	Incomplete outcome	Incomplete outcome	Free of Selective	Free of Selective	Other biases- major	Other biases- major
Study	data	data	Reporting	Reporting	baseline imbalance	baseline imbalance
	Judgement	Reason	Judgement	Reason	Judgement	Reason
Boyle 2015	Low risk	no missing data	Unclear	insufficient information	Low risk	appears free of other biases
	High Diek		Unclear	Not enough information provided to	Low Risk	
Bresnihan 1998	High Risk	less than 80% completion		assess selective reporting	LOW RISK	No major baseline imabalances
		"The full analysis set for the primary analysis included all randomised patients who				
		received at least one dose of study				
D 2042	Ulah Diah	medication and had at least one post- baseline assessment."	Unclear	Not enough information provided to assess selective reporting	Low Risk	No secion baseline insubalesses
Burmester 2013	High Risk	Dascille assessment.	Officieal	assess selective reporting	LOW INISK	No major baseline imabalances
		"Efficacy analyses were based on a modified intent-to-treat population, including patients				
		who received any test article and provided				
		efficacy data at baseline and at any subsequent visit The last-observation-				"there were no significant differences among the groups in the baseline
		carried-forward (LOCF) approach was used				characteristics with the exception of the
		to account for missing data points. LOCF imputation was also applied to patients who		Not enough information provided to		percentage of patients receiving previous corticosteroids and
Combe 2009	High Risk	discontinued for unsatisfactory response."	Low Risk	assess selective reporting	High Risk	the mean number of previous DMARD"
				Not enough information provided to		
Coombs 2009	Unclear	No data presented	Unclear	assess selective reporting	Unclear	No baseline data presented
		"Efficacy analyses were conducted in the				
		intention-to-treat population (all randomly				
		assigned and treated patients analysed in the arm they were randomly assigned to)				
		with non-responder imputation for				
		categorical variables (eg, DAS28 remission, ACR response), last observation carried				
		forward until patient withdrawal for missing		N. 1 . 6 . 6		
Dougados 2013	High Risk	joint counts and no additional imputation of missing values."	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
	111311111111	,		Not enough information provided to		
Doyle 2013	Unclear	No data presented	Unclear	assess selective reporting	Unclear	No baseline data presented
Edwards 2004	Low Risk	Reasons documented for dropouts. For patie	unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
Edwards 2004	LOW FROM	Reasons documented for dropodis. For patie	Choca	access sciedare reporting	LOW HOR	No major baseline imabalances
				Not enough information provided to		Baseline characteristics were similar
Flesichmann 2012 (Aug)	Low Risk	more than 80% completed the study	Unclear	assess selective reporting	Low Risk	among the treatment groups
Flesichmann 2012 (March)	Low Risk	3 types of imputation were used to address missing data.	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
1 loodillianii 2012 (Malori)		· ·		1 0		Tro major bassimo imabalaness
		"The safety population included all patients who received at least one dose of				
		tocilizumab or adalimumab and had at least				
		one post-dose safety assessment. The intention-totreat population included patients				
		who received at least one dose of				
		tocilizumab or adalimumab and had at least one efficacy measurement. The per-protocol				
		population included patients in the intention-				
Gabay 2013	High Digit	to-treat population who had not had any major protocol violations."	Unclear	Not enough information provided to assess selective reporting	Low Risk	No maio has alias imala da sas
Gabay 2013	High Risk	major protocor violations.	Officieal	Not enough information provided to	LOW INION	No major baseline imabalances
Genovese 2002	High Risk	Significantly more AE withdrawls in MTX grou	Unclear	assess selective reporting	Low Risk	No major baseline imabalances
		proportion of missing outcomes compared				
		with observed event risk not enough to induce clinically relevant bias in intervention				protocol failure - deviation from study
Hobbs 2015	low risk	effect estimate	Unclear risk	insuffucent information	high risk	protocol
		Efficacy analyses were performed in				
		the intent-to-treat (ITT) population				
		(randomised patients who received ≥ 1 administration of study medication)				
		with non-responder imputation of				
		missing data used for binary response variables (eg, DAS28-ESR				
		remission and ACR response)."				
		(p.37). Comment: Withdrawals due to AEs in the tocilizumab group were				
		8.7% compared to 9.1% in the				
		placebo group. Total withdrawals were 19.9% in the tocilizumab group				
		compared to 27.2% in the placebo				
		group. 553/556 randomised patients were included in the ITT population.				
		3 people were omitted since they did				
		not receive Tocilizumab.		Commont: The exclusion		
Huizinga 2015	Low Risk		Unclear	Comment: The protocol is not available.	Low Risk	No major baseline imabalances
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Jobanputra 2012	High Risk	At 12 months, the authors provided data for the 39 and 34 patients still remaining in each study group respectively as well as a modified ITT population results. The modified method is described as follows: "Data for the modified intention to treat population with baseline values carried forward for those who discontinued therapy within 1 year."	Unclear	Not enough information provided to assess selective reporting	High Risk	imbalances in concomitant treatments
Johnsen 2006	High Risk	"A patient who had a negative ACR-N or who had missing evaluations due to premature withdrawal from the study (before 24 weeks of treatment) had the ACR-N set to zero for that evaluation. The treatment effect was tested using 2-way analysis of variance (ANOVA). All patients who received at least 1 dose of study medication were included in the efficacy analyses."	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
Jones 2010	High Risk	"The intention-to-treat (ITT) population included all randomised patients who received at least one infusion of the study treatment; depending on the purpose of analysis, ITT patients initially randomised to placebo were excluded."	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
		"The primary analysis was conducted on an intention-to-treat population Four patients were withdrawn from the study before the start of treatment, leaving 147 patients for the safety analysis (Fig. 1). Efficacy analysis was performed for 142 patients for whom sufficient clinical data were available. Sixteen patients (twelve in the E group and four in another) were withdrawn from the study by week 24 for the reasons given in Fig. 1." Insufficient data is presented as a reason why efficacy analysis was not performed on 2 patients in the ETN group and 3 patients in the ETN+MTX group. Moreover 12 more natients were lost in the ETN group than in		Not enough information provided to		
Kameda 2010	High Risk	patients were lost in the ETN group than in ETN+MTX group.	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
Keystone 2009	High Risk	No mention of whether ITT analysiswas performed or how missing data was handled.	Low Risk	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
Kremer 2009	Low Risk	more than 80% completion	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
Kremer 2010	High Risk	"Efficacy data from all randomized patients were analyzed by assigned treatment group using an intent-to-treat approach" However, patients assigned to lower dosages or inactive control were allowed to escape at 16 weeks to higher dosage or active treatment.	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
				Not enough information provided to		Imbalance in baseline demographic
Kremer 2013	Low Risk	more than 80% completion	Unclear	assess selective reporting	High Risk	and disease characteristics
MacIsaac 2014	Low risk	no missing data	Unclear	insufficient information	Low risk	appears free of other biases
		"Three hundred fifty-nine patients were randomly allocated to the 7 treatment groups. Patient flow through the trial and randomization to each treatment arm are shown in Figure 1. Approximately equal numbers of patients were randomly allocated to each arm of the study. During the trial, 60 patients withdrew (34 patients withdrew due to adverse events and/or possible drugrelated toxicity). Of the 359 patients randomized to receive study medication, all were included in the safety population, and 354 patients were included in the full-analysis set (5 patients were excluded from the full-analysis set because of a protocol		Not enough information provided to		
Maini 2006	High Risk	violation)."	Low Risk	assess selective reporting	Low Risk	No major baseline imabalances
				Not enough information provided to		"Differences between the groups did not otherwise achieve statistical
Mathias 2000	Unclear	"A total of 34 (9.7%) of 352 patients discontinued treatment	Unclear	assess selective reporting	Low Risk	significance"
		(7, 7, 16, and 4 in the placebo and adalimumab 20, 40,		Not enough information provided to		Imbalance in baseline disease
Miyasaka 2008	Low Risk	and 80 mg groups, respectively)."	Unclear	assess selective reporting	High Risk	characteristics

Maraland 1000	Low Risk	Reasons for withdrawal clearly specified with methods stated to deal with missing data	Unclear	Not enough information provided to assess selective reporting	Low Risk	Aside from differences in concurrent medications (more patients in the 25-mg group were receiving corticosteroids and more placebo recipients were receiving NSAIDs), no baseline imbalances were detected.
Moreland 1999	LOW NISK	statistical analysis was performed using the	Officieal	assess selective reporting	LOW NISK	baseiiile iiiibalalices were detected.
		intention-to-treat approach		Not enough information provided to		
Moreland 2012	Low Risk	fashion	Unclear	assess selective reporting  Not enough information provided to	Low Risk	No major baseline imabalances
Nishimoto 2004	High Risk	Many placebo dropouts	Unclear	assess selective reporting	Low Risk	No major baseline imabalances
		"All patients receiving at least one dose of				
Nishimoto 2007	High Risk	study drug were included in the efficacy and safety analysis."	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
Ohta 2014	Low risk	no missing data	Unclear risk	insuffucent information	Low risk	appears free of other biases
		proportion of missing outcomes compared with observed event risk not enough to induce clinically relevant bias in intervention				
Ostergaard 2015	low risk	effect estimate	Unclear risk	insuffucent information	Low risk	appears free of other biases
		"Intent-to-treat analyses with the last observation carried forward (LOCF) were		Not enough information provided to		
Pavelka 2009	High Risk	used to compare the two treatment arms."	Unclear	assess selective reporting	Low Risk	No major baseline imabalances
Pope 2014	High rick	High withdrawal rate and per protocol analysis was used	Unclear	insufficient information	Low risk	No major basalina imahalangas
Pope 2014	High risk	analysis was asca	Officieal	insufficient information	LOWTISK	No major baseline imabalances
						"Baseline demographics and disease
Strand 2006	Low Risk	more than 80% completion at 24 weeks	Unclear	Not enough information provided to assess selective reporting	Low Risk	characteristics were comparable across treatment groups."
		·		, ,		<u> </u>
Tada 2012	Unclear	No mention of whether ITT analysiswas performed or how missing data was handled.	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major basalina imahalanga
1444 2012	Officical	performed of flow missing data was mandied.	Officical	Not enough information provided to	LOW NISK	No major baseline imabalances
Takeuchi 2013	High Risk	less than 80% completion	Unclear	assess selective reporting	Low Risk	No major baseline imabalances
Takeuchi 2013a	Low Risk	more than 80% completion	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
				Not enough information provided to		
Takeuchi 2013b	Low Risk	more than 80% completion	Unclear	assess selective reporting  Not enough information provided to	Low Risk	No major baseline imabalances
van der Heidje 2006	Low Risk	more than 80% completion	Low Risk	assess selective reporting	Low Risk	No major baseline imabalances
van der Heijde (TEMPO) 2007	High Risk	See table	High Risk	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
		"Efficacy analyses were performed for the intention to treat (ITT) population, defined as all randomised patients who received at least one double blind injection of study drug and				
		for whom any assessment of efficacy under double blind conditions was available All patients randomly allocated to receive adalimumab and who received at least one				
van de Putte 2003	High Risk	double blind conditions was available All patients randomly allocated to receive	Unclear	Not enough information provided to assess selective reporting	Low Risk	No major baseline imabalances
van de Putte 2003	High Risk	double blind conditions was available All patients randomly allocated to receive adalimumab and who received at least one dose of adalimumab were included in the safety analyses."  Patients who dropped out were followed up at 1, 2, 3, and 6 months after treatment; An intention to treat analysis was performed that included patients who were randomised and who received at least one injection of the randomised study drug. Patients not completing the trial	Unclear	· ·	Low Risk	No major baseline imabalances
van de Putte 2003	High Risk	double blind conditions was available All patients randomly allocated to receive adalimumab and who received at least one dose of adalimumab were included in the safety analyses."  Patients who dropped out were followed up at 1, 2, 3, and 6 months after treatment; An intention to treat analysis was performed that included patients who were randomised and who received at least one injection of the randomised	Unclear	· ·	Low Risk	There were no statistically significant differences in the demographic characteristics and baseline disease activity between the treatment groups
		double blind conditions was available All patients randomly allocated to receive adalimumab and who received at least one dose of adalimumab were included in the safety analyses."  Patients who dropped out were followed up at 1, 2, 3, and 6 months after treatment; An intention to treat analysis was performed that included patients who were randomised and who received at least one injection of the randomised study drug. Patients not completing the trial (that is, who were withdrawn or required rescue) despite fulfilling ACR criteria were considered nonresponders upon withdrawing or entering rescue. Withdrawals occurred in 118/434 (27.2%) adalimumab treated patients and 62/110 (56.4%) placebo treated patients.  "One patient in the ETN group did not receive drug and was withdrawn from the		Not enough information provided to assess selective reporting		There were no statistically significant differences in the demographic characteristics and baseline disease
		double blind conditions was available All patients randomly allocated to receive adalimumab and who received at least one dose of adalimumab were included in the safety analyses."  Patients who dropped out were followed up at 1, 2, 3, and 6 months after treatment; An intention to treat analysis was performed that included patients who were randomised and who received at least one injection of the randomised study drug. Patients not completing the trial (that is, who were withdrawn or required rescue) despite fulfilling ACR criteria were considered nonresponders upon withdrawing or entering rescue. Withdrawals occurred in 118/434 (27.2%) adalimumab treated patients and 62/110 (56.4%) placebo treated patients.  "One patient in the ETN group did not		assess selective reporting  Not enough information provided to		There were no statistically significant differences in the demographic characteristics and baseline disease
van de Putte 2004	High Risk	double blind conditions was available All patients randomly allocated to receive adalimumab and who received at least one dose of adalimumab were included in the safety analyses."  Patients who dropped out were followed up at 1, 2, 3, and 6 months after treatment; An intention to treat analysis was performed that included patients who were randomised and who received at least one injection of the randomised study drug. Patients not completing the trial (that is, who were withdrawn or required rescue) despite fulfilling ACR criteria were considered nonresponders upon withdrawing or entering rescue. Withdrawals occurred in 118/434 (27.2%) adalimumab treated patients and 62/110 (56.4%) placebo treated patients.  "One patient in the ETN group did not receive drug and was withdrawn from the study, leaving 314 patients in the intent-to-	Unclear	Not enough information provided to assess selective reporting  Not enough information provided to assess selective reporting  Not enough information provided to assess selective reporting	Low Risk	There were no statistically significant differences in the demographic characteristics and baseline disease activity between the treatment groups
van de Putte 2004 van Riel 2006	High Risk Low Risk	double blind conditions was available All patients randomly allocated to receive adalimumab and who received at least one dose of adalimumab were included in the safety analyses."  Patients who dropped out were followed up at 1, 2, 3, and 6 months after treatment; An intention to treat analysis was performed that included patients who were randomised and who received at least one injection of the randomised study drug. Patients not completing the trial (that is, who were withdrawn or required rescue) despite fulfilling ACR criteria were considered nonresponders upon withdrawing or entering rescue. Withdrawals occurred in 118/434 (27.2%) adalimumab treated patients and 62/110 (56.4%) placebo treated patients.  "One patient in the ETN group did not receive drug and was withdrawn from the study, leaving 314 patients in the intent-to-treat analysis."  Patient reported outcomes were analyzed from Riel 2006 trial. The number of patients included in analysis for HAQ did not match those that were originally randomized to the	Unclear	Not enough information provided to assess selective reporting  Not enough information provided to assess selective reporting  Not enough information provided to assess selective reporting	Low Risk	There were no statistically significant differences in the demographic characteristics and baseline disease activity between the treatment groups.  No major baseline imabalances