



Diabetes and Tuberculosis Co-Management in High-Burden Settings: A Narrative Review of Integrated Service Models

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Received: 30 January 2026; Accepted: 6 May 2026; Published: 13 August 2026

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Abstract

International guidance recommends bidirectional screening for tuberculosis and diabetes where both are prevalent, and integrated services have been established in several countries to deliver it. The evidence that integration works is weaker and more one-sided than the recommendation implies. In a comparison of eight Malawian hospitals, of which one had integration measures, tuberculosis screening among people with diabetes increased and loss to follow-up in both diseases fell, but the evidence for increased diabetes screening among people with tuberculosis was limited. The yields differ by a wide margin in the same direction: screening people with diabetes for tuberculosis in a multi-province Chinese study found active disease in 0.80 per cent, while screening people with tuberculosis for diabetes in a Kerala programme found a prevalence of 44 per cent. A scoping review of the collaborative framework concluded that evidence that diabetes is a risk factor for tuberculosis remains inconclusive.

Keywords: Tuberculosis; Diabetes; Bidirectional screening; Integrated care; Low- and middle-income countries

Introduction

Tuberculosis and diabetes coexist at scale in several of the countries carrying the largest burden of each, and the number of people affected by both is projected to rise [1,2,3]. Diabetes has been reported to raise the risk of tuberculosis and to worsen its treatment outcomes, and tuberculosis complicates glycaemic control [4,5,20,30]. The convergence of the two epidemics has been described for more than a decade [30], and systematic review has examined comorbidity prevalence and its associated factors [24,25].

International guidance has responded with a collaborative framework recommending bidirectional screening, so that people presenting with either condition are assessed for the other [6,7]. Integrated clinics have been established in several high-burden countries to deliver this [8,9,22,23]. Clinical management of concurrent disease and its service implications have been set out separately [22], as have the implications of rising diabetes for tuberculosis control [23,26].

This review examines what integrated models have achieved where they have been evaluated, how the yield differs between

the two directions of screening, and how secure the epidemiological premise underneath the recommendation is.

Material and Methods

Search strategy: PubMed and the archives of the major infectious disease, global health and diabetes journals were searched for evaluations of integrated tuberculosis and diabetes services. Search terms combined tuberculosis and diabetes with bidirectional screening, integrated care, collaborative framework and low- and middle-income countries. Reference lists of the scoping review [6] and the principal comparative study [10] were screened by hand for primary sources.

Eligibility: Studies were included if they evaluated integrated service models, reported screening yields in either direction, or examined the association between the two conditions. Programme descriptions without outcome data are cited for the models they describe and are identified as such.

Data extraction and handling: Setting, design, direction of screening and the reported yield or outcome were extracted as published. The direction of screening is stated with every yield

figure, because the two directions produce results differing by more than an order of magnitude and the term bidirectional obscures this. This review reports published findings and does not constitute guidance on service design or clinical management in any setting. No pooling or re-analysis was performed. Figures 1 to 6 and Tables 1 to 3 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

Yield in each direction: A large multi-province study in China screened people with diabetes for active tuberculosis and found a prevalence of 0.80 per cent, demonstrating feasibility while identifying operational difficulties including insufficient staffing and the need for simpler screening algorithms [11,12]. A study in Kerala integrating diabetes screening into directly observed treatment clinics found diabetes in 44 per cent of people with tuberculosis (Figure 1) [11,13].

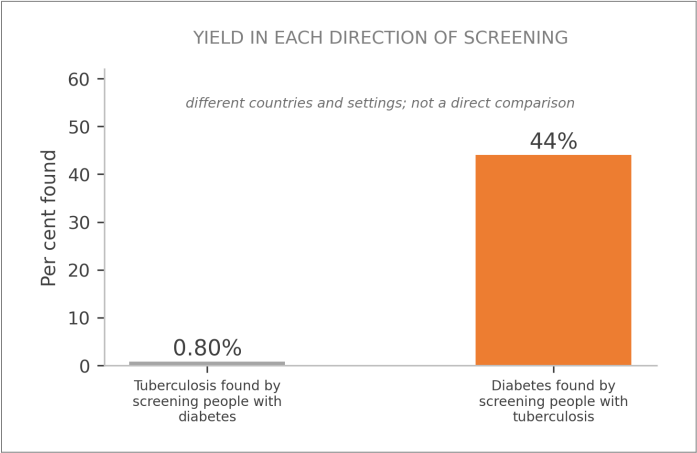


Figure 1: Yield in each direction of screening, in different settings [11,12,13]

What integration changed: A retrospective chart review compared eight Malawian hospitals, one with integration measures and seven without, covering patients registered between 2016 and August 2019. The analysis included 557 people with diabetes, mean age 54, and 987 people with tuberculosis, mean age 41 (Figure 3). Tuberculosis screening for people with diabetes increased, loss to follow-up in both diseases was reduced, and treatment success among people with tuberculosis improved. Evidence for an increase in diabetes screening among people with tuberculosis was limited (Figure 2) [10].

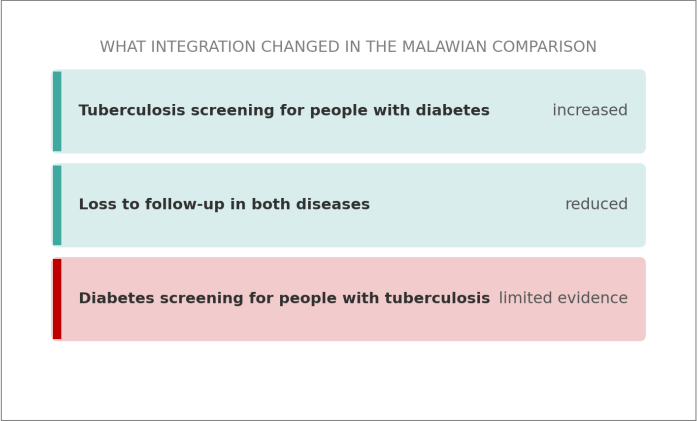


Figure 2: What integration changed in the Malawian comparison [10]

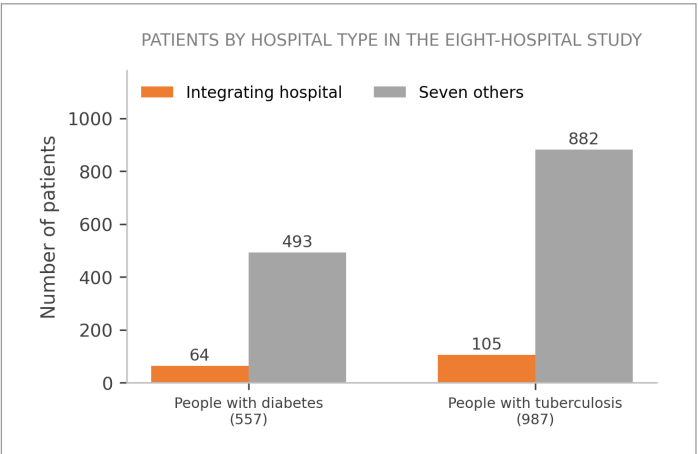


Figure 3: Patients by hospital type in the eight-hospital study [10]

How small the comparison was: Of the 557 people with diabetes, 64 (11.5 per cent) were from the integrating hospital, as were 105 of the 987 people with tuberculosis (10.6 per cent) [10]. The investigators concluded that decisions about which hospitals should integrate ought to weigh disease burden, local barriers and existing guidance against what they described as rather weak evidence of effect on bidirectional screening coverage and treatment outcomes [10].

Outcome	Direction of effect	Strength as reported
Tuberculosis screening in diabetes	Increased	Observed [10]
Loss to follow-up, both diseases	Reduced	Observed [10]
Treatment success in tuberculosis	Improved	Observed [10]
Diabetes screening in tuberculosis	Unclear	Limited evidence [10]

Table 1: Findings of the eight-hospital comparison, as reported by the original investigators [10]

The epidemiological premise: The risk of tuberculosis among people with diabetes has been estimated at approximately threefold that of the general population [4,6]. A scoping review of implementation of the collaborative framework found that this was generally supported, but that two included studies reported low diabetes prevalence among people with tuberculosis, and

concluded that evidence that diabetes is a risk factor for tuberculosis remains inconclusive and requires further study (Figure 4) [6,21]. A research agenda addressing the converging epidemics has been proposed to close exactly this question [21].

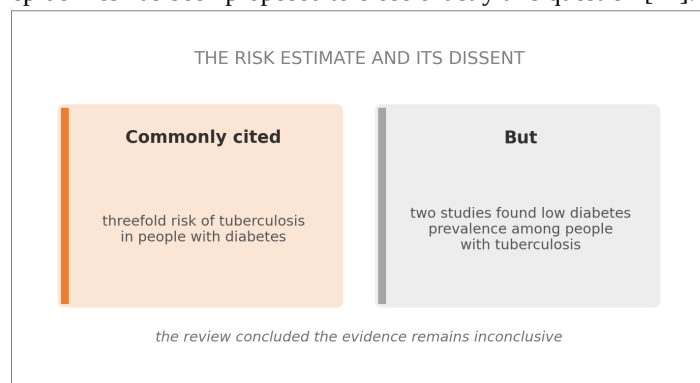


Figure 4: The commonly cited risk estimate and the dissent from it [4,6]

Feasibility and acceptability: The same review found bidirectional screening implemented mainly within existing healthcare facilities, in both rural and urban settings, indicating that established systems can be used to co-manage the two conditions [6,14]. Integration of screening for non-communicable diseases into a tuberculosis programme in Delhi produced high yield and was reported as feasible and acceptable to patients and providers where the identified challenges could be overcome [15]. An Ethiopian study reported good acceptability of integrated care within a tuberculosis control programme [16].

What made it work and what did not: A pilot in rural India identified task sharing with non-physician health workers, digital support and doorstep free care delivery as the principal enablers, and inadequate awareness, insufficient training and overburdened community health workers as the key barriers (Figure 5) [16,17]. Task shifting to non-physician workers for non-communicable disease management has been found feasible across several contexts [17], and integration of tuberculosis services with care for other comorbidities has been argued for on the same grounds [33].

The Malawian comparison is the closest thing to an evaluation of integration and it points the same way. Tuberculosis screening among people with diabetes increased and loss to follow-up fell, but the evidence for improved diabetes screening among people with tuberculosis was limited [10]. That is integration succeeding in the lower-yield direction and not demonstrably succeeding in the higher-yield one, which is close to the opposite of what a service would want.

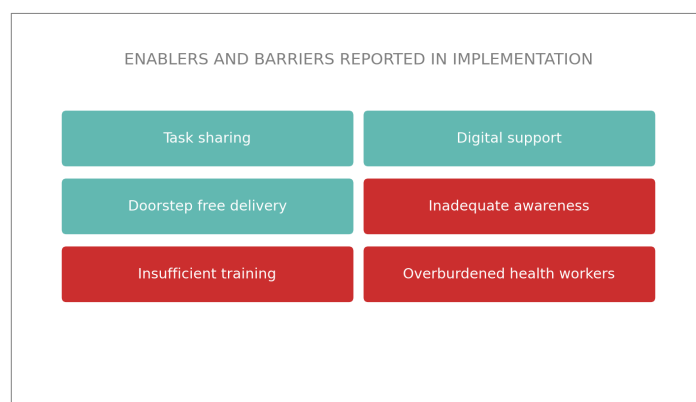


Figure 5: Enablers and barriers reported in implementation [16,17]

Background prevalence varies: In one high-burden southern African country, a national survey reported impaired fasting glycaemia in 10 per cent of participants, a later outpatient survey reported diabetes in 7.3 per cent and prediabetes in 6.5 per cent, and a survey restricted to people living with HIV reported diabetes in 6 per cent and prediabetes in 30 per cent (Figure 6) [18,19]. The national tuberculosis programme there recommends diabetes screening for people with tuberculosis, and it is not routinely implemented [18]. Undiagnosed diabetes among people with tuberculosis has been reported at high levels in peripheral facilities elsewhere [31], and bidirectional screening has been evaluated at tertiary level in southern India [34].

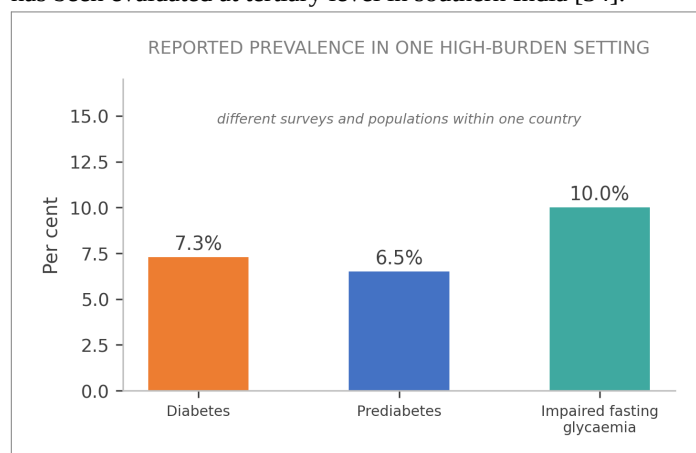


Figure 6: Reported prevalence in one high-burden setting [18,19]

Setting	Screening direction	Reported yield
China, multi-province	Tuberculosis in diabetes	0.80% [11,12]
Kerala, India	Diabetes in tuberculosis	44% [11,13]
Southern Africa, outpatients	Diabetes prevalence	7.3% [18]
Southern Africa, people with HIV	Diabetes prevalence	6% [18]

Table 2: Reported yields and prevalence by setting and screening direction

Claim	Status in the reviewed literature
Bidirectional screening is feasible	Supported in rural and urban settings [6,14]
Integration improves tuberculosis outcomes	Observed in one comparison [10]
Integration improves diabetes screening	Limited evidence [10]
Diabetes raises tuberculosis risk	Described as inconclusive [6]
Workforce is the limiting factor	Reported consistently [11,17]

Table 3: What the reviewed literature does and does not support

Transient hyperglycaemia complicates the higher-yield direction: Diabetes detected during acute tuberculosis may reflect stress hyperglycaemia that resolves as the infection is treated, rather than established disease [4,20]. Studies differ in whether they re-test after treatment, which means the prevalence found by screening people with tuberculosis is an upper bound rather than a settled figure [5,24,25]. That does not remove the case for screening in that direction, but it changes what a positive result means at the point it is obtained.

The wider comorbidity argument: Tuberculosis coexists with several non-communicable conditions, and integration has been argued for on grounds broader than diabetes alone [33]. The Delhi programme screened for a range of non-communicable diseases and their risk factors within routine tuberculosis care and reported high yield with acceptability to patients and providers [15]. If the limiting factor is workforce rather than any single test, that framing matters, because the marginal cost of adding a condition to an existing contact is lower than the cost of creating the contact [11,17].

Discussion

The word bidirectional does a great deal of work in this literature and conceals the most consistent finding in it. Screening people with tuberculosis for diabetes and screening people with diabetes for tuberculosis are not symmetrical activities. In the studies reviewed here they returned 44 per cent and 0.80 per cent respectively, in different countries and populations, but a difference of that magnitude is not explicable by setting alone [11,12,13].

The asymmetry has a straightforward explanation and an awkward implication. Diabetes is common and its prevalence rises with the age and adiposity of the screened population, while active tuberculosis is comparatively rare even where incidence is high. A programme that screens every person with tuberculosis for diabetes will find a great deal; one that screens every person with diabetes for tuberculosis will find little at considerable cost. Those are different propositions and the collaborative framework recommends both [6,7].

The study cannot bear much weight and its authors say so. One integrating hospital against seven others, with 64 and 105 patients respectively in the integrating arm, is a comparison of a service rather than of a policy, and it is retrospective [10]. Their

own conclusion, that decisions to integrate should weigh local burden and barriers against rather weak evidence of effect, is more cautious than the framework it evaluates.

Underneath all of this sits an unsettled premise. The threefold risk estimate is widely cited, and the scoping review that examined implementation of the framework concluded that the evidence for diabetes as a risk factor for tuberculosis remains inconclusive, with two included studies reporting low diabetes prevalence among people with tuberculosis [6]. A screening policy built on an association that its own evidence review describes as unresolved deserves to be described that way rather than as settled.

There is a design point that follows from the asymmetry without needing further evidence. If screening people with tuberculosis for diabetes has a yield of the order reported in Kerala, that activity justifies itself on detection alone and does not depend on the contested risk association [6,13]. Screening in the opposite direction has a low yield and its case rests substantially on that association, which is the part the evidence has not closed [6,21]. Treating the two as a single policy obscures that they stand or fall on different grounds.

What would settle it is a prospective comparison of integrated against separate services with screening coverage and treatment outcomes as pre-specified endpoints in both directions [6,10]. The existing evaluations were not designed for that, and the one closest to it involved a single integrating hospital [10]. Until then the recommendation rests on feasibility, which is well demonstrated, rather than on effectiveness, which is not [6,14].

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Study limitations

The limitations belong to the underlying literature. The principal comparative study is retrospective, involves a single integrating hospital, and is not powered for the comparisons it reports [10]. Yields from different countries are set alongside one another although populations, screening thresholds and diagnostic methods differ, so the contrast between directions is illustrative rather than a direct comparison [11,12,13]. Diabetes diagnosed during acute tuberculosis may reflect transient stress hyperglycaemia rather than established disease, which inflates prevalence in that direction and is inconsistently addressed [4,5]. The scoping review pools heterogeneous implementation reports of varying quality [6]. Programme evaluations are frequently conducted by the teams delivering the programme [15,16]. Co-infection with HIV alters both the epidemiology and the service context substantially in several of the settings described, and is not held constant [18,19]. And no randomised comparison of integrated against separate services exists, so the effects attributed to integration remain associations [6,10]. Whether glucose-lowering treatment alters tuberculosis incidence or prognosis has been reviewed and not resolved [28], modelling suggests diabetes trends bear on global tuberculosis targets [26], and national programme guidance varies in how it handles the comorbidity [27,29,32].

Conclusion

Integrated tuberculosis and diabetes services are feasible, acceptable and established in several high-burden settings, and where evaluated they were associated with better tuberculosis screening among people with diabetes and reduced loss to follow-up in both conditions. Two things qualify the recommendation. The two directions of screening are not equivalent: one returned 44 per cent and the other 0.80 per cent, and the direction that integration was shown to improve is the lower-yield one. And the epidemiological premise is less settled than the framework built on it, with the review of its own implementation concluding that evidence for diabetes as a risk factor for tuberculosis remains inconclusive. The case for screening people with tuberculosis for diabetes is strong on yield alone; the case for the reverse rests on an association that has not been closed.

Acknowledgements

The authors thank the investigators who reported both directions of screening separately rather than under a single heading, which is what makes the asymmetry described here visible.

Funding

No dedicated funding from public, commercial or charitable sources supported the preparation of this review.

Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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Citation: Stavrou E, Barreto T, Zilinskaite R. "Diabetes and Tuberculosis Co-Management in High-Burden Settings: A Narrative Review of Integrated Service Models". DOI: 10.5281/zenodo.22261632