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SYSTEMATIC REVIEW

Prevalence of non-communicable diseases among household contacts of people with tuberculosis: A systematic review and individual participant data meta-analysis

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Abstract

Objective: To investigate the prevalence of non-communicable diseases among household contacts of people with tuberculosis.

Methods: We conducted a systematic review and individual participant data meta-analysis. We searched Medline, Embase and the Global Index Medicus from inception to 16 May 2023. We included studies that assessed for at least one non-communicable disease among household contacts of people with clinical tuberculosis. We estimated the non-communicable disease prevalence through mixed effects logistic regression for studies providing individual participant data, and compared it with estimates from aggregated data meta-analyses. Furthermore, we compared age and sex-standardised non-communicable disease prevalence with national-level estimates standardised for age and sex.

Results: We identified 39 eligible studies, of which 14 provided individual participant data (29,194 contacts). Of the remaining 25 studies, 18 studies reported aggregated data suitable for aggregated data meta-analysis. In individual participant data analysis, the pooled prevalence of diabetes in studies that undertook biochemical testing was 8.8% (95% confidence interval [CI], 5.1%–14.9%, four studies). Age-and sex-standardised prevalence was higher in two studies (10.4% vs. 6.9% and 11.5% vs. 8.4%) than the corresponding national estimates and similar in two studies. Prevalence of diabetes mellitus based on self-report or medical records was 3.4% (95% CI 2.6%–4.6%, 14 studies). Prevalence did not significantly differ compared to estimates from aggregated data meta-analysis. There were limited data for other non-communicable diseases.

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Conclusion: The prevalence of diabetes mellitus among household contacts was high while that of known diabetes was substantially lower, suggesting the underdiagnosis. tuberculosis household contact investigation offers opportunities to deliver multifaceted interventions to identify tuberculosis infection and disease, screen for non-communicable diseases and address shared risk factors.

KEYWORDS
chronic diseases, diabetes mellitus, systematic review, tuberculosis

BACKGROUND

In 2022, an estimated 10.6 million people developed tuberculosis (TB), and 1.3 million died globally [1]. Almost 98% of TB deaths occur in low- and middle-income countries, where populations also face a rapidly rising burden of non-communicable diseases [1, 2]. Around 16 million people die from non-communicable diseases annually in low- and middle-income countries, while the number of people with an non-communicable disease rose from to 3.5 billion between 2010 and 2019 [3]. Cardiovascular diseases account for most non-communicable disease deaths, with risk increased in the presence of other non-communicable diseases such as diabetes and chronic kidney diseases [2].

There are complex interactions between TB and several non-communicable diseases. TB and one or more non-communicable diseases are often diagnosed concurrently, and the presence of one disease increases the risk of development of another [4]. People with diabetes and chronic kidney diseases have a higher incidence of TB disease than those without these conditions [5, 6]. Conversely, people diagnosed with TB may be at greater risk of subsequent development of non-communicable diseases, and potentially with greater severity [7]. For example, hyperglycaemia is more prevalent in people with TB than those without TB, even though this increase in blood glucose levels may be limited to the early post-TB diagnosis phase [7]. Other studies suggest that TB is a risk factor for development of COPD [8], lung cancer [9] and cardiovascular diseases [10, 11].

In addition to interactions between TB and non-communicable disease states, both have shared determinants, such as age, sex, HIV infection, smoking, alcohol and air pollution [12–14]. These shared determinants contribute to the overlapping epidemics in low- and middle-income countries, which are now accelerating due to rapidly aging populations and urbanisation, and shifts in socio-economic and behavioural environments.

The overlapping risk profile and disease burden of non-communicable diseases and TB is likely to be common among household contacts of people diagnosed with TB, because of the shared determinants. The clustering of non-communicable diseases and non-communicable disease risk factors within households is reported in the general population [15, 16]. However, evidence on the non-communicable disease burden among TB contacts has not been systematically reviewed. Understanding the burden of non-communicable diseases could help inform the provision of integrated care for both TB and non-communicable diseases in households affected by TB, for example, as part of contact tracing activities. Therefore, we conducted a systematic review and individual participant data meta-analysis of contact tracing studies to evaluate the prevalence of non-communicable diseases among household contacts of people with TB.

METHODS

The protocol of this systematic review has been pre-registered (CRD42021248455). The review was conducted and reported following the Preferred Reporting Items for a Systematic Review and Meta-analysis of Individual Participant Data (PRISMA-IPD) [17]. This individual participant data meta-analysis was approved by the University College London Research Ethics Committee (21569/001).

Eligibility criteria and search strategy

We included studies in low- and middle-income countries that assessed household contacts of people diagnosed with TB for the presence of at least one non-communicable disease. Non-communicable diseases of interest were: diabetes; hypertension; chronic kidney diseases or renal disease; cardiovascular diseases; chronic respiratory disease; dyslipidaemia; cancer; and mental health conditions. Case definitions for these non-communicable diseases and detailed eligibility criteria are described in Appendix S1.

We searched for studies from inception to 16 April 2021 using Medline (OVID), Embase and the Global Index Medicus, subsequently updated to 16 May 2023. Abstracts presented between January 2016 and April 2021 at the Union World Conference on Lung Health, the American Thoracic Society Conference and the European Respiratory Society International Congress were also searched. Reference lists of included papers were reviewed. No language limitation was applied. The detailed search strategy was developed in consultation with a librarian and is presented in Appendix S1.

Study selection, data extraction and quality assessment

Screening of titles and abstracts, review of full-text articles, data extraction and quality assessment were done independently by

two reviewers (YH and one of FM, KM or AT). Discrepancies were resolved through discussions.

We requested individual participant data from the study authors by email (variables requested in Appendix S1). We made at least two attempts to contact the study authors. For studies where individual participant data could not be obtained, we extracted aggregated data from study papers for the above variables. We checked individual participant data for consistency with data reported in study publications and potentially invalid and implausible values. Issues raised were resolved by contacting the study authors. We treated height and weight which are biologically implausible as missing, following criteria used in a previous study (height <111.8 cm or >228.6 cm and weight <24.9 kg or >453.6 kg) [18].

We assessed the quality of included studies using an adapted version of the National Institute of Health (NIH) quality assessment tool for observational cohort and cross-sectional studies [19]. The tool assessed (1) the participation rate of index people diagnosed with TB and (2) of contacts; (3) the diagnostic method of clinical TB (bacteriologically confirmed as per the WHO definition [20] or not bacteriologically confirmed), (4) the definition of household contacts and (5) the methods used to diagnose non-communicable diseases.

STATISTICAL ANALYSIS

Detailed statistical methods are available in Appendix S1.

Prevalence of non-communicable disease based on individual participant data meta-analysis

Where data were available, we estimated the prevalence of each non-communicable disease in household contacts aged ≥15 years. We conducted the analyses in two ways: (1) accounting for clustering within households using generalised estimating equations restricted to studies with household identifiers and (2) including all studies with no adjustment for household clustering. Because these two approaches showed similar results, we primarily reported results based on the inclusion of all studies with data, ignoring clustering within households. We used mixed effects logistic regressions to estimate prevalence, accounting for clustering of participants within studies (i.e., one-stage meta-analysis) [21]. We reported non-communicable disease prevalence estimates in forest plots with I-squared statistics. Furthermore, we pooled the prevalence of known diabetes by region; however, limited data precluded similar analyses for other non-communicable disease variables.

To further explore sources of heterogeneity, we performed additional analyses. First, we analysed associations between non-communicable diseases and contact characteristics (age, sex, current smoking status and BMI) using mixed-effects logistic regressions, including one variable at a time. Second, we conducted meta-analyses of non-communicable disease prevalence after excluding a study that only included contacts aged ≥30 years. Third, we repeated these meta-analyses restricting to contacts aged ≥30 years.

Next, we compared the prevalence of diabetes (due to limited data for other non-communicable diseases) with the national estimates from the 2019 Global Burden of Disease study [3]. Both estimates were standardised for age and sex using country-specific population estimates in 2019 [3].

Additionally, we compared the prevalence of each non-communicable disease between household contacts who were diagnosed with TB as part of contact investigations, and those not diagnosed with TB. We calculated the pooled prevalence for each group using a one-stage meta-analysis and estimated odds ratios (ORs) and 95% confidence intervals (CIs) for non-communicable disease presence via mixed-effects logistic regression models.

Finally, to evaluate the level of diabetic control in contacts with known diabetes, we estimated the median and interquartile range (IQR) of HbA1c from studies that provided such data. We reported these summary statistics across imputed datasets and the proportion of contacts with an HbA1c level below the standard target of 7.0% [22], including 95% CI.

Association between non-communicable disease in index persons with TB and contacts

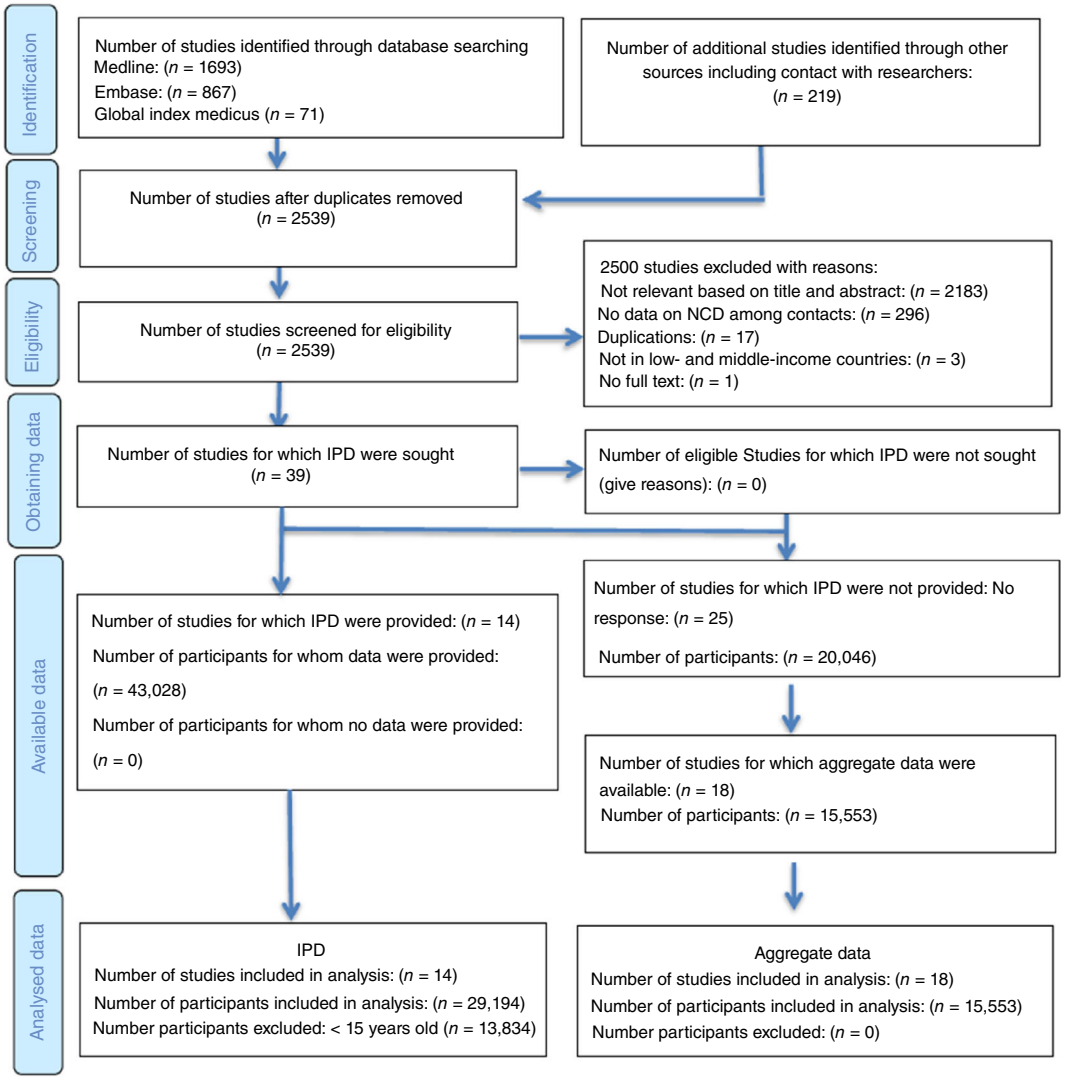
We aimed to determine whether contacts and index individuals tend to share the same non-communicable diseases, suggesting the clustering of non-communicable diseases in households affected by TB. To this end, we evaluated whether contacts of index individuals with an non-communicable disease were more likely to also have the same non-communicable disease compared to contacts of those without an non-communicable disease. To investigate this, we employed a multilevel logistic regression model using non-communicable disease status among index persons as the main exposure, and status among contacts as the outcome.

Handling of missing data

We conducted multiple imputation by multilevel fully-conditional specification to impute both outcomes and predictors [23]. For each outcome, we conducted imputations separately, restricting to studies that reported the outcome. We generated 20 multiply-imputed data sets with 20 iterations between successive imputations. Model outputs were combined using Rubin's rules [24].

Sensitivity analysis

In sensitivity analysis, we repeated the analysis of non-communicable disease prevalence using an alternative



	IPD		Aggregated data	
Outcomes	# studies included	# participants included	# studies included	# participants included
Diabetes	4	8680	6	5404
Known diabetes	14	29194	12	8506
Hypertension	4	17303	2	1107
Cardiovascular disease	4	12383	0	0
Renal disease	6	14229	3	1784
Depression	1	838	0	0

FIGURE 1 Study selection.

multiple imputation that ignored clustering within households. Second, we repeated the analyses, but excluding studies with missing data on outcomes in >50% of contacts. Third, we conducted a quantitative bias analysis using individual participant data. This aimed to explore how misclassifying diabetes status impacted the observed association between known diabetes among index people with TB and known diabetes among contacts [25]. We estimated and presented the true associations between diabetes among index people with TB and diabetes among contacts after correcting misclassification, assuming various levels of accuracy (i.e., sensitivity and specificity) of known diabetes.

Meta-analysis of aggregated data

To explore the bias due to data availability, we conducted an aggregated data meta-analysis of the prevalence of non-communicable disease using studies without individual participant data.

TABLE 1 Characteristics of studies with individual participant data.

Study	Country	*N*	Eligible age[b]	Index TB: Site/ bacteriological confirmation	Definition of household contacts	Diagnosis of diabetes	Other non-communicable diseases
Acuna-Villaorduna, 2022	Brazil	894	≥15 years	PTB/bac+	Sleeping under the same roof ≥5 days/week, sharing meals ≥5 days/ week, watching TV together on week nights or weekends, or other significant contact (85% of these visited the household ≥18 days/ month).	Not defined.	Renal disease; not defined.
Becerra, 2019	Peru	521	≥15 years	PTB/bac+	Lived in the same household as an index patient at the time the index person was enrolled in the study were invited to participate.	Not defined.	Hypertension, renal disease, heart disease; all of them were not defined.
Bekken, 2020	India	144	≥15 years	PTB/bac+	Living ≥75% of the time in the same household as the index person with TB and sharing the same kitchen.	Not defined.	Not reported.
Diaz, 2021	Colombia	138	≥15 years	PTB and EPTB/ bac+ and CD	Not reported.	Self-report.	Not reported.
Galea, 2022	Peru	838	≥15 years	PTB/bac+	Living in the same household as an index person with TB at the time the index subject is enrolled in the study.	Not defined.	Depression defined as PHQ-9 scores 5–27. Heart disease and hypertension not defined.
Grandjean, 2011	Peru	1113	≥15 years	Unspecified/ MDR-TB	Any individual who lived with the index case for >1 day each week in the period during which the index person was symptomatic with TB disease.	Not defined.	Renal disease and heart disease; both of them were not defined.
Grandjean, 2015	Peru	620	≥15 years	Unspecified/ MDR-TB	Any person living in the same house as the index person for >1 day a week.	Not defined.	Not reported.
Marin, 2017	Colombia	2464	≥18 years	PTB/bac+	Had spent time regularly (weekly) in the same household as the index person for at least a month prior to the time when the index person's diagnosis was confirmed.	Not defined.	Renal disease. "Health status upon enrolment was established by physical examination performed by a physician and specific enquiry on immunosuppressive conditions related to medication intake and concurrent diseases."
Martinson, 2021	South Africa	6695	≥15 years	PTB/bac+	All individuals who shared dwelling airspace by either having slept overnight at least once, or shared at least two meals in the same household as	RBG and self-reported.	Hypertension (BP measurement and known diagnosis). Only a subset of contacts (9.7%) had a BP measurement.

(Continues)

TABLE 1 (Continued)

Study	Country	*N*	Eligible age[b]	Index TB: Site/ bacteriological confirmation	Definition of household contacts	Diagnosis of diabetes	Other non-communicable diseases
					the index person in the 14 days prior to the index person's diagnosis of TB.		
Restrepo, 2018[a]	South Africa	323	30–65 years	PTB/bac+	Sharing at least 5 h per week in a house or closed space with a person with confirmed pulmonary TB.	RBG and point-of-care HbA1c in all.	Hypertension (self-report), renal disease and heart disease; both were not defined. These were asked only in participants with HbA1c ≥6.5% and randomly selected participants with HbA1c <6.5%.
Shivakumar, 2018	India	359	≥18 years	PTB/bac+	Resided with an adult with TB for at least 3 months before their TB diagnosis in their household.	All tested for HbA1c. DM was defined as previously diagnosed, self-reported DM or HbA1c ≥6.5%.	Renal disease; not defined.
Shu, 2017	Peru	174	≥15 years	PTB/bac+	Adult contacts of the index person who spent at least 1 day per week with the patient.	Not defined.	Not reported.
Verrall, 2022	Indonesia	1383	≥15 years	PTB/bac+	Had lived with the index person for >5 h a week and had no previous TB.	RBG in all and HbA1c for all tested for RBG >100.	Not reported.
Vo, 2023	Vietnam	2079	≥15 years	PTB and EPTB/ bac+ and CD	Persons sharing a kitchen with the index person for one or more nights in the past 3 months prior to treatment initiation of the index person.	Not defined.	Not reported.

Abbreviations: bac+, bacteriologically confirmed; BP, blood pressure; CD, clinically diagnosed; DM, diabetes; EPTB, extrapulmonary TB; MDR-TB, multidrug-resistant TB; PHQ, patient health questionnaire; PTB, pulmonary TB; RBG, random blood glucose; TB, tuberculosis.
[a]The study reported data from the Texas-Mexico border and South Africa, but we included data from South Africa only.
[b]The minimum eligible age is set at 15 years, regardless of the original age eligibility criteria, since the meta-analysis excluded participants below 15 years of age.

All analyses were performed using R Statistical Software (ver 4.3.1; R Core Team 2023) [26].

ASSESSMENT OF REPORTING BIASES

We assessed publication bias by creating a funnel plots where there were at least 10 studies in the meta-analysis [27]. We assessed the degree of asymmetry using Egger's tests [28].

RESULTS

Search results and study characteristics

From the review of 2537 records identified, 37 studies were considered potentially eligible, and their individual participant data were sought; 12 provided individual participant data (Figure 1) [29–39]. Additionally, one study was identified through contacting experts [40] and one through conference abstract searching [41], from which the authors provided individual participant data. Thus, individual participant data from 14 studies were included, comprising 29,194 contacts; 11 of them included data on 8260 index people with TB.

Among 25 studies ($N = 20{,}046$) for which individual participant data could not be obtained, aggregated data could be extracted from 18 studies ($N = 15{,}553$) [42–59]. The remaining seven studies did not report the prevalence of individual non-communicable diseases among contacts.

Among 14 studies with individual participant data made available, five were from Peru [29, 32, 33, 36, 38] and the rest were in various countries (Table 1). Studies in South America

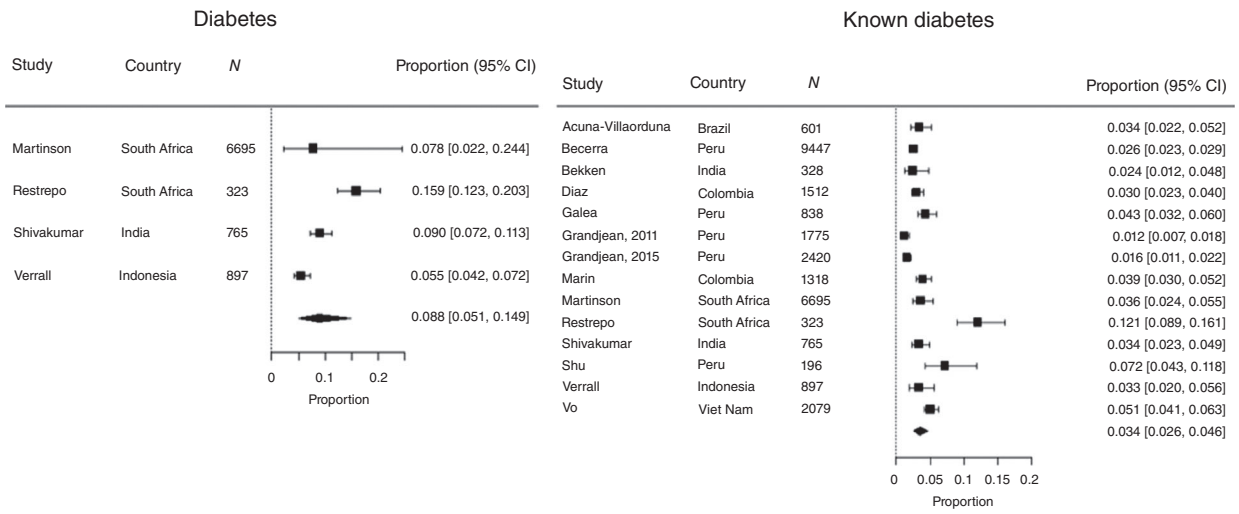


FIGURE 2 Prevalence of diabetes and known diabetes. Estimates are based on the pooling of 20 imputed datasets. The numerators vary across the imputed datasets, and thus are not presented. Diabetes: I-squared = 90.4% (95% CI 78.4%–95.7%), $p \leq 0.001$, $tau^2 = 0.26$. Known diabetes: I-squared = 91.5% (95% CI 87.5%–94.2%), $p \leq 0.001$, $tau^2 = 0.33$.

accounted for most participants (eight studies, 18,107 participants), followed by Africa (two studies, 7018 participants) and Asia (four studies, 4069 participants). Across studies, the median age of contacts was 35 years, and the majority (59.1%) were female (Table A1). The study by Restrepo et al. included only contacts aged ≥30 years, while the other studies included those aged at least 15 or 18 years. Characteristics of participants by studies are available in Table A2. Data on diabetes were available in four studies [35, 37, 40, 41], and on known diabetes in 14 studies. The availability of other non-communicable disease was variable (four studies for hypertension [29, 38, 40, 41], four for cardiovascular diseases [29, 32, 38, 41], five for renal disease [29, 32, 34, 41, 60], and one for depression [38]) (Table 1, Table A2, Figure A1). In seven studies with data, 0.2%–5.8% of contacts were diagnosed with TB. We did not find issues that could undermine individual participant data integrity. Characteristics of studies without individual participant data are presented in Table A3.

Quality of included studies is summarised in Table A4. Eleven studies included index TB patients with bacteriological confirmation, with the remainder including people with both bacteriologically-confirmed and clinically-diagnosed TB. All but one study provided a clear definition of household contacts. Three studies used a combination of blood glucose and HbA1c measurement to diagnose diabetes, and one used blood glucose alone [35, 37, 41]. Diabetes status was missing in 75.6% (5069/6695) in one study [40]; however, the other three studies had <1% of missing data [35, 37, 41]. One study defined depression as Patient Health Questionnaire-9 scores ≥5 [38]. Ascertainment methods of other diseases were insufficiently defined (Table 1). In the study by Restrepo et al [41]., the history of hypertension, renal disease and cardiovascular diseases were sought only in participants with HbA1c ≥6.5% and randomly selected participants with HbA1c <6.5%.

Prevalence of non-communicable diseases

Based on 14 studies with data made available, the pooled prevalence of known diabetes among household contacts was 3.4% (95% CI 2.6%–4.6%) (Figure 2). Prevalence ranged from 1.2% in a study in Peru [32] to 12.1% in a study in South Africa [41]. There was no evidence that the prevalence of known diabetes varied by region ($p = 0.061$) (Figure A2).

Four studies used blood tests to identify previously undiagnosed diabetes in addition to known diabetes. The pooled prevalence of diabetes (including known and newly identified diabetes) was 8.8% (95% CI 5.1%–14.9%, Figure 2).

The age-sex standardised prevalence of diabetes mellitus ranged from 5.4% to 13.2% (Figure 3). The point estimates were higher than the standardised national prevalence estimates in two studies, in South Africa (13.2%, 95% CI 9.3%–18.4% vs. 10.2%, 95% CI 8.8%–11.5%) [41] and India (11.5%, 95% CI 8.7%–15.0% vs. 8.4%, 95% CI 6.9%–9.9%), but with overlapping 95% CI [35]. Another study in South Africa had a large CI due to missing data [40], and in a study in Indonesia, the estimate was similar to the national estimate (5.4%, 95% CI 4.0%–7.3% vs. 5.3%, 95% CI 4.4%–6.2%) [39].

In three studies with data, the median HbA1c level among contacts with known diabetes was 8.6% (IQR 7.3%–11.0%), and 20.1% of these contacts had HbA1c levels below 7.0% (95% CI 13.3%–29.2%).

Data on other non-communicable diseases were limited (Figures A3–A5). Hypertension was reported in four studies, with prevalence ranging from 8.6% (95% CI 6.9%–10.7%) in a study in Peru to 42.4% (95% CI 34.8%–50.3%) in the study by Restrepo et al. in South Africa (Figure A3). Due to this large heterogeneity, we did not undertake meta-analysis of the prevalence estimates. The pooled prevalence of renal and cardiovascular disease was 1.0% (95% CI 0.4%–2.7%) and 1.6% (95% CI 0.7%–3.5%),

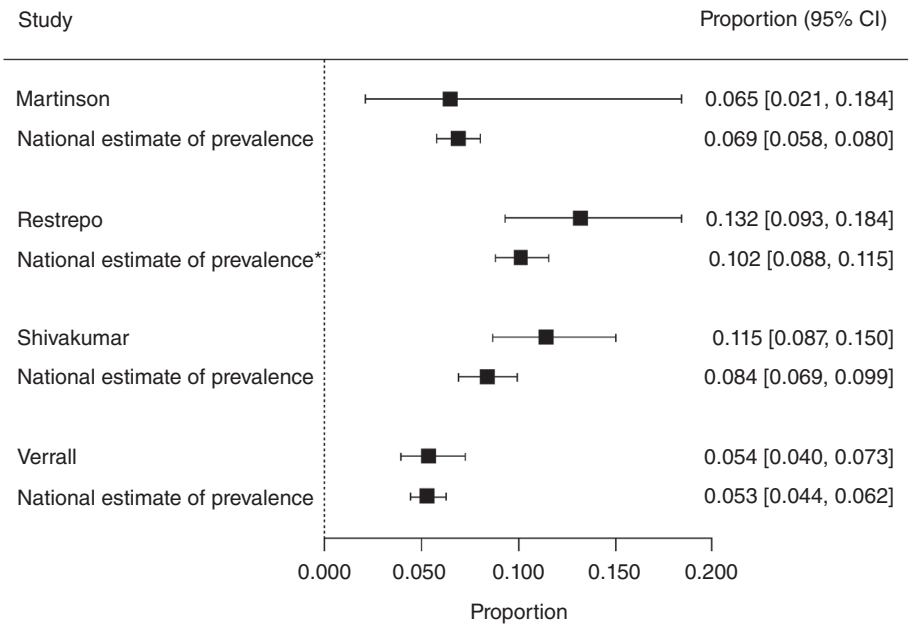


FIGURE 3 Age-sex-standardised prevalence of diabetes and the national standardised estimates. CI, confidence interval; GBD, global burden of disease. National estimates of prevalence are based on the 2019 Global Burden of Disease estimates. Both study and national estimates are standardised for age and sex using 2019 national population estimates. *To align with the Restrepo et al. study, the population is limited to those aged ≥30 years.

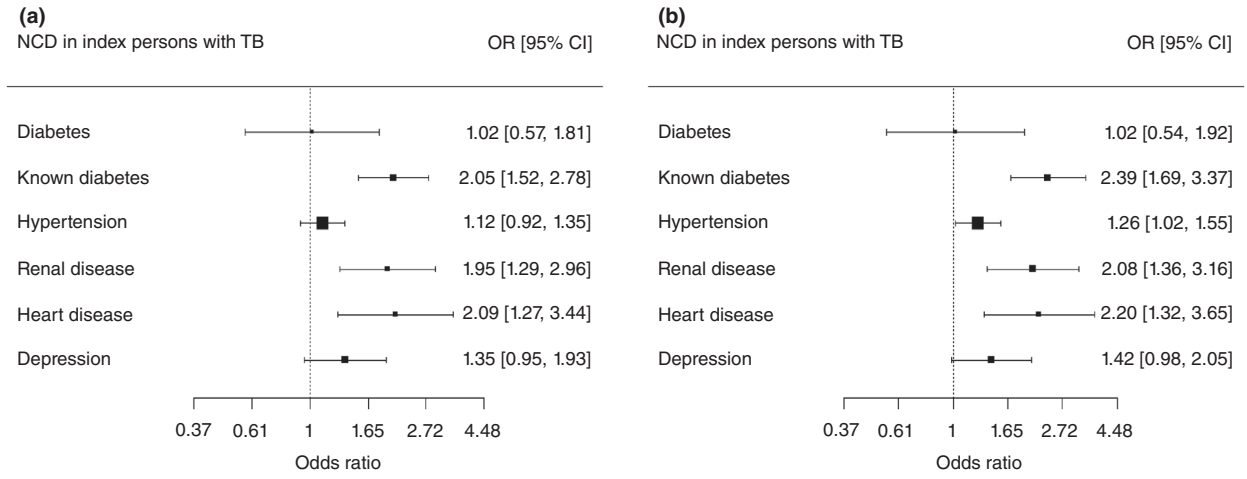


FIGURE 4 Associations between non-communicable disease in index people with TB and non-communicable disease in contacts. (a) Odds ratios were adjusted for age and sex of index people with TB. (b) Odds ratios were adjusted for age and sex of both index people with TB and household contacts. CI, confidence interval; OR, odds ratio; TB, tuberculosis. The odds ratios indicate the association between non-communicable disease in index people with TB and the same non-communicable disease in contacts (i.e., clustering of non-communicable disease).

respectively (Figures A4 and A5). Based on one study, the prevalence of depression was 22.0% (95% CI 19.3%–24.8%) [38].

Contacts who were older or female were more likely to have known diabetes, diabetes, hypertension, renal disease and cardiovascular diseases (Table A5). Similarly, contacts with a greater BMI were more likely to have known diabetes, diabetes and hypertension. Non-communicable disease prevalence did not differ significantly between contacts with and without TB (Table A6).

When restricted to contacts aged 30 years and older (Figures A6–A10), the variation in diabetes and hypertension prevalence across studies decreased, although the hypertension prevalence in the Restrepo et al. study remained higher compared to another study in South Africa (42.4, 95% CI 34.8%–50.3% vs. 26.3%, 95% CI 23.2%–39.6%). When this study was excluded from the meta-analyses, the pooled prevalence of diabetes was 7.3% (95% CI 4.1%–12.8%) and for hypertension was 11.4% (95% CI 7.7%–16.5%) (Table A7). The estimates for other

conditions were similar to those from the primary analyses.

The prevalence estimates accounting for clustering within households are presented in Table A8, and were similar to main estimates.

Association between non-communicable disease in index people with TB and non-communicable disease in contacts

When adjusted for age and sex of index people with TB, diabetes in index people with TB was not significantly associated with the presence of diabetes in contacts (odds ratio [OR] 0.84, 95% CI 0.51%–1.40%, $p = 0.95$) (Figure 4). In contrast, known diabetes, renal disease and cardiovascular diseases in people with TB were associated with the presence of the same non-communicable disease in contacts (e.g., for known diabetes, OR 2.05, 95% CI 1.52%–2.78%, $p < 0.001$). These associations remained when additionally adjusting for the age and sex of contacts (Figure 4). Depression had a similar association, although not statistically significant (OR 1.42, 95% CI 0.98%–2.05%, $p = 0.061$).

Sensitivity analysis

The prevalence of non-communicable disease was similar in a sensitivity analysis that applied multiple imputation ignoring households and another that excluded studies with missing data on outcomes in >50% of contacts (Table A9).

The quantitative bias analysis indicates that the observed association might be explained by differential misclassification of diabetes status (Figure A11). For example, when we assume a sensitivity of self-reported diabetes at 60% for individuals living with a household member diagnosed with diabetes, compared to 40% in those without any household member with diagnosed diabetes, the confidence interval for the true association overlapped with null.

Meta-analysis of aggregated data

The prevalence of non-communicable disease did not differ significantly by the availability of individual participant data, and there was no evidence of publication bias (Figures A12–A16).

Two studies without individual participant data reported the prevalence of self-reported diabetes in a control group [47, 56]. In one study in India, the prevalence of self-reported diabetes among household contacts was 2.8% (10/359) compared to 4.7% (17/361) in individuals in the same community (prevalence ratio 0.59, 95% CI 0.27%–1.27%) [47]. In another study in Chile, the prevalence was 4.9% (7/144) versus 3.2% (1/31) (prevalence ratio 1.51, 95% CI 0.19%–11.81%) when compared to healthy volunteers [56].

DISCUSSION

To our knowledge, this is the first study that synthesised the evidence on the prevalence of non-communicable diseases among contacts of people with TB. The findings revealed a high prevalence of diabetes among these contacts in contrast to the low proportion of those already diagnosed with diabetes (8.8% vs. 3.4%). This discrepancy is consistent with studies reporting a low sensitivity of self-reported diabetes [61, 62]. The gap indicates the underdiagnosis of diabetes among contacts of people with TB. If left untreated, these contacts remain at an elevated risk for TB. This calls for integrated screening and management strategies targeted at households affected by TB to bridge the diagnostic gap. Notably, a similar diagnostic gap exists in the general population. In response to this, one of the global targets set in 2022 is to diagnose 80% of all people with diabetes [63]. Integrated screening during contact investigations could serve as a collaborative model of care, helping reach this target. The prevalence of other non-communicable disease was much lower than the national estimates, most likely due to the reliance on self-report.

Our review suggests that contacts were more likely to have known diabetes and other non-communicable diseases when their index people with TB had the same conditions. This pattern may be a result of shared healthcare access within households, which increases the likelihood of non-communicable disease diagnoses rather than a true rise in prevalence. The sensitivity analysis similarly indicated that the observed association might be explained by differences in detection probabilities rather than true differences in prevalence. This might reflect more frequent underreporting among individuals from lower socio-economic backgrounds, who often have limited access to healthcare, as is usually the case for people with TB and their families. Household contact tracing could present an excellent opportunity to screen for diabetes and other non-communicable diseases among household members who otherwise lack access to care. For diabetes based on laboratory tests, no association was found with diabetes among index people with TB. However, since the confidence interval was wide, the clustering of diabetes and other non-communicable disease in households affected by TB cannot be excluded.

There has been a global push for the integrated screening and management of TB and its comorbidities, notably diabetes [64, 65]. Despite this, policy adoption and implementation remain suboptimal. Recent data reveals that 20 of the 30 countries with a high TB burden refer to diabetes screening in TB patients in their guidelines but less than one-third have included it in their national strategic plans [66]. Moreover, programmatic data on the implementation are lacking. Contact investigation is a critical component of TB programmes, serving as a gateway for TB preventive treatment and improved TB detection. Leveraging this for non-communicable disease screening benefits people with TB as well as their families, promoting a holistic approach. Such a household-wide

integration can address multiple diseases that are risk factors for TB and, if left unmanaged, can worsen both TB and non-communicable disease outcomes.

In our study, the prevalence of diabetes among contacts with TB did not differ significantly from those without TB in the same household. This appears to contrast with the well-established association between diabetes and TB development which suggest higher prevalence of diabetes in TB cases. The point prevalence of diabetes among contacts with TB was lower than that reported among TB cases in a systematic review though direct comparisons are challenging due to differences in settings and populations [67]. The lower prevalence in our study could partly be attributed to the earlier identification of TB through contact investigation, as opposed to passively detected TB cases. However, the wide confidence interval for the diabetes prevalence (8.4%, 95% CI 2.7%–22.9%) in our study suggests that the upper range is still consistent with an increased prevalence. Similar diabetes prevalence observed between contacts in the same household with and without TB might also suggest clustering of predisposing factors between the groups, given our control group is from the same households rather than a comparison with the general population.

There is limited information about the health of TB affected households. We found a small number of studies that undertook standard assessments for non-communicable diseases, limiting our ability to combine data in individual participant data analysis. Furthermore, the comparative non-communicable disease burden relative to other households is unclear. We attempted to compare with the general population through age and sex standardisation; however, the results were inconclusive due to wide confidence intervals and the indirect nature of comparisons. Another review, using data from national TB prevalence surveys, suggested that smoking may cluster in TB-affected households, but data on non-communicable diseases were similarly sparse [68]. A recent study in India reported that over a third of household contacts had undernutrition [69]. The prevalence was higher than the state average, possibly due to the poor socioeconomic status of TB affected households. Nonetheless, comparative data on undernutrition among other households in the same community or different settings are lacking. The lack of information about the health status of TB-affected households is a missed opportunity to develop targeted healthcare strategies. This review highlighted the need for more studies using standard non-communicable disease diagnostic methods (e.g., HbA1c for diabetes) among household contacts. Additionally, there is a necessity to investigate other conditions that may commonly affect these individuals. Conducting such studies would help improve health interventions tailored to the specific needs of TB-affected households.

A limitation of this review was the small proportion (38%) of eligible studies that provided individual participant data. Challenges in data retrieval are common, especially when including non-randomised studies [70]. Low data retrieval rates may result in bias. We mitigated this risk by conducting a meta-analysis using aggregate data, which did not suggest a substantial difference in the estimates by the availability of datasets. Moreover, the number of studies available per region was small, limiting regional sub-group analyses to known diabetes, with data from Africa confined to South Africa. Given the documented variability in diabetes prevalence across regions—with higher rates in South America and Southeast Asia compared to Africa [71]—a similar variation in contact prevalence might be expected, though this remains unconfirmed. Lastly, Restrepo et al. collected data on hypertension, chronic kidney diseases and cardiovascular diseases only in participants with HbA1c ≥6.5% and randomly selected participants with HbA1c <6.5%. However, we were able to recover missing information using multiple imputation including diabetes status (i.e., HbA1c ≥6.5%). Thus, the difference in the hypertension prevalence is likely to be attributed to other factors such as the likelihood of diagnosis since most hypertension cases were based on self-report.

CONCLUSION

Our study showed a high prevalence of diabetes among contacts, compared to a low prevalence of known diabetes, highlighting a gap in the diagnosis. This suggests a need for integrated screening and management targeted to households affected by TB. It, however, remains inconclusive whether contacts have a higher prevalence of diabetes than the general population. Future studies should address this knowledge gap by applying systematic diabetes screening with a control group from the same geographic areas. Furthermore, prospective household control studies using standard diagnostic methods are needed to address limited data on other non-communicable diseases.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The individual participant data database is stored within the UCL Data Repository and can be shared subject to the approval of the corresponding authors of the original studies.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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