Database	PubMed and Cochrane
Date	30/03/2021
Result	379
User Query	("Arthritis, Psoriatic"[Mesh] OR "Spondylitis, Ankylosing"[Mesh]) AND ("Infections"[Mesh] OR "Safety"[Mesh]) AND ((TNF-inhibitors) OR (etanercept) OR (adalimumab) OR (infliximab) OR (golimumab) OR (certolizumab pegol) OR (baricitinib) OR (tofacitinib) OR (upadacitinib) OR (filgotinib) OR (abatacept) OR (apremilast) OR (secukinumab) OR (ixekizumab) OR (ustekinumab) OR (guselkumab) OR (bimekizumab) OR (deucravacitinib) OR (briankizumab) OR (brodalumab) OR (tildrakizumab) OR (risankizumab) OR (brazikumab) OR (mirikizumab))

Supplementary table 1. *Full electronic search strategy*

Section/ Checklist item	#	Explanation and/or examples	Reported on page #
Reporting of background should include			
Problem definition	1		#3-4
Hypothesis statement	2		#3-4
Description of study outcome(s)	3		#4
Type of exposure or intervention used	4		#4- 6
Type of study designs used	5		#4- 6
Study population	6		#4 -6
Reporting of search strategy should include			
Qualifications of searchers	7	eg, librarians and investigators	#1
Search strategy including time period included in the synthesis and keywords	8		#4- 5
Effort to include all available studies, including contact with authors	9		#6
Databases and registries searched	10		#5
Search software used, name and version, including special features used	11	eg, explosion	#7
Use of hand searching	12	eg, reference lists of obtained articles	#5
List of citations located and those excluded, including justification	13		#FIGURE 1
Method of addressing articles published in languages other than English	14		# FIGURE 1
Method of handling abstracts and unpublished studies	15		# FIGURE 1
Description of any contact with authors	16		#6
Reporting of methods should include			
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	17		#6
Rationale for the selection and coding of data	18	eg, sound clinical principles or convenience	#6

Documentation of how data were classified and coded	19	eg, multiple raters, blinding, and interrater reliability	#6
Assessment of confounding	20	eg, comparability of cases and controls in studies where appropriate	NA
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	21		#9
Assessment of heterogeneity	22		#23; 31
Description of statistical methods in sufficient detail to be replicated	23	eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis	#6
Provision of appropriate tables and graphics	24		yes
Reporting of results should include			
Graphic summarizing individual study estimates and overall estimate	25		#FIGURE 2-6
Table giving descriptive information for each study included	26		#TABLE 1
Results of sensitivity testing	27	eg, subgroup analysis	# supplementary table 6-8
Indication of statistical uncertainty of findings	28		#figure 2-6
Reporting of discussion should include			
Quantitative assessment of bias	29	eg, publication bias	#figure 5
Justification for exclusion	30	eg, exclusion of non–English-language citations	#figure 1
Assessment of quality of included studies	31		# supplementary figure 9
Reporting of conclusions should include			
Consideration of alternative explanations for observed results	32		#9-15
Generalization of the conclusions	33	ie, appropriate for the data presented and within the domain of the literature review	# 9-15
Guidelines for future research	34		# 15
Disclosure of funding source	35		# 15

Supplementary table 2. *MOOSE Checklist: A proposed Reporting checklist for Authors, Editors, and Reviewers of Meta-analyses of Observational Studies)*

Selection
1) Representativeness of the exposed cohort
a) Truly representative (one star)
b) Somewhat representative (one star)
c) Selected group

d) No description of the derivation of the cohort

2) Selection of the non-exposed cohort

a) Drawn from the same community as the exposed cohort (one star)

b) Drawn from a different source

c) No description of the derivation of the non-exposed cohort

3) Ascertainment of exposure

a) Secure record (e.g., surgical record) (one star)

b) Structured interview (one star)

c) Written self-report

d) No description

e) Other

4) Demonstration that outcome of interest was not present at start of study

a) Yes (one star)

b) No

Comparability

1) Comparability of cohorts on the basis of the design or analysis controlled for confounders

a) The study controls for age, sex and marital status (one star)

b) Study controls for other factors (list) _____ (one star)

c) Cohorts are not comparable on the basis of the design or analysis controlled for confounders

Outcome

1) Assessment of outcome

a) Independent blind assessment (one star)

b) Record linkage (one star)

c) Self report

d) No description

e) Other

2) Was follow-up long enough for outcomes to occur

a) Yes (one star)

b) No

3) Adequacy of follow-up of cohorts

a) Complete follow up- all subject accounted for (one star)

b) Subjects lost to follow up unlikely to introduce bias- number lost less than or equal to 20% or description of those lost suggested no different from those followed. (one star)

c) Follow up rate less than 80% and no description of those lost

d) No statement

Supplementary table 3. *Newcastle-Ottawa Quality Assessment Form for Cohort Studies*

	Serious infections			Non-serious infections		
	RCT	OLE	OBS	RCT	OLE	OBS
Number of studies	56	*19*	*14*	38	8	10
Number of patients	12186	6506	*16 098*	7418	2430	3047
PsA, n (%)	7804 (64)	3346 (51)	12183 (75)	4623 (62)	635 (26)	1999 (65)
AS or nr-AxSpA, n (%)	4382 (36)	3160 (49)	3915 (25)	2795 (38)	1795 (74)	1048 (35)
Number of women, %	43.3	*38.5*	*49.4*[12]	42.6	37.7[5]	51.6
Mean age, year	44.9	*44.2*	*48.04*[12]	43.8	43.6[7]	49.4
Mean disease duration, year	8,1	*8.7*	*11,2*[10]	8.4	10.4[6]	9.5
Mean TJC	21.5[22]	NA	NA	21[14]	NA	NA
Mean SJC	11.6[22]	NA	NA	11.7[14]	NA	NA
Mean DAS 28	4.9[14]	NA	NA	4.9[8]	NA	NA
Mean HAQ	1.2[29]	NA	NA	1.2[17]	NA	NA
Concomitant CTC (%)	14.6[42]	*12.6*[9]	*28.3*[7]	12.2[28]	10.3[3]	23.6[5]
Concomitant csDMARDs, (%)	54.5[54]	*31*[14]	*35.9*[7]	47.5[37]	34,1[5]	40.7[8]
Concomitant NAIDS, (%)	78.8[35]	*72.3*[7]	*49.1*[4]	74.2[25]	83.8[3]	34.9[6]
Previous biologic	18.5[50]	19.2[14]	*33.4*[7]	20.5[34]	38.5[4]	59.6[6]
Mean BASDAI	6.6[21]	NA	NA	6.6[16]	NA	NA
Mean CRP	14.1[36]	*14.1*[9]	*13.4*[6]	13.5[26]	14.8[6]	8[3]
Mean BMI	29[24]	*28.7*[3]	*22.8*[4]	28[14]	27.3[3]	27.6[4]

Supplementary table 4. *Characteristics of patients treated with bDMARD or tDMARD included in RCT, OLE and observational studies.*

TJC: tender joint count; SJC: Swollen joint count; HAQ: health Assessment Questionnaire; DAS: Disease activity score; CTC: glucocorticoids; DMARD: Disease modifying anti-rheumatic drugs ; NSAID: non steroid anti-inflammatory drugs; PsA : Psoriatic arthritis; SpA : spondyloarthritis; BASDAI : Bath Ankylosing Spondylitis Disease Activity Index; CRP : C-reactive protein; BMI : Body mass index.

NA: not applicable.

	Incidence per 100 PY			
	Random-effects model	[95% CI]	I^2	p
Study design				
Retrospective	1.93	0.89-3.34	63	0.02
Prospective	1.58	0.68-2.83	95	0.01
Multicentric	1.56	0.80-2.54	92	0.01
Monocentric	2.09	0.19-5.83	72	0.03
NOS score				
High ≥ 6	1.56	0.74-2.65	94	0.01
Low ≤ 5	1.95	0.61-3.97	74	0.01
Class of treatment				
TNF inhibitor	1.87	0.96- 3.07	70	0.01
IL-17 inhibitor	0.35	(0.00-9.02)	8	0.30
Pathology				
Axial SpA	1.71	0.1- 4.94	76	0.01
Psoriatic arthritis	1.43	0.72- 2.35	84	0.01
Psoriatic arthritis and axial SpA	2.87	0.00-47.34	94	0.01

Supplementary table 5. *Subgroup analyses for serious infections in observational studies*

	k	Univariable analysis Coefficient [95% CI]	p
Year of publication	8	0.019 [-0.024; 0.062]	0.38
Total follow-up weeks	8	0.0006 [-0.0004; 0.0017]	0.23
Number of patients	8	0.0001 [-0.006; 0.0007]	0.87
Number of patients with CTC	4	-0.0013 [-0.0051; 0.0025]	0.49
Number of patients with csDMARD	5	0.0003 [-0.0012; 0.0017]	0.73
Number of patients with previous biotherapy	5	-0.0007 [-0.0020; 0.0006]	0.32

Supplementary table 6. *Meta-regression analyses for serious infections in observational studies*
CTC: glucocorticoids; csDMARD: conventional synthetic disease modifying anti-rheumatic drugs.

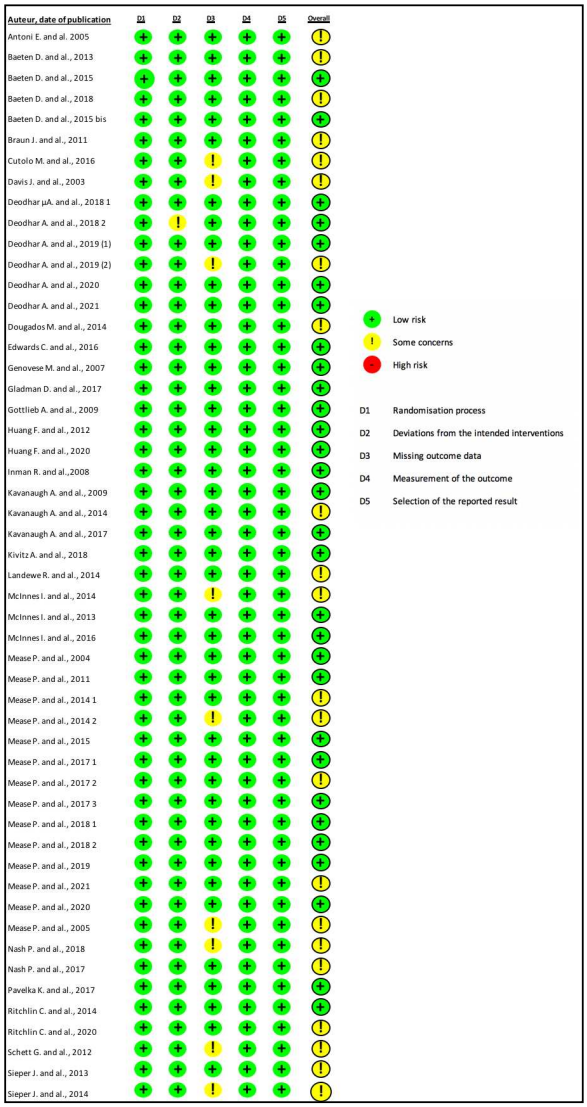
	Incidence per 100 PY			
	Random-effects model	[95% CI]	I^2	p
Study design				
Retrospective	11.70	0.00-42.65	97	<0.01
Prospective	18.12	2.11-49.27	99	<0.01
Multicentric	13.51	2.12-34.31	99	<0.01
Monocentric	18.06	0.00-77.36	98	<0.01
NOS score				
High ≥ 6	14.70	0.89-44.39	99	<0.01
Low ≤ 5	15.76	0.46-50.93	97	<0.01

Supplementary table 7. *Subgroup analyses for non-serious infections in observational studies*

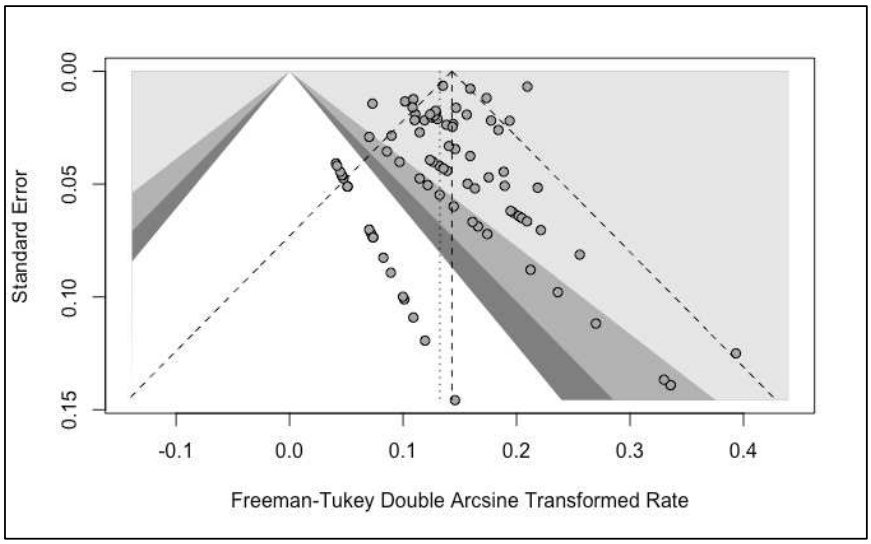
	k	Univariable analysis Coefficient [95% CI]	p	Multivariable analysis Coefficient [95% CI]	p
Randomized controlled trials					
Year of publication	37	-0.016 [-0.027; -0.0054]	0.0032	-0.013 [-0.023; -0.0022]	0.19
Total follow-up weeks	37	-0.0061 [-0.012; 0.00]	0.05	-0.005 [-0.010; 0.010Ø	0.10
Number of patients	37	-0.0003 [-0.0007; 0.0001]	0.13		
Number of patients CTC	28	-0.0021[-0.0043; 0.0001]	0.057		
Number of patients csDMARDs	36	-0.0007[-0.0013; -0.001]	0.03	-0.0004 [-0.0010; 0.0002]	0.15
Number of patients previous biotherapy	34	0.0002[-0.0006; 0.0010]	0.62		
Open label extension of RCTs					
Year of publication	8	-0.023 [-0.050; 0.0042]	0.098		
Total follow-up weeks	8	0.0006 [-0.0020; 0.0032]	0.64		
Number of patients	8	0.0002 [-0.0008; 0.0012]	0.66		
Number of patients CTC	0				
Number of patients csDMARDs	0				
Number of patients previous biotherapy	0				
Observational cohort studies					
Year of publication	10	0.012[-0.044; 0.067]	0.68		
Total follow-up weeks	9	0.0001[-0.0013;0.0015]	0.93		
Number of patients	10	-0.003[-0.0008;0.0002]	0.27		
Number of patients CTC	5	-0.0020[-0.0061; 0.0021]	0.34		
Number of patients csDMARDs	7	-0.0004[-0.0020; 0.0012]	0.64		
Number of patients previous biotherapy	7	-0.0008[-0.0016; -0.000]	0.040		

Supplementary table 8. *Meta-regression analyses for non-serious infections infections*

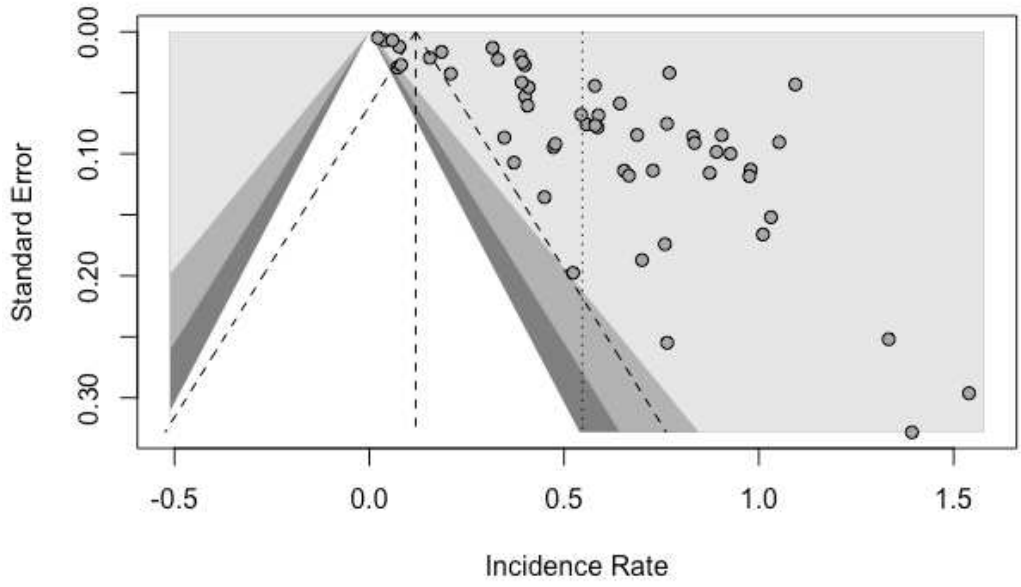
CTC: glucocorticoids; csDMARD: conventional synthetic disease modifying anti-rheumatic drugs.



Supplementary table 9. *Evaluation of bias for RCTs using Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) performed by one independent author (MS)*



Supplementary figure 1. *Funnel plot of IR of SI for the search of publication bias*



Supplementary figure 2. *Funnel plot of IR of NSI, for the search of publication bias*