

Figure 1 Study selection process

| Study | Country | | | | Relative Risk (95% Cl) | Quality of Study |
|--|----------------|------------|---------------|-------|---------------------------|---------------------|
| Cohort study | | TB/DM | TB/non-DM | | | |
| Kim et al, 1995 | South Korea | 170/8015 | 4935/806698 | * | 3.58 (3.08-4.16) | Low |
| John ea al, 2001 | India | 19/87 | 145/1162 | | 2.24 (1.38-3.65) | Low |
| Leung et al, 2008 | Hong Kong | 94/6444 | 383/35672 | - | 1.77 (1.41-2.24) | High |
| Baker et al, 2012 | Taiwan | 13/1652 | 44/16063 | | 2.09 (1.10-3.95) | High |
| Dobler et al, 2012 | Australia | 271/802087 | 6005/19053196 | | 1.48 (1.04-2.10) | High |
| Chen et al, 2013 | China | 4/1312 | 113/176215 - | | 2.43 (0.84-7.00) | High |
| Pealing et al, 2015 | UK | 190/222731 | 779/1218616 | - | 1.30 (1.01-1.67) | High |
| Lee et al, 2016 | Taiwan | 63/11260 | 264/112286 | - | 1.70 (1.27-2.27) | High |
| Subtotal (I-squared = | = 89.7%, p<0.0 | 001*) | | | 1.95 (1.38-2.76) | |
| Case-control stud | dy | DM/TB | DM/non-TB | | | |
| Morietal, 1992 | USA | 16/46 | 5/46 | | 5.20 (1.22-22.10) | Low |
| Coker et al, 2006 | Russia | na/334 | na/334 | | 7.83 (2.37-25.89) | Low |
| Leegaard et al, 2011 | Denmark | 156/2950 | 539/14274 | • | 1.18 (0.96-1.45) | High |
| Jurcev-S et al, 2013 | Croatia | 31/300 | 17/300 | | 2.38 (1.05-5.38) | Low |
| Davis et al, 2016 | Kazakhstan | 40/562 | 9/1038 | | 13.96 (6.37-30.56) | Low |
| Ndishimye et al, 2017 | Romania | 21/150 | 7/150 | | 3.32(1.36-8.08) | Low |
| Subtotal (I-squared = | = 90.1%, p<0.0 | 001*) | | | 3.98 (1.53-10.37) | |
| High-quality studies (I-squared = 44.1%, p=0.097*) | | | | < | 1.50 (1.28-1.76) | |
| - | | | | | (Test for RR=1 : Z=4 | .91 p<0.001 |
| | | | 0.5 | 1 2 4 | 8 | |
| | | | Polativ | Dick | | |

Figure 2 Estimates of effect of DM on active TB in each study and pooled relative risk in cohort studies, case-control studies, and high-quality studies

Relative Risk: Rate ratio in cohort studies and odds ratio in case-control studies, 95% CI: 95% confidence interval, P value*: Test of heterogeneity, na: data not available



Figure 3 Stratum-specific association between DM and TB: level of control of DM (a), Age (b), and Sex (c)

| 1. Population characteristics (Number of studie | s) | Relative Risk (95%Cl) | 1 2 | P value | l² residua | Adju: I R |
|--|--------------|--------------------------------------|------------|---------|---------------|--------------|
| Region | | | | 0.015 | 80% | 73 |
| Asia(6) | | 2.24(1.59, 3.16) | 87% | | | |
| Former Soviet nation(2) | | 11.40(4.32, 30.10) | 0.001 | | | |
| Europe(4) | — . | 1.54(0.88, 2.68) | 90% | | | |
| Australia(1) | _ . | 1.48(0.63, 32.51) | | | | |
| Background TB incidence | | | | 0.036 | 66% | 44 |
| Low(3) | — | 1.46(0.85, 2.50) | 0% | | | |
| Moderate(8) High(3) | | 2.41(1.52, 3.81) 3.96(2.50, 6.27) | 76% 60% | | | |
| Median are of narticinants | | 0.00(2.00, 0.21) | 0070 | 0.33 | 81% | 50 |
| $\leq 40 \text{ yo}(4)$ | | 2 89(1 28 6 53) | 80% | 0.33 | 0170 | 37 |
| >=40 yo(6) - | | 1.80(0.63, 5.15) | 66% | | | |
| 2. Study characteristics (Number of studies) | 1 | | | | | |
| Study type | | | | 0 118 | 90% | 5% |
| Cohort(8) | | 1.96(1.23, 3.12) | 90% | | 2070 | 57 |
| Case-control(6) | | 3.59(1.64, 7.89) | 90% | | | |
| Study quality | | | | 0.001 | 58% | 82 |
| High(7) | - • | 1.54(1.15, 2.05) | 44% | | | |
| Low(7) | | 3.83(2.36, 6.23) | 67% | | | |
| Median follow-up time of study | | | | 0.008 | 36% | 80 |
| <4 year(4)) | _ . - | 2.97(2.16, 4.08) | 49% | | | |
| >=4year(4) | - | 1.56(1.04, 2.33) | 16% | | | |
| Sample size | | | | 0.011 | 90% | 50 |
| Sample size of all bracket >=10 (9) | | 1.83(1.34, 2.51) | 92% | | | |
| Sample size of any bracket <10 (4) | | 5.52(2.40, 11.40) | 00% | | | |
| Method of DM diagnosis | | | | 0.018 | 90% | 47 |
| Self report only(5) Lab data or code or DM prescription (9) | . | 4.66(2.47, 8.81) 1.86(0.90, 3.86) | 69% 92% | | | |
| TB type | | | | 0.185 | 76% | 17 |
| AII TB | | 2.08(1.35, 3.21) | 81% | | | |
| РТВ | | 3.63(1.53, 8.60) | 0% | | | |
| Regression model included smoking | | | | 0.569 | 90% | -1 |
| Not Included(5) | | 2.13(1.11, 4.10) | 95% | | | |
| Included(9)) | | 2.66(1.16, 6.11) | 81% | | | |
| Regression model included | | | | 0.886 | 84% | -1 |
| Not Included(4) | | 2.58(1.20, 5.46) | 87% | | | |
| Included(10) | • | 2.41(0.98, 5.92) | 83% | | | |
| Regression model included BMI | | | | 0.155 | 89% | 79 |
| Not Included(9) | | 2.99(1.85, 4.84) | 92% | | | |
| Included(5) | | 1.76(0.83, 3.76) | 21% | | | |
| | | | | | | |
| ariate meta-regression 0.5 | 1 2 4 | | | | 55% | 77 |
| Background TB incidence | | | | 0.72 | 0070 | |
| Low(3) | + | 1.48(0.99, 2.21) | | | | |
| Moderate(8) High(3) | * | 1.61(0.97, 2.69) 1.76(1.05, 2.92) | | | | |
| | - | | | | | |
| | - | 1 40/0 00 0 00 | | 0.04 | | |
| Low(7) | | 1.48(0.99, 2.22) 3.39(1.55, 7.39) | | | | |
| | - | , | | | | |
| | | | _ | | | _ |
| I 0.5 | 1 2 4 | | | | | |

Figure 4 Estimated effect of DM on TB stratified by population characteristics and study characteristics

Background TB incidence (per 100,000 person-years): low <15, moderate 15-100, high >100, Study quality: high 8-9, low -7 (the numbers of stars in Newcastle-Ottawa Scale), I²: % variation due to between-study heterogeneity in group computed from Der Simonian-Laird random effect model, P value: test of linear trend (meta-regression), I² residual: % residual variation due to heterogeneity, Adjusted R²: Proportion of between-study variance, Bivariate meta-regression included only the background TB incidence and study quality in the model.



Figure 5 Funnel plot with pseudo 95% confidence limits of the studies included in metaanalysis



Figure 6 Relationships between factors and the strength of the effect of DM on TB



s.e of logRR: standard error of log (Relative Risk)

Figure 7 Funnel plots with pseudo 95% confidence limits of the studies, grouped by quality of study (a), and health expenditure per capita (b)



Figure 8 Association between study quality and estimated effect of DM on TB (a), and association between health expenditure per capita and estimated effect of DM on TB in all studies (b) and in high-quality studies (c)