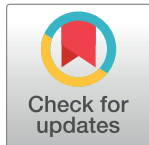


RESEARCH ARTICLE

Diabetes mellitus and tuberculosis, a systematic review and meta-analysis with sensitivity analysis for studies comparable for confounders

Joseph Rodrigue Foe-Essomba^{1,2,3}, Sebastien Kenmoe⁴, Serges Tchatchouang⁵, Jean Thierry Ebogo-Belobo⁶, Donatien Serge Mbaga⁷, Cyprien Kengne-Ndé⁸, Gadji Mahamat⁷, Ginette Irma Kame-Ngasse⁶, Efiengab Atembeh Noura⁶, Chris Andre Mbongue Mikangue⁷, Alfloditte Flore Feudjio⁹, Jean Bosco Taya-Fokou⁷, Sabine Aimee Touangnou-Chamda⁷, Rachel Audrey Nayang-Mundo¹⁰, Inès Nyebe⁷, Jeannette Nina Magoudjou-Pekam⁹, Jacqueline Félicité Yéngué¹¹, Larissa Gertrude Djukou⁹, Cynthia Paola Demeni Emoh⁷, Hervé Raoul Tazokong⁷, Arnol Bowo-Ngandji⁷, Eric Lontchi-Yimagou¹², Afi Leslie Kaiyven¹³, Valerie Flore Donkeng Donfack³, Richard Njoum⁴, Jean Claude Mbanya¹², Wilfred Fon Mbacham¹⁴, Sara Eyangoh^{3*}



1 Camdiagnostic, Ministry of Scientific Research and Innovation, Yaounde, Cameroon, **2** Faculty of Medicine and Biomedical Sciences, The University of Yaounde I, Yaounde, Cameroon, **3** Department of Mycobacteriology, Centre Pasteur of Cameroon, Yaounde, Cameroon, **4** Virology Department, Centre Pasteur of Cameroon, Yaounde, Cameroon, **5** Bacteriology Department, Centre Pasteur of Cameroon, Yaounde, Cameroon, **6** Medical Research Centre, Institute of Medical Research and Medicinal Plants Studies, Yaounde, Cameroon, **7** Department of Microbiology, The University of Yaounde I, Yaounde, Cameroon, **8** Evaluation and Research Unit, National AIDS Control Committee, Yaounde, Cameroon, **9** Department of Biochemistry, The University of Yaounde I, Yaounde, Cameroon, **10** Department of Microbiology, Protestant University of Central Africa, Yaounde, Cameroon, **11** Department of Animals Biology and Physiology, The University of Yaounde I, Yaounde, Cameroon, **12** Laboratory for Molecular Medicine and Metabolism, The University of Yaounde I, Yaounde, Cameroon, **13** Institute of Biomedical and Clinical Research, University of Exeter, Exeter, United Kingdom, **14** The Biotechnology Centre, The University of Yaounde I, Yaounde, Cameroon

* eyangoh@pasteur-yaounde.org

OPEN ACCESS

Citation: Foe-Essomba JR, Kenmoe S, Tchatchouang S, Ebogo-Belobo JT, Mbaga DS, Kengne-Ndé C, et al. (2021) Diabetes mellitus and tuberculosis, a systematic review and meta-analysis with sensitivity analysis for studies comparable for confounders. *PLoS ONE* 16(12): e0261246. <https://doi.org/10.1371/journal.pone.0261246>

Editor: Antonio Palazón-Bru, Universidad Miguel Hernandez de Elche, SPAIN

Received: May 17, 2021

Accepted: November 28, 2021

Published: December 10, 2021

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0261246>

Copyright: © 2021 Foe-Essomba et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Introduction

Meta-analyses conducted so far on the association between diabetes mellitus (DM) and the tuberculosis (TB) development risk did not sufficiently take confounders into account in their estimates. The objective of this systematic review was to determine whether DM is associated with an increased risk of developing TB with a sensitivity analyses incorporating a wider range of confounders including age, gender, alcohol consumption, smoke exposure, and other comorbidities.

Methods

Pubmed, Embase, Web of Science and Global Index Medicus were queried from inception until October 2020. Without any restriction to time of study, geographical location, and DM and TB diagnosis approaches, all observational studies that presented data for associations between DM and TB were included. Studies with no abstract or complete text, duplicates,

Data Availability Statement: All relevant data are within the paper and its S1–S3 Figs, S1–S8 Tables files.

Funding: - Initials: SK - Grant number:

VARIAFRICA-TMA2019PF-2705 - URL: <http://www.edctp.org/projects-2/edctp2-projects/edctp-preparatory-fellowships-2019/> - The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. This project is part of the EDCTP2 programme supported by the European Union under grant agreement TMA2019PF-2705.

Competing interests: The authors have declared that no competing interests exist.

and studies with wrong designs (review, case report, case series, comment on an article, and editorial) or populations were excluded. The odds ratios (OR) and their 95% confidence intervals were estimated by a random-effect model.

Results

The electronic and manual searches yielded 12,796 articles of which 47 were used in our study (23 case control, 14 cross-sectional and 10 cohort studies) involving 503,760 cases (DM or TB patients) and 3,596,845 controls. The size of the combined effect of TB risk in the presence of DM was OR = 2.3, 95% CI = [2.0–2.7], $I^2 = 94.2\%$. This statistically significant association was maintained in cohort (OR = 2.0, CI 95% = [1.5–2.4], $I^2 = 94.3\%$), case control (OR = 2.4, CI 95% = [2.0–2.9], $I^2 = 93.0\%$) and cross-sectional studies (OR = 2.5, CI 95% = [1.8–3.5], $I^2 = 95.2\%$). The association between DM and TB was also maintained in the sensitivity analysis including only studies with similar proportions of confounders between cases and controls. The substantial heterogeneity observed was mainly explained by the differences between geographic regions.

Conclusions

DM is associated with an increased risk of developing latent and active TB. To further explore the role of DM in the development of TB, more investigations of the biological mechanisms by which DM increases the risk of TB are needed.

Review registration

PROSPERO, [CRD42021216815](https://doi.org/10.1371/journal.pone.0261246).

Introduction

About 25% of the global population is infected with *Mycobacterium tuberculosis* (MTB) [1], including nearly 10 million new cases of active tuberculosis (TB) and 1.5 million deaths recorded each year [2]. These statistics have crowned TB as one of the leading causes of death from infectious diseases worldwide. MTB infections are more prevalent in developing regions of Southeast Asia (44%), Africa (25%) and the West Pacific (18%), with 2/3 of cases recorded in India, Indonesia, China, Philippines, Pakistan, Nigeria, Bangladesh and South Africa [2]. The International Diabetes Federation estimated that nearly half a billion people (about 10% of the global population) were living with diabetes mellitus (DM) each year, including more than 4 million deaths [3]. This incidence is predicted to increase by more than 10% by 2045, leading to about 700 million cases. The majority of people living with DM are registered in the urban areas of low-and middle-income countries where TB is also dominant. Five of 8 countries with the highest incidence of TB are among the 10 countries with the highest prevalence of DM [2, 3].

Compared to patients with TB only, patients with TB and DM are more likely to have more severe clinical pictures, greater infectivity, treatment failure for TB, relapses after recovery, and high mortality [4–8]. The global escalation of DM and TB epidemics is therefore detrimental and especially for low-resource countries where a very high proportion of DM remains undiagnosed or untreated due to poor resourced health systems [9, 10]. This high increase of DM patients in areas with high TB endemicity is of great concern to TB control efforts because

numerous studies have suggested that DM increases the risk of developing latent and active TB [11, 12]. Diabetes mellitus is indeed a disease that can alter the host's immunity and lead to increased susceptibility to several diseases including tuberculosis [13]. The association between DM and TB has been established in several systematic reviews including active TB [14, 15], latent TB [16] and multidrug-resistant TB [17, 18]. There are multiple confounding factors for the association between DM and TB, the main ones being: HIV infections [19, 20], undernutrition [21], smoking and alcoholism [22, 23]. Although all of these reviews have been devoted to the association between DM and TB, apart from adjusting analyses for age [14, 24], other major confounding factors such as HIV infection, alcohol or smoke exposure have received very little attention. In view of the increasing incidence of DM epidemic, further evidence of the association of DM and TB would be of crucial importance in the fight against the double DM-TB epidemic [25]. Furthering this knowledge could include implications such as the implementation of education, prevention, two-way early detection and co-management programs for MD and TB [26]. In this meta-analysis, including a sensitivity analysis with studies with similar proportions of confounders among cases and controls, we further assess the association between DM and TB.

Methods

Literature search

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed for the preparation (PROSPERO ID = CRD42021216815, https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021216815) and writing of this review (S1 Table). A comprehensive search strategy for relevant articles was applied in several electronic databases including Pubmed, Embase, Web of Science, and Global Index Medicus. We searched from the date the databases were created to October 2020. The search terms covered exposure (DM) and outcome (TB) (S2 Table). Beyond this electronic search, we performed an additional review of the bibliographic references of relevant works for additional inclusions.

Inclusion and non-inclusion criteria

We included in the present review, all observational studies (cohort, case-control and cross-sectional) which investigated the association between DM and TB without any restriction by geographic location, time and DM and TB diagnostic approaches. The studies included were those written in English or French. Excluded from this review were studies for which we did not have access to the abstract and/or full-text, duplicates, studies with designs or populations inappropriate for the purposes of the present work.

Study selection and data extraction

The results of the manual and electronic search were screened by two investigators (JETB and SK) using the Rayyan review application. Eligibility and data extraction from full texts were carried out by all investigators in this review. The following parameters were extracted from the included articles: first author, year of publication, study design, sampling approach, timing (retrospectively/prospectively) of (exposure follow up, timing of DM and TB testing), country, study period and duration, age range of participants, DM and TB testing approaches, DM and TB case definition, inclusion and exclusion criteria, pairing parameters, data on qualitative and quantitative confounding factors and data on the total numbers of cases (diabetic or TB) and controls. Qualitative confounders included gender, smoking, alcohol consumption, HIV infection, malignant diseases, chronic kidney diseases, and several other socio-demographic

and co-morbidities. Quantitative confounders included age, body mass index, and several other blood components. Discussion and consensus among investigators were used if there were any disagreement.

Quality assessment

The quality of the included observational studies was assessed according to the Joanna Briggs Institute scale (S3 Table) [27]. The cross-sectional, case-control and cohort studies consisted of 8, 10 and 11 questions respectively with the expected answers being (Yes, No, Unclear or Not applicable). We attributed 1 mark for the answers (Yes) and 0 for the other answers (No, Unclear and Not applicable). We rated studies as having low, moderate, and high risk of bias according to total marks per study. All investigators in this study independently collected answers to the Joanna Briggs Institute scale questions in duplicate. Disagreements were resolved by discussion and consensus.

Statistical analysis

We opted to group the results according to study designs (cross-sectional, control cases, and cohorts). We selected the data from the reference methods (culture for active TB, IGRA for latent TB, and OGTT for DM) in studies reporting multiple data on the relationship between DM and TB for the same population. The odds ratio (OR), its confidence interval (95% CI) and the prediction interval were calculated using random-effects models on the R software version 4.0.3 [28]. Egger's test (< 0.1) and funnel charts (asymmetric distribution) were used to indicate the existence of publication bias [29]. The Chi-square test and the I² and H indices were used to estimate heterogeneity in the estimates [30]. Subgroup analyses and metaregression were used to investigate the parameters responsible for the heterogeneity. Parameters included in these subgroup analyses included sampling method, number of study sites, timing of DM and TB testing, country, country income level [31], and study duration. P values < 0.05 indicated statistical significance. Sensitivity analyses that included only studies with a low risk of bias and studies comparable with regard to confounding factors were performed to enhance the accuracy of our results. We determined the comparability of studies with confounding factors using Chi-square, Fisher or Student's T-test as reported previously [32].

Results

Study selection

The electronic search yielded 12,742 articles from PubMed (6725), Web of Science (6123), Embase (693), and Global Index Medicus (201). Manual search yielded 54 additional articles (Fig 1). From these, the eligibility review resulted in 201 articles and the exclusion brought this number to 154 (S4 Table) and finally the inclusion resulted 47 articles used (49 effect estimates) in this review [33–79].

Summary characteristics of included studies

The detailed description of the individual characteristics of the included studies is presented in Table 1. The included studies were published between 1992 and 2020. Cases (TB), controls (non-TB), exposed (diabetics) and unexposed (non-diabetics) were recruited from 1976 to 2018. The majority of studies had a case-control design (23/49), while 16 were cross-sectional and 10 cohort studies. No investigator of the included studies performed a prospective follow-up of exposed/unexposed subjects in the included studies. Five studies were representative of the national population. Included studies were performed in 18 countries spread across

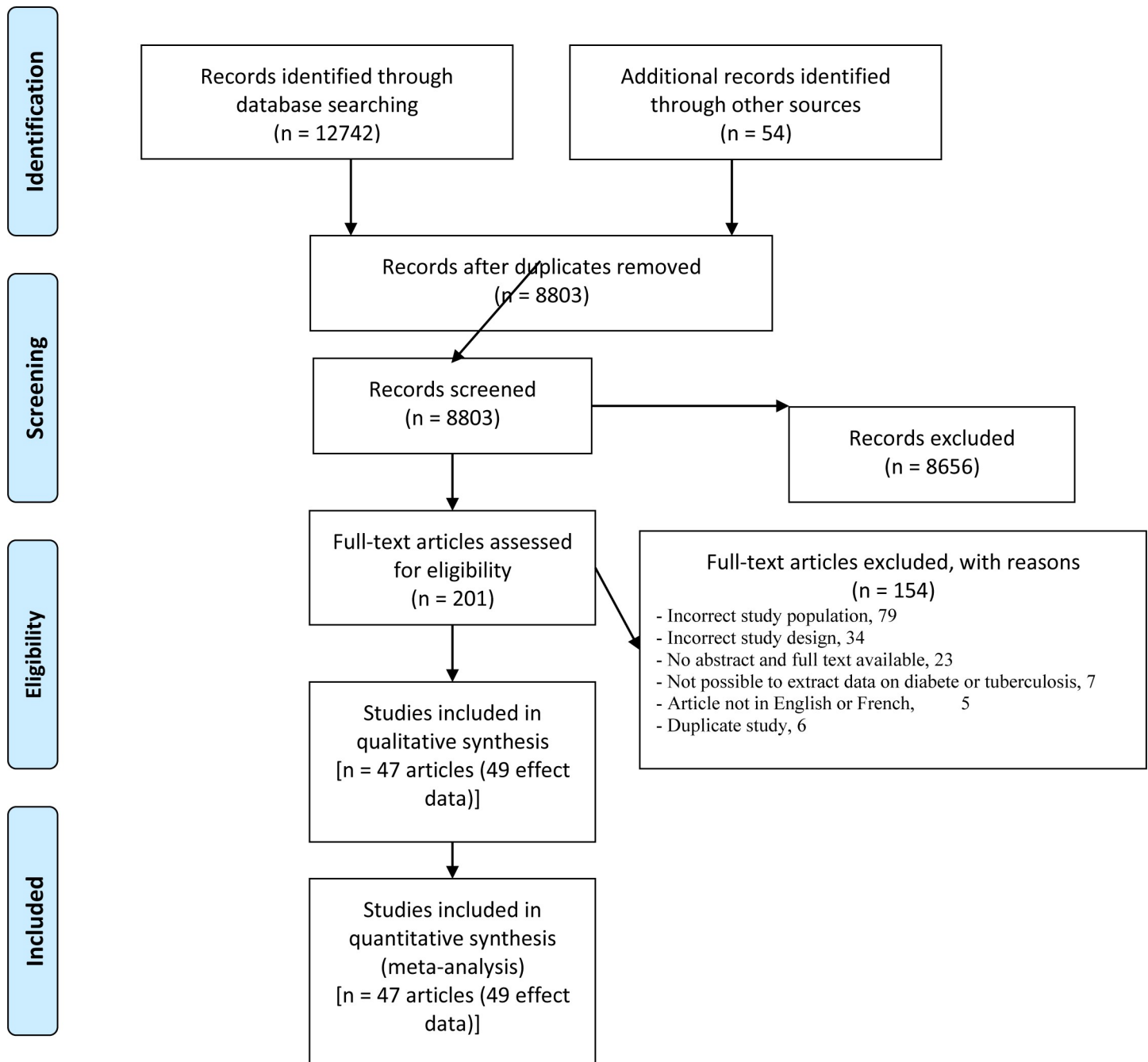


Fig 1. PRISMA flow-chart of studies selected for the meta-analysis.

<https://doi.org/10.1371/journal.pone.0261246.g001>

different regions of the world and more particularly in China (16/49) and the United States of America (11/49). High-income countries (26/49) were the most represented and only one study was conducted in low-income countries [46]. The vast majority of studies recruited adults over 15 years old. Apart from studies with multiple diagnostic methods, the International Classification of Diseases (ICD) code was the most widely used approach for DM (10/26) and TB (11/20). Nineteen included studies paired reference with controls with at least one parameter.

Table 1. Individual characteristics of included studies.

Study Design	Country	Study period	TB stage	TB diagnosis approach	DM diagnosis approach	Controls	Matched parameters between cases and controls	Author, Year
Case control	Indonesia	Mar/2001-Mar/2005	Active TB	Clinical, chest X-rays, Microscopy	Fasting blood glucose	Presumed healthy controls	Age, Gender, county of residence	Alisjahbana, 2006 [33]
Cross sectional	China	Aug/2001-Dec/2004	Active TB	ICD code, Medical records	ICD code, Medical records	Non-DM	Unclear/ Not reported	Baker, 2012 [34]
Cross sectional	United States of America	2011–2012	Latent TB infection	IGRA Test, Tuberculin skin test	Doctor-diagnosed DM, Glycated hemoglobin A1c test	Non-TB diseases	Unclear/ Not reported	Barron, 2018 –DM [35]
Cross sectional	United States of America	2011–2012	Latent TB infection	IGRA Test, Tuberculin skin test	Doctor-diagnosed DM, Glycated hemoglobin A1c test	Non-TB diseases	Unclear/ Not reported	Barron, 2018 – PreDM [35]
Case control	Tanzania	Jun/2012-Dec/2013	Active TB	Clinical, chest X-rays, Microscopy	Fasting blood glucose, Oral glucose tolerance test, Glycated hemoglobin A1c test	Presumed healthy controls	Age, Gender	Boillat-blanc, 2016 [36]
Case control	United States of America	Sep/1998-Dec/2003	Active TB	ICD code	ICD code	Presumed healthy controls	Unclear/ Not reported	Brassard, 2006 [37]
Case control	United States of America	1988–1990	Active TB	Microscopy, Culture, PCR	Unclear/ Not reported	Non-TB diseases	Unclear/ Not reported	Buskin, 1994 [38]
Cross sectional	China	Jan/1983- Dec/2003	Active TB	Clinical, chest X-rays, Culture	Unclear/ Not reported	Non-TB diseases	Unclear/ Not reported	Chen, 2006 [39]
Case control	China	1997–2010	Active TB	ICD code	ICD code	Presumed healthy controls	Age, Gender, Recruitment time	Chung, 2014 [40]
Case control	United States of America	1976–1980	Active TB	Doctor-diagnosed TB	Doctor-diagnosed DM, Oral glucose tolerance test	Non-TB diseases	Unclear/ Not reported	Corris, 2012 [41]
Case control	Kazakhstan	Jun/ 2012- May/ 2014	Active TB	Clinical, chest X-rays, Culture	Doctor-diagnosed DM	Presumed healthy controls	County of residence	Davis, 2017 [42]
Case control	Tanzania	Apr/2006-Jan/2009	Active TB	Microscopy, Culture	Fasting blood glucose, Oral glucose tolerance test	Presumed healthy controls	Age, Gender	Faurholt-Jepsen, 2011 [44]
Cross sectional	Tanzania	Apr/ 2006— Mar/ 2009	Active TB	Culture	Fasting blood glucose, Oral glucose tolerance test	Presumed healthy controls	Age, Gender	Faurholt-Jepsen, 2014 [43]
Cohort	United States of America	Jan/ 2001— Dec/ 2011	Active TB	chest X-rays	ICD code, Fasting blood glucose	Non-DM	Unclear/ Not reported	Golub, 2019 [45]
Case control	Guinea-Bissau	July/2010-July/2011	Active TB	Clinical, chest X-rays, Microscopy	Fasting blood glucose, Random blood sugar test	Presumed healthy controls	Unclear/ Not reported	Haraldsdottir, 2015 [46]
Cross sectional	United States of America	October/ 2013-August/ 2014	Latent TB infection	chest X-rays, IGRA Test	Glycated hemoglobin A1c test	Non-TB diseases	Unclear/ Not reported	Hensel, 2016 [47]
Case control	Bangladesh	Jan/2008-Jul/2008	Active TB	Microscopy	Oral glucose tolerance test	Non-TB diseases	Unclear/ Not reported	Hossain, 2014 [48]
Case control	United Kingdom	1990–2001	Active TB	Medical records	Medical records	Presumed healthy controls	Age, Gender, County of residence	Jick, 2006 [49]
Case control	Croatia	2006–2008	Active TB	Culture	Unclear/ Not reported	Non-TB diseases	Age, Gender, county of residence	Jurcev-Savicevic, 2013 [50]

(Continued)

Table 1. (Continued)

Study Design	Country	Study period	TB stage	TB diagnosis approach	DM diagnosis approach	Controls	Matched parameters between cases and controls	Author, Year
Cross sectional	Thailand	Mar/2012-Mar/2013	Latent TB infection	Tuberculin skin test, IGRA Test	Unclear/ Not reported	Presumed healthy controls	Unclear/ Not reported	Khawcharoenporn, 2015 [51]
Cohort	Korean	1988–1990	Active TB	chest X-rays, Microscopy, Culture	Glucose oxidase test	Non-DM	Unclear/ Not reported	Kim, 1995 [52]
Cross sectional	India	May/2014-Nov/2015	Active TB	Tuberculin skin test, Microscopy, Culture	Clinical, Random blood sugar test	Presumed healthy controls	Unclear/ Not reported	Kubiak, 2019 [53]
Cohort	China	2000–2011	Active TB	ICD code	ICD code	Presumed healthy controls	Age, Gender	Kuo, 2013 [54]
Case control	China	1998–2011	Active TB	ICD code	ICD code	Non-TB diseases	Age, Gender	Lai, 2014 [55]
Cohort	China	1997–2007	Active TB	ICD code	ICD code	Non-DM	Age, Gender, Recruitment time	Lee, 2013 [56]
Case control	China	2006–2017	Active TB	Clinical, Medical records, chest X-rays, Microscopy, Culture	ICD code, Medical records, Fasting blood glucose, Glycated hemoglobin A1c test	Non-TB diseases	Unclear/ Not reported	Lee, 2014 [58]
Cohort	China	Mar/2005-Dec/2012	Active TB	ICD code, Medical records	Fasting blood glucose	Non-DM	Unclear/ Not reported	Lee, 2016 [57]
Case control	Denmark	Jan/1980-Dec/2008	Active TB	ICD code	Clinical, Medical records, Glycated hemoglobin A1c test	Non-TB diseases	Age, Gender, county of residence	Leegaard, 2011 [59]
Cohort	China	Jan/2000—Dec/2005	Active TB	Clinical, Medical records, chest X-rays, Histopathology, Culture	Glycated hemoglobin A1c test	Non-DM	Unclear/ Not reported	Leung, 2008 [60]
Cohort	China	2000–2009	Active TB	ICD code	ICD code	Non-DM	Age, Gender, Recruitment time	Lin, 2017 [62]
Cohort	China	2005–2013	Latent TB infection	Clinical, chest X-rays, Tuberculin skin test, IGRA Test	Doctor-diagnosed DM	Non-DM	Unclear/ Not reported	Lin, 2019 [61]
Case control	India	Jan/1983-Dec/1989	Active TB	Tuberculin skin test	Medical records, Fasting blood glucose, Any glucose level	Non-TB diseases	Unclear/ Not reported	Mori, 1992 [63]
Case control	Romania	Mar/2014—Mar/2015	Active TB	Microscopy, Culture, PCR	Unclear/ Not reported	Non-TB diseases	Age, Gender, county of residence	Ndishimye, 2017 [64]
Case control	United States of America	1991	Active TB	ICD code	ICD code	Non-TB diseases	Unclear/ Not reported	Pablos-Méndez, 1997 [65]
Cohort	United Kingdom	Jan/1990-Dec/2012	Active TB	ICD code	ICD code	Non-DM	Age, Gender	Pealing, 2015 [66]
Case control	Brazil	Aug/2008-Apr/2010	Active TB	Clinical, Microscopy, Culture	Fasting blood glucose, Oral glucose tolerance test	Non-TB diseases	Age, Gender	Pereira, 2016 [67]
Case control	United States of America	1999–2001	Active TB	ICD code	ICD code	Non-TB diseases	Unclear/ Not reported	Pérez, 2006 [68]
Cohort	China	2002–2011	Active TB	ICD code	ICD code	Non-DM	Gender	Shen, 2014 [69]
Case control	Japan	Jan/2015-Dec/2018	Active TB	Clinical, chest X-rays, IGRA Test, Microscopy, Culture, PCR	Doctor-diagnosed DM	Non-TB diseases	County of residence	Shimouchi, 2020 [70]

(Continued)

Table 1. (Continued)

Study Design	Country	Study period	TB stage	TB diagnosis approach	DM diagnosis approach	Controls	Matched parameters between cases and controls	Author, Year
Cross sectional	China	Mar/2011-Feb/2012	Latent TB infection	ELISA, Microscopy, Culture	Unclear/ Not reported	Non-TB diseases	Unclear/ Not reported	Shu, 2012 [71]
Cross sectional	United States of America	Apr/2005-Mar/2012	Latent TB infection	Tuberculin skin test, IGRA Test	Medical records	Non-DM	Unclear/ Not reported	Suwanpimolkul, 2014 [72]
Cross sectional	United States of America	Apr/2005-Mar/2012	Active TB	Tuberculin skin test, IGRA Test	Medical records	Non-DM	Unclear/ Not reported	Suwanpimolkul, 2014 [72]
Cross sectional	Malaysia	Oct/2014-Dec/2015	Latent TB infection	Clinical, chest X-rays, Tuberculin skin test, Microscopy	Fasting blood glucose, Glycated hemoglobin A1c test, Random blood sugar test	Non-DM	Unclear/ Not reported	Swarna Nantha, 2017 [73]
Cross sectional	China	Jan/2011-Dec/2012	Latent TB infection	Medical records, chest X-rays, IGRA Test	Unclear/ Not reported	Non-TB diseases	Unclear/ Not reported	Ting, 2014 [74]
Case control	Republic of Kiribati	Jun/2010-Mar/2012	Latent TB infection	Clinical, Doctor-diagnosed DM, chest X-rays, Tuberculin skin test, Microscopy, Culture	Glycated hemoglobin A1c test	Non-TB diseases	Unclear/ Not reported	Viney, 2015 [75]
Cross sectional	China	Sep/2010-Dec/2012	Active TB	Clinical, chest X-rays, Microscopy	Fasting blood glucose	Non-TB diseases	County of residence	Wang, 2013 [76]
Cross sectional	Indonesia	2014–2015	Active TB	Doctor-diagnosed DM	Doctor-diagnosed DM	Non-TB diseases	Unclear/ Not reported	Wardhani, 2019 [77]
Cross sectional	China	Jan/2002-Dec/2004	Active TB	Culture	Medical records	Presumed healthy controls	Unclear/ Not reported	Wu, 2007 [78]
Case control	Kazakhstan	Jun/2012-Jan/2013	Active TB	Clinical, chest X-rays, Microscopy, Culture, PCR	Unclear/ Not reported	Presumed healthy controls	Age	Zhussupov, 2016 [79]

DM: Diabetes Mellitus; ICD: International Classification of Diseases; TB: Tuberculosis.

<https://doi.org/10.1371/journal.pone.0261246.t001>

Risk of bias in included studies

The methodological quality of the included studies is shown in S5 Table. Overall, the included studies had a low risk of bias (32/49). Most of the included studies collected data and considered confounding factors in the analysis of the association between DM and the TB development risk. In cohort studies, diabetic and nondiabetic patients were generally recruited from the same population, diagnosed with DM and TB in the same way, tested for absence of TB at the start of the follow-up, and followed up with a completeness rate. TB and non-TB patients recruited from case control studies were generally comparable and diagnosed with TB and DM in the same way. In cross-sectional studies, the study context and inclusion criteria for participants were well defined.

Meta-analysis

In this meta-analysis, 503,760 cases (diabetic or TB) and 3,596,845 controls were considered to calculate the combined effect of the association between DM and the TB risk. Regarding the study design, the 49-effect estimate showed an increased risk of developing TB in diabetic patients (OR = 2.3, 95% CI = [2.0–2.7]) (Fig 2). This overall effect was associated with substantial heterogeneity ($I^2 = 94.2\%$ [93.0–95.1]). The association between DM and the risk of developing TB was conserved in the 10 cohort (OR = 2.0, CI 95% = [1.5–2.4]), the 23 case-control

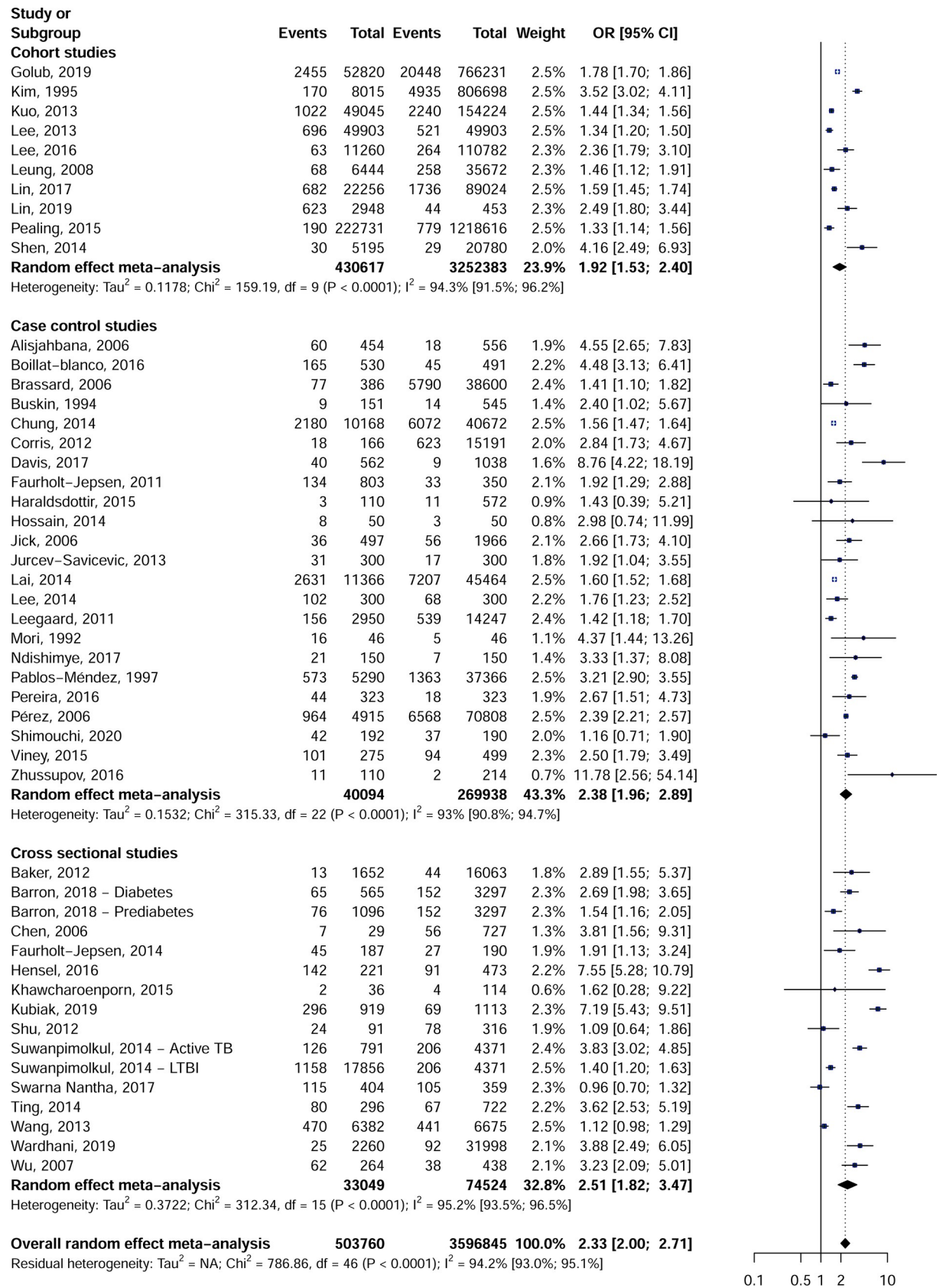


Fig 2. Association between diabetes mellitus and risk of tuberculosis in cohort, case control and cross-sectional studies.

<https://doi.org/10.1371/journal.pone.0261246.g002>

(OR = 2.4, CI 95% = [2.0–2.9]) and 16 cross-sectional studies (OR = 2.5, CI 95% = [1.8–3.5]). A significant publication bias was recorded in the cross-sectional (p Egger = 0.058) and the case-control studies (p Egger = 0.093) unlike the cohort studies (p Egger = 0.417) which did not present any publication bias (Table 2, S1–S3 Figs). Considering only studies with low risk of bias sensitivity analysis did not reveal any difference from the overall results. The data collected for 81 qualitative variables and 16 quantitative variables considered to be confounding factors enabled us to select studies that had similar proportions in references and controls (S6 and S7 Tables). For cohort studies, sensitivity analyses including only comparable studies for confounding factors showed similar results to overall results, including factors such as HIV infection, malignancies and age. For the case-control studies, the same trend was observed for the sensitivity analysis including only comparable studies mainly for alcohol drinkers, chronic kidney disease, drug users, HIV infected patients, tobacco exposure, and age. For the cross-sectional studies, on the other hand, the overall effect observed was lost for the sensitivity analyses including only comparable studies for certain confounding factors including chronic kidney disease, patients with cirrhosis of the liver or malignant diseases.

Source of heterogeneity examination

The potential sources of heterogeneity were explored by the subgroup analyses. These sources included country, UNSD region, country income level, TB stage (active vs latent), and type of controls (S8 Table). In the cohort, control and cross-sectional designs only the geographic location (countries and UNSD regions) contributed to a source of heterogeneity (p subgroup difference <0.05). In cohort studies, however, all subcategories showed an association between DM and the risk of developing TB.

Discussion

This systematic review included 47 articles examining the association between DM and TB. Regardless of study design, region of origin, stage of TB (latent or active TB), type of controls (non-DM, non-TB, or presumed healthy), this meta-analysis suggests that DM increases the risk of developing TB. The overall effect observed suggests that patients with DM are two times more likely to develop TB than non-diabetics. This overall effect persisted in the sensitivity analysis including only studies with similar proportions of common confounders between cases and controls.

The statistically significant association between DM and TB observed in this review is consistent with those reported previously. A first qualitative review in 2007 with 9 included studies reported effect estimates ranging from 1.5 to 7.8 fold the risk of TB in DM patients [80]. Two other meta-analyses that included studies with patients with active TB and whose age-adjusted estimates were reported in 2008 and 2018 [14, 24]. One of these meta-analyses reported an estimated 3.1-fold effect for 3 cohort studies and the second an estimated 1.5-fold effect for 14 studies with low risk of bias. A final meta-analysis with studies recruiting patients with latent TB revealed no significant association for one cohort study and a weak association for 12 cross-sectional studies [16]. Compared to these previous systematic reviews, we included over 10 additional articles and used a very rigorous methodology including calculating effect estimates of primary data from included studies and taking into account a wide range of confounding factors of the association between DM and TB listed in the articles included [35, 43, 45, 48, 53, 58, 61, 62, 64, 67, 70, 73, 77, 79]. Little is known about the biological mechanisms that underlie a high risk of developing TB in patients with DM. Several hypotheses linked to an alteration of immune function in diabetics have however been suggested to explain this association between DM and TB [81–84]. These hypotheses include, but not limited to:

Table 2. TB development in people with and without DM and influence of confounders.

	OR (95% CI)	95% Prediction interval	N Studies	N LRTI cases	N controls	H (95% CI)	I ² (95%CI)	P heterogeneity	P Egger test
Cohort studies									
Overall	1.9 [1.5–2.4]	[0.8–4.4]	10	430617	3252383	4.2 [3.4–5.2]	94.3 [91.5–96.2]	< 0.001	0.417
Low risk of bias	1.6 [1.4–1.7]	[1.1–2.2]	7	414459	2424452	2.9 [2.1–4]	88.2 [78.2–93.7]	< 0.001	0.496
Asbestosis	1.6 [1.5–1.7]	NA	1	22256	89024	NA	NA	1	NA
Autoimmune disorders	1.3 [1.2–1.5]	NA	1	49903	49903	NA	NA	1	NA
Bet nut use	2.4 [1.8–3.1]	NA	1	11260	110782	NA	NA	1	NA
Chronic kidney disease	1.8 [1.7–1.9]	NA	1	52820	766231	NA	NA	1	NA
HIV infection	1.5 [1.3–1.7]	NA	2	72159	138927	2.3 [1.1–4.7]	81 [19.2–95.6]	0.022	NA
Male gender	1.8 [1.2–2.5]	[0.3–9.4]	4	83798	195379	2.6 [1.7–4.1]	85.4 [63.9–94.1]	< 0.001	0.377
Malignant disease	1.8 [1.7–1.8]	NA	2	59264	801903	1.4	49	0.161	NA
Pneumoconiosis	1.6 [1.5–1.7]	NA	1	22256	89024	NA	NA	1	NA
Age	1.5 [1.3–1.7]	NA	2	72159	138927	2.3 [1.1–4.7]	81 [19.2–95.6]	0.022	NA
Case control studies									
Overall	2.4 [2–2.9]	[1–5.5]	23	40094	269938	3.8 [3.3–4.4]	93 [90.8–94.7]	< 0.001	0.093
Low risk of bias	2.2 [1.7–2.9]	[0.8–6.2]	13	28831	144497	2.6 [2.1–3.3]	85.4 [76.6–90.9]	< 0.001	0.05
Adenotonsillectomy	1.6 [1.5–1.7]	NA	1	11366	45464	NA	NA	1	NA
Central sewage system	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Chronic kidney disease	1.9 [1.4–2.6]	[0.3–14]	3	710	814	1.7 [1–3.1]	64.7 [0–89.9]	0.059	0.271
Co_morbidity	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Currently rent home	11.8 [2.6–54.1]	NA	1	110	214	NA	NA	1	NA
Drinker	3.2 [2.9–3.5]	[2.5–3.9]	4	5850	38388	1.2 [1–1.9]	26.3 [0–72.1]	0.254	0.101
Drug user	3.8 [1.8–7.9]	[0–16592.3]	3	1012	1488	2.2 [1.2–3.9]	79.5 [34.7–93.5]	0.008	0.916
Ever injected heroin	8.8 [4.2–18.2]	NA	1	562	1038	NA	NA	1	NA
Ever smoked heroin	8.8 [4.2–18.2]	NA	1	562	1038	NA	NA	1	NA
Ever used opium	8.8 [4.2–18.2]	NA	1	562	1038	NA	NA	1	NA
Extra pulmonary lesion	1.8 [1.2–2.5]	NA	1	300	300	NA	NA	1	NA
Family history of diabetes mellitus	3 [0.7–12]	NA	1	50	50	NA	NA	1	NA
Hepatitis C infection, Anti_HCV	11.8 [2.6–54.1]	NA	1	110	214	NA	NA	1	NA

(Continued)

Table 2. (Continued)

	OR (95% CI)	95% Prediction interval	N Studies	N LRTI cases	N controls	H (95% CI)	I ² (95%CI)	P heterogeneity	P Egger test
HIV infection	1.5 [1.3–1.8]	[0.5–4.6]	3	3360	14761	2 [1.1–3.6]	74.9 [16.8–92.4]	0.019	0.277
Hyperlipidaemia	1.6 [1.5–1.6]	NA	1	10168	40672	NA	NA	1	NA
Illicit drug use	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Immunosuppressive therapy	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Living in a crowded home	4.6 [2.6–7.8]	NA	1	454	556	NA	NA	1	NA
Male gender	2.1 [1.6–2.7]	[0.9–4.9]	10	26090	117338	2.1 [1.5–2.8]	77.2 [58.2–87.6]	< 0.001	0.036
Malignant disease	1.8 [1.2–2.5]	NA	1	300	300	NA	NA	1	NA
Marital status, Single	2.1 [1.5–3.1]	NA	2	953	500	1.1	17.3	0.272	NA
Other chronic diseases	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Pancreatitis	2.4 [1–5.7]	NA	1	151	545	NA	NA	1	NA
Physical activity	3 [0.7–12]	NA	1	50	50	NA	NA	1	NA
Poly_drug resistant	1.8 [1.2–2.5]	NA	1	300	300	NA	NA	1	NA
Previous hospitalizations	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Prisoners	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Smoke Exposure	2.5 [2–3.3]	[1.4–4.4]	4	702	16807	1 [1–1.5]	0 [0–53.1]	0.806	0.86
Transplantation	1.9 [1–3.5]	NA	1	300	300	NA	NA	1	NA
Age	2.4 [1.6–3.7]	[0.6–10.1]	5	4756	15561	2.9 [2–4.3]	88.5 [75.8–94.5]	< 0.001	0.393
Cigarettes smoked in a week	8.8 [4.2–18.2]	NA	1	562	1038	NA	NA	1	NA
Cross sectional studies									
Overall	2.5 [1.8–3.5]	[0.6–9.7]	16	33049	74524	4.6 [3.9–5.3]	95.2 [93.5–96.5]	< 0.001	0.058
Low risk of bias	2.4 [1.6–3.5]	[0.5–11.4]	12	30309	41171	5.2 [4.4–6.1]	96.3 [94.8–97.3]	< 0.001	0.15
Anemia	1.1 [0.6–1.9]	NA	1	91	316	NA	NA	1	NA
Atrial fibrillation	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Autoimmune disorders	2.1 [0.9–4.7]	NA	2	387	1038	3.7 [2–6.7]	92.5 [74.7–97.8]	< 0.001	NA
Bronchial asthma	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Bronchiectasis	3.2 [2.1–5]	NA	1	264	438	NA	NA	1	NA
Chronic kidney disease	1.9 [0.7–4.6]	NA	2	700	1081	5.4 [3.3–8.9]	96.6 [90.9–98.7]	< 0.001	NA
Chronic liver disease	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Chronic obstructive pulmonary disease	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Drinker	5 [2.6–9.6]	NA	2	1873	16536	2.6 [1.3–5.3]	85.5 [41.6–96.4]	0.009	NA
Gout	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Health care worker	3.6 [2.5–5.2]	NA	1	296	722	NA	NA	1	NA
Hemodialysis patients	1.9 [0.9–4.1]	NA	2	355	754	3.1 [1.6–5.9]	89.5 [60.9–97.2]	0.002	NA

(Continued)

Table 2. (Continued)

	OR (95% CI)	95% Prediction interval	N Studies	N LRTI cases	N controls	H (95% CI)	I ² (95%CI)	P heterogeneity	P Egger test
Hepatitis B infection, HBsAg	2.5 [1.3–4.8]	[0.2–29.5]	5	2315	8153	4.5 [3.4–6]	95.1 [91.2–97.3]	< 0.001	0.597
Hepatitis C infection, Anti_HCV	3.5 [1.5–7.8]	[0–71340.3]	3	1346	4497	4.8 [3.3–7.1]	95.7 [90.7–98]	< 0.001	0.811
HIV infection	5.2 [3.1–8.7]	NA	2	517	1195	2.8 [1.4–5.6]	87.6 [51.8–96.8]	0.005	NA
Ischaemic heart disease	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Liver cirrhosis	2.1 [0.9–4.7]	NA	2	387	1038	3.7 [2–6.7]	92.5 [74.7–97.8]	< 0.001	NA
Living in a crowded home	2.9 [1.6–5.4]	NA	1	1652	16063	NA	NA	1	NA
Male gender	2.5 [1.6–4]	[0.5–11.9]	7	3841	24363	3.1 [2.3–4.2]	89.9 [81.7–94.4]	< 0.001	0.883
Malignant disease	2.6 [1.6–4.3]	[0.3–22.7]	4	680	2203	2.2 [1.4–3.6]	79.8 [46.4–92.4]	0.002	0.962
Osteoarthritis	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Residence in an indigenous community	2.9 [1.6–5.4]	NA	1	1652	16063	NA	NA	1	NA
Self_reported history of renal failure	7.2 [5.4–9.5]	NA	1	919	1113	NA	NA	1	NA
Smoke Exposure	3 [1.8–5.2]	[0.4–22.9]	5	2825	20871	3.1 [2.2–4.5]	89.8 [79–95]	< 0.001	0.467
Syphilis	7.5 [5.3–10.8]	NA	1	221	473	NA	NA	1	NA
Thyroid disorder	1 [0.7–1.3]	NA	1	404	359	NA	NA	1	NA
Total Bilirubin (mg_dL), Not Normal	2 [1.4–3]	NA	2	1661	6594	2.6 [1.3–5.3]	85.4 [40.9–96.4]	0.009	NA
Age	2.3 [1.5–3.6]	NA	2	216	917	1.3	41.1	0.193	NA
Body mass index	7.5 [5.3–10.8]	NA	1	221	473	NA	NA	1	NA
Dialysis duration	1.8 [0.8–4.2]	NA	2	120	1043	2.4 [1.1–4.8]	82 [23.9–95.7]	0.018	NA
Hemoglobin	1.1 [1–1.3]	NA	1	6382	6675	NA	NA	1	NA

<https://doi.org/10.1371/journal.pone.0261246.t002>

depressed cellular immunity, alveolar macrophage dysfunction, low levels of interferon gamma, reduction of interleukin-12, and micronutrient deficiency. We recognize several potential limitations to this review. In addition to the fact that most of the included studies used multiple diagnostic approaches for TB and DM, other diagnostic methods including ICD codes, medical records and self-reported data may be associated with some inaccuracies. Different risk factors have been reported for pulmonary TB compared to extra-pulmonary TB. Very few included studies, however, differentiated pulmonary TB from extrapulmonary TB [85, 86]. Similarly, very few included studies reported information on DM types (1 or 2 and pre-DM or DM) and participant glycaemic control. However, these are conditions that influence susceptibility to TB [87]. Very few included studies reported treatment status for participant for TB. Normalization of glycaemic status has been established for TB patients receiving treatment [88, 89]. This could therefore have been the cause of the misclassification of cases and controls in the included studies. The above limitations would justify the substantial heterogeneity recorded in this meta-analysis. As previously reported [90], very few studies

included in this meta-analysis were from Africa, thus compromising the generalizability of these results globally. It should also be noted that Africa has the highest rate of undiagnosed DM in the world and may therefore have a specific profile of the association between DM and TB [91].

Due to the inclusion of only observational studies in this meta-analysis, a causal link between DM and the risk of TB cannot be suggested. However, the results of this meta-analysis further strengthen the level of evidence for the association between DM and the risk of TB development. We therefore encourage specific studies on the association between DM and TB in the context of Africa. We advocated public health programs to prevent DM such as strengthening education on risk factors for DM and physical activities and sports. Patients with DM only and healthcare professionals should be educated about their increased risk of active or latent TB development. Two-way screening and management programs for DM and TB including latent TB would help reduce the incidence and burden associated with this double epidemic. Interventional studies to demonstrate the causal link between DM and TB are needed in the future. Further research on the biological mechanism by which DM increases the risk of TB are needed.

Supporting information

S1 Fig. Funnel chart for publications of the association between diabetes and tuberculosis in cohort studies.

(PDF)

S2 Fig. Funnel chart for publications of the association between diabetes and tuberculosis in case control studies.

(PDF)

S3 Fig. Funnel chart for publications of the association between diabetes and tuberculosis in cross-sectional studies.

(PDF)

S1 Table. Preferred reporting items for systematic reviews and meta-analyses checklist.

(PDF)

S2 Table. Search strategy in Pubmed.

(PDF)

S3 Table. Items for risk of bias assessment.

(PDF)

S4 Table. Main reasons of non-inclusion of eligible studies.

(PDF)

S5 Table. Risk of bias assessment.

(PDF)

S6 Table. P-value of Khi-2 and Fisher exact tests for qualitative confounding factors.

(PDF)

S7 Table. P-value of Student test for quantitative confounding factors.

(PDF)

S8 Table. Subgroup analyses of the association between diabetes and tuberculosis.

(PDF)

Author Contributions

Conceptualization: Joseph Rodrigue Foe-Essomba, Sebastien Kenmoe, Jean Claude Mbanya, Wilfred Fon Mbacham, Sara Eyangoh.

Data curation: Joseph Rodrigue Foe-Essomba, Sebastien Kenmoe, Serges Tchatchouang, Jean Thierry Ebogo-Belobo, Donatien Serge Mbaga, Cyprien Kengne-Ndé, Gadj Mahamat, Ginette Irma Kame-Ngasse, Efietngab Atembeh Noura, Chris Andre Mbongue Mikangue, Alfloditte Flore Feudjio, Jean Bosco Taya-Fokou, Sabine Aimee Touangnou-Chamda, Rachel Audrey Nayang-Mundo, Inès Nyebe, Jeannette Nina Magoudjou-Pekam, Jacqueline Félicité Yéngué, Larissa Gertrude Djukouo, Cynthia Paola Demeni Emoh, Hervé Raoul Tazokong, Arnol Bowo-Ngandji, Eric Lontchi-Yimagou.

Formal analysis: Sebastien Kenmoe, Cyprien Kengne-Ndé.

Funding acquisition: Sebastien Kenmoe.

Methodology: Joseph Rodrigue Foe-Essomba, Sebastien Kenmoe, Serges Tchatchouang, Jean Thierry Ebogo-Belobo, Donatien Serge Mbaga, Cyprien Kengne-Ndé, Gadj Mahamat, Ginette Irma Kame-Ngasse, Efietngab Atembeh Noura, Chris Andre Mbongue Mikangue, Alfloditte Flore Feudjio, Jean Bosco Taya-Fokou, Sabine Aimee Touangnou-Chamda, Rachel Audrey Nayang-Mundo, Inès Nyebe, Jeannette Nina Magoudjou-Pekam, Jacqueline Félicité Yéngué, Larissa Gertrude Djukouo, Cynthia Paola Demeni Emoh, Hervé Raoul Tazokong, Arnol Bowo-Ngandji, Eric Lontchi-Yimagou, Afi Leslie Kaiyven, Valerie Flore Donkeng Donfack, Richard Njouom, Jean Claude Mbanya, Wilfred Fon Mbacham, Sara Eyangoh.

Project administration: Sebastien Kenmoe, Jean Claude Mbanya, Wilfred Fon Mbacham, Sara Eyangoh.

Supervision: Sara Eyangoh.

Validation: Sebastien Kenmoe, Serges Tchatchouang, Jean Thierry Ebogo-Belobo, Donatien Serge Mbaga, Gadj Mahamat, Ginette Irma Kame-Ngasse, Efietngab Atembeh Noura, Chris Andre Mbongue Mikangue, Alfloditte Flore Feudjio, Jean Bosco Taya-Fokou, Sabine Aimee Touangnou-Chamda, Rachel Audrey Nayang-Mundo, Inès Nyebe, Jeannette Nina Magoudjou-Pekam, Jacqueline Félicité Yéngué, Larissa Gertrude Djukouo, Cynthia Paola Demeni Emoh, Hervé Raoul Tazokong, Arnol Bowo-Ngandji, Eric Lontchi-Yimagou, Afi Leslie Kaiyven, Valerie Flore Donkeng Donfack, Richard Njouom, Jean Claude Mbanya, Wilfred Fon Mbacham, Sara Eyangoh.

Writing – original draft: Joseph Rodrigue Foe-Essomba, Sebastien Kenmoe.

Writing – review & editing: Joseph Rodrigue Foe-Essomba, Sebastien Kenmoe, Serges Tchatchouang, Jean Thierry Ebogo-Belobo, Donatien Serge Mbaga, Cyprien Kengne-Ndé, Gadj Mahamat, Ginette Irma Kame-Ngasse, Efietngab Atembeh Noura, Chris Andre Mbongue Mikangue, Alfloditte Flore Feudjio, Jean Bosco Taya-Fokou, Sabine Aimee Touangnou-Chamda, Rachel Audrey Nayang-Mundo, Inès Nyebe, Jeannette Nina Magoudjou-Pekam, Jacqueline Félicité Yéngué, Larissa Gertrude Djukouo, Cynthia Paola Demeni Emoh, Hervé Raoul Tazokong, Arnol Bowo-Ngandji, Eric Lontchi-Yimagou, Afi Leslie Kaiyven, Valerie Flore Donkeng Donfack, Richard Njouom, Jean Claude Mbanya, Wilfred Fon Mbacham, Sara Eyangoh.

References

1. Cohen A, Mathiasen VD. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. *The European respiratory journal*. 2019; 54(3). <https://doi.org/10.1183/13993003.00655-2019> PMID: 31221810.
2. World Health O. Global tuberculosis report 2020. Geneva: World Health Organization; 2020 2016.
3. Foundation ID. IDF Diabetes Atlas 2019. 9th Edition ed2019.
4. Baker MA, Harries AD, Jeon CY, Hart JE, Kapur A, Lönnroth K, et al. The impact of diabetes on tuberculosis treatment outcomes: a systematic review. *BMC medicine*. 2011; 9:81. Epub 2011/07/05. <https://doi.org/10.1186/1741-7015-9-81> PMID: 21722362; PubMed Central PMCID: PMC3155828.
5. Lönnroth K, Roglic G, Harries AD. Improving tuberculosis prevention and care through addressing the global diabetes epidemic: from evidence to policy and practice. *The lancet Diabetes & endocrinology*. 2014; 2(9):730–9. Epub 2014/09/10. [https://doi.org/10.1016/S2213-8587\(14\)70109-3](https://doi.org/10.1016/S2213-8587(14)70109-3) PMID: 25194886.
6. Singla R, Khan N. Does diabetes predispose to the development of multidrug-resistant tuberculosis? *Chest*. 2003; 123(1):308–9; author reply 9. Epub 2003/01/16. PMID: 12527642.
7. Stevenson CR, Forouhi NG, Roglic G, Williams BG, Lauer JA, Dye C, et al. Diabetes and tuberculosis: the impact of the diabetes epidemic on tuberculosis incidence. *BMC Public Health*. 2007; 7(1):234. <https://doi.org/10.1186/1471-2458-7-234> PMID: 17822539
8. Diabetes Dixon B. and tuberculosis: an unhealthy partnership. *The Lancet Infectious diseases*. 2007; 7(7):444. Epub 2007/06/29. [https://doi.org/10.1016/S1473-3099\(07\)70144-5](https://doi.org/10.1016/S1473-3099(07)70144-5) PMID: 17597568.
9. Beran D, Yudkin JS. Diabetes care in sub-Saharan Africa. *Lancet (London, England)*. 2006; 368(9548):1689–95. Epub 2006/11/14. [https://doi.org/10.1016/S0140-6736\(06\)69704-3](https://doi.org/10.1016/S0140-6736(06)69704-3) PMID: 17098088.
10. Harries AD, Murray MB, Jeon CY, Ottmani SE, Lönnroth K, Barreto ML, et al. Defining the research agenda to reduce the joint burden of disease from diabetes mellitus and tuberculosis. *Tropical medicine & international health: TM & IH*. 2010; 15(6):659–63. Epub 2010/04/22. <https://doi.org/10.1111/j.1365-3156.2010.02523.x> PMID: 20406430; PubMed Central PMCID: PMC4465347.
11. Odone A, Houben RM, White RG, Lönnroth K. The effect of diabetes and undernutrition trends on reaching 2035 global tuberculosis targets. *The lancet Diabetes & endocrinology*. 2014; 2(9):754–64. Epub 2014/09/10. [https://doi.org/10.1016/S2213-8587\(14\)70164-0](https://doi.org/10.1016/S2213-8587(14)70164-0) PMID: 25194888.
12. Restrepo BI. Convergence of the tuberculosis and diabetes epidemics: renewal of old acquaintances. *Clin Infect Dis*. 2007; 45(4):436–8. Epub 2007/07/20. <https://doi.org/10.1086/519939> PMID: 17638190; PubMed Central PMCID: PMC2900315.
13. Harries AD, Lin Y, Satyanarayana S, Lönnroth K, Li L, Wilson N, et al. The looming epidemic of diabetes-associated tuberculosis: learning lessons from HIV-associated tuberculosis. *The international journal of tuberculosis and lung disease: the official journal of the International Union against Tuberculosis and Lung Disease*. 2011; 15(11):1436–44, i. Epub 2011/09/10. <https://doi.org/10.5588/ijtld.11.0503> PMID: 21902876.
14. Jeon CY, Murray MB. Diabetes Mellitus Increases the Risk of Active Tuberculosis: A Systematic Review of 13 Observational Studies. *PLoS Medicine*. 2008; 5(7):e152. <https://doi.org/10.1371/journal.pmed.0050152> PMID: 18630984
15. Al-Rifai RH, Pearson F, Critchley JA, Abu-Raddad LJ. Association between diabetes mellitus and active tuberculosis: A systematic review and meta-analysis. *PLOS ONE*. 2017; 12(11):e0187967. <https://doi.org/10.1371/journal.pone.0187967> PMID: 29161276
16. Lee M-R, Huang Y-P, Kuo Y-T, Luo C-H, Shih Y-J, Shu C-C, et al. Diabetes mellitus and latent tuberculosis infection: a systemic review and meta-analysis. *Clinical Infectious Diseases*. 2016:ciw836. <https://doi.org/10.1093/cid/ciw836> PMID: 27986673
17. Liu Q, Li W, Xue M, Chen Y, Du X, Wang C, et al. Diabetes mellitus and the risk of multidrug resistant tuberculosis: a meta-analysis. *Scientific Reports*. 2017; 7(1):1090. <https://doi.org/10.1038/s41598-017-01213-5> PMID: 28439071
18. Tegegne BS, Mengesha MM, Teferra AA, Awoke MA, Habtewold TD. Association between diabetes mellitus and multi-drug-resistant tuberculosis: evidence from a systematic review and meta-analysis. *Systematic reviews*. 2018; 7(1):161. <https://doi.org/10.1186/s13643-018-0828-0> PMID: 30322409
19. Martinez L, Sekandi JN, Castellanos ME, Zalwango S, Whalen CC. Infectiousness of HIV-Seropositive Patients with Tuberculosis in a High-Burden African Setting. *Am J Respir Crit Care Med*. 2016; 194(9):1152–63. Epub 2016/11/01. <https://doi.org/10.1164/rccm.201511-2146OC> PMID: 27181053; PubMed Central PMCID: PMC5114446.
20. Peters JS, Andrews JR, Hatherill M, Hermans S, Martinez L, Schurr E, et al. Advances in the understanding of Mycobacterium tuberculosis transmission in HIV-endemic settings. *The Lancet Infectious*

- diseases. 2019; 19(3):e65–e76. Epub 2018/12/18. [https://doi.org/10.1016/S1473-3099\(18\)30477-8](https://doi.org/10.1016/S1473-3099(18)30477-8) PMID: 30554995; PubMed Central PMCID: PMC6401310.
21. Harries AD, Nkhoma WA, Thompson PJ, Nyangulu DS, Wirima JJ. Nutritional status in Malawian patients with pulmonary tuberculosis and response to chemotherapy. *Eur J Clin Nutr.* 1988; 42(5):445–50. Epub 1988/05/01. PMID: 3396531.
 22. Lin HH, Ezzati M, Chang HY, Murray M. Association between tobacco smoking and active tuberculosis in Taiwan: prospective cohort study. *Am J Respir Crit Care Med.* 2009; 180(5):475–80. Epub 2009/06/23. <https://doi.org/10.1164/rccm.200904-0549OC> PMID: 19542475.
 23. Lönnroth K, Williams BG, Stadlin S, Jaramillo E, Dye C. Alcohol use as a risk factor for tuberculosis—a systematic review. *BMC Public Health.* 2008; 8:289. Epub 2008/08/16. <https://doi.org/10.1186/1471-2458-8-289> PMID: 18702821; PubMed Central PMCID: PMC2533327.
 24. Hayashi S, Chandramohan D. Risk of active tuberculosis among people with diabetes mellitus: systematic review and meta-analysis. *Tropical Medicine & International Health.* 2018; 23(10):1058–70. <https://doi.org/10.1111/tmi.13133> PMID: 30062731
 25. Executive B. Global strategy and targets for tuberculosis prevention, care and control after 2015: Report by the Secretariat. 2014.
 26. Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *The Lancet Infectious Diseases.* 2009; 9(12):737–46. [https://doi.org/10.1016/S1473-3099\(09\)70282-8](https://doi.org/10.1016/S1473-3099(09)70282-8) PMID: 19926034
 27. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetc R, et al. Chapter 7: Systematic reviews of etiology and risk. *Joanna Briggs Institute Reviewer's Manual.* Joanna Briggs Institute Reviewer's Manual. The Joanna Briggs Institute ed: Aromataris E, Munn Z; 2017.
 28. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemporary Clinical Trials.* 2015; 45 (Pt A):139–45. <https://doi.org/10.1016/j.cct.2015.09.002> PMID: 26343745
 29. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ: British Medical Journal.* 1997; 315(7109):629–34. <https://doi.org/10.1136/bmj.315.7109.629> PMID: 9310563
 30. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine.* 2002; 21(11):1539–58. <https://doi.org/10.1002/sim.1186> PMID: 12111919
 31. Nelson JF, Ship II. Intraoral carcinoma: predisposing factors and their frequency of incidence as related to age at onset. *Journal of the American Dental Association (1939).* 1971; 82(3):564–8. Epub 1971/03/01. <https://doi.org/10.14219/jada.archive.1971.0080> PMID: 5276260.
 32. Kenmoe S, Kengne-Nde C, Modiyinji AF, Bigna JJ, Njouom R. Association of early viral lower respiratory infections and subsequent development of atopy, a systematic review and meta-analysis of cohort studies. *PLoS One.* 2020; 15(4):e0231816. <https://doi.org/10.1371/journal.pone.0231816> PMID: 32330171.
 33. Alisjahbana B, van Crevel R, Sahiratmadja E, den Heijer M, Maya A, Istriana E, et al. Diabetes mellitus is strongly associated with tuberculosis in Indonesia. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease.* 2006; 10(6):696–700. PMID: 16776459
 34. Baker MA, Lin H-H, Chang H-Y, Murray MB. The risk of tuberculosis disease among persons with diabetes mellitus: a prospective cohort study. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America.* 2012; 54(6):818–25. <https://doi.org/10.1093/cid/cir939> PMID: 22238171
 35. Barron MM, Shaw KM, Bullard KM, Ali MK, Magee MJ. Diabetes is associated with increased prevalence of latent tuberculosis infection: Findings from the National Health and Nutrition Examination Survey, 2011–2012. *Diabetes Research and Clinical Practice.* 2018; 139:366–79. <https://doi.org/10.1016/j.diabres.2018.03.022> PMID: 29574108
 36. Boillat-Blanco N, Ramaiya KL, Mganga M, Minja LT, Bovet P, Schindler C, et al. Transient Hyperglycemia in Patients With Tuberculosis in Tanzania: Implications for Diabetes Screening Algorithms. *Journal of Infectious Diseases.* 2016; 213(7):1163–72. <https://doi.org/10.1093/infdis/jiv568> PMID: 26609005
 37. Brassard P, Kezouh A, Suissa S. Antirheumatic drugs and the risk of tuberculosis. *Clin Infect Dis.* 2006; 43(6):717–22. Epub 2006/08/17. <https://doi.org/10.1086/506935> PMID: 16912945.
 38. Buskin SE, Gale JL, Weiss NS, Nolan CM. Tuberculosis risk factors in adults in King County, Washington, 1988 through 1990. *American journal of public health.* 1994; 84(11):1750–6. <https://doi.org/10.2105/ajph.84.11.1750> PMID: 7977912
 39. Chen C-H, Lian J-D, Cheng C-H, Wu M-J, Lee W-C, Shu K-H. Mycobacterium tuberculosis infection following renal transplantation in Taiwan. *Transplant Infectious Disease.* 2006; 8(3):148–56. <https://doi.org/10.1111/j.1399-3062.2006.00147.x> PMID: 16913973

40. Chung W-S, Lin C-L, Hung C-T, Chu Y-H, Sung F-C, Kao C-H, et al. Tuberculosis increases the subsequent risk of acute coronary syndrome: a nationwide population-based cohort study. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease*. 2014; 18(1):79–83. <https://doi.org/10.5588/ijtld.13.0288> PMID: 24365557
41. Corris V, Unwin N, Critchley J. Quantifying the association between tuberculosis and diabetes in the US: a case-control analysis. *Chronic Illness*. 2012; 8(2):121–34. <https://doi.org/10.1177/1742395312440294> PMID: 22387690
42. Davis A, Terlikbayeva A, Aifah A, Hermosilla S, Zhumadilov Z, Berikova E, et al. Risks for tuberculosis in Kazakhstan: implications for prevention. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease*. 2017; 21(1):86–92. <https://doi.org/10.5588/ijtld.15.0838> PMID: 28157470
43. Faurholt-Jepsen D, Aabye MG, Jensen AV, Range N, Praygod G, Jeremiah K, et al. Diabetes is associated with lower tuberculosis antigen-specific interferon gamma release in Tanzanian tuberculosis patients and non-tuberculosis controls. *Scandinavian Journal of Infectious Diseases*. 2014; 46(5):384–91. <https://doi.org/10.3109/00365548.2014.885657> PMID: 24621055
44. Faurholt-Jepsen D, Range N, PrayGod G, Jeremiah K, Faurholt-Jepsen M, Aabye MG, et al. Diabetes Is a Risk Factor for Pulmonary Tuberculosis: A Case-Control Study from Mwanza, Tanzania. *PLoS ONE*. 2011; 6(8):e24215. <https://doi.org/10.1371/journal.pone.0024215> PMID: 21912626
45. Golub JE, Mok Y, Hong S, Jung KJ, Jee SH, Samet JM. Diabetes mellitus and tuberculosis in Korean adults: impact on tuberculosis incidence, recurrence and mortality. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease*. 2019; 23(4):507–13. <https://doi.org/10.5588/ijtld.18.0103> PMID: 31064631
46. Haraldsdottir TL, Rudolf F, Bjerregaard-Andersen M, Joaquim LC, Stochholm K, Gomes VF, et al. Diabetes mellitus prevalence in tuberculosis patients and the background population in Guinea-Bissau: a disease burden study from the capital Bissau. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2015; 109(6):400–7. <https://doi.org/10.1093/trstmh/trv030> PMID: 25918218
47. Hensel RL, Kempker RR, Tapia J, Oladele A, Blumberg HM, Magee MJ. Increased risk of latent tuberculosis infection among persons with pre-diabetes and diabetes mellitus. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease*. 2016; 20(1):71–8. <https://doi.org/10.5588/ijtld.15.0457> PMID: 26688531
48. Hossain M. Glucose Intolerance in Pulmonary Tuberculosis: A Case-Control Study. *Chest*. 2014; 145(3):140A. <https://doi.org/10.1378/chest.1823698>
49. Jick SS, Lieberman ES, Rahman MU, Choi HK. Glucocorticoid use, other associated factors, and the risk of tuberculosis. *Arthritis and rheumatism*. 2006; 55(1):19–26. Epub 2006/02/08. <https://doi.org/10.1002/art.21705> PMID: 16463407.
50. Jurcev-Savicevic A, Mulic R, Ban B, Kozul K, Bacun-Ivcek L, Valic J, et al. Risk factors for pulmonary tuberculosis in Croatia: a matched case-control study. *BMC Public Health*. 2013; 13(1):991. <https://doi.org/10.1186/1471-2458-13-991> PMID: 24144113
51. Khawcharoenporn T, Apisarnthanarak A, Phetsuksiri B, Rudeeaneksin J, Srisingngam S, Mundy LM. Tuberculin skin test and QuantiFERON-TB Gold In-tube Test for latent tuberculosis in Thai HIV-infected adults. *Respirology*. 2015; 20(2):340–7. Epub 2014/11/28. <https://doi.org/10.1111/resp.12442> PMID: 25428131.
52. Kim SJ, Hong YP, Lew WJ, Yang SC, Lee EG. Incidence of pulmonary tuberculosis among diabetics. *Tubercle and Lung Disease*. 1995; 76(6):529–33. [https://doi.org/10.1016/0962-8479\(95\)90529-4](https://doi.org/10.1016/0962-8479(95)90529-4) PMID: 8593374
53. Kubiak RW, Sarkar S, Horsburgh CR, Roy G, Kratz M, Reshma A, et al. Interaction of nutritional status and diabetes on active and latent tuberculosis: a cross-sectional analysis. *BMC infectious diseases*. 2019; 19(1):627. <https://doi.org/10.1186/s12879-019-4244-4> PMID: 31311495
54. Kuo MC, Lin SH, Lin CH, Mao IC, Chang SJ, Hsieh MC. Type 2 diabetes: an independent risk factor for tuberculosis: a nationwide population-based study. *PLoS One*. 2013; 8(11):e78924. Epub 2013/11/16. <https://doi.org/10.1371/journal.pone.0078924> PMID: 24236069; PubMed Central PMCID: PMC3827305.
55. Lai S-W, Lin C-L, Liao K-F, Tsai S-M. Increased risk of pulmonary tuberculosis among patients with appendectomy in Taiwan. *European Journal of Clinical Microbiology & Infectious Diseases*. 2014; 33(9):1573–7. <https://doi.org/10.1007/s10096-014-2112-0> PMID: 24781006
56. Lee M-C, Lee C-H, Shu C-C, Pong W-B, Lan C-C, Wang J-Y, et al. The impact of diabetes mellitus and its control on the development of tuberculosis: a nationwide longitudinal study in Taiwan: IMPACT OF DM TREATMENT ON RISK OF TB. *Pharmacoepidemiology and Drug Safety*. 2013; 22(9):995–1003. <https://doi.org/10.1002/pds.3491>

57. Lee P-H, Fu H, Lai T-C, Chiang C-Y, Chan C-C, Lin H-H. Glycemic Control and the Risk of Tuberculosis: A Cohort Study. *PLoS medicine*. 2016; 13(8):e1002072. <https://doi.org/10.1371/journal.pmed.1002072> PMID: 27505150
58. Lee P-H, Lin H-C, Huang AS-E, Wei S-H, Lai M-S, Lin H-H. Diabetes and risk of tuberculosis relapse: nationwide nested case-control study. *PloS One*. 2014; 9(3):e92623. <https://doi.org/10.1371/journal.pone.0092623> PMID: 24663327
59. Leegaard A, Riis A, Kornum JB, Prahj JB, Thomsen VO, Sorensen HT, et al. Diabetes, Glycemic Control, and Risk of Tuberculosis: A population-based case-control study. *Diabetes Care*. 2011; 34(12):2530–5. <https://doi.org/10.2337/dc11-0902> PMID: 21972407
60. Leung CC, Lam TH, Chan WM, Yew WW, Ho KS, Leung GM, et al. Diabetic control and risk of tuberculosis: a cohort study. *American journal of epidemiology*. 2008; 167(12):1486–94. <https://doi.org/10.1093/aje/kwn075> PMID: 18400769
61. Lin C-H, Kuo S-C, Hsieh M-C, Ho S-Y, Su I-J, Lin S-H, et al. Effect of diabetes mellitus on risk of latent TB infection in a high TB incidence area: a community-based study in Taiwan. *BMJ Open*. 2019; 9(10):e029948. <https://doi.org/10.1136/bmjopen-2019-029948> PMID: 31662365
62. Lin H-F, Liao K-F, Chang C-M, Lai S-W, Tsai P-Y, Sung F-C. Anti-Diabetic Medication Reduces Risk of Pulmonary Tuberculosis in Diabetic Patients: A Population-based Cohort Study in Taiwan. *KUWAIT MEDICAL JOURNAL*. 2017; 7.
63. Mori MA, Leonardson G, Welty TK. The benefits of isoniazid chemoprophylaxis and risk factors for tuberculosis among Oglala Sioux Indians. *Archives of internal medicine*. 1992; 152(3):547–50. PMID: 1546917
64. Ndishimye P, Domokos B, Stillo J, Seghrouchni F, Mrabet O, Homorodean D, et al. A case control study of risk factors associated with pulmonary tuberculosis in romania: experience at a clinical hospital of pneumology. *Clujul medical (1957)*. 2017; 90(1):54–9. <https://doi.org/10.15386/cjmed-652> PMID: 28246498
65. Pablos-Méndez A, Blustein J, Knirsch CA. The role of diabetes mellitus in the higher prevalence of tuberculosis among Hispanics. *American journal of public health*. 1997; 87(4):574–9. <https://doi.org/10.2105/ajph.87.4.574> PMID: 9146434
66. Pealing L, Wing K, Mathur R, Prieto-Merino D, Smeeth L, Moore DAJ. Risk of tuberculosis in patients with diabetes: population based cohort study using the UK Clinical Practice Research Datalink. *BMC medicine*. 2015; 13:135. <https://doi.org/10.1186/s12916-015-0381-9> PMID: 26048371
67. Pereira SM, Araújo GSd, Santos CAdST, Oliveira MGd, Barreto ML. Association between diabetes and tuberculosis: case-control study. *Revista de saude publica*. 2016; 50:82. <https://doi.org/10.1590/S1518-8787.2016050006374> PMID: 28099656
68. Pérez A, Brown HS, Restrepo BI. Association between tuberculosis and diabetes in the mexican border and non-border regions of texas. *The American journal of tropical medicine and hygiene*. 2006; 74(4):604–11. <https://doi.org/10.4269/ajtmh.2006.74.604> PMID: 16606993
69. Shen T-C, Lin C-L, Wei C-C, Liao W-C, Chen W-C, Chen C-H, et al. Increased Risk of Tuberculosis in Patients With Type 1 Diabetes Mellitus: Results From a Population-Based Cohort Study in Taiwan. *Medicine*. 2014; 93(16):e96. <https://doi.org/10.1097/MD.000000000000096> PMID: 25310745
70. Shimouchi A, Tsuda Y, Komukai J, Matsumoto K, Yoshida H, Ohkado A. Characteristics of individuals with tuberculosis in an urban, poor population in Osaka City, Japan—a case-control study. *Western Pacific surveillance and response journal: WPSAR*. 2020; 11(1):22–8. <https://doi.org/10.5365/wpsar.2018.9.1.005> PMID: 32963888
71. Shu C-C, Wu V-C, Yang F-J, Pan S-C, Lai T-S, Wang J-Y, et al. Predictors and Prevalence of Latent Tuberculosis Infection in Patients Receiving Long-Term Hemodialysis and Peritoneal Dialysis. *PLoS ONE*. 2012; 7(8):e42592. <https://doi.org/10.1371/journal.pone.0042592> PMID: 22916137
72. Suwanpimolkul G, Grinsdale JA, Jarlsberg LG, Higashi J, Osmond DH, Hopewell PC, et al. Association between diabetes mellitus and tuberculosis in United States-born and foreign-born populations in San Francisco. *PloS One*. 2014; 9(12):e114442. <https://doi.org/10.1371/journal.pone.0114442> PMID: 25478954
73. Swarna Nantha Y, Puri A, Mohamad Ali SZ, Suppiah P, Che Ali SA, Ramasamy B, et al. Epidemiology of latent tuberculosis infection among patients with and without diabetes mellitus. *Family practice*. 2017; 34(5):532–8. <https://doi.org/10.1093/fampra/cmz017> PMID: 28369346
74. Ting W-Y, Huang S-F, Lee M-C, Lin Y-Y, Lee Y-C, Feng J-Y, et al. Gender disparities in latent tuberculosis infection in high-risk individuals: a cross-sectional study. *PloS One*. 2014; 9(11):e110104. <https://doi.org/10.1371/journal.pone.0110104> PMID: 25369472
75. Viney K, Cavanaugh J, Kienene T, Harley D, Kelly PM, Sleight A, et al. Tuberculosis and diabetes mellitus in the Republic of Kiribati: a case-control study. *Tropical Medicine & International Health*. 2015; 20(5):650–7. <https://doi.org/10.1111/tmi.12462> PMID: 25598275

76. Wang Q, Ma A, Han X, Zhao S, Cai J, Ma Y, et al. Prevalence of Type 2 Diabetes among Newly Detected Pulmonary Tuberculosis Patients in China: A Community Based Cohort Study. *PLoS ONE*. 2013; 8(12):e82660. <https://doi.org/10.1371/journal.pone.0082660> PMID: 24367535
77. Wardhani I, Sudaryo MK. Relationship between Diabetes Mellitus and Tuberculosis in Indonesia. *Indian Journal of Public Health Research & Development*. 2019; 10(2):392. <https://doi.org/10.5958/0976-5506.2019.00321.8>
78. Wu H-P, Pan Y-H, Hua C-C, Shieh W-B, Jiang B-Y, Yu T-J. Pneumoconiosis and liver cirrhosis are not risk factors for tuberculosis in patients with pulmonary infection. *Respirology*. 2007; 12(3):416–9. <https://doi.org/10.1111/j.1440-1843.2007.01033.x> PMID: 17539848
79. Zhussupov B, Hermosilla S, Terlikbayeva A, Aifah A, Ma X, Zhumadilov Z, et al. Risk Factors for Primary Pulmonary TB in Almaty Region, Kazakhstan: A Matched Case-Control Study. *Iranian journal of public health*. 2016; 45(4):441–50. PMID: 27252913
80. Stevenson CR, Critchley JA, Forouhi NG, Roglic G, Williams BG, Dye C, et al. Diabetes and the risk of tuberculosis: a neglected threat to public health? *Chronic Illness*. 2007; 3(3):228–45. <https://doi.org/10.1177/1742395307081502> PMID: 18083679
81. Young F, Critchley JA, Johnstone LK, Unwin NC. A review of co-morbidity between infectious and chronic disease in Sub Saharan Africa: TB and diabetes mellitus, HIV and metabolic syndrome, and the impact of globalization. *Globalization and health*. 2009; 5:9. Epub 2009/09/16. <https://doi.org/10.1186/1744-8603-5-9> PMID: 19751503; PubMed Central PMCID: PMC2753337.
82. Ottmani SE, Murray MB, Jeon CY, Baker MA, Kapur A, Lönnroth K, et al. Consultation meeting on tuberculosis and diabetes mellitus: meeting summary and recommendations. *The international journal of tuberculosis and lung disease: the official journal of the International Union against Tuberculosis and Lung Disease*. 2010; 14(12):1513–7. Epub 2010/12/25. PMID: 21180207.
83. Biochemistry Brownlee M. and molecular cell biology of diabetic complications. *Nature*. 2001; 414(6865):813–20. Epub 2001/12/14. <https://doi.org/10.1038/414813a> PMID: 11742414.
84. Martinez N, Kornfeld H. Diabetes and immunity to tuberculosis. *Eur J Immunol*. 2014; 44(3):617–26. Epub 2014/01/23. <https://doi.org/10.1002/eji.201344301> PMID: 24448841; PubMed Central PMCID: PMC4213860.
85. Antony SJ, Harrell V, Christie JD, Adams HG, Rumley RL. Clinical differences between pulmonary and extrapulmonary tuberculosis: a 5-year retrospective study. *Journal of the National Medical Association*. 1995; 87(3):187–92. Epub 1995/03/01. PMID: 7731067; PubMed Central PMCID: PMC2607831.
86. Sreeramareddy CT, Panduru KV, Verma SC, Joshi HS, Bates MN. Comparison of pulmonary and extrapulmonary tuberculosis in Nepal- a hospital-based retrospective study. *BMC Infect Dis*. 2008; 8:8. Epub 2008/01/26. <https://doi.org/10.1186/1471-2334-8-8> PMID: 18218115; PubMed Central PMCID: PMC2245948.
87. McMahon MM, Bistrrian BR. Host defenses and susceptibility to infection in patients with diabetes mellitus. *Infectious disease clinics of North America*. 1995; 9(1):1–9. Epub 1995/03/01. PMID: 7769211.
88. Oluboyo PO, Erasmus RT. The significance of glucose intolerance in pulmonary tuberculosis. *Tubercle*. 1990; 71(2):135–8. Epub 1990/06/01. [https://doi.org/10.1016/0041-3879\(90\)90010-6](https://doi.org/10.1016/0041-3879(90)90010-6) PMID: 2219464.
89. Tabarsi P, Baghaei P, Marjani M, Vollmer WM, Masjedi MR, Harries AD. Changes in glycosylated haemoglobin and treatment outcomes in patients with tuberculosis in Iran: a cohort study. *J Diabetes Metab Disord*. 2014; 13(1):123. Epub 2015/01/01. <https://doi.org/10.1186/s40200-014-0123-0> PMID: 25551103; PubMed Central PMCID: PMC4280034.
90. Bailey SL, Ayles H. Association between diabetes mellitus and active tuberculosis in Africa and the effect of HIV. *Tropical Medicine & International Health*. 2017; 22(3):261–8. <https://doi.org/10.1111/tmi.12822> PMID: 27935650
91. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract*. 2010; 87(1):4–14. Epub 2009/11/10. <https://doi.org/10.1016/j.diabres.2009.10.007> PMID: 19896746.