

Appendix 1. MEDLINE search strategy

- #1 randomized controlled trial [pt]
- #2 controlled clinical trial [pt]
- #3 randomized [tiab]
- #4 placebo [tiab]
- #5 clinical trials as topic [mesh: noexp]
- #6 randomly [tiab]
- #7 trial [ti]
- #8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
- #9 animals [mh] NOT humans [mh]
- #10 #8 NOT #9
- #11 TNF- α antagonist OR etanercept OR adalimumab OR infliximab OR golimumab
OR certolizumab
- #12 #10 AND #11

Appendix 2. Screening for tuberculosis (TB) and incidence of TB in the included studies

First Author	Screening for TB (methods)	Treatment group(n=7912)		Control group(n=3967)	
		Events	No. of patients	Events	No. of patients
Ho-Youn KIM ¹⁶	Yes (not mentioned)	1	65	0	63
Rutgeerts ¹⁷	Yes (chest radiograph and PPD)	1	243	0	121
Baranauskaite ¹⁸	Yes (not mentioned)	1	57	0	58
Barker ¹⁹	Yes (not mentioned)	1	653	0	215
Braun ²⁰	Yes (not mentioned)	1	35	0	35
Breedveld ²¹	Yes (PPD)	1	542	0	257
Chen ²²	Yes (chest radiograph)	1	35	0	12
Colombel ²³	Yes (chest radiograph and PPD)	1	338	0	170
Couriel ²⁴	Yes (chest radiograph)	1	29	2	28
Judson ²⁵	Yes (not mentioned)	1	55	0	58
Kavanaugh ²⁶	Yes (PPD)	1	515	0	517
Kennedy ²⁷	Yes (QuantiFeron)	1	85	0	44
Keystone ²⁸	Yes (not mentioned)	1	419	0	200
Keystone ²⁹	Yes (chest radiograph and PPD)	5	783	0	199
Maini ³⁰	Yes (not mentioned)	1	340	0	88
Nam ³¹	Yes (not mentioned)	1	55	0	57
Reich ³²	Yes (chest X-ray and PPD)	1	117	0	59
Schiff ³³	No	2	328	0	318
Schiff ³⁴	Yes (chest X-ray and PPD)	2	165	0	110
Sieper ³⁵	Yes (chest X-ray and PPD)	1	106	0	52
Smolen ³⁶	Yes (chest X-ray and PPD)	5	492	0	127

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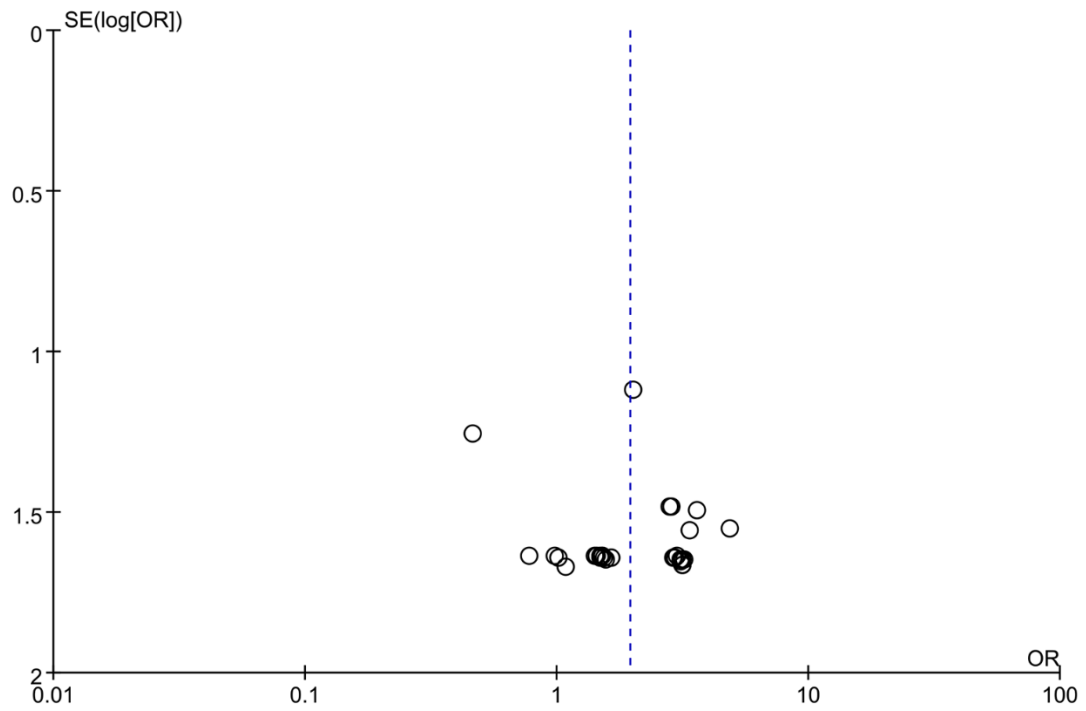
First Author	Screening for TB (methods)	Treatment group(n=7912)		Control group(n=3967)	
		Events	No. of patients	Events	No. of patients
St Clair ³⁷	Yes (not mentioned)	4	751	0	298
Suzuki ³⁸	Yes (chest X-ray and PPD)	1	177	0	96
Tam ³⁹	No	1	20	0	20
Van Den Bosch ⁴⁰	Yes (chest radiograph)	1	20	0	20
van der Heijde ⁴¹	Yes (not mentioned)	1	454	0	228
van Vollenhoven ⁴²	Yes (not mentioned)	1	79	0	76
Wenzel ⁴³	No	1	233	0	78
Westhovens ⁴⁴	Yes (chest radiograph and PPD)	4	721	1	363

PPD: Purified Protein Derivative.

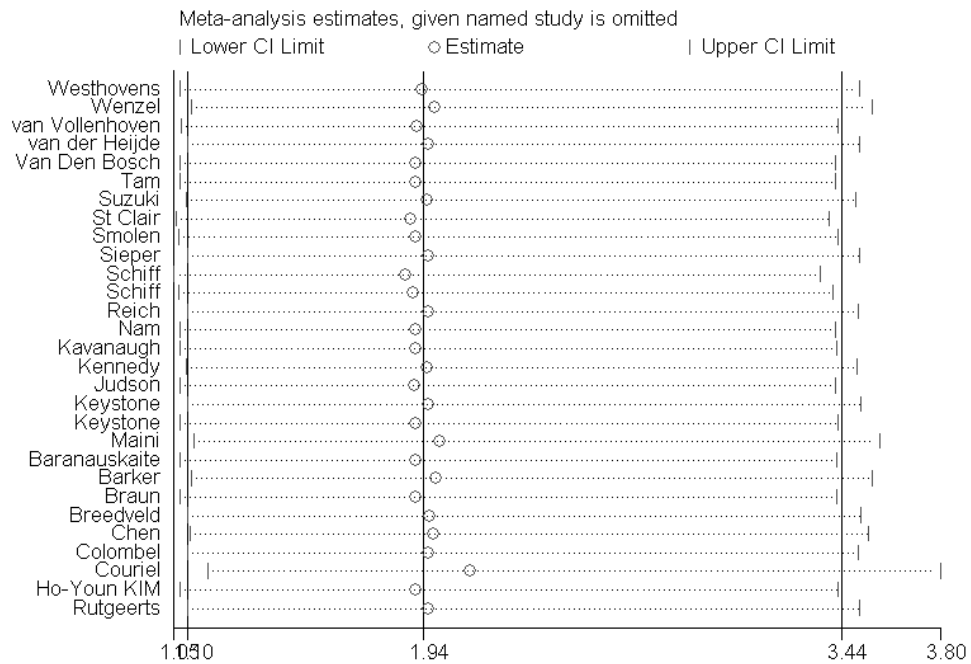
Appendix 3. Risk of bias summary: review authors' evaluation about each risk of bias item for each included study

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Baranauskaite 2012	?	?	+	+	+	+	+
Barker 2011	+	+	+	+	+	+	+
Braun 2002	+	+	+	+	+	+	+
Breedveld 2006	?	?	+	+	+	+	+
Chen 2009	?	?	+	+	+	+	+
Colombel 2010	?	?	+	+	+	+	+
Couriel 2009	?	?	+	+	+	+	+
Ho-Youn KIM 2007	?	?	+	+	+	+	+
Judson 2014	+	+	+	+	+	+	+
Kavanaugh 2013	+	+	+	+	+	+	+
Kennedy 2014	?	?	+	+	+	+	+
Keystone 2004	?	?	+	+	+	+	+
Keystone 2008	?	?	+	+	+	+	+
Maini 1999	?	?	+	+	+	+	+
Nam 2014	+	+	+	+	+	+	+
Reich 2012	+	+	+	+	+	+	+
Rutgeerts 2005	+	+	+	+	+	+	+
Schiff 2008	?	?	+	+	+	+	+
Schiff 2014	?	?	+	+	+	+	+
Sieper 2014	+	+	+	+	+	+	+
Smolen 2009	?	?	+	+	+	+	+
St Clair 2004	+	+	+	+	+	+	+
Suzuki 2014	+	?	+	+	+	+	+
Tam 2012	+	+	+	+	+	+	+
Van Den Bosch 2002	+	+	+	+	+	+	+
van der Heijde 2007	+	+	+	+	+	+	+
van Vollenhoven 2011	+	?	+	+	+	+	+
Wenzel 2009	+	+	+	+	+	+	+
Westhovens 2006	?	?	+	+	+	+	+

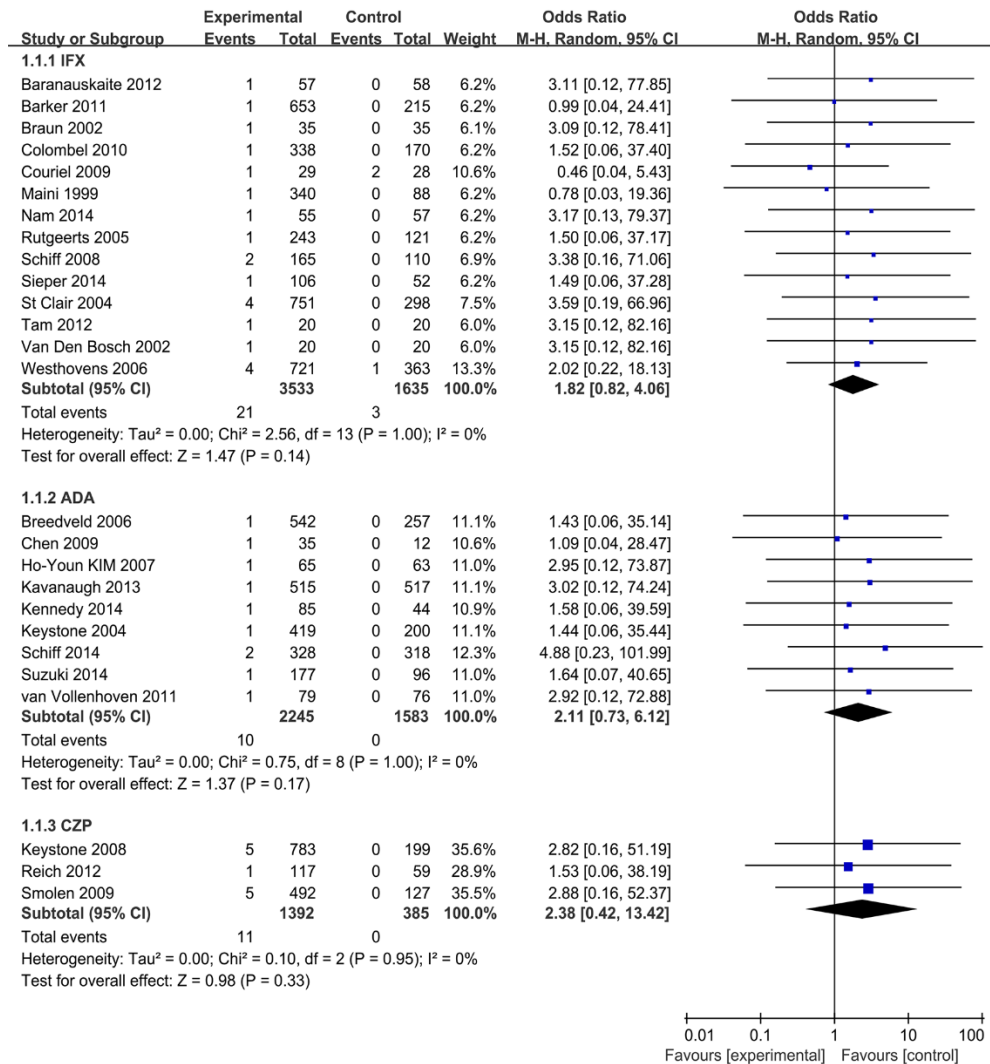
Appendix 4. Funnel plot for RCTs included in this meta-analysis



Appendix 5. Sensitivity analysis of the influence of each individual study on the pooled ORs by omitting individual studies



Appendix 6. Subgroup analysis of TB risk of IFX, ADA and CZP



Appendix 7. GRADE assessment of tuberculosis risk associated with TNF- α antagonists

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TNF- α antagonists	Control	Relative (95% CI)	Absolute		
Outcome: tuberculosis risk												
29	Randomized trials	serious	no serious inconsistency	no serious indirectness	serious	none	45/7912 (0.57%)	3/3967 (0.08%)	OR 1.94 (1.10, 3.44)	1 more per 1000 (from 0 more to 2 more)	⊕⊕○○ LOW	IMPORTANT