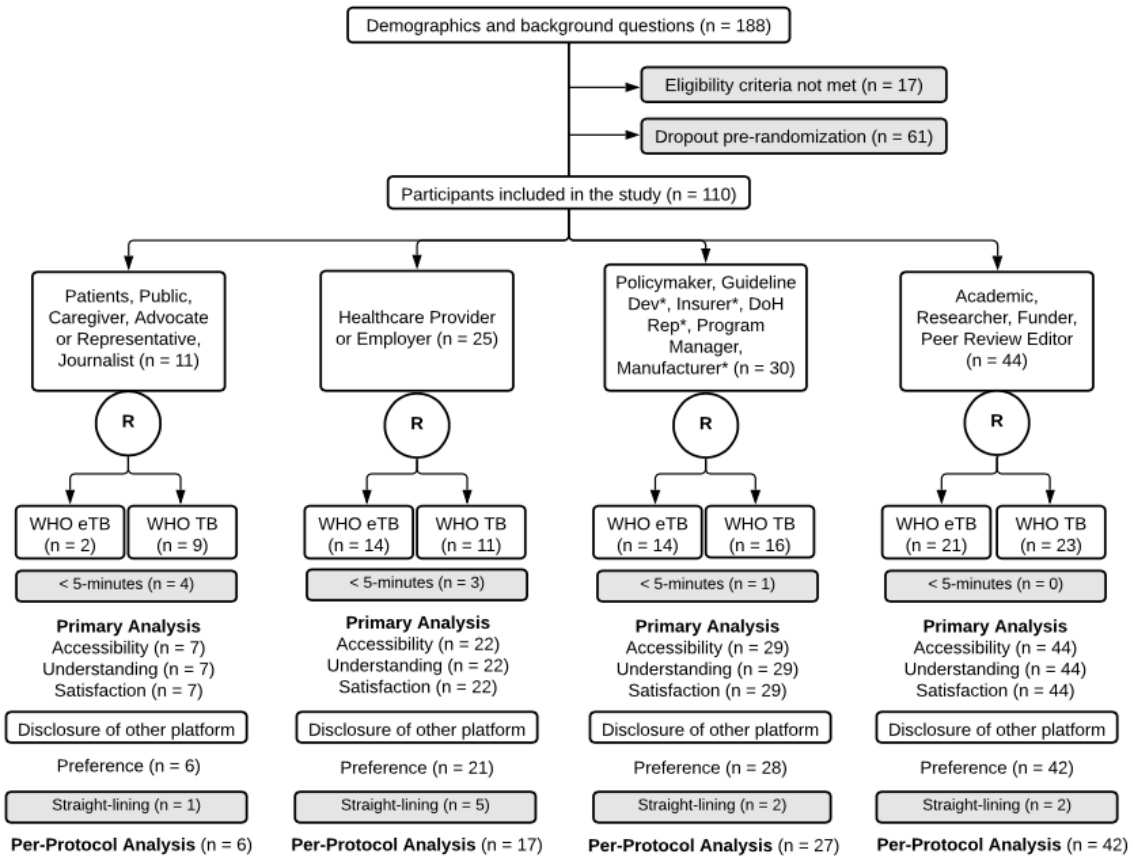
2.3.11.3. Dropouts, missing data, and poor-quality responses

We used available case analysis for data from participants who responded to some survey questions after being assigned to the intervention. In order to prevent dropouts and missing data, we implemented the following strategies: (1) we disseminated short emails to target stakeholder groups with a direct link to the survey, (2) we informed participants that the survey would require 15 minutes, (3) participants who completed the survey had the option to enter a draw for a gift card, (4) all outcome questions were mandatory, and (5) participants were randomized only after the collection of baseline characteristics.

We defined participants who spent less than five minutes on the survey as inappropriate in our analyses, with the rationale that practical comprehension and completion of the survey, based on pilot testing, could not be performed in

five minutes. The average survey completion time was 15 minutes. This was anticipated to prevent analysis of erroneous responses from participants who sought to simply gain access to the content of the survey or enter the gift card draw. For the per-protocol analysis, we used a pre-defined but unknown SurveyMonkey® algorithm which flagged poor-quality responses for straight-lining. Straight-lining is defined by SurveyMonkey® as responses to questions with the same answer option or pattern. Participants flagged for straight-lining, as well as those who spent less than five minutes on the survey, were removed from the per-protocol analysis.

Figure 1. Flow of participants through the study and samples for analyses



*Abbreviations: Guideline Dev: Guideline developer, Insurer: Insurer of health services, DoH Rep: Department of health representative, Manufacturer: Drug or device manufacturer

2.4. Results

Between February 26 and March 24, 2021, 188 participants enrolled in the study. Of these, 61 dropped out prior to randomization and 17 did not satisfy the eligibility criteria. A total of 110 participants were randomized. Of these, eight were removed for less than five-minute completion time, leaving 102 for the primary analysis. In this sample, 51% (52/102) were female, 93% (95/102) were between the ages of 26 and 65, 58% (59/102) worked or lived in a low-and middle-income country (LMIC), 28% (29/102) in a high-income country

(HIC), and 14% (14/102) in both. A total of 42 countries were represented. The majority of participants 87% (89/102) held a professional or graduate degree, and at least three years 90% (92/102) of TB-related work experience. Most participants also considered themselves to be comfortable 30% (31/102) or very comfortable 59% (60/102) with basic information and communication technologies. Participant strata comprised of 7% (7/102) in the patient group, 22% (22/102) in the healthcare provider group, 28% (29/102) in the policy maker group, and 43% (44/102) in the academic group. We found no differences in study outcomes between strata, so here we provide non-stratified data by group.

Table 2. Baseline characteristics of participants per group

Characteristic	WHO eTB (n = 49)	WHO TB (n = 53)
Gender: n (%)		
Female	22 (45)	30 (56)
Male	27 (55)	21 (40)
Other	-	1 (2)
Prefer not to respond	-	1 (2)
Age (years): n (%)		
< 25	1 (2)	1 (2)
26-35	12 (23)	13 (22)
36-45	18 (35)	20 (34)
46-55	10 (20)	13 (22)
56-65	6 (12)	10 (17)
66-75	3 (6)	2 (3)
Prefer not to respond	1 (2)	-
Setting: n (%)		
HIC	11 (23)	18 (34)
LMIC	29 (59)	30 (57)
HIC and LMIC	9 (18)	5 (9)
Education: n (%)		

Primary	-	1 (2)
College	1 (2)	1 (2)
Bachelor	4 (8)	3 (6)
Professional	6 (12)	13 (24)
Graduate	23 (47)	23 (43)
Professional and graduate	15 (31)	12 (23)
TB work (years): n (%)		
< 1	1 (2)	2 (4)
1-2	2 (4)	3 (6)
3-5	4 (8)	6 (11)
6-9	7 (14)	4 (7)
> 10	33 (68)	38 (72)
Not applicable	2 (4)	-

Abbreviations: WHO, World Health Organization; TB, Tuberculosis; HIC, high income country; LMIC, low- and middle-income country

2.4.1. Accessibility of Information

Across four domains, participants assigned to the new WHO eTB catalogue rated the information as more accessible, on average, compared to the conventional WHO TB website (see Table 3). The largest mean differences were noted for the statements "it was easy to find the information" (MD 1.4; 95% CI: 0.8, 2.0; $p < 0.001$) and "this website was easy to navigate" (MD 1.5; 95% CI: 0.9, 2.1; $p < 0.001$). Participants assigned to the WHO eTB catalogue also rated, on average, that it was easier to understand the information (MD 0.8; 95% CI: 0.3, 1.3; $p = 0.004$) and that the information was presented in a way that would help them make a decision (MD 0.8; 95% CI: 0.3, 1.3; $p = 0.003$).

Table 3. Overall accessibility of information [mean (SD)]

Domain	WHO eTB (n = 49)	WHO TB (n = 53)	MD (95% CI)	P-value
It was easy to find the information.[a]	5.6 (1.3)	4.1 (1.8)	1.4 (0.8, 2.0)[b]	< 0.001
It was easy to understand the information.[a]	5.6 (1.1)	4.9 (1.6)	0.8 (0.3, 1.3)[b]	0.004

The information was presented in a way that would help me make a decision.[a]	5.7 (1.2)	4.9 (1.4)	0.8 (0.3, 1.3)	0.003
This website was easy to navigate.[a]	5.5 (1.5)	4.0 (1.8)	1.5 (0.9, 2.1)[b]	< 0.001

Abbreviations: SD, standard deviation; WHO, World Health Organization; TB, tuberculosis; MD, mean difference; CI, confidence interval
[a] Likert-scale from 1 = strongly disagree to 7 = strongly agree
[b] Equal variances could not be assumed using Levene's test, degrees of freedom adjusted

2.4.2. Understanding

There was no significant difference in correct responses to the question on recommendation strength (10%; 95% CI: -8, 28; p = 0.294) or certainty of evidence (6%; 95% CI: -13, 25; p = 0.530) between participants who completed the activity in accessing a recommendation with WHO eTB or WHO TB. However, participants assigned to WHO eTB were significantly more likely to locate the EtD table accompanying the recommendation than participants assigned to WHO TB (RD 57%; 95% CI 43, 73; p < 0.001) (see Table 4).

Table 4. Percentage (%) of participants who responded correctly to understanding questions

Question	WHO eTB (n = 49)	WHO TB (n = 53)	Risk Difference (95% CI)	P-value[a]
What is the recommendation strength?	76	66	10 (-8, 28)	0.294
What is the certainty of evidence?	57	51	6 (-13, 25)	0.530
On which page does the evidence to decision (EtD) table for this recommendation start?	65	8	57 (43, 73)	< 0.001

[a] Pearson's chi-square

2.4.3. Satisfaction

Participants assigned to WHO eTB were, on average, more satisfied with the presentation of the home page (MD 1.7; 95% CI: 1.1, 2.3; p < 0.001) and

individual recommendations page (MD 0.7; 95% CI: 0.2, 1.2; p = 0.011) compared to WHO TB. There was no statistically significant difference in participant satisfaction for the list of recommendations page between WHO eTB and WHO TB (MD 0.4; 95% CI: -0.1, 0.9; p = 0.143) (see Table 5).

Table 5. Satisfaction with the presentation of platform pages [mean (SD)]

Page	WHO eTB (n = 49)	WHO TB (n = 53)	MD (95% CI)	P-value
Home page[a]	5.7 (1.0)	4.1 (1.8)	1.7 (1.1, 2.3)[b]	< 0.001
List of recommendations[a]	5.6 (1.1)	5.2 (1.4)	0.4 (-0.1, 0.9)[b]	0.143
Individual recommendation[a]	5.8 (1.1)	5.1 (1.4)	0.7 (0.2, 1.2)[b]	0.011

Abbreviations: SD, standard deviation; WHO, World Health Organization; TB, tuberculosis; MD, mean difference; CI, confidence interval
[a] Likert-scale from 1 = very dissatisfied to 7 = very satisfied
[b] Equal variances could not be assumed using Levene's test, degrees of freedom adjusted

2.4.4. Preference

Overall, participants (n = 97), on average, "somewhat preferred WHO eTB" after reviewing demonstrations of both platforms (4.9; SD 1.8). There was no statistically significant difference in mean preference between participants who were assigned to WHO eTB (5.0; SD 1.7), or WHO TB (4.7; SD 2.0) (p = 0.481). Both arms were left-skewed toward this preference (p < 0.001) (see Appendix F).

2.4.5. Per-protocol analysis

No differences in statistical significance were identified for any outcomes in the per-protocol analysis (n = 92). See Appendix F for the full results of this analysis.

2.5. Discussion

2.5.1. Main Findings

The primary aim of this RCT was to determine if the WHO eTB catalogue of recommendations improved the accessibility of WHO TB recommendations for stakeholders of interest. Participants represented a diverse group of users and potential users of TB recommendations. Our results suggest that the WHO eTB catalogue improves the accessibility of these recommendations for stakeholders when compared to the conventional method. Specifically, participants found, on average, that the information presented in WHO eTB was easier to find, easier to understand, that it was presented in a way that would help them make a decision, and that the website was easier to navigate.

We sought to corroborate accessibility with the secondary outcome of understanding, and we found that the eTB catalogue did not improve the ability of stakeholders to correctly identify the strength and certainty of evidence for an individual recommendation. However, it did significantly improve the ability of participants to access supporting evidence and decisions underpinning the recommendations (EtD). Furthermore, stakeholders were, on average, more satisfied with the presentation of the WHO eTB home page and presentation of individual recommendations. Overall, participants somewhat preferred the eTB catalogue to the conventional WHO TB website.

2.5.2. Research in Context

To our knowledge, this is the first RCT comparing stakeholder feedback on the presentation of two guideline platforms. Nevertheless, several studies have explored stakeholder perceptions of guideline development and presentation, as well as the factors that influence their uptake. One qualitative study by Fearns, et al.[14] explored public perceptions of clinical practice guidelines and found that participants desired information to help them make decisions, but current numerical formats may not always be accessible to a public audience. Additionally, a content analysis by Santesso, et al.[15] found that patient versions of guidelines may not always address stakeholder needs, as they rarely include important EtD information, such as beliefs, values and preferences, accessibility, costs, and feasibility. Furthermore, a realist review by Kastiner, et al.[16] which sought to identify the factors associated with guideline uptake, found that effective communication of content, including simple, clear and persuasive language, improved the implementability of guidelines by stakeholders.

This trial expands on the methods of previous RCTs used to evaluate the presentation of guideline information, specifically, comparing new GRADE SoF tables to conventional formats. These studies evaluated participant understanding, accessibility, satisfaction and preference.[10,12,13] Carrasco-Labra,

et al.[10] and Vandvik, et al.[13] identified that stakeholders preferred the presentation of risk differences over absolute risk estimates, as well as the inclusion of narrative statements to supplement numerical data. Furthermore, Akl, et al.[17] found that participants demonstrated a better understanding of strength of recommendations and quality of evidence when this information was presented as symbols, rather than numbers. Similar to our trial, these studies objectively evaluated perceptions of new to conventional formats to identify areas of improvement.

2.5.3. Strengths and Limitations

This study had several strengths. First, we used a randomized design conducted and reported in accordance with the CONSORT statement on randomised trials which reduces the risk of confounding, selection and reporting bias.[9] Second, we used several previously validated outcomes from similar trials.[10–13] Third, we gathered feedback from a diverse group of stakeholders, thus improving the generalizability of findings.

This study also has some limitations. First, the ability to blind participants was limited, as some may have been aware of eTB development. We consider this probability to be small, as the main publication and awareness campaigns began after the majority of participants had been recruited. Our a priori interim analysis did not suggest differences in the results before and after these

campaigns, thus further reducing the possibility that this impacted the findings (to be verified for the final manuscript). Second, data were collected using an online survey, thus there was limited control over the environment in which the survey was performed. Third, participants often claimed to be part of more than one stakeholder group (e.g. a healthcare provider involved in research), but they were required to select just one for stratification. Fourth, we did not power our trial to conclusively evaluate results by participant strata.

2.5.4. Implications for Policy and Practice

Tuberculosis guideline recommendations developed by the WHO assist stakeholders in making evidence-informed decisions on TB prevention, diagnosis, treatment, and care.[2,3] According to the Guidelines International Network (G-I-N) and the National Institute for Health and Care Excellence (NICE), stakeholder engagement is important to ensuring that guideline products are feasible and acceptable to end-users.[18,19] This study engaged stakeholders in evaluating the presentation of recommendations through the outcomes of accessibility, understanding, and satisfaction, which are surrogates for the correct implementation of evidence in practice. Thus, our findings suggest that the new WHO eTB catalogue will help stakeholders make evidence-informed decisions on TB in support of the WHO End TB strategy.[2]

2.5.5. Implications for Research

This study demonstrates that RCTs may be used to compare stakeholder feedback on guideline platforms. Future studies should seek to explain the findings of this trial through qualitative and user testing techniques, such as the study by Rosenbaum, et al. for SoF tables.[11] Furthermore, additional trials should focus on specific stakeholder groups, such as patients and the public, to determine optimal ways to present recommendations.

2.6. Conclusion

The new WHO eTB catalogue of recommendations improved the accessibility of WHO TB recommendations and supporting evidence for stakeholders of interest. Our findings support the continued use, promotion and quality improvement of WHO eTB. Researchers should consider the use of RCTs to evaluate stakeholder feedback on guideline presentation in the future.

2.7. References

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Development Groups. :34.

2.8. APPENDIX A: CONSORT Checklist

Appendix A. CONSORT Checklist Page numbers reflect independent manuscript for publication

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Page 1
	1b	Structured summary of trial design, methods, results, and conclusions	Page 2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Page 5
	2b	Specific objectives or hypotheses	Page 5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Page 6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	Page 7
	4b	Settings and locations where the data were collected	Page 7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Page 9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Pages 9
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	Page 12
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Page 13
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Page 13
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Page 13

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Page 13
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Page 14
	11b	If relevant, description of the similarity of interventions	Page 14
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Page 14
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Page 15
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Page 17
	13b	For each group, losses and exclusions after randomisation, together with reasons	Page 18
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Page 18
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Page 19
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Page 19
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Page 20
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Page 21
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Page 22
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	TBD
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Page 23
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Page 23
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Page 23-TBD
Other information			
Registration	23	Registration number and name of trial registry	Page 3
Protocol	24	Where the full trial protocol can be accessed, if available	Page 3
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Page 3

2.9. APPENDIX B: Questionnaire

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WHO Tuberculosis Guidelines Feedback

Welcome

Study Name: Exploring Stakeholder Perceptions of the World Health Organization's Tuberculosis Guidelines

Purpose: Thank you for participating in this survey! We would like to gain your perspective on the presentation of Tuberculosis (TB) guidelines and recommendations offered by the World Health Organization (WHO). This information will be used to improve the accessibility of WHO TB recommendations.

This survey will take approximately 15 minutes.
As a thank you, you will be invited to enter a draw for one of five $50 Amazon gift cards at the end.

Confidentiality: This survey is anonymous and all information will remain confidential. Survey responses will be secured on a password protected device only to be accessed by the research team. No personally identifiable information will be shared with individuals or organizations outside of the research team. We will only collect personal identifying information (your name and email) at the end of the survey if you agree to be contacted for follow-up questions.

Risks: We do not foresee any risks from your participation.

Voluntary Participation: Your participation in this survey is voluntary. You are free to leave the survey at any time. If you choose to leave, we will only be able to remove your responses if you have provided us with your name and email. Otherwise, the anonymous information cannot be removed.

Ethics Approval: This study has been reviewed by the Hamilton Integrated Research Ethics Board (HiREB). If you have any questions about your rights as a research participant, please call the Office of the Chair, HiREB at 1-905-521-2100 x 42013

Researcher Contacts: Micayla Matthews, matthm9@mcmaster.ca; Holger Schünemann, schuneh@mcmaster.ca

Consent: Your filling out of the survey provides consent for participation in this study. Thank you in advance for your participation.

WHO Tuberculosis Guidelines Feedback

Demographics

To better understand your perspective, we will begin by asking you a few anonymous questions about yourself.

* 1. In what role(s) are you participating in this survey? Check all that apply.

- [ ] Patient
- [ ] Caregiver
- [ ] Member of the public
- [ ] Patient advocate or patient group representative
- [ ] Healthcare provider
- [ ] Healthcare employer
- [ ] Policymaker
- [ ] Guideline developer
- [ ] Other (please specify)
- [ ] Insurer of health services (public or private)
- [ ] Department of health representative
- [ ] Member of a professional association
- [ ] Program manager
- [ ] Drug or device manufacturer
- [ ] Academic, researcher or funder of research
- [ ] Peer review editor (for journals or guidelines)
- [ ] Journalist

* 2. In which setting(s) do you currently work or live?

- ( ) Low and middle income country (LMIC)
- ( ) High income country (HIC)
- ( ) Both LMIC and HIC
- ( ) Prefer not to respond

Please list which country (or countries) you currently work or live.

* 3. What is the highest level of school you have completed?

- ◯ Some primary or secondary school
- ◯ High school diploma or equivalent (e.g. GED)
- ◯ Certificate or College diploma
- ◯ Bachelor's degree
- ◯ Professional degree (e.g. MD, DDS, JD)
- ◯ Graduate degree (e.g. Masters, PhD)
- ◯ Both professional and graduate degrees
- ◯ Prefer not to respond
- ◯ Other (please specify)

* 4. How many years have you been involved in tuberculosis-focused work?

- ◯ < 1 year
- ◯ 1-2 years
- ◯ 3-5 years
- ◯ 6-9 years
- ◯ > 10 years
- ◯ Not applicable (e.g. I am a patient)
- ◯ Prefer not to respond

* 5. What is your age?

- ◯ < 25
- ◯ 26-35
- ◯ 36-45
- ◯ 46-55
- ◯ 56-65
- ◯ 66-75
- ◯ 76 <
- ◯ Prefer not to respond

* 6. What is your gender?

- Female
- Male
- Other
- Prefer not to respond

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WHO Tuberculosis Guidelines Feedback

Accessing WHO Tuberculosis Guidelines

* 7. In what role are you most likely to access WHO tuberculosis guidelines? Select the one category that describes you best.

- Patient, Public, Caregiver, Patient Advocate/Representative, or Journalist
- Healthcare Provider or Employer
- Policymaker, Guideline Developer, Insurer, Department of Health Representative, Program Manager, or Manufacturer
- Academic, Researcher, Funder, or Peer Review Editor

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WHO Tuberculosis Guidelines Feedback

Background (A)

* 8. Have you ever accessed **any** tuberculosis guidelines, recommendations or policy advice in the past?

- Yes
- No
- Unsure

* 9. Do you plan on accessing **any** tuberculosis guidelines, recommendations or policy advice in the future?

- ◯ Yes
- ◯ No
- ◯ Unsure

* 10. Specifically, have you ever accessed **WHO** tuberculosis guidelines, recommendations or policy advice?

- ◯ Yes
- ◯ No
- ◯ Unsure

* 11. How comfortable are you with basic information and communication technologies? (e.g. internet search, smartphone, email)

Very uncomfortable	Uncomfortable	Somewhat uncomfortable	Neutral	Somewhat comfortable	Comfortable	Very comfortable
◯	◯	◯	◯	◯	◯	◯

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WHO Tuberculosis Guidelines Feedback

WHO eTB Guidelines (A)

We are interested in your perspective on the WHO eTB Guidelines website available [at this link]. Please explore the website and follow the short instructions below to access a recommendation.

A 50.0% You seek to determine whether a centralized or decentralized model of care is recommended for patients with multidrug resistant tuberculosis (MDR-TB).

- Use the search function to find this recommendation.
- Click on the recommendation.

What is the recommendation strength?

B 50.0% You seek to determine whether latent tuberculosis infection (LTBI) testing and treatment should be considered for prisoners.

- Use the search function to find this recommendation.
- Click on the recommendation.

What is the recommendation strength?

- ◯ Strong recommendation for the intervention
- ◯ Conditional recommendation for the intervention
- ◯ Strong recommendation against the intervention
- ◯ Conditional recommendation against the intervention
- ◯ Recommendation not found

* 13. What is the certainty of the evidence?

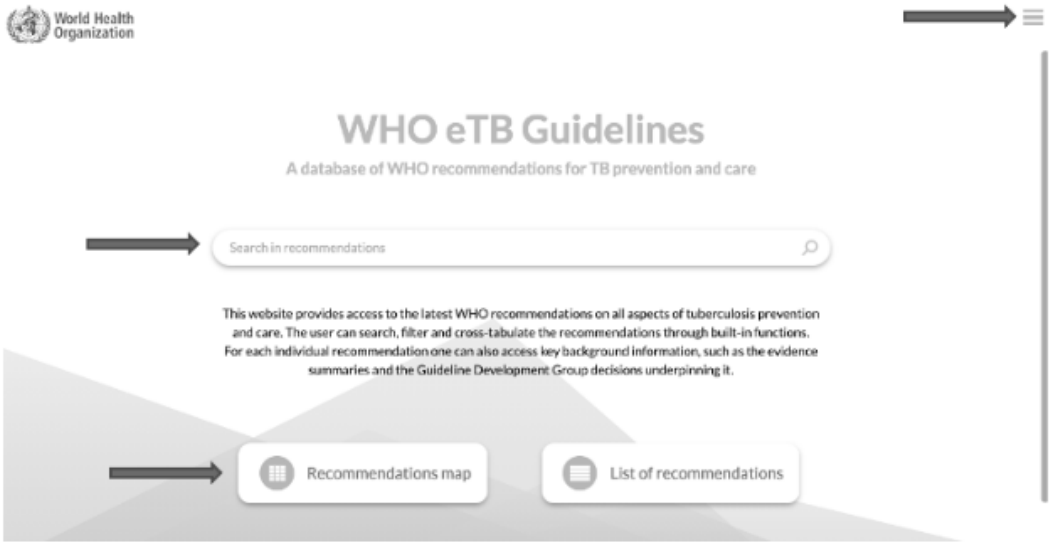
- ◯ Moderate
- ◯ Low
- ◯ Very Low
- ◯ Low to very low
- ◯ Recommendation not found

* 14. On which page does the evidence to decision (EtD) table for this recommendation start?

- ◯ Page 16
- ◯ Page 5
- ◯ Page 82
- ◯ Page 2
- ◯ EtD not found

Home Page

This is an image of the WHO eTB Guidelines home page. You can explore its functions [at this link].



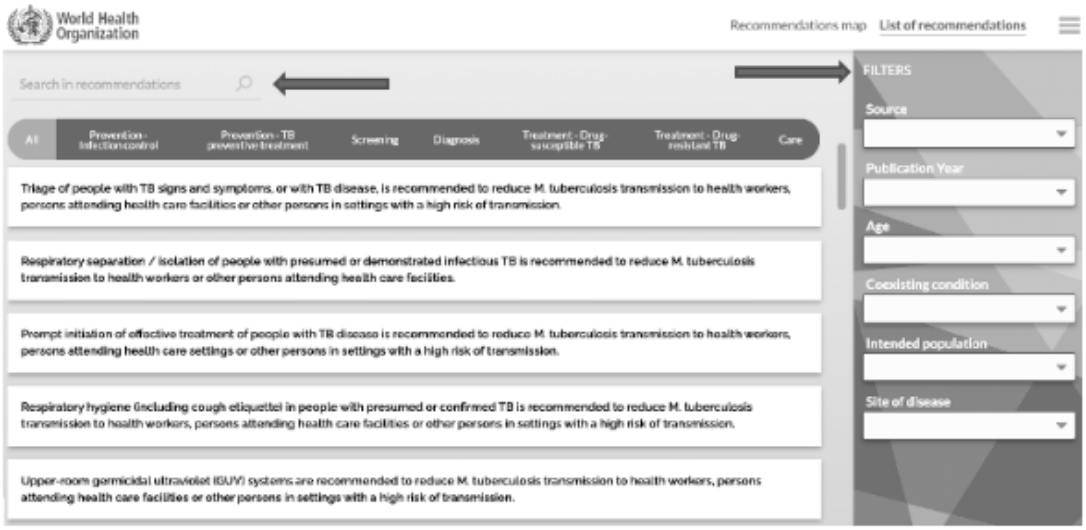
* 15. How satisfied are you with the presentation of the home page?

Very Dissatisfied	Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Satisfied	Very Satisfied
○	○	○	○	○	○	○

Please share what you like or dislike (optional).

List of Recommendations

This is an image of the list of recommendations page. You can explore its functions [at this link].



* 16. How satisfied are you with the presentation of the list of recommendations page?

Very Dissatisfied	Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Satisfied	Very Satisfied
○	○	○	○	○	○	○

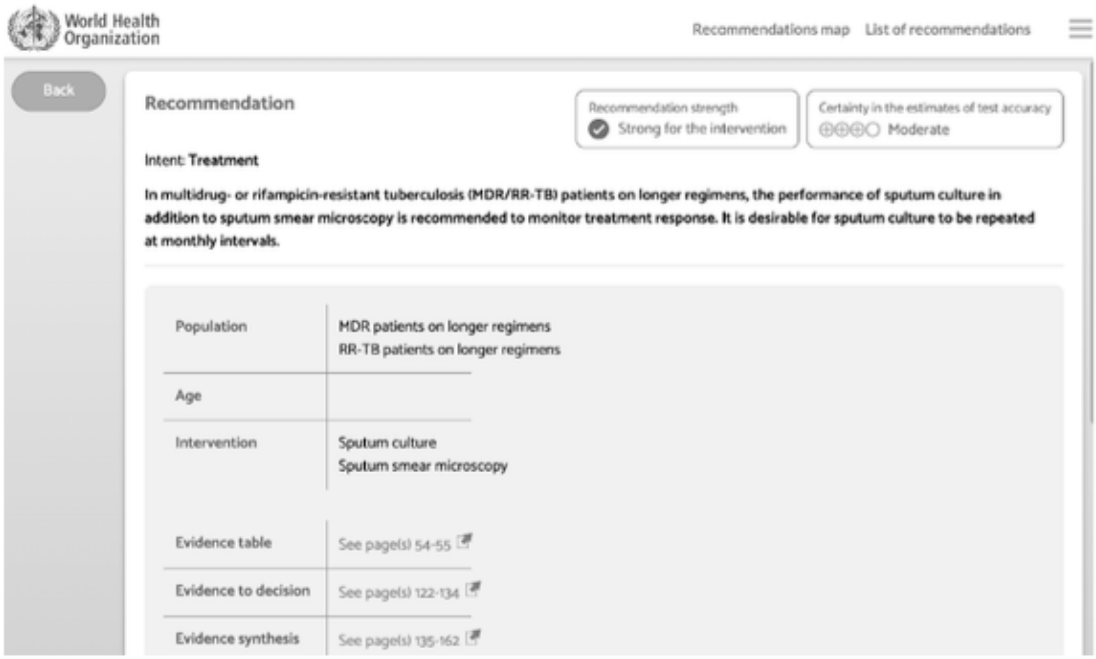
Please share what you like or dislike (optional).

* 17. In which order would you prefer recommendations to be organized on this page?

- ○ In the order found in the original guideline
- ○ In the order of the patient care cascade (i.e. case-finding, diagnosis, linkage to care, etc.)
- ○ In the order of publication year (new to old)
- ○ In the order of publication year (old to new)
- ○ No preference
- ○ Other order (please specify)

Individual Recommendation

This image is an example of an individual recommendation available on the WHO eTB Guidelines website. You can explore its functions [at this link].



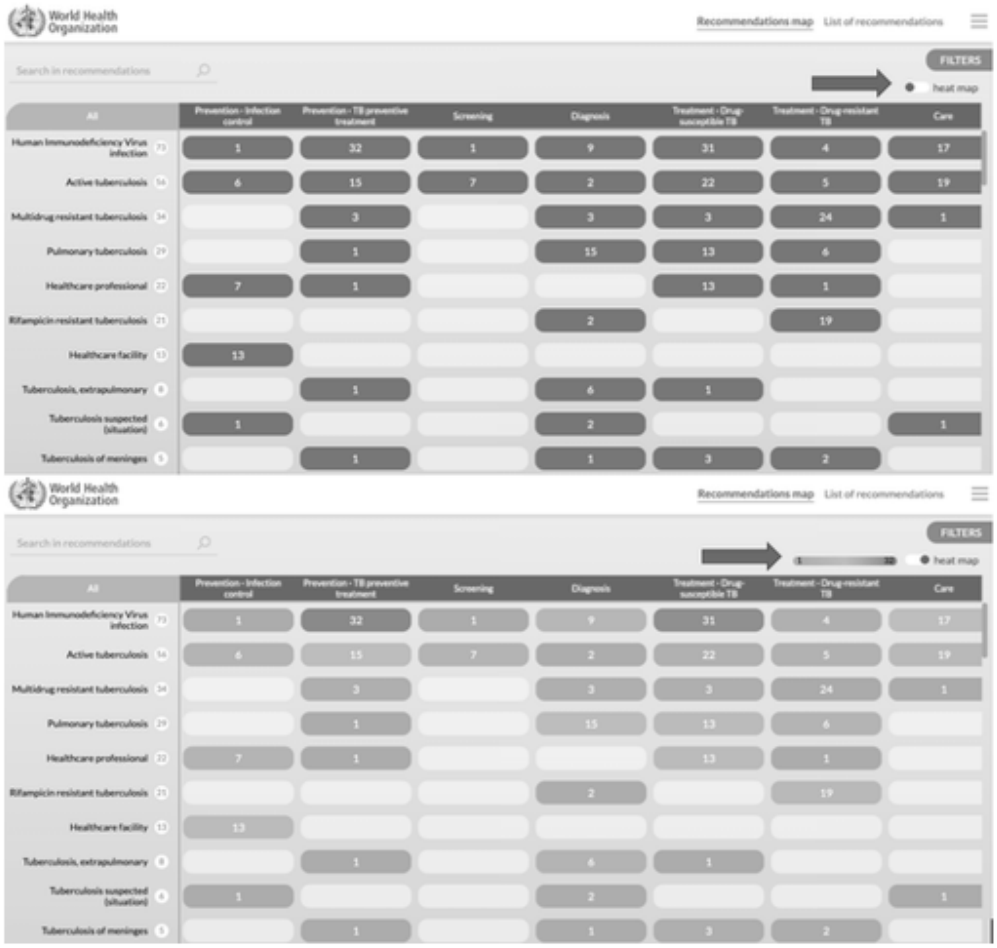
* 18. How satisfied are you with the presentation of this individual recommendation?

Very Dissatisfied	Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Satisfied	Very Satisfied
○	○	○	○	○	○	○

Please share what you like or dislike (optional).

Recommendations Map

The two images below are recommendation maps. Recommendation mapping organizes the evidence on a topic in order to identify clusters and gaps. It involves dividing recommendations by the populations and interventions they address. The second image is a "heat map" which is meant to aid in visualizing the distribution of evidence. These functions can be explored [at this link].



* 19. How satisfied are you with the presentation of the recommendations map?

Very Dissatisfied	Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Satisfied	Very Satisfied
○	○	○	○	○	○	○

Please share what you like or dislike (optional).

* 20. Please answer the following questions on your experience with the accessibility of the **WHO eTB Guidelines** website.

	Strongly Disagree	Disagree	Somewhat Disagree	Neutral	Somewhat Agree	Agree	Strongly Agree
It was easy to find the information.	○	○	○	○	○	○	○
It was easy to understand the information.	○	○	○	○	○	○	○
The information was presented in a way that would help me make a decision.	○	○	○	○	○	○	○
This website was easy to navigate.	○	○	○	○	○	○	○

21. Please provide any final comments or suggestions on the WHO eTB Guidelines website, including how to make it more accessible or relevant to you (optional).

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WHO Tuberculosis Guidelines Feedback

WHO Tuberculosis Guidelines Website (A)

We are interested in your perspective on the WHO Tuberculosis Guidelines website available [at this link]. Please explore the website and follow the short instructions below to access a recommendation.

A 50.0% You seek to determine whether a centralized or decentralized model of care is recommended for patients with multidrug tuberculosis (MDR-TB).

- Use the search function to browse Tuberculosis (TB) publications.
- Locate the most recent guideline on drug resistant tuberculosis.
- Open the document and search for the recommendation.

What is the recommendation strength?

B 50.0% You seek to determine whether latent tuberculosis infection (LTBI) testing and treatment should be considered for prisoners.

- Use the search function to browse Tuberculosis (TB) publications.
- Locate the most recent guideline on tuberculosis treatment.
- Open the document and search for the recommendation.

What is the recommendation strength?

- ◯ Strong recommendation for the intervention
- ◯ Conditional recommendation for the intervention
- ◯ Strong recommendation against the intervention
- ◯ Conditional recommendation against the intervention
- ◯ Recommendation not found

* 23. What is the certainty of the evidence?

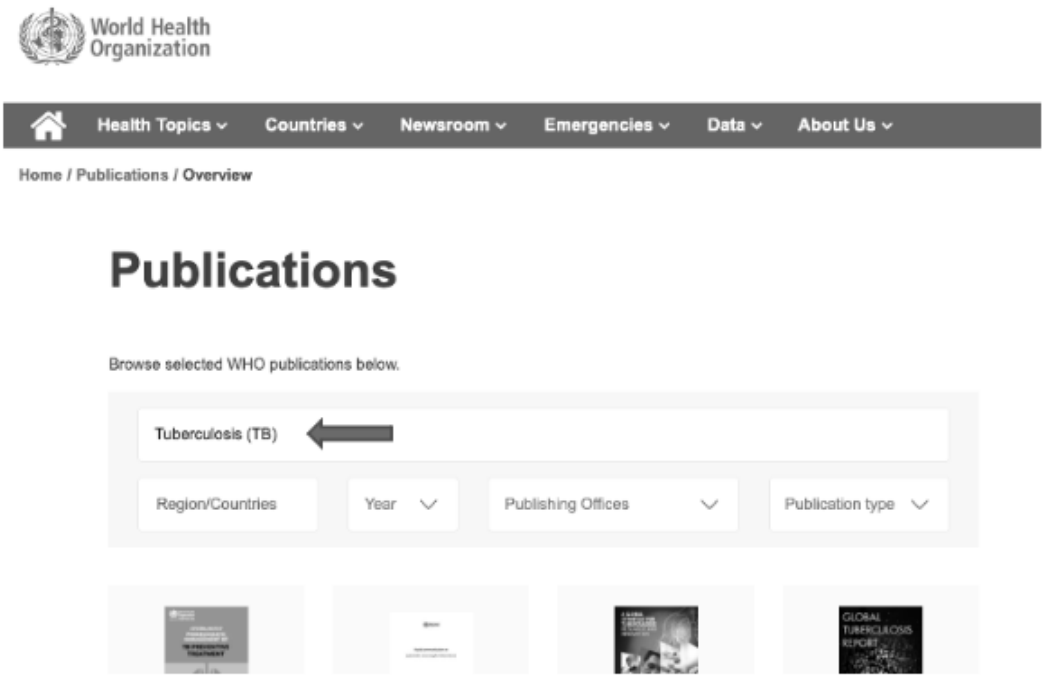
- ◯ Moderate
- ◯ Low
- ◯ Very Low
- ◯ Low to very low
- ◯ Recommendation not found

* 24. On which page does the evidence to decision (EtD) table for this recommendation start?

- ◯ Page 16
- ◯ Page 5
- ◯ Page 82
- ◯ Page 2
- ◯ EtD not found

Home Page

This is an image of the WHO publications home page. You can explore its functions at [this link].



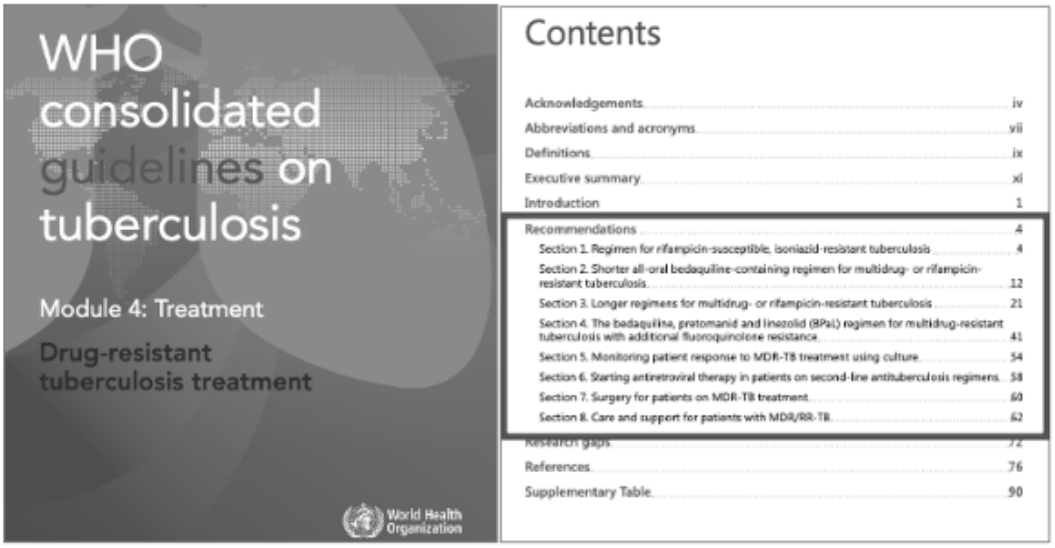
* 25. How satisfied are you with the presentation of the home page?

Very Dissatisfied	Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Satisfied	Very Satisfied
○	○	○	○	○	○	○

Please share what you like or dislike (optional).

List of Recommendations

The image below is an example of recommendations listed in a WHO Tuberculosis Guideline document.



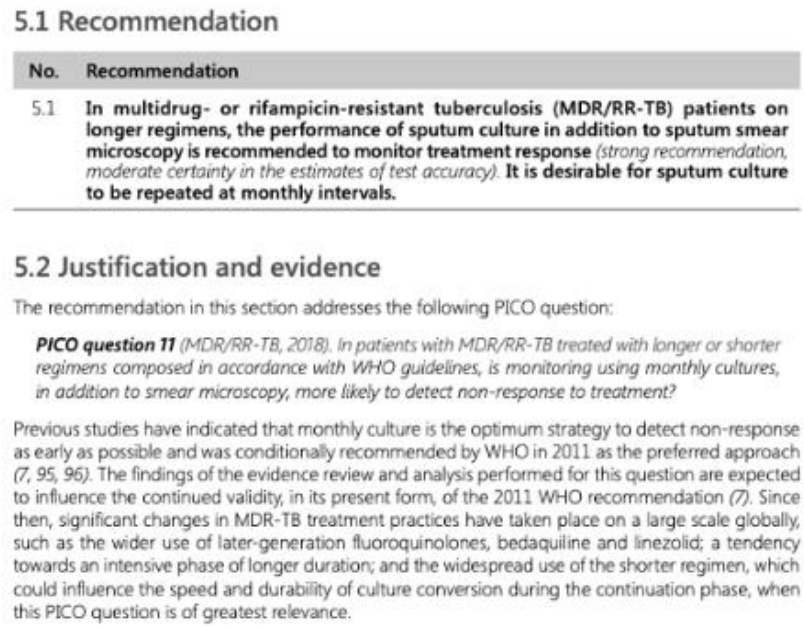
* 26. How satisfied are you with the presentation of the list of recommendations?

Very Dissatisfied	Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Satisfied	Very Satisfied
○	○	○	○	○	○	○

Please share what you like or dislike (optional).

Individual Recommendation

This image is an example of an individual recommendation available in a WHO Tuberculosis Guideline document.



5.1 Recommendation

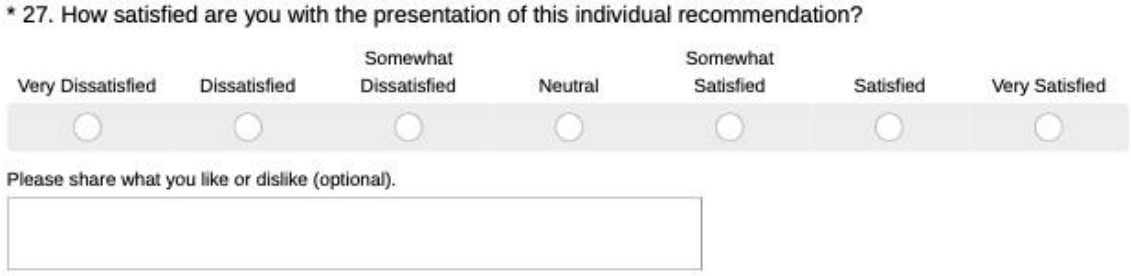
No.	Recommendation
5.1	**In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, the performance of sputum culture in addition to sputum smear microscopy is recommended to monitor treatment response** *(strong recommendation, moderate certainty in the estimates of test accuracy).* **It is desirable for sputum culture to be repeated at monthly intervals.**

5.2 Justification and evidence

The recommendation in this section addresses the following PICO question:

> ***PICO question 11*** *(MDR/RR-TB, 2018). In patients with MDR/RR-TB treated with longer or shorter regimens composed in accordance with WHO guidelines, is monitoring using monthly cultures, in addition to smear microscopy, more likely to detect non-response to treatment?*

Previous studies have indicated that monthly culture is the optimum strategy to detect non-response as early as possible and was conditionally recommended by WHO in 2011 as the preferred approach *(7, 95, 96)*. The findings of the evidence review and analysis performed for this question are expected to influence the continued validity, in its present form, of the 2011 WHO recommendation *(7)*. Since then, significant changes in MDR-TB treatment practices have taken place on a large scale globally, such as the wider use of later-generation fluoroquinolones, bedaquiline and linezolid; a tendency towards an intensive phase of longer duration; and the widespread use of the shorter regimen, which could influence the speed and durability of culture conversion during the continuation phase, when this PICO question is of greatest relevance.



* 27. How satisfied are you with the presentation of this individual recommendation?

Very Dissatisfied	Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Satisfied	Very Satisfied
○	○	○	○	○	○	○

Please share what you like or dislike (optional).

* 28. Please answer the following questions on your experience with the accessibility of the **WHO Tuberculosis Guidelines** website.

	Strongly Disagree	Disagree	Somewhat Disagree	Neutral	Somewhat Agree	Agree	Strongly Agree
It was easy to find the information.	○	○	○	○	○	○	○
It was easy to understand the information.	○	○	○	○	○	○	○
The information was presented in a way that would help me make a decision.	○	○	○	○	○	○	○
This website was easy to navigate.	○	○	○	○	○	○	○

29. Please provide any final comments on your experience with the WHO Tuberculosis Guidelines website (optional).

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WHO Tuberculosis Guidelines Feedback

Preference (A)

The purpose of this project is to compare the accessibility of recommendations from the current WHO Tuberculosis Guidelines website, to an alternative WHO eTB Guidelines website.

- **[Click here] for a short demonstration of the current WHO Tuberculosis Guidelines website.**
- **[Click here] for a short demonstration of the alternative WHO eTB Guidelines website.**

* 30. Between the WHO Tuberculosis Guidelines (current website), and the WHO eTB Guidelines (alternative website), which do you prefer?

Strongly Prefer WHO Tuberculosis Guidelines	Prefer WHO Tuberculosis Guidelines	Somewhat Prefer WHO Tuberculosis Guidelines	Same Preference for WHO Tuberculosis and eTB Guidelines	Somewhat Prefer WHO eTB Guidelines	Prefer WHO eTB Guidelines	Strongly Prefer WHO eTB Guidelines
○	○	○	○	○	○	○

31. Please provide any final comments on either website (optional).

* 32. What additional resources would you like to see as part of WHO Tuberculosis Guidelines in the future? Check all that apply.

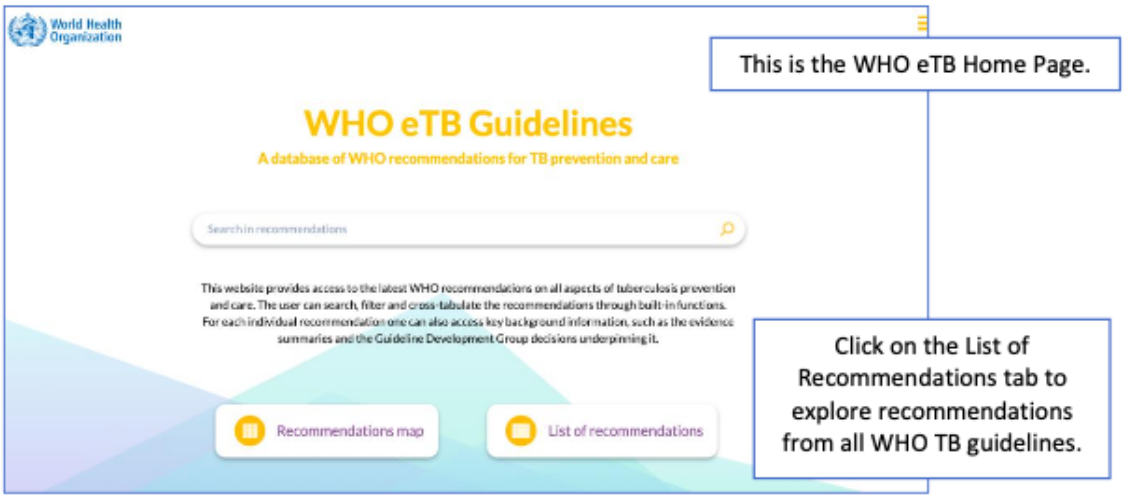
- [ ] Plain language summaries of evidence and recommendations
- [ ] Decision aids (example: flowcharts, decision scoring system, etc.)
- [ ] Implementation tools (example: WHO ENGAGE-TB manual to promote community engagement, etc.)
- [ ] Translation to other languages
- [ ] Unsure
- [ ] Other resources (please specify)

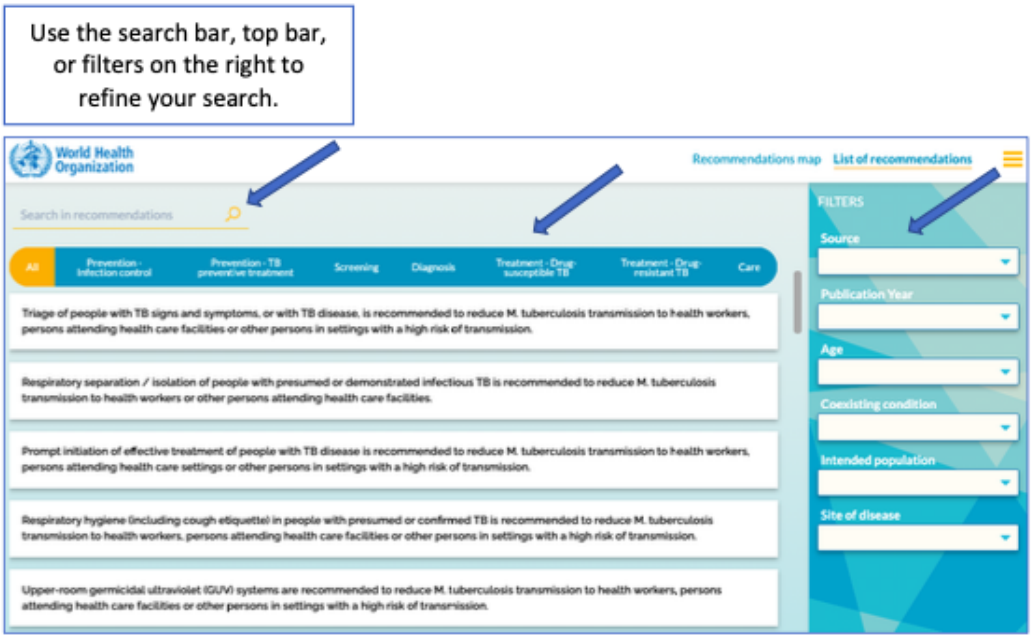
2.10. APPENDIX C: Understanding Question Descriptions

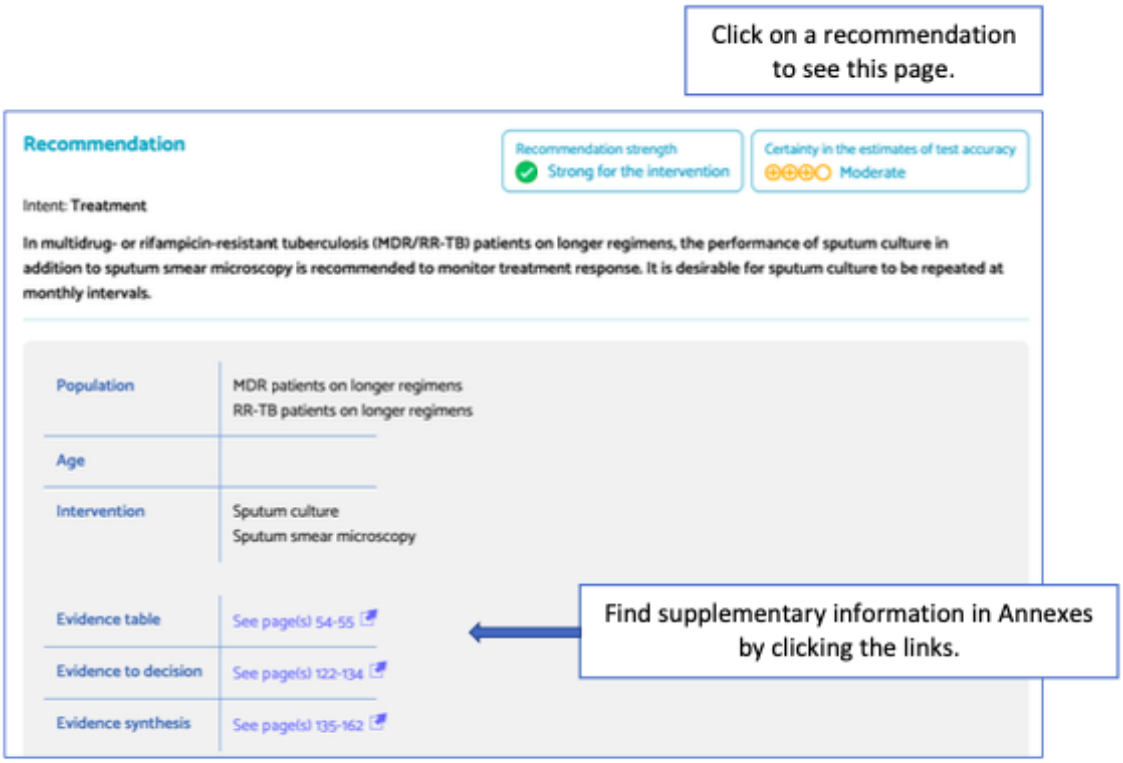
Platform	Guideline Reference	Recommendation Statement	Survey Instructions	Understanding Questions	Answer Key
WHO eTB	WHO consolidated guidelines on tuberculosis. Module 4: Treatment. Drug-resistant tuberculosis treatment. World Health Organization, 2020. License: CC BY-NC-SA 3.0 IGO.	A decentralized model of care is recommended over a centralized model for patients on MDR-TB treatment.	You seek to determine whether a centralized or decentralized model of care is recommended for patients with multidrug resistant tuberculosis (MDR-TB). • Use the search function to find this recommendation. • Click on the recommendation.	1. What is the recommendation strength? 2. What is the certainty of evidence? 3. On which page does the evidence to decision (EtD) table for this recommendation start?	1. Conditional recommendation for the intervention 2. Very low 3. 82 (Guidelines for treatment of drug-susceptible tuberculosis and patient care 2017 update, Annex 4, PICO 11)
WHO TB	WHO consolidated guidelines on tuberculosis. Module 4: Treatment. Drug-resistant tuberculosis treatment. World Health Organization, 2020. License: CC BY-NC-SA 3.0 IGO.	A decentralized model of care is recommended over a centralized model for patients on MDR-TB treatment.	You seek to determine whether a centralized or decentralized model of care is recommended for patients with multidrug resistant tuberculosis (MDR-TB). • Use the search function to browse Tuberculosis (TB) publications. • Locate the most recent guideline on drug resistant tuberculosis. • Open the document and search for the recommendation.	1. What is the recommendation strength? 2. What is the certainty of evidence? 3. On which page does the evidence to decision (EtD) table for this recommendation start?	1. Conditional recommendation for the intervention 2. Very low 3. 82
WHO eTB	WHO consolidated guidelines on tuberculosis. Module 1: Prevention.	Systematic LTBI testing and treatment may be considered for prisoners, health workers,	You seek to determine whether latent tuberculosis infection (LTBI) testing and treatment should be considered for prisoners.	1. What is the recommendation strength? 2. What is the certainty of evidence?	1. Conditional recommendation for the intervention 2. Low to very low 3. 5
	Tuberculosis preventative treatment. World Health Organization, 2020. License: CC BY-NC-SA 3.0 IGO.	immigrants from other countries with a high TB burden, homeless people and people who use drugs.	• Use the search function to find this recommendation. • Click on the recommendation.	3. On which page does the evidence to decision (EtD) table for this recommendation start?	
WHO TB	WHO consolidated guidelines on tuberculosis. Module 1: Prevention. Tuberculosis preventative treatment. World Health Organization, 2020. License: CC BY-NC-SA 3.0 IGO.	Systematic LTBI testing and treatment may be considered for prisoners, health workers, immigrants from other countries with a high TB burden, homeless people and people who use drugs.	You seek to determine whether latent tuberculosis infection (LTBI) testing and treatment should be considered for prisoners. • Use the search function to browse Tuberculosis (TB) publications. • Locate the most recent guideline on tuberculosis treatment. • Open the document and search for the recommendation.	1. What is the recommendation strength? 2. What is the certainty of evidence? 3. On which page does the evidence to decision (EtD) table for this recommendation start?	1. Conditional recommendation for the intervention 2. Low to very low 3. 5

2.11. APPENDIX D: Preference Demonstrations

Accessing Tuberculosis Recommendations using the **WHO eTB Guidelines** Website
Short Demonstration

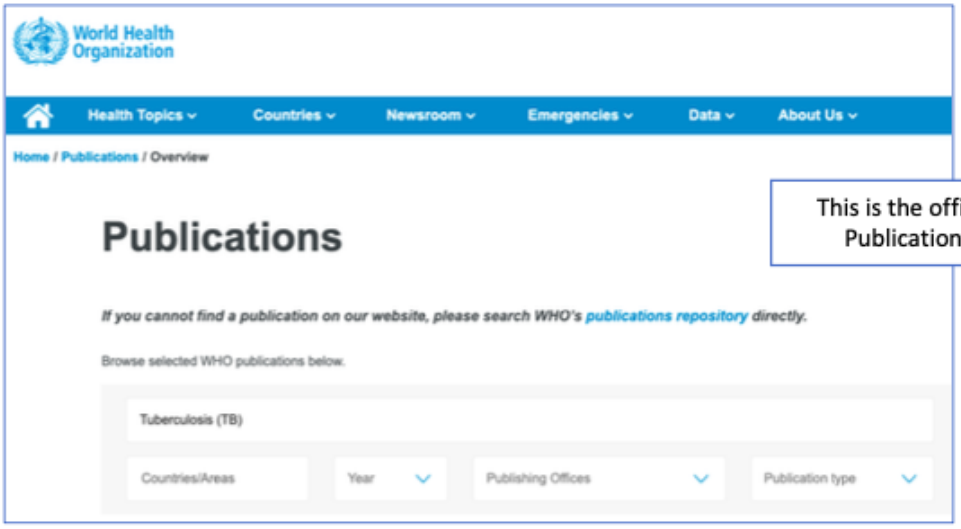


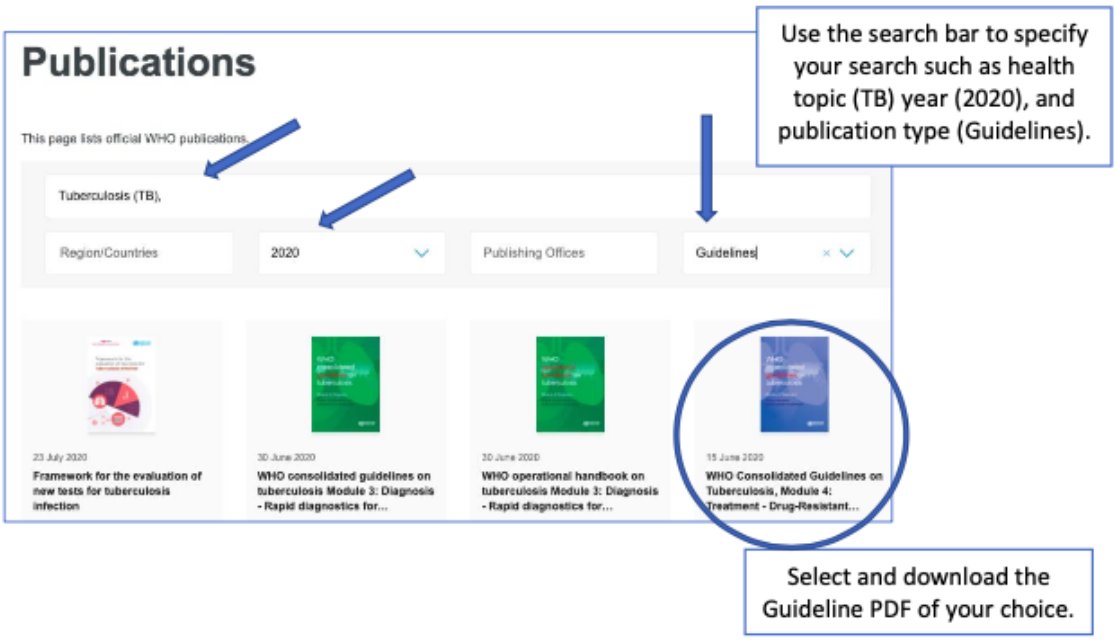



Click on a recommendation to see this page.
Recommendation
Recommendation strength
Strong for the intervention
Certainty in the estimates of test accuracy
Moderate
Intent: Treatment
In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, the performance of sputum culture in addition to sputum smear microscopy is recommended to monitor treatment response. It is desirable for sputum culture to be repeated at monthly intervals.
Population
MDR patients on longer regimens
RR-TB patients on longer regimens
Age
Intervention
Sputum culture
Sputum smear microscopy
Evidence table
See page(s) 54-55
Evidence to decision
See page(s) 122-134
Evidence synthesis
See page(s) 135-162
Find supplementary information in Annexes by clicking the links.

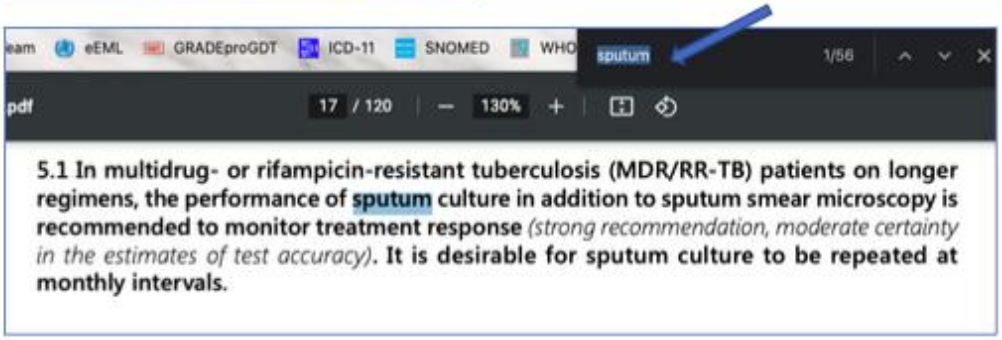

Click on the recommendations map to see all WHO TB recommendations organized by their population and intervention.
World Health Organization
Recommendations map
List of recommendations
FILTERS
heat map
All
Prevention - Infection control
Prevention - TB preventive treatment
Screening
Diagnosis
Treatment - Drug-susceptible TB
Treatment - Drug-resistant TB
Tuberculosis
Human Immunodeficiency Virus infection
Active tuberculosis
Multidrug resistant tuberculosis
Pulmonary tuberculosis
Human immunodeficiency virus infection
Rifampicin resistant tuberculosis
Healthcare professional

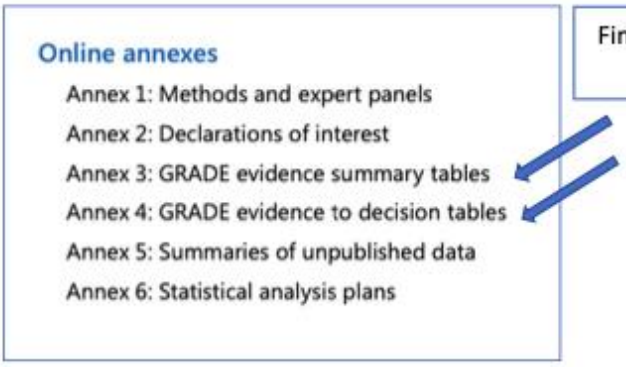
Accessing TB Recommendations using the **WHO Tuberculosis Guidelines** Website
Short Demonstration





Use the table of contents or Ctrl+F with keywords to search the document for recommendations.





Find supplementary information in Annexes at the end of the document or online.

2.12. APPENDIX E: Analysis Plan

1. Primary Analyses

We reported the results of the primary analyses for both the preplanned interim analysis (February 26 to March 24, 2021) and final analysis (February 26 to April _, 2021). The interim analysis was scheduled based on the thesis defence date of the first author (MM) and was not used to stop the study or draw final conclusions. We conducted these analyses in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement for reporting randomised trials using IBM SPSS® (Statistical Package for Social Sciences) version 23.

1.1. Descriptive Analysis

We summarized participant baseline characteristics and outcomes using descriptive statistics, including means and standard deviations (SD) for continuous variables, and proportions for categorical variables.

1.2. Primary Inferential Analysis

We performed one primary interim and final analysis with all randomized participants, except for those who completed the survey in less than five minutes. We determined the five-minute cut-off a priori because, based on user testing, we deemed it impossible to complete the work in that time (average completion time was 15 minutes).

1.2.1. Primary Outcome: Accessibility

For the primary outcome of accessibility, we performed t-tests to compare the means and standard deviations (SDs) between the intervention and control groups for each of the four domains. We reported the mean differences (MD), standard errors (SE), and associated p-values. Levene's test of equal variances was used for all t-tests, and degrees of freedom were adjusted when Levene's test was $p < 0.05$. Three decimal places were used for reporting all p-values, with values less than 0.001 reported as < 0.001.

1.2.2. Secondary Outcome: Understanding

For the secondary outcome of understanding, we used χ^2 tests to compare the proportion of correct responses between groups for

each of the three questions. We reported the risk differences, 95% confidence intervals (CIs) and associated p-values.

1.2.3. Secondary Outcome: Satisfaction

For the secondary outcome of satisfaction, we used t-tests to compare the means and SDs between the intervention and control groups for each of the three pages. We reported the mean differences (MD), standard errors (SE), and associated p-values. Levene's test of equal variances was used for all t-tests, and degrees of freedom were adjusted when Levene's test was $p < 0.05$. Three decimal places were used for reporting all p-values, with values less than 0.001 reported as < 0.001.

1.2.4. Secondary Outcome: Preference

For the secondary outcome of preference, we present overall preference pooled between groups as a mean (SD). We also present the mean (SD) preference for both trial arms and used t-tests to compare means. Skewness, Shapiro-Wilk tests, and Histograms were used to evaluate whether the distribution was shifted toward the same preference in both arms.

1.3. Per-Protocol Inferential Analysis

We performed one interim and final per-protocol analysis excluding participants who were flagged by pre-defined but unknown SurveyMonkey® algorithm which flagged poor-quality responses of straight-lining (see below). We used the same analysis plan as described in the primary analysis.

1.4. Dropouts, missing data, and poor-quality responses

We used available case analysis for data from participants who responded to some survey questions after being assigned to the intervention. In order to prevent dropouts and missing data, we implemented the following strategies: (1) we disseminated short emails to target stakeholder groups with a direct link to the survey, (2) we informed participants that the survey would require 15 minutes, (3) participants who completed the survey had the option to enter a draw for a gift card, (4) all outcome questions were mandatory, and (5)

participants were randomized only after the collection of baseline characteristics.

We defined participants who spent less than five minutes on the survey as inappropriate in our analyses, with the rationale that practical comprehension and completion of the survey, based on pilot testing, could not be performed in five minutes. The average survey completion time was 15 minutes. This was anticipated to prevent analysis of erroneous responses from participants who sought to simply gain access to the content of the survey or enter the gift card draw. For the per-protocol analysis, we used a pre-defined but unknown SurveyMonkey® algorithm which flagged poor-quality responses for straight-lining. Straight-lining is defined by SurveyMonkey® as responses to questions with the same answer option or pattern. Participants flagged for straight-lining, as well as those who spent less than five minutes on the survey, were removed from the per-protocol analysis.

2. Secondary Analyses

We performed the following secondary analyses with the full trial data (February 26 to April _, 2021).

2.1. Regression Analysis

We performed multivariable linear and logistic regression to explore the relationships between covariates of 'stakeholder experience' and the outcomes of accessibility, understanding, satisfaction, and preference. The covariates of interest included history of accessing TB guidelines (dichotomous – 2 categories), years of TB work experience (ordinal – 5 categories), comfort with information technology (ordinal – 7 categories), and education (ordinal – 3 categories). We presented the results as overall model fit using adjusted R^2 and F-statistics with associated p-values. The individual contributions of explanatory variables were assessed using β coefficients, 95% CIs and associated p-values. Signs of coefficients were examined for theoretical appropriateness and interaction terms were explored using knowledge of relationships between covariates. We verified regression assumptions and assessed outliers using Cook's distance as a measure of influence, and centered leverage.

2.2. Qualitative Analysis of Free-Text Responses

Qualitative data were collected using free-text responses provided under Likert-scale questions and independent comment boxes. Qualitative analysis may be part of a separate, mixed-methods manuscript. Chapter 3 describes the interim results of this qualitative analysis and quality improvement work.

2.3. Outcome Validity and Reliability

Several randomized controlled trials have established the face and external validity for the outcomes used in this trial (accessibility, understanding, satisfaction, and preference). However, these outcomes have not been statistically tested for reliability. In anticipation of using these outcomes in future studies, an accompanying study may test the reliability these outcomes by assessing factors of internal consistency, parallel/alternate forms, inter-rater agreement, and teat-retest reliability.

2.13. APPENDIX F: Analysis Results

1. **Preference outcome distributions for interim primary analysis (n = 97)**

   Overall, participants (n = 97), on average, "somewhat preferred WHO eTB" (4.9; SD 1.8), after reviewing demonstrations of both platforms. There was no statistically significant difference in mean preference between participants who were assigned to WHO eTB (5.0; SD 1.7), or WHO TB (4.7; SD 2.0) (p = 0.481). Both arms were left-skewed toward this preference (p < 0.001).

   Figure 1. Histograms for preference by intervention arm (eTB and WHO TB)

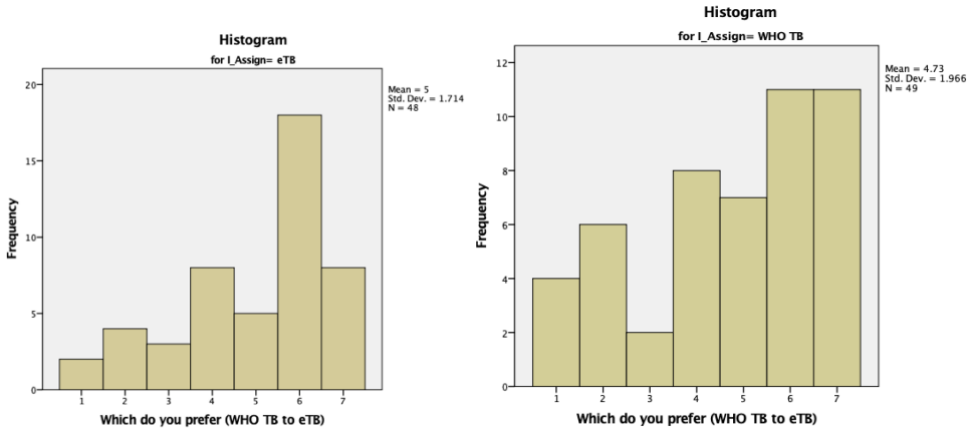


Table 1. Shapiro-Wilk test

Shapiro-Wilk	Statistic	Degrees of freedom	P-value
WHO eTB (n = 48)	0.873	48	< 0.001
WHO TB (n = 49)	0.888	49	< 0.001

Table 2. Skewness test

Skewness	Statistic	Standard error
WHO eTB (n = 48)	-0.821	0.343
WHO TB (n = 49)	-0.556	0.340

Table 3. Preference toward a platform [mean (SD)]

Question	WHO eTB (n = 48)	WHO TB (n = 49)	t (df)	P-value
Between the WHO TB website and the WHO eTB catalogue, which do you prefer?[a]	5.0 (1.7)	4.7 (2.0)	0.71 (95)	0.481

Abbreviations: SD, standard deviation; WHO, World Health Organization; TB, tuberculosis; df, degrees of freedom

[a] Likert-scale from 1 = strongly prefer WHO TB to 7 = strongly prefer eTB

2. **Interim per-protocol analysis results (n = 92)**
   No changes in statistical significance were identified for any outcomes between the primary (n = 102) and per-protocol analyses (n = 92). The results of the per-protocol analyses are reported below.

Accessibility of information

Across four domains, participants assigned to the new WHO eTB catalogue rated the information as more accessible, on average, compared to the conventional WHO TB website (see Table 4). The largest mean differences were noted for the statements "it was easy to find the information" (MD 1.3; SE 0.33; p < 0.001) and "this website was easy to navigate" (MD 1.5; SE 0.34; p < 0.001). Participants assigned to the WHO eTB catalogue also rated, on average, that it was easier to understand the information (MD 0.7; SE 0.29; p = 0.013) and that the information was presented in a way that would help them make a decision (MD 0.7; SE 0.27; p = 0.010).

Table 4. Overall accessibility of information [mean (SD)]

Domain	WHO eTB (n = 43)	WHO TB (n = 49)	MD (SE)	P-value
It was easy to find the information.[a]	5.5 (1.3)	4.1 (1.8)	1.3 (0.33)[b]	< 0.001
It was easy to understand the information.[a]	5.6 (1.2)	4.9 (1.6)	0.7 (0.29)[b]	0.013
The information was presented in a way that would help me make a decision.[a]	5.6 (1.3)	4.9 (1.4)	0.7 (0.27)	0.010
This website was easy to navigate.[a]	5.4 (1.5)	4.0 (1.8)	1.5 (0.34)[b]	< 0.001

Abbreviations: SD, standard deviation; WHO, World Health Organization; TB, tuberculosis; df, MD, mean difference; SE, standard error

[a] Likert-scale from 1 = strongly disagree to 7 = strongly agree

[b] Equal variances could not be assumed using Levene's test, degrees of freedom adjusted

Understanding

There was no significant difference in correct responses to recommendation strength (p = 0.429) or certainty of evidence (p = 0.494) between participants who completed the activity in accessing a recommendation with WHO eTB or WHO TB. However, participants assigned to WHO eTB were significantly more likely to locate the EtD table accompanying the recommendation than participants assigned to WHO TB (p < 0.001) (see Table 5).

Table 5. Percentage (%) of participants who responded correctly to understanding questions

Question	WHO eTB (n = 43)	WHO TB (n = 49)	P-value[a]
What is the recommendation strength?	77	69	0.429
What is the certainty of evidence?	58	51	0.494
On which page does the evidence to decision	70	8	< 0.001

(EtD) table for this recommendation start?
[a] Pearson's chi-square

Satisfaction

Participants assigned to WHO eTB were, on average, more satisfied with the presentation of the home page (MD 1.7; SE 0.31; p < 0.001) and individual recommendations page (MD 0.6; SE 0.27; p = 0.038) compared to WHO TB. There was no statistically significant difference in satisfaction with the list of recommendations page between WHO eTB and WHO TB (MD 0.3; SE 0.26; p = 0.351) (see Table 6).

Table 6. Satisfaction with the presentation of platform pages [mean (SD)]

Page	WHO eTB (n = 43)	WHO TB (n = 49)	MD (SE)	P-value
Home page[a]	5.7 (1.0)	4.0 (1.8)	1.7 (0.31)[b]	< 0.001
List of recommendations[a]	5.5 (1.1)	5.2 (1.3)	0.2 (0.26)[b]	0.351
Individual recommendation[a]	5.7 (1.2)	5.1 (1.4)	0.6 (0.27)	0.038

Abbreviations: SD, standard deviation; WHO, World Health Organization; TB, tuberculosis; MD, mean difference; SE, standard error
[a] Likert-scale from 1 = very dissatisfied to 7 = very satisfied
[b] Equal variances could not be assumed using Levene's test, degrees of freedom adjusted

Preference

Overall, participants (n = 87), on average, "somewhat preferred WHO eTB" (4.8; SD 1.9), after reviewing demonstrations of both platforms. There was no statistically significant difference in mean preference between participants who were assigned to WHO eTB (4.9; SD 1.8), or WHO TB (4.8; SD 2.0) (p = 0.671). Both arms were left-skewed toward this preference (p < 0.001).

Table 7. Preference toward a platform [mean (SD)]

Question	WHO eTB (n = 42)	WHO TB (n = 45)	t (df)	P-value
Between the WHO TB website and the eTB catalogue, which do you prefer?[a]	4.9 (1.8)	4.8 (2.0)	0.43 (85)	0.671

Abbreviations: SD, standard deviation; WHO, World Health Organization; TB, tuberculosis; df, degrees of freedom
[a] Likert-scale from 1 = strongly prefer WHO TB to 7 = strongly prefer eTB

Figure 2. Histograms for preference by intervention arm (eTB and WHO TB)

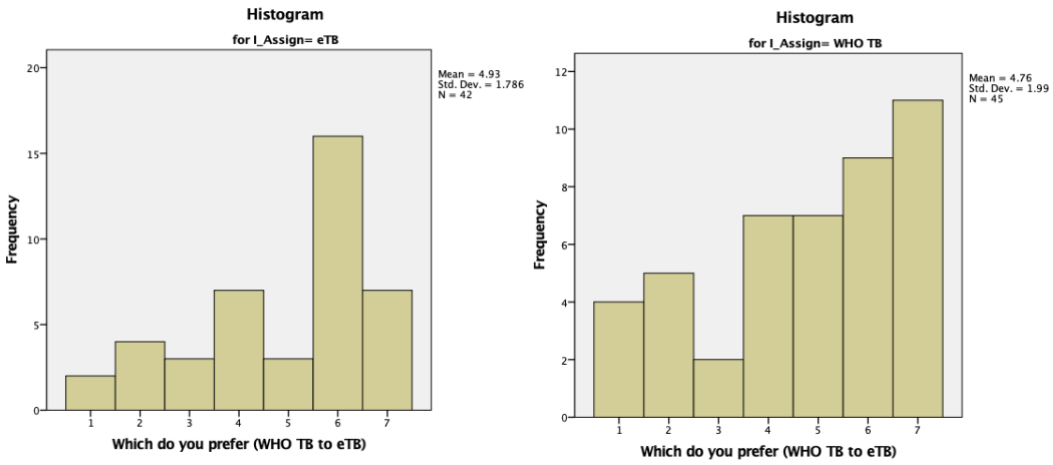


Table 8. Shapiro-Wilk test

Shapiro-Wilk	Statistic	Degrees of freedom	P-value
WHO eTB (n = 48)	0.870	42	< 0.001
WHO TB (n = 49)	0.885	45	< 0.001

Table 9. Skewness test

Skewness	Statistic	Standard error
WHO eTB (n = 48)	-0.751	0.365
WHO TB (n = 49)	-0.569	0.354

CHAPTER 3: QUALITY IMPROVEMENT

3.1. Background

Quality improvement (QI) methodology seeks to achieve measurable advances in system efficiency, effectiveness, and performance.[1] It is a cyclical process whereby gaps in these systems are identified, interventions are developed, and they are subsequently tested to ensure they are achieving planned objectives. This is often accomplished through the use of established improvement processes such as the Plan-Do-Study-Act (PDSA) cycle.[1-3]

The WHO eTB catalogue was developed with the objective of improving stakeholder accessibility and use of the World Health Organization's (WHO) tuberculosis (TB) recommendations and supplementary information, such as evidence to decision (EtD) and summary of findings (SoF) tables. The interim results of the randomized controlled trial (RCT) in Chapter 2 have highlighted areas where objectives have been met, as well as areas in need of further exploration. This chapter describes the mixed-methods QI processes and frameworks used to explore feedback from trial participants.

3.2. Methods

This QI work included the same stakeholders who participated in the RCT in Chapter 2. Refer to Chapter 2 for the complete methods on survey design and participant recruitment.

3.2.1. Quantitative Methods

We anticipated the need for stakeholder perspectives on two multiple-choice questions of interest. Participants who were randomized to the new WHO eTB catalogue were asked "in which order would you prefer recommendations to be organized on this [list of recommendations] page?" Participants were presented with the following options: in the order found in the original guideline, in the order of the patient care cascade (i.e. case-finding, diagnosis, linkage to care, etc.), publication year (new to old), publication year (old to new), no preference, or other order (please specify).

Furthermore, we were interested in stakeholder perspectives on the prioritization of future services. All survey participants were asked "what additional resources would you like to see as part of WHO tuberculosis guidelines in the future? Check all that apply." Participants were presented with the following options: plain language summaries of evidence and recommendations, decision aids, implementation tools, translation to other languages, unsure, and other resources (please specify). Descriptive analyses were performed using SurveyMonkey® software.

3.2.2. Qualitative Methods

In order to explore the results of the RCT and gather feedback for QI, we

collected qualitative data in free-text boxes under Likert-scale and independent questions. Participants were asked to "please share what you like or disklike (optional)", and to share "any final comments on your experience (optional)". We developed themes using a semantic coding and deductive thematic process that built on preconceived theories of knowledge translation (KT)[5-8] and user experience (UX)[9,10]. Furthermore, we developed a QI framework to address these themes with content and information technology developers. Table 1 describes the stages of this process.

Table 1. Stages and Descriptions of Qualitative Analysis

Stages	Descriptions
Sorting & Familiarization	Anonymous free-text statements were reviewed and sorted according to the quality improvement objective. Non-actionable and incoherent statements were removed from the analysis.
Semantic Coding	Statements were coded based on their explicit content.
Deductive Thematic Analysis	Recurring themes were combined with reference to guideline knowledge translation theory (presentation, awareness, perceptions of relevance)[5-8] and user experience theory (ergonomic and hedonic quality).[9,10]
Interpretation & Connection to Prior Work	Themes were interpreted and defined with supporting quotes. The qualitative findings were explored in relation to randomized controlled trial findings.
Quality Improvement Framework Development	Statements were sorted into a quality improvement framework to describe the nature of the problem, its perceived priority, and to explore possible solutions.

3.3. Results

These are the results of a pre-planned interim analysis with survey data

collected between February 26 and March 24, 2021. These preliminary findings will not be used to draw final conclusions. These results will be revised when the full trial data are available.

3.2.1. Quantitative Results

We received 55 responses to the question "in which order would you prefer recommendations to be organized on this [list of recommendations] page?" Of these respondents, 40% (22/55) preferred in the order of the patient care cascade, 29% (16/55) by publication year (new to old), 16% (9/55) in the order of the original guideline, 2% (1/55) by publication year (old to new), 2% (1/55) other, and 11% (6/55) claimed no preference.

We received 112 responses to the question "what additional resources would you like to see as part of WHO tuberculosis guidelines in the future? Check all that apply." Of these respondents, 65% (73/112) confirmed that they would like to see decision aids, 62% (69/112) would like plain language summaries of evidence and recommendations, 55% (62/112) would like implementation tools, and 47% (62/112) would like to see translation to other languages.

3.2.2. Qualitative Results

A total of 75 free-text responses were received from trial participants. Of these,

19 were positive non-actionable statements such as "well summarized and referenced" or "easy to find information", and nine were neutral or incoherent statements. The remaining 47 statements were coded and categorized into the following five themes: purpose (n = 7), navigation (n = 18), presentation (n = 9), organization (n = 9), and outreach (n = 4). See Table 2 for descriptions and quotes from each theme.

Table 2. WHO eTB Survey Qualitative Feedback Themes

Theme	Description of Findings	Quotes
Purpose	Some participants (n = 7) expressed challenges with understanding the purpose of the platform, especially the recommendations map and heat map.	"I do not know how I will use the heat map. I would like an example."
Navigation	Several participants (n = 18) experienced challenges with navigating the platform. These challenges included problems with searching, inability to find information, and challenges moving between website pages.	"It took too many clicks and too much scrolling to find the recommendation and strength after entering the search."
Presentation	Some participants (n = 9) identified issues with visual attractiveness and presentation of the platform. Participants provided suggestions to increase font size, make recommendation statements more prominent, and add column labeling to the recommendations map.	"Clear separation of links but I would have expected the intervention to be the main text, not the strength. Makes reading through them more difficult."
Organization	Several participants (n = 9) provided suggestions for improving the organization of recommendations. Specifically, it was important to participants that they knew they were accessing the most updated recommendation. There was also a suggestion to tailor sections of the platform to	"Please make sure that the newest publications are found first and the older ones stored in an archive part of the website."

	specific stakeholder groups such as the public, clinicians, and researchers.	
Outreach	There were a few suggestions (n = 4) for additional dissemination and outreach strategies. These included the use of social media, connecting the platform with the work of other organizations, and creating a mobile application.	"The website is good. But the mobile app version will make the website more accessible."

We subsequently organized this feedback using the QI framework described in Table 3. This framework was developed in collaboration with WHO eTB catalogue content and information technology developers. It allowed us to identify the nature of the problem as described by stakeholders, categorize it by priority, and explore possible solutions.

Table 3. WHO eTB Quality Improvement Framework

Category	Options	Description	Example
Problem or Suggestion Identified (Verbatim)	-	Description of issue or proposed solution as explained by the stakeholder.	"I would need a bit more time to familiarize myself with it. Perhaps a short video would help."
Problem or Suggestion (Theme)		Theme of the issue or proposed solution.	Navigation
Nature of the Problem	Technology, Content, Both	Depending on the nature of the problem, the solution may be addressed by information technology developers, content abstractors, or both.	Content
Page	Home, List, Map, About, Rec, Overall	Location of the issue on the platform.	Overall, Map
Number of Times Mentioned	-	The number of times the problem is mentioned by stakeholders may influence its priority.	12

Priority	Low, Moderate, High	A collaborative judgement in the priority of addressing the issue based on number of times mentioned and the perceived urgency of the problem.	High
Possible Solutions	-	Possible solutions are identified that consider proposed stakeholder solutions and feasibility.	Create instructional videos and add written instruction for use of each page.
Solution Identified	Yes – Full, Yes – Partial, Not Feasible	Whether a full or partial solution has been identified, or whether a change is not feasible.	Yes - Full
Time Estimate	-	Estimated time for making changes if applicable.	3 months
Resolved	Yes – Fully, Yes – Partially, No	Whether issue has been fully, partially, or not resolved.	-
Comments and Explanations	-	Comments and explanations justifying decisions.	-

3.4. Discussion

This chapter describes the mixed-methods and QI frameworks used to explore interim feedback from the RCT participants. These participants were a diverse group of users and potential users of WHO TB guidelines, recommendations and policy advice. Five themes emerged from the qualitative responses: purpose, navigation, presentation, organization, and outreach. These themes were developed with reference to theories on KT and UX, which include that an individual's decision to engage with guidelines and technology may be influenced by interface presentation, understanding of the content's relevance, the user's ability to reach goals with efficiency, and perceived visual quality and

originality.[5-10] We identified that some participants experienced challenges with understanding the purpose of the eTB catalogue and map. Furthermore, despite measured improvements in accessibility, several participants experienced challenges navigating the platform. Creating instructional content that describes the purpose of the WHO eTB catalogue, as well as tutorials for proper navigation should be prioritized.

These emerging themes may also be explored in relation to the interim trial results. First, we found no statistical difference in participant understanding of the strength and certainty between WHO eTB and WHO TB. Strength was correctly identified by 76%, and certainty by 57% of WHO eTB participants. Thus, there were still many participants who were unable to locate and understand this information. This may be partially explained by the theme of navigation, including participant-identified issues with the search function or moving between platform pages. Second, while participants were more satisfied, on average, with the presentation of the WHO eTB home page and individual recommendations, we found no statistical difference in satisfaction with the list of recommendations page. This may be partially explained by the theme of organization, as some participants felt the order of recommendations on the list view could be improved. Finally, in anticipation of making improvements to the list view, we identified that the majority of participants preferred recommendations to be listed by patient care cascade (40%) or by

publication year (new to old) (29%). Participants also suggested archiving older recommendations that have been updated. Strategies to further improve the list of recommendations should be explored using our QI framework.

3.6. References

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CHAPTER 4: CONCLUSION

4.1. Discussion

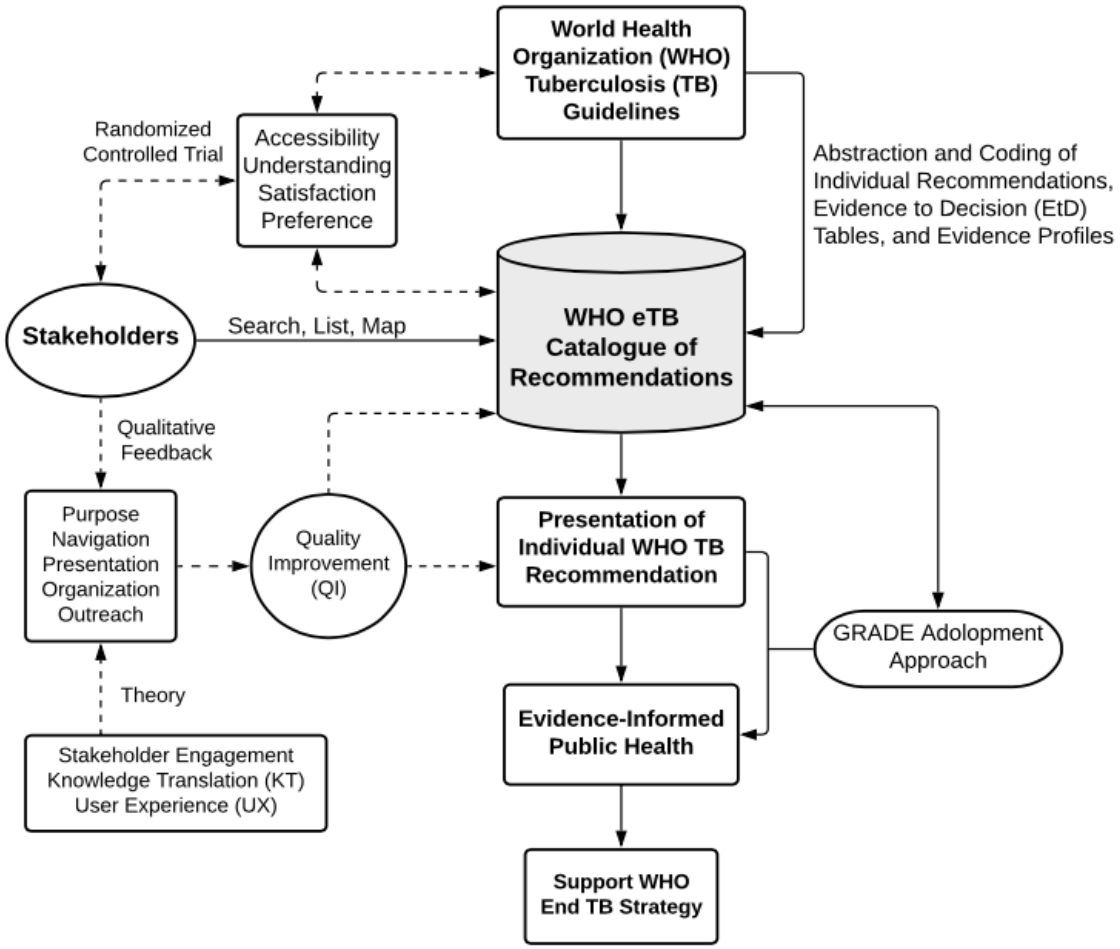
4.1.1. Main Findings

This thesis represents an effort to improve the accessibility and use of the World Health Organization's (WHO) tuberculosis (TB) guideline recommendations through stakeholder engagement. It involved the development of a two-arm superiority randomized controlled trial (RCT) administered using an online survey to compare stakeholder feedback on the accessibility of information, understanding, satisfaction, and preference between the new WHO eTB catalogue and the conventional method of accessing these recommendations. Study participants represented a diverse group of users and potential users of TB guidelines. Our interim results suggest that the WHO eTB catalogue does improve accessibility, understanding, and satisfaction for stakeholders of interest.

This thesis also represents an effort to integrate an RCT into a traditional quality improvement (QI) framework. The implementation of an RCT to gather stakeholder feedback allowed for the objective comparison of these two platforms. The findings of this RCT highlighted areas of success, as well as areas that we must continue to explore and improve. These results were explored in relation to five themes derived from the interim qualitative analysis: purpose, navigation, presentation, organization and outreach. Furthermore, a

QI framework was developed to systematically and transparently address these findings. See Figure 1 for a comprehensive flow diagram of this work.

Figure 1. WHO eTB Catalogue of Recommendations Process Flow Diagram



4.1.2. Strengths and Limitations

This thesis has several strengths. First, it complemented the efforts of the WHO to improve the accessibility and use of WHO TB recommendations through a combination of stakeholder engagement, user experience, knowledge translation, and quality improvement methods. Second, this

feedback was collected from a diverse group of users and potential users of WHO TB recommendations including the public, clinicians, policymakers, and academics, thus improving the generalizability of findings. Third, stakeholders participated in an RCT where they were not aware that they were comparing "new" to "conventional" methods, thus minimizing the consequence of social-desirability bias, in addition to balancing confounders. Fourth, the quantitative results of the RCT were triangulated with qualitative feedback from free-text boxes to further explore these findings and engage in quality improvement.

This thesis also has some limitations. First, stakeholder feedback was collected exclusively using an online questionnaire, which did not include interviews or individual user testing. More comprehensive qualitative feedback would have been useful to identify further areas of improvement and explain the results of the RCT. Second, the nature of an anonymous online survey meant that it was not possible to confirm whether the survey was completed by the person who received the link, or whether they used additional strategies or materials to respond to questions. Third, participant strata in the RCT were not sufficiently powered to detect subgroup effects, thus there was limited exploration of these findings by individual stakeholder groups.

4.1.3. Implications for Public Health and Policy

The WHO eTB catalogue of recommendations was developed as part of the WHO and McMaster TB QI project to improve the ability of stakeholders to source, use, and implement WHO TB recommendations across a variety of settings. This catalogue has the potential to bridge gaps between the evidence available in these recommendations, and clinical, public health and policy practice. The work of this thesis helps to ensure that the WHO eTB catalogue meets these objectives. Stakeholder ability to access and use these recommendations supports Evidence-Informed Public Health (EIPH), which is the process of integrating science-based interventions with community preferences in order to improve population health.[1] Ultimately, this work supports the WHO End TB Strategy by contributing to the pillars of patient-centered care, bold policies and supportive systems, and intensified research and innovation.[2]

4.1.4. Research Implications & Future Directions

This thesis contributes to the emerging field of experimental studies on methods by demonstrating the ways in which randomized controlled trials may be used to compare guideline platforms with the unit of analysis as the participant applying these methods. Future studies should seek to explain the findings of this RCT through more robust qualitative and user testing techniques. Furthermore, additional trials should target specific stakeholder

groups, such as patients and the public, to determine optimal ways to present WHO TB recommendations for these groups.

This work helps to shift the perspective on QI from the more common before and after comparisons to QI based in randomized controlled trials. Although QI is often described as distinct from research, this work demonstrates the ways in which they may be complementary. Thus, future research should continue to explore ways in which we can integrate research into QI frameworks. Finally, future directions of WHO TB recommendation development may consider the stakeholder priorities identified in Chapter 3, including the development of decision aids and plain language summaries.

4.2. Conclusion

The new WHO eTB catalogue of recommendations improved the accessibility of WHO TB recommendations and supporting evidence for stakeholders of interest. This thesis supports the continued use, promotion, and quality improvement of WHO eTB. Researchers should consider the use of randomized controlled trials and quality improvement frameworks to evaluate stakeholder feedback on guideline presentation in the future.

3.3. References

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