BMJ Open

Implementation of the WHO's collaborative framework for the management of tuberculosis and diabetes: a scoping review

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ABSTRACT

Objective To map evidence on the implementation of the WHO's collaborative framework for the management of tuberculosis (TB) and diabetes mellitus (DM) comorbidity, globally.

Design Scoping review.

Methods Guided by Arksey and O'Malley's scoping review framework, this review mapped literature on the global implementation of the framework for the management of TB and DM comorbidity, globally. An extensive literature search for peer-reviewed studies, theses, studies in the press and a list of references from the selected studies was conducted to source-eligible studies. PubMed, Google Scholar, Web of Science, Science Direct, the EBSCOhost platform (academic search complete, health source: nursing/academic edition, CINAHL with full text), Scopus and the WHO library were used to source the literature. We performed title screening of articles using keywords in the databases, after which two independent reviewers (RS and PV) screened abstracts and full articles. Studies from August 2011 to May 2021 were included in this review and the screening was guided by the inclusion and exclusion criteria. Findings were analysed using the thematic content analysis approach and results presented in the form of a narrative report. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension was used as a checklist and for explaining the scoping review process.

Results This review found evidence of the WHO TB-DM collaborative framework's implementation in 35 countries across the globe. TB-DM comorbidity was identified in patients through bidirectional screening of both patients with TB and patients with DM in rural and urban settings.

Conclusion Due to the paucity of evidence on mechanisms of collaboration, we recommend further research in other implementing countries to identify techniques used for diagnosis and integration of TB and DM services, in order to ensure that effective and joint management of TB-DM comorbidity in populations is achieved.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The search strategy was rigorous and covered an extensive range of databases to give a comprehensive review of the global implementation of the WHO collaborative framework.

⇒ All included studies underwent quality appraisal using an approved tool, namely: the Mixed Method Appraisal Tool.

⇒ This review only included articles published in English language and this may have excluded some relevant studies published in other languages. This review was guided by Arksey and O'Malley's framework, a widely used framework for conducting scoping reviews, which ensures a clear methodological and transparent process that can be replicated.

INTRODUCTION

Current tuberculosis (TB)-diabetes mellitus (DM) co-epidemic imposes strain on the strategies to control rising TB and DM prevalence across the globe.[1 2] Healthcare systems are also being challenged to rethink diagnostic accuracy, co-management of the two diseases, and re-evaluation of the vertical nature of TB and DM management.[3] The past decade has shown that the TB-DM co-epidemic has severe public health consequences, mainly because TB affects one-fourth of the global population.[4]

DM is one of the top four non-communicable diseases causing mortality worldwide; and in the year 2019, approximately 1.5 million deaths were attributed to DM, globally.[5] Globally, an estimated 15% of people with TB can be associated with DM.[6] The 22 countries known to bear 80% of the global TB burden had TB infections due to DM, thereby contributing 10% of all TB cases recorded in 2010, a figure that increased to 15% in 2013.[7] Low/middle-income countries (LMICs) carry an estimated 80% and 90% of DM and TB burden, respectively.[6] Nine of the top 10 countries identified to have the highest TB-DM incidence, globally, are from LMICs.[7]

The increased risk of TB infections has been associated with DM, which affects the immune system leading to poor treatment outcomes, the likelihood of disease recurrence and

increased risk of death.[8 9] Populations with DM are three to four times more likely to develop TB, as compared with the general populations.[2 8] In 2011, the WHO and International Union Against Tuberculosis and Lung Disease (Union) launched a policy framework to address the growing TB-DM co-epidemic, known as the collaborative framework for the management of TB and DM.[10] This framework outlines recommendations to guide countries in the care, prevention, and control of TB and DM worldwide.[10] The recommendations are to be used by policymakers and implementers to curb the TB-DM co-epidemic and complement the existing systems set up for the prevention and management of TB and DM.[3] The focus is on: (1) improving detection and management of TB in patients with DM, (2) improving detection and management of DM in patients with TB, and (3) establishing mechanisms of joint coordination at regional, district, and/or local levels (sensitive to country-specific factors), with representation from all relevant stakeholders.[10]

The WHO and Union encourage findings from implementation research to strengthen the existing recommendations for healthcare systems.[10] In this review, we mapped evidence on the implementation of the WHO-Union collaborative framework, globally. Results from this scoping review provide current data on the state of implementation, reveal existing gaps in current literature and ultimately inform the refinement of questions for further primary research.

METHODS

Study design

The methodology for this scoping review, as outlined in the published protocol,[11] was guided by Arksey and O'Malley's framework and Levac *et al*'s[12] methodological enhancement for scoping review projects.[13] This review mapped literature on the implementation of the WHO collaborative framework for the management of TB-DM comorbidity, published between August 2011 and May 2021. We conducted a systematic search to synthesise published and unpublished literature (grey literature) articles to answer the research question. The research question considered a range of studies including qualitative, quantitative and mixed methods. Arksey and O'Malley's framework gives five clear steps to be used for exploring core concepts in a specific research area.[13] These steps are: identifying the research question, identifying relevant studies, study selection, charting the data, collating, summarising and reporting the results.[13] This process helped in identifying the existing evidence in the research area. We also followed guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) extension for Scoping Reviews: checklist and explanation for reporting purposes (online supplemental file 1).[14]

Eligibility of the research question

This scoping review followed the Population, Concept, Context framework to determine the eligibility of the

Table 1	PCC framework
P—Population	Individuals with TB Individuals with DM
C—Concept	WHO collaborative framework implementation
C—Context	Global
DM, diabetes mellitus; TB, tuberculosis.	

primary research question (table 1).[13] Based on the framework, the study population was individuals with TB and individuals with DM, the concept was the WHO collaborative framework implementation and the context was global.

Identify the research question

The main research question: What is the evidence on the implementation of the WHO's TB-DM collaborative framework, globally?

Subquestions:

1. What is the evidence of DM detection and management in patients with TB?
2. What is the evidence of TB detection and management in patients with DM?
3. What is the evidence of collaboration between TB and DM programmes?
4. What is the evidence of a referral system for patients with DM suspected to have TB for diagnosis and management?
5. What is the evidence of a referral system for patients with TB suspected to have DM for diagnosis and management?

Identifying relevant studies

Search strategy

We conducted a comprehensive search technique for published and unpublished (grey literature) articles relevant to answer our research question. We piloted our search strategy in December 2019 in PubMed and CINAHL via EBSCOhost, followed by analysis of the text words contained in the title and abstract and of the index terms used to describe the article, guided by the Joanna Briggs Institute's manual for evidence synthesis.[15] Our overall search was updated in seven electronic databases in May 2021 (online supplemental appendix 1), including: PubMed and CINAHL via EBSCOhost, Web of Science, Science Direct, Scopus, Google Scholar and WHO library. Our search approach included Boolean terms (AND, OR) and Medical Subject Headings terms. The search keywords were: 'Diabetes', 'Type 2 Diabetes', 'Tuberculosis', 'Comorbidity', 'Implementation' and 'Framework'. All studies suitable for inclusion had their reference lists further assessed for potential inclusion. Grey literature articles were accessed by searching for policy documents, treatment guidelines and reports by ministries of health, and health agencies through their websites or links. Studies obtained through database

searches were exported to EndNote library for further abstract and full article screening, respectively. The 'Find full text' option in the EndNote library was used to automatically obtain PDFs of exported studies.

Study selection

The first reviewer (RS) conducted the database search based on a broad inclusion criterion. This search focused on the title of the articles. The full texts of all the articles that were selected as potentially eligible for inclusion in this review were obtained. Two independent reviewers (RS and PV) then conducted abstracts and full article screenings in order to identify articles that met all the inclusion criteria. Any disagreements between the two independent reviewers were resolved through discussion. Arrangements had been made for a third reviewer to resolve any disagreements between the two independent reviewers. However, no disagreements emerged, hence the third reviewer was not consulted.

Inclusion and exclusion criteria

The eligibility criteria were developed to ensure the inclusion of specific information relating to the research questions in the studies. Our inclusion criteria in this review involved studies presenting evidence of TB-DM comorbidity among populations with TB and DM. We also considered studies presenting evidence of bidirectional screening for TB and DM, as well as studies presenting evidence of mechanisms of collaboration in the management of TB and DM. All these studies had to be published in English language, between August 2011 and May 2021, given that the framework was first launched in 2011.

Studies presenting evidence on type 1 diabetes and those focusing on TB or HIV were excluded. This review only included articles on type 2 diabetes and excluded type 1 diabetes because type 2 diabetes contributes 90%–95% of all diabetes cases, globally, and shares socioeconomic, environmental, and behavioural factors with TB.[16 17] Also excluded were studies published prior to August 2011 and those published in other languages apart from English language.

Data charting

To extract relevant information and characteristics of studies, we developed a form electronically, using Google forms, pretested it and used feedback to refine the tool. The selected studies were thoroughly read for data extraction of bibliographical details and ensuring that relevant outcomes were extracted, including: (a) author(s) and date of publication, (b) aim(s) or research questions, (c) primary source data, study population, (d) geographical setting (rural/urban), (e) study design, (f) most relevant finding, (g) most significant finding, (h) study limitations and implications, as well as (i) interpretations and conclusions from the authors.

Collating, summarising and reporting results

The results from existing studies were summarised and presented in a narrative format. This summary was analysed using thematic content analysis. Data extracted were structured around the following outcomes: bidirectional screening of TB and DM, feasibility of screening and co-management of TB/DM comorbidity. The themes emerging from the analysis were examined to determine whether or not they addressed the research questions. Furthermore, the researchers explored linkages between the findings, study aim, and the implications for future research, policy, and practice.

Quality of evidence

Two independent reviewers conducted quality assessment by appraising the included studies using the Mixed Method Appraisal Tool (MMAT) V.2018.[18] The MMAT is a critical appraisal tool designed for the appraisal stage of systematic mixed studies reviews, like reviews that include qualitative, quantitative and mixed-methods studies. The tool may also be used to assess the methodological quality of five different types of studies: qualitative research, randomised controlled trials, non-randomised studies, quantitative descriptive studies and mixed techniques studies (online supplemental appendix 2). The MMAT evaluates the appropriateness of the study aim, study design, methodology including the recruitment of participants, data collection, data analysis, results presentation, authors' discussion and conclusions. Any disagreements between the two independent reviewers were resolved through discussion. The tool does not permit for quality scoring of included studies, therefore we did not provide overall quality scores.[18]

The quality of evidence had little variations across the studies. Most of the 82 studies had good methodological rigour across all the MMAT criteria. Out of the 82 included studies, 4 were poorly appraised; as these studies did not report on the validity and reliability of the measurement, neither did they report on the response rate, hence the risk of non-response bias could not be determined. Furthermore, the sample of the studies was not representative of the target population, as no standard measure was used to determine the sample size. The sample strategy of the studies was not clearly stated, and this could have led to sampling bias. Additionally, one of the mixed-methods studies did not adhere to the quality criteria of each tradition of the methods used in the study.

RESULTS

The initial search through the electronic databases, including published studies and grey literature, yielded a total of 1442 articles. One thousand and seventy-two (1072) articles were excluded at a database search stage, because they did not meet the inclusion criteria. Sixty-four duplicates were removed, leaving us with 306 articles that were screened for abstracts. A total of 200 articles were removed at the abstract screening stage based on the exclusion criteria. The researchers further screened the remaining 106 full-text articles and excluded 24 articles (online supplemental appendix 3) with the following
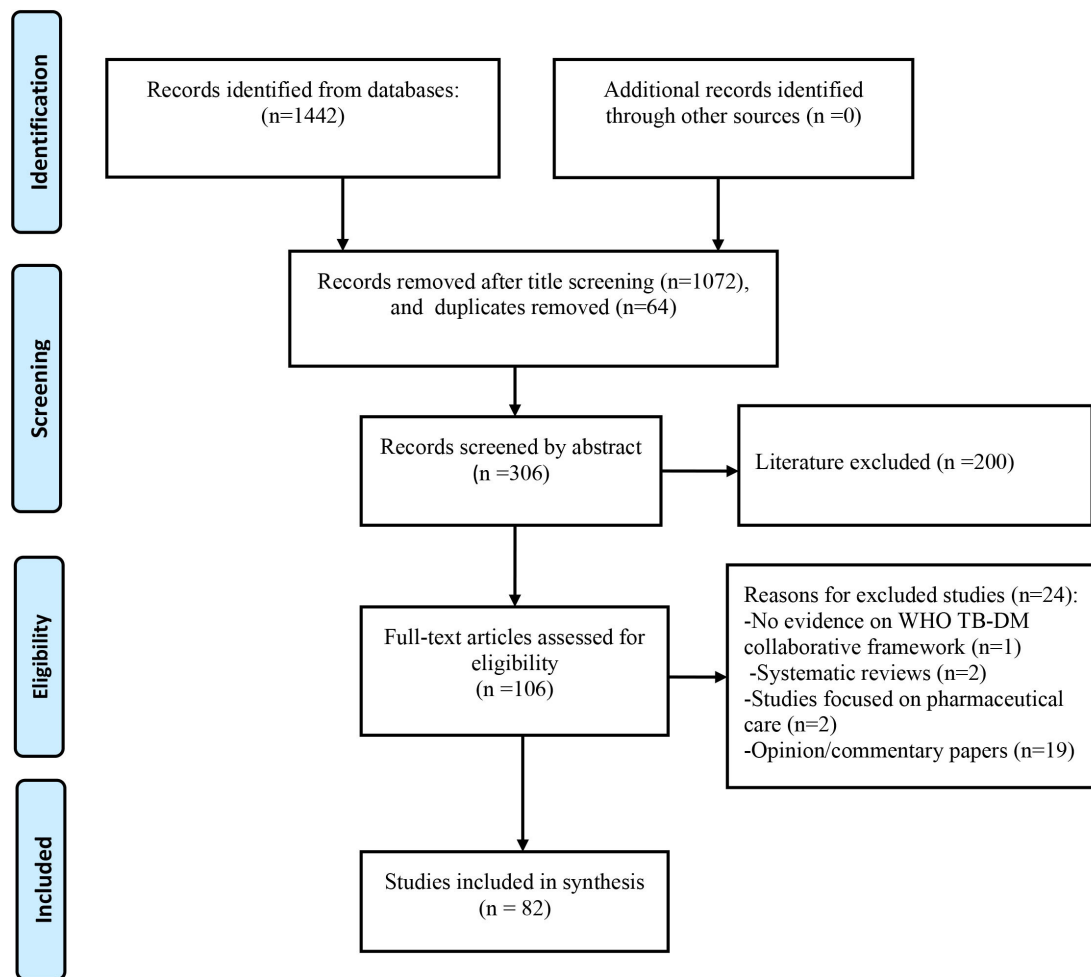
Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram. From: Moher *et al.*[129] DM, diabetes mellitus; TB, tuberculosis.

reasons: 19 studies were opinion/commentary papers, 2 were systematic reviews, 2 focused on pharmaceutical care and the last one had no evidence on WHO TB-DM collaborative framework. Figure 1 shows the PRISMA flow diagram demonstrating the screening results from each stage.

Characteristics of included studies

A total of 82[9 19–98] articles from 35 countries including India, China, the USA, Pakistan, Taiwan, Ethiopia, Tanzania and Nigeria met our inclusion criteria and were included in the quality assessment stage. These were 5 qualitative, 75 quantitative and 2 mixed-methods studies. The WHO is made up of 194 member states, but our review found studies from only 35 countries, mostly India (n=25),[19 20 44–51 53–55 58 60 61 63 81 82 94 95 99–101] China (n=10),[65–67 70 71 84 85 97 102] Ethiopia (n=4),[34 35 94 103] Nigeria (n=3)[25 36 86] and the USA (n=2).[26 28] Online supplemental appendix 4 summarises the characteristics of the different studies. The findings from this review provided evidence on the feasibility of screening, bidirectional screening (screening patients with TB for DM, screening patients with DM for TB), co-management, and challenges and

opportunities, in line with the recommendations of the collaborative framework.[10 104]

Feasibility of screening

The Bali declaration was expected to accelerate the implementation of the collaborative framework for the care and control of diabetes and TB.[104] A major emphasis was on operational and clinical research, globally, designed to establish evidence to strengthen the current recommendations and propose appropriate indicators.[104] Our review of publications showed evidence supporting the feasibility of bidirectional screening. Study findings demonstrated that it was possible to conduct screening in both rural and urban settings.[55 68] The different settings also indicated varying TB-DM prevalence rates in rural and urban regions in various countries.[38 48 67 78] Additionally, our findings supported routine screening, especially in high-risk populations.[20 28 55 61 63 65 72 78 79]

A predominant number of publications on screening in healthcare settings revealed that screening can be integrated into routine practices in the healthcare system.[21 32 53 60 62 65 68–70 81 98 99 105–107]

Bidirectional screening

One of the public health actions proposed for averting the impact of the looming TB-DM co-epidemic is screening patients with TB for DM and vice-versa.[104] This review identified publications on screening to provide evidence on suitable approaches used by various countries and settings. Majority (60%) of the included studies focused on screening patients with TB for DM,[19 20 22 28 34–36 38 40 41 46–51 57 59 61 65–67 71 72 76–80 82 108–112] a phenomenon that permeated throughout various countries spreading across the five geographical regions, especially Asia. The DM prevalence among patients with TB varied within countries, such as India (5%–25%)[19 20 46 48 51 54 58 59 61 82] and China (6.3%–12.4%).[65 66] DM prevalence was reported by the studies to be higher in older male patients with TB than female counterparts and mostly in urban settings.[19 46 72 113]

Fewer studies focused on screening patients with DM for TB, and this was attributed to the low availability of TB management strategies in DM facilities.[33 68 70 81 86 100 114] These studies were conducted in the USA, India, Tanzania, Korea, Bangladesh, China, Taiwan, Nigeria and Iran. Generally, the risk of TB in patients with DM is about three times higher compared with the general population, a pattern that was also confirmed in our review.[16 115] Results ranged from as low as 1.8-fold in South Korea to 7-fold in Tanzania, higher than the general population.[21 62] In one study conducted in India, TB was not prevalent among patients with DM.[53] Male patients with DM were found to be at increased risk of TB than their female counterparts.[21 26 52 60 70] Higher TB rates among older men were attributable to sedentary lifestyles, high body mass index (BMI) levels and smoking practice.[60 70] Age and gender were identified as important risk factors for TB.[60]

Co-management

Several studies highlighted the minimum or lack of integration between TB and DM units and the parallel paths of care for patients with TB-DM comorbidity. This is shown by the quotes below:

> Endocrinologist treats diabetes, and we treat TB (p4).[37]
>
> We treat diabetes and that's it (p6).[37]
>
> Since our main task is TB treatment, the primary treatment is focused on TB (p6).[37]
>
> A TB patient should have tests for diabetes but generally diabetes patients don't go for TB tests (p7).[100]

There was more evidence on case detection than co-management of TB and DM.[29 37] Patients with TB-DM comorbidity did not appear to receive comparable treatment, and this may be due to more funding being available to TB, compared with diabetes and the limited number of staff trained in co-management.[37 114]

> We haven't received any funding or training, especially for this screening…I think, currently the training is not adequate. It should be given more often (p7).[100]

Individuals with the dual TB-DM condition were found to have better outcomes when jointly managed.[114]

Opportunities and challenges

Implementation of the collaborative framework in various countries revealed the opportunities and challenges among healthcare workers, patients and the healthcare system. One of the opportunities identified was the feasibility to implement screening in the existing healthcare systems.[22 72] However, it is still important that policies that support integrated screening in routine health service delivery be developed.[78] Timely diagnosis and management of TB-DM comorbidity were improved by implementing cost-effective measures, recording screening and user-friendly approaches.[22 60 72 78 80 99] Some of the challenges encountered were lack of awareness of bidirectional screening by patients, while some healthcare providers were not aware of guidelines for bidirectional screening.[56]

> See madam, what can I tell about this [screening for DM]? Doctors can only talk about this [screening TB patients for DM] (p7).[56]
>
> I don't know about that [any national guidelines] (p7).[56]

DISCUSSION

This scoping review mapped existing literature on the implementation of the TB-DM collaborative framework, globally, and provides an overview of the extent of implementation from 2011 to 2021. Our review found evidence of research in 35 countries, predominantly from LMICs. India and China showed greatest research outputs on the implementation of the collaborative framework, and this may be due to high TB burden being observed in these countries.[10 67] Findings pointed to the feasibility of bidirectional screening, opportunities and challenges, as well as fewer publications on the collaboration of TB and DM programmes, thereby highlighting gaps in evidence on the integration of services for the management of TB-DM comorbidity.

Several studies in this review focused on screening patients with TB for DM as compared with screening patients with DM for TB and this was congruent with the findings of Workneh *et al*.[103] Additionally, there were limited articles on screening patients with TB for DM in African countries and this was consistent with what had been reported in a prior study conducted in Ghana.[39] This is probably because of inadequate support for DM facilities to screen for TB. Fewer articles showed evidence of screening both patients with TB and patients with DM in the same study. This review showed that screening can be implemented in both urban and rural settings with varying prevalence rates across geographical settings, thereby rendering the link between prevalence and the type of setting (rural vs urban) weak. This is in contrast with the findings of the study by Sulaiman *et al*, who

found prevalence rates to be the same in urban and rural centres.[116]

Bidirectional screening was found to be mainly implemented in healthcare facilities and this revealed that the existing healthcare systems can be used to co-manage individuals with TB-DM comorbidity, similar to findings by a review conducted in India.[117] Routine screening in high-risk populations was demonstrated by some studies in our review and was linked to early detection of TB or DM, subsequently leading to more effective management and outcomes. This was also reported in other studies.[16 19 22 60 118]

The risk of patients with DM developing TB has been estimated to be threefold as compared with the general population.[10] While this was generally confirmed by the findings of this review, two studies produced contrary findings, which revealed low DM prevalence in patients with TB.[27 76] Therefore, evidence suggesting that DM is a risk factor for TB remains inconclusive and further studies are required.

Consistent with recommendations from other studies, evidence from this review points to the need for more awareness on bidirectional screening for both patients and healthcare workers.[46 54 67 119] Individuals with the coinfection were not found to be receiving comparable care for each disease, which may be contributing to the growing TB-DM comorbidity and adversely affecting the global efforts towards the control of TB.[37 77 78 120]

A key recommendation by the WHO-Union collaborative framework is joint management to improve health outcomes of patients with TB-DM comorbidity.[10] Health systems in this review were having challenges in managing TB and DM jointly, due to existing systems of care that offered vertical healthcare,[37 114] which is supported by a review on the double burden of TB and DM.[121] The silo approach in most healthcare systems with regard to communicable and non-communicable diseases was a barrier to integrating care for individuals with the dual condition. Although not identified in this research, an article published in India showed that collaboration is also hindered due to patients with TB being largely managed in public health facilities, as compared with patients with DM, who are mostly being cared for in private health facilities.[122]

Some studies have shown that individuals with coinfection have different experiences of care in health facilities, when compared with patients with only one condition.[56 114] Their experiences spanned from the unavailability of joint consultation, so patients had to see a separate specialist for the different conditions, to the indecisiveness of health workers on whether to admit individuals with the comorbidity in DM or TB wards.[37 114] This may be due to the perception that TB-DM comorbidity is a complicated condition that may lead to relapse, treatment failure, or death and requiring specialist attention.[37 123 124] Patients and healthcare professionals had to find ways to integrate required medication, addressing medication-related issues, and more education to help patients understand the comorbidity.[114] There is a need for clear guidelines, diagnostics and refresher training for healthcare workers.[114 125] Other studies support our findings that joint management improves early diagnosis and health outcomes.[16 126]

Limitations

Our review is subject to important limitations. This review included only articles published in English language, which may have excluded some relevant studies published in other languages. We only identified one non-English article, which was in Spanish, and this too may be reflective of our incompetence in other languages. Only a single reviewer carried out title and abstract screening. The database search conducted by two independent reviewers may have yielded additional relevant studies. Despite the generally relevant key words used while searching for relevant articles in different databases, other terms may also exist. Nonetheless, the study strictly followed the framework provided by Arksey and O'Malley's framework to map evidence on the implementation of the WHO's collaborative framework for the management of TB and diabetes comorbidity, globally. Despite these limitations, we believe that our search strategy was comprehensive in reviewing relevant literature for this review.

Implications for practice

In line with other recommendations,[127] our findings suggest that free glucose tests, integration of DM and TB services, patient counselling and routine screening are factors that enhance effective screening.[47 57] In areas where bidirectional screening was not effective, factors such as inadequate staffing, poor supply of laboratory supplies for DM diagnosis and poor patient awareness of bidirectional screening were highlighted.[56] Recommendations from screening studies emphasise the importance of policies that support integrating screening in routine health delivery, cost-effective measures, recording screening results in reports and user-friendly approaches, to improve timely diagnosis and management.[80 128]

Conclusion

This review revealed that bidirectional screening is feasible and can potentially improve the diagnosis and co-management of individuals with TB and DM. Additionally, the study demonstrates that gaps still exist in research aimed at providing evidence of improved techniques for detecting TB-DM comorbidity. There is an urgent need for health systems to integrate TB and DM services.

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