Contents

Supplementary 1. Summary of included comparator arm studies, with additional data column to table 1.

Randomised control trials													
Study	**Design**	**Duration (weeks)**	**No. in study**	**Drug**	**No. on drug**	**Dose**	**Age**	**Female**	**Black**	**White**	**Duration disease**	**Concomitant medications**	**Predicted FVC**	**Primary Outcome**
Culver et al., 2023	**RCT**	**24**	**37**	**Efzofitimod**	**9**	**5mg/kg**	**50.8 ± 9.8**	**55.6**	**66.7**	**33.3**	**2.9 ± NR^**	**CS (100), MTX (33.3), AZA (11.1)**	**83.8 ± 16.6**	**TEAE-free survival at wk 24**
				Efzofitimod	**8**	**3mg/kg**	**51.8 ± 11.4**	**50**	**25**	**75**	**4.3 ± NR^**	**CS (100), LEF (12.5)**	**83.8 ± 7.3**	
				Efzofitimod	**8**	**1mg/kg**	**54.5 ± 11.3**	**50**	**37.5**	**62.5**	**5.3 ± NR^**	**CS (100), MTX (25), HCQ (12.5)**	**68.3 ± 9.7**	
				Placebo	**12**	**NA**	**52.5 ± 10.2**	**58.3**	**25**	**75**	**2.9 ± NR^**	**CS (100), MTX (33.3), AZA (16.7)**	**77.3 ± 11.5**	
Judson et al., 2014	**RCT**	**28**	**173**	**Ustekinumab**	**60**	**180mg -> 90mg**	**49.8 ± 10.2**	**48.3**	**31.7**	**63.3**	**NR**	**CS (76.7), MTX (20), AZA (1.7)**	**64.3 ± NR**	**Change at wk 16 in % predicted FVC**
				Golimumab	**55**	**200mg -> 100mg**	**50.0 ± 9.4**	**49.1**	**29.1**	**65.5**	**NR**	**CS (80), MTX (21.8), AZA (7.3)**	**68.0 ± NR**	
				Placebo	**58**	**NA**	**49.5 ± 9.5**	**50**	**39.7**	**55.2**	**NR**	**CS (70.7), MTX (18.9), AZA (5.2)**	**68.4 ± NR**	
Pariser et al., 2013	**RCT**	**12**	**15**	**Adalimumab**	**10**	**80mg -> 40mg**	**46.0 ± NR**	**80**	**100**	**0**	**9.8 ± NR**	**NR**	**NR**	**PGA score of 2 or less**
				Placebo	**5**	**NA**	**52.6 ± NR**	**80**	**80**	**20**	**5.6 ± NR**	**NR**	**NR**	
Baughman et al., 2006	**RCT**	**24**	**138**	**Infliximab**	**47**	**5mg/kg**	**46.5 ± 8.7**	**40.4**	**36.2**	**59.6**	**5.8 ± 6.1**	**CS only (51.1), csDMARD only (8.5), CS+csDMARD (40.4)**	**69.5 ± 8.6**	**Change at wk 24 in % predicted FVC**
				infliximab	**46**	**3mg/kg**	**49.3 ± 9.4**	**47.8**	**17.4**	**78.3**	**8.0 ± 6.2**	**CS only (43.5), csDMARD only (8.7), CS+csDMARD (47.8)**	**67.7 ± 9.6**	
				Placebo	**45**	**NA**	**45.3 ± 9.4**	**42.2**	**35.6**	**64.4**	**7.0 ± 6.2**	**CS only (57.8), csDMARD only (4.4), CS+csDMARD (37.8)**	**68.8 ± 11.1**	

Judson et al., 2008	**Analysis Baughman 2006**	**24**	**138**	**Infliximab**	**93**	**3mg/kg or 5mg/kg**	**47.8 ± 9.1**	**44.1**	**26.9**	**68.8**	**6.9 ± 6.2**	**NR**	**68.6 ± 9.1**	**Change at wk 24 in ePOST**
				Placebo	**45**	**NA**	**45.3 ± 9.4**	**42.2**	**35.6**	**64.4**	**7.0 ± 6.2**	**NR**	**68.8 ± 11.1**	
Baughman et al., 2005	**RCT**	**26**	**18**	**Etanercept**	**9**	**25mg**	**NR**	**88.9**	**77.8**	**NR**	**NR**	**CS (55.6), MTX (100), AZA (0)**	**68 ± NR**	**Ophthalmologist exam atr 6m**
				Placebo	**9**	**NA**	**NR**	**100**	**55.6**	**NR**	**NR**	**CS (22.2), MTX (100), AZA (0)**	**92 ± NR**	
*Rossman et al., 2006**	**RCT**	**6**	**19**	**Infliximab**	**13**	**5mg/kg**	**46.77 ± 2.31**	**61.5**	**38.5**	**61.5**	**NR**	**CS (69.2), MTX (NR), AZA (NR)**	**50.6 ± 4.4**	**Change at wk 6 in % predicted FVC**
				Placebo	**6**	**NA**	**49.33 ± 4.92**	**16.7**	**50**	**50**	**NR**	**CS (66.7), MTX (NR), AZA (NR)**	**56.8 ± 5.2**	
Kron et al., 2023	**RCT**	**4**	**16**	**Anakinra + SOC**	**7**	**100mg per day**	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**Change in hs-CRP at 28 days**
				SOC	**9**	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**NR**	**SOC**

Single arm trials

Study	Design	Duration (weeks)	Total N	Drug	Drug N	Dose	Age	Female	Black	White	Duration disease	Concomitant medications	Predicted FVC	Primary Outcome
Friedman et al., 2021	**Open-label**	**16**	**5**	**Tofacitinib**		**5mg BD**	**40.8 ± NR**	**20**	**20**	**80**	**2.75 ± NR**	**CS (100), MTX (NR), AZA (NR)**	**86.6 ± NR**	**≥ 50% reduction in CS at wk 16**
Damsky et al., 2022	**Open-label**	**26**	**10**	**Tofacitinib**		**5mg BD**	**56 ± NR**	**40**	**60**	**40**	**13.2 ± NR**	**CS (50), MTX (40), AZA (0), HCQ (10)**	**NR**	**Change in CSAMI activity score at 6 months**
Utz et al., 2003	**Open-label**	**52**	**17**	**Etanercept**		**25mg twice weekly**	**49.4 ± 10.7**	**58.8**	**11.8**	**88.2**	**NR**	**NR**	**91.1 ± 16.5**	**NA**
Sweiss et al., 2014	**Open-label**	**52**	**11**	**Adalimumab**		**40mg weekly**	**45.3 ± 12.7**	**90.9**	**100**	**0**	**NR**	**CS (45.5), MTX (36.4), AZA (9.1), LEF (9.1), MMF (36.4), CYC (9.1)**	**61 ± 12**	**Change from baseline to Week 24 in % predicted FVC**
Kullberg et al., 2020	**Open-label**	**26**	**13**	**Infliximab**		**3-5mg**	**47.6 ± 5.1**	**15.4**	**0**	**100**	**4.94 ± 5.0**	**CS (92), MTX (16.7)[#], AZA (0)**	**70 ± NR**	**NA**
Vorselaars et al., 2015	**Open-label**	**26**	**56**	**Infliximab**		**5mg/kg**	**48.7 ± 10.1**	**35.7**	**NR**	**87.5**	**6.8 ± 7.1**	**CS (42.9), MTX (82.1), AZA (7.1), LEF (1.8)**	**78.8 ± NR**	**NA**

Sweiss et al., 2014	**Open-label**	**52**	**10**	**Rituximab**	**1g weeks 0 and 2**	**49 ± NR^**	**30**	**30**	**60**	**NR**	**NR**	**57.3 ± 14.2**	**Safety**
*Baker et al., 2023**	**Open-label prior to RCT**	**16**	**15**	**Sarilumab**	**200mg**	**57.0 ± NR^**	**20**	**20**	**73.3**	**5.17 ± NR^**	**CS (100), DMARDs (33.3)**	**92.0 ± NR^**	**Flare-free survival on CS taper. Flare was defined as the need for rescue, significant worsening of disease, or cessation of study intervention.**

Supplementary 2a. Risk-of-bias assessment of the included comparator studies using Version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2).

	Bias					
Study	Randomisation Process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Culver, 2023						
Judson, 2014						
Parisier, 2013						
Baughman, 2006						
Baughman, 2005						
Rossman, 2006						
Baker, 2023						
Kron, 2023						

Green, low risk of bias.
Yellow, some concerns of risk of bias.
Red, high risk of bias

Although Kron et al is not a randomised study, it was analysed using the RoB to allow comparison

Supplementary 2b. Risk-of-bias assessment of the included single armed studies using the Newcastle Ottawa Scale (NOS).

	Bias					
Study	Representativeness of the cohort	Ascertainment of the exposure	Demonstration that the outcome of interest was not present at start of the study	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up
Friedman et al., 2021						
Damsky et al., 2022						
Utz et al., 2003						
Sweiss et al., 2014a (adalimumab)						
Kullberg et al., 2020						
Vorselaars et al., 2015						
Sweiss et al., 2014b (rituximab)						

Green, low risk of bias.
Yellow, some concerns of risk of bias.
Red, high risk of bias

Two NOS criteria were excluded as studies did not include a control arm; selection of the non-exposed cohort and comparability of cohorts.

Supplementary 3. Vote counting data synthesis based on the direction of effect across outcomes, presented by drug, trial, and outcome

Authors	Study type	N	Pulmonary	Cutaneous	Cardiac/Ocular	e-POST	IS dose	18F-FDG-PET	PRO
Infliximab									
Rossman	RCT	13	VC: 15.2± 9.9, NS CXR: 31%, NS Dyspnoea: 0.38±0.21, NS						SF36: 0.39, NS
Baughman/ Judson	RCT	93	FVC: 2.5^, p=0.038 6WMD: 7.6±6.6 Borg's: 0.1±1.8, NS CXR: 0.9±2.9, p=0.001			2.09±0.32, p=0.002			SGRQ: 3.7±1.5, NS
Vorselaars	Single arm	56	PFT: 6.6^	Skin lesion: 4 of 4			Reduce GC: 8.8mg, p=0.001	SUV 3.93, p<0.0001	PGA: 8.2, p=0.009 SF36: 14.6, p<0.0001
Kullberg	Single arm	13	FVC: 0.07 (-0.01 to 0.15)*				Reduce IS: 7 of 13		
Adalimumab									
Sweiss	Single arm	11	FVC: 3 (-3 to 13) 6WMD: 20 (-90 to 124)* Borg: 0.5 (0 to 1)* CXR: 2 of 6 improved						PGA: 25 (10-42)*
Pariser	RCT	10	FVC: 0.09^	PGA ≤2:OR 2.5(0.2,141)* TL area: 32%, p=0.023 TL vol: 59%, NS					SHQ: 0.47 DLQI: 3.08, NS
Etanercept									
Utz	Single arm	17	FVC: 4 of 17 CXR: 2 of 17 mMRC dyspnoea: 5 of 17						SF36: NR, NS
Baughman	RCT	9			OGA: 2 of 9		Reduce GC: 2 of 9		
Golimumab									
Judson	RCT	55	FVC: 1.15 ± 1.41^, NS 6MWD: 12.5 ± 14.9^, NS	SPGA: 9 of 17 SASI: 2.57, NS TL score: 2.3, NS		3^, p=0.004	Reduce GC: 34 of 42, p=0.01		PGA: NR, NS SAT: NR, NS FAS: NR, NS SGRQ: NR, NS SF36: NR, NS
Rituximab									
Sweiss	RCT	10	FVC: 2.9 (-4.9 to 14)*, NS CXR: NR 6MWD: 19 (-38 to 80)*						
Ustekinumab									
Judson	RCT	60	FVC -0.15±1.30, NS 6MWD: -13.2±13.6, NS	sPGA: 3 of 21 TL score: 1.2, NS SASI: 0.5, NS		1^, NS	Reduce GC: 27 of 46, NS		PGA, NR, NS SF36 , NR, NS SAT, NR, NS

									FAS, NR, NS SGRQ, NR, NS
Sarilumab									
Baker	RCT	15	FVC: -3	SASI: 0 (-13 to 1)*		0			PGA: -2.5 HAQ: 0 FACIT-F: 1
Anakinra									
Kron	Single arm	16			LVEF: 5 (-3.4 to 14.7), NS			Cardiac PET: 17%, NS	
Efzofitimod									
Culver	RCT	9	FVC: 2.5^				Reduce GC: 58.1%		SAT: 7.77, p=0.01 FAS: 16.17, p=0.022 KSQ: 6.42, p=0.018
Tofacitinib									
Friedman	RCT	5	FVC: 1^* CXR: 2 of 5				Reduce GC: 3 of 5		SGRQ: 18.5
Damsky	Single arm	10		CSAMI: 83% (40%–100%)			Reduce GC: 4 of 5	5 of 8	

Legend:
Red box: unsupportive; Yellow box: Uncertain; Green box: supportive. FVC: % Force vital capacity ; CXR: Chest X-ray; 6MWD: 6-min walking distance ; Borg: Borg Dyspnea Scale; DLQI: Dermatology Life Quality Index questionnaire; CSAMI: Cutaneous Sarcoidosis Activity and Morphology Instrument; sGPA: Static Physician's Global Assessment; SASI: Sarcoidosis Activity and Severity Index; ePOST: extrapulmonary physician organ severity tool; IS: immunosuppression; GC: Glucocorticoid; PGA: Patient global assessment; HAQ: Health Assessment Questionnaire; FAS: Fatigue Assessment Scale; SHQ: Sarcoidosis Health Questionnaire; KSQ: King's Sarcoidosis Questionnaire;
SAT: Sarcoidosis Assessment Tool; FACIT: Functional Assessment of Chronic Illness Therapy; SF36: 36-Item Short Form Health Survey; St Georges Respiratory Questionnaire.
Median and IQR presented unless specified. # = mean value presented with SD. * = value calculated using data in text, table or figure
P value = statistically significance when compared with placebo in RCT, and statistically significance when compared with baseline in single arm studies
For scores when a negative value indicates improvement, this was converted to a positive value e.g Borg Dyspnea Scale

Outcomes and MCID:
FVC: % Force vital capacity, MCID: 3-5.2% in Scleroderma (32), 2-6 in PFT (31)
6MWD: 6-min walking distance; MCID: 14-30.5m (41)
Borg Dyspnea Scale, range 0-10; MCID: 1 (42)
DLQI: Dermatology Life Quality Index questionnaire, range 0-30; MCID: 4 (43)
CSAMI: Cutaneous Sarcoidosis Activity and Morphology Instrument, range 0-165; MCID: 5 (44)
sGPA: Static Physician's Global Assessment; range 0-5 MCID: 2 (45)
SASI: Sarcoidosis Activity and Severity Index, range 0-72; MCID not established (46)
ePOST: extrapulmonary physician organ severity tool; range 0-102 MCID not established (47)
PGA: Patient global assessment; range 1-10, MCID: 2 (40)
HAQ: Health Assessment Questionnaire, range 0-3 MCID 0.25 (48)
FAS: Fatigue Assessment Scale; range 10-50, MCID:4 (49)
SHQ: Sarcoidosis Health Questionnaire, range 0-7; MCID not established (39)
KSQ: King's Sarcoidosis Questionnaire; MCID: 8 (40)

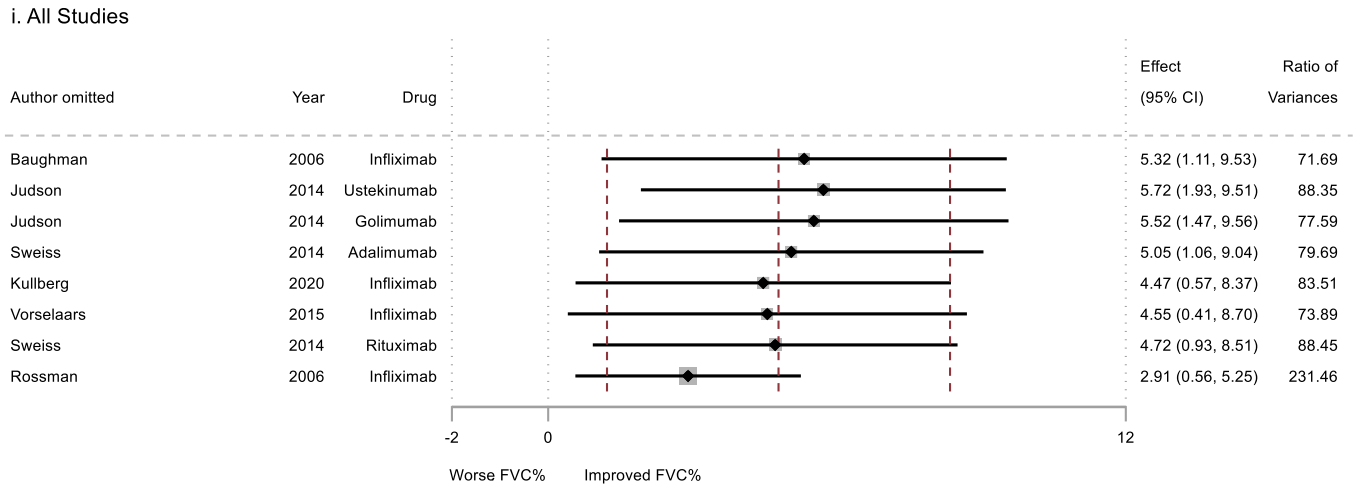
SAT: Sarcoidosis Assessment Tool; range 29-203; MCID not established (50)
FACIT: Functional Assessment of Chronic Illness Therapy; range 0-52; MCID: 4 (51)
SF36: 36-Item Short Form Health Survey, range 0-100; MCID 2-4 (52)
St Georges Respiratory Questionnaire, range 0-100; MCID 5-8 (52)

Supplementary 4. Improvement in pulmonary function

	Study design	Study duration	Drug	Number on drug	Lung outcome	Mean or medium	SD or IQR or CI
Baughman et al., 2006	RCT	24	Infliximab	47	% change in FVC at 24 weeks	2.5	SD 0.7
Judson et al., 2014	RCT	28	Ustekinumab	60	% change in FVC at 16 weeks	-0.15	CI -2.68 to 2.38
Judson et al., 2014	RCT	28	Golimumab	55	% change in FVC at 16 weeks	1.15	CI -1.64 to 3.95
*Baker et al., 2023**	RCT	16	Sarilumab	2	% change in FVC at 16 weeks	-3.0^	NR
					Absolute change in FVC at 16 weeks	-110ml^	NR
Sweiss et al., 2014	Open-label	24	Adalimumab	11	% change in FVC at 24 weeks	3	CI-3 to 13
Kullberg et al., 2020	Open-label	26	Infliximab	12	% change in FVC at 26 weeks	8~	11.8~
Vorselaars et al., 2015	Open-label	26	Infliximab	56	% change in FVC at 26 weeks	6.64	9.38*
Sweiss et al., 2014	Open-label	24	Rituximab	10	% change in FVC at 24 weeks	6.61~	17.9~
Friedman et al., 2021	Open-label	16	Tofacitinib	5	% change in FVC at 16 weeks	1	NR
*Rossman et al., 2006**	RCT	6	Infliximab	13	% change in FVC at 6 weeks	15.22	9.91

^median and not mean published
~ mean and SD calculated using published data.
* SD calculated using published data.

Supplementary 5. Leave one out analysis i) for all studies and ii) restricted to studies of anti-



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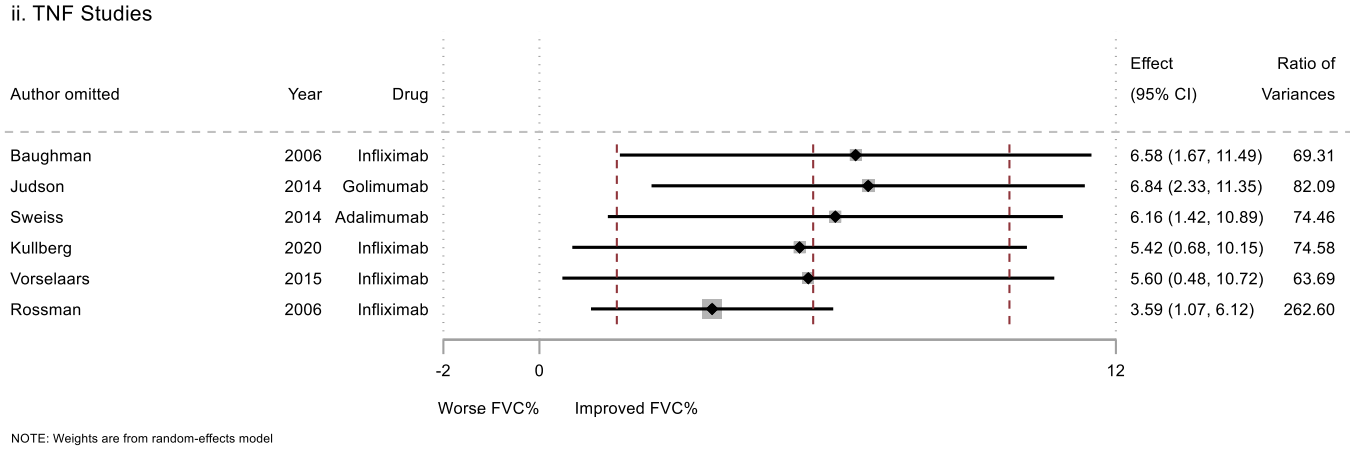
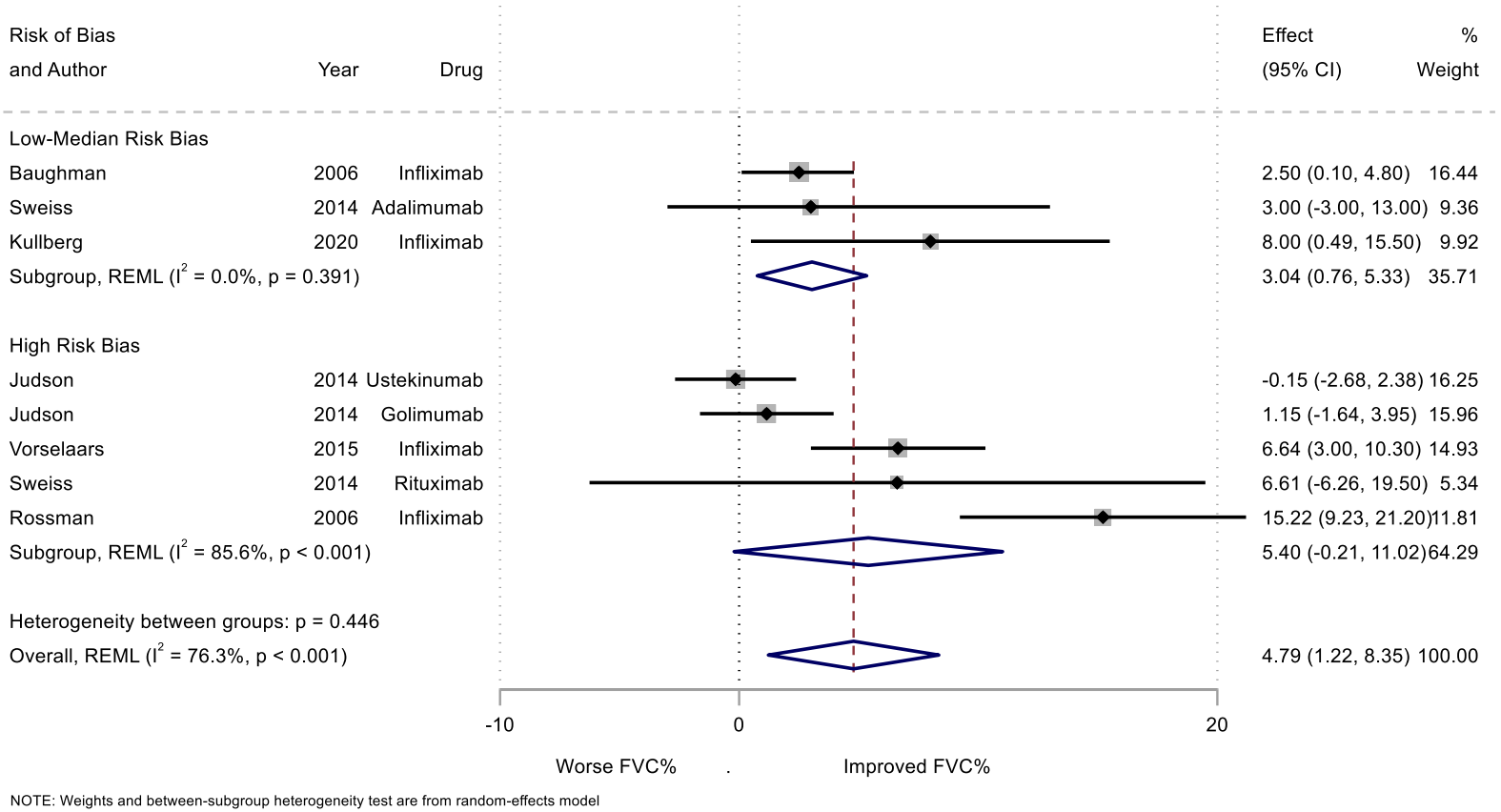


Supplementary 6. Sensitivity analysis restricting to studies without high risk of bias



NOTE: Weights and between-subgroup heterogeneity test are from random-effects model

Supplementary 7. Funnel plots, assessing potential publication bias in pairwise meta-analysis, primary outcome