Supplemental Material

Risk factors for pulmonary TB recurrence, relapse and reinfection: a systematic review and meta-analysis
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Appendix 1 PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pag 3-4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 4
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 4
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 4
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 4
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review,	Page 5

Section and Topic	Item #	Checklist item	Location where item is reported
		ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Appendix 7
Study characteristics	17	Cite each included study and present its characteristics.	Appendix 6 – Table S1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table S3 – S4
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 5
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 5-6
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 6
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 6
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 6
	23b	Discuss any limitations of the evidence included in the review.	Page 6
	23c	Discuss any limitations of the review processes used.	Page 6
	23d	Discuss implications of the results for practice, policy, and future research.	Page 7
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Abstract – Page 2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not applicable
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 8
Competing interests	26	Declare any competing interests of review authors.	Page 8
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supplementary material

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Appendix 2 Search strategy

Search strategy PUBMED

((((((((((("tuberculosis"[MeSH Terms]) OR "tuberculosis"[Title/Abstract])) AND (((("recurrence"[MeSH Terms]) OR recurren*[Tite/Abstract])) OR ((((reinfection*[Title/Abstract]) OR relapse*[Title/Abstract])) OR "reactivation*"[Title/Abstract]))))))) NOT (((""addresses""[Publication Type] OR ""autobiography""[Publication Type] OR ""bibliography""[Publication Type] OR ""book illustrations""[Publication Type] OR ""case reports""[Publication Type] OR ""comment""[Publication Type] OR ""dictionary""[Publication Type] OR ""directory""[Publication Type] OR ""editorial""[Publication Type] OR ""electronic supplementary materials""[Publication Type] OR ""ephemera""[Publication Type] OR ""expression of concern""[Publication Type] OR ""festschrift""[Publication Type] OR ""government publications""[Publication Type] OR ""guideline""[Publication Type] OR ""interactive tutorial""[Publication Type] OR ""interview""[Publication Type] OR ""lectures""[Publication Type] OR ""legal cases""[Publication Type] OR ""legislation""[Publication Type] OR ""letter""[Publication Type] OR ""news""[Publication Type] OR ""newspaper article""[Publication Type] OR ""patient education handout""[Publication Type] OR ""periodical index""[Publication Type] OR ""personal narratives""[Publication Type] OR ""pictorial works""[Publication Type] OR ""popular works""[Publication Type] OR ""portraits""[Publication Type] OR ""practice guideline""[Publication Type] OR ""technical report""[Publication Type] OR OR ""video audio media""[Publication Type] OR ""webcasts""[Publication Type]))))) NOT Animals[Mesh:noexp])

Filters: Publication date from 1980/01/01; English; Spanish; French

Cochrane Library

"tuberculosis":ti,ab,kw AND "recurrence":ti,ab,kw or "relapse":ti,ab,kw or "reinfection":ti,ab,kw or "reactivation":ti,ab,kw

Filters: Publication date from 1980/01/01

Scielo

(ti:(tuberculosis) OR ab:(tuberculosis)) AND ((ti:(recurren$)or ab:(recurren$)) OR (ti:(reinfección)or ab:(reinfección)) OR (ab:(recaída) OR ti:(recaída)) OR (ti:(reactivación)or ab:(reactivación))

Lilacs

(tw:((tw:((tw:("tuberculosis")) AND (tw:(reinfección)) OR (tw:(recurren*)) OR (tw:(reactivación)) OR (tw:(recaída)) AND (db:("LILACS")))))) NOT (type_of_study:("case_reports")) AND (instance:"regional") AND (la:("es" OR "en"))

Appendix 3 Quality assessment criteria using QUIPS-tool

Domains	Signaling items	Risk of bias ratings	Specific criteria used for this review
1. Study participation	(a) Adequate participation in the study by eligible persons (b) Description of the target population or population of interest (c) Description of the baseline study sample (d) Adequate description of the sampling frame and recruitment (e) Adequate description of the period and place of recruitment (f) Adequate description of inclusion and exclusion criteria	High: the relationship between the PF and outcome is very likely to be different for participants and eligible non-participants Moderate: the relationship between the PF and outcome may be different for participants and eligible non-participants Low: the relationship between the PF and outcome is unlikely to be different for participants and eligible non-participants	Eligible refers to successfully treated TB patients (cured or treatment completed). We considered a cut-off of 2/3 of eligible participants for consider adequate participation. Several studies only report characteristics of the treatment cohort and not of successfully treated TB patients. However, we did not consider this to have a major impact on the quality of the study. Lack of any description of participants was considered to downgrade quality in this domain.
2. Study attrition	(a) Adequate response rate for study participants (b) Description of attempts to collect information on participants who dropped out (c) Reasons for loss to follow-up are provided (d) Adequate description of participants lost to follow-up (e) There are no important differences between participants who completed the study and those who did not	High: the relationship between the PF and outcome is very likely to be different for completing and non-completing participants Moderate: the relationship between the PF and outcome may be different for completing and non-completing participants Low: the relationship between the PF and outcome is unlikely to be different for completing and non-completing participants	We considered a cut-off of 2/3 of completing participants for this domain. In case the study has a greater percentage of lost to follow up, we downgrade the quality in this domain for those studies that lack of a description of lost to follow up participants.
3. Prognostic factor measurement	(a) A clear definition or description of the PF is provided (b) Method of PF measurement is adequately valid and reliable (c) Continuous variables are reported or appropriate cutpoints are used (d) The method and setting of measurement of PF is the same for all study participants (e) Adequate proportion of the study sample has complete data for the PF (f) Appropriate methods of imputation are used for missing PF data	High: the measurement of the PF is very likely to be different for different levels of the outcome of interest Moderate: the measurement of the PF may be different for different levels of the outcome of interest Low: the measurement of the PF is unlikely to be different for different levels of the outcome of interest	We provided an overall evaluation for all risk factors evaluated in the study. HIV and Diabetes mellitus diagnosis not being based on specified of laboratory methods was considered to decrease the quality
4. Outcome measurement	(a) A clear definition of the outcome is provided (b) Method of outcome measurement used is adequately valid and reliable (c) The method and setting of outcome measurement is the same for all study participants	High: the measurement of the outcome is very likely to be different related to the baseline level of the PF Moderate: the measurement of the outcome may be different related to the baseline level of the PF Low: the measurement of the outcome is unlikely to be different related to the baseline level of the PF	We downgraded quality if recurrences were only or mostly based on clinical radiological TB diagnoses. For relapses and reinfections, we considered a threshold of >88% for availability of genotyping for both episodes.
5. Adjustment for other prognostic factors	(a) All other important PFs are measured (b) Clear definitions of the important PFs measured are provided	High: the observed effect of the PF on the outcome is very likely to be distorted by another factor related to PF and outcome	We considered as low risk of bias for those studies that adjust at minimum for age, sex and HIV.

Domains	Signaling items	Risk of bias ratings	Specific criteria used for this review
	(c) Measurement of all important PFs is adequately valid and reliable (d) The method and setting of PF measurement are the same for all study participants (e) Appropriate methods are used to deal with missing values of PFs, such as multiple imputation (f) Important PFs are accounted for in the study design (g) Important PFs are accounted for in the analysis	Moderate: the observed effect of the PF on outcome may be distorted by another factor related to PF and outcome Low: the observed effect of the PF on outcome is unlikely to be distorted by another factor related to PF and outcome	In case the study did not perform multivariate analysis, we downgraded quality.
6. Statistical analysis and reporting	(a) Sufficient presentation of data to assess the adequacy of the analytic strategy (b) Strategy for model building is appropriate and is based on a conceptual framework or model (c) The selected statistical model is adequate for the design of the study (d) There is no selective reporting of results	High: the reported results are very likely to be spurious or biased related to analysis or reporting Moderate: the reported results may be spurious or biased related to analysis or reporting Low: the reported results are unlikely to be spurious or biased related to analysis or reporting	
Overall assesment	In order to provide and overall assessment of quality, we use the following criteria based on previous results Good quality: Low risk of bias in all domains Poor quality: High risk of bias in any of six domains Fair quality: The study did not match criteria for good or poor quality		

Table adapted from: Riley R D, Moons K G M, Snell K I E, Ensor J, Hooft L, Altman D G et al. A guide to systematic review and meta-analysis of prognostic factor studies *BMJ* 2019; 364 :k4597 doi:10.1136/bmj.k4597

Appendix 4 Supplementary tables

Table S1: Characteristics of included studies

Authors (year)	**Country (region or city)**	**Number of recurrences**	**Source of risk factor information**	**Length of follow up (years, unless specified)**	**Type of follow up***	**Diagnostic method of recurrent episode**	**Genotyping methods used and percentage availability of DNA samples for genotyping**
Clinical trials							
Balasubramaniam et al (1990)	India (Madras)	52	Trial database	5	Active	Culture	
Castelo et al (1989)	Brazil (Sao Paulo)	27	Trial database	1	Active	Culture	
Chaulet et al (1995)	Algeria	1	Trial database	2	Active	Culture	
Combs et al (1990)	United States	16	Trial database	96 weeks	Active	Clinical and radiological diagnosis or AFB smear microscopy and culture	
East and Central African/BMRC (1986)	Kenia, Zambia, Tanzania, Uganda	24	Trial database	2	Active	Clinical and radiological diagnosis or AFB smear microscopy and culture	
Fitzgerald et al (2000)	Haiti (Port au Prince)	15	Medical records	1.5	Passive	Clinical and radiological diagnosis or AFB smear microscopy and culture	
Gillespie et al (2014)	South Africa, India, Tanzania, Kenya, Thailand, Malaysia, Zambia, China, Mexico	123	Trial database	12-14 months	Active	Culture	
Gopalan et al (2018) ‡	India (Chennai, Vellore, and Madurai, south India)	16	Trial database	1	Active	AFB smear microscopy and culture	
Hong Kong Chest Service (1982)	China (Hong Kong)	22	Trial database	1.5	Active	Culture	
Hong Kong TBRC / Madras BMRC (1991)	Hong Kong, China	17	Trial database	First treatment	5 years	Active	
Jasmer Lorna et al (2004)	United States and Canada	81	Trial database	2	Active	Culture	RFLP, Polymorphic guanine-cytosine–rich sequence–based RFLP analysis (93%)
Jawahar et al (2013)	India (Chennai and Madurai, South India)	40	Trial database	2	Active	Clinical and radiological diagnosis or AFB smear microscopy and culture	

Jindani et al (2014)	South Africa, Zimbabwe, Botswana, and Zambia	38		Trial database	4 months	Active	Culture	
Johnson et al (2000)	Uganda (Kampala)	18		Medical records	2	Active	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Johnson et al (2009)	Uganda, Brazil and Philippines.	18		Trial database	2	Active	Clinical and radiological diagnosis and microbiological diagnosis	RFLP (89%)
Kennedy et al (1996)	Tanzania (Kilimanjaro)	7		Medical records	0.5	Active	Clinical and radiological diagnosis or AFB smear microscopy and culture	
Lienhardt et al (2011)	Africa, Asia, and Latin America	42		Trial database	12 months	Active	Culture	
Madras/BMRC (1989) **	China (Hong Kong)	82		Trial database	4.5	Not specified	AFB smear microscopy and culture	
Merle et al (2014)	Cotonou, Benin; Conakry, Guinea; Nairobi, Kenya; Dakar, Senegal; Durban, South Africa.	148		Trial database	2	Active	Culture	
Nie et al (2021)	China	34		Trial database	1	Active	AFB smear microscopy and culture	
Parthasarathy et al (1991)	India (Madras and Bangalore)	85		Trial database	2 after start	Active	Culture	
Perriens et al (1995)	Democratic Republic of the Congo (Kinshasa)	19		Medical records	0.5	Passive	AFB smear microscopy and culture	
Singapore/BMRC (1981)	Singapore, China, Malay and India	18		Trial database		Active	Culture	
Singapore/BMRC (1988)	Singapore	11		Trial database	2	Active	Clinical and radiological diagnosis or AFB smear microscopy and culture	
Singapore/BMRC (1991)	Singapore	10		Trial database	1.5	Active	Culture	
Somner et al (1990)	Britain	10		Trial database		Not specified	AFB smear microscopy and culture	
Su et al (2001)	Taiwan (Taipei)	1		Trial database	2	Active	Clinical and radiological diagnosis or AFB smear microscopy and culture	
Teo et al (1999)	Singapore	14		Trial database	5	Active	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Tuberculosis Research Centre (1997)	India (Madurai)	65		Trial database	2	Not specified	AFB smear microscopy and culture	
Wu et al (2015)	Taiwan	0		Trial database	1	Active	Culture	
Zierski et al (1981)	Poland	54		Trial database	2.5	Not specified	AFB smear microscopy and culture	

Prospective longitudinal studies							
Anaam et al (2019)	Yemen	71	TB registers	5	Active	AFB smear microscopy and culture	
Chaisson et al (1996)	Haiti (Cité Soleil)	13	Medical records; HIV testing	3.5	Pasive	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Chang et al (2004)	China (Hong Kong)	113	Medical records	2	Pasive	Clinical and radiological diagnosis and culture	
Charalambous et al (2008) §	South Africa (Free State Province)	42	TB registers/Medical records	1.02 (Mean follow up)	Active	Clinical and radiological diagnosis and AFB smear microscopy and culture	RFLP (38%)
Connolly et al (1999)	South Africa (KwaZulu-Natal)	19	HIV testing	1.2 (Mean follow up)	Passive and Active	AFB smear microscopy	
Crampin et al (2010)	Malawi (Karonga)	53	TB registers	10.8	Active	Clinical and radiological diagnosis and AFB smear microscopy and culture	RFLP, Spoligotyping (79%)
Fox et al (2018)	Vietnam	498	Local TB registers/Interview	2	Mixed	AFB smear microscopy	
Gupte et al (2021)	India and South Africa	39	Meidcal records	At First treatment	18 months	Active	
Hang et al (2015)	Vietnam (Hanoi)	30	Structured questionnaire.	1.3		AFB smear microscopy and culture	
Hawken et al (1993) ‡	Kenya (Nairobi)	11	TB registers/Medical records	1.25	Active	AFB smear microscopy and culture	RFLP (27%)
Huyen et al (2013)	Vietnam (Mekong River Delta)	35	TB registers/Medical records	1.5	Active	AFB smear microscopy and culture	Spoligotyping (100%)
Jimenez Corona et al (2013)	Mexico (Veracruz)	74	Medical records	5.14 (Mean follow-up)	Active	AFB smear microscopy and culture	RFLP, Spoligotyping (51%)
Kassim et al (1995)	Nigeria (Abidjan)	20	Medical records	1.5	Active	AFB smear microscopy, Clinically diagnosed extrapulmonary tuberculosis	
Kim et al 2021	Cheongju, South Korea	6	Medical records	2014-2019	Active	Clinical-radiological, AFB smear microscopy or AFB smear culture	
Liu et al (2021)	China	141	Structured questionnaire	2	Active	Clinical and radiological diagnosis and AFB smear microscopy, culture and Molecular genotyping	WGS (27%)

Mave et al (2021)	India (Pune)	19	Medical records	1	Active	Clinical-radiological, AFB smear microscopy, AFB smear culture, Molecular (Genotype, Xpert, Xpert Ultra)	
Perriens et al (1991)	Democratic Republic of the Congo	20	HIV surveys	1	Pasive	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Pettit et al (2011)	United States of America (Tennesee)	20	National TB registers/Medical records	1	Passive	Non specified	RFLP, Spoligotyping, MIRU VNTR (75%)
Pulido et al (1997) ‡	Spain (Madrid)	15	Medical records	2.63 (Mean follow up)	Passive	AFB smear microscopy and culture	
Shen et al (2017)	China (Shanghai)	710	Local TB registers	2000-2012	Passive	Culture	MIRU VNTR (20%)
Sonnenberg et al (2001) §	South Africa (Gauteng)	65	TB registers/Medical records	2.09 (Mean follow up)	Active	Culture	RFLP (60%)
Suryanto et al (2008)	Indonesia (South Sulawesi)	12	Study records	4.3 years from trearment	Active	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Thomas et al (2005)	India (Tamil Nadu)	62	TB registers/Medical records	1.5	Active	AFB smear microscopy and culture	
Thomas et al (2019)	India (Chennai and Pune)	20	Interview	2	Active	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Velayutham et al (2018)	India (Tamil Nadu, Karnataka, Delhi, Maharashtra, Madhya Pradesh and Kerala)	158	Medical record/patient interview.	1	Active	AFB smear microscopy and culture	
Vree et al (2007)	Northern Vietnam	21	Structured questionnaire and TB registers	1.62 (Mean follow up)	Active	AFB smear microscopy	
Westerlund et al (2015)	Peru (Lima)	58	Questionaires	10	Active	Not specified	
Retrospective longitudinal studies							
Cudahy et al (2020)	South Africa (KwaZulu-Natal)	35	Medical records	6	Passive	AFB smear microscopy, AFB smear culture and Molecular (Genotype, Xpert, Xpert Ultra)	MIRU-VNTR (88%)
Dangisso et al (2018)	Ethiopia (Dale and Yirgalem)	101	Medical records	2002-2013	Active	The term TB recurrence was used to describe a recorded (on TB registry) re-diagnosis of	

						TB after successful completion of DOTS. We confirmed the re-diagnosis through interview.	
Datiko et al (2009)	Ethiopia (Dale and Wonsho, Sidama)	15	TB registers/Medical records	1998-2006	Active	AFB smear microscopy	
Franke et al (2012) ¶	Peru (Lima)	26	Medical records	3.3 y (Mean follow up)	Active	Culture	
Jiang et al (2022)	China	7143	Medical records	2005–2018	Passive	Clinical and radiological diagnosis and AFB smear microscopy, culture and Molecular (Genotype, Xpert)	
Jo et al (2014)	South Korea (Seoul)	6	Medical records	1	Passive	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Luzze et al (2013)	Uganda (Kampala)	171	Medical records	1.24 (Mean follow-up)	Active	Culture	RFLP (57%)
Ma et al (2018) ‖	Beijing (China)	16	Medical records	3	Active	AFB smear microscopy and culture	
Marx et al (2014)	South Africa (Cape Town)	203	Local TB registers	1996-2008	Passive	AFB smear microscopy and culture	RFLP. / WGS (64%)
Moreno-Martinez et al (2007)	Mexico (Soconusco, Chiapas)	39	Standardisez questionaire	1	Passive	AFB smear microscopy and culture	
Nahid et al (2007)	United States of America (San Francisco)	16	Medical records	1	Passive	Culture	
Nettles et al (2004)	United States of America (Baltimore)	14	Local TB registers	1	Active	Culture	
Picon et al (2007)	Brazil (Rio Grande do Sul, Porto Alegre)	26	Local TB registers	7.7 years (Mean follow-up)	Passive	AFB smear microscopy and culture	
Ruan et al (2021)	China (Hangzhou City)	479	National TB registers	Median 1565 days	Passive	Clinical-radiological, AFB smear microscopy or AFB smear culture	RFLP and WGS
Sun et al (2017)	China (Henan Province)	69	Interview and medicla records	9	Passive	AFB smear microscopy and culture	
Wang et al (2015) ‡ ‖	Taiwan	18	TB registry and medical records	2	Passive	AFB smear microscopy and culture	
Wu et al (2015)	China (Changning, Shanghai)	7	Medical recorsds	5 years	Passive	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Case-control studies							

Ahmad-Khan et al (2016)	Pakistan (Rawalpindi)	166	Interview	2005-2006	NA	Clinical and radiological diagnosis and AFB smear microscopy	
Eksombatchai et al (2022)	Republic of Korea		National TB registers	2006-2008	NA	Clinical and radiological diagnosis and AFB smear microscopy	
ElSahly et al (2004)	United States of America (Houston and Harris County, Texas)	100	TB registers/Medical records	1995-2000	NA	Non specified	
Faustini et al (2008)	Italy (Lazio region)	20	TB registry and medical records	6 y	NA	Clinical and radiological diagnosis and AFB smear microscopy and culture	
Lee et al (2014)	Taiwan	300	Local TB registers	3 – 4 y	NA	AFB smear microscopy and culture	
Pillay et al (2021)	South Africa (KwaZulu-Natal)	139	Trial database	4 years	Non specified	Non specified	
Racil et al (2012)	Tunisia	64	Not specified	1995-2007	NA	Not specified	
Tian et al (2014)	China (Tian and Han Region)	480	Medical records	12 y	NA	Not specified	
Systematic review							
Romanowski et al (2018)	Multicentric RCT		Trial records	1.5-2Y	Active	AFB smear microscopy and culture	MIRU VNTR
Cross sectional study							
William et al (2021)	Indonesia	5	Medical records	2015-2018	NA	Clinical-radiological, AFB smear microscopy or AFB smear culture	

* active: patients were followed up to determine the presence or absence of a recurrent TB episode
passive: routine TB register based; patients self-present at health facilities
† For case control studies, the study period when recurrences were identified is provided
‡ HIV positive population
§ Gold miners
¶ MDR patients
‖ Diabetes
**Smear negative

Table S2: Modelling methods for multivariate analysis

Authors	Modelling method for regression.	Method for selection of risk factors for inclusion in multivariable modelling.	Method for inclusion or exclusion of risk factors	Criteria used for inclusion or exclusion	Set of variables adjusted for
Ahmad-Khan et al (2016)	Not specified	preselection of established risk factors	Not specified	Not specified	Age
Anaam et al (2019)	Logistic	retain only those significant from univariable analysis	Full model approach	P-value (<0.1)	Literate, Unemployment, Smoking, Khat chewing , Cavitation, Weight, Diabetes, Non Adherence
Chang et al (2004)	Conditional logistic	preselection of established risk factors	Forward	Not specified	Treatment-related Factors, Sex, Age, Socio-demografic factors, type and extend of TB diseseae
Charalambous et al (2008)	Cox	preselection of established risk factors	Not specified	Likelihood ratio	Silicosis, age and HIV status.
Crampin et al (2010)	Poisson	preselection of established risk factors	Not specified	No aplica (si no excluye/incluye)	Age, sex, time-band
Dangisso et al (2018)	Cox	retain only those significant from univariable analysis	Full model approach	P-value (<0.2)	Age group, Residence, Treatment category, Education, Wealth index
Picon et al (2007)	Cox	retain only those significant from univariable analysis	Full model approach	P-value (<0.2)	HIV-positivity , Treatment compliance
ElSahly et al (2004)	Logistic	retain only those significant from univariable analysis + preselection of established risk factors	Full model approach	P-value (<0.2)	Foreign born, Unemployment, Not married, Use of public transportation, Pulmonary disease on first episode, use of DOT on first episode, HIV/AIDS diagnosis and having a family physician
Faustini et al (2008)	Logistic	retain only those significant from univariable analysis	Full model approach	P-value (<0.1)	Gender, Foreign status , Residence , Length of therapy, TB site and modified therapy
Fitzgerald et al (2000)	Cox	Not specified	Not specified	Not specified	age and duration of tuberculosis symptoms
Fox et al (2018)	Cox	preselection of established risk factors+ retain only those significant from univariable analysis	Not specified	-	Age, gender, hemoptysis, HIV status, prior TB, self-reported drug-resistant TB, interaction between age and gender, and clustering at the district level.
Franke et al (2012)	Cox	retain only those significant from univariable analysis	Forward	p<=0.1 and 10% change	Baseline, resistance to at least 5 drugs, age and XDR tuberculosis diagnosis
Hang et al (2015)	Cox	Not specified	Not specified	Not specified	Resistance to SM, RMP, and INH, MTB strains (ancient Beijing, modern Beijing and others)
Hawken et al (1993)	Poisson	all candidate risk factors considered	Full model approach	Likelihood ratio test.	Age
Huyen et al (2013)	Cox	retain only those significant from univariable analysis	Not specified	P-value (P < 0.05)	History of TB treatment, Previously treated , M. tuberculosis genotype, drug resistance
Jimenez Corona et al (2013)	Cox	preselection of established risk factors+ retain only those significant from univariable analysis	Forward	P-value (p < 0.20)	"relevant confounding factors"
Jo et al (2014)	Logistic	retain only those significant from univariable analysis	Not specified	P-value (P < 0.05)	Age, sex, BMI, Diabetes mellitus, type and extend of disease.
Johnson et al (2009)	Cox	retain only those significant from univariable analysis	Backward	P-value (<0.05)	Sex, age, type and extent of disease, treatment related factors, body mass index, hemoglobin.
Lee et al (2014)	Conditional logistic regression	preselection of established risk factors	Forward	Not specified	"all potential risk factors for TB based on literature review"
Luzze et al (2013)	Cox	all candidate risk factors considered	Not specified	Not specified	HIV and other risk factors
Moreno-Martinez et al (2007)	Logistic	Unclear	Forward	Not specified	Sex

Pettit et al (2011)	Logistic	all candidate risk factors considered	Not specified	Not specified	All covariates in the table were included in the disease risk score except for the exposure of interest and tobacco use, due to collinearity with chronic lung disease.
Pulido et al (1997)	Cox	retain only those significant from univariable analysis	Not specified	P-value (<=0.1)	Not specified
Racil et al (2012)	Not specified	Not specified	Not specified	Not specified	Not specified
Shen et al (2017)	Cox	preselection of established risk factors + retain significant values	Full model approach	p values less than 0.2 from the univariable analysis	Sex, age, treatment history and drug resistance profiles
Sonnenberg et al (2001)	Cox	all candidate risk factors considered	Forward	Not specified	“age and other risk factors “
Sun et al (2017)	Cox	preselection of established risk factors + retain significant values	Not specified	P-value (<0.05)	Male sex, Age, Drug resistance, Education and Income
Thomas et al (2005)	Logistic	retain only those significant from univariable analysis	Forward	Not specified	Drug regularity, DST profile, Smoking
Thomas et al (2019)	Poisson	preselection of established risk factors	Not specified	Not specified	Age, BMI, family income, HIV coinfection, diabetes, chest x-ray cavity and smear.
Tian et al (2014)	Logistic	retain only those significant from univariable analysis	Forward	P-value (p < 0.25 o HR > 1.5)	Smoking, Alcoholism, HIV positive, COPD , Diabetes mellitus , Immunosuppressor treatment , Malnutrition ,Use of DOTS on first episode
Velayutham et al (2018)	Poisson	all candidate risk factors considered	Full model approach	Not specified	Smoking , BMI<16, Alcohol, Missed doses in Intensive phase of treatment>12, Diabetes mellitus, Respiratory symptom at end of treatment
Wang et al (2015)	Cox	retain only those significant from univariable analysis	Stepwise	P-value (<0.15)	Age, sex, year of TB diagnosis, diabetes related factors, culture positivity after 2 months of treatment, duration of anti-TB treatment , adherence
Westerlund et al (2015)	Cox	preselection of established risk factors	Forward	Likelihood ratio test	Sex, MDR-TB, HIV and smoking, other respiratory diseases, age and BMI, treatment delay, and diabetes
Ruan et al (2021)	Cox	preselection of established risk factors	Not specified	Not specified	Sex,age,cavitation,sputum positive at 2mo and prolonged treatment
Pillay et al (2021)	Cox	preselection of established risk factors	Not specified	Not specified	WHO stage of the disease, BMI, lung cavities, age, CD4 count, VL, gender and previous history of TB
Patrick George Tobias Cudahy et al (2020)	Cox	all candidate risk factors considered	Not specified	Not specified	M. tuberculosis heterogeneity, HIV,age, education, mari- tal status, and AFB sputum smear grade
Mave et al (2021)	Cox	all candidate risk factors considered	Not specified	Not specified	Sex, age, household income, smoking, alcohol, body mass index, daily vs intermittent TB regimen, and smear grade
Liu et al (2021)	Logistic	preselection of established risk factors+ retain only those significant from univariable analysis	Not specified	P-value (<0.01)	Patient age, sex, bilateral cavitation, treatment history, smoking, and occupation.
Jiang et al (2022)	Cox	all candidate prognostic factors considered	Full model approach	Not specified	Sex, age, occupation and all the other variables in table.

Table S3: Risk of bias assessment using QUIPS Tool for studies reporting undifferentiated recurrences

Study	Study participation	Study attrition	Risk factor measurement	Outcome measurement	Adjustment for other risk factors	Statistical analysis and reporting	Overall assessment
Ahmad Khan et al (2016)	Low	NA	Low	Low	Low	Low	Good
Anaam et al (2019)	Low	Moderate	Low	Low	Moderate	Low	Fair
Balasubramanian et al (1990)	Low	Low	Low	Low	Low	Low	Good
Castelo et al (1989)	Low	High	Low	Low	Low	Low	Poor
Chaisson et al (1996)	Low	Moderate	Low	Moderate	High	High	Poor
Chang et al (2004)	Low	Low	Low	Moderate	Low	Low	Fair
Charalambous et al (2008)	Moderate	Moderate	Low	Low	Low	Low	Fair
Chaulet et al (1995)	Low	Low	Low	Low	Low	Low	Good
Combs et al (1990)	Low	High	Low	Low	High	High	Poor
Connolly et al (1999)	Low	Low	Low	Low	High	High	Poor
Crampin et al (2010)	Moderate	Moderate	Low	Moderate	Low	Moderate	Fair
Cudahy et al (2020)	Low	Low	Moderate	Low	Low	Low	Fair
Dangisso et al (2018)	Low	Low	Low	Moderate	High	Low	Poor
Datiko et al (2009)	Low	Low	Low	Low	High	Low	Poor
East and Central African/BMRC (1986)	Low	Low	Low	Low	Low	Low	Good
Eksombatchai et al (2022)	Low	NA	Low	Low	Low	Low	Good
El Sahly et al (2004)	Low	NA	Moderate	Low	Moderate	Low	Fair
Faustini et al (2008)	Low	NA	Moderate	Low	Low	Low	Fair
Fitzgerald et al (2000)	Low	Moderate	Low	Moderate	High	Low	Poor
Fox et al (2018)	Low	Low	Low	Low	Low	Low	Good
Franke et al (2012)	Low	Low	Moderate	Moderate	Moderate	Moderate	Fair
Gopalan et al (2018)	Low	Low	Low	Low	Low	Low	Good
Gupte et al (2021)	Low	NA	Low	Low	Low	Low	Good
Hang et al (2015)	Low	Moderate	Low	Low	Low	Moderate	Fair
Hawken et al (1993)	Low	Moderate	Moderate	Low	Moderate	Moderate	Fair

Hong Kong Chest Service (1982)	Low	Low	Low	Low	Low	Low	Good
Hong Kong TBRC / Madras BMRC (1991)	Low	Low	Low	Low	Low	Low	Good
Huyen et al (2013)	Low	Low	Low	Low	Moderate	Low	Fair
Jasmer Lorna et al (2004)	Low	Moderate	Low	Low	High	Low	Poor
Jawahar et al (2013)	Low	Low	Low	Low	Low	Low	Good
Jiang et al (2022)	Low	Low	Low	Moderate	Moderate	Low	Fair
Jimenez Corona et al (2013)	Low	Moderate	Low	Low	Moderate	Low	Fair
Jo et al (2014)	Low	High	Moderate	Moderate	Moderate	Moderate	Poor
Johnson et al (2000)	Low	Low	Low	Low	High	High	Poor
Kassim et al (1995)	Moderate	Moderate	Low	Low	High	High	Poor
Kennedy et al (1996)	Low	Low	Low	Low	High	High	Poor
Kim et al (2021)	Low	Low	Low	Moderate	High	High	Poor
Lienhard et al (2011)	Low	Low	Low	Low	Low	Low	Good
Liu et al (2021)	Low	Moderate	Low	Low	Moderate	Low	Fair
Luzze et al (2013)	Low	Moderate	Low	Low	Low	Low	Fair
Ma et al (2018)	Low	Low	Low	Low	High	High	Poor
Madras BMRC (1989)	Low	Low	Low	Low	Low	Low	Good
Marx et al (2014)	Low	Moderate	Low	Low	High	Low	Poor
Mave et al (2021)	Low	Low	Low	Moderate	Low	Moderate	Fair
Merle et al (2014)	Low	Low	Low	Low	Low	Low	Good
Moreno Martinez et al (2009)	Low	Moderate	Low	Low	High	High	Poor
Nahid et al (2007)	Low	Moderate	Low	Low	High	High	Poor
Nettles et al (2004)	Low	Moderate	Low	Low	High	High	Poor
Nie et al (2021)	Low	Low	Low	Low	Low	Low	Good
Parthasarathy et al (1991)	Low	Low	Low	Low	Low	Low	Good
Perriens et al (1991)	Low	Moderate	Low	Low	High	High	Poor
Perriens et al (1995)	Low	Moderate	Low	Low	High	High	Poor
Pettit et al (2011)	Low	Low	Low	Moderate	Low	Low	Fair

Picon et al (2007)	Low	Moderate	Moderate	Low	Low	Low	Fair
Pillay et al (2021)	Low	Na	Low	High	Low	Low	Poor
Pin Hui Lee et al (2014)	Low	NA	Moderate	Low	High	High	Poor
Pulido et al (1997)	Low	Low	Low	Low	Low	Low	Good
Racil et al (2012)	Low	NA	Moderate	Moderate	Moderate	High	Poor
Ruan et al (2021)	Low	Low	Low	Low	High	Moderate	Poor
Shen et al (2017)	Low	Moderate	Low	Low	Low	Low	Fair
Singapore/BMRC (1981)	Low	Low	Low	Low	Low	Low	Good
Singapore/BMRC (1988)	Low	Low	Low	Low	Low	Low	Good
Singapore/BMRC (1991)	Low	Low	Low	Low	Low	Low	Good
Somner et al (1980)	Low	Low	Low	Low	Low	Low	Good
Sonnenberg et al (2001)	Low	Low	Low	Low	Low	Low	Good
Su et al (2002)	Low	Moderate	Low	Low	Low	Low	Fair
Sun et al (2017)	Low	Low	Low	Moderate	Low	Low	Fair
Suryanto et al (2008)	Low	Low	Low	Moderate	Low	Low	Fair
Teo et al (1999)	Low	Low	Low	Low	Low	Low	Good
Thomas et al (2004)	Moderate	Low	Moderate	Low	High	Low	Poor
Thomas et al (2019)	High	High	Low	Moderate	Low	Low	Poor
Tian et al (2014)	Low	NA	Low	Moderate	Low	Low	Fair
Tuberculosis Research Centre (1997)	Low	Low	Low	Low	Low	Low	Good
Velayutham et al (2018)	Low	Low	Low	Moderate	Low	Low	Fair
Vree et al (2007)	Low	Low	Moderate	Low	High	High	Poor
Wang et al (2015)	Low	Low	Low	Moderate	Low	Low	Fair
Westerlund et al (2015)	Low	Low	Low	Moderate	Low	Low	Fair
William et al (2021)	Low	High	Low	High	High	High	Poor
Wu et al (2015)	Low	Low	Low	Low	Low	Low	Good
Wu et al (2016)	Low	Low	Moderate	Moderate	High	High	Poor
Zierski et al (1981)	Low	Low	Low	Low	Low	Low	Good

NA: Study attrition domain was not applicable for case control studies.

Table S4: Risk of bias assessment using QUIPS Tool for studies reporting relapses and reinfections

Study	Study participation	Study attrition	Risk factor measurement	Outcome measurement	Adjustment for other risk factors	Statistical analysis and reporting	Overall assessment
Charalambous et al (2008)	Low	Moderate	Low	High	High	Low	Poor
Crampin et al (2010)	Moderate	Moderate	Low	Moderate	Low	Moderate	Fair
Gillespie et al (2014)	Low	Low	Low	Low	Low	Low	Good
Hawken et al (1993)	Low	Moderate	Low	High	High	Moderate	Poor
Huyen et al (2013)	Low	Low	Low	Low	Low	Low	Good
Jasmer Lorna et al (2004)	Low	Moderate	Moderate	Low	High	Low	Poor
Jimenez Corona et al (2013)	Low	Low	Low	Moderate	High	Low	Poor
Jindani et al (2014)	Low	Low	Low	Low	Low	Low	Good
Johnson et al (2009)	Low	Low	Low	Low	Low	Low	Good
Lienhard et al (2011)	Low	Low	Low	Low	Low	Low	Good
Luzze et al (2013)	Low	Low	Low	Low	Low	Low	Good
Marx et al (2014)	Low	Moderate	Low	Low	High	Low	Poor
Merle et al (2014)	Low	Low	Low	Low	Low	Low	Good
Pettit et al (2011)	Low	Low	Low	Moderate	High	Low	Poor
Shen et al (2017)	Low	Moderate	Low	High	Low	Low	Poor
Sonnenberg et al (2001)	Low	Low	Low	Moderate	Low	Low	Fair

Table S5 Individual study risk factor estimates for undifferentiated recurrences

Study	Effect measure	Number of observations	Number of missing data	Risk factor	Risk factor as reported by study	Estimate	p-value	Adjusted estimate	p-value
Anaam et al (2019)	OR	751		Low TB treatment adherence (yes)	Non adherence	3.73 (2.21-6.31)	<0.001	3.22 (1.76-5.87)	<0.001
Picon et al (2007)	RR	610		Low TB treatment adherence (yes)	Non compliance	4.02 (1.79-9.01)	0.001	6.43 (2.02-20.44)	0.002
Pulido et al (1997)*	HR	187		Low TB treatment adherence (yes)	Poor compliance with therapy	3.3 (1.2-12.1)			
Thomas et al (2005)	OR	491	12	Low TB treatment adherence (yes)	Drug regularity irregular	2.6 (1.5-4.7)	<0.001	2.5 (1.4-4.6)	
Picon et al (2007)	RR	607	3	Advanced radiographical extent of TB disease (yes)	Advanced tuberculosis	2.06 (0.83-5.12)	0.122		
Hang et al (2015)	HR	388		Advanced radiographical extent of TB disease (yes)	Presence of infiltrate on cxr >3zones	0.79 (0.27-2.25)			
Jo et al (2014)	OR	317		Advanced radiographical extent of TB disease (yes)	moderately to far advanced disease	2.5 (0.5-12.3)	0.268	3.08 (0.4-23.78)	0.282
Luzze et al (2013)	HR	1334	367	Advanced radiographical extent of TB disease (yes)	Extent of disease (end of treatment): far advanced	2 (1.3-3.1)		1.3 (0.8-2.1)	
Chang et al (2004)	OR	339		Alcohol consumption (yes)	History of habitual alcohol drinking	1.4 (0.7-2.8)			
Picon et al (2007)	RR	610		Alcohol consumption (yes)	Alcohol	1.9 (0.85-4.25)	0.121		
Franke et al (2012)	HR	367		Alcohol consumption (yes)	Alcohol or substance use	0.58 (0.14-2.47)	0.46		
Lee et al (2014)	OR	600		Alcohol consumption (yes)	History of alcohol use	2.39 (1.51-3.77)	<0.001	1.79 (1.79-3.33)	0.06
Thomas et al (2005)	OR	486	17	Alcohol consumption (yes)	Drinking (alcoholism) no	2.3 (1.3-4.1)	<0.1		
Tian et al (2014)	HR	480		Alcohol consumption (yes)	Alcohol	1.79 (1.04-3.09)	0.036		
Velayutham et al (2018)	Relative risk	1108		Alcohol consumption (yes)	Taking alcohol during treatment and or follow-up	1.46 (1.07-2)	0.017	1.06 (0.66-1.71)	0.81
Anaam et al (2019)	OR	751		Body mass index <18.5 (yes)	Bmi <=18.5	2.37 (1.43-3.93)	0.001	1.66 (0.86-3.19)	0.129
Chang et al (2004)	OR	339		Body mass index <18.5 (yes)	Initial body weight □< 50 kg	1.7 (1-2.8)		1.79 (0.9-3.59)	
Franke et al (2012)	HR	348		Body mass index <18.5 (yes)	Low bmi (<18.5 in women or <20 in	0.68 (0.25-1.87)	0.45		

					men) or malnutrition				
Jo et al (2014)	OR	317		Body mass index <18.5 (yes)	Bmi < 18.5 kg/m2	1.15 (0.13-10.53)	0.901	0.6 (0.19-18.4)	0.597
Luzze et al (2013)	HR	1701		Body mass index <18.5 (yes)	Bmi <18.9	1.3 (0.9-1.7)			
Thomas et al (2005)	OR	489	14	Body mass index <18.5 (yes)	Initial weight <42 kg	1.3 (0.7-2.3)	0.4		
Tian et al (2014)	HR	480		Body mass index <18.5 (yes)	Malnutrition	2.33 (1.32-4.12)	0.003	1.91 (1.11-4.291)	0.019
Velayutham et al (2018)	Relative risk	1108		Body mass index <18.5 (yes)	Bmi < 18.5	0.99 (0.47-2.07)	0.97	0.77 (0.26-2.27)	0.64
Anaam et al (2019)	OR	751		Cavitary disease (yes)	Cavitation	2.08 (1.27-3.42)	0.004	2.01 (1.16-3.46)	0.012
Chang et al (2004)	OR	339		Cavitary disease (yes)	cavitation on initial chest radiograph	1.8 (1.1-2.9)		2.39 (1.14-5.05)	
Charalambous et al (2008)	HR	503	106	Cavitary disease (yes)	Cavitation	1.1 (0.5-2.5)	0.85		
Picon et al (2007)	RR	595	15	Cavitary disease (yes)	Cavitation	1.55 (0.37-6.56)	0.551		
Franke et al (2012)	HR	389		Cavitary disease (yes)	Bilateral chest cavitatons	0.88 (0.41-1.9)	0.74		
Hang et al (2015)	HR	388		Cavitary disease (yes)	Cavitation	0.75 (0.36-1.59)			
Jo et al (2014)	OR	317		Cavitary disease (yes)	Cavitary disease	1.6 (0.29-8.92)	5.91	1.02 (0.16-6.47)	0.981
Kim et al (2021)*	RR	355		Cavitary disease (yes)	Cavitary disease	6.75 (0.8-57.22)			
Lee et al (2014)	OR	575	25	Cavitary disease (yes)	Initial cavitation`	1.4 (0.93-2.1)	0.1	1.02 (0.62-1.68)	0.94
Liu et al (2022)	OR	1897		Cavitary disease (yes)	Bilateral cavitation	1.51 (1.02-2.22)		1.56 (1.05-2.32)	0.029
Luzze et al (2013)	HR	1432	269	Cavitary disease (yes)	Cavitation	1.6 (1.2-2.3)		1.4 (1-1.9)	
Nettles et al (2004)*	Relative risk	393		Cavitary disease (yes)	Cavitation	1.14 (0.36-3.55)			
Qiao Lin Ruan et al (2021)	HR	479		Cavitary disease (yes)	Pulmonary cavitiy	1.51 (1.24-1.84)	<0.001	1.51 (1.25-1.82)	<0.001
Shen et al (2017)	HR	13067	350	Cavitary disease (yes)	Cavitation	1.43 (1.23-1.67)	<0.001	1.27 (1.06-1.51)	<0.01
Charalambous et al (2008)	HR	496	113	Chronic lung disease (yes)	Silicosis advanced	0.6 (0.2-1.9)		0.6 (0.2-2)	0.31
Luzze et al (2013)	HR	1435	266	Chronic lung disease (yes)	Fibrosis	1.4 (1-2)		1.2 (0.8-1.7)	
Pettit et al (2011)	OR	98		Chronic lung disease (yes)	Chronic lung disease	4.01 (1.15-13.94)	0.03	5.28 (1.16-24.04)	0.03
Tian et al (2014)	HR	480		Chronic lung disease	Copd	1.49 (0.87-2.56)	0.144		

Anaam et al (2019)	OR	751		Diabetes mellitus (yes)	Diabetes	4.04 (2.18-7.48)	<0.001	3.78 (1.84-7.8)	<0.001
Picon et al (2007)	RR	610		Diabetes mellitus (yes)	Diabetes	0.04 (0-16.68)	0.301		
Eksombatchai et al (2022)*	RR	199571		Diabetes mellitus (yes)	Diabetes	1.33 (1.26, 1.41)	<0.001		
Franke et al (2012)	HR	360		Diabetes mellitus (yes)	Diabetes	5.96 (1.75-20.29)	0.004	10.47 (2.17-50.6)	0.004
Jo et al (2014)	OR	317		Diabetes mellitus (yes)	Diabetes mellitus	0.98 (0.97-1)	0.908	0.78 (0.62-1.23)	0.897
Lee et al (2014)	OR	600		Diabetes mellitus (yes)	Dm	1.67 (1.18-2.38)	0.004	1.96 (1.22-3.15)	0.005
Mave et al (2021)	Rate Ratio	799		Diabetes mellitus (yes)	Diabetes	0.62 (0.3-1.27)	0.19	0.73 (0.31-1.7)	0.46
Patrick George Tobias Cudahy et al (2020)	HR	333		Diabetes mellitus (yes)	Diabetes	2.34 (0.56-9.77)	0.24		
Shen et al (2017)	HR	12896	521	Diabetes mellitus (yes)	Diabetes	1.43 (1.17-1.75)	0.001	1.4 (1.13-1.76)	<0.01
Tian et al (2014)	HR	480		Diabetes mellitus (yes)	Diabetes	3.56 (1.86-6.82)	<0.001	3.288 (1.301-8.312)	0.012
Velayutham et al (2018)	Relative risk	1108		Diabetes mellitus (yes)	Diabetes	0.58 (0.37-0.9)			
Wu et al (2016)*	RR	196	5	Diabetes mellitus (yes)	Diabetes	5.87 (1.26-27.4)	0.024		
Anaam et al (2019)	OR	751		Illiteracy (yes)	Illiterate	2.07 (1.26-3.38)	0.004	1.54 (0.87-2.73)	0.143
Dangisso et al (2018)	HR	1711	78	Illiteracy (yes)	No education	1.4 (0.9-2.1)		1 (0.6-1.5)	
Datiko et al (2009)	HR	355		Illiteracy (yes)	Literate : no	1.42 (0.53-5.00)	0.5		
Sun et al (2017)	HR	234		Illiteracy (yes)	Education <= primary school	1.95 (1.14-3.35)	0.01	1.72 (0.88-3.35)	0.11
Thomas et al (2005)	OR	486	17	Illiteracy (yes)	Literate; no	0.83 (0.48-1.66)	0.7		
Bartacek et al 2009	RR	945		Fixed-dose combination TB drug (yes)		1.15 (0.83-1.59)			
Chaulet et al (1995)*	RR	209		Fixed-dose combination TB drug (yes)		2.86 (0.12-69.42)			
Singapore BMRC (1991)*	RR	265		Fixed-dose combination TB drug (yes)		3.74 (0.81-17.27)			
Su et al (2002)*	RR	51		Fixed-dose combination TB drug (yes)		2.89 (0.12-67.64)			
Suryanto et al (2008)*	IRR	172		Fixed-dose combination TB drug (yes)	-	3.56 (0.78-16.24)	0.08		

Teo et al (1999)*	RR	271		Fixed-dose combination TB drug (yes)		4.21 (1.22-14.59)			
Chaisson et al (1996)	Rate Ratio	427		HIV (yes)	HIV	2.39 (0.78-7.59)			
Charalambous et al (2008)	HR	508	101	HIV (yes)	HIV	2.5 (1.2-5.3)		3 (1.3-7)	0.01
Connolly et al (1999)*	Rate Ratio	403		HIV (yes)	HIV	1.08 (0.42-2.87)			
Crampin et al (2010)	Rate Ratio	584		HIV (yes)	HIV	1.6 (0.9-2.7)	0.1	1.4 (0.8-2.4)	0.22
Picon et al (2007)	RR	279	331	HIV (yes)	HIV	11.25 (3.38-37.43)	<0.001	8.04 (2.35-27.5)	0.001
Faustini et al (2008)	OR	360	10	HIV (yes)	HIV	0.77 (0.04-13.57)			
Fitzgerald et al (2000)	RR	233		HIV (yes)	HIV	10.7 (1.4-81.6)	0.004		
Fox et al (2018)	HR	9825		HIV (yes)	HIV	1.3 (1.01-1.71)	P<0.05.	1.7 (1.1-2.4)	P<0.05.
Hang et al (2015)	HR	401		HIV (yes)	HIV	0.66 (0.09-4.85)			
Jasmer Lorna et al (2004)*	Rate Ratio	85		HIV (yes)	HIV	1.11 (0.61-1.90)			
Johnson et al (2000)	Rate Ratio	225		HIV (yes)	HIV	2.47 (0.51-59.32)			
Kassim et al (1995)*	Rate Ratio	835		HIV (yes)	HIV	1.75 (0.67-5.49)			
Kennedy et al (1996)*	Rate Ratio	168		HIV (yes)	HIV	0.71 (0.15-3.86)			
Luzze et al (2013)	HR	1700	1	HIV (yes)	HIV	1.3 (0.9-1.8)		1.1 (0.7-1.6)	
Nahid et al (2007)	Rate Ratio	800		HIV (yes)	HIV	9.23 (2.94-42.05)			
Nettles et al (2004)*	Relative risk	393		HIV (yes)	HIV	4.98 (1.71-14.54)			
Patrick George Tobias Cudahy et al (2020)	HR	333		HIV (yes)	HIV	0.77 (0.39-1.53)	0.46	0.99 (0.48-2.05)	0.99
Perriens et al (1991)*	Rate Ratio	385		HIV (yes)	HIV	3.05 (1.18-7.44)			
Perriens et al (1995)*	Rate Ratio	523		HIV (yes)	HIV	0.91 (0.36-2.33)			
Pettit et al (2011)	OR	98		HIV (yes)	HIV	2.67 (0.77-9.18)	0.12	5.01 (1.07-23.39)	0.04
Sonnenberg et al (2001)	Rate Ratio	326		HIV (yes)	HIV	2.49 (1.52-4.19)			
Tian et al (2014)	HR	407	73	HIV (yes)	HIV	1.5 (0.78-2.88)	0.222		
Velayutham et al (2018)	Relative risk	1108		HIV (yes)	HIV	1.34 (0.55-3.29)			
Anaam et al (2019)	OR	751		Male sex (yes)	Male	1.49 (0.89-2.48)	0.127		

Crampin et al (2010)	Rate Ratio	584.00		Male sex (yes)	Male	0.59 (0.34-1.01)			
Datiko et al (2009)	HR	368.00		Male sex (yes)	Male	1.8 (0.6-5.5)	0.3		
Picon et al (2007)	RR	610		Male sex (yes)	Male	2.1 (0.84-5.22)	0.111		
Faustini et al (2008)	OR	352	8	Male sex (yes)	Male	1.43 (0.53-3.81)		1.98 (0.3-12.83)	
Fox et al (2018)	HR	9825.00		Male sex (yes)	Male	1.3 (1.1-1.4)	P<0.05.	1.04 (0.7-1.5)	P>=0.05.
Franke et al (2012)	HR	402.00		Male sex (yes)	Male	1.64 (0.71-3.85)	0.24		
Hang et al (2015)	HR	403.00		Male sex (yes)	Male	0.4 (0.11-2)			
Jiang et al (2022)	HR	7143		Male sex (yes)	Male	1.42 (1.34-1.49)	<0.001	1.29 (1.22-1.36)	<0.001
Jo et al (2014)	OR	317		Male sex (yes)	Male gender	0.94 (0.15-5.68)	0.941	0.64 (0.12-3.44)	0.602
Lee et al (2014)	OR	600		Male sex (yes)	Male	1.41 (0.99-2)	0.06	1.41 (1.41-2.31)	0.17
Liu et al (2022)	OR	1897		Male sex (yes)	Male	1.79 (1.10-2.86)		1.33 (0.79-2.27)	0.28
Luzze et al (2013)	HR	1701		Male sex (yes)	Male	1.1 (0.8-1.4)			
Nettles et al (2004)*	Relative risk	393		Male sex (yes)	Male	2.03 (0.58-7.16)			
Patrick George Tobias Cudahy et al (2020)	HR	333		Male sex (yes)	Male gender	1.13 (0.57-2.22)	0.71		
Pettit et al (2011)	OR	98		Male sex (yes)	Male	6.47 (1.39-30.26)	0.02		
Qiao Lin Ruan et al (2021)	HR	479		Male sex (yes)	Male	1.77 (1.46-2.13)	<0.001	1.61 (1.3-2)	<0.001
Shen et al (2017)	HR	13147		Male sex (yes)	Male	1.49 (1.22-1.81)	<0.001	1.4 (1.1-1.75)	<0.01
Sun et al (2017)	HR	234.00		Male sex (yes)	Male	1.04 (0.58-1.85)	0.89	0.99 (0.55-1.81)	0.98
Thomas et al (2005)	OR	503		Male sex (yes)	Male	1.8 (0.8-3.9)	0.1		
Tian et al (2014)	HR	480		Male sex (yes)	Male	1 (0.58-1.72)	1		
Velayutham et al (2018)	Relative risk	1108		Male sex (yes)	Male	2.23 (1.47-3.4)	<0.001	2.43 (1.29-4.58)	0.006
Vree et al (2007)*	RR	304		Male sex (yes)	Male	1.19 (0.5-2.84)			
Fox et al (2018)	HR	9825		MDR (vs no resistance)	Self reported MDR	9.9 (9-11)	P<0.05.	8.4 (7.4-9.6)	P<0.05.
Hang et al (2015)	HR	397		MDR (vs no resistance)	Resistance to RIF	3.63 (0.86-15.26)		3.1 (0.66-14.55)	
Huyen et al (2013)	HR	35		MDR (vs no resistance)	MDR	4.23	0.029	1.58 (0.46-5.41)	0.466
Luzze et al (2013)	HR	932	769	MDR (vs no resistance)	Resistant to H and/or R	1.1 (0.6-2.2)			

Shen et al (2017)	HR	7768		MDR (vs no resistance)	MDR	3.12 (2.27-4.11)	<0.001	2.9 (2.2-3.84)	<0.001
Sun et al (2017)	HR	234		MDR (vs no resistance)	MDR	3.37 (1.98-5.73)	<0.001	2.75 (1.58-4.79)	<0.001
Thomas et al (2005)	OR	487	16	MDR (vs no resistance)	Resistant to H and/or R	3.6 (1.5-8.5)	<0.01	4.8 (2-11.6)	
Anaam et al (2019)	OR	751		Smear or culture positivity at 2 months treatment (yes)	Smear positivity at 2 months	1.81 (0.73-4.48)	0.2		
Chang et al (2004)	OR	231	108	Smear or culture positivity at 2 months treatment (yes)	Persistence of positive culture after 2–3 mo of treatment	2.5 (0.8-7.2)			
Picon et al (2007)	RR	610		Smear or culture positivity at 2 months treatment (yes)	Negative sputum conversion at month 4	1.68 (0.55-5.61)	0.396		
Hang et al (2015)	HR	403		Smear or culture positivity at 2 months treatment (yes)	Smear positivity at 2 months	1.84 (0.75-4.5)			
Jo et al (2014)	OR	317		Smear or culture positivity at 2 months treatment (yes)	Positive afb culture at 2 months of treatment	8.12 (1.4-47.44)	0.021	7.08 (1.25-42.23)	0.068
Nettles et al (2004)*	Relative risk	42		Smear or culture positivity at 2 months treatment (yes)	Smear positivity at 2 months	0.98 (0.06-16.65)			
Qiao Lin Ruan et al (2021)	HR	479		Smear or culture positivity at 2 months treatment (yes)	Sputum positivity at 2 months	1.56 (1.14-2.13)	0.001	1.39 (1.05-1.81)	0.02
Thomas et al (2005)	OR	503		Smear or culture positivity at 2 months treatment (yes)	No smear conversion at 2 months	1.1 (0.5-2.2)	0.9		
Vree et al (2007)*	RR	278	26	Smear or culture positivity at 2 months treatment (yes)	Smear positivity at 2 months	1.79 (0.29-11.25)			
Chang et al (2004)	OR	339		Previous TB episode (yes)	History of tuberculosis	1.1 (0.5-2.2)			
Dangisso et al (2018)	HR	1789		Previous TB episode (yes)	Retreatment vs new patient	3.1 (1.6-5.9)		2.7 (1.4-5.3)	
Fox et al (2018)	HR	9825		Previous TB episode (yes)	Prior TB	3.3 (3-3.6)	P<0.05.	2.3 (2-2.7)	P<0.05.

Huyen et al (2013)	HR	35.00			Previous TB episode (yes)	Previously treated	1.5	0.471	0.61 (0.19-1.9)	0.393
Jo et al (2014)	OR	317			Previous TB episode (yes)	Previous history of TB treatment	0.97 (0.11-8.5)	0.981	0.56 (0.06-5.81)	0.63
Liu et al (2022)	OR		1897		Previous TB episode (yes)	Previous TB treatment	2.49 (1.71-3.61)		2.22 (1.52-3.26)	<0.001
Patrick George Tobias Cudahy et al (2020)	HR	333			Previous TB episode (yes)	Previous treatment for tuberculosis	0.59 (0.2-1.67)	0.32		
Shen et al (2017)	HR	13147			Previous TB episode (yes)	Retreated case	1.84 (1.55-2.19)	<0.001	1.8 (1.45-2.2)	<0.001
Chang et al (2004)	OR	339			Any drug resistance (yes)	Resistance in the initial drug sensitivity pattern	1.8 (0.7-4.4)			
Charalambous et al (2008)	HR	545		64	Any drug resistance (yes)	Resistance	0.8 (0.2-1.9)	0.76		
Crampin et al (2010)	Rate Ratio	584			Any drug resistance (yes)	Resistance	4.2 (2-8.5)			
Velayutham et al (2018)	Relative risk	1108			Any drug resistance (yes)	Baseline drug resistant	0.92 (0.48-1.76)	0.81		
East and Central Africa (1986)*	RR	609			Rifampicin less than 6 months vs 6 months	Regimen less than 6 months	3 (1.08-8.35)			
Jawahar et al (2013)*	HR	400			Rifampicin less than 6 months vs 6 months	Moxifloxacin vs standard treatment	1.41 (0.6-3.32)	0.432		
Jawahar et al (2013)*	HR	400			Rifampicin less than 6 months vs 6 months	Gatifloxacin vs standard regimen	2.26 (1.05-4.87)	0.04		
Luzze et al (2013)	HR	1701			Rifampicin less than 6 months vs 6 months	$6H_3E_3$ vs standard regimen	1.9 (1.2-2.9)		1.6 (0.9-2.7)	
Madras BMRC (1989)*	RR	459			Rifampicin less than 6 months vs 6 months	Regimen less than 6 months	0.5 (0.18-1.34)			
Singapore BMRC (1981)*	RR	318			Rifampicin less than 6 months vs 6 months	Regimen less than 6 months	12.78 (1.68-97.12)			
Singapore BMRC (1981)*	RR	314			Rifampicin less than 6 months vs 6 months	Regimen less than 6 months	7.6 (1.77-32.67)			
Tuberculosis Research Centre (1997)*	RR	777			Rifampicin less than 6 months vs 6 months	Regimen less than 6 months	1.98 (1.14-3.47)			
Velayutham 2020	RR	675			Rifampicin less than 6 months vs 6 months	Regimen less than 6 months	1.99 (0.96-4.09)			

Combs et al (1990)*	RR	616		Rifampicin more than 6 months vs 6 months	Regimen more than 6 months	1 (0.37-2.72)			
Hong Kong TBRC / Madras BMRC (1991)*	RR	99		Rifampicin more than 6 months vs 6 months	Regimen more than 6 months	0.2 (0.05-0.85)			
Luzze et al (2013)	HR	1701		Rifampicin more than 6 months vs 6 months	6RH	0.7 (0.4-1.1)		0.8 (0.5-1.4)	
Somner et al (1990)	RR	665		Rifampicin more than 6 months vs 6 months	Regimen more than 6 months	0.08 (0.02-0.38)			
Dangisso et al (2018)	HR	1789		Rural resident (vs urban)	Rural vs urban	1.6 (0.9-2.6)		1.5 (0.9-2.8)	
Fox et al (2018)	HR	9825		Rural resident (vs urban)	Urban setting	0.71 (0.62-0.77)	P<0.05.	0.71 (0.625-0.83)	P<0.05.
Jiang et al (2022)	HR	7143		Rural resident (vs urban)	Residence urban vs rural	1.07 (1-1.14)	0.025	0.99 (0.92-1.07)	0.855
Vree et al (2007)*	RR	304		Rural resident (vs urban)	Rural vs urban	0.39 (0.1-1.48)			
Anaam et al (2019)	OR	751		Smear positivity at diagnosis (yes)	Smear positive	0.77 (0.34-1.77)	0.546		
Chang et al (2004)	OR	339		Smear positivity at diagnosis (yes)	Initial sputum smear	1.2 (0.8-2.1)			
Faustini et al (2008)	OR	298	62	Smear positivity at diagnosis (yes)	Smear+	1.2 (0.38-3.81)			
Jiang et al (2022)	HR	7143		Smear positivity at diagnosis (yes)	Bacterial results positive vs negative	1.25 (1.19-1.31)	<0.001	1.27 (1.21-1.33)	<0.001
Jo et al (2014)	OR	317		Smear positivity at diagnosis (yes)	Positive afb smear at treatment initiation	1.33 (0.24-7.35)	0.747	0.59 (0.1-3.61)	0.567
Shen et al (2017)	HR	13363	54	Smear positivity at diagnosis (yes)	Smear positive	1.61 (1.26-2.07)	<0.001	1.59 (1.19-2.14)	<0.01
Ahmad Khan et al (2016)	OR	332		Smoking (yes)	Ever smoked	2.05 (1.32-3.19)		1.86	
Anaam et al (2019)	OR	751		Smoking (yes)	Smoking	2.1 (1.18-3.75)	0.012	2.18 (1.07-4.47)	0.032
Chang et al (2004)	OR	339		Smoking (yes)	Ever-smokers	1.3 (0.7-2.3)			
Franke et al (2012)	HR	367.00		Smoking (yes)	Ever smoked cigarettes	1.02 (0.24-4.38)	0.98		
Lee et al (2014)	OR	600		Smoking (yes)	History of smoking	1.54 (1.1-2.15)	0.01	1.17 (0.71-1.93)	0.54
Liu et al (2022)	OR	1897		Smoking (yes)	Smoking	1.37 (0.97-1.93)		1.32 (0.91-1.91)	0.146
Pettit et al (2011)	OR	98		Smoking (yes)	Smoking	16.85 (2.06-137.76)	0.008		
Thomas et al (2005)	OR	486	17	Smoking (yes)	Smoking	2.8 (1.5-5.2)	<0.001	3.1 (1.6-6)	

Tian et al (2014)	HR	480	Smoking (yes)	Smoking	2.41 (1.29-4.49)	0.005	2.387 (1.328-4.291)	0.004
Velayutham et al (2018)	Relative risk	1108	Smoking (yes)	Smoking during treatment and or follow-up	1.53 (1.12-2.1)	0.007	1.13 (0.7-1.84)	0.61

*Estimates were calculated based on data provided by the study

Table S6 Individual study risk factor estimates for relapses

Study	Effect measure	Number of observations	Number of missing data	Risk factor	Estimate	p-value	Adjusted estimate	p-value
Romanowski et al (2017)	OR	1187		HIV infection (yes)	2.2 (1.2-3.9)		2.6 (1.4-4.6)	
Sonnenberg et al (2001)	HR	326		HIV infection (yes)	0.61 (0.26-1.4)		0.58 (0.24-1.4)	
Luzze et al (2013)	HR	97	1	HIV infection (yes)	0.8 (0.5-1.2)		0.4 (0.2-0.8)	
Charalambous et al (2008)	Relative risk	503	106	HIV infection (yes)	2.53 (0.29-22.5)			
Crampin et al (2010)	Rate Ratio	584		HIV infection (yes)	0.8 (0.4-1.8)			
Hawken et al (1993)*	Relative risk	196		HIV infection (yes)	11.78 (0.57-241.63)			
Jasmer Lorna et al (2004)	Relative risk	75		HIV infection (yes)	1.01 (0.57-1.78)			
Marx et al (2014)	Relative risk	1624		HIV infection (yes)	0.37 (0.05-2.72)			
Pettit et al (2011)	Relative risk	1079		HIV infection (yes)	1.62 (0.36-7.3)			
Shen et al (2017)	HR	12848		Male sex (yes)	3.33 (1.54-7.23)	<0.01	3.14 (1.44-6.85)	0.004
Romanowski et al (2017)	OR	1189		Male sex (yes)	1.9 (1-3.5)		2.1 (1.1-4)	
Crampin et al (2010)	Rate Ratio	584		Male sex (yes)	0.59 (0.28-1.25)			
Huyen et al (2013)	HR	23		Male sex (yes)	1.495 (-)	0.446		
Marx et al (2014)	Relative risk	1624		Male sex (yes)	1.4 (0.84-2.32)			
Johnson et al (2009)	HR	386		Male sex (yes)	1.09 (0.4-3)	0.867		
Johnson et al (2009)	HR	386		Rifampicin less than 6 months vs 6 months	4.47 (1.27-15.68)	0.019	4.14 (1.17-14.63)	0.0273
Gillespie et al (2014)	RR			Rifampicin less than 6 months vs 6 months	4.63 (2.64-8.14)			
Jindani et al (2014)	RR			Rifampicin less than 6 months vs 6 months	1.39 (0.93-2.08)			
Merle et al (2014)	RR			Rifampicin less than 6 months vs 6 months	0.3 (0.17-0.53)			

*Estimates were calculated based on data provided by the stud

Table S7 Individual study risk factor estimates for reinfections

Study	Effect measure	Number of observations	Number of missing data	Risk factor	Estimate	p-value	Adjusted estimate	p-value
Luzze et al (2013)	HR	97	1	HIV infection (yes)	0.8 (0.3-2.5)		0.6 (0.1-3.6)	
Sonnenberg et al (2001)	HR	326		HIV infection (yes)	18.9 (2.5-145)		18.7 (2.4-143)	
Charalambous et al (2008)	Relative risk	508		HIV infection (yes)	6.33 (0.82-49.1)			
Crampin et al (2010)	Rate Ratio	584		HIV infection (yes)	13.5 (1.8-103.7)			
Hawken et al (1993)*	Relative risk	196		HIV infection (yes)	7.72 (0.32-186.65)			
Jasmer Lorna et al (2004)	Relative risk	75		HIV infection (yes)	2.09 (0.19-22.97)			
Marx et al (2014)	Relative risk	1624		HIV infection (yes)	2.23 (0.95-5.26)			
Pettit et al (2011)	Relative risk	1078		HIV infection (yes)	56.23 (2.92-1082.09)			

*Estimates were calculated based on data provided by the study

Table S8 Summary table of adjusted estimates *

	Undifferentiated recurrence			
Risk factor	**Min**	**Median**	**Max**	**N significant / n total†**
Socio demographic factors				
Male sex (yes)	0.64	1.40	2.43	5/9
Low TB related knwoledge (yes)	2.28	2.30	2.60	5/5
Co-morbidites				
HIV infection (yes)	0.99	2.11	33.80	6/9
Diabetes mellitus (yes)	0.73	1.90	10.47	6/8
Body mass index < 18.5 (yes)	0.60	1.66	1.91	1/5
TB disease characteristics (first episode)				
Cavitary disease (yes)	0.70	1.34	2.39	4/8
MDR (vs no resistance)	1.58	3.10	12.85	5/7
Previous TB episode (yes)	0.56	1.80	2.70	3/5
Smear or culture positivity at 2 months treatment (yes)	1.39	2.65	7.08	3/4
TB treatment related factors (first episode)				
Low TB treatment adherence (yes)	2.50	3.11	6.43	3/4
Behavioural factors				
Smoking (yes)	1.02	2.18	3.10	5/9

*We summary all adjusted estimates despite the factors consider for adjustment. Residual confounding is plausible.
†**N significant:** number of studies where the factor is significantly different from 1 over the total number of studies reporting the factor

Table S9: GRADE assessment of certainty of evidence

Certainty assessment							Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
UNDIFFERENTIATED RECURRENCES								
Socio-demographic characteristics								
Male sex								
23	Observational studies + randomised trials	serious[a]	serious[b]	not serious	not serious	none	Low⨁⨁◯◯	
Illiteracy (yes)								
5	Observational studies + randomised trials	serious[a]	serious[b]	serious[c]	not serious	none	Very low⨁◯◯◯	
Rural resident (vs urban)								
4	Observational studies + randomised trials	serious[a]	Very serious[b]	not serious	not serious	non	Very low⨁◯◯◯	
Behavioural characteristics of the patient								
Smoking (yes)								
9	Observational studies + randomised trials	serious[a]	not serious	serious[c]	not serious	none	Low⨁⨁◯◯	
Alcohol consumption (yes)								
7	Observational studies + randomised trials	serious[a]	not serious	serious[c]	not serious	none	Low⨁⨁◯◯	
Clinical characteristics of the previous TB episode								
Cavitary disease (yes)								
13	Observational studies + randomised trials	serious[a]	not serious	not serious	not serious	none	Moderate⨁⨁⨁◯	
Positivity at 2 months (undifferentiated recurrence)								
8	Observational studies + randomised trials	serious[a]	not serious	serious[c]	not serious	none	Low⨁⨁◯◯	
Previous TB episode (yes)								
7	Observational studies + randomised trials	serious[a]	Very serious[f]	not serious	not serious	none	Very low⨁◯◯◯	
MDR (vs no resistance)								
6	Observational studies + randomised trials	serious[a]	very serious[f]	not serious	not serious	very strong association	Moderate⨁⨁⨁◯	
Smear positivity at diagnosis (yes)								
5	Observational studies + randomised trials	serious[a]	not serious	not serious	not serious	none	Moderate⨁⨁⨁◯	
Any drug resistance (yes)								
5	Observational studies + randomised trials	serious[a]	very serious[f]	very serious[c]	not serious	none	Very low⨁◯◯◯	
Advanced radiographical extent of TB disease (yes)								
4	Observational studies + randomised trials	serious[a]	not serious	serious[c]	not serious	none	Low⨁⨁◯◯	
Treatment characteristics of the previous TB episode								
Rifampicin less than 6 months vs 6 months								
9	randomised trials	not serious	serious[b]	serious[g]	not serious	none	Low⨁⨁◯◯	
Rifampicin more than 6 months vs 6 months								

4	randomised trials	serious[i]	very serious[f]	very serious[g]	not serious	none	Very low ⊕◯◯◯	
Fixed dose combination TB drug (yes)								
6	randomised trials	not serious	not serious	not serious	not serious	none	High ⊕⊕⊕⊕	
Low TB treatment adherence (yes)								
4	Observational studies + randomised trials	serious	not serious	serious[c]	not serious	none	Low ⊕⊕◯◯	
Co-morbidities								
HIV infection (yes)								
23	Observational studies + randomised trials	serious[a]	serious[b]	not serious	not serious	none	Low ⊕⊕◯◯	
Body mass index <18.5 (yes)								
	Observational studies + randomised trials	serious[a]	not serious	very serious[c]	not serious	none	Very low ⊕◯◯◯	
Chronic lung disease (yes)								
4	Observational studies + randomised trials	not serious	serious[b]	serious[c]	not serious	none	Low ⊕⊕◯◯	
Diabetes mellitus (yes)								
12	Observational studies + randomised trials	serious[a]	very serious[f]	not serious	not serious	none	Very low ⊕◯◯◯	
RELAPSES								
Socio-demographic characteristics								
Male sex (yes)								
5	Observational studies + randomised trials	serious[a,j]	serious[b]	not serious	not serious	none	Low ⊕⊕◯◯	
Co-morbidities								
HIV infection (yes)								
9	Observational studies + randomised trials	serious[a,j]	serious[b]	not serious	not serious	none	Low ⊕⊕◯◯	
Treatment characteristics of the previous TB episode								
Rifampicin less than 6 months vs 6 months								
4	randomised trials	serious[i]	Very serious[f]	serious[g]	not serious	none	Very low ⊕◯◯◯	
REINFECTIONS								
Co-morbidities								
HIV infection (yes)								
8	Observational studies + randomised trials	serious[a,j]	not serious	not serious	not serious	Strong association	Moderate ⊕⊕⊕◯	

Explanations

a. We downgraded quality in the risk of bias domain because unadjusted estimates were used.
b. Moderate heterogeneity detected based on I2 and/or forest plot inspection.
c. Definitions for risk factors vary between studies
f. High heterogeneity detected based on I2 and/or forest plot inspection
g. Different regimens (duration, frequency, or composition) lead to downgrade quality due to indirectness
i. Lack of attrition and control for confounding lead to downgrade due to risk of bias.
j. Methodological heterogeneity may arise from differences in genotyping methods and availability of sample

Appendix 5 Supplementary figures

Figure S1 Forest plot Undifferentiated recurrence: Male sex (yes)

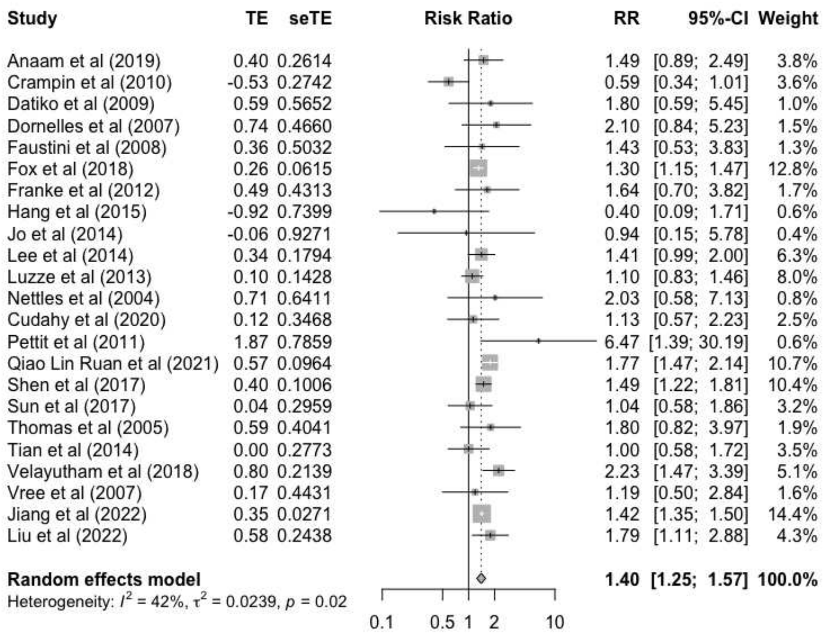


Figure S2 Forest plot Undifferentiated recurrence: Illiteracy (yes)

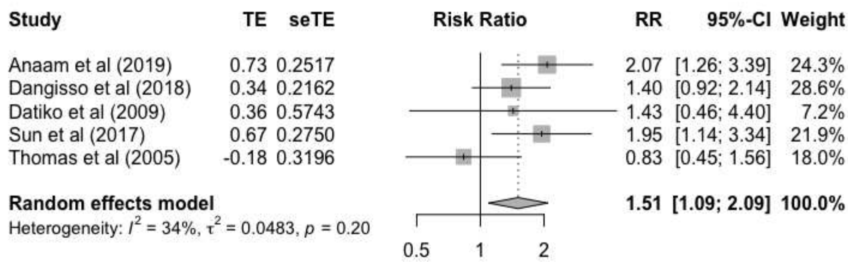


Figure S3 Forest plot Undifferentiated recurrence: Rural resident (vs urban)

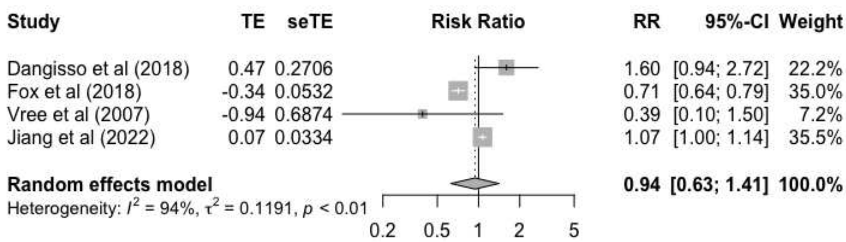


Figure S4 Forest plot Undifferentiated recurrence: Smoking (yes)

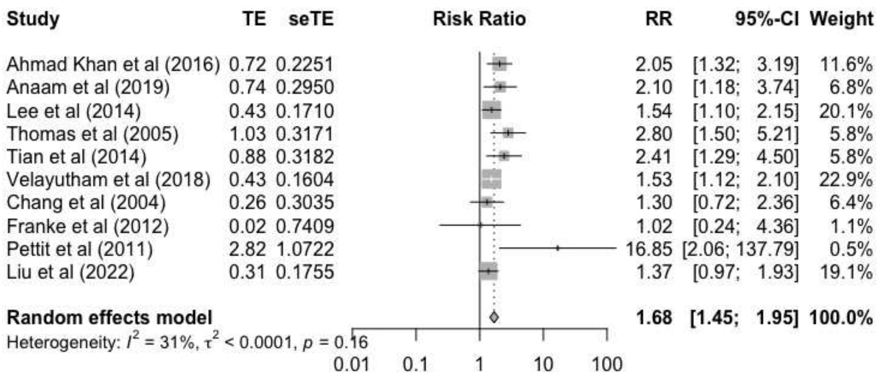


Figure S5 Forest plot Undifferentiated recurrence: Alcohol consumption (yes)

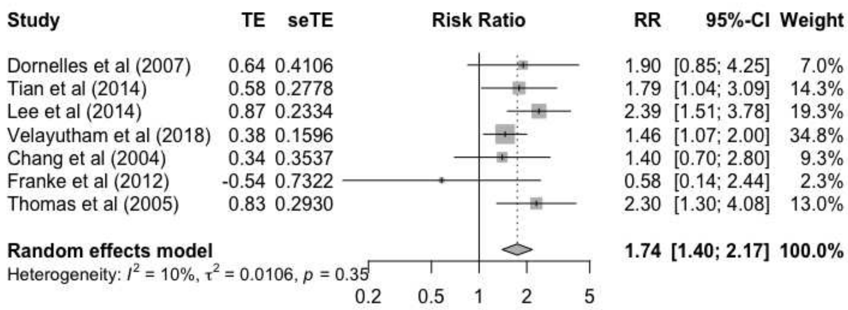


Figure S6 Forest plot Undifferentiated recurrence: Cavitary disease (yes)

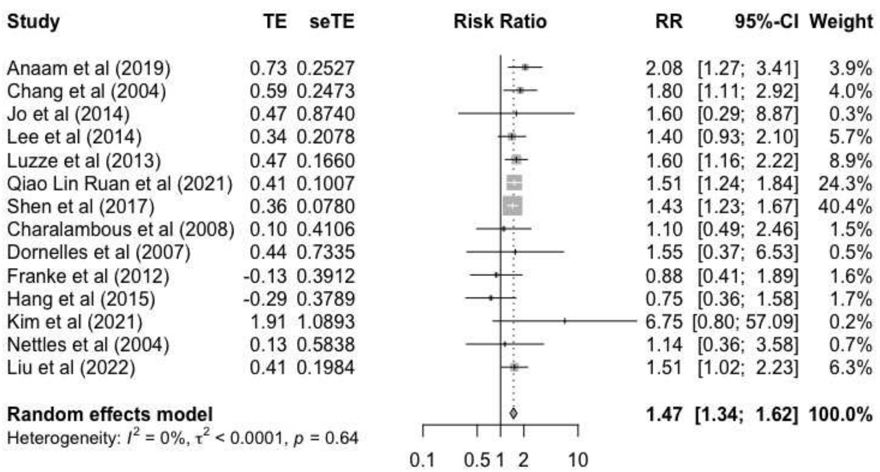


Figure S7 Forest plot Undifferentiated recurrence: Smear positivity at diagnosis (yes)

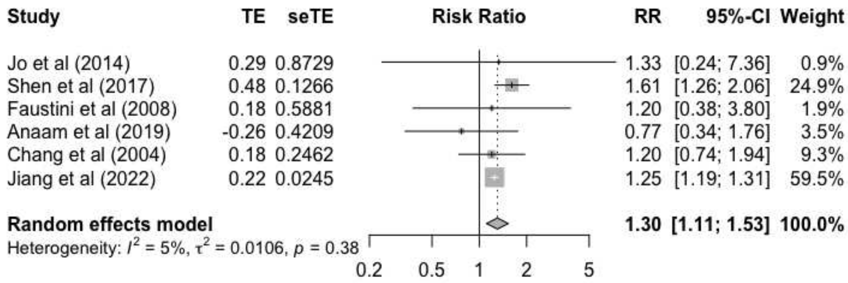


Figure S8 Forest plot Undifferentiated recurrence: Smear or culture positivity at 2 months treatment (yes)

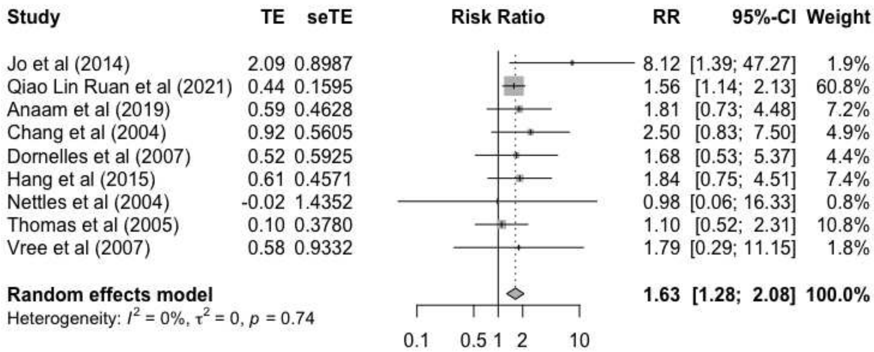


Figure S9 Forest plot Undifferentiated recurrence: Previous TB episode (yes)

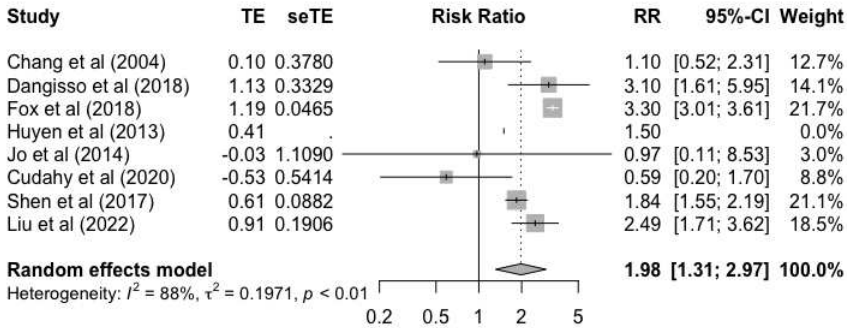


Figure S10 Forest plot Undifferentiated recurrence: Multidrug resistance (vs no resistance)

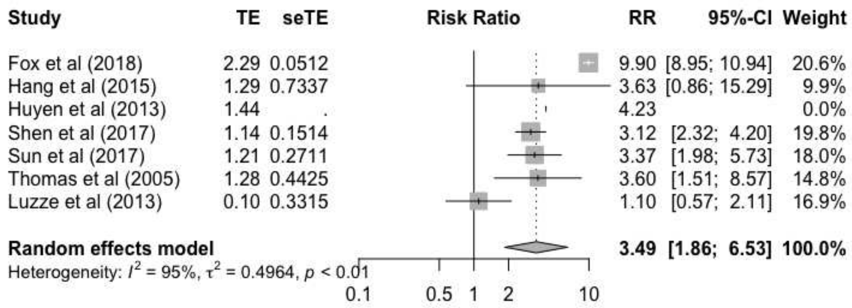


Figure S11 Forest plot Undifferentiated recurrence: Any drug resistance (yes)

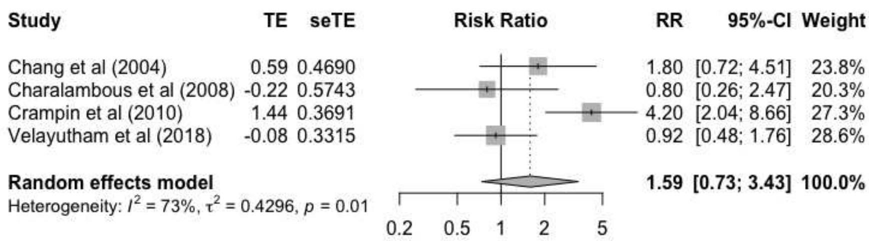


Figure S12 Forest plot Undifferentiated recurrence: Advanced radiographical extent of TB disease

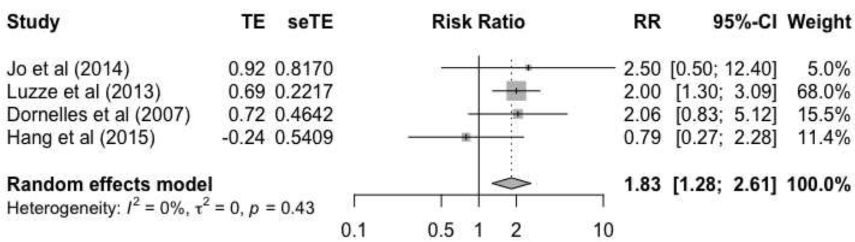


Figure S13 Forest plot Undifferentiated recurrence: Rifampicin less than 6 months vs 6 months

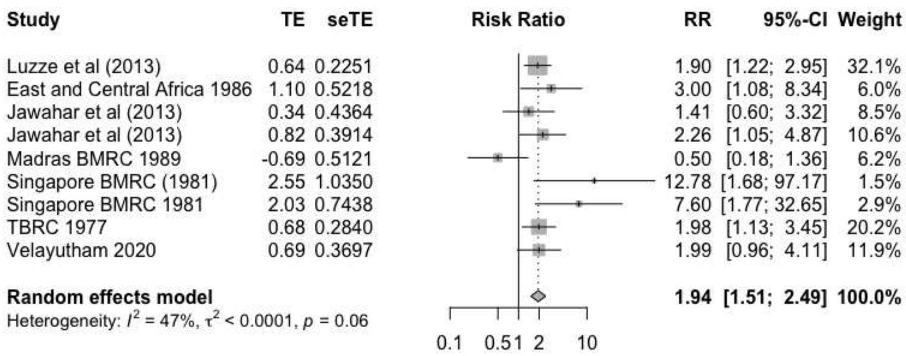


Figure S14 Forest plot Undifferentiated recurrence: Rifampicin more than 6 months vs 6 months

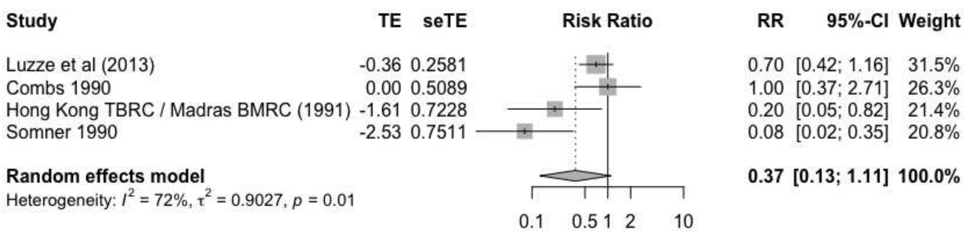


Figure S15 Forest plot Undifferentiated recurrence: Fixed-dose combination TB drug (yes)

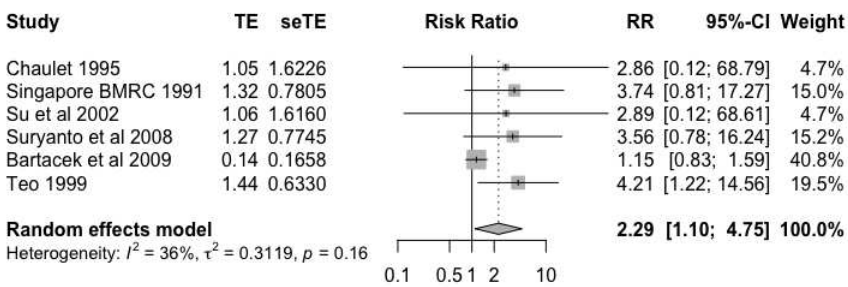


Figure S16 Forest plot Undifferentiated recurrence: Low TB treatment adherence (yes)

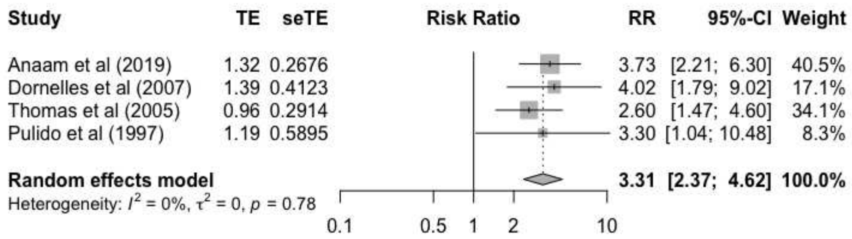


Figure S7 Forest plot Undifferentiated recurrence: HIV infection (yes)

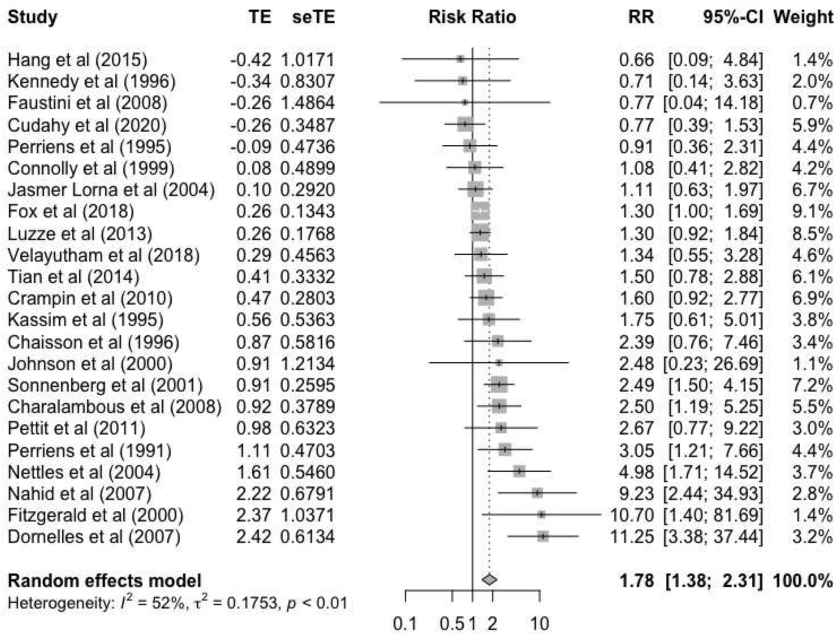


Figure S18 Forest plot Undifferentiated recurrence: Body mass index <18.5 (yes)

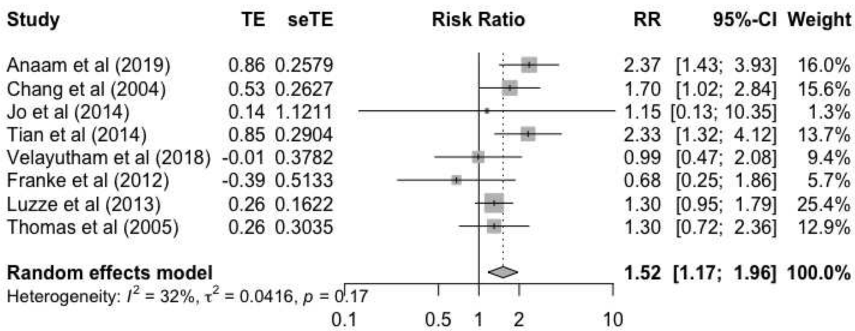


Figure S19 Forest plot Undifferentiated recurrence: Chronic lung disease (yes)

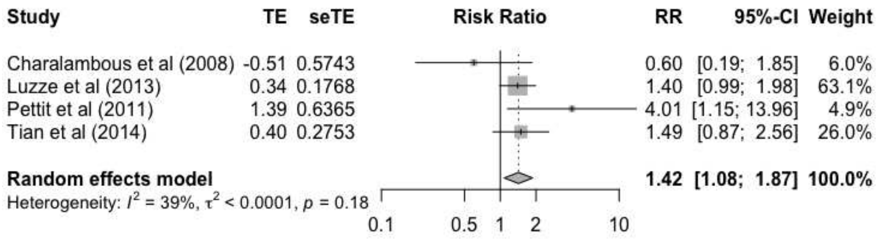


Figure S20 Forest plot Undifferentiated recurrence: Diabetes mellitus (yes)

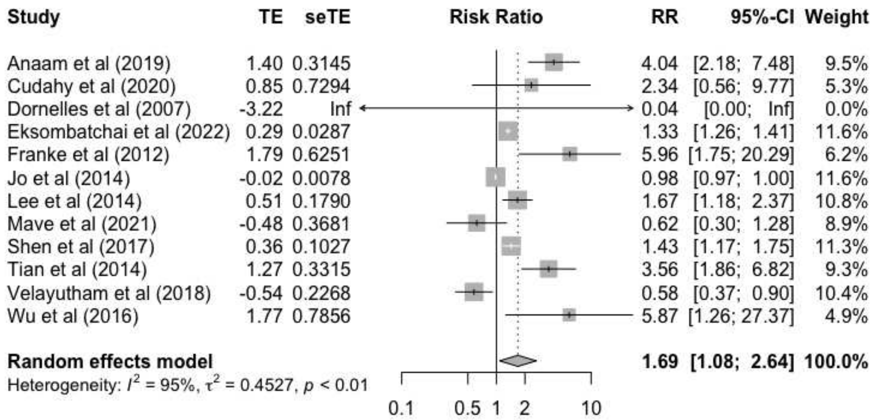


Figure S21 Forest plot Relapses Male sex (yes)

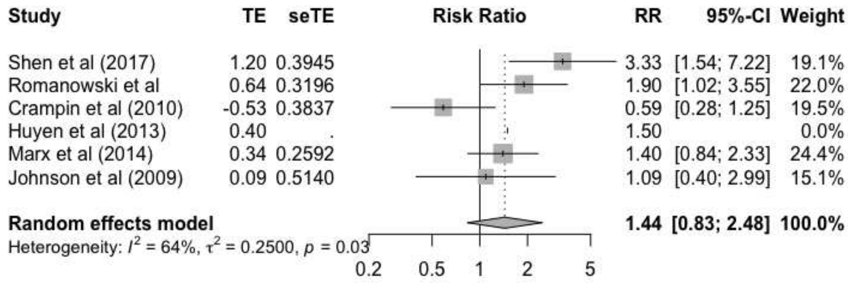


Figure S22 Forest plot Relapses HIV infection (yes)

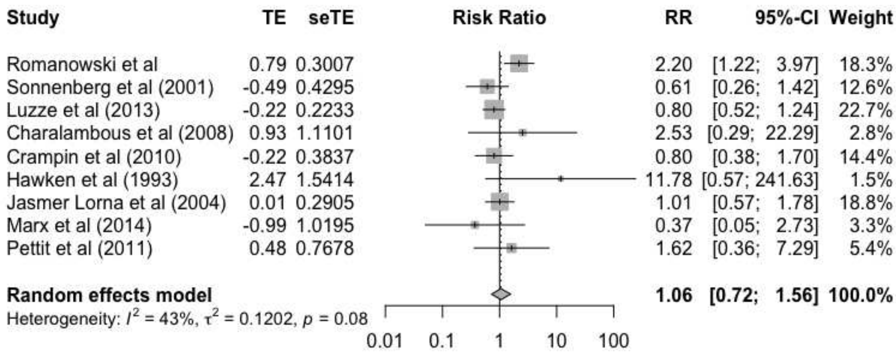


Figure S23 Forest plot Relapses Rifampicin less than six months

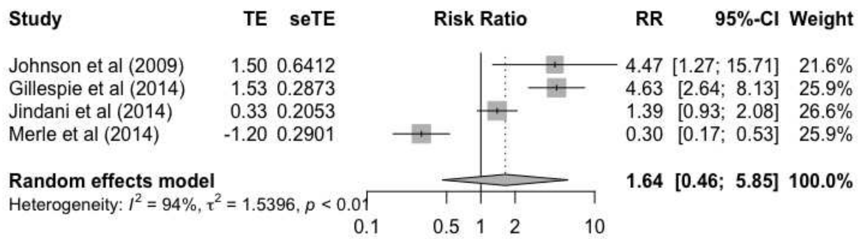


Figure S24 Forest plot Reinfections HIV infection (yes)

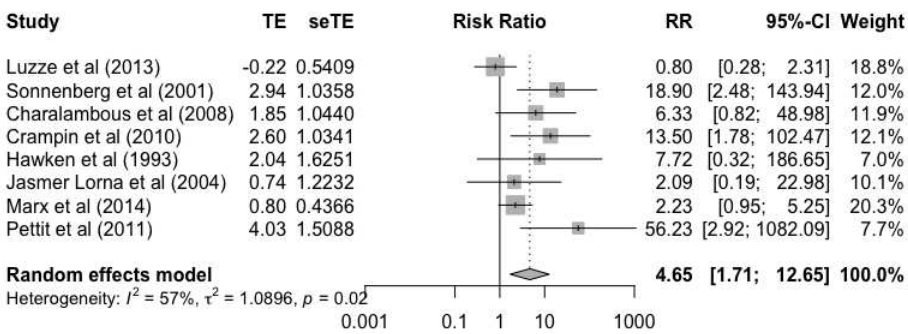
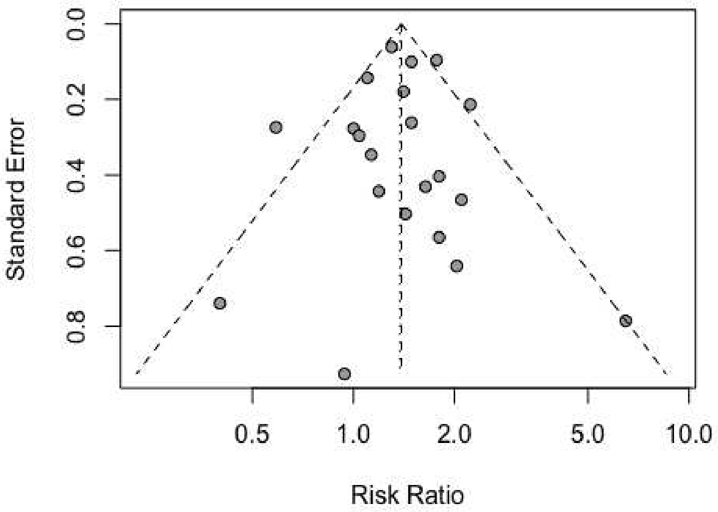
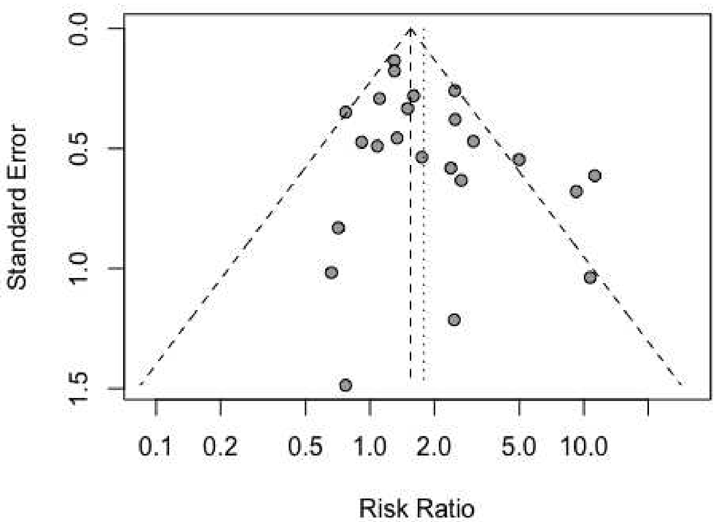


Figure S25 Funnel plot Undifferentiated recurrence: Male sex (yes)



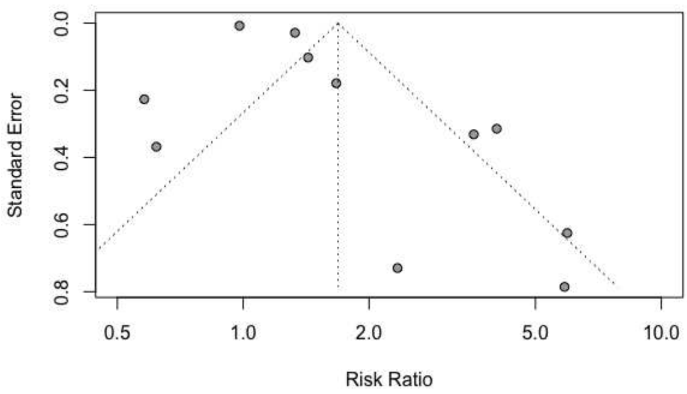
Egger's test: p=0.06830.8992

Figure S26 Funnel plot Undifferentiated recurrence: HIV infection (yes)



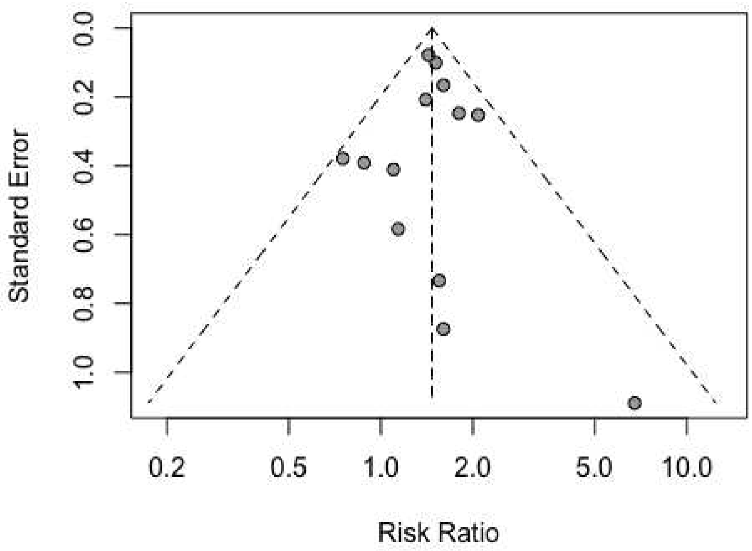
Egger's test: p=0.0683

Figure S27 Funnel plot Undifferentiated recurrence: Diabetes mellitus (yes)



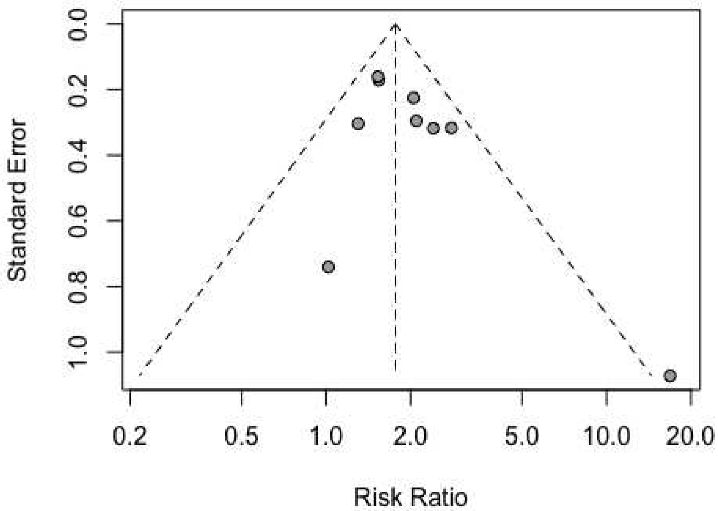
Egger's test: p= 0.9229

Figure S28 Funnel plot Undifferentiated recurrence: Cavitary disease (yes)



Egger's test: p= 0.9229

Figure S29 Funnel plot Undifferentiated recurrence: Smoking (yes)



Egger's test: p= 0.0843

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Definition of recurrent TB does not match WHO definition

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