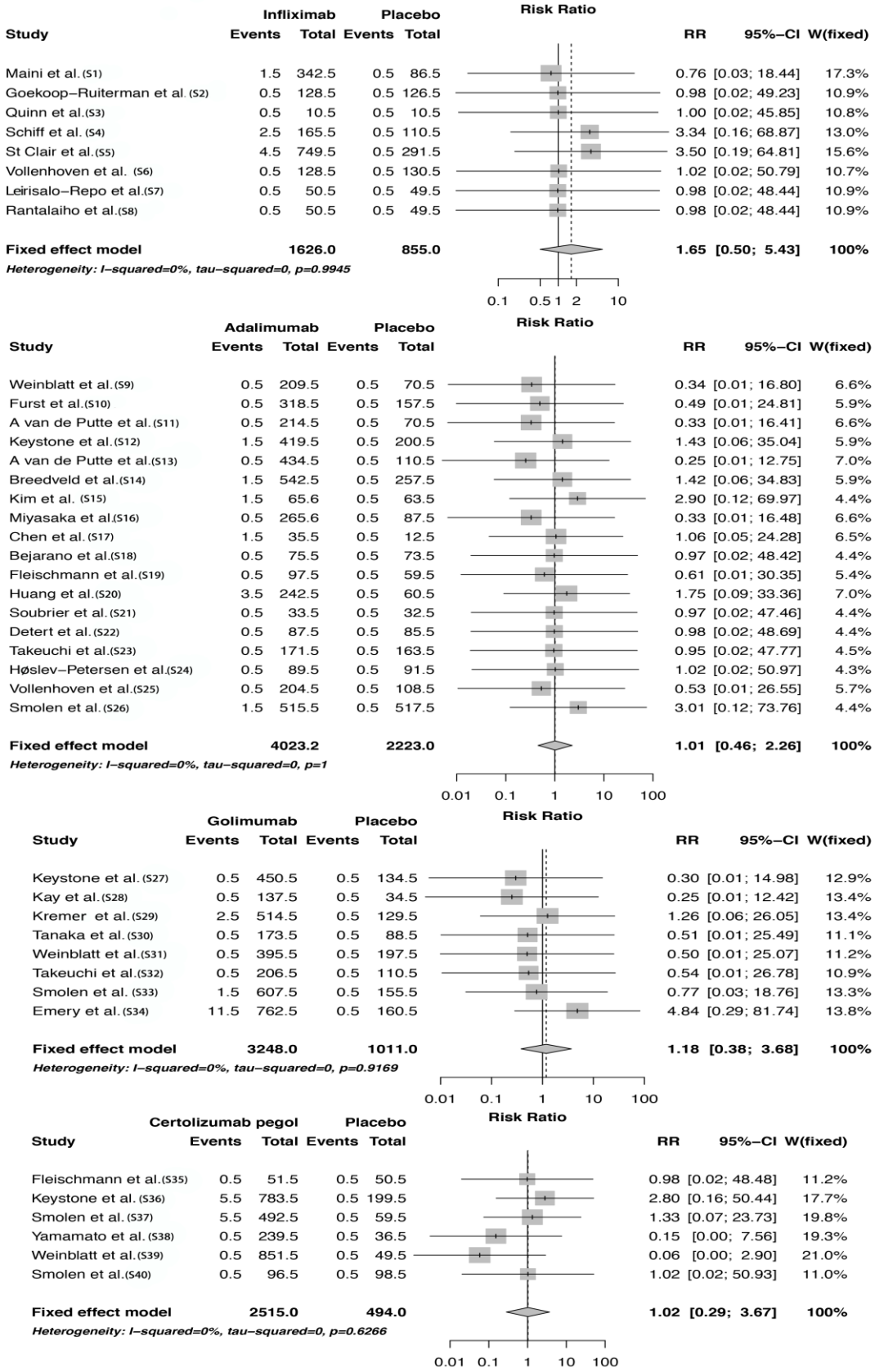
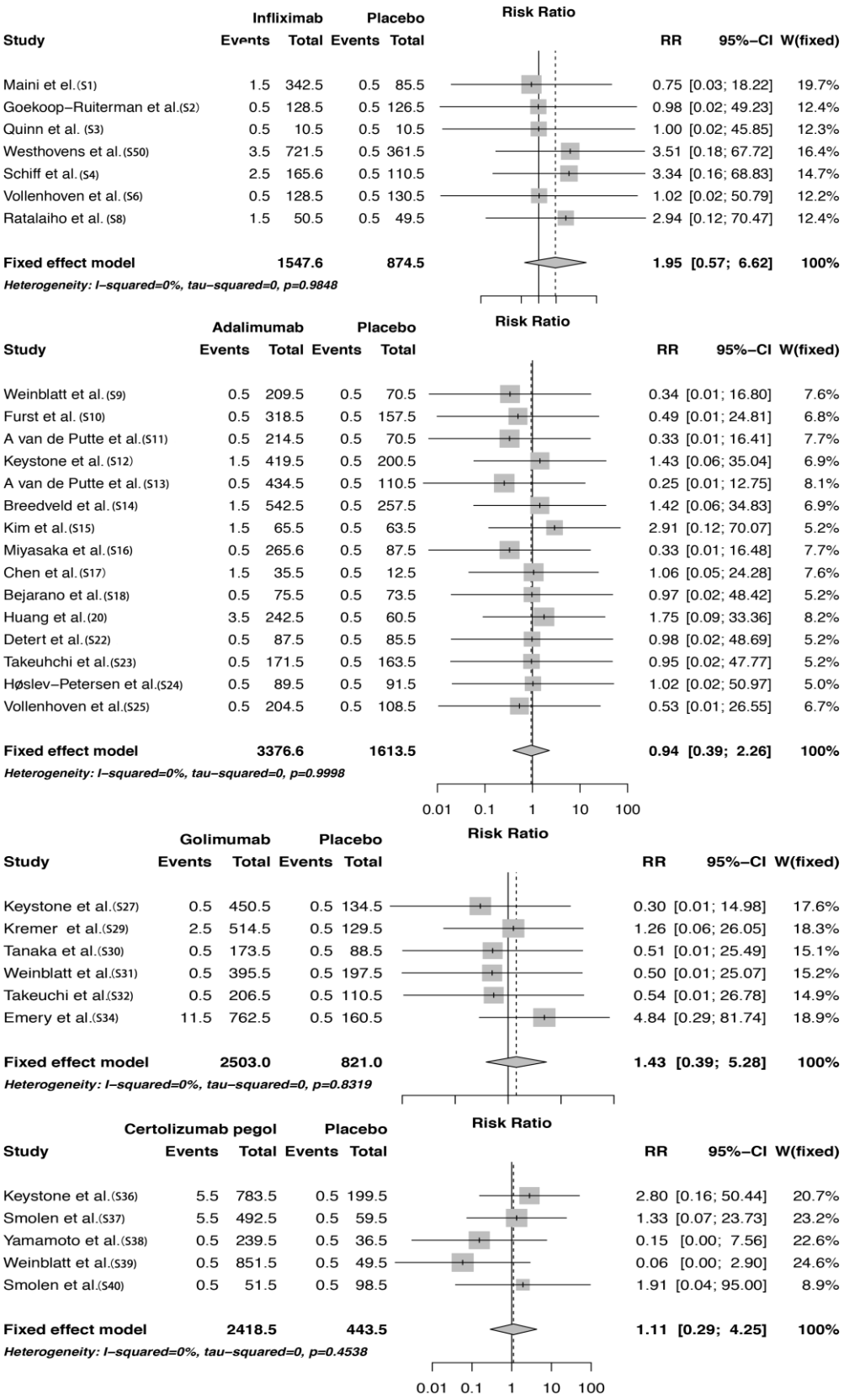
Online supplement to: The Risk of Tuberculosis in Patients with Rheumatoid Arthritis Treated with Tumor Necrosis Factor-α Antagonist: A Metaanalysis of Both Randomized Controlled Trials and Registry/Cohort Studies. *The Journal of Rheumatology.* doi:10.3899/jrheum.150057

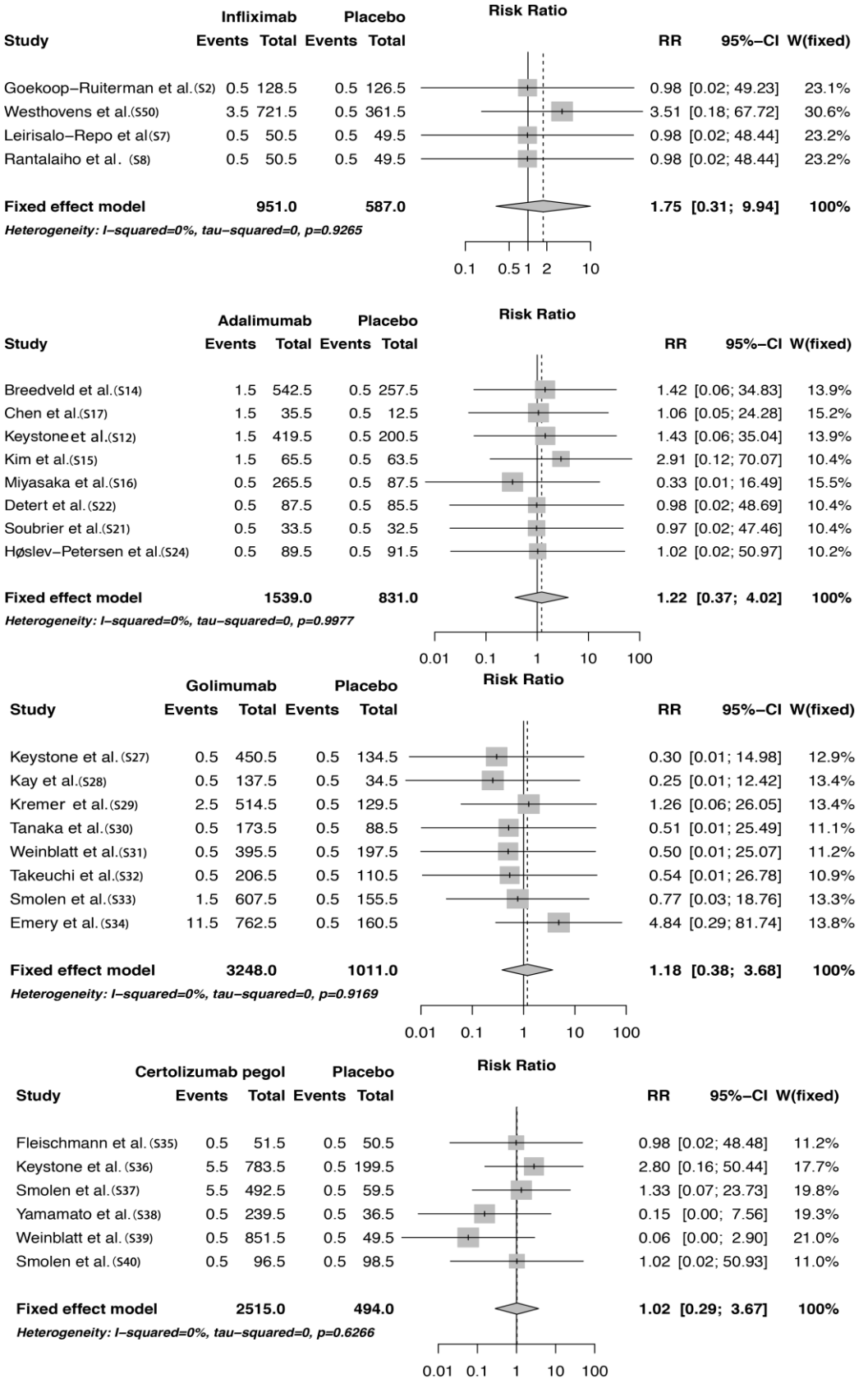
ONLINE SUPPLEMENTARY DATA



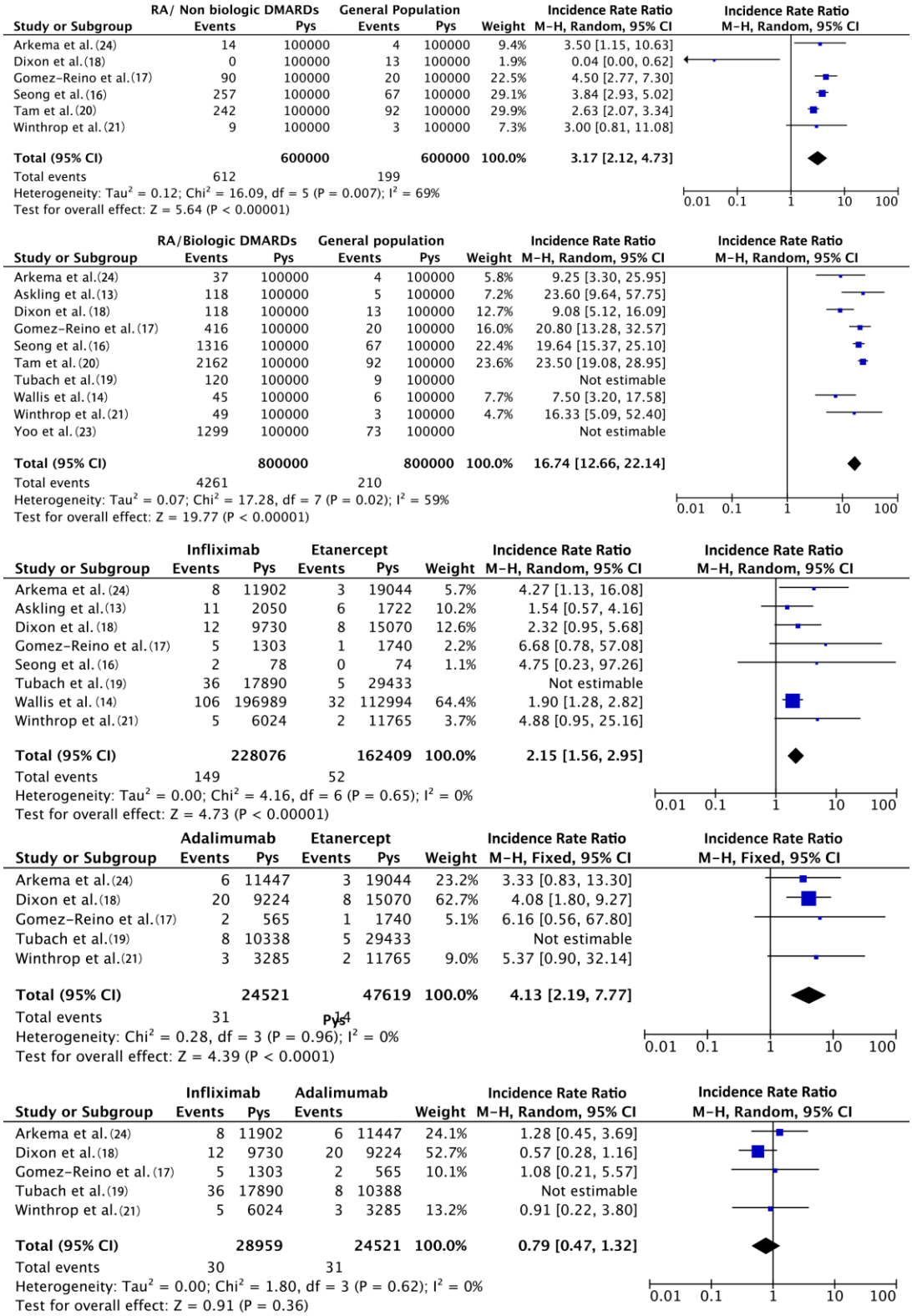
Supplementary Figure 1. Forest plot of the TB risk ratio of each TNF antagonist vs the control in RCTs.



Supplementary Figure 2. Forest plot of TB risk ratio of each TNF antagonist versus placebo in RCTs, excluding the possibly biased articles.



Supplementary Figure 3. Forest plot of the TB risk ratio of each TNF antagonist versus the control in RCTs, excluding studies without latent tuberculosis screening and prophylaxis.



Supplementary Figure 4. Forest plot of the TB risk ratio of 1) RA/Non biologic DMARDs vs. General population; 2) RA/Biologic DMARDs vs. General population; 3) Infliximab vs. Etanercept; 4) Adalimumab vs. Etanercept; 5) Infliximab vs. Adalimumab, excluding the 3 articles with diseases other than RA. RA: rheumatoid arthritis; Pys: patient years; DMARDs: disease modifying anti-rheumatic drugs.

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Supplementary Table 1. Check list for quality assessment and scoring of nonrandomized studies

Check list
Selection
1. Assignment for TNF-alpha antagonists treatment: (if reported, one star)
2.The exposed cohorts were representative in comparison with the general RA population: (if yes, one star)
3. PPD test done at the start of the study :(if yes, one star)
Comparability
4. Group comparable for 1,2,3 (if yes, two stars, one star was assigned if one group differed or was not reported, no star was assigned if two group differed)
5. Group comparable for 4,5 （5 is only compared among TNF alpha antagonists exposed cohorts）(if yes, two stars, one star was assigned if one group differed or was not reported, no star was assigned if two group differed)
Outcome assessment
6. Clearly defined TB cases:(if yes, one star)
7. Adequacy of follow-up: (if follow up>90%, one star)
Comparability variables: 1=age; 2=gender; 3=Diabetes; 4=PPD test positivity; 5=Prophylaxis.

Supplementary Table 2. Characteristics of the randomized controlled trials

Author	Intervention（Placebo）	patient	TB case	Follow up(wks)
Weinblatt (S9)	ADA 20mg(eow)+MTX ADA 40mg(eow)+MTX ADA 80mg(eow)+MTX Pla+MTX	69 67 73 70	0	24
Furst (S10)	ADA 40mg(eow) Pla	318 157	0	24
A van de Putte (S11)	ADA 20mg(qw) ADA 40mg(qw) ADA 80mg(qw) Pla	72 70 72 70	0	12
Keystone (S12)	ADA 20mg(qw)+MTX ADA 40mg(eow)+MTX Pla+MTX	212 207 200	0 1 0	52
A van de Putte (S13)	ADA 20mg(eow) ADA 40mg(eow) ADA 20mg(qw) ADA 40mg(qw) Pla	106 113 112 103 110	0	26
Breedveld (S14)	ADA 40mg(eow) ADA 40mg(eow)+MTX Pla+MTX	274 268 257	0 1 0	104

Kim.(S15)	ADA 40mg(eow)+MTX Pla+MTX	65 63	1 0	24
Miyasaka (S16)	ADA 20mg(eow) ADA 40mg(eow) ADA 80mg(eow) Pla	87 91 87 87	0	24
Chen (S17)	ADA 40mg(eow)+MTX Pla+MTX	35 12	1 0	23
Bejarano (S18)	ADA(eow)+MTX Pla+MTX	75 73	0	56
Fleischmann (S19)	ADA 40mg(eow)+tofacitinib Pla	97 59	0	24
Huang (S20)	ADA 40mg(eow)+MTX ADA 80 mg(eow)+MTX Pla+MTX	121 121 60	3	24
Soubrier (S21)	ADA 40mg(eow)+MTX MTX	33 32	0	52
Detert (S22)	ADA 40mg(eow)+MTX Pla+MTX	87 85	0	48
Takeuchi (S23)	ADA 40mg(eow)+MTX MTX	171 163	0	26
HØslev-Petersen (S24)	ADA 40mg(eow)+MTX Pla+MTX	89 91	0	52
Vollenhoven (S25)	ADA 40mg(eow)+MTX Pla+MTX	204 108	0	26
Smolen(S26)	ADA 40mg(eow)+MTX Pla+MTX	515 517	1 0	78
Moreland (S47)	ETA 10mg(biw) ETA 25mg(biw) Pla	76 78 80	0	26
Genovese (S43)	ETA 10mg(biw) ETA 25mg(biw) MTX	166 177 169	0	104
Keystone (S49)	ETA 25mg(biw) ETA 50mg(qw) Pla	153 214 53	0	16
Van der Heijide (S48)	ETA 25mg(biw) ETA 25mg(biw)+MTX Pla+MTX	223 231 228	0	104
Combe (S41)	ETA 25mg(biw)	103	0	24

	ETA 25mg(biw)+Sulfasalazine	101		
	Pla+Sulfasalazine	50		
Emery (S42)	ETA 50mg(qw)+MTX	274	0	52
	Pla+MTX	268		
Kim (S45)	ETA 25mg(biw)+MTX	197	0	16
	DMARD+MTX	103		
Moreland (S47)	ETA 50mg(qw)+MTX	244	0	104
	MTX+Sulfasalazine	132		
Iannone (S44)	ETA 50mg(qw)	13	0	54
	ETA 50mg(qw)+MTX	7		
	MTX	9		
Maini (S1)	INF 3mg/kg(q4w)	86	1	30
	INF 3mg/kg(q8w)	89	0	
	INF 10mg/kg(q4w)	80	0	
	INF 10mg/kg(q8w)	87	0	
	Pla	86	0	
Goekoop-Ruiterman (S2)	INF 3mg/kg(q8w)+DMARDs	128	0	52
	DMARDs	126		
St.Clair (S5)	INF 3mg/kg(q8w)	372	3	54
	INF 6mg/kg(q8w)	377	1	
	Pla+MTX	291	0	
Quinn (S3)	INF 3mg/kg(q8w)+MTX	10	0	54
	PLa+MTX	10		
Westhovens (S50)	INF 3mg/kg(q8w)+MTX	360	0	22
	INF 10mg/kg(q8w)+MTX	361	3	
	Pla+MTX	361	0	
Schiff (S4)	INF 3mg/kg(q8w)+MTX	165	2	26
	Pla+MTX	110	0	
Vollenhoven (S6)	INF 3mg/kg(q8w)+MTX	128	0	54
	Sulfasalazine+MTX	130		
Leirisalo-Repo (S7)	INF 3mg/kg(q8w)+FIN-RACo	50	0	104
	Pla+FIN-RACo	49		
Rantalaiho (S8)	INF 3mg/kg+FIN-RACo	50	0	260
	Pla+FIN-RACo	49		
Kay (S28)	GOL 50mg(q4w)+MTX	37	0	52
	GOL 50mg(q2w)+MTX	32		
	GOL 100mg(q4w)+MTX	33		
	GOL 100mg(q2w)+MTX	35		
	Pla+MTX	34		

Keystone (S27)	GOL 50mg(q4w)+MTX	212	0	24
	GOL 100mg(q4w)+MTX	105		
	GOL 100mg(q4w)+Pla	133		
	Pla+MTX	134		
Kremer (S29)	GOL 2mg/kg(q12w)	257	0	48
	GOL 4mg/kg(q12w))	257	2	
	Pla+MTX	129		
Tanaka (S30)	GOL 50mg(q4w)+MTX	86	0	24
	GOL 100mg(q4w)+MTX	87		
	Pla+MTX	88		
Weinblatt (S31)	GOL 2mg/kg(q8w)+MTX	395	0	24
	Pla+MTX	197		
Takeuchi (S32)	GOL 50mg(q4w)	102	0	16
	GOL 100mg(q4w)	104		
	Pla	110		
Smolen (S33)	GOL 50mg(q4w)	279	0	160
	GOL 100mg(q4w)	328	1	
	Pla	155		
Emery (S34)	GOL 50mg(q4w)+MTX	293	4	104
	GOL 100mg(q4w)+MTX	312	5	
	GOL 100mg(q4w)+Pla	157	2	
	Pla+MTX	160		
Keystone (S36)	CIMZIA 200mg(q2w)+MTX	392	2	52
	CIMZIA 400mg(q2w)+MTX	389	3	
	Pla+MTX	199		
Smolen (S37)	CIMZIA 200mg(q2w)+MTX	248	3	24
	CIMZIA 400mg(q2w)+MTX	246	2	
	Pla+MTX	125		
Fleischmann (S35)	CIMZIA 400mg(q4w)+MTX	111	0	24
	Pla+MTX	109		
Weinblatt (S39)	CIMZIA 200mg(q2w)	846	0	12
	Pla	209		
Yamamoto (S38)	CIMZIA 100mg(q2w)+MTX	72	0	24
	CIMZIA 200mg(q2w)+MTX	82		
	CIMZIA 400mg(q2w)+MTX	85		
	Pla+MTX	77		
Smolen (S40)	CIMZIA 200mg(q2w)+DMARDs	96	0	52
	Pla+DMARDs	98		

TB: tuberculosis; INF: infliximab; ADA: adalimumab; ETA: etanercept;GOL: golimumab; CIMZIA: certolizumab pegol; Pla:placebo; MTX: methotrexate; wks: weeks.

Supplementary Table 3. Characteristics of the registry and cohort studies

Author	Country	Local TB IR（per 100000 pys）	TB IR of RA/Non biologic DMARDs （per 100000pys）	TB IR of RA/biologic DMARDs （per 100000pys）			
				Total	INF	ADA	ETA
Asking et al. (24)	Sweden	5	18.5	118	145	N	80
Wallis et al. (14)	USA	5.6	N	44.5	53.8	N	28.3
Sichletidis et al. (15)	Greece	19	N	449	N	N	N
Seong et al. (16)	South Korea	67.2	257.4	2558	2558	N	0
Gomez-Reino et al. (17)	Spain	20	90	172	383	176	114
Favalli et al. (25)	Italy	N	N	126.6	258.6	112.9	38.79
Dixon et al. (18)	Britain	12.3	0	118	123	217	53
Tubach et al. (19)	France	8.7	N	119.6	187.5	215	9.3
Tam et al. (20)	Hong Kong	91.8	241.8	2162	N	N	N
Winthrop et al. (21)	USA	2.8	8.7	49	83	91	17
Atzni et al. (22)	Italy	N	N	126.6	258.6	112.9	38.8
Yoo et al. (23)	South Korea	72.6	N	1298.7	4109.6	0	N
Arkema et al. (24)	Sweden	3.5	14.3	39.4	67.2	52.4	15.7

IR: incidence rate; pys: person years; TB: tuberculosis; RA: rheumatoid arthritis; DMARDs: disease modifying anti-rheumatic drugs; N=data not available.

Supplementary Table 4. The evaluation of bias for randomized controlled trials

Study	Sequence Generation	Allocation Concealment	Blinding of participant and personnel	Incomplete Outcome Data	Blinding of outcome assessment	Selective outcome reporting	Other sources of bias*
Adalimumab							
Weinblatt (S9)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Furst (S10)	Unclear	Unclear	Low	Low	Unclear	Low	Low
A van de Putte (S11)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Keystone (S12)	Unclear	Unclear	Low	Low	Unclear	Low	Low
A van de Putte (S13)	High	Unclear	Low	Low	Unclear	Low	Low
Breedveld (S14)	Unclear	Unclear	Low	Low	Low	Low	Low
Kim (S15)	Unclear	Unclear	Low	Low	Unclear	Low	Unclear
Miyasaka (S16)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Chen (S17)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Bejarano (S18)	Low	Low	Low	Low	Unclear	Low	Low
Fleischman (S19)	Unclear	Unclear	Low	Low	Unclear	Low	Unclear
Huang (S20)	Unclear	Unclear	Low	Low	Unclear	Low	Unclear
Soubrier (S21)	Unclear	Unclear	High	Low	Unclear	Low	Low
Detert (S22)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Takeuchi (S23)	Unclear	Unclear	Low	Low	Low	Low	Low
Hørslev-Petersen (S24)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Vollenhoven (S25)	Low	Low	Low	Low	Unclear	Low	Low
Smolen (S26)	Low	Low	Low	Low	Unclear	Unclear	Low
Etanercept							
Moreland (S47)	Unclear	Low	Low	Low	Unclear	Low	Low
Genovese (S43)	Unclear	Unclear	Low	Low	Low	Low	Low
Keystone	Unclear	Unclear	Low	Low	Unclear	Low	Low

(S49)							
Van der Heijide(S48)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Combe(S41)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Emery (S42)	Low	Low	Low	Low	Unclear	Low	Low
Kim (S45)	Low	Low	High	Low	Unclear	Unclear	High
Klareskog (S46)	Low	Low	Low	Low	Unclear	Low	Low
Iannone (S44)	High	Low	High	Low	Unclear	Low	High
Infliximab							
Maini (S1)	Low	Low	Low	Low	Unclear	Low	Low
Goekoop-Ruiterman(S2)	Low	Low	Unclear	Low	Low	Low	Unclear
St.Clair (S5)	Low	Unclear	Unclear	Low	Unclear	Low	High
Quinn (S3)	Unclear	Unclear	Low	Unclear	Low	Low	Low
Westhovens (S50)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Schiff (S4)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Vollenhoven (S6)	Low	Unclear	Low	Low	Unclear	Low	Low
Leirisalo-Repo (S7)	Low	Unclear	High	Low	Unclear	Low	Low
Rantalaiho (S8)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Golimumab							
Kay (S28)	Unclear	Unclear	Low	Low	Low	Low	High
Keystone (S27)	Low	Low	Low	Unclear	Unclear	Low	Low
Kremer (S29)	Unclear	Unclear	Low	Low	Low	Low	Low
Tanaka (S30)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Weinblatt (S31)	Low	Low	Low	Low	Unclear	Low	Unclear
Takeuchi (S32)	Unclear	Unclear	Low	Low	Unclear	Low	Low
Smolen (S33)	Unclear	Unclear	Low	Low	Low	Low	High
Emery (S34)	Low	Low	Low	Low	Unclear	Low	Low
Certolizumab Pegol							
Keystone (S36)	Unclear	Unclear	Low	Low	Unclear	Low	Low

Smolen (S37)	Unclear	Unclear	Low	Low	Unclear	Low	Unclear
Fleischmann (S35)	Low	Low	Low	Low	Unclear	Low	High
Weinblatt (S39)	Low	Low	Low	Low	Unclear	Low	Low
Yamamoto (S38)	Low	Low	Low	Low	Unclear	Low	Low
Smolen (S40)	Low	Unclear	High	Low	Unclear	Low	Low

* In the dimension of other sources of bias, high risk is graded when the sponsors of the research evolved in the data collection of adverse events.

Supplementary Table 5. Percentage of the studies with LTBI screening and prophylaxis.

Drugs	LTBI patients included studies		LTBI patients excluded studies (%)	Unclear(%)
	Prophylaxis(%)	Non-prophylaxis(%)		
Infliximab	1 (11.1%)	5（55.6%）	2（22.2%）	1（11.1%）
Etanercept	1 (11.1%)	5（55.6%）	2（22.2%）	1（11.1%）
Adalimumab	5 (27.8%)	10 (55.6%)	2 (11.1%)	1 (5.6%)
Golimumab	7 (87.5%)	0 (0%)	1 (12.5%)	0 (0%)
Certolizumab Pegol	2 (33.3%)	0 (0%)	4 (66.7%)	0 (0%)

LTBI: latent tuberculosis infection.

Supplementary Table 6. Reported adjusted incidence rate/hazard ratios from non-RCTs

Authors	Year	RA/Biologic DMARDs vs. General population	RA /non Biologic DMARDs vs. General population	INF/ETA	ADA/ETA
Askling (13)	2005	N	N	N	N
Wallis (14)	2004	N	N	N	N
Sichletidis (15)	2006	N	N	N	N
Seong (16)	2007	30.1	8.9	N	N
Gomez-Reino (17)	2007	N	N	N	N
Tubach (19)	2009	13.41	N	10.3	16.28
Dixon (18)	2009	N	N	3.1	4.2
Tam (20)	2010	34.92	2.35	N	N
Winthrop (21)	2012	N	N	N	N
Atzni (22)	2012	N	N	N	N
Yoo (23)	2014	N	N	N	N
Arkema (24)	2014	N	N	2 (Hazard ratio)	2.3 (Hazard ratio)

RA: rheumatoid arthritis; DMARDs: disease modifying anti-rheumatic drugs; INF: infliximab; ADA: adalimumab; ETA: etanercept.

References for 50 randomized controlled trials

S1. Maini R, St Clair EW, Breedveld F, Furst D, Kalden J, Weisman M, et al. Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. ATTRACT Study Group. Lancet 1999;354:1932-9.

S2. Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, van Zeben D, Kerstens PJ, Hazes JM, et al. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. Arthritis Rheum 2005;52:3381-90.

S3. Quinn MA, Conaghan PG, O'Connor PJ, Karim Z, Greenstein A, Brown A, et al. Very early treatment with infliximab in addition to methotrexate in early, poor-prognosis rheumatoid arthritis reduces magnetic resonance imaging evidence of synovitis and damage, with sustained benefit after infliximab withdrawal: results from a twelve-month randomized, double-blind, placebo-controlled trial. Arthritis Rheum 2005;52:27-35.

S4. Schiff M, Keiserman M, Codding C, Songcharoen S, Berman A, Nayiager S, et al. Efficacy and safety of abatacept or infliximab vs placebo in ATTEST: a phase III, multi-centre, randomised, double-blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate. Ann Rheum Dis 2008;67:1096-103.

S5. St Clair EW, van der Heijde DM, Smolen JS, Maini RN, Bathon JM, Emery P, et al. Combination of infliximab and methotrexate therapy for early rheumatoid arthritis: a randomized, controlled trial. Arthritis Rheum 2004;50:3432-43.

S6. Vollenhoven RF, Ernestam S, Geborek P, Petersson IF, Coster L, Waltbrand E, et al. Addition of infliximab compared with addition of sulfasalazine and hydroxychloroquine to methotrexate in patients with early rheumatoid arthritis (Swefot trial): 1-year results of a randomised trial. Lancet 2009;374:459-66.

S7. Leirisalo-Repo M, Kautiainen H, Laasonen L, Korpela M, Kauppi MJ, Kaipiainen-Seppanen O, et al. Infliximab for 6 months added on combination therapy in early rheumatoid arthritis: 2-year results from an investigator-initiated, randomised, double-blind, placebo-controlled study (the NEO-RACo Study). Ann Rheum Dis 2013;72:851-7.

S8. Rantalaiho V, Kautiainen H, Korpela M, Hannonen P, Kaipiainen-Seppanen O, Mottonen T, et al. Targeted treatment with a combination of traditional DMARDs produces excellent clinical and radiographic long-term outcomes in early rheumatoid arthritis regardless of initial infliximab. The 5-year follow-up results of a randomised clinical trial, the NEO-RACo trial. Ann Rheum Dis 2014;73:1954-61.

S9. Weinblatt ME, Keystone EC, Furst DE, Moreland LW, Weisman MH, Birbara CA, et al. Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: the ARMADA trial. Arthritis Rheum 2003;48:35-45.

S10. Furst DE, Schiff MH, Fleischmann RM, Strand V, Birbara CA, Compagnone D, et al. Adalimumab, a fully human anti tumor necrosis factor-alpha monoclonal antibody, and concomitant standard antirheumatic therapy for the treatment of rheumatoid arthritis: results of STAR (Safety Trial of Adalimumab in Rheumatoid Arthritis). J Rheumatol 2003;30:2563-71.

S11. A van de Putte LB, Atkins C, Malaise M, Sany J, Russell AS, van Riel PL, et al. Efficacy and safety of adalimumab as monotherapy in patients with rheumatoid arthritis for whom previous disease modifying antirheumatic drug treatment has failed. Ann Rheum Dis 2004;63:508-16.

S12. Keystone EC, Kavanaugh AF, Sharp JT, Tannenbaum H, Hua Y, Teoh LS, et al. Radiographic, clinical, and functional outcomes of treatment with adalimumab(a Human Anti-Tumor Necrosis Factor monoclonal Antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy: A randomized, placebo-controlled, 52-week trial. Arthritis Rheum 2004;50:1400-1411.

S13. A van de Putte LB, Rau R, Breedveld FC, Kalden JR, Malaise MG, M van Riel PLCM, et al. Efficacy and safety of the fully human anti-tumour necrosis factor a monoclonal antibody adalimumab (D2E7) in DMARD refractory patients with rheumatoid arthritis: a 12 week, phase II study. Ann Rheum Dis 2003;62:1168-1177.

S14. Breedveld FC, Weisman MH, Kavanaugh AF, Cohen SB, Pavelka K, van Vollenhoven R, et al. The PREMIER study: A multicenter, randomized, double-blind clinical trial of combination therapy with adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early, aggressive rheumatoid arthritis who had not had previous methotrexate treatment. Arthritis Rheum 2006;54:26-37.

S15. Kim Ho-Youn LS-K, Song Yeong-Wook, Yoo Dae-Hyun, KOH Eun-Mi, Yoo Bin, Luo-Allison. A randomized, double-blind, placebo-controlled, phase III study of the human anti-tumor necrosis factor antibody adalimumab administered as subcutaneous injections in Korean rheumatoid arhritis patients treated with methotrexate. APLAR journal of rheumatology 2007;10:9-16.

S16. Miyasaka N, Investigators CS. Clinical investigation in highly disease-affected rheumatoid arthritis patients in Japan with adalimumab applying standard and general evaluation: the CHANGE study. Mod Rheumatol 2008;18:252-62.

S17. Chen DY, Chou SJ, Hsieh TY, Chen YH, Chen HH, Hsieh CW, et al. Randomized, double-blind, placebo-controlled, comparative study of human anti-TNF antibody adalimumab in combination with methotrexate and methotrexate alone in Taiwanese patients with active rheumatoid arthritis. J Formos Med Assoc 2009;108:310-9.

S18. Bejarano V, Quinn M, Conaghan PG, Reece R, Keenan AM, Walker D, et al. Effect of the early use of the anti-tumor necrosis factor adalimumab on the prevention of job loss in patients with early rheumatoid arthritis. Arthritis Rheum 2008;59:1467-74.

S19. Fleischmann R, Cutolo M, Genovese MC, Lee EB, Kanik KS, Sadis S, et al. Phase IIb dose-ranging study of the oral JAK inhibitor tofacitinib (CP-690,550) or adalimumab monotherapy versus placebo in patients with active rheumatoid arthritis with an inadequate response to disease-modifying antirheumatic drugs. Arthritis Rheum 2012;64:617-29.

S20. Huang F, Zhang FC, Bao CD, Tao Y, Gu JR, Xu JH, et al. [Adalimumab plus methotrexate for the treatment of rheumatoid arthritis: a multi-center randomized, double-blind, placebo-controlled clinical study.]. Zhonghua Nei Ke Za Zhi 2009;48:916-21.

S21. Soubrier M, Puechal X, Sibilia J, Mariette X, Meyer O, Combe B, et al. Evaluation of two strategies (initial methotrexate monotherapy vs its combination with adalimumab) in management of early active rheumatoid arthritis: data from the GUEPARD trial. Rheumatology (Oxford) 2009;48:1429-34.

S22. Detert J, Bastian H, Listing J, Weiss A, Wassenberg S, Liebhaber A, et al. Induction therapy with adalimumab plus methotrexate for 24 weeks followed by methotrexate monotherapy up to week 48 versus methotrexate therapy alone for DMARD-naive patients with early rheumatoid arthritis: HIT HARD, an investigator-initiated study. Ann Rheum Dis 2013;72:844-50.

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