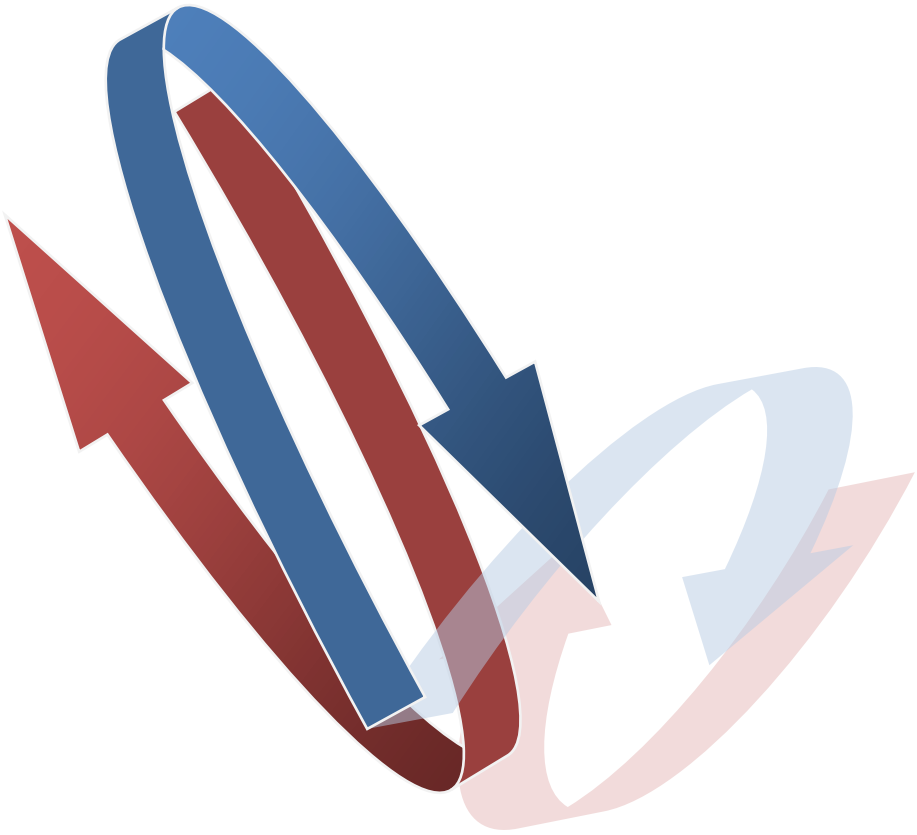
Collaborative Framework for Care and Control of Tuberculosis and Diabetes

SUPPORT MATERIAL



International Union Against Tuberculosis and Lung Disease
Health solutions for the poor

World Health Organization

Collaborative framework for care and control of tuberculosis and diabetes.

WHO/HTM/TB/2011.15

1.Tuberculosis - prevention and control. 2.Tuberculosis - etiology. 3.Tuberculosis - complications. 4.Diabetes complications. 4.Diabetes mellitus - prevention and control. 5.Health programs and plans. 6.Guidelines. I.World Health Organization. II.International Union against Tuberculosis and Lung Disease

ISBN 978 92 4 150225 2 (NLM classification: WF 200)

Provisional collaborative framework, 2011

Expiry date, 2015

1. Associations between diabetes and tuberculosis infection, tuberculosis disease and drug-resistant tuberculosis

Table 1. Summary of the four cross-sectional studies on the association between diabetes and tuberculosis infection included in the meta-analysis

Study	Country; population	Study period	Background TB incidence*	Exposure	Outcome	Adjusted variables
Marton et al., 1963 (1)	Hungary; people with and without diabetes of similar age, sex, region	Summer 1960	>100**	Diabetes diagnosis by medical records	TST (≥10mm) among people with negative X-rays	None
Woeltje et al., 1998 (2)	USA.; patients receiving haemodialysis	Jun. 1996 – Aug. 1996	4.1**	Diabetes diagnosis by medical records	TST (≥10mm, >=5 mm for HIV+)	None
Brock et al., 2006 (3)	Denmark, HIV-positive individuals	Oct. 2004 – Jan. 2005	<10	Diabetes diagnosis by medical records	QFT-IT (≥0.35 IU/mL IFN-γ)	None
Chan-Yeung et al., 2006 (4)	Hong Kong (SAR China); elderly aged >65 years	2002–2003	98.9	Diabetes diagnosis by medical records	TST (≥10mm)	Age, marital status, education, place of birth, smoking, drug abuse, past TB, CVD, arthritis, fracture, ischemic heart disease, COPD, cancer, liver disease, BMI, feeding method, Norton score

* Background Incidence of TB per 100 000 person-years ** Data obtained from external source

TST = tuberculin skin testing; HIV = human immunodeficiency virus; CVD = cardiovascular disease; COPD = chronic obstructive pulmonary disease

Table 2. Summary of the 16 observational studies on the association between diabetes and active tuberculosis included in the meta-analysis

Type of Study	Study	Country; population	Study period	Background TB incidence*	Exposure	Outcome	Adjusted variables
Prospective cohort	Kim et al., 1995 (5)	Republic of Korea; civil servants	1988–1990	306	DM diagnosed as ≥119mg/dl at screening, followed by FBG ≥150mg/dl and PPBG ≥180 mg/dl	PTB determined by X-ray	Age^
	John et al., 2001 (6)	India; renal transplant patients in Vellore	1986–1999	168**	DM diagnosed as FBG >120 mg/dL or PPBG >200 mg/dL; or two elevated levels of either measurement	All TB diagnosed by X-ray, AFB, gastric juice, or culture	Age, chronic liver disease, other co-existing infections (CMV, PCP, nocardiosis, deep mycoses), immunosuppressive meds
	Chen et al., 2006 (7)	Taiwan (China); renal transplant recipients in Taichung	1983–2003	66.7	DM diagnosis from medical chart	All TB diagnosed by 1) positive culture, 2) presence of granuloma in biopsy, 3) typical chest x-ray finding, OR 4) clinical presentation consistent with TB and favorable response to Tx	Age, gender, dialysis duration, HBV and HCV infection, graft rejection >3, immunosuppressive medications
	Leung et al., 2008 (8)	Hong Kong (SAR China); elderly aged >65 years	Jan. 2000 – Dec. 2000	90	DM determined by FBG >7.0mmol/L	All TB diagnosed by bacteriology, X-ray, histology, or response to TB Tx	Age, sex, smoking, alcohol, language, marital status, education, housing, employment, SES, BMI, cardiovascular disease, hypertension, COPD/asthma, malignancy, recent weight loss, recent hospitalization, activities and daily living scores
Case-control	Mori et al., 1992 (9)	USA; Oglala Sioux indians in South Dakota	1986	90.9	DM determined by anti-diabetic treatment; or ≥ 11.1 mmol/L at screening or ≥ 7.8 mmol/L FBG	Clinically diagnosed TB, not otherwise specified	Age, sex, alcohol abuse, isoniazid therapy, residence
	Buskin et al., 1994 (10)	USA; residents seen at TB clinic in Washington DC	1988–1990	9	DM by self-report	All TB defined by CDC 1990	Age
	Rosenman et al., 1996 (11)	USA; male residents registered at the New Jersey Department of Health	Jan. 1985 – May 1987	9.5	DM by self-report	All TB diagnosed by positive culture, OR physician's diagnosis with anti-TB medication	Age, gender, race
	Pablo-Mendez et al., 1997 (12)	USA; civilians in California (based on discharge records)	1991	17.3**	DM diagnosis from medical chart coded as ICD-9 : 250.0 - 250.9	All TB coded as ICD-9 010-018	Age, sex, race, poor education, median income, health insurance, HIV-related conditions, chronic renal insufficiency, alcohol-related conditions, drug use and two-way interactions
	Jick et al., 2005 (13)	UK; general practice research database	1990–2001	3	DM determined by anti-diabetic treatment	All TB treated with anti-TB medication	Age, sex, index date, amount of computerized medical history, glucocorticoid use, smoking, BMI, pulmonary disease, use of anti-rheumatic or immunosuppressive agents
	Alisjahbana et al., 2006 (14)	Indonesia; Bandung and Jakarta,	Mar. 2001 – Mar. 2005	263**	DM determined by FBG ≥126 mg/dl	PTB diagnosed by clinical presentation, X-ray, confirmed by AFB in sputum	Age
	Brassard et al., 2006 (15)	USA; PharMetrics Database with ≥1 prescription for anti-rheumatic medicines	Sept.1998 – Dec. 2003	5.6	DM diagnosis from medical chart coded as ICD-9 : 250.0 - 250.9	All TB coded as ICD-9 010-018	Age, sex, silicosis, chronic renal failure, haemodialysis, solid organ transplant, head and neck cancer, NSAIDS, steroids, Cox-2 inhibitors
	Coker et al., 2006 (16)	Russian Federation; residents in the city of Samara	Jan. 2003 – Dec. 2003	118**	DM by self-report	PTB diagnosed by positive culture	Age, sex, relative with TB, drinking raw milk, assets, number of co-habiting persons, employment, financial security, smoking, alcohol, illicit drugs, history of imprisonment
	Perez et al., 2006 (17)	USA; residents of 15 Texas/Mexico border counties (based on discharge records)	1999–2001	13.1	DM diagnosis from medical chart coded as ICD-9 : 250.0 - 250.9	All TB coded as ICD-9 010-018	Age, sex, race^, insurance, chronic renal failure, nutrition deficit, income, education, border^
	Wu et al., 2007 (18)	Keelung, Taiwan (China); TB cases and controls with lower respiratory infections without pneumonia OR contacts of TB cases without TB disease	Jan. 2002 – Dec. 2004	87**	DM diagnosis from medical chart	PTB confirmed by culture	Age, gender, pneumoconiosis, bronchiectasis, liver cirrhosis, haemodialysis, lung cancer

| Type of Study | Study | Country; population | Study period | Background TB | Exposure | Outcome | Adjusted variables |

				incidence*			
Other"	Ponce-de-Leon et al., 2004 (19)	Mexico; civilians in Veracruz	Mar. 1995 – Apr. 2003 for TB case accrual; 2005 for diabetes survey	28	DM previously diagnosed by a physician; or FBG ≥ 126 mg/dl or ≥ 200 mg/dl for random samples	All TB diagnosed by positive AFB or postiive culture	Age^, and standardized by sex
	Dyck et al., 2007 (20)	Canada; aboriginals in Saskatchewan	Jan. 1986 – Dec. 2001 for TB case accrual; Jan. 1991 – Dec. 1995 for diabetes survey	44	DM from medical chart coded as ICD-9 : 250	All TB cases reported to Saskatchewan Health	Age^

* Background incidence of TB per 100 000 person-years ** Data obtained from external source; ^ Stratum-specific relative risks were pooled by inverse-variance weighting method

Other: neither of the studies by Ponce-de-Leon et al. and Dyck et al. was specified as cohort or case-control. Case accrual occurred prospectively, while the underlying distribution of diabetes was determined during a different time after baseline.

AFB = acid fast bacilli stain; BMI = body mass index; CMV = cytomegalovirus; DM = diabetes mellitus; FBG = fasting blood glucose; NSAIDS = non-steroidal anti-inflammatory medicines; PCP = pneumocystis pneumonia; PPBG = post-prandial blood glucose; PTB = pulmonary TB; Tx = treatment

Table 3. Association between diabetes (DM) and active tuberculosis in studies stratifying by glucose control

Study	Diabetes strata	Relative risk	95% confidence interval
Pablo-Mendez et al., 1997 (12)	No DM	1	--
	Type II DM; uncomplicated	1.08	(0.98–1.20)
	Type I DM; uncomplicated	1.47	(1.25, 1.73)
	Poor control / complicated	2.75	(2.46, 3.06)
Leung et al., 2008 (8)	No DM	1	--
	DM; HbA1c<7%	0.81	(0.44, 1.48)
	DM HbA1c≥7%	2.56	(1.95, 3.35)

Table 4. Summary of studies on the association between diabetes (DM) and drug-resistant tuberculosis (DR-TB)

Study	Country	Study design	Study period	Method of ascertaining DM	Adjusted variables
STUDIES ON DM AND DR-TB (NO DISTINCTION BETWEEN MDR-TB)					
Studies on DM and primary DR-TB					
Subhash et al., 2003 (21)	South India	Cross-sectional	Jan. 1997 – Dec. 1999	FBG>140mg/dl; or known diabetics on antidiabetic medication or diet control	None
Singla et al., 2006 (22)	Riyadh, Saudi Arabia	Cross-sectional; DM vs. no DM	Jan. 1998 – Dec. 1999	FBG >140mg/dl in repeat testings	None
Kong et al., 2008 (23)	Seoul, Republic of Korea	Cross-sectional	Sept. 2005 – Sept. 2007	Medical records	None
Studies on DM and acquired DR-TB					
Subhash et al., 2003 (21)	South India	Cross-sectional	Jan. 1997 – Dec. 1999	FBG>140mg/dl; or known diabetics on antidiabetic medication or diet control	None
Ito et al., 2004 (24)	Tokyo, Japan	Cross-sectional	Jan. 1993 – Dec. 2003	Not reported	None
Studies on DM and DR-TB (no distinction between primary or acquired)					
Borchardt et al., 1995 (25)	Northern Germany	Cross-sectional	Jan. 1984 – Dec. 1993	Medical records	None
Arevalo et al., 1996 (26)	Southeastern Spain	Cross-sectional	Jan. 1988 – Oct. 1994	Medical records	Age, sex, chest hospital, pulmonary TB, smear positive, previous anti-TB treatment, cavitary lung disease, alcohol dependency, COPD, corticosteroids, neoplasia, IDUs, hepatic cirrhosis
Lee et al., 2001 (27)	Seoul, Republic of Korea	Cross-sectional	Mar. 1995 – Feb. 2000	Medical records	None
Moniruzzaman et al., 2006 (28)	British Columbia, Canada	Cross-sectional	1990–2001	Medical records	None
STUDIES ON DM AND MDR-TB					
Studies on DM and primary MDR-TB					
Wang et al., 2001 (29)	Taipei, Taiwan (China)	Cross-sectional	Jan. 1996 – Dec. 1999	Medical records	None
Min et al., 2005 (30)	Masan, Republic of Korea	Cross-sectional	Jan. 2001 – Jun. 2003	Medical records	Age, smoking
Studies on DM and acquired MDR-TB					
Wang et al., 2001 (29)	Taipei, Taiwan	Cross-sectional	Jan. 1996 – Dec. 1999	Medical records	None
Studies on DM and MDR-TB (no distinction between primary or acquired)					
Fujino et al., 1998 (31)	Japan	Cross-sectional MDR vs. matched non-MDR	Jan. 1994 – Dec. 1996	Not reported	Matched by age, sex, time of hospitalization; adjusted for previous treatment, non-compliance with treatment, alcohol dependency, high bacillary AFB smear and culture
Bashar et al., 2001 (32)	New York City, USA	Cross-sectional; DM vs. no DM	1987–1997	Medical records	
Toungoussova et al. 2002 (33)	Archangels, Oblast, Russian Federation	Cross-sectional	1998–2000	Medical records	None
Liaw et al., 2004 (34)	Taipei, Taiwan (China)	Cross-sectional; MDR vs. non-MDR	Jan. 1998 – Dec. 2002	Medical records	None
Kim et al., 2005 (35)	Seoul, Republic of Korea	Cross-sectional	Mar. 1999 – Mar. 2003	Not reported	None
Telles et al., 2005 (36)	Sao Paulo, Brazil	Cross-sectional; Population-based	Mar. 2000 – May 2002	Self-reported	None
Fisher-Hoch et al., 2008 (37)	Texas, USA	Cross-sectional	1996–2003	Self-reported	Age, gender, alcohol and drug dependency, HIV, previous TB
Tanrikulu et al., 2008 (38)	South-east Turkey	Cross-sectional	Dec. 2001 – Apr. 2005	Medical records	None
Suarez Garcia et al., 2009 (39)	Madrid, Spain	Cross-sectional	Sept. 1997 – Dec. 2006	Medical records	None
STUDIES ON DM AND XDR-TB					
Jeon et al., 2008 (40)	Masan, Republic of Korea	Cross-sectional	2005–2007	Self-reported	Sex, cumulative duration of treatment

FBG = fasting blood glucose; COPD = chronic obstructive pulmonary disease; IDU = intravenous drug use; AFB = acid fast bacilli; HIV = human immunodeficiency virus

Figure 1. Association between diabetes and tuberculosis (TB) infection in four cross-sectional studies

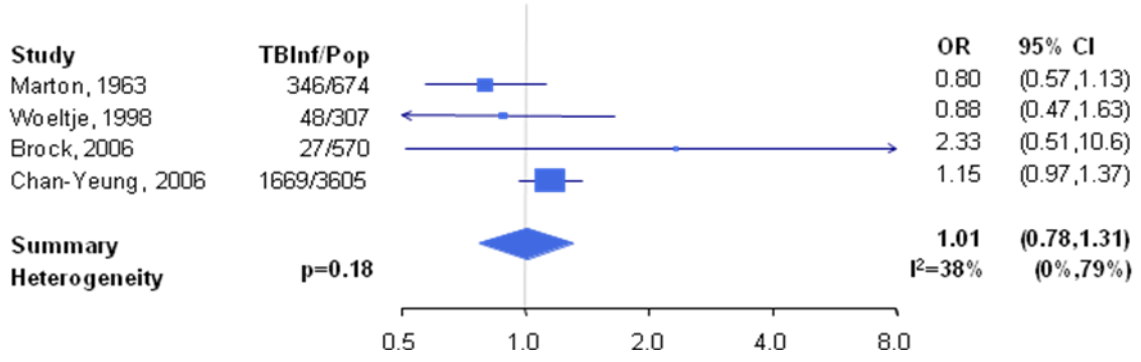
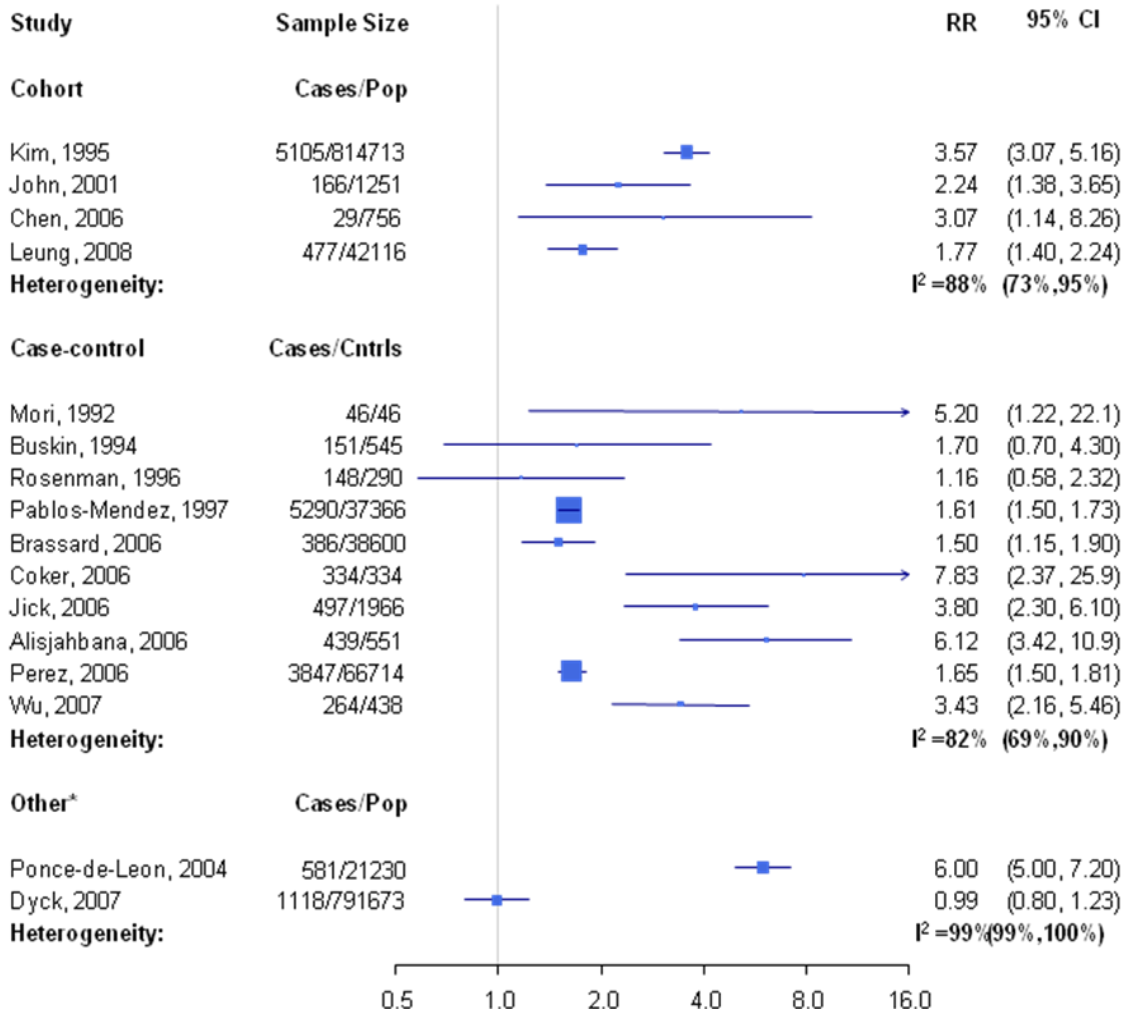


Figure 2. Association between diabetes and active tuberculosis in 16 observational studies, with age-adjustment



* These studies were not specified as prospective cohort or case-control. TB case accrual occurred prospectively, while the underlying distribution of diabetes was determined during a different time period after baseline.
Note: Arrows indicate the truncation of confidence intervals due to limited space on forest plot.

Figure 3. Funnel plot to examine the possibility of publication bias among studies on the association between diabetes and active tuberculosis

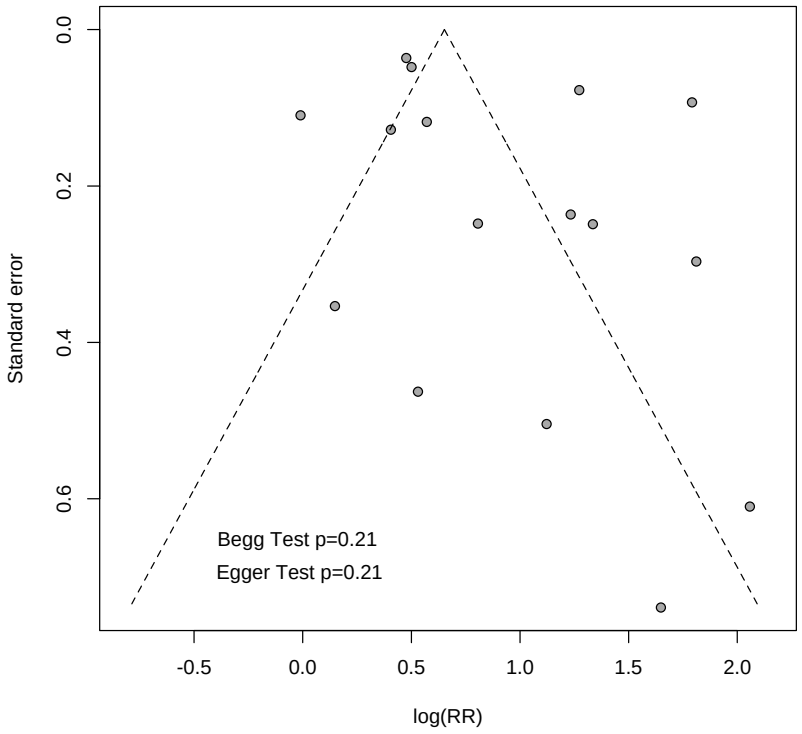


Figure 4. Association between diabetes (DM) and drug-resistant TB (DRTB) in 20 observational studies

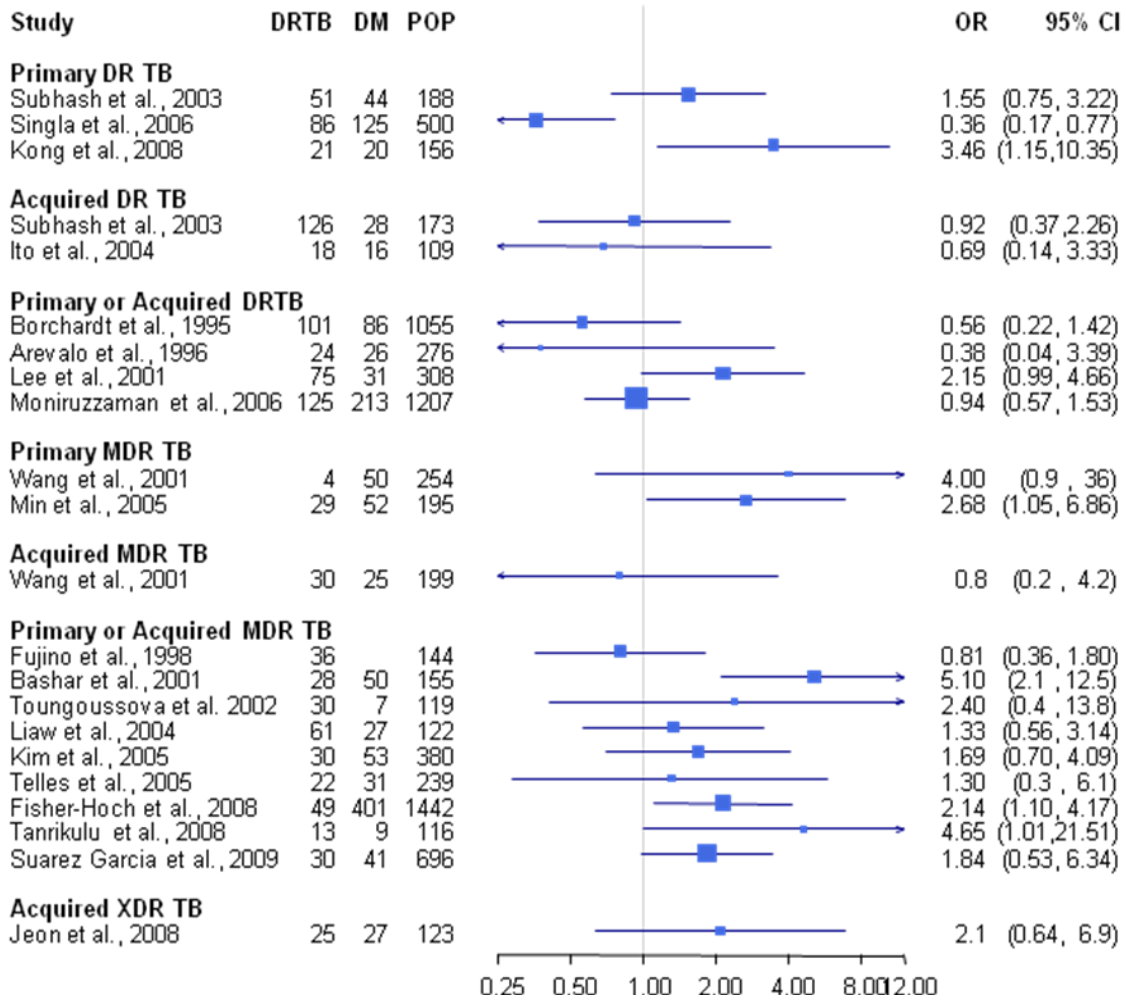
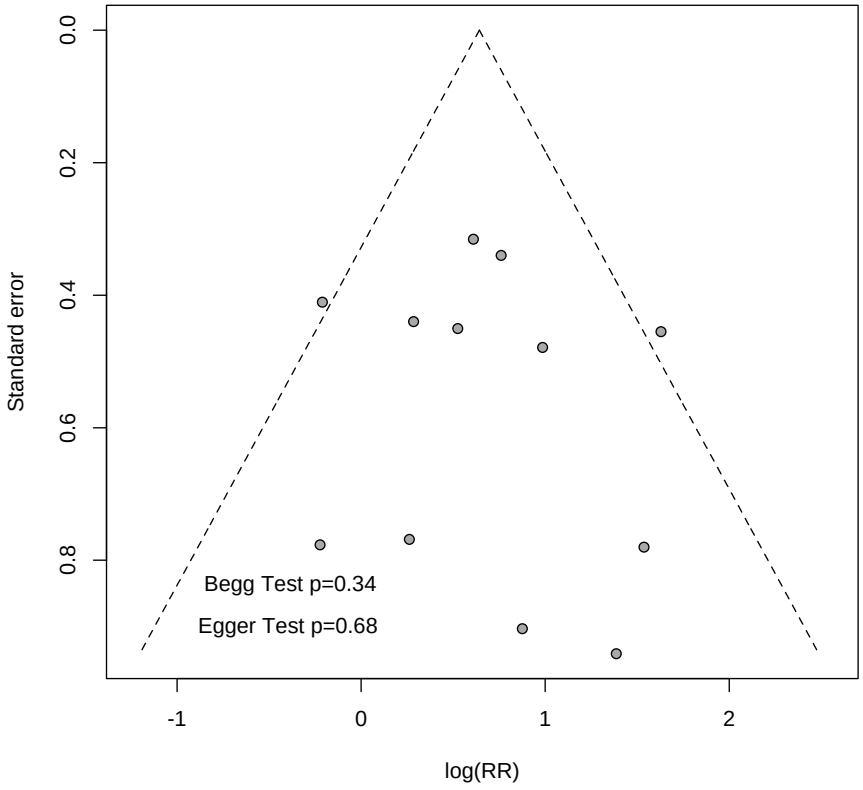


Figure 5. Funnel plot to examine the possibility of publication bias among studies on the association between diabetes and primary or acquired multidrug-resistant tuberculosis



References

1. Marton S et al. Representative tuberculosis mass examinations in diabetics in hungary. *Acta Tuberc Pneumol Scand*, 1963, 43:29-38.

2. Woeltje KF et al. Tuberculosis infection and anergy in hemodialysis patients. American Journal of Kidney Diseases, 1998, 31(5):848–852.

3. Brock I et al. Latent tuberculosis in HIV positive, diagnosed by the *M. tuberculosis* specific interferon-gamma test. *Respiratory Research*, 2006, 7:56.

4. Chan-Yeung M et al. Prevalence and determinants of positive tuberculin reactions of residents in old age homes in Hong Kong. *International Journal of Tuberculosis and Lung Disease*, 2006, 10(8):892–898.

5. Kim SJ et al. Incidence of pulmonary tuberculosis among diabetics. *Tubercle and Lung Disease*, 1995, 76(6):529–533.

6. John GT et al. Risk factors for post-transplant tuberculosis. *Kidney International*, 2001, 60(3):1148–1153.

7. Chen CH et al. Mycobacterium tuberculosis infection following renal transplantation in Taiwan. *Transplant Infectious Diseases*, 2006, 8(3):148–156.

8. Leung CC et al. Diabetic control and risk of tuberculosis: a cohort study. *American Journal of Epidemiology*, 2008, 167(12):1486–1494.

9. 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):547–550.

10. Buskin SE et al. Tuberculosis risk factors in adults in King County, Washington, 1988 through 1990. *American Journal of Public Health*, 1994, 84(11):1750–1756.

11. Rosenman KD, Hall N. Occupational risk factors for developing tuberculosis. *American Journal of Industrial Medicine*, 1996, 30(2):148–154.

12. Pablos-Mendez 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):574–579.

13. Jick SS et al. Glucocorticoid use, other associated factors, and the risk of tuberculosis. *Arthritis & Rheumatism*, 2006, 55(1):19–26.

14. Alisjahbana B et al. Diabetes mellitus is strongly associated with tuberculosis in Indonesia. *International Journal of Tuberculosis and Lung Disease*, 2006, 10(6):696–700.

15. Brassard P, Kezouh A, Suissa S. Antirheumatic drugs and the risk of tuberculosis. *Clinical Infectious Diseases*, 2006, 43(6):717–722.

16. Coker R et al. Risk factors for pulmonary tuberculosis in Russia: case-control study. Bmj 2006 Jan 14;332(7533):85-7.

17. Perez A, Brown HS 3rd, Restrepo BI. Association between tuberculosis and diabetes in the Mexican border and non-border regions of Texas. *American Journal of Tropical Medicine and Hygiene*, 2006, 74(4):604–611.

18. Wu HP et al. Pneumoconiosis and liver cirrhosis are not risk factors for tuberculosis in patients with pulmonary infection. *Respirology*, 2007, 12(3):416–419.

19. Ponce-De-Leon A et al. Tuberculosis and diabetes in southern Mexico. *Diabetes Care*, 2004, 27(7):1584–1590.

20. Dyck RF et al. The relationship between diabetes and tuberculosis in Saskatchewan: comparison of registered Indians and other Saskatchewan people. *Canadian Journal of Public Health*, 2007, 98(1):55–59.

21. Subhash HS et al. Drug resistant tuberculosis in diabetes mellitus: a retrospective study from south India. *Tropical Doctor*, 2003, 33(3):154–156.

22. Singla R et al. Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. *International Journal of Tuberculosis and Lung Disease*, 2006, 10(1):74–79.

23. Kong J et al. The prevalence of initial drug resistance among pulmonary tuberculosis patients. *Tuberculosis and Respiratory Diseases*, 2008, 64(2):95–101.

24. Ito K et al. Drug resistance in recurrent cases of tuberculosis. *Kekkaku*, 2004, 79(8):461–467.

25. Borchardt J et al. Drug-resistant tuberculosis in northern Germany: a retrospective hospital-based study of 1,055 patients from 1984 until 1993. European Respiratory Journal, 1995, 8(7):1076–1083.

26. Arevalo M et al. Risk factors associated with drug-resistant Mycobacterium tuberculosis in Castilla-la-Mancha (Spain). *European Respiratory Journal*, 1996, 9(2):274–278.

27. Lee JH, Chang JH. Drug-resistant tuberculosis in a tertiary referral teaching hospital of Korea. *Korean Journal of Internal Medicine*, 2001, 16(3):173–179.

28. Moniruzzaman A et al. A population-based study of risk factors for drug-resistant TB in British Columbia. *International Journal of Tuberculosis and Lung Disease*, 2006, 10(6):631–638.

29. Wang PD, Lin RS. Drug-resistant tuberculosis in Taipei, 1996–1999. *American Journal of Infection Control*, 2001, 29(1):41–47.

30. Min J et al. Risk factors for primary multidrug resistant tuberculosis. *Tuberculosis and Respiratory Diseases*, 2005, 59(6):600–605.

31. Fujino T et al. Attributable factors to the emergence of multidrug-resistant Mycobacterium tuberculosis based on the observation of consecutive drug resistance test results. *Kekkaku*, 1998, 73(7):471–476.

32. Bashar M et al. Increased incidence of multidrug-resistant tuberculosis in diabetic patients on the Bellevue Chest Service, 1987 to 1997. *Chest*, 2001, 120(5):1514–1519.

33. Toungoussova S et al. Drug resistance of *Mycobacterium tuberculosis* strains isolated from patients with pulmonary tuberculosis in Archangels, Russia. *International Journal of Tuberculosis and Lung Disease*, 2002, 6(5):406–414.

34. Liaw YS et al. Drug resistance pattern of Mycobacterium tuberculosis in a university hospital in Taiwan, 1998–2002. *Journal of the Formosan Medical Association*, 2004, 103(9):671–677.

35. Kim DK et al. The prevalence and risk factors of drug resistant pulmonary tuberculosis investigated at one university hospital in Seoul. *Tuberculosis and Respiratory Diseases*, 2005, 58(3):243–247.

36. Telles MA et al. A population-based study of drug resistance and transmission of tuberculosis in an urban community. International Journal of Tuberculosis and Lung Disease, 2005, 9(9):970–976.

37. Fisher-Hoch SP et al. Type 2 diabetes and multidrug-resistant tuberculosis. *Scandinavian Journal of Infectious Diseases*, 2008, 40(11–12):888–893.

38. Tanrikulu AC et al. Risk factors for drug resistant tuberculosis in southeast Turkey. *Tropical Doctor*, 2008, 38(2):91–93.

39. Suarez-Garcia I et al. Risk factors for multidrug-resistant tuberculosis in a tuberculosis unit in Madrid, Spain. *European Journal of Clinical Microbiology and Infectious Diseases*, 2009, 28(4):325–330.

40. Jeon CY et al. Extensively drug-resistant tuberculosis in South Korea: risk factors and treatment outcomes among patients at a tertiary referral hospital. *Clinical Infectious Diseases*, 2008, 46(1):42–49.

2. Associations between diabetes and tuberculosis treatment outcomes

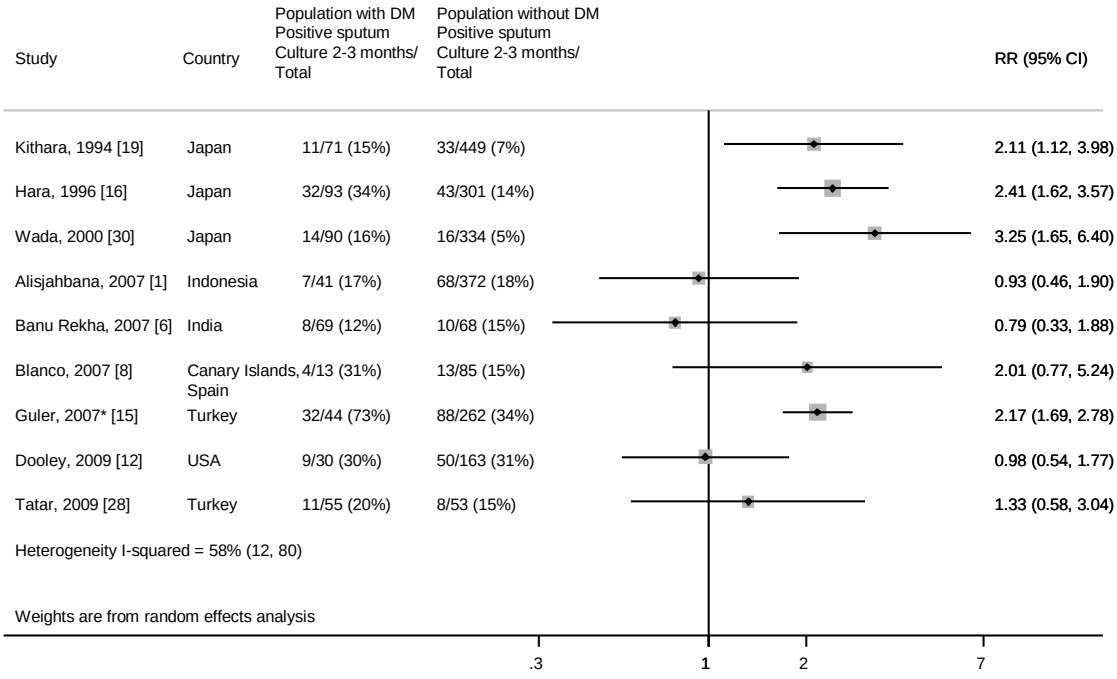
Table. Characteristics of included studies for the association between DM and TB outcomes

Study	Type of study	Country	Type of TB	Total (N)	Population with diabetes (N)	Outcomes						Definition of diabetes (DM)
						Sputum culture conversion 2–3 months	Failure and death	Death	Adjusted variables for death outcome	Relapse	Recurrent drug resistance	
Alisjahbana (1)	Prospective cohort	Indonesia	Pulmonary TB	634	94	√	√	√	–	–	–	Two measurements of FBG >126 mg/dL
Ambrosetti (2)	Prospective cohort	Italy	Undifferentiated TB	778	32	–	√	√	–	–	–	Medical records
Ambrosetti (3)	Prospective cohort	Italy	Undifferentiated TB	838	50	–	√	√	–	–	–	Medical records
Ambrosetti (4)	Prospective cohort	Italy	Undifferentiated TB	715	40	–	√	√	–	–	–	Medical records
Anunnatsiri (5)	Retrospective cohort	Thailand	Pulmonary TB	226	117	–	√	–	–	–	–	Medical records
Banu Rekha (6)	Retrospective analysis of three concurrent studies	India	Pulmonary TB	190	92	√	–	–	–	–	–	Medical records, FBG
Bashar (7)	Retrospective case-control	USA	Undifferentiated TB	155	50	–	–	√	–	–	–	Medical records
Blanco (8)	Retrospective cohort	Canary Islands (Spain)	Pulmonary TB	98	14	√	–	–	–	–	–	Medical records
Centis (9)	Prospective cohort	Italy	Undifferentiated TB	1,162	56	–	√	√	–	–	–	Medical records
Centis (10)	Prospective cohort	Italy	Undifferentiated TB	906	40	–	√	√	–	–	–	Medical records
Chiang (11)	Retrospective cohort	Taiwan (China)	Pulmonary TB	1,127	241	–	√	√	–	–	–	Medical records
Dooley (12)	Retrospective cohort	USA	Undifferentiated TB	297	42	√	–	√	Age, HIV, weight, foreign birth	–	–	Medical records, non-FBG >200mg/dL, DM medications
Fielder (13)	Retrospective cohort	USA	Pulmonary TB	174	22	–	–	√	Age	–	–	Medical records
Fisher-Hoch (14)	Retrospective cohort	Mexico and USA	Undifferentiated TB	2878	688	–	–	√	–	–	√	Self report
Guler (15)	Retrospective cohort	Turkey	Pulmonary TB	306	44	√	–	–	–	–	–	Medical records
Hara (16)	Retrospective cohort	Japan	Pulmonary TB	624	112	√	–	–	–	–	–	Medical records
Hasibi (17)	Retrospective cohort	Iran	Disseminated TB	50	6	–	–	√	–	–	–	Medical records
Ito (18)	Retrospective cohort	Japan	Undifferentiated TB	109	16	–	–	–	–	–	√	Medical records
Kitahara (19)	Retrospective cohort	Japan	Pulmonary TB	520	71	√	–	√	–	–	–	Medical records
Kourbatova (20)	Retrospective case-control	Russian Federation	Undifferentiated TB	460	20	–	–	√	–	–	–	Medical records
Maalej (21)	Retrospective case-control	Tunisia	Pulmonary TB	142	60	–	–	√	–	√	–	Medical records
Mboussa (22)	Retrospective cohort	Republic of the Congo	Pulmonary TB	132	32	–	√	√	–	√	–	Two measurements of FBG ≥126 mg/dL
Oursler (23)	Retrospective cohort	USA	Pulmonary TB	139	18	–	–	√	Age, HIV, Renal, COPD	–	–	Medical records
Pina (24)	Retrospective cohort	Spain	Undifferentiated TB	1,511	73	–	–	√	–	–	–	Medical records
Ponce-De-Leon (25)	Prospective cohort	Mexico	Pulmonary TB	581	172	–	√	√	–	–	–	Medical records (FBG ≥126 mg/dL or non-FBG ≥200 mg/dL sensitivity anal)
Singla (26)	Retrospective cohort	Saudi Arabia	Pulmonary TB	692	187	–	√	√	–	√	–	2 measurements of FBG >140 mg/dL

Subhash (27)	Retrospective cohort	India	Undifferentiated TB	361	72	–	–	–	–	–	√	FBG >140 mg/dL, medical records and DM medication or diet
Tatar (28)	Retrospective cohort	Turkey	Undifferentiated TB	78	156	|√	–	√	–	–	–	Medical records
Vasankari (29)	Retrospective cohort	Finland	Pulmonary TB	629	92	–	–	√	–	–	–	Treatment with DM medications
Wada (30)	Retrospective cohort	Japan	Pulmonary TB	726	143	√	–	–	–	√	–	Medical records
Wang (31)	Retrospective cohort	Taiwan (China)	Pulmonary TB	453	75	–	–	–	–	–	√	Medical records
Wang (32)	Retrospective cohort	Taiwan (China)	Pulmonary TB	217	74	–	√	√	Age, sex	–	–	Medical records and DM medication or FBG>126 mg/dL
Zhang (33)	Retrospective Cohort	China	Pulmonary TB	203	2141	–	–	–		√	–	Medical records or non-FBG ≥126 mg/dL

DM = diabetes mellitus; COPD = chronic obstructive pulmonary disease; FBG = fasting blood glucose

Figure 1. Risk of remaining sputum culture positive after 2-3 months of treatment for TB patients with DM compared with TB patients without DM. Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% CIs.



*The RR for Guler et al. (15) was calculated using the OR, CI and total number of patients with and without DM provided in the paper.

Figure 2. Begg's funnel plot with pseudo 95% confidence limits for all studies with sputum cultures at 2-3 months

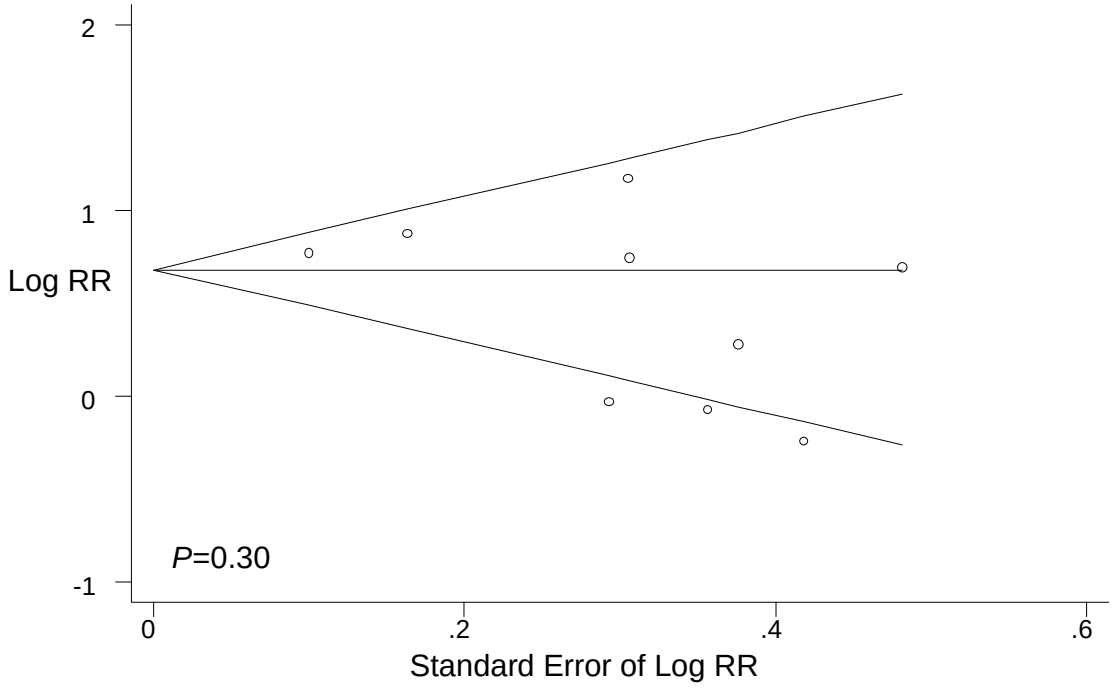


Figure 3. Risk of failure and death for TB patients with DM compared with TB patients without DM. Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% CIs. The diamond is centered on the summary RR of the observational studies, and the width indicates the corresponding 95% CI.

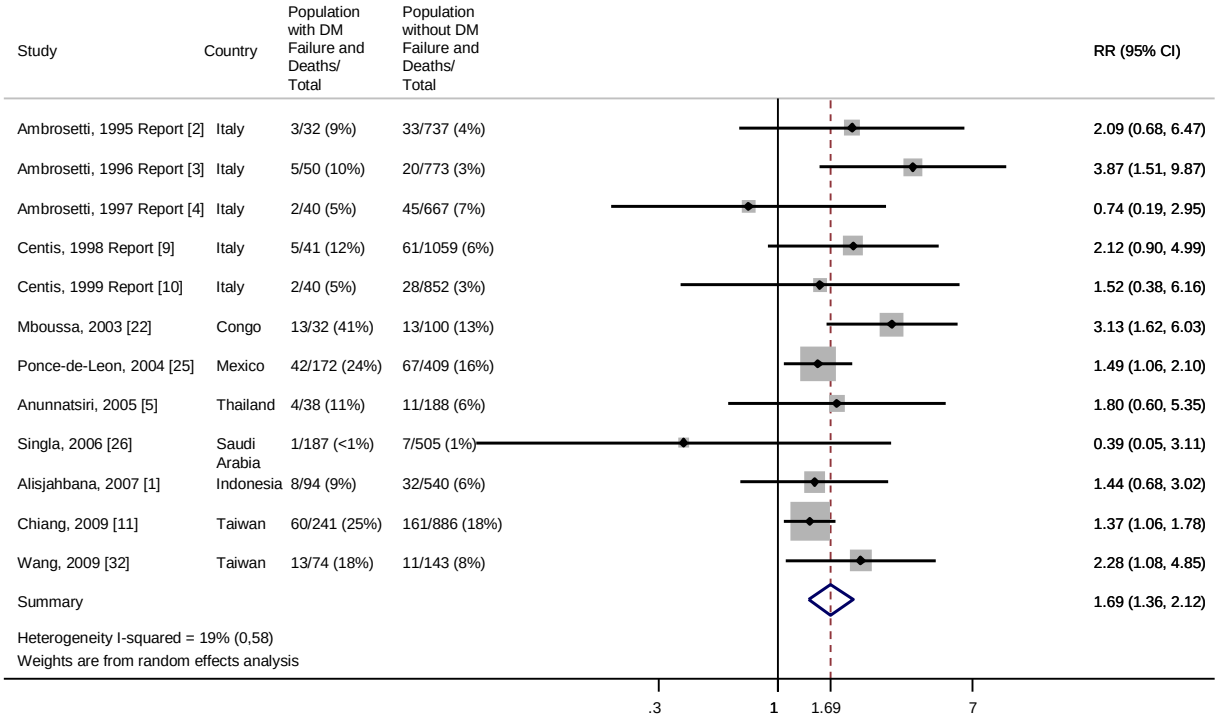


Figure 4. Begg's funnel plot with pseudo 95% confidence limits for all studies with the combined outcome of failure and death.

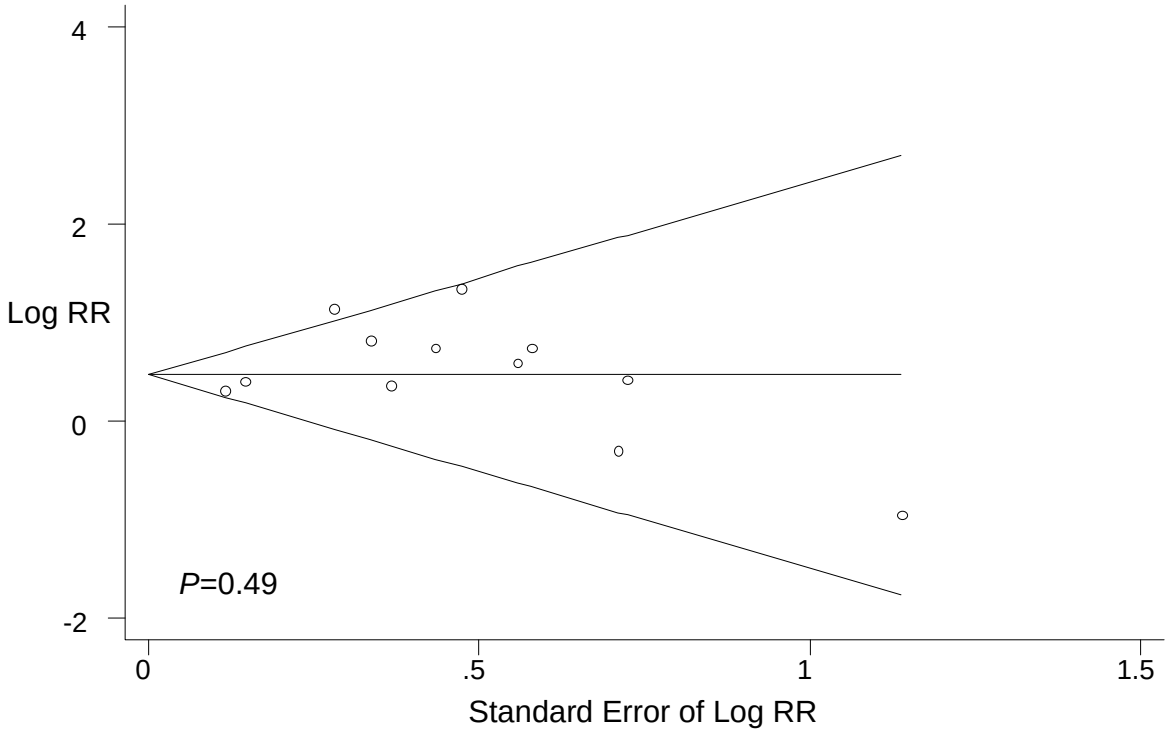


Figure 5. Risk of death for TB patients with DM compared with TB patients without DM. Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% CIs. The diamond is centered on the summary RR of the observational studies, and the width indicates the corresponding 95% CI.

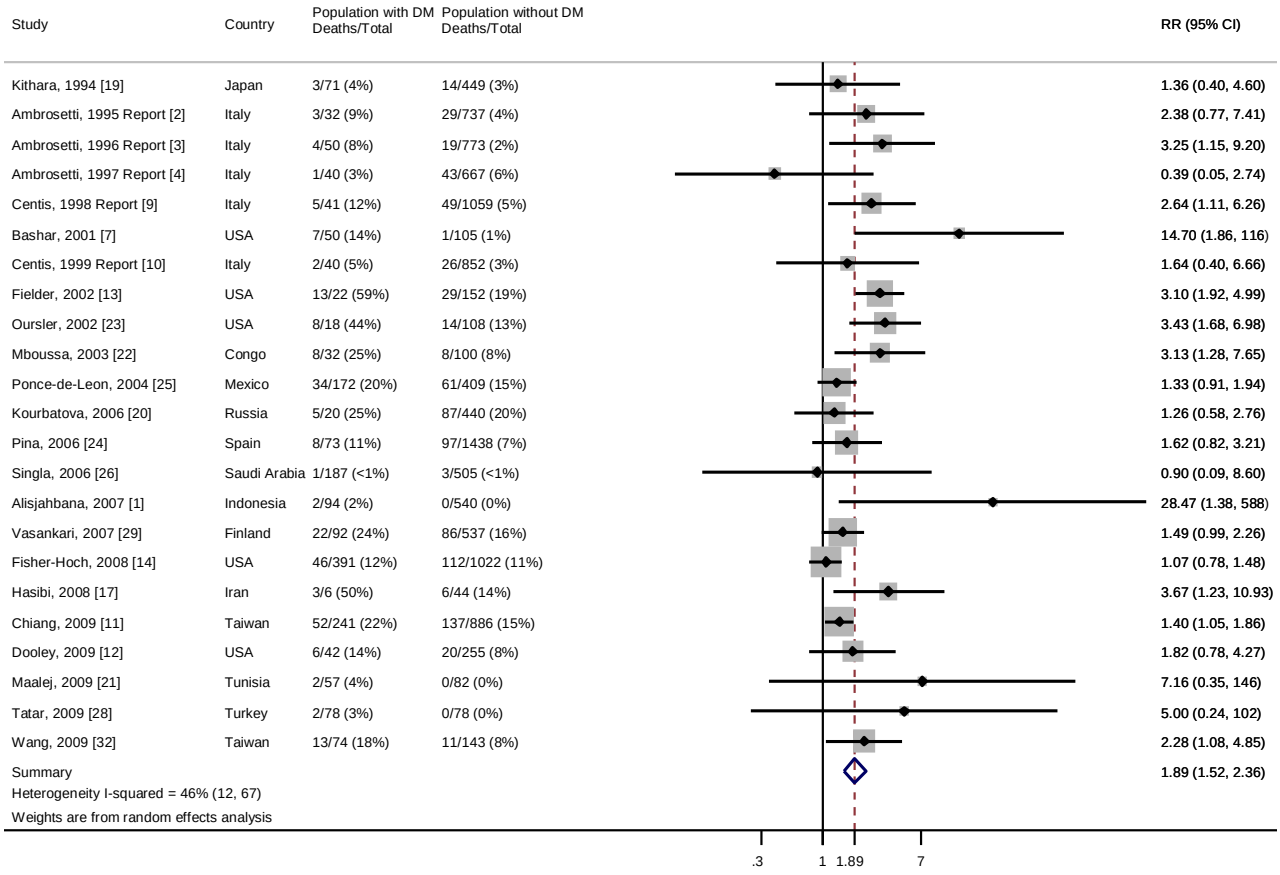


Figure 6. Begg's funnel plot with pseudo 95% confidence limits for all studies with the outcome of death.

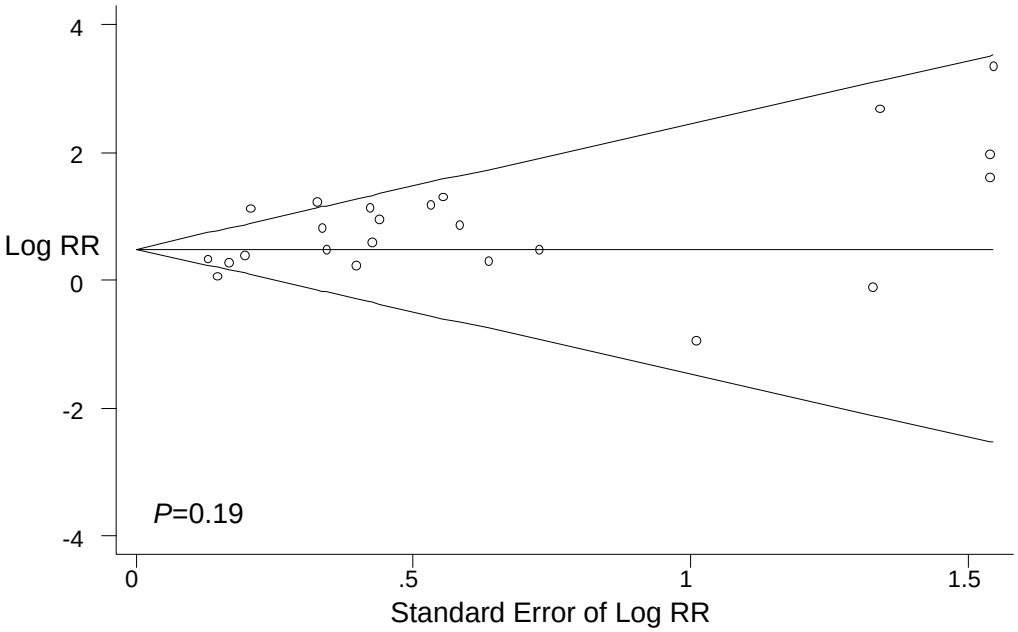


Figure 7. Adjusted odds of death for TB patients with DM compared with TB patients without DM, for all studies with the outcome of death adjusted for age and other confounding factors. Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% CIs. The diamond is centered on the summary OR of the observational studies, and the width indicates the corresponding 95% CI.

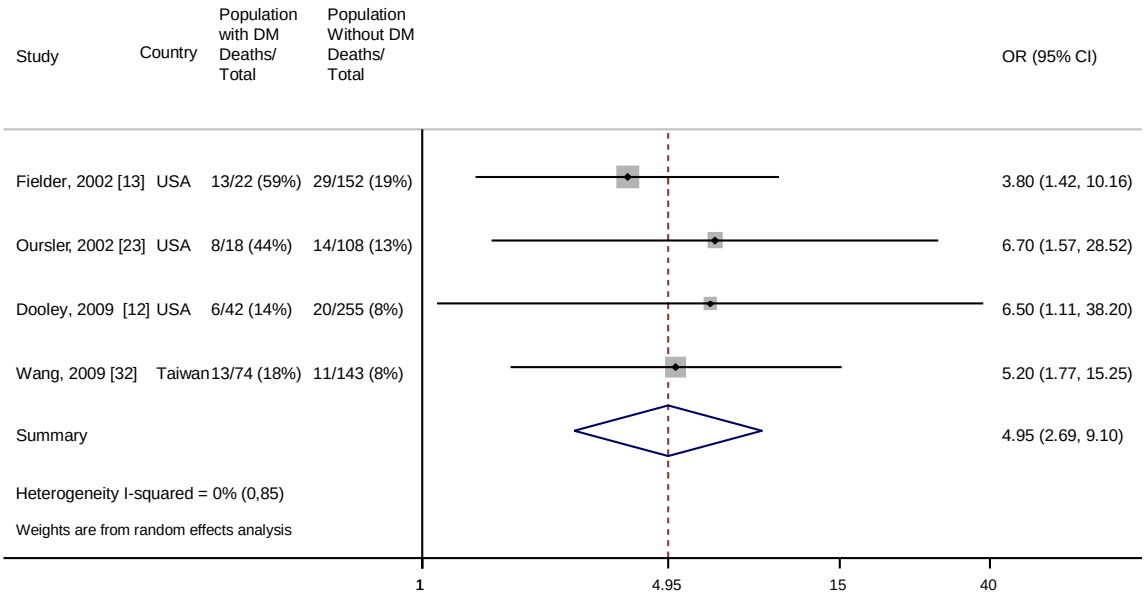


Figure 8. Begg's funnel plot with pseudo 95% confidence limits for all studies with the outcome of death adjusted for age and other confounding factors.

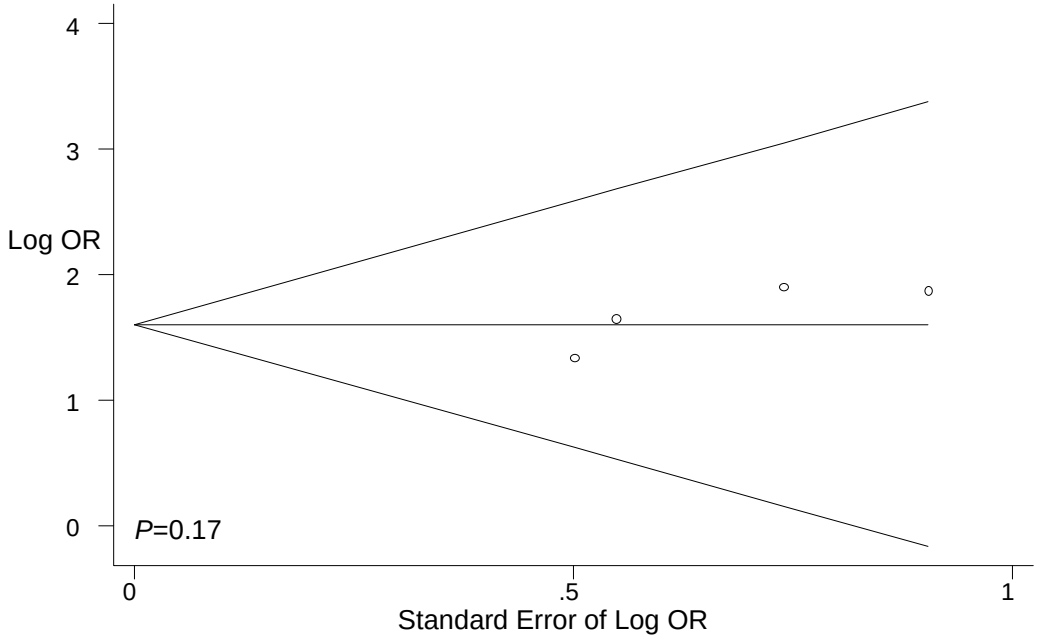


Figure 9. Risk of TB relapse for TB patients with DM compared with TB patients without DM. Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% CIs. The diamond is centered on the summary RR of the observational studies, and the width indicates the corresponding 95% CI.

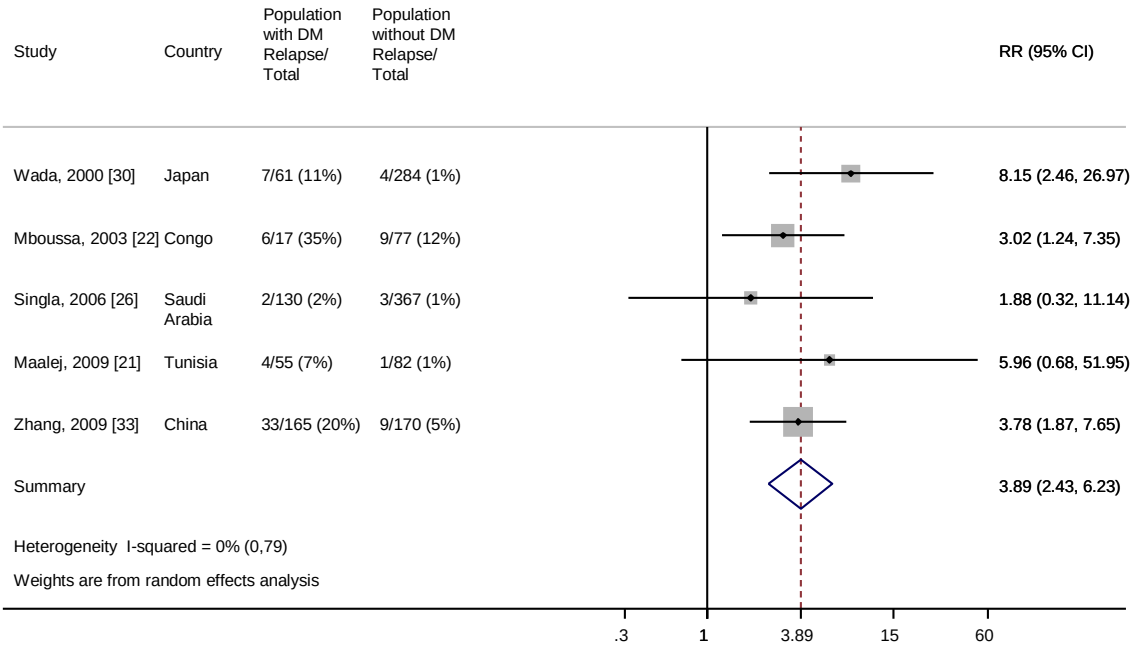


Figure 10. Begg's funnel plot with pseudo 95% confidence limits for all studies with TB relapse.

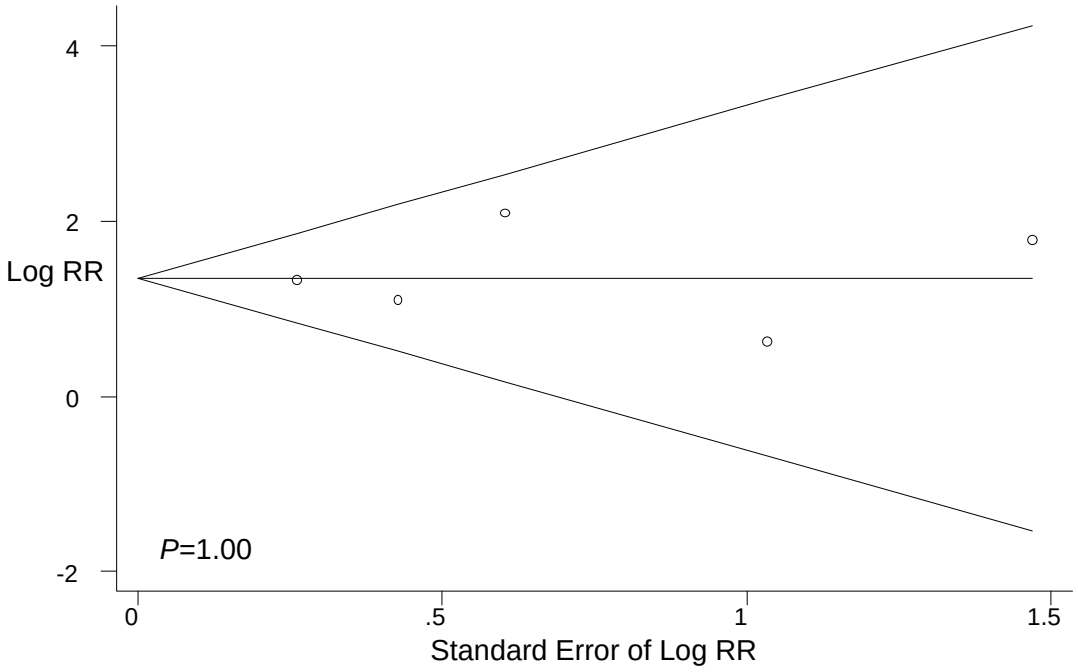


Figure 11. The odds of recurrent TB that is DR, comparing patients with DM to patients without DM. Size of the square is proportional to the precision of the study-specific effect estimates, and the bars indicate the corresponding 95% CIs. The diamond is centered on the summary OR of the observational studies, and the width indicates the corresponding 95% CI.

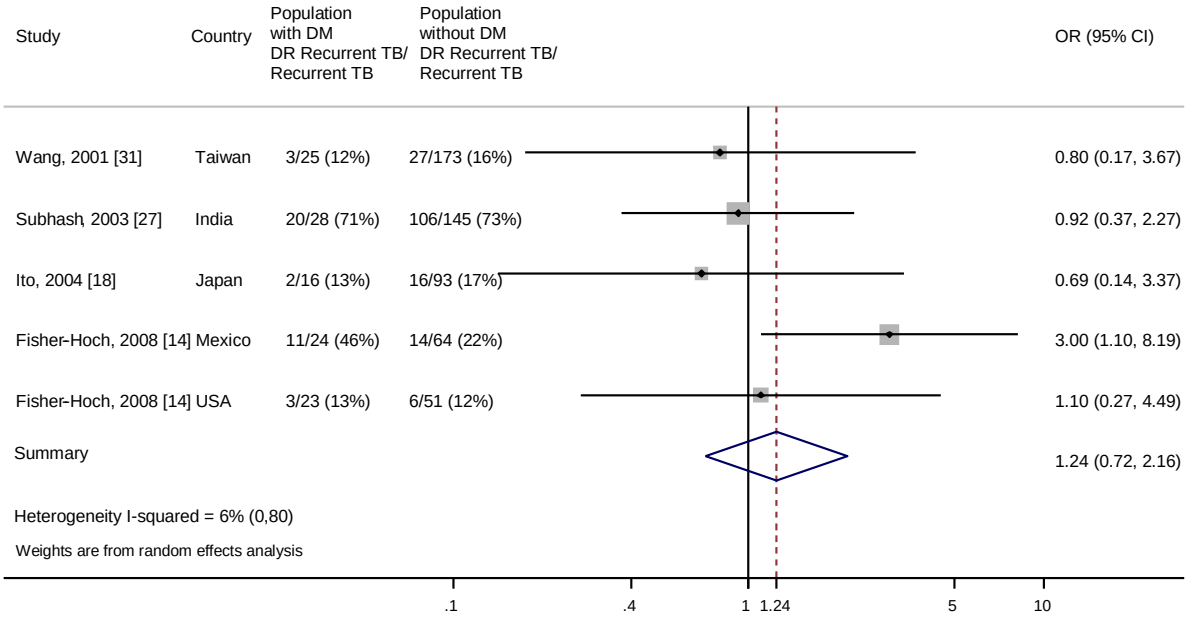
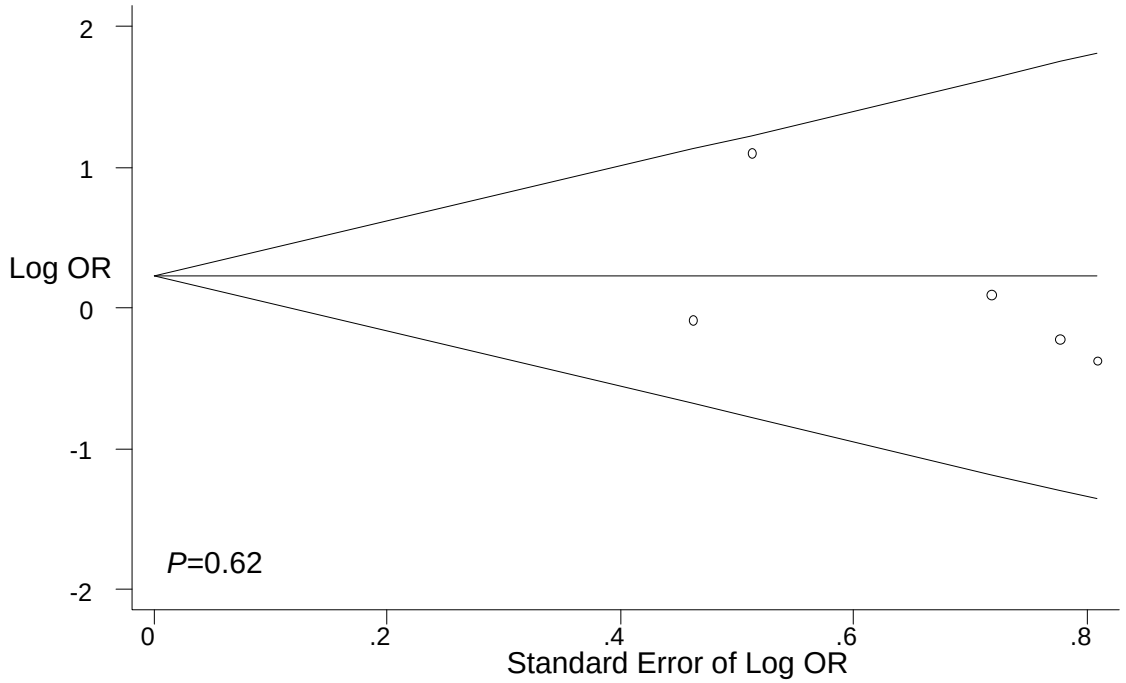


Figure 12. Begg's funnel plot with pseudo 95% confidence limits for all studies with recurrent TB that is DR.



References

1. Alisjahbana B et al. The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis. *Clinical Infectious Diseases*, 2007, 45:428–435.

2. Ambrosetti M et al. The Italian AIPO study on tuberculosis treatment results, report 1995. National AIPO “Tuberculosis” Study Group. *Monaldi Archives for Chest Disease*, 1999, 54:49–54.

3. Ambrosetti M et al. The Italian AIPO study on tuberculosis treatment results, report 1996. National AIPO “Tuberculosis” Study Group. Associazione Italiana Pneumologi Ospedalieri. *Monaldi Archives for Chest Disease*, 1999, 54:237–241.

4. Ambrosetti M et al. The Italian AIPO study on tuberculosis treatment results, report 1997. National AIPO “Tuberculosis” Study Group. *Monaldi Archives for Chest Disease*, 1999, 54:407–412.

5. Anunnatsiri S, Chetchotisakd P, Wanke C. Factors associated with treatment outcomes in pulmonary tuberculosis in Northeastern Thailand. *Southeast Asian Journal of Tropical Medicine and Public Health*, 2005, 36:324–330.

6. Banu Rekha VV et al. Sputum conversion at the end of intensive phase of Category-1 regimen in the treatment of pulmonary tuberculosis patients with diabetes mellitus or HIV infection: An analysis of risk factors*. Indian Journal of Medical Research*, 2007, 126:452–458.

7. Bashar M et al. Increased incidence of multidrug-resistant tuberculosis in diabetic patients on the Bellevue Chest Service, 1987 to 1997. *Chest*, 2001, 120:1514–1519.

8. Blanco JAG et al. Tobacco smoking and sputum smear conversion in pulmonary tuberculosis. *Medicina Clinica*, 2007, 128:565–568.

9. Centis R, Ianni A, Migliori GB: Evaluation of tuberculosis treatment results in Italy, report 1998. Tuberculosis section of the National AIPO Study Group on Infectious Disease and the SMIRA Group. *Monaldi Archives for Chest Disease*, 2000, 55:293–298.

10. Centis R, Migliori GB. Evaluation of tuberculosis treatment results in Italy, report 1999. *Monaldi Archives for Chest Disease*, 2002, 57:297–305.

11. Chiang CY et al. Tuberculosis outcomes in Taipei: factors associated with treatment interruption for 2 months and death. *International Journal of Tuberculosis and Lung Disease*, 2009, 13:105–111.

12. Dooley KE et al. Impact of diabetes mellitus on treatment outcomes of patients with active tuberculosis. *American Journal of Tropical Medicine and Hygiene,* 2009, 80:634–639.

13. Fielder JF et al. A high tuberculosis case-fatality rate in a setting of effective tuberculosis control: implications for acceptable treatment success rates. *International Journal of Tuberculosis and Lung Disease*, 2002, 6:1114–1117.

14. Fisher-Hoch SP et al, Nuevo Santander Tuberculosis Trackers. Type 2 diabetes and multidrug-resistant tuberculosis. *Scandinavian Journal of Infectious Diseases*, 2008, 40:888–893.

15. Guler M et al. Factors influencing sputum smear and culture conversion time among patients with new case pulmonary tuberculosis. *International Journal of Clinical Practice*, 2007, 61:231–235.

16. Hara H. From the aspects of complicated diseases. *Kekkaku*, 1996, 71:47–56.

17. Hasibi M et al. Epidemiological, clinical, laboratory findings, and outcomes of disseminated tuberculosis in Tehran, Iran. *Southern Medical Journal*, 2008, 101:910–913.

18. Ito K et al. Drug resistance in recurrent cases of tuberculosis. *Kekkaku*, 2004, 79:461–467.

19. Kitahara Y et al. An investigation on risk factors relating to the treatment difficulty in originally treated pulmonary tuberculosis cases. *Kekkaku*, 1994, 69:503–511.

20. Kourbatova EV et al. Risk factors for mortality among adult patients with newly diagnosed tuberculosis in Samara, Russia. *International Journal of Tuberculosis and Lung Disease*, 2006, 10:1224–1230.

21. Maalej S et al. Pulmonary tuberculosis and diabetes. A retrospective study of 60 patients in Tunisia. *Presse Medicale*, 2009, 38:20–24.

22. Mboussa J et al. Course of pulmonary tuberculosis in diabetics. *Rev Pneumol Clin*, 2003, 59:39–44.

23. Oursler KK et al. Survival of patients with pulmonary tuberculosis: clinical and molecular epidemiologic factors. *Clinical Infectious Diseases*, 2002, 34:752–759.

24. Pina JM, Dominguez A et al. Excess mortality due to tuberculosis and factors associated to death in and annual cohort of patients diagnosed of tuberculosis. *Revista Clinica Espanola*, 2006, 206:560–565.

25. Ponce-De-Leon A et al. Tuberculosis and diabetes in southern Mexico. *Diabetes Care*, 2004, 27:1584–1590.

26. Singla R et al. Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. *International Journal of Tuberculosis and Lung Disease*, 2006, 10:74–79.

27. Subhash HS et al. Drug resistant tuberculosis in diabetes mellitus: a retrospective study from south India. *Tropical Doctor*, 2003, 33:154–156.

28. Tatar D et al. Tuberculosis in diabetics: features in an endemic area. *Japanese Journal of Infectious Diseases*, 62:423–427.

29. Vasankari T et al. Risk factors for poor tuberculosis treatment outcome in Finland: a cohort study. *BMC Public Health*, 2007, 7:291.

30. Wada M. The effectiveness of pyrazinamide-containing six-month short course chemotherapy. *Kekkaku*, 2000, 75:665–673.

31. Wang PD, Lin RS. Drug-resistant tuberculosis in Taipei, 1996–1999. *American Journal of Infection Control*, 2001, 29:41–47.

32. Wang CS et al. Impact of type 2 diabetes on manifestations and treatment outcome of pulmonary tuberculosis. *Epidemiology and Infection*, 2009, 137:203–210.

33. Zhang Q, Xiao H, Sugawara I. Tuberculosis complicated by diabetes mellitus at Shanghai Pulmonary Hospital, China. *Japanese Journal of Infectious Diseases*, 62:390–691.

3. Summary of studies on screening for tuberculosis in diabetes patients and screening for diabetes in tuberculosis patients, and studies on tuberculosis preventive therapy in patients with diabetes

Table 1. Summary of studies on screening for tuberculosis among people with diabetes and selected comparison population

Table 2. Summary of results of screening for tuberculosis in people with diabetes and selected comparisons

Table 3. Summary of studies on screening for tuberculosis infection among people with diabetes and selected comparison population

Table 4. Summary of results of screening for tuberculosis infection in people with diabetes and selected comparisons

Table 5. Summary of studies on screening for diabetes among tuberculosis patients and selected comparison populations

Table 6. Summary of results on screening for diabetes in tuberculosis patients and selected comparisons

Figure. The decreasing trend of hyperglycaemia in tuberculosis patients receiving anti-tuberculosis treatment

Text. Summary of two studies on tuberculosis preventive therapy in patients with diabetes

Note: Tables 1, 2, 5, 6; the figure and the text reflect findings from the following published review: Jeon CY et al., Bi-directional screening for tuberculosis and diabetes: a systematic review. *Tropical Medicine and International Health*, 2010, 15: 1300–1314 (doi: 10.1111/j.1365-3156.2010.02632.x).

Table 1. Summary of studies on screening for tuberculosis among people with diabetes and selected comparison population

Study	Region, Country	Study Period	Diabetes diagnosis methods	TB identification method	% insulin depen-dent	% male	Age distribution	Comparison Population
Studies on screening for prevalent TB in DM								
Boucot et al., 1952[1]	Philadelphia, United States	1946	Diabetics referred by clinics (FBG >=130mg/dl; Random BG>=170mg/dl with glycosuria)	PTB by chest X-ray	74%	Among DM 31%; Among TB 45%	Among DM 14% <40 years; Among TB 13% <40 years	Non diabetic industrial workers of Philadelphia in 1942**
Oscarsson and Silwer, 1958[2]	County of Kristianstad, Swedan	March 1954	Diabetics identified by medical records	PTB by chest X-ray	64%	Among DM 45%, Among TB 52%	Among DM 18% <40 years; Among TB 26% <40 years	Residents of county of Kristianstad in 1953**
Opsahl et al., 1961[3]	Korea	N/R	Diabetic patients at The National Medical Center	PTB by chest X-ray	43%	Among DM 63%; Among TB N/R	Among DM 35% <40 years; Among TB N/A	Patients applying to the surgical out-patients department for diseases other than TB
Davidovich et al., 1963[4]	Rosario, Argentina	N/R	Diabetic patients at the clinic identified by medical records	PTB by chest X-ray	N/R	Among DM 22%; Among TB 25%	Among DM 12% < 45 year; Among TB 25% <45 years	No comparison
Marton et al., 1963[5]	Hungary	Summer 1960	Diabetic patients of hospital; and nondiabetic controls	PTB by chest X-ray, followed by sputum culture	N/R	Among DM 44%; Among TB 58%	Among DM: Mean 59; Among TB: Mean 60	Non diabetics of similar age and sex distribution from the same hospital
Golli et al., 1975[6]	Germany	N/R	Diabetic patients registered in the diabetes center in Berlin	PTB by chest X-ray	38%	Among DM 62%, Among TB 92%	Among DM 11% <=40; Among TB 17%<=40	No comparison
Gill et al., 1984[7]	Soweto, South Africa	N/R	Diabetics <30 years with insulin dependence by medical records	PTB by chest X-ray	100%	Among DM 50%; Among TB N/R	Among DM Mean 21.7,SD 4.8; 100% <30 years; Among TB N/R	No comparison
Tripathy et al., 1984[8]	Adra, India	N/R	Diabetics identified by medical records	PTB by sputum smear on three consecutive days	N/R	Among DM N/R; Among TB 78%	Among DM 24% <40 years; Among TB 12% <40 years	No comparison
Ezung et al., 2002[9]	Imphal, India	N/R	Diabetics at diabetic clinic; DM established by clinical symptoms and by WHO criteria	PTB by chest X-ray, and sputum smear	N/R	Among DM 65%, Among TB 74%	Among DM 12% <=40 years; Among TB 15% <=40	No comparison
Webb et al., 2009[10]	Western Cape, South Africa	Sept 2006 - Jan 2007	Type 1 diabetics diagnosed by pediatric endocrinologist	TB by chest X-ray, suggestive symptoms, and positive Mantoux test	100%	Among DM 42%, Among TB 67%	100% <21 years for DM and TB	No comparison
Studies on screening for incident TB in DM								
Lester, 1984[11]	Ethiopia	Apr 1976 – Jul 1983	Diabetic patients at a hospital diagnosed by FBG >140mg/dl, Random BG >200mg/dl OR history of diabetes treatment	PTB by chest X-ray, sputum smears; OR positive Mantoux test with suggestive clinical presentation	40%	Among DM 50%, Among TB 69%	Among DM 53% <40 years; Among TB 79%<40 years	No comparison
Kim et al., 1995[12]	South Korea	1988-1990	Civil servants with DM diagnosed by random >=119mg/dl, FBG >=150mg/dl and >=180 mg/dl post meal	PTB by chest X-ray, smear microscopy and culture	N/R	Among DM 96%, Among TB 98%	>=20	Korean civil servants without diabetes

N/R = not reported; PTB = pulmonary tuberculosis; DM = diabetes mellitus; FBG = fasting blood glucose

Table 2. Summary of results of screening for tuberculosis in people with diabetes and selected comparisons

Study	Pop Size of Diabetics	Number of TB	Number of TB Diagnosed prior to screening	TB Prevalence or incidence in diabetics (per 100,000)	TB Prevalence or Incidence for Comparison (per 100,000)	Prevalence or Incidence Ratio	Prevalence or Incidence Difference (per 100,000)	Number needed to screen to detect 1 TB case^
Studies on screening for prevalent TB in DM								
Boucot et al., 1952[1]	3106	261	87	8403*	4300*	2.0	4103	24
Oscarsson and Silwer, 1958[2]	1270	46	N/R	3622*	880*	4.1	2742	36
Opsahl et al., 1961[3]	116	42	13	36206*	10359*	3.5	25848	4
Davidovich et al., 1963[4]	100	4	N/R	4000*	--	--	--	--
Marton et al., 1963[5]	802	16	8	1995	997	2.0	998	100
Golli et al., 1975[6]	304	12	N/R	3947*	--	--	--	--
Gill et al., 1984[7]	66	7	3	10606*	--	--	--	--
Tripathy et al., 1984[8]	219	9	N/R	4110	--	--	--	--
Ezung et al., 2002[9]	100	6	N/R	6000	--	--	--	--
Webb et al., 2009[10]	258	9	2	3488	--	--	--	--
Studies on screening for incident TB in DM								
Lester, 1984[11]	849	29	N/R	488†	--	--	--	--
Kim et al., 1995[12]	8015	45	Excluded at baseline	281†	55	5.1	226	442

--No appropriate comparison could be identified
^ computed by taking the inverse of prevalence difference
* The TB cases were determined only by X-ray, thus TB prevalence may be overestimated
† The cumulative incidence in the diabetic were divided by the number of years of follow-up
N/R = not reported; DM = diabetes mellitus

Table 3. Summary of studies on screening for TB infection among diabetics and selected comparison population

Study	Region, Country	Study Period	Diabetes diagnosis methods	TB identification method	% insulin depen-dent	% male	Age distribution	Comparison Population
Davidovich et al., 1963[4]	Rosario, Argentina	Not specified	Diabetic patients at the clinic identified by medical records	TB infection by Mantoux Test (no distinction made for BCG vaccinated)	N/A	Among DM 22%, Among TB N/A	Among DM 12% < 45 years, Among TB N/A	Annual prevalence of TB in Argentina 1964**[13]
Marton et al., 1963[5]	Hungary	Summer 1960	Diabetic patients of hospital; and nondiabetic controls	TB infection TST (>=10mm) among negative X-rays	N/A	Among DM 44%, Among TB N/A	Among DM Mean 58.8 for men, 60.2 for women; Among TB N/A	Non diabetics of similar age and sex distribution from the same region
Hernandez Garcia et al., 1992[14]	Elche, Spain	1986-1990	Diabetics registered at health center; identified by medical records	TB infection by TST(>=10 mm)	12% TIDM	Among DM 34%, Among TB N/A	Among DM mean 62, SD 11.4, Among TB N/A	No comparison
Mansilla Bermejo et al., 1995[15]	Ciudad Real, Spain	Jun 1994 - Jul 1994	Diabetics registered at health center	TB infection by Mantoux test >=5 mm at first test, for BCG vaccinated >14mm; OR >=18mm at second test, or difference of >14 mm between first and second tests	32%	Among DM 38%, Among TB N/A	Among DM mean 68, SD 9.9; Among TB	No comparison
Webb et al., 2009[10]	Western Cape, South Africa	Sept 2006 - Jan 2007	<21 year olds with T1DM diagnosed by pediatric endocrinologist	TB infection by Mantoux test (>=10mm)	100%	Among DM 42%, Among TB 67%	<21	Western Cape pediatric population**

** Information on comparison group obtained in external source cited in the original paper, in other medical literature, or obtained from public database (WHO)
OGTT=oral glucose tolerance test, FBG=fasting blood glucose, PTB=pulmonary tuberculosis, TST=tuberculin skin testing, BCG=bacillus Calmette-Guerin, T1DM=type 1 diabetes mellitus

Table 4. Summary of results of screening for tuberculosis infection in people with diabetes and selected comparisons

Study	Pop Size of Diabetics	Number of TB infection	TB infection prevalence in diabetics	TB infection Prevalence in comparison	Prevalence Ratio	Prevalence Difference	Number needed to screen to detect 1 TB infection case*
Davidovich et al., 1963[4]	100	95	95.0%	24.8%	3.8	70.2%	1
Marton et al., 1963[5]	324	188	58.0%	63.2%	0.9	-5.2%	N/A
Hernandez Garcia et al., 1992[14]	257	118	45.9%	--	--	--	
Mansilla Bermejo et al., 1995[15]	154	97	63.0%	--	--	--	
Webb et al., 2009[10]	258	77	29.8%	30.0%	1.0	-0.2%	N/A

--No appropriate comparison could be identified

* computed by taking the inverse of prevalence difference; N/A = not applicable because prevalence difference was a negative number

Table 5. Summary of studies on screening for diabetes among tuberculosis patients and selected comparison populations

Study	Region, Country	Study Period	TB diagnosis method	DM diagnosis method	Timing of DM diagnosis	% Male	Age distribution	Comparison Population
Studies in which DM was screened for all study participants after TB Tx initiation								
Nichols, 1957[16]	Denver, Colorado, U.S.	N/R	TB inpatients seen at the Fitzsimons Army Hospital	DM defined by following criteria 1. OGTT peak sugar > 180 mg/dl, 2. OGTT > 130mg/dl at 2 hr and 3. More than a trace of glycosuria	7-9 mo post Tx start	Among TB 100%; Among DM 100%	Among TB: Mean 27.9, Range 18-53; Among DM: Mean 33.4	No comparison
Kishore et al., 1973[17]	Agra, India	Apr 1971 - Oct 1971	PTB patients diagnosed by clinical examination, sputum smear, or X-ray	DM defined by WHO 1965 criteria, OGTT(100g) 2hr >130mg/dl	3 mo post Tx start	Among TB 66%; Among DM 74%	Among TB: Mean 29.4, Range 13-61, 84%<40; Among DM: N/R	Health subjects of comparable age and sex, without family history of diabetes and tuberculosis
Kovaleva et al., 1975[18]	Moscow, Russia	N/R	TB inpatients	DM defined by FBG >120mg/dl, OGTT(50g) >200m/dl at 1hr, >160mg/dl at 2 hr; exclude previous diagnosed DM	post Tx start (unspecified time)	Among TB 76%; Among DM N/R	Among TB: 60%<=50; Among DM: 33%<=50	No comparison
Goyal et al., 1978[19]	Uttar Pradesh, India	N/R	PTB patients diagnosed by clinical examination, sputum smear and X-ray	DM defined by WHO 1965 criteria, OGTT and cortisone primed GTT	3 mo post Tx start	Among TB 85%; Among DM N/R	Among TB: 69% <=40; Among DM: N/R	Healthy individuals of comparable age and sex without family history of diabetes and pulmonary tuberculosis
Singh et al., 1984[20]	Delhi, India	N/R	PTB outpatients, diagnosed by X-ray and bacteriologically confirmed	DM defined by WHO 1980 criteria, FBG >=120 mg/dl, OGTT (75g) 0.5 hr – 2hr >=180mg/dl after eating	12 wk post Tx start	Among TB 65%; Among DM N/R	Among TB: Mean 30.5, Range 19-60; Among DM: N/R	No comparison
Oluboyo and Erasmus, 1990[21]	Ilorin, Nigeria	N/R	Newly diagnosed PTB patients diagnosed by sputum smear and X-ray	DM defined by WHO 1980 criteria, OGTT (75g), FBG	3 mo post Tx start	Among TB 56%; Among DM N/R	Among TB: Mean 34.9, SD 14.4; Among DM: N/R	Health individuals matched by age, sex and BMI
Balde et al., 2006[22]	Conakry, Guinea	Feb 2002-May 2002	TB patients from the registry	DM defined by WHO 1999 criteria; known diabetic confirmed with FBG in capillary >1.1g/L (corresponding to venous 126mg/dl); random glycaemia in capillary > 2g/L with clinical signs	post Tx start (unspecified time)	Among TB 66%, Among DM 69%	Among TB: Mean 31, Range 14-75; Among DM: Mean 47.1, SD 13.1	No comparison

Studies in which DM was screened before TB Tx initiation								
Nanda and Tripathy, 1968[23]	Orissa, India	N/R	PTB patients diagnosed by clinical examination, X-ray and bacteriology	DM defined by FBG>120mg/dl, OR PPGTT peak sugar >180mg/dl, OR 2 hr >130mg/dl	At diagnosis	Among TB 83%; Among DM N/R	Among TB: 54%<=40; Among DM: 50%<=40	No comparison
Jawad et al., 1995[24]	Nazimabad, Pakistan	N/R	PTB patients diagnosed by X-ray and sputum smear	DM defined by WHO 1985 criteria, OGTT(75g); previously known diabetics excluded	At diagnosis	Among TB 59%; Among DM N/R	Among TB: Mean 39.3; 74.6% <40; Among DM: N/R	Urban population of Baluchistan, Pakistan, 1995**
Basoglu et al., 1999[25]	Izmir, Turkey	N/R	PTB patients diagnosed by clinical examination, X-ray and sputum smear	DM defined by OGTT(75g) 0.5 or 1hr and 2hr >200 mg/dl	At diagnosis	Among TB 78%; Among DM N/R	Among TB: Mean 41.9, Range 15-82; Among DM: Mean 53.9, Range 37-82	No comparison
Alisjahbana et al., 2006[26]	Jakarta and Badung, Indonesia	Mar 2001-Mar 2005	Primary TB patients with clinical symptoms and suggestive X-ray, confirmed by + smear	DM defined by FBG >=126mg/dl	At diagnosis	Among TB 52%; Among DM N/R	Among TB: Median 30, Range 15-75; Among DM: Median 45	Randomly selected control of the same sex, age (+/- 10%) from same region
Studies in which timing of DM diagnosis relative to TB Tx is unclear								
Higashi, 1967[27]	Kyushu, Japan	Jul 1966	TB inpatients in 23 TB sanatoria	DM defined by glycosuria and venous blood 2hr after meal >120mg/dl, or capillary blood 2 hr after meal >140mg/dl	Unclear	Among TB 64%; Among DM 71%	Among TB: 45.3% <40; Among DM: 20.3%<40	No comparison
Roychowdhury and Sen, 1980[28]	Calcutta, India	Apr 1975 - Mar 1976	TB inpatients diagnosed by smear, culture, X-ray or clinical symptoms suggestive of TB	DM defined by OGTT(100g) >140mg/dl at 2hr, Potential DM defined by 131-140mg/dl	Unclear	Among TB 83%; Among DM N/R	Among TB: 70%<45; Among DM: 67%<45	No comparison
Deshmukh and Shaw, 1984[29]	Jamshedpur, India	N/R	PTB patients diagnosed by clinical, radiological and bacteriological methods	DM defined by glucosuria and FBG >120mg/dl, OGTT (75g)>140mg/dl	Unclear	Among TB 64%; Among DM 72%	Among TB: 60% <45; Among DM: 17% <45	No comparison
Tripathy et al., 1984[8]	Adra, India	N/R	PTB patients diagnosed by sputum smear	DM defined by WHO 1965 criteria, OGTT (100g)	Variable	Among TB: N/R; Among DM N/R	Among TB: 66% <40; Among DM: 52% <40	No comparison
Mugusi et al., 1990[30]	Dar es Salaam, Tanzania	N/R	PTB patients diagnosed by sputum smear	DM defined by WHO 1985 criteria, OGTT (75g) >=10mmol/L or FBG >6.7 mmol/L	Unclear	Among TB 69%; Among DM N/R	Among TB: Mean 35, Range 14-88; Among DM: N/R	Urban community in Dar es Salaam
Ponce-de-Leon et al., 2004[31]	Veracruz, Mexico	Mar 1995 - Mar 2003	PTB patients confirmed by sputum smear or culture	DM defined by E11FBG>=126mg/dl OR >=200mg/dl for random samples	Unclear	Among TB 66%; Among DM N/R	Among TB: Mean 44, Range19-86; Among DM: Mean 53, Range 23-82	General population of state of Veracruz (ENSA2000 diabetes survey)**
Golsha et al., 2009[32]	Gorgan, Iran	2001 - 2005	TB patients with 2 + smears or 1+ smear with abnormal X-ray, OR physician's diagnosis with response to Tx	DM defined by FBG >126mg/dl	Unclear	Among TB 53%; Among DM 43%	Among TB: Mean 50.2, SD 19, 30%<=40; Among DM 7% <=40	General population of Iran (National survey of diabetes conducted in 2005)**

** Comparison data from external source

N/R = not reported, PTB = pulmonary tuberculosis, FBG = fasting blood glucose, OGTT = oral glucose tolerance test, BMI = body mass index, PPGTT = prednisone-primed glucose tolerance test, Tx = TB treatment

Table 6. Summary of results on screening for diabetes in tuberculosis patients and selected comparisons

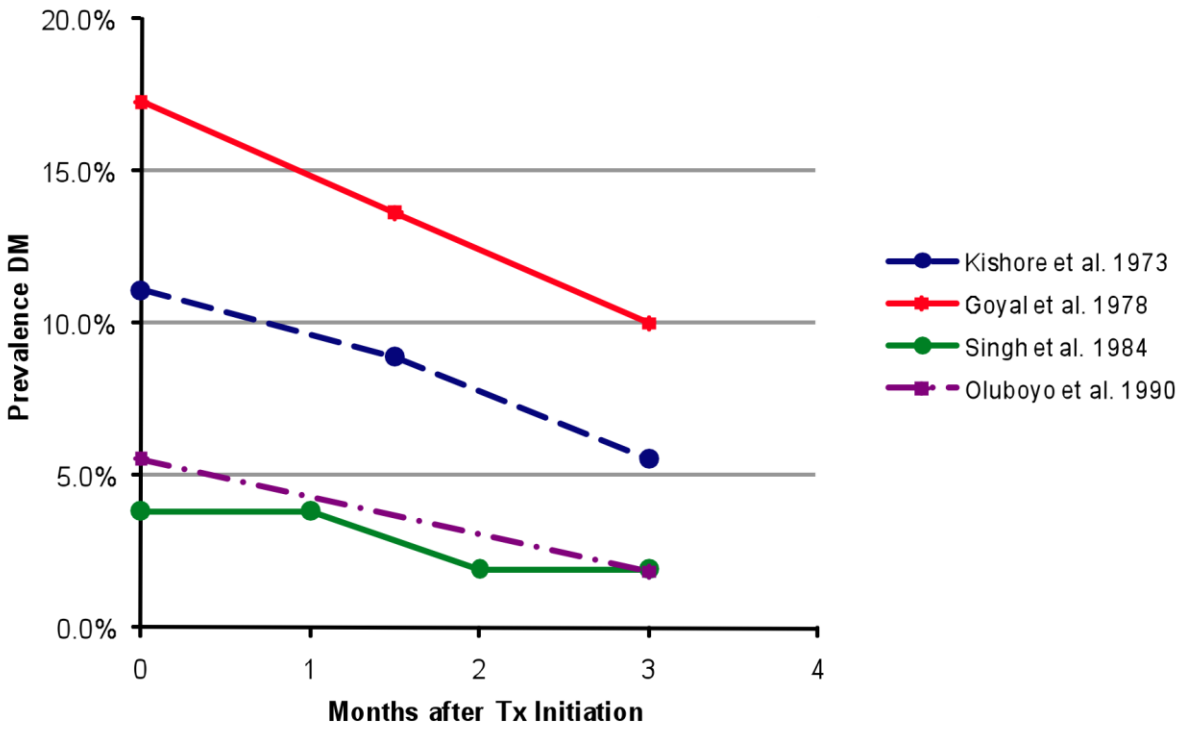
Study	Pop Size of TB patients	Number of DM in TB patients	Diagnosed prior to screening	DM Prevalence in TB	DM Prevalence in Comparison	Prevalence or Incidence Ratio	Prevalence or Incidence Difference	Number needed to screen to detect 1 DM case^
Studies in which DM was screened for all study participants after TB Tx initiation								
Nichols, 1957[16]	178	9	N/R	5.1%	--	--	--	--
Kishore et al., 1973[17]	90	5	4	5.6%	2.0%	2.78	3.6%	28
Kovaleva et al., 1975[18]	771	27	0	3.5%	--	--	--	--
Goyal et al., 1978[19]	110	11	10	10.0%	1.3%	8.00	8.8%	11
Singh et al., 1984[20]	52	1	N/R	1.9%	--	--	--	--
Oluboyo and Erasmus, 1990[21]	54	1	N/R	1.9%	0%*	Infinity	1.9%	54
Balde et al., 2006[22]	388	13	9	3.4%	--	--	--	--
Studies for which DM was screened before TB Tx initiation								
Nanda and Tripathy, 1968[23]	200	24	N/R	12.0%	--	--	--	--
Jawad et al., 1995[24]	106	21	N/R	19.8%	10.8%	1.83	9.0%	11
Basoglu et al., 1999[25]	58	5	N/R	8.6%	--	--	--	--
Alisjahbana et al., 2006[26]	454	60	N/R	13.2%	3.2%	4.08	10.0%	10
Studies in which timing of screening of DM is unclear								
Higashi, 1967[27]	6065	222	109	3.7%	--	--	--	--
Roychowdhury and Sen, 1980[28]	961	199	N/R	20.7%	--	--	--	--
Deshmukh and Shaw, 1984[29]	2434	138	60	5.7%	--	--	--	--
Tripathy et al., 1984[8]	1359	29	9	2.1%	--	--	--	--
Mugusi et al., 1990[30]	506	34	N/R	6.7%	0.9%	7.81	5.9%	17
Ponce-de-Leon et al., 2004[31]	525	185	172	35.2%	7.6%	4.63	27.6%	4
Golsha et al., 2009[32]	243	56	N/R	23.0%	7.7%	2.99	15.3%	7

* No DM was found a control population of 54 health individuals who were also screened for DM
^ computed by taking the inverse of prevalence difference

--No appropriate comparison could be identified

Tx = TB treatment

Figure. The decreasing trend of hyperglycaemia in tuberculosis patients receiving anti-tuberculosis treatment



Summary of two studies on tuberculosis preventive therapy in patients with diabetes

We identified two observational studies in which people with diabetes had been administered chemopropylaxis for prevention of TB. In a study conducted in Germany [33] in the 1950s, 63 diabetes patients who had completed a course of treatment for active TB were subsequently treated with isoniazid for 6–24 months while a comparison group of 164 people with diabetes completing treatment for active TB was not treated. While the comparison group accrued 18 cases of recurrent TB over a mean of 2.3 years of follow up time, the intervention group experienced no recurrent TB over 1.6 years of follow up time. In a second study conducted in the Russian Federation in the 1960s [34], investigators administered ftivazid, a Russian analog of isoniazid, to 2006 diabetes patients and compared their course to 387 controls who were not treated. Treated patients were reported to experience 2–3 times lower incidence of TB compared with controls who did not receive any ftivazid during a follow-up period of five years. The study did not report raw numbers of TB cases, specify whether the follow-up period occurred during the intervention or afterwards, nor indicate the reasons for not administering ftivazid in the control group.

References

1. Boucot KR et al. Tuberculosis among diabetics: the Philadelphia survey. *American Review of Tuberculosis*, 1952, 65(1:2):1–50.
2. Oscarsson PNS, H. Incidence and coincidence of diabetes mellitus and pulmonary tuberculosis in a Swedish county. *Acta Med Scand Suppl*, 1958, 335:22–48.
3. Opsahl R, Riddervold HO, Wessel A. Pulmonary *tuberculosis* in mitral stenosis and *diabetes* mellitus. *Acta Tuberculosea Scandinavica*, 1961, 40:290–296.
4. Davidovich D, Aiello CR, Hassan IA. [Antitubercular preventive examination in diabetics.] Sem Med, 1963, 122:781–784.
5. Marton S et al. [Representative tuberculosis mass examinations in diabetics in Hungary.] *Acta tuberculosea et pneumologica Scandinavica*, 1963, 43:29–38.
6. Golli V et al. [Incidence of pulmonary tuberculosis in diabetics (author's transl)]. *MMW Munch Med Wochenschr*, 1975, 117(3):93–96.
7. Gill GV, Huddle KR, Krige LP. Intensive health screening of young Black diabetics. *South African Medical Journal*, 1984, 65(20):815–816.
8. Tripathy SR et al. Diabetes mellitus and pulmonary tuberculosis. A prospective study. *Indian Journal of Tuberculosis*, 1984, 31(3):122–125.
9. Ezung T et al. Pulmonary tuberculosis and diabetes mellitus--a study. *Journal of the Indian Medical Association*, 2002, 100(6):376, 8–9.
10. Webb EA et al. High prevalence of *Mycobacterium tuberculosis* infection and disease in children and adolescents with type 1 diabetes mellitus. International Journal of Tuberculosis and Lung Disease, 2009, 13(7):868–874.
11. Lester FT. Tuberculosis in Ethiopian diabetics. *Ethiopian Medical Journal*, 1984, 22(3):129–133.
12. Kim SJ et al. Incidence of pulmonary tuberculosis among diabetics. Tubercle and Lung Disease, 1995, 76(6):529–533.
13. *Indices Epidemiologicos Actuales De la Tuberculosis en la Ciudad de Buenos Aires*. Vol. Tomo 1: XI Congreso Argentino de Tisiologia y Neumonologia, 1967:25–27.
14. Hernandez Garcia P, Martinez Cruz F, Cayuelas Martinez T. [PPD and chemoprophylaxis in diabetes mellitus]. *Aten Primaria*, 1992, 9(2):106–108.
15. Mansilla Bermejo MJ et al. [Tuberculin test in diabetic patients in a health center]. *Aten Primaria*, 1995, 16(3):154–157.
16. Nichols GP. Diabetes among young tuberculous patients; a review of the association of the two diseases. *American Review of Tuberculosis*, 1957, 76(6):1016–1030.
17. Kishore B et al. Manifest, chemical and latent chemical diabetes in pulmonary tuberculosis. *Journal of Associations of Physicians of India*, 1973, 21(10):875–881.
18. Kovaleva SI, Gaponova SA, Abrosimova NN. [Diabetes mellitus in patients with pulmonary tuberculosis]. *Probl Tuberk*, 1975, (3):43–45.
19. Goyal BN et al. Study of diabetic status in pulmonary tuberculosis. *Journal of Diabetes Association in India*, 1978,18:191–197.
20. Singh MM, Biswas SK, Shah A. Impaired glucose tolerance in active pulmonary tuberculosis. *Indian Journal of Tuberculosis*, 1984, 31(3):118–121.
21. Oluboyo PO, Erasmus RT. The significance of glucose intolerance in pulmonary tuberculosis. *Tubercle*, 1990, 71(2):135–138.
22. Balde NM et al. Associated tuberculosis and diabetes in Conakry, Guinea: prevalence and clinical characteristics. *International Journal of Tuberculosis and Lung Disease*, 2006, 10(9):1036–1040.
23. Nanda CN, Tripathy SN. Association of diabetes mellitus with pulmonary tuberculosis. *Journal of Associations of Physicians of India*, 1968, 16(10):741–746.

24. Jawad F et al. Glucose intolerance in pulmonary tuberculosis. *Journal of Pakistan Medical Association*, 1995, 45(9):237–238.
25. Basoglu OK et al. The oral glucose tolerance test in patients with respiratory infections. *Monaldi Archives for Chest Disease*, 1999, 54(4):307–310.
26. Alisjahbana B et al. Diabetes mellitus is strongly associated with tuberculosis in Indonesia. *International Journal of Tuberculosis and Lung Disease*, 2006, 10(6):696–700.
27. Higashi H. [Screening test for diabetes in tuberculous sanatoria]. *Iryo*, 1967, 21(3):361–368.
28. Roychowdhury AB, Sen PK. Diabetes in tuberculosis patients. *Journal of the Indian Medical Association*, 1980, 74(1):8–15.
29. Deshmukh PA, Shaw T. Pulmonary tuberculosis and diabetes mellitus. *Indian Journal of Tuberculosis*, 1984, 31(3):114–117.
30. Mugusi F et al. Increased prevalence of diabetes mellitus in patients with pulmonary tuberculosis in Tanzania. *Tubercle*, 1990, 71(4):271–276.
31. Ponce-De-Leon A et al. Tuberculosis and diabetes in southern Mexico. *Diabetes Care*, 2004, 27(7):1584–1590.
32. Golsha R et al. Pulmonary tuberculosis and some underlying conditions in Golestan Province of Iran, during 2001–2005. *Journal of Clinical and Diagnostic Research*, 2009, 3(1):1302–1306.
33. Pfaffenberg R, Jahler H. [Isoniazid & recurrence of tuberculosis in diabetics.]. *Z Tuberk*, 1958, 111(3–4):167–173.
34. Lesnichii AV, Karpina LZ. [Experience with the chemoprophylaxis of pulmonary tuberculosis in diabetes mellitus patients]. *Probl Tuberk*, 1969, 47(12):1–3.