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The Effects of bDMARDs on Quality of Life in Patients with Psoriatic Arthritis: Meta-analysis

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The Effects of bDMARDs on Quality of Life in Patients with

2	Psoriatic	Arthritis:	Meta-ana	lysis
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1 Abstract

- **Objectives:** To determine the effects of biological disease-modifying anti-rheumatic
- drugs (bDMARDs) on the quality of life (QoL) among patients with psoriatic arthritis
- 4 (PsA).
- **Design:** Meta-analysis.
- 6 Data sources and eligibility criteria: PubMed, Web of Science, Cochrane Library,
- 7 CNKI, WanFang, and VIP databases were searched to collect randomized controlled
- 8 trials (RCTs), which were conducted to evaluate the effect of bDMARDs in treatment
- 9 of patients with PsA and reported QoL-related outcomes, from inception to November
- 10 2020.
- 11 Data extraction and synthesis: Outcomes about Health Assessment Questionnaire
- 12 Disability Index (HAQ-DI), Dermatology Life Quality Index (DLQI), physical
- component summary (PCS) and mental component summary (MCS) of the Short Form
- 14 36 (SF-36), EuroQol Visual Analogue Scale (EQ-VAS), Psoriasis Area Severity Index
- 15 (PASI) 50/75/90/100 were extracted by two reviewers independently. Data were pooled
- using the fixed or random effects methods and considered as mean difference (MD) or
- 17 risk ratio (RR) with 95% CI.
- **Results:** Out of 2281 articles screened, 29 RCTs (with 40 articles reported) were
- included. Pooled estimates showed that bDMARDs were superior versus placebo on all
- 20 outcomes. Against methotrexate (MTX) and tofacitinib, bDMARDs showed no
- 21 statistically significant advantages or even significant disadvantages. Similar results
- 22 were found for bDMARDs+MTX versus MTX. For HAQ-DI, the results of the
- subgroups of bDMARDs vs. placebo, bDMARDs+MTX vs. MTX, bDMARDs vs.
- 24 tofacitinib, bDMARDs vs. MTX, were -0.24 (MD, 95% CI, -0.27, -0.21), -0.22 (MD,
- 25 95% CI, -0.58, 0.14), -0.01(MD, 95% CI, -0.05, 0.04), -0.03 (MD, 95% CI, -0.04, -
- 26 0.02) respectively.
- 27 Conclusions: Compared with placebo, bDMARDs taken by patients with PsA appear
- 28 to significantly improve the QoL. Compared with other therapeutic agents, more studies

1	are still required to confirm the effect of single and combined bDMARDs use further.
2	
3	Keywords: psoriatic arthritis; bDMARDs; quality of life; meta-analysis
4	
5	Strengths and limitations of this study
6	• The effects of bDMARDs on QoL among patients with PsA have not been
7	previously studied. Therefore, the results of this meta-analysis can inform
8	evidence-based decision-making in clinical practice.
9	• Subgroup analyses with the hierarchical structure were conducted to determine the
10	source of heterogeneity, according to the experimental groups and control groups
11	firstly, then category of bDMARDs, variety of bDMARDs, duration of PsA.
12	Because most of the included RCTs were multi-center studies, subgroup analysis
13	on the basis of countries and regions was not conduct to evaluate the effects of
14	bDMARDs on the QoL of different races patients.
15	• The follow-up period for all included studies didn't exceed 24 weeks, so that the
16	long-term effects can't be assessed.
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1. Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease that can lead to structural damage and disability, resulting in impaired quality of life (QoL), physical function, and working ability. [1-3] Scotti L et al. [4] synthesized results of twenty-eight studies and found that the prevalence and incidence rates of PsA are respectively 133 every 100,000 subjects and 83 every 100,000 person-years. PsA develops in up to 30% of patients with psoriasis. [5] Rosen CF et al. [6] found the QoL of patients with PsA is significantly lower than that of patients with psoriasis. Therefore, one of the main objectives of treating PsA is to improve the QoL of patients. Currently, the QoL of patients with PsA can be measured by the questionnaires including the Short Form 36 (SF-36) questionnaire, Health Assessment Questionnaire (HAQ), Nottingham Health Profile (NHP), EuroQoL 5 domains (EQ-5D), Psoriasis Area and Severity Index (PASI), Disease Activity for Psoriatic Arthritis (DAPSA), Psoriasis Disability Index (PDI), Dermatology Life Quality Index (DLQI), Skindex-29, Skindex-17, Psoriasis Arthritis Quality of Life (PsAQoL), [7-10] etc. Among these questionnaires, the higher scores of SF-36 and EQ-5D indicate higher levels of quality of life, while others are the opposite [11-16]. As a great advancement in the treatment of PsA, the biological disease-modifying

As a great advancement in the treatment of PsA, the biological disease-modifying anti-rheumatic drugs (bDMARDs) can decrease inflammation and block structural progression effectively, which have been proven.^[17-18] The bDMARDs are widely recommended by management guidelines,^[1,19] including the tumor necrosis factor inhibitor (TNFi, e.g. etanercept, infliximab, adalimumab, golimumab, certolizumab pegol), interleukin-17 inhibitor (IL-17i, e.g. ustekinumab, guselkumab, risankizumab), interleukin-12/23 inhibitor (IL-12/23i, e.g. secukinumab, ixekizumab, brodalumab).^[1,20] Ruyssen-Witrand A et al.^[21], Lu C et al. ^[22], and Lemos LL et al. ^[23] studied the efficacy and safety of bDMARDs in treating PsA, they found that the physical summarized component (PSC) of SF-36 score was improved, HAQ score and PASI score were decreased, but the change of mental summarized component (MSC) of SF-36 score was

not significant. It indicated that the effects of bDMARDs on QoL in PsA need to be further studied.

The purpose of this study is to conduct a meta-analysis of randomized controlled trials (RCTs) related to bDMARDs in treating PsA, to comprehensively evaluate the effects of bDMARDs on QoL with multiple outcome indicators, and to provide evidence for supporting pharmacists' and physicians' clinical actions and decisions in treating PsA. The SF-36, HAQ, NHP, and EQ-5D are generic instruments, scores measured by them are the primary outcomes of this study. The scores measured by other disease-specific instruments are the secondary outcomes.

2. Materials and methods

2.1 Search strategy and study selection

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.^[24] To identify RCTs reporting the effects of bDMARDs on QoL, two independent authors (YQL and ZJD) electronically conducted the searches in PubMed, Web of Science, the Cochrane Library, China National Knowledge Infrastructure (CNKI), WanFang Database, and VIP Datebase, from inception to November 2020. The keywords used for database search were: patients, including "psoriatic arthritis"; intervention, including "etanercept" or "infliximab" or "adalimumab" or "golimumab" or "certolizumab" or "ustekinumab" or "guselkumab" or "risankizumab" or "tildrakizumab" "secukinumab" or "ixekizumab" or "brodalumab" or "tumor necrosis factor inhibitor" or "TNFi" or "interleukin-12/23 inhibitor" or "IL-12/23i" or "interleukin-17 inhibitor" or "IL-17i" or "biologic"; and outcomes, including "health-related quality of life" or "HRQoL" or "Dermatology Life Quality Index" or "DLQI" or "disease activity index for psoriatic arthritis" or "DAPSA" or "psoriasis area and severity index" or "PASI" or "short form-36" or "SF-36" or "health assessment questionnaire" or "HAQ" or "Nottingham Health Profile" or "NHP" or "EuroQol-5D" or "EQ-5D" or "psoriasis disability index" or "PDI" or "Skindex-29" or "Skindex-17" or "PsAQoL" or "quality

- of life". To avoid missing any related study, authors checked reference lists of eligible
- 2 articles as an additional search. Researches were limited to RCTs published in English
- 3 and Chinese. The complete electronic search strategy for PubMed is provided in
- 4 supplementary table S1.

2.2 Inclusion and exclusion criteria

Studies were independently selected by two authors (YQL and ZJD), and they achieved good agreement (κ =0.879). Studies were included if they met the following inclusion criteria: (i) the trial was a human study conducted in patients with PsA; (ii) the experimental group was treated with bDMARDs or bDMARDs combined with other non-bDMARDs, while placebo and other non-bDMARDs was used as the control group; (iii) the study provided appropriate data (means and standard deviation [SD] of continuous outcomes, the events number of dichotomous outcomes) for each group present at baseline and end of intervention for DLQI, DAPSA, PASI, SF-36, HAQ, NHP, EQ-5D, PDI, Skindex, and PsAQoL. Other studies, including animal experiments, in-vitro studies, case reports, observational studies, systematic reviews, duplicate publications, study protocols without findings, or congress abstracts without full texts were excluded.

2.3 Data extraction and quality assessment

Two authors (YQL and ZJD) independently extracted data from each selected RCTs using a standard abstraction excel sheet (κ =0.962). The extracted data included trial name, sample size, characteristics of participants, duration of treatment, and outcomes of interest. The methodological quality of the selected RCTs was evaluated by two independent investigators (YQL and ZJD) using the Cochrane Collaboration risk of bias tool (κ =0.971).^[25] The Cochrane Collaboration risk of bias tool used the following criteria for quality assessment: randomization generation, allocation concealment, blinding of participants and outcome assessment, incomplete outcome data, and selective outcome reporting, and other sources of bias. Any disagreement between authors was resolved by discussion and final consensus between authors or a

third author (FC) approved the findings.

2.4 Data synthesis and statistical analysis

All statistical analyses were conducted using Review Manager V.5.3 software (Cochrane Collaboration, Copenhagen, Denmark) and STATA software version 16.0 (Stata Corp., College Station, TX). The risk ratio (RR) with 95% CI was used to evaluate dichotomous outcomes, and the mean difference (MD) with 95% CI was generated to evaluate continuous outcomes. Heterogeneity was assessed by using the I^2 estimate and the P-value of the χ^2 -test. If the P-value >0.10 and I^2 <50%, the assumption of homogeneity was made and the fixed-effects model (FE) was used for analyses. Otherwise, heterogeneity was assumed, the random-effects model (RE) was used to analyze and its source should be further determined by sensitivity analysis or subgroup analysis. Sensitivity analyses were conducted using a leave-one-out method to determine the effect of each trial on the reliability of overall pooled effect sizes. Further, subgroup analyses were carried out to determine the source of heterogeneity according to the potential moderator variables. First, the subgroup analyses were conducted according to the experimental groups and control groups (bDMARDs vs. placebo, bDMARDs+ methotrexate [MTX] vs. MTX, bDMARDs vs. tofacitinib, bDMARDs vs. MTX), which was probably the biggest cause of heterogeneity. Then, each subgroup was analyzed according to the following variables: category of bDMARDs (TNFi, IL-12/23i, IL-17i), variety of bDMARDs (etanercept, infliximab, adalimumab, etc.), duration of PsA (<6 years, 6-9 years, ≥9 years, unclear), duration of treatment (<24 weeks, \geq 24 weeks). The funnel plot, as well as Egger's test were used to determine any possible publication bias.

3. Results

3.1 Search Results

The detailed step-by-step process of article identification and selection is presented in figure 1. In online searches, initially, 2281 articles were identified. After duplicates and irrelevant articles were removed, 40 articles^[26-65] (29 RCTs reported)

- were ultimately included in the meta-analysis. There was a total of 9720 participants.
- 2 Twenty RCTs have reported the effects of bDMARDs on HAQ Disability Index (HAQ-
- 3 DI), 20 RCTs on SF-36 PCS, 16 RCTs on SF-36 MCS, 1 RCT on SF-36 score, 8 RCTs
- 4 on DLQI, 3 RCTs on EuroQol Visual Analogue Scale (EQ-VAS), 2 RCTs on PsAQoL,
- 5 1 RCT on DAPSA, 7 RCTs on the proportion of participants achieving 50%
- 6 improvement from baseline in PASI (PASI 50), 2 RCTs on PASI 70, 23 RCTs on PASI
- 7 75, 20 RCTs on PASI 90, 7 RCTs on PASI 100 and 1 RCT on PASI score. Among
- 8 them, HAQ-DI, DLQI, PsAQoL, DAPSA, and PASI scores are negative outcomes,
- 9 higher scores indicate worse health-related QoL, while the others are opposite. The
- detailed characteristics of selected RCTs are summarized in supplementary table S2.
- 11 The methodological quality assessment of RCTs based on the Cochrane Collaboration
- 12 risk of bias tool is shown in figure 2. Meta-analysis was not performed for the outcomes
- reported in less than 3 RCTs.

3.2 Main outcomes

- Forest plots demonstrating the effects of bDMARDs on QoL were provided in
- supplementary figure S1-S9. The pooled effect sizes of all outcomes were summarized
- in table 1. The results showed that bDMARDs taken by patients with PsA can decrease
- 18 HAQ-DI (MD=-0.22; 95% CI, -0.25, -0.18; *P* < 0.00001; *P*: 100%), DLQI (MD=-4.36;
- 19 95% CI, -5.76, -2.96; P < 0.00001; P: 99%), and improve SF-36 PCS (MD=3.89; 95%
- 20 CI, 3.44, 4.34; P < 0.00001; P: 99%), SF-36 MCS (MD=1.82; 95% CI, 1.24, 2.40; P
- 21 <0.00001; *I*²: 98%), EQ-VAS (MD=5.27; 95% CI, 1.21, 9.34; *P* <0.00001; *I*²: 99%),
- 22 PASI 50 (RR=4.09; 95% CI, 2.71, 6.16; P<0.00001; I²: 82%), PASI 75 (RR=4.73; 95%
- 23 CI, 3.77, 5.95; P <0.00001; I²: 84%), PASI 90 (RR=5.44; 95% CI, 4.30, 6.89; P
- 24 <0.00001; *P*: 66%), PASI 100 (RR=9.11; 95% CI, 6.75, 12.31; *P* <0.00001; *P*: 26%)
- significantly. The changes in all outcomes meant that the bDMARDs can effectively
- improve the QoL of patients with PsA.

Table 1 Meta-analysis of RCTs that examined the effects of bDMARDs on QoL

Outcomes	Number of	Effect	Effect	05% CI	I ² (%)	P-value
Outcomes	trials	model	size	95% CI	12 (%)	P-value

Primary outcome	Primary outcomes							
HAQ-DI	20	RE	-0.22	-0.25, -0.18	100	< 0.00001		
SF-36 PCS	20	RE	3.89	3.44, 4.34	99	< 0.00001		
SF-36 MCS	16	RE	1.82	1.24, 2.40	99	< 0.00001		
EQ-VAS	3	RE	5.27	1.21, 9.34	99	0.01		
Secondary outcom	mes							
DLQI	8	RE	-4.36	-5.76, -2.96	99	< 0.00001		
PASI 50	7	RE	4.09	2.71, 6.16	82	< 0.00001		
PASI 75	23	RE	4.73	3.77, 5.95	84	< 0.00001		
PASI 90	20	RE	5.44	4.30, 6.89	66	< 0.00001		
PASI 100	7	FE	9.11	6.75, 12.31	26	< 0.00001		

HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36, DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; PASI 50/75/90/100, the proportion of participants achieving 50%/75%/90%/100% improvement from baseline in Psoriasis Area Severity Index; FE, fixed-effects model; RE, random-effects model.

3.3 Sensitivity analysis

With the exclusion of any single study, the heterogeneity did not change materially in terms of any outcomes. After excluding NCT02181673 (GO-VIBRANT), post-sensitivity pooled MD for EQ-VAS was 3.71 (95% CI: -0.58, 7.99), which differed from pre-sensitivity significantly. We did not find any statistical significant difference between pre- and post-sensitivity pooled MDs or RRs for HAQ-DI, SF-36 PCS, SF-36 MCS, DLQI, PASI 50, PASI 75, and PASI 90. The detailed results of sensitivity analyses are presented in table 2.

Table 2 Sensitivity analysis of RCTs that examined the effects of bDMARDs on QoL

43								
43 44	Pre-sensitivity analysis			Upper &	Post-sensitivity analysis			
45 Outcomes 46 47	Number of trials	Pooled estimates	95% CI	lower of effect size	Pooled estimates	95% CI	Excluded trials	
48 HAQ-DI	20	-0.22	-0.25, -0.18	Upper	-0.19	-0.23, -0.15	Mease PJ 2000	
19				Lower	-0.25	-0.28, -0.21	NCT00265096 (GO-REVEAL)	
50 SF-36 PCS	20	3.89	3.44, 4.34	Upper	4.12	3.67, 4.56	NCT01877668 (OPAL Broaden)	
52				Lower	3.76	3.30, 4.22	NCT00265096 (GO-REVEAL)	
SF-36 MCS	16	1.82	1.24, 2.40	Upper	2.22	1.63, 2.81	NCT01877668 (OPAL Broaden)	
54 55				Lower	1.70	1.11, 2.29	NCT00265096 (GO-REVEAL)	
66 EQ-VAS	3	5.27	1.21, 9.34	Upper	9.66	5.34, 13.98	NCT01877668 (OPAL Broaden)	
57 58				Lower	3.71	-0.58, 7.99	NCT02181673 (GO-VIBRANT)	
59 DLQI	8	-4.36	-5.76, -2.96	Upper	-3.50	-5.00, -2.00	NCT01392326 (FUTURE 1)	

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3					Lower	-5.67	-6.71, -4.62	NCT01695239 (SPIRIT-P1)
•	PASI 50	7	4.09	2.71, 6.16	Upper	4.83	2.75, 8.49	NCT01087788 (RAPID-PsA)
6					Lower	3.30	2.29, 4.78	NCT00265096 (GO-REVEAL)
8	PASI 75	23	4.73	3.77, 5.95	Upper	5.10	4.26, 6.09	NCT01877668 (OPAL Broaden)
9					Lower	4.50	3.60, 5.62	NCT00265096 (GO-REVEAL)
10	PASI 90	20	5.44	4.30, 6.89	Upper	5.84	4.39, 7.78	NCT02404350 (FUTURE 5)
12					Lower	5.13	4.06, 6.50	NCT01392326 (FUTURE 1)

- HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component
- 2 summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36;
- 3 DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; PASI 50/75/90,
- 4 the proportion of participants achieving 50%/75%/90% improvement from baseline in Psoriasis
- 5 Area Severity Index.

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3.4 subgroup analysis

Following subgroup analyses, heterogeneity was changed among some of the strata of subgroups. In regard to the subgroup of bDMARDs vs. placebo, there was a significant difference between pre- and post-subgroup analysis for HAQ-DI in strata of golimumab (MD=0.08; 95% CI, -0.53, 0.69) and strata of < 24 weeks (MD=-0.50; 95% CI, -1.09, 0.09), SF-36 MCS in strata of adalimumab (MD=1.00; 95% CI, -0.50, 2.49) and strata of < 24 weeks (MD=-0.50; 95% CI, -1.09, 0.09), DLQI in strata of adalimumab, ixekizumab, and 6-9 years, PASI 75 in strata of infliximab. Similar results were found for HAQ-DI and SF-36 MCS in the subgroup of bDMARDs+MTX vs. MTX, HAQ-DI, SF-36 MCS, EQ-VAS, and PASI 75 in the subgroup of bDMARDs vs. tofacitinib, SF-36 MCS in the subgroup of bDMARDs vs. MTX. In general, bDMARDs had obvious advantages in improving the QoL of PsA compared with placebo, but bDMARDs plus MTX compared with MTX, bDMARDs compared with tofacitinib, and bDMARDs compared with MTX had no obvious advantages or even disadvantages in improving the QoL of PsA. Taking the outcome of HAQ-DI as an example, the results of the subgroups of bDMARDs vs. placebo, bDMARDs+MTX vs. MTX, bDMARDs vs. tofacitinib, bDMARDs vs. MTX, were -0.24 (MD, 95% CI, -0.27, -0.21), -0.22 (MD, 95% CI, -0.58, 0.14), -0.01(MD, 95% CI, -0.05, 0.04), -0.03 (MD, 95% CI, -0.04, -0.02) respectively. The detailed results of the subgroup analysis are presented in supplementary table S3.

3.5 Publication bias

- 2 Since the funnel chart requires a certain amount of literature, this study drew
- 3 funnel charts for the outcomes that include more than 10 RCTs. As presented in figure
- 4 3, there was potential publication bias for the outcomes including HAQ-DI, SF-36 PCS,
- 5 SF-36 MCS, PASI 75, PASI 90. The P-value was calculated by Egger's test based on
- 6 these outcomes also suggested the presence of publication bias.

4. Discussion

- 8 This meta-analysis focused on the effects of bDMARDs on QoL in patients with
- 9 PsA, involving a total of 29 RCTs and 9720 participants. Through the quantitative
- analysis of 9 outcomes, it was found that bDMARDs could effectively improve the QoL
- of patients with PsA. By comparing the minimal results of the research on the minimal
- 12 clinically important difference (MCID) related to the concerned outcomes, it was found
- that the decrease of HAQ-DI (MD=-0.22; 95% CI, -0.25, -0.18) was a probable
- clinically meaningful effect (< -0.131) [66-67]. Similar results were found for SF-36 PCS
- 15 (MD=3.89; 95% CI, 3.44, 4.34; > 2.1) [68-71], SF-36 MCS (MD=1.82; 95% CI, 1.24,
- 2.40; > 1.33)^[69-71], and DLQI (MD=-4.36; 95% CI, -5.76, -2.96; < -2.24) ^[72], but not
- 17 for EQ-VAS (MD=5.27; 95% CI, 1.21, 9.34, < 5.35) [73-76].
- Since the medicines in experimental and control groups had large differences in
- 19 the effects on QoL, subgroup analysis was conducted according to the experimental
- 20 groups and control groups. The results showed that there was obvious dissimilarity in
- 21 subgroups of bDMARDs compared with placebo, tofacitinib, and methotrexate,
- concerning HAQ-DI, SF-36 PCS, SF-36 MCS, EQ-VAS, and PASI 75. The bDMARDs
- 23 had a significant effect on improving the QoL compared with placebo, but more
- 24 experimental data were required to confirm the effects of bDMARDs compared with
- 25 tofacitinib and methotrexate.
- Looking specifically at the subgroup of bDMARDs vs. placebo, variety of
- 27 bDMARDs and duration of treatment were probable sources of heterogeneity.
- 28 Infliximab, golimumab, adalimumab, and ixekizumab had no significant difference

1 from placebo concerning one or two of HAQ-DI, SF-36 MCS, DLQI, and PASI 75,

which might be due to the efficacy of these bDMARDs can not be reflected on the

change of QoL. The bDMARDs had no significant difference from placebo in the

subgroup of duration of treatment < 24 weeks, which might indicate that long-term use

of bDMARDs can improve the QoL of patients.

In our study, quantitative analysis was not performed on the outcomes that reported in less than 3 RCTs, including SF-36 score, PsAQoL, DAPSA, PASI 70, and PASI score. According to NCT02376790 (SEAM-PsA) [50-61], etanercept or plus MTX could decrease DAPSA and improve SF-36 score compared with MTX, but without statistical difference. The results of NCT01087788 (RAPID-PsA) [43-44] and NCT01392326 (FUTURE 1) [45-46] showed that certolizumab pegol and secukinumab could significantly decrease PsAQoL compared with placebo. As for PASI 70, Hong Tao et al. [27] found that infliximab plus MTX got more significant improvement than MTX, while NCT02065713 (GO-DACT)[53] found that golimumab plus MTX had no difference form MTX. Besides, Hong Tao et al. [27] found that in MTX group. Taken together, the quantitative analysis results of the effects of bDMARDs on the QoL of PsA patients is robust.

The patients who have taken bDMARDs showed an improvement in term of SF-36 PCS, EQ-VAS, PASI 50, and PASI 90, which was consistent with the results of previous studies [21-23]. Our meta-analysis got an improvement in term of SF-36 MCS, which was inconsistent with the results of Lemos LL et al [23]. Furthermore, this meta-analysis comprehensively and specifically analyzed the effects of bDMARDs on the QoL of patients with PsA, and quantitatively analyzed some other outcomes including HAQ-DI and DLQI, which were not studied before. The results of this meta-analysis can be used as a powerful supplement to the evidence for the reasonable clinical application of bDMARDs.

However, there were several limitations of this meta-analysis. First, all the

- included studies were published in English and Chinese, and the results of Egger's test indicated the presence of publication bias. Second, most of the included RCTs were multi-center studies. It was difficult to conduct subgroup analysis on the basis of countries and regions to evaluate the effects of bDMARDs on the QoL of different races patients. Third, the follow-up period for all included studies didn't exceed 24 weeks, so that the long-term effects can't be assessed. Thus, more studies which are relevant to the longer follow-up period of bDMARDs in the treatment of PsA are required in the future to confirm the long-term effect of bDMARDs on the QoL of PsA patients.
 - 5. Conclusions
 - In summary, our meta-analysis demonstrated that bDMARDs used in patients with PsA compared with placebo appeared to significantly improve the QoL. Compared with therapeutic agents, more studies are still required to confirm the effect of single and combined bDMARDs use further.

- Figure 1 Flowchart of the study selection. RCT, randomized controlled trial.
- Figure 2 Quality assessment of included RCTs using Cochrane's risk of bias tool, RCT, randomized
- 17 controlled trial.
- Figure 3 Funnel plots of HAQ-DI, SF-36 PCS, SF-36 MCS, PASI 75, and PASI 90. HAQ-DI,
- 19 Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of
- the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36; PASI 75/90,
- 21 the proportion of participants achieving 75%/90% improvement from baseline in Psoriasis Area
- 22 Severity Index.

- Contributors YQL substantially contributed to the conception and design of the research, and the acquisition, analysis and interpretation of data; involved in drafting
- 26 the manuscript and revising it critically for important intellectual content; ZJD
- substantially contributed to the acquisition, analysis and interpretation of data; involved
- in drafting the manuscript and revising it critically for important intellectual content;

- 1 YL substantially contributed to the conception and design of the research; involved in
- 2 revising the manuscript critically for important intellectual content; FC substantially
- 3 contributed to the conception and design of the research, and the acquisition, analysis
- 4 and interpretation of data; involved in revising the manuscript critically for important
- 5 intellectual content. All authors give their approval for the manuscript to be submitted
- 6 in BMJ Open and agree to be accountable for all aspects of the work.

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Competing Interests None declared.

- 13 Patient and public involvement Patients and/or the public were not involved in the
- design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

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- study was based solely on the summary results of previously published articles.
- 20 Individual patient data were not obtained or accessed.

- **Data availability statement** All data relevant to the study are included in the article,
- 23 supplementary materials, or can be found from references. No additional data are
- 24 available.

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6 2016;71:493-500.

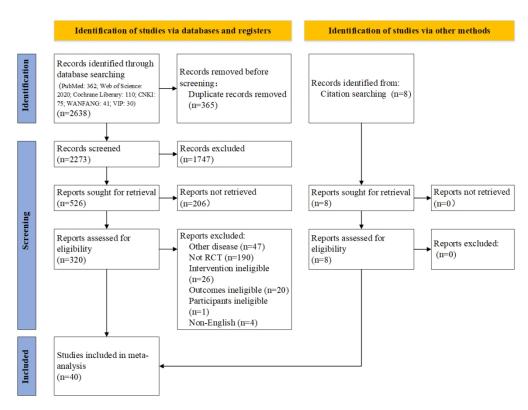


Figure 1 Flowchart of the study selection. RCT, randomized controlled trial.

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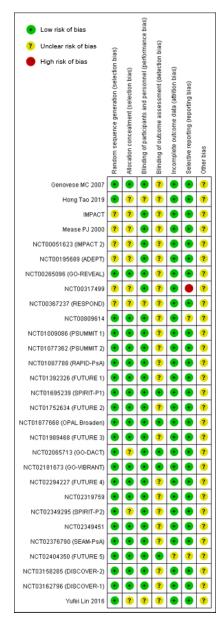
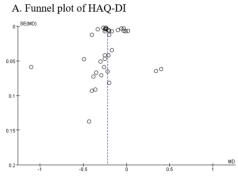
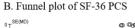
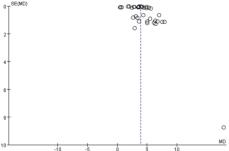


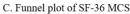
Figure 2 Quality assessment of included RCTs using Cochrane's risk of bias tool, RCT, randomized controlled trial.

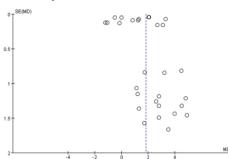
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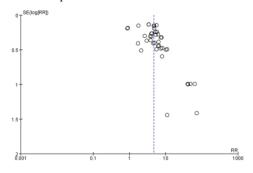








D. Funnel plot of PASI 75



E. Funnel plot of PASI 90

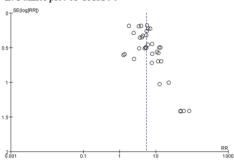


Figure 3 Funnel plots of HAQ-DI, SF-36 PCS, SF-36 MCS, PASI 75, and PASI 90. HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36; PASI 75/90, the proportion of participants achieving 75%/90% improvement from baseline in Psoriasis Area Severity Index.

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Content

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Table S2. Subgroup analysis of RCTs that examined the effect of bDMARDs on QoL7
Figure S1 Forest plot of HAQ-DI
Figure S2. Forest plot of SF-36 PCS
Figure S3. Forest plot of SF-36 MCS
Figure S4. Forest plot of DLQI
Figure S5. Forest plot of EQ-VAS
Figure S6. Forest plot of PASI 50
Figure S7. Forest plot of PASI 75
Figure S8. Forest plot of PASI 90
Figure S9. Forest plot of PASI 100

Table S1. Full electronic search strategy of PubMed

#1 "arthritis, psoriatic" [MeSH Terms] #2 "etanercept" [Title/Abstract] OR "infliximab" [Title/Abstract] OR "adalimumab" [Title/Abstract] OR "golimumab"[Title/Abstract] OR "certolizumab"[Title/Abstract] OR "ustekinumab"[Title/Abstract] OR "guselkumab"[Title/Abstract] OR "risankizumab"[Title/Abstract] OR "tildrakizumab"[Title/Abstract] OR "secukinumab"[Title/Abstract] OR "ixekizumab"[Title/Abstract] OR "brodalumab"[Title/Abstract] OR "tumor necrosis factor inhibitor"[Title/Abstract] OR "TNFi"[Title/Abstract] OR "IL-12/23i"[Title/Abstract] "interleukin-12/23 inhibitor"[Title/Abstract] OR "IL-17i"[Title/Abstract] OR "interleukin-17 inhibitor"[Title/Abstract] OR "biologic"[Title/Abstract] #3 "health-related quality of life"[All Fields] OR "HRQoL"[All Fields] OR "Dermatology Life Quality Index"[All Fields] OR "DLQI"[All Fields] OR "disease activity index for psoriatic arthritis"[All Fields] OR "DAPSA"[All Fields] OR "psoriasis area and severity index"[All Fields] OR "PASI"[All Fields] OR "short form-36"[All Fields] OR "SF-36"[All Fields] OR "health assessment questionnaire"[All Fields] OR "HAQ"[All Fields] OR "Nottingham Health Profile" [All Fields] OR "NHP" [All Fields] OR "EuroQol-5D" [All Fields] OR "EQ-5D"[All Fields] OR "psoriasis disability index"[All Fields] OR "PDI"[All Fields] OR "Skindex-29"[All Fields] OR "Skindex-17" [All Fields] OR "quality of life" [All Fields] OR "PsAQoL" [All Fields] **#4** #1 AND #2 AND #3

Table S2. Characteristics of included studies

Trial name[Ref.]	Treatment arms and doses	Sample size (male, %)	Age, years	Duration of PsA, years	Duration of treatment	Presented outcomes
Genovese MC 2007	Adalimumab 40 mg SC q2w	51 (56.9)	50.4±11.0	755±7.0	12 weeks	1235
[26]	Placebo	49 (51.0)	47.7±11.3	.∾ 7 © 2±7.0		
Hong Tao 2019 [27]	Infliximab 3mg /kg IV at weeks 0,2,6,14,22,24 +MTX	33 (57.58)	35.63±6.12	3. ≦ 6±1.29	24 weeks	1012
	MTX 15.36±1.69 mg q1w	33 (54.55)	35.94±6.25	3. 8 2±1.28		
IMPACT [28]	Infliximab 5 mg/kg at weeks 0, 2, 6, 14	52 (57.7)	45.7±11.1	1 <u>₹</u> 7±9.8	16 weeks	11)
	Placebo	52 (57.7)	45.2±9.7	1 <mark>₹</mark> .0±6.6		
Mease PJ 2000 [29]	Etanercept 25 mg SC BIW	30 (53)	46.0*	9.0*	12 weeks	1111
	Placebo	30 (60)	43.5*	9 .5*		
NCT00051623	Infliximab 5 mg/kg IV at weeks 0, 2, 6, 14, 22	100 (71)	47.1±12.8	% 4±7.2	24 weeks	123
(IMPACT 2) [30,31,32]	Placebo	100 (51)	46.5±11.3	7 2 5±7.8		91112
NCT00195689	Adalimumab 40 mg SC at weeks 0, 2, 4, then q4w	151 (56.3)	48.6±12.5	928±8.3	24 weeks	1235
(ADEPT) [33,34,35]	Placebo	162 (54.9)	49.2±11.1	9 2 2±8.7		9111213
NCT00265096 (GO-	Golimumab 50 mg SC q4w	146 (61)	45.7±10.7	7 <u>5</u> 2±6.8	24 weeks	123
REVEAL) [36,37]	Golimumab 100 mg SC q4w	146 (59)	48.2±10.9	7 <u>.</u> 7±7.8		91112
	Placebo	113 (61)	47.0±10.6	∞ 16±7.9		
NCT00317499 [38]	Etanercept 25 mg SC BIW	101 (57)	47.6	22 9	24 weeks	911
	Placebo	104 (45)	47.3	9.2		
NCT00367237	Infliximab 5 mg/kg at weeks 0, 2, 6, 14 + MTX	56 (48.2)	40.1±12.3	2 <u>5</u> 8±2.6	16 weeks	11112
(RESPOND) [39]	MTX 15 mg q1w	54 (61.1)	42.3±10.5	3 <mark>5</mark> 7±2.7		
NCT00809614 [40]	Secukinumab 10 mg/kg SC on days 1, 22	28 (32)	46.7±11.3	623±6.8	24 weeks	2
	Placebo	14 (43)	47.6±8.1	5 <mark>€</mark> 1±3.8		

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NCT01009086	Ustekinumab 45 mg SC at weeks 0,2, then q12w	205 (51.7)	48.0 (39.0-55.0)*	3.4(7.2-9.2)*	24 weeks	1235
(PSUMMIT 1) [41]	Ustekinumab 90 mg SC at weeks 0,2, then q12w	204 (56.9)	47.0 (38.5-54.0)*	4.9(\frac{1}{1.7-8.3})*		1
	Placebo	206 (52.4)	48.0 (39.0-57.0)*	3.6 (2.0-9.7)*		
NCT01077362	Ustekinumab 45 mg at weeks 0, 4, then q12w	103 (46.6)	49.0(40.0-56.0)*	5.3(8/3-12.2)*	24 weeks	1235
(PSUMMIT 2) [42]	Ustekinumab 90 mg at weeks 0, 4, then q12w	105 (46.7)	48.0(41.0-57.0)*	4.5(1.7-10.3)*		1112
	Placebo	104 (49.0)	48.0(38.5-56.0)*	5.5 (2.3-12.2)*		
NCT01087788	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 200	138 (46.4)	48.2±12.3	9 <u>6</u> ±8.5	24 weeks	1235
(RAPID-PsA) [43,44]	mg q2w			ded		791112
	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 400	135 (45.9)	47.1 ± 10.8	851±8.3		
	mg q4w			- http:		
	Placebo	136 (41.9)	47.3±11.1	7 <u>3</u> 9±7.7		
NCT01392326	Secukinumab 75 mg/kg IV at weeks 2, 4, then 75 mg	202 (41.6)	48.8±12.2	njop	24 weeks	1235
(FUTURE 1) [45,46]	SC q4w			en.b		7112
	Secukinumab 75 mg/kg IV at weeks 2, 4, then 150 mg	202 (47.5)	49.6±11.8	<u> </u>		
	SC q4w			njopen.bmj.com/ on		
	Placebo	202 (47.5)	48.5±11.2	_		
NCT01695239	Ixekizumab 80 mg SC q2w	107 (42.1)	49.1 ± 10.1	6 <u>2</u> ±6.4	24 weeks	1235
(SPIRIT-P1) [47,48]	Ixekizumab 80 mg SC q4w	103 (46.6)	49.8 ± 12.6	7嘉 ± 8.0		6(1)(12(13)
	Adalimumab 40 mg SC q2w	101 (50.5)	48.6 ± 12.4	$6\% \pm 7.5$		
	Placebo	106(45.3)	50.6 ± 12.3	6\$\div \pm 6.9		
NCT01752634	Secukinumab 300 mg SC q1w to week 4 then q4w	100 (51)	46.9±12.6	gue:	24 weeks	121112
(FUTURE 2) [49]	Secukinumab 150 mg SC q1w to week 4 then q4w	100 (55)	46.5±11.7	guest. Protected by		
	Secukinumab 75mg SC q1w to week 4 then q4w	99 (47)	48.6 ± 11.4	rote		
	Placebo	98 (41)	49.9±12.5	ctec		

		Уорен		njopen-2021-05849		
NCT01877668	Adalimumab 40 mg SC q2w	106 (53)	47.4 ± 11.3	53 ± 5.3	3 months	1236
(OPAL Broaden)	Tofacitinib 5 mg orally BID	107 (47)	49.4 ± 12.6	$7\frac{1}{8} \pm 8.2$		11)
[50][51]	Tofacitinib 10 mg orally BID	104 (40)	46.9 ± 12.4	5∰±5.8		
	Placebo	105 (47)	47.7 ± 12.3	6 <u>₹</u> ±6.4		
NCT01989468	Secukinumab 300 mg SC at weeks 1, 2, 3, 4, then q4w	139 (48.2)	49.3±12.9	8:3±9.2	24 weeks	121112
(FUTURE 3) [52]	Secukinumab 150 mg SC at weeks 1, 2, 3, 4, then q4w	138 (44.2)	50.1 ± 11.7	7 <u>§</u> 7±8.5		
	Placebo	137 (43.1)	50.1 ± 12.6	€ <u>€</u> 6±6.9		
NCT02065713 (GO-	Golimumab 50 mg SC q4w + MTX	21 (81.0)	46.2 (15.5)*	3.8 (6.7)*	24 weeks	91012
DACT) [53]	MTX 15 mg orally q1w and increased 5 mg q4w until	22 (87.0)	44.1 (24.6)*	4. (6.1)*		
	25 mg q1w			http		
NCT02181673 (GO-	Golimumab 2 mg/kg IV at weeks 0, 4, then q8w	241 (50.6)	45.7 ± 11.3	6 ± 6.0	24 weeks	1235
VIBRANT) [54,55]	Placebo	239 (53.1)	46.7 ± 12.5	$5\vec{8} \pm 5.9$		6111213
NCT02294227	Secukinumab 150 mg SC q4w LD	114 (41.2)	48.3±12.2	5.6±7.3	16 weeks	21112
(FUTURE 4) [56]	Secukinumab 150 mg SC q4w no-LD	113 (45.1)	50.4 ± 11.8	5 <mark>=</mark> 7±7.7		
	Placebo	114 (39.5)	48.5±12.2	6 9±7.6		
NCT02319759 [57]	Guselkumab 100 mg SC at weeks 0, 4, then q8w	100 (52)	47.4±12.8	7 . 0±7.2	24 weeks	1239
	Placebo	49 (49)	44.2±12.4	€9±7.2		111213
NCT02349295	Ixekizumab 80 mg SC q4w	122 (52)	52.6±13.6	1₹0±9.6	24 weeks	123
(SPIRIT-P2) ^[58]	Ixekizumab 80 mg SC q2w	123 (41)	51.7±11.9	989±7.4		111213
	Placebo	118 (47)	51.5±10.4	£2±7.3		
NCT02349451 [59]	Adalimumab 40 mg SC q1w	72 (54.2)	50.5±12.0	8 5 4±9.2	12 weeks	1112
	Placebo	24 (50.0)	50.5 ± 12.0	7 <u>-</u> 6±7.2		
NCT02376790	Etanercept 50 mg SC q1w	284 (53.2)	48.5±13.5	3 6 1±6.0	24 weeks	1234
(SEAM-PsA) [60,61]	Etanercept 50 mg SC + MTX orally q1w	283 (50.9)	48.1 ± 12.7	3 <u>≅</u> 0±6.0		8
		5		±6.0 ±6.0 by copyright.		

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	MTX 20 mg orally q1w	284 (43.7)	48.7±13.1	₹ 356±6.8		
		. ,				
NCT02404350	Secukinumab 300 mg SC q4w LD	222 (48.6)	48.9 ± 12.8	$6\frac{3}{18}\pm 8.3$	16 weeks	1112
(FUTURE 5) [62]	Secukinumab 150 mg SC q4w LD	220 (50.5)	48.4 ± 12.9	6 ₫ ±7.1		
	Secukinumab 150 mg SC q4w no-LD	222 (54.1)	48.8 ± 11.8	$6 = \pm 6.1$		
	Placebo	332 (48.5)	49.0 ± 12.1	$6\cancel{8} \pm 7.6$		
NCT03158285	Guselkumab 100mg SC at weeks 0,4, then q4w	245 (58)	45.9±11.5	5€5±5.9	24 weeks	123
(DISCOVER-2) [63]	Guselkumab 100mg SC at weeks 0,4, then q8w	248 (52)	44.9±11.9	5 <u>\$</u> 1±5.5		111213
	Placebo	246 (48)	46.3 ± 11.7	5 2 8±5.6		
NCT03162796	Guselkumab 100 mg SC q4w	128 (52)	47.4±11.6	€6±6.3	24 weeks	123
(DISCOVER-1) [64]	Guselkumab 100 mg SC at weeks 0, 4, then q8w	127 (54)	48.9 ± 11.5	64±5.9		111213
	Placebo	126 (48)	49.0 ± 11.1	7 <u>2</u> ±7.6		
Yufei Lin 2016 [65]	Infliximab 5mg /kg IV at weeks 0,2,6,12 + MTX	42 (61.90)	44.01±10.33	3. 6 2±2.11	24 weeks	14)
	MTX 7.5-15 mg orally q1w and increased to 15-25 mg	42 (66.67)	43.59 ± 10.29	$3.\frac{2}{3}1\pm2.12$		
	q1w			<u>m</u>		
	qlw			ے <u>.</u> م		

MTX: methotrexate; IV: intravenous; SC: subcutaneous; qXw: once every X weeks; BID: twice daily; BIW: twice weekly LD: loading dose; ---: not reported; ① HAQ-DI, Health Assessment Questionnaire Disability Index; ②SF-36 PCS, physical component summary of the Short Form 36; ③SF-36 MCS, mental component summary of the Short Form 36; ④SF-36 score, the Short Form 36 score; ⑤DLQI, Dermatology Life Quality Index; ⑥F②-VAS, EuroQol Visual Analogue Scale; ⑦PsAQoL, Psoriasis Arthritis Quality of Life; ⑧DAPSA, Disease Activity for Psoriatic Arthritis; ⑨PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index; ⑪PASI 70, the proportion of participants achieving 70% improvement from baseline in Psoriasis Area Severity Index; ⑪PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index; ⑪PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; ⑩PASI score, Psoriasis Area Severity Index score.

^{*} Data are reported as median (IQR);

Table S2. Subgroup analysis of RCTs that examined the effect of bDMARDs on QoL

Groups	Outcomes	K	Effect size	95% CI	I^{2} (%)	P-value
DMARDs	HAQ-DI					
s. Placebo	Total	31	-0.24	-0.27, -0.21	99	< 0.0000
	Category of bDMARD					
	TNFi	11	-0.25	-0.43, -0.07	98	0.006
	IL-12/23i	9	-0.26	-0.29, -0.23	97	< 0.0000
	IL-17i	11	-0.22	-0.27, -0.16	99	< 0.0000
	Variety of bDMARD					
	Etanercept	1	-1.10	-1.22, -0.98		< 0.0000
	Infliximab	1	-0.40	-0.58, -0.22		< 0.0001
	Adalimumab	4	-0.20*	-0.22, -0.19	21	< 0.0000
	Golimumab	3	0.08	-0.53, 0.69	99	0.79
	Certolizumab pegol	2	-0.30*	-0.39, -0.21	1	< 0.0000
	Ustekinumab	4	-0.21*	-0.25, -0.17	0	< 0.0000
	Guselkumab	5	-0.27	-0.31, -0.24	98	< 0.0000
	Secukinumab	7	-0.17	-0.23, -0.11	99	< 0.0000
	Ixekizumab	4	-0.32	-0.46, -0.18	98	< 0.0000
	Duration of PsA					
	< 6 years	7	-0.23	-0.26, -0.21	95	< 0.0000
	6-9 years	14	-0.19	-0.26, -0.13	99	< 0.0000
	≥ 9 years	5	-0.46	-0.65, -0.28	99	< 0.0000
	Unclear	5	-0.18	-0.25, -0.11	99	< 0.0000
	Duration of treatment					
	< 24 weeks	3	-0.50	-1.09, 0.09	99	0.09
	≥ 24 weeks	28	-0.22	-0.25, -0.19	99	< 0.0000
	SF-36 PCS					
	Total	33	4.22	3.82, 4.61	99	< 0.0000
	Category of bDMARD					
	TNFi	10	5.75	4.35, 7.14	88	< 0.0000
	IL-12/23i	9	4.06	3.66, 4.46	96	< 0.0000
	IL-17i	14	3.78	3.05, 4.50	99	< 0.0000
	Variety of bDMARD					
	Infliximab	1	6.40	3.90, 8.90		< 0.0000
	Adalimumab	4	4.47	2.50, 6.44	79	< 0.0000
	Golimumab	3	7.06*	6.06, 8.05	0	< 0.0000
	Certolizumab pegol	2	5.85*	4.48, 7.22	0	< 0.0000
	Ustekinumab	4	3.47*	2.74, 4.22	6	< 0.0000
	Guselkumab	5	4.22	3.77, 4.67	98	< 0.0000
	Secukinumab	10	3.30	2.50, 4.11	99	< 0.0000
	Ixekizumab	4	5.22	4.67, 5.78	64	< 0.0000
	Duration of PsA					
	< 6 years	9	3.37	2.97, 3.77	97	< 0.0000
	6-9 years	15	4.87	3.76, 5.99	99	< 0.0000

≥9 years	4	5.58	4.84, 6.31	79	< 0.00001
Unclear	5	3.97	3.27, 4.67	99	< 0.00001
Duration of treatment					
< 24 weeks	4	3.04	2.62, 3.46	92	< 0.00001
≥ 24 weeks	29	4.42	3.98, 4.86	99	< 0.00001
SF-36 MCS					
Total	25	2.24	1.80, 2.69	97	< 0.00001
Category of bDMARD					
TNFi	10	2.93	1.19, 4.67	89	0.0009
IL-12/23i	9	1.75	1.28, 2.22	96	< 0.00001
IL-17i	6	2.50	1.46, 3.54	99	< 0.00001
Variety of bDMARD					
Infliximab	1	3.50	0.24, 6.76		0.04
Adalimumab	4	1.00	-0.50, 2.49	60	0.19
Golimumab	3	4.47*	3.22, 5.72	0	< 0.00001
Certolizumab pegol	2	3.78*	2.11, 5.44	28	0.0002
Ustekinumab	4	2.21*	1.27, 3.15	0	< 0.00001
Guselkumab	5	1.65	1.13, 2.17	98	< 0.00001
Secukinumab	2	2.30	0.34, 4.26	100	0.02
Ixekizumab	4	2.89*	2.67, 3.11	32	< 0.00001
Duration of PsA					
< 6 years	7	1.61	0.94, 2.28	98	< 0.00001
6-9 years	12	2.10	1.51, 2.70	79	< 0.00001
≥ 9 years	4	2.90	2.40, 3.40	61	< 0.00001
Unclear	2	2.30	0.34, 4.26	100	0.02
Duration of treatment					
< 24 weeks	2	0.11	-1.13, 1.36	27	0.86
≥ 24 weeks	23	2.40	1.97, 2.82	97	< 0.00001
EQ-VAS					
Total	5	8.76	5.32, 12.20	71	< 0.00001
Category of bDMARD					
TNFi	3	9.05	3.75, 14.35	85	0.0008
IL-17i	2	8.31*	3.85, 12.77	0	0.0003
Variety of bDMARD					
Adalimumab	2	6.72*	6.13, 7.31	0	< 0.00001
Golimumab	1	14.70	10.44, 18.96		< 0.00001
Ixekizumab	2	8.31*	3.85, 12.77	0	0.0003
Duration of PsA			ŕ		
< 6 years	1	6.73	6.14, 7.32		< 0.00001
6-9 years	4	9.66	5.34, 13.98	58	< 0.0001
Duration of treatment			•		
< 24 weeks	1	6.73	6.14, 7.32		< 0.00001
≥ 24 weeks	4	9.66	5.34, 13.98	58	< 0.0001
			,		

DLQI

Total	14	-4.36	5.76 2.06	00	< 0.00001
	14	-4.30	-5.76, -2.96	99	< 0.00001
Category of bDMARD TNFi	6	-3.38	5 52 1 22	92	0.002
IL-12/23i	-		-5.53, -1.23		
_	4	-5.39*	-6.15, -4.63	0	< 0.00001
IL-17i	4	-4.79	-6.81, -2.77	99	< 0.00001
Variety of bDMARD					0.4-
Adalimumab	3	-2.31	-5.60, 0.98	89	0.17
Golimumab	1	-6.20	-7.56, -4.84		< 0.00001
Certolizumab pegol	2	-3.46	-6.40, -0.53	90	0.02
Ustekinumab	4	-5.39*	-6.15, -4.63	0	< 0.00001
Secukinumab	2	-9.05	-9.93, -8.17	98	< 0.00001
Ixekizumab	2	-0.17*	-0.99, 0.65	0	0.69
Duration of PsA					
< 6 years	4	-5.39*	-6.15, -4.63	0	< 0.00001
6-9 years	6	-1.70	-3.59, 0.19	92	0.08
≥ 9 years	2	-5.12*	-6.35, -3.89	0	< 0.00001
Unclear	2	-9.05	-9.93, -8.17	98	< 0.00001
Duration of treatment					
< 24 weeks	1	-1.70	-4.21, 0.81		0.18
≥ 24 weeks	13	-4.53	-5.97, -3.10	99	< 0.00001
PASI 50					
Total	8	4.54	2.98, 6.91	81	< 0.00001
Category of bDMARD					
TNFi	7	4.92	3.00, 8.07	83	< 0.00001
IL-12/23i	1	2.97	1.90, 4.65		< 0.00001
Variety of bDMARD					
Etanercept	1	2.69	1.68, 4.30		< 0.0001
Infliximab	1	9.83	5.06, 19.09		< 0.00001
Adalimumab	1	6.50	3.34, 12.64		< 0.00001
Golimumab	2	9.59	5.55, 16.56	0	< 0.00001
Certolizumab pegol	2	2.63	2.03, 3.40	0	< 0.00001
Guselkumab	1	2.97	1.90, 4.65		< 0.00001
Duration of PsA					
6-9 years	4	6.93	3.33, 14.42	80	< 0.00001
≥9 years	4	3.06	2.20, 4.25	54	< 0.00001
PASI 75			·		
Total	38	5.06	4.36, 5.88	51	< 0.00001
Category of bDMARD					
TNFi	13	7.19	4.26, 12.16	74	< 0.00001
IL-12/23i	9	5.06	3.93, 6.51	56	< 0.00001
IL-17i	16	5.09*	4.45, 5.82	12	< 0.00001
Variety of bDMARD			,		
Etanercept	2	8.34*	2.83, 24.62	0	0.0001
Infliximab					
	2	65.64*	13.30, 322.82	0	0.31

	. 1 12 1	4	4.50	1 72 12 22	0.0	0.002
	Adalimumab	4	4.58	1.72, 12.22	89	0.002
	Golimumab	3	18.30	2.23, 149.96	84	0.007
	Certolizumab pegol	2	4.06*	2.79, 5.91	0	< 0.00001
	Ustekinumab	4	6.50*	4.79, 8.83	2	< 0.00001
	Guselkumab	5	4.10*	3.44, 4.87	46	< 0.00001
	Secukinumab	12	5.10*	4.41, 5.89	21	< 0.00001
	Ixekizumab	4	5.03*	3.51, 7.22	2	< 0.00001
	Duration of PsA					
	< 6 years	9	4.68	3.57, 6.13	57	< 0.00001
	6-9 years	17	5.89*	5.15, 6.72	38	< 0.00001
	\geq 9 years	7	5.92	3.33, 10.51	57	< 0.00001
	Unclear	5	4.23	2.43, 7.36	68	< 0.00001
	Duration of treatment					
	< 24 weeks	9	5.13*	4.37, 6.02	37	< 0.00001
	≥ 24 weeks	29	5.27	4.37, 6.35	56	< 0.00001
	PASI 90					
	Total	32	5.89*	4.85, 7.15	41	< 0.00001
	Category of bDMARD					
	TNFi	9	9.45*	6.62, 13.50	49	< 0.00001
	IL-12/23i	7	6.66*	5.21, 8.50	0	< 0.00001
	IL-17i	16	5.27*	4.44, 6.25	45	< 0.00001
	Variety of bDMARD					
	Infliximab	1	82.76	5.17, 1325.04		0.002
	Adalimumab	3	7.64	1.43, 40.80	65	0.02
	Golimumab	3	16.48	2.33, 116.59	65	0.005
	Certolizumab pegol	2	7.11*	3.78, 13.36	0	< 0.00001
	Ustekinumab	2	9.93*	4.42, 22.34	0	< 0.00001
	Guselkumab	5	6.32*	4.89, 8.17	0	< 0.00001
	Secukinumab	12	5.12	3.72, 7.03	51	< 0.00001
	Ixekizumab	4	6.27*	5.50, 7.15	39	< 0.00001
	Duration of PsA					
	< 6 years	6	7.52*	5.62, 10.07	0	< 0.00001
	6-9 years	17	5.78*	4.89, 6.84	38	< 0.00001
	≥ 9 years	4	5.52	2.83, 10.78	51	< 0.00001
	Unclear	5	5.44	2.40, 12.31	69	< 0.0001
	Duration of treatment					
	< 24 weeks	6	4.60*	3.73, 5.67	44	< 0.00001
	≥ 24 weeks	26	7.20*	6.10, 8.50	30	< 0.00001
bDMARDs+	HAQ-DI	2	-0.22	-0.58, 0.14	86	0.23
MTX vs.	SF-36 PCS	1	2.00	1.90, 2.10		< 0.00001
MTX	SF-36 MCS	1	0.00	-0.10, 0.10		1.00
	PASI 50	1	1.76	1.06, 2.92		0.03
	PASI 75	1	1.79	1.31, 2.44		0.0002
	PASI 90	2	1.97	1.45, 2.70	0	< 0.0001
						-

bDMARDs	HAQ-DI	2	-0.01	-0.05, 0.04	96	0.84
vs.	SF-36 PCS	2	0.63*	0.49, 0.77	36	< 0.00001
Tofacitinib	SF-36 MCS	2	-1.15*	-1.32, -0.97	0	< 0.00001
	EQ-VAS	2	-1.81	-3.61, -0.02	95	0.05
	PASI 75	2	0.90*	0.69, 1.17	0	0.43
bDMARDs	HAQ-DI	1	-0.03	-0.04, -0.02		< 0.00001
vs. MTX	SF-36 PCS	1	1.80	1.70, 1.90		< 0.00001
	SF-36 MCS	1	-0.50	-0.60, -0.40		< 0.00001

bDMARDs, the biological disease-modifying anti-rheumatic drugs; TNFi, the tumor necrosis factor inhibitor; IL-17i, interleukin-17 inhibitor; IL-12/23i, interleukin-12/23 inhibitor; HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36, DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; PASI 50/75/90, the proportion of participants achieving 50%/75%/90% improvement from baseline in Psoriasis Area Severity Index; K: Number of data reported in included studies;

^{*} fixed effect

Figure S1 Forest plot of HAQ-DI. HAQ-DI, Health Assessment Questionnaire Disability Index.

	Ехре	rimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean			Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	-0.3	0.5	51	-0.1	0.3	49	2.1%	-0.20 [-0.36, -0.04]	
Mease PJ 2000		0.23	30	-0.1		30	2.5%	-1.10 [-1.22, -0.98]	
NCT00051623 (IMPACT 2)	-0.4	0.66	100	0	0.66	100	1.9%	-0.40 [-0.58, -0.22]	_
NCT00195689 (ADEPT)	-0.4	0.5	151	-0.1	0.4	162	2.6%	-0.30 [-0.40, -0.20]	
NCT00265096 (GO-REVEAL) A NCT00265096 (GO-REVEAL) B	0.33	0.55	146 146	-0.01 -0.01	0.49	113 113	2.4%	0.34 [0.21, 0.47] 0.40 [0.28, 0.52]	
NCT00263036 (GO-REVEAL) B NCT00367237 (RESPOND)	-0.99		56	-0.56		54	1.3%	-0.43 [-0.70, -0.16]	
NCT01009086 (PSUMMIT 1) A		0.47	205	-0.09		206	2.8%	-0.21 [-0.29, -0.13]	
NCT01009086 (PSUMMIT 1) B	-0.34		204	-0.09		206	2.7%	-0.25 [-0.34, -0.16]	
NCT01077362 (PSUMMIT 2) A	-0.17	0.29	103	0	0.2	104	2.9%	-0.17 [-0.24, -0.10]	-
NCT01077362 (PSUMMIT 2) B	-0.25		105	0	0.2	104	2.8%	-0.25 [-0.33, -0.17]	-
NCT01087788 (RAPID-PsA) A	-0.52		138	-0.17		136	2.3%	-0.35 [-0.48, -0.22]	
NCT01087788 (RAPID-PsA) B	-0.43		135	-0.17		136	2.5%	-0.26 [-0.38, -0.14]	
NCT01392326 (FUTURE 1) A NCT01392326 (FUTURE 1) B	-0.41 -0.4		202 202	-0.17 -0.17		202 202	3.2% 3.2%	-0.24 [-0.25, -0.23] -0.23 [-0.24, -0.22]	
NCT01695239 (SPIRIT-P1) A	-0.53		107	-0.15	0.5	106	2.2%	-0.38 [-0.52, -0.24]	
NCT01695239 (SPIRIT-P1) B	-0.44		103	-0.15	0.5	106	2.3%	-0.29 [-0.43, -0.15]	
NCT01695239 (SPIRIT-P1) C	-0.37		101	-0.15	0.5	106	2.4%	-0.22 [-0.35, -0.09]	
NCT01752634 (FUTURE 2) A	-0.56	0.05	100	-0.31	0.06	98	3.2%	-0.25 [-0.27, -0.23]	•
NCT01752634 (FUTURE 2) B	-0.48		100	-0.31		98	3.2%	-0.17 [-0.19, -0.15]	•
NCT01752634 (FUTURE 2) C	-0.32		99	-0.31	0.06	98	3.2%	-0.01 [-0.03, 0.01]	.1
NCT01877668 (OPAL Broaden) A	-0.38		106	-0.35		107	3.2%	-0.03 [-0.04, -0.02]	1
NCT01877668 (OPAL Broaden) B	-0.38		106		0.05	104	3.2%	0.02 [0.01, 0.03]	
NCT01877668 (OPAL Broaden) C NCT01989468 (FUTURE 3) A	-0.38 -0.38		106 139	-0.18 -0.17		105 137	3.2% 3.2%	-0.20 [-0.21, -0.19] -0.21 [-0.22, -0.20]	
NCT01989468 (FUTURE 3) B	-0.27		138	-0.17		137	3.2%	-0.10 [-0.11, -0.09]	•
NCT02181673 (GO-VIBRANT)	-0.63		237	-0.14	0.5	236	2.7%	-0.49 [-0.58, -0.40]	
NCT02319759	-0.42		100	-0.06		49	1.9%	-0.36 [-0.54, -0.18]	
NCT02349295 (SPIRIT-P2) A	-0.6	0.1	122	-0.2	0.1	118	3.2%	-0.40 [-0.43, -0.37]	*
NCT02349295 (SPIRIT-P2) B	-0.4	0.1	123	-0.2	0.1	118	3.2%	-0.20 [-0.23, -0.17]	*
NCT02376790 (SEAM-PsA) A	-0.44		258	-0.41		252	3.2%	-0.03 [-0.04, -0.02]	
NCT02376790 (SEAM-PsA) B	-0.47		283	-0.41		252	3.2%	-0.06 [-0.07, -0.05]	. '
NCT03158285 (DISCOVER-2) A		0.03	245	-0.13 -0.13		246	3.2%	-0.27 [-0.28, -0.26]	
NCT03158285 (DISCOVER-2) B NCT03162796 (DISCOVER-1) A	-0.37 -0.4	0.03	248 128	-0.13		246 126	3.2% 3.2%	-0.24 [-0.25, -0.23] -0.33 [-0.34, -0.32]	
NCT03162796 (DISCOVER-1) B	-0.32		127	-0.07		126	3.2%	-0.25 [-0.26, -0.24]	•
, -									
Total (95% CI)			5050				100.0%	-0.22 [-0.25, -0.18]	• • • • • • • • • • • • • • • • • • • •
Heterogeneity: Tau ² = 0.01; Chi ² = 8			(P < 0.	00001);	$I^2 = 10$	10%			-1 -0.5 0 0.5 1
Test for overall effect: Z = 10.93 (P <	< 0.00001)							Favours [experimental] Favours [control]

Figure S2. Forest plot of SF-36 PCS. SF-36 PCS, physical component summary of the Short Form 36.

	Expe	rimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	5.7	8.5	49	2.8	7.1	45	1.3%	2.90 [-0.26, 6.06]	-
NCT00051623 (IMPACT 2)	7.7	9.8	100	1.3	8.2	100	1.7%	6.40 [3.90, 8.90]	-
NCT00195689 (ADEPT)	9.3	10.1	140	1.4	9.6	152	1.8%	7.90 [5.64, 10.16]	-
NCT00265096 (GO-REVEAL) A	7.42	9.17	146	0.67	8.72	113	1.9%	6.75 [4.56, 8.94]	-
NCT00265096 (GO-REVEAL) B	8.22	9.64	146	0.67	8.72	113	1.9%	7.55 [5.31, 9.79]	-
NCT00809614	15.2	28.1	28	-2.61	26	14	0.1%	17.81 [0.67, 34.95]	
NCT01009086 (PSUMMIT 1) A	4.46	8.96	205	1.38	5.6	206	2.5%	3.08 [1.63, 4.53]	-
NCT01009086 (PSUMMIT 1) B	5.76	7.69	204	1.38	5.6	206	2.7%	4.38 [3.08, 5.68]	-
NCT01077362 (PSUMMIT 2) A	3.76	7.37	99	1.13	3.61	97	2.4%	2.63 [1.01, 4.25]	 -
NCT01077362 (PSUMMIT 2) B	4.52	7.75	97	1.13	3.61	97	2.3%	3.39 [1.69, 5.09]	
NCT01087788 (RAPID-PsA) A	8.4	10.1	138	2.1	7.2	136	2.0%	6.30 [4.23, 8.37]	-
NCT01087788 (RAPID-PsA) B	7.6	8.1	135	2.1	7.2	136	2.2%	5.50 [3.67, 7.33]	-
NCT01392326 (FUTURE 1) A	5.41	0.52	202	1.82	0.72	202	3.4%	3.59 [3.47, 3.71]	
NCT01392326 (FUTURE 1) B	5.91	0.53	202	1.82	0.72	202	3.4%	4.09 [3.97, 4.21]	•
NCT01695239 (SPIRIT-P1) A	7.7	8.6	107	2.7	7.7	106	1.9%	5.00 [2.81, 7.19]	
NCT01695239 (SPIRIT-P1) B	7.7	9.8	103	2.7	7.7	106	1.7%	5.00 [2.61, 7.39]	
NCT01695239 (SPIRIT-P1) C	6.3	8.3	101	2.7	7.7	106	1.9%	3.60 [1.42, 5.78]	
NCT01752634 (FUTURE 2) A	7.25	0.74	100	1.95	0.97	98	3.4%	5.30 [5.06, 5.54]	•
NCT01752634 (FUTURE 2) B	6.39	0.73	100	1.95	0.97	98	3.4%	4.44 [4.20, 4.68]	
NCT01752634 (FUTURE 2) C	4.38	0.75	99	1.95	0.97	98	3.4%	2.43 [2.19, 2.67]	
NCT01877668 (OPAL Broaden) A	6.23	0.75	106	5.51	0.73	107	3.4%	0.72 [0.52, 0.92]	•
NCT01877668 (OPAL Broaden) B	6.23	0.75	106	5.69	0.74	104	3.4%	0.54 [0.34, 0.74]	
NCT01877668 (OPAL Broaden) C	6.23	0.75	106	2.68	0.79	105	3.4%	3.55 [3.34, 3.76]	•
NCT01989468 (FUTURE 3) A	6.46	0.59	139	2.94	0.83	137	3.4%	3.52 [3.35, 3.69]	•
NCT01989468 (FUTURE 3) B	3.42	0.6	138	2.94	0.83	137	3.4%	0.48 [0.31, 0.65]	
NCT02181673 (GO-VIBRANT)	9.4	8.1	237	2.4	6.1	236	2.7%	7.00 [5.71, 8.29]	-
NCT02294227 (FUTURE 4) A	3.42	0.58	114	0.63	0.59	114	3.4%	2.79 [2.64, 2.94]	•
NCT02294227 (FUTURE 4) B	3.44	0.58	113	0.63	0.59	114	3.4%	2.81 [2.66, 2.96]	•
NCT02319759	6.59	7.47	100	0.46	6.51	49	1.8%	6.13 [3.79, 8.47]	
NCT02349295 (SPIRIT-P2) A	8.9	1.3	122	3.3	1.4	118	3.3%	5.60 [5.26, 5.94]	•
NCT02349295 (SPIRIT-P2) B	8.2	1.2	123	3.3	1.4	118	3.3%	4.90 [4.57, 5.23]	•
NCT02376790 (SEAM-PsA) A	7.8	0.6	256	6	0.6	253	3.4%	1.80 [1.70, 1.90]	•
NCT02376790 (SEAM-PsA) B	8	0.6	257	6	0.6	253	3.4%	2.00 [1.90, 2.10]	•
NCT03158285 (DISCOVER-2) A	7.04	0.46	245	3.42	0.46	246	3.4%	3.62 [3.54, 3.70]	•
NCT03158285 (DISCOVER-2) B	7.39		248	3.42		246	3.4%	3.97 [3.89, 4.05]	•
NCT03162796 (DISCOVER-1) A	6.87		128	1.96	0.65	126	3.4%	4.91 [4.75, 5.07]	
NCT03162796 (DISCOVER-1) B		0.65	127	1.96		126	3.4%	4.14 [3.98, 4.30]	
Total (95% CI)			5166			5020	100.0%	3.89 [3.44, 4.34]	
Heterogeneity: Tau2 = 1.58; Chi2 = 5	612.48. d	f= 36	(P < 0.	00001):	$ ^2 = 99$	9%			-20 -10 0 10 20
Test for overall effect: Z = 16.79 (P <									
									Favours (control) Favours (experimental)

Figure S3. Forest plot of SF-36 MCS. SF-36 MCS, mental component summary of the Short Form 36.

	Ехр	erimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	1.1	7.4	49	-0.6	7.8	45	2.0%	1.70 [-1.38, 4.78]	
NCT00051623 (IMPACT 2)	3.9	11.9	100	0.4	11.6	100	1.9%	3.50 [0.24, 6.76]	
NCT00195689 (ADEPT)	1.8	9.3	140	0.6	10.4	152	2.7%	1.20 [-1.06, 3.46]	
NCT00265096 (GO-REVEAL) A	3.37	10.55	146	-0.6	12.13	113	2.2%	3.97 [1.15, 6.79]	
NCT00265096 (GO-REVEAL) B	4.29	11.03	146	-0.6	12.13	113	2.1%	4.89 [2.03, 7.75]	
NCT01009086 (PSUMMIT 1) A	3.19	9.11	205	1.46	7.84	206	3.3%	1.73 [0.09, 3.37]	-
NCT01009086 (PSUMMIT 1) B	4.68	9.26	204	1.46	7.84	206	3.3%	3.22 [1.56, 4.88]	_
NCT01077362 (PSUMMIT 2) A	1.72	8.65	99	0.6	6.1	97	2.9%	1.12 [-0.97, 3.21]	
NCT01077362 (PSUMMIT 2) B	3.19	10.84	97	0.6	6.1	97	2.5%	2.59 [0.11, 5.07]	
NCT01087788 (RAPID-PsA) A	5.5	10.2	138	0.7	9.9	136	2.6%	4.80 [2.42, 7.18]	
NCT01087788 (RAPID-PsA) B	3.5	9.6	135	0.7	9.9	136	2.6%	2.80 [0.48, 5.12]	
NCT01392326 (FUTURE 1) A	3.7	0.6	202	2.4	0.9	202	4.6%	1.30 [1.15, 1.45]	
NCT01392326 (FUTURE 1) B	5.7	0.6	202	2.4	0.9	202	4.6%	3.30 [3.15, 3.45]	•
NCT01695239 (SPIRIT-P1) A	3.1	10.4	107	1.8	9.5	106	2.3%	1.30 [-1.37, 3.97]	
NCT01695239 (SPIRIT-P1) B	4.6	11.9	103	1.8	9.5	106	2.1%	2.80 [-0.12, 5.72]	
NCT01695239 (SPIRIT-P1) C	4.6	9.5	101	1.8	9.5	106	2.4%	2.80 [0.21, 5.39]	
NCT01877668 (OPAL Broaden) A	3.13	0.94	106	4.35	0.91	107	4.6%	-1.22 [-1.47, -0.97]	+
NCT01877668 (OPAL Broaden) B	3.13	0.94	106	4.2	0.91	104	4.6%	-1.07 [-1.32, -0.82]	+
NCT01877668 (OPAL Broaden) C	3.13	0.94	106	3.27	0.98	105	4.6%	-0.14 [-0.40, 0.12]	+
NCT02181673 (GO-VIBRANT)	5.3	10.2	237	0.8	7.4	236	3.4%	4.50 [2.89, 6.11]	
NCT02319759	4.95	9.06	100	0.42	6.74	49	2.4%	4.53 [1.94, 7.12]	
NCT02349295 (SPIRIT-P2) A	3.6	1.2	122	0.9	1.3	118	4.5%	2.70 [2.38, 3.02]	-
NCT02349295 (SPIRIT-P2) B	4	1.2	123	0.9	1.3	118	4.5%	3.10 [2.78, 3.42]	-
NCT02376790 (SEAM-PsA) A	2.8	0.6	256	3.3	0.6	253	4.6%	-0.50 [-0.60, -0.40]	•
NCT02376790 (SEAM-PsA) B	3.3	0.6	257	3.3	0.6	253	4.6%	0.00 [-0.10, 0.10]	†
NCT03158285 (DISCOVER-2) A	4.22	0.55	245	2.14	0.55	246	4.6%	2.08 [1.98, 2.18]	•
NCT03158285 (DISCOVER-2) B	4.17	0.54	248	2.14	0.55	246	4.6%	2.03 [1.93, 2.13]	
NCT03162796 (DISCOVER-1) A	3.6	0.73	128	2.37	0.73	126	4.6%	1.23 [1.05, 1.41]	
NCT03162796 (DISCOVER-1) B	3.2	0.73	127	2.37	0.73	126	4.6%	0.83 [0.65, 1.01]	*
Total (95% CI)			4335			4210	100.0%	1.82 [1.24, 2.40]	•
Heterogeneity: Tau² = 1.88; Chi² = 39	958.02, (df= 28 ((P < 0.0	0001); I	= 99%)		-	-4 -2 0 2 4
Test for overall effect: Z = 6.19 (P < 0	.00001)								-4 -2 U 2 4 Favours [control] Favours [experimental]
	,								ravours (control) - ravours (experimental)

Figure S4. Forest plot of DLQI. DLQI, Dermatology Life Quality Index.

	Expe	rimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	-3.4	4.5	32	-1.7	5.3	28	6.2%	-1.70 [-4.21, 0.81]	
NCT00195689 (ADEPT)	-6.1	6.3	66	-0.7	6.7	66	6.5%	-5.40 [-7.62, -3.18]	
NCT01009086 (PSUMMIT 1) A	-6.35	6.75	129	-1.35	5.25	132	7.1%	-5.00 [-6.47, -3.53]	
NCT01009086 (PSUMMIT 1) B	-7.05	6.74	134	-1.35	5.25	132	7.1%	-5.70 [-7.15, -4.25]	
NCT01077362 (PSUMMIT 2) A	-6.35	8.27	103	-0.7	4.51	104	6.8%	-5.65 [-7.47, -3.83]	
NCT01077362 (PSUMMIT 2) B	-6	6.01	105	-0.7	4.51	104	7.1%	-5.30 [-6.74, -3.86]	
NCT01087788 (RAPID-PsA) A	-6.3	7.5	138	-1.3	4.7	136	7.1%	-5.00 [-6.48, -3.52]	
NCT01087788 (RAPID-PsA) B	-3.3	5.1	135	-1.3	4.7	136	7.3%	-2.00 [-3.17, -0.83]	
NCT01392326 (FUTURE 1) A	-7.9	0.6	108	0.7	0.8	109	7.7%	-8.60 [-8.79, -8.41]	*
NCT01392326 (FUTURE 1) B	-8.8	0.6	108	0.7	0.8	109	7.7%	-9.50 [-9.69, -9.31]	•
NCT01695239 (SPIRIT-P1) A	-0.5	0.52	107	-0.3	6.1	106	7.3%	-0.20 [-1.37, 0.97]	-
NCT01695239 (SPIRIT-P1) B	-0.44	0.53	103	-0.3	6.1	106	7.3%	-0.14 [-1.31, 1.03]	-
NCT01695239 (SPIRIT-P1) C	-0.37	0.44	101	-0.3	6.1	106	7.3%	-0.07 [-1.23, 1.09]	
NCT02181673 (GO-VIBRANT)	-8.1	7.7	194	-1.9	5.9	195	7.2%	-6.20 [-7.56, -4.84]	
Total (95% CI)			1563			1569	100.0%	-4.36 [-5.76, -2.96]	•
Heterogeneity: Tau ² = 6.63; Chi ² :	= 954.91	. df = 1	13 (P <	0.0000	1); 2=	99%			+
Test for overall effect: Z = 6.09 (P			٧.						-10 -5 0 5 10
									Favours [experimental] Favours [control]

Figure S5. Forest plot of EQ-VAS. EQ-VAS, EuroQol Visual Analogue Scale.

	Expe	rimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
NCT01695239 (SPIRIT-P1) A	11.9	25	107	3.3	21.1	106	12.0%	8.60 [2.39, 14.81]	
NCT01695239 (SPIRIT-P1) B	11.3	25.8	103	3.3	21.1	106	11.8%	8.00 [1.60, 14.40]	
NCT01695239 (SPIRIT-P1) C	9.1	22.1	101	3.3	21.1	106	12.3%	5.80 [-0.09, 11.69]	•
NCT01877668 (OPAL Broaden) A	13.1	2.14	106	14	2.1	107	16.6%	-0.90 [-1.47, -0.33]	-
NCT01877668 (OPAL Broaden) B	13.1	2.14	106	15.83	2.09	104	16.6%	-2.73 [-3.30, -2.16]	•
NCT01877668 (OPAL Broaden) C	13.1	2.14	106	6.37	2.24	105	16.6%	6.73 [6.14, 7.32]	•
NCT02181673 (GO-VIBRANT)	20.2	24.2	237	5.5	23.1	236	14.1%	14.70 [10.44, 18.96]	
Total (95% CI)			866			870	100.0%	5.27 [1.21, 9.34]	-
Heterogeneity: Tau² = 25.86; Chi² = 1	619.38, 0	df = 6 (P < 0.0	0001); F	= 999	%			-10 -5 0 5 10
Test for overall effect: Z = 2.54 (P = 0).01)								Favours [control] Favours [experimental]

Figure S6. Forest plot of PASI 50. PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index.

	Experime	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
NCT00051623 (IMPACT 2)	75	83	8	87	10.3%	9.83 [5.06, 19.09]	
NCT00195689 (ADEPT)	52	69	8	69	10.3%	6.50 [3.34, 12.64]	
NCT00265096 (GO-REVEAL) A	77	102	6	73	9.4%	9.18 [4.23, 19.93]	
NCT00265096 (GO-REVEAL) B	87	106	6	73	9.4%	9.99 [4.62, 21.60]	
NCT00317499	47	101	18	104	11.9%	2.69 [1.68, 4.30]	
NCT01087788 (RAPID-PsA) A	67	90	24	86	12.7%	2.67 [1.86, 3.83]	-
NCT01087788 (RAPID-PsA) B	55	76	24	86	12.6%	2.59 [1.80, 3.74]	_
NCT02065713 (GO-DACT)	16	20	10	22	11.6%	1.76 [1.06, 2.92]	
NCT02319759	85	98	14	48	12.0%	2.97 [1.90, 4.65]	
Total (95% CI)		745		648	100.0%	4.09 [2.71, 6.16]	•
Total events	561		118				
Heterogeneity: Tau ^z = 0.31; Chi ^z =	45.41, df=	8 (P <	0.00001)	; l² = 8:	2%	 - 0.1	05 0.2 1 5 20
Test for overall effect: Z = 6.72 (P	< 0.00001)					0.0	Favours [control] Favours [experimental]

Figure S7. Forest plot of PASI 75. PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index.

tudy or Subgroup	Experim Events		Contr Events		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% Cl
MPACT	35	52	0	52	0.6%	71.00 [4.47, 1127.60]	
ease PJ 2000	5	19	ō	19	0.5%	11.00 [0.65, 186.02]	
CT00051623 (IMPACT 2)	60	83	1	87	1.0%	62.89 [8.92, 443.47]	
CT00195689 (ADEPT)	41	69	1	69	1.0%	41.00 [5.80, 289.75]	
CT00265096 (GO-REVEAL) A	57	102	1	73	1.0%	40.79 [5.78, 287.91]	
CT00265096 (GO-REVEAL) B	70	106	1	73	1.0%	48.21 [6.85, 339.27]	
CT00317499	23	101	3	104	1.8%	7.89 [2.45, 25.48]	
CT00367237 (RESPOND)	33	34	19	35	3.3%	1.79 [1.31, 2.44]	-
CT01009086 (PSUMMIT 1) A	83	145	16	146	3.0%	5.22 [3.22, 8.47]	
CT01009086 (PSUMMIT 1) B	93	149	16	146	3.0%	5.70 [3.53, 9.19]	-
CT01077362 (PSUMMIT 2) A	41	80	4	80	2.1%	10.25 [3.85, 27.28]	
CT01077362 (PSUMMIT 2) B	45	81	4	80	2.1%	11.11 [4.19, 29.45]	
CT01087788 (RAPID-PsA) A	56	90	13	86	2.9%	4.12 [2.43, 6.97]	—
CT01087788 (RAPID-PsA) B	46	76	13	86	2.9%	4.00 [2.35, 6.82]	—
CT01392326 (FUTURE 1) A	70	108	9	109	2.7%	7.85 [4.13, 14.90]	
CT01392326 (FUTURE 1) B	66	108	9	109	2.7%	7.40 [3.89, 14.09]	—
CT01695239 (SPIRIT-P1) A	37	52	4	41	2.2%	7.29 [2.83, 18.80]	
CT01695239 (SPIRIT-P1) B	33	41	4	41	2.2%	8.25 [3.21, 21.18]	
CT01695239 (SPIRIT-P1) C	20	37	4	41	2.1%	5.54 [2.09, 14.72]	
CT01752634 (FUTURE 2) A	26	41	7	43	2.6%	3.90 [1.90, 7.98]	
CT01752634 (FUTURE 2) B	28	58	7	43	2.6%	2.97 [1.43, 6.14]	
CT01752634 (FUTURE 2) C	14	50	7	43	2.4%	1.72 [0.76, 3.87]	<u> </u>
CT01877668 (OPAL Broaden) A	30	77	35	82	3.2%	0.91 [0.63, 1.33]	1
CT01877668 (OPAL Broaden) B CT01877668 (OPAL Broaden) C	30 30	77 77	31 12	70	3.2%	0.88 [0.60, 1.29]	1
, ,	30 29		12	82	2.8%	2.66 [1.47, 4.82]	
CT01989468 (FUTURE 3) A	29 34	62 68	6	59 59	2.4%	4.60 [2.06, 10.27]	
CT01989468 (FUTURE 3) B CT02181673 (GO-VIBRANT)	127	241	26	239	2.4% 3.2%	4.92 [2.22, 10.88] 4.84 [3.31, 7.10]	_ _
CT02294227 (FUTURE 4) A	29	55	5	62	2.3%	6.54 [2.72, 15.71]	
CT02294227 (FUTURE 4) B	27	54	5	62	2.3%	6.20 [2.57, 14.97]	
CT02319759	77	98	6	48	2.5%	6.29 [2.95, 13.38]	
CT02349295 (SPIRIT-P2) A	38	68	10	67	2.8%	3.74 [2.04, 6.89]	
CT02349295 (SPIRIT-P2) B	41	68	10	67	2.8%	4.04 [2.21, 7.39]	
CT02349451	19	33	3	11	2.1%	2.11 [0.77, 5.79]	
CT02404350 (FUTURE 5) A	155	222	41	332	3.3%	5.65 [4.19, 7.63]	-
CT02404350 (FUTURE 5) B	132	220	41	332	3.3%	4.86 [3.58, 6.60]	-
CT02404350 (FUTURE 5) C	129	222	41	332	3.3%	4.71 [3.46, 6.40]	-
CT03158285 (DISCOVER-2) A	144	184	42	183	3.3%	3.41 [2.59, 4.49]	-
CT03158285 (DISCOVER-2) B	139	176	42	183	3.3%	3.44 [2.61, 4.54]	-
CT03162796 (DISCOVER-1) A	77	89	11	78	2.9%	6.13 [3.53, 10.67]	
CT03162796 (DISCOVER-1) B	62	82	11	78	2.9%	5.36 [3.06, 9.40]	
				4032	100.0%	4.73 [3.77, 5.95]	♦
otal (95% CI)		3855					
otal events	2331		527				
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%	H	1001 01 1 10 10
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%	H	
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%	t o	.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; l² = 84	1%	t	.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%		.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; l² = 84	1%	4	.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; l² = 84	4%	1	.001 0.1 1 10 10 Favours (control) Favours (experimental)
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	4%	7	.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	4%	4	0.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	4%	7	.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal (95% CI) otal events eterogeneity: Tau ^a = 0.39; Chi ^a = 2 est for overall effect: Z = 13.34 (P <	48.01, df=			; I² = 84	1%	1	0.001 0.1 1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%		0.001 0.1 10 10 Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%	7	Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%	7	Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	4%		Favours [control] Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I*= 84	4%		Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I*= 84	4%		0.001 0.1 10 10 Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I*= 84	1%		Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I² = 84	1%		Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I ^z = 84	4%		Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I ^z = 84	1%		Favours (control) Favours (experimental)
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I ^z = 84	1%		Favours [control] Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; F= 84	4%		Favours [control] Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; F= 84	4%		Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; F= 84	1%		Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; P= 84	1%		Favours [control] Favours [experimental]
otal events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; F= 84	4%		Favours [control] Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; ² = 84	1%		Favours [control] Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; ² = 84	1%		Favours [control] Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; I ^a = 84	1%		Favours [control] Favours [experimental]
ital events eterogeneity: Tau² = 0.39; Chi² = 2	48.01, df=			; ² = 84	4%		Favours (control) Favours (experimental)

Figure S8. Forest plot of PASI 90. PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index.

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Hong Tao 2019	29	33	16	33	4.9%	1.81 [1.25, 2.63]	-
NCT00051623 (IMPACT 2)	39	83	0	87	0.6%	82.76 [5.17, 1325.04]	
NCT00195689 (ADEPT)	29	69	0	69	0.6%	59.00 [3.68, 946.75]	
NCT00265096 (GO-REVEAL) A	33	102	0	73	0.6%	48.14 [3.00, 773.11]	
NCT00265096 (GO-REVEAL) B	34	106	0	73	0.6%	47.72 [2.97, 766.16]	- ·
NCT00367237 (RESPOND)	24	34	10	35	4.2%	2.47 [1.40, 4.36]	
NCT01077362 (PSUMMIT 2) A	24	80	3	80	2.4%	8.00 [2.51, 25.51]	
NCT01077362 (PSUMMIT 2) B	36	81	3	80	2.4%	11.85 [3.80, 36.93]	
NCT01087788 (RAPID-PsA) A	42	90	5	86	3.1%	8.03 [3.33, 19.33]	
NCT01087788 (RAPID-PsA) B	27	76	5	86	3.1%	6.11 [2.48, 15.07]	
NCT01392326 (FUTURE 1) A	53	108	4	109	2.8%	13.37 [5.01, 35.66]	
NCT01392326 (FUTURE 1) B	49	108	4	109	2.8%	12.36 [4.62, 33.07]	
NCT01695239 (SPIRIT-P1) A	29	52	2	41	1.9%	11.43 [2.90, 45.13]	
NCT01695239 (SPIRIT-P1) B	28	41	2	41	1.9%	14.00 [3.57, 54.97]	
NCT01695239 (SPIRIT-P1) C	14	37	2	41	1.9%	7.76 [1.89, 31.88]	
NCT01752634 (FUTURE 2) A	20	41	4	43	2.8%	5.24 [1.96, 14.04]	
NCT01752634 (FUTURE 2) B	19	58	4	43	2.8%	3.52 [1.29, 9.61]	
NCT01752634 (FUTURE 2) C	6	50	4	43	2.3%	1.29 [0.39, 4.27]	
NCT01989468 (FUTURE 3) A	21	62	4	59	2.8%	5.00 [1.82, 13.69]	
NCT01989468 (FUTURE 3) B	25	68	4	59	2.8%	5.42 [2.00, 14.68]	
NCT02065713 (GO-DACT)	5	20	4	22	2.4%	1.38 [0.43, 4.42]	
NCT02181673 (GO-VIBRANT)	84	241	15	239	4.4%	5.55 [3.30, 9.34]	-
NCT02294227 (FUTURE 4) A	20	55	1	62	1.1%	22.55 [3.13, 162.52]	
NCT02294227 (FUTURE 4) B	11	54	1	62	1.1%	12.63 [1.68, 94.67]	
NCT02319759	65	98	3	48	2.5%	10.61 [3.52, 32.03]	
NCT02349295 (SPIRIT-P2) A	30	68	8	67	3.7%	3.69 [1.83, 7.46]	
NCT02349295 (SPIRIT-P2) B	34	68	8	67	3.8%	4.19 [2.10, 8.37]	
NCT02349451	15	33	2	11	2.0%	2.50 [0.68, 9.25]	
NCT02404350 (FUTURE 5) A	119	222	31	332	4.9%	5.74 [4.02, 8.20]	-
NCT02404350 (FUTURE 5) B	81	220	31	332	4.9%	3.94 [2.70, 5.75]	-
NCT02404350 (FUTURE 5) C	70	222	31	332	4.8%	3.38 [2.29, 4.97]	-
NCT03158285 (DISCOVER-2) A	112	184	18	183	4.6%	6.19 [3.93, 9.74]	-
NCT03158285 (DISCOVER-2) B	121	176	18	183	4.6%	6.99 [4.46, 10.96]	· ·
NCT03162796 (DISCOVER-1) A	56	89	9	78	4.0%	5.45 [2.89, 10.29]	-
NCT03162796 (DISCOVER-1) B	41	82	9	78	3.9%	4.33 [2.26, 8.31]	→
Total (95% CI)		3211		3386	100.0%	5.44 [4.30, 6.89]	•
Total events	1445		265				
Heterogeneity: Tau² = 0.26; Chi² =	99.58, df=	34 (P <	0.00001); l ² = 61	6%		1 1 1
Test for overall effect: $Z = 14.08$ (P							0.001 0.1 1 10 10 Favours [control] Favours [experimental]

Figure S9. Forest plot of PASI 100. PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index.

•										
	Experim	ental	Conti	rol		Risk Ratio		Risk	Ratio .	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fix	ed, 95% CI	
NCT00195689 (ADEPT)	20	69	0	69	1.1%	41.00 [2.53, 664.71]				
NCT01695239 (SPIRIT-P1) A	22	52	1	41	2.5%	17.35 [2.44, 123.36]				_
NCT01695239 (SPIRIT-P1) B	22	41	1	41	2.2%	22.00 [3.11, 155.67]				
NCT01695239 (SPIRIT-P1) C	9	37	1	41	2.1%	9.97 [1.33, 75.00]			-	_
NCT02181673 (GO-VIBRANT)	50	241	11	239	24.5%	4.51 [2.41, 8.44]			-	
NCT02319759	39	98	3	48	8.9%	6.37 [2.07, 19.56]				
NCT02349295 (SPIRIT-P2) A	24	68	3	67	6.7%	7.88 [2.49, 24.94]				
NCT02349295 (SPIRIT-P2) B	19	68	3	67	6.7%	6.24 [1.94, 20.11]				
NCT03158285 (DISCOVER-2) A	82	184	5	183	11.1%	16.31 [6.77, 39.30]			-	
NCT03158285 (DISCOVER-2) B	80	176	5	183	10.9%	16.64 [6.90, 40.09]				
NCT03162796 (DISCOVER-1) A	40	89	5	78	11.8%	7.01 [2.91, 16.88]			-	
NCT03162796 (DISCOVER-1) B	21	82	5	78	11.4%	4.00 [1.58, 10.07]				
Total (95% CI)		1205		1135	100.0%	9.11 [6.75, 12.31]			•	
Total events	428		43							
Heterogeneity: Chi ² = 14.89, df = 1			3%				0.002	0.1	1 10	50
Test for overall effect: $Z = 14.40$ (P	~ 0.00001	,						Favours [control]	Favours [expering	nental]



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item 27	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page1/line1-2
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page2/line1-28 and Page3/line1
INTRODUCTION		Describe the rationale for the review in the context of existing knowledge	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page4/line1-28 and Page25/line1-2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page5/line3-9
METHODS		<u>Q.</u> Q.	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page6/line6-17
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to the studies. Specify the date when each source was last searched or consulted.	Page5/line15-18
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page5/line18-28 and Page6/line1-4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page6/line6-7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each reports whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page6/line19-20
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each successful to decide which results to collect.	Page6/line20-22
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page6/line20-22
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page6/line22-27
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page7/line5-7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
)	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was perior model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page7/line7-12
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page7/line13-23
	13f	Describe any sensitivity analysesecondicated toyassess/volumess logithecsynthesized are sultisle lines.xhtml	Page7/line12-13



PRISMA 2020 Checklist

		20	
Section and Topic	Item #	Checklist item 52	Location where item is reported
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases)	Page7/line22-23
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page7/line5-7
RESULTS	•	o ri	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the rember of studies included in the review, ideally using a flow diagram.	Page7/line26-28 and Page 8/line1-13
, L	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were exiguded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary table S2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Figure 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary figure S1-S9
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Supplementary table S2 and Figure 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page8/line15-26
; '	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Supplementary table S3
8	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page9/line7-13
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page11/line2-6 and Figure 3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 1
DISCUSSION	•	gu	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page11/line8-28 and Page12/line1-18
3	23b	Discuss any limitations of the evidence included in the review.	Page13/line1-8
)	23c	Discuss any limitations of the review processes used.	N/A
)	23d	Discuss implications of the results for practice, policy, and future research.	Page12/line19-2
OTHER INFORMA	TION	Q P	
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
protocol	24b	Indicate where the review protocological ibevancessed; not/state that abprotocol/was/abt prepared lines.xhtml	N/A

.1136/bmjopen-20



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
5	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
7 Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the regiew.	Page14/line8-9
8 Competing 9 interests	26	Declare any competing interests of review authors.	Page14/line11
10 Availability of 11 data, code and 12 other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page14/line22-2 4

13
14 From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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The Effects of bDMARDs on Quality of Life in Patients with Psoriatic Arthritis: Meta-analysis

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The Effects of bDMARDs on Quality of Life in Patients with

2	Psoriatic	Arthritis:	Meta-anal	ysis
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- Jiangsu, China; cpucf@163.com; +86 13805153128.
- Word Count 3197.

1 Abstract

- **Objectives:** To determine the effects of biological disease-modifying anti-rheumatic
- drugs (bDMARDs) on the quality of life (QoL) among patients with psoriatic arthritis
- 4 (PsA).
- **Design:** Meta-analysis.
- 6 Data sources and eligibility criteria: PubMed, Web of Science, Cochrane Library,
- 7 CNKI, WanFang, and VIP databases were searched to collect randomized controlled
- 8 trials (RCTs), which were conducted to evaluate the effect of bDMARDs in treatment
- 9 of patients with PsA and reported QoL-related outcomes, from inception to November
- 10 2020 and updated on 19 February 2022.
- 11 Data extraction and synthesis: Outcomes about Health Assessment Questionnaire
- 12 Disability Index (HAQ-DI), Dermatology Life Quality Index (DLQI), physical
- component summary (PCS) and mental component summary (MCS) of the Short Form
- 14 36 (SF-36), EuroQol Visual Analogue Scale (EQ-VAS), Psoriasis Area Severity Index
- 15 (PASI) 50/75/90/100 were extracted by two reviewers independently. Data were pooled
- using the fixed or random effects methods and considered as mean difference (MD) or
- 17 risk ratio (RR) with 95% CI.
- **Results:** Out of 3190 articles screened, 37 RCTs (with 47 articles reported) were
- included. Pooled estimates showed that bDMARDs were superior versus placebo on all
- 20 outcomes. Against methotrexate (MTX) and tofacitinib, bDMARDs showed no
- 21 statistically significant advantages or significant disadvantages. Similar results were
- found for bDMARDs+MTX versus MTX. For HAQ-DI, the results of the subgroups of
- 23 bDMARDs vs. placebo, bDMARDs+MTX vs. MTX, bDMARDs vs. tofacitinib,
- 24 bDMARDs vs. MTX, were -0.21 (MD, 95% CI, -0.23, -0.18), -0.22 (MD, 95% CI, -
- 25 0.58, 0.14), -0.01(MD, 95% CI, -0.05, 0.04), -0.03 (MD, 95% CI, -0.04, -0.02)
- 26 respectively.
- 27 Conclusions: Compared with placebo, bDMARDs taken by patients with PsA appear
- to significantly improve the QoL. Compared with other therapeutic agents, more studies

1 are required to confirm the effect of single and combined bDMARDs use further.

Keywords: psoriatic arthritis; bDMARDs; quality of life; meta-analysis

Strengths and limitations of this study

- This is the first meta-analysis focusing on the effects of biological diseasemodifying anti-rheumatic drugs (bDMARDs) on the quality of life (QoL) among
 patients with psoriatic arthritis (PsA).
- Subgroup analyses with the specific hierarchical structure were conducted to
 determine the source of heterogeneity, according to the experimental groups and
 control groups firstly, then category of bDMARDs, variety of bDMARDs, duration
 of PsA.
- Meta-analysis was not performed for the outcomes reported in less than 3 RCTs, and funnel charts was not drawn for the outcomes reported in less than 10 RCTs.
- The results of Egger's test indicated the presence of publication bias, but the trim and fill method were not used to explore publication bias.
 - There was a lack of stratification for countries or regions and long-term effects (exceeding 24 weeks) of bDMARDs for specific analysis due to the limited clinical data.

1. Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease that can lead to structural damage and disability, resulting in impaired quality of life (QoL), physical function, and working ability. [1-3] Scotti L et al. analyzed results of 28 studies and found that the prevalence and incidence rates of PsA are respectively 133 per 100,000 subjects and 83 per 100,000 person-years.^[4] PsA develops in up to 30% of patients with psoriasis.^[5] Rosen CF et al. reported that the QoL of patients with PsA is significantly lower than that of patients with psoriasis. [6] Therefore, one of the main objectives of treating PsA is to improve the QoL of patients. Currently, the QoL of patients with PsA can be measured by the questionnaires including the Short Form 36 (SF-36) questionnaire, Health Assessment Questionnaire (HAQ), Nottingham Health Profile (NHP), EuroQoL 5 domains (EQ-5D), Psoriasis Area and Severity Index (PASI), Disease Activity for Psoriatic Arthritis (DAPSA), Psoriasis Disability Index (PDI), Dermatology Life Quality Index (DLQI), Skindex-29, Skindex-17, Psoriasis Arthritis Quality of Life (PsAQoL), etc. [7-10] Among these questionnaires, the higher scores of SF-36 and EQ-5D indicate higher levels of quality of life, while others are the opposite. [11-16]

As a great advancement in the treatment of PsA, biological disease-modifying anti-rheumatic drugs (bDMARDs) have been proven to decrease inflammation and block structural progression effectively.^[17-18] The bDMARDs are widely recommended by management guidelines,^[1,19] including tumor necrosis factor inhibitors (TNFi, e.g. etanercept, infliximab, adalimumab, golimumab, certolizumab pegol), interleukin-17 inhibitors (IL-17i, e.g. ustekinumab, guselkumab, risankizumab), and interleukin-12/23 inhibitors (IL-12/23i, e.g. secukinumab, ixekizumab, brodalumab).^[1,20] Ruyssen-Witrand A et al.^[21], Lu C et al. ^[22], and Lemos LL et al. ^[23] studied the efficacy and safety of bDMARDs in treating PsA, and found that the physical summarized component (PSC) of SF-36 score was improved, HAQ score and PASI score were decreased, but the change of mental summarized component (MSC) of SF-36 score was

not significant. This indicated that the effects of bDMARDs on QoL in PsA need to be further evaluated.

The purpose of this study is to conduct a meta-analysis of randomized controlled trials (RCTs) related to bDMARDs in treating PsA, to comprehensively evaluate the effects of bDMARDs on QoL with multiple outcome indicators, and to provide evidence for supporting pharmacists' and physicians' clinical actions and decisions in treating PsA. The SF-36, HAQ, NHP, and EQ-5D are generic instruments, scores measured by them are the primary outcomes of this study. The scores measured by other disease-specific instruments are the secondary outcomes.

2. Materials and methods

2.1 Search strategy and study selection

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.^[24] To identify RCTs reporting the effects of bDMARDs on QoL, two independent authors (YQL and ZJD) electronically conducted the searches in PubMed, Web of Science, the Cochrane Library, China National Knowledge Infrastructure (CNKI), WanFang Database, and VIP Datebase, from inception to November 2020 and updated on 19 February 2022. The keywords used for database searches were: patients, including "psoriatic arthritis"; intervention, including "etanercept" or "infliximab" or "adalimumab" or "golimumab" or "certolizumab" or "ustekinumab" or "guselkumab" or "risankizumab" or "tildrakizumab" or "secukinumab" or "ixekizumab" or "brodalumab" or "tumor necrosis factor inhibitor" or "TNFi" or "interleukin-12/23 inhibitor" or "IL-12/23i" or "interleukin-17 inhibitor" or "IL-17i" or "biologic"; and outcomes, including "healthrelated quality of life" or "HRQoL" or "Dermatology Life Quality Index" or "DLQI" or "disease activity index for psoriatic arthritis" or "DAPSA" or "psoriasis area and severity index" or "PASI" or "short form-36" or "SF-36" or "health assessment questionnaire" or "HAQ" or "Nottingham Health Profile" or "NHP" or "EuroQol-5D" or "EQ-5D" or "psoriasis disability index" or "PDI" or "Skindex-29" or "Skindex-17"

- 1 or "PsAQoL" or "quality of life". To avoid missing any related study, authors checked
- 2 the reference citation sections of eligible articles as an additional level of searching.
- 3 Research articles were limited to those regarding RCTs that were published in English
- 4 or Chinese. The complete electronic search strategy for PubMed is provided in
- 5 supplementary table S1.

2.2 Inclusion and exclusion criteria

Studies were independently selected by two authors (YQL and ZJD), and they achieved good agreement (κ =0.942). Studies were included if they met the following inclusion criteria: (i) the trial was a human study conducted on patients with PsA; (ii) the experimental group was treated with bDMARDs or bDMARDs combined with other non-bDMARDs, while placebo and other non-bDMARDs were used as the control groups; (iii) the study provided appropriate data (means and standard deviation [SD] of continuous outcomes, the events number of dichotomous outcomes) for each group present at baseline and end of intervention for DLQI, DAPSA, PASI, SF-36, HAQ, NHP, EQ-5D, PDI, Skindex, and PsAQoL. Other studies, including animal experiments, in vitro studies, case reports, observational studies, systematic reviews, duplicate publications, study protocols without findings, or congress abstracts without full texts were excluded.

2.3 Data extraction and quality assessment

Two authors (YQL and ZJD) independently extracted data from each selected RCTs using a standard abstraction excel sheet (κ =0.959). The extracted data included trial name, sample size, characteristics of participants, duration of treatment, and outcomes of interest. The methodological quality of the selected RCTs was evaluated by two independent investigators (YQL and ZJD) using the Cochrane Collaboration risk of bias tool (κ =0.853).^[25] The Cochrane Collaboration risk of bias tool used the following criteria for quality assessment: randomization generation, allocation concealment, blinding of participants and outcome assessment, incomplete outcome data, and selective outcome reporting, and other sources of bias. Any disagreement

between the reviewing authors was resolved by discussion and final consensus or when

a third author (FC) approved the findings.

2.4 Data synthesis and statistical analysis

All statistical analyses were conducted using Review Manager V.5.3 software (Cochrane Collaboration, Copenhagen, Denmark) and STATA software version 16.0 (Stata Corp., College Station, TX). The risk ratio (RR) with 95% CI was used to evaluate dichotomous outcomes, and the mean difference (MD) with 95% CI was generated to evaluate continuous outcomes. Heterogeneity was assessed by using the I^2 estimate and the P-value of the χ^2 -test. If the P-value >0.10 and I^2 <50%, the assumption of homogeneity was made and the fixed-effects model (FE) was used for analyses. Otherwise, heterogeneity was assumed, the random-effects model (RE) was used to analyze and its source should be further determined by sensitivity analysis or subgroup analysis. Sensitivity analyses were conducted using a leave-one-out method to determine the effect of each trial on the reliability of overall pooled effect sizes. Further, subgroup analyses were carried out to determine the source of heterogeneity according to the potential moderator variables. First, the subgroup analyses were conducted according to the experimental groups and control groups (bDMARDs vs. placebo, bDMARDs+ methotrexate [MTX] vs. MTX, bDMARDs vs. tofacitinib, bDMARDs vs. MTX), which was probably the biggest cause of heterogeneity. Then, each subgroup was analyzed according to the following variables: category of bDMARDs (TNFi, IL-12/23i, IL-17i), variety of bDMARDs (etanercept, infliximab, adalimumab, etc.), duration of PsA (<6 years, 6-9 years, ≥9 years, unclear), duration of treatment (<24 weeks, ≥24 weeks). The funnel plot, as well as Egger's test, were used to determine any possible publication bias.

3. Results

26 3.1 Search Results

The detailed step-by-step process of article identification and selection is presented in figure 1. In online searches, 3190 articles were identified initially. After

duplicates and irrelevant articles were removed, 47 articles^[26-72] (37 RCTs reported) were ultimately included in the meta-analysis. There was a total of 14115 participants in those RCTs. Twenty-five RCTs have reported the effects of bDMARDs on HAQ Disability Index (HAQ-DI), 23 RCTs on SF-36 PCS, 18 RCTs on SF-36 MCS, 1 RCT on SF-36 score, 8 RCTs on DLQI, 3 RCTs on EuroQol Visual Analogue Scale (EQ-VAS), 2 RCTs on PsAQoL, 2 RCT on DAPSA, 7 RCTs on the proportion of participants achieving 50% improvement from baseline in PASI (PASI 50), 2 RCTs on PASI 70, 27 RCTs on PASI 75, 26 RCTs on PASI 90, 10 RCTs on PASI 100 and 1 RCT on PASI score. Among them, HAQ-DI, DLQI, PsAQoL, DAPSA, and PASI scores are negative outcomes, and higher scores indicate worse health-related QoL, while the others are opposite. The detailed characteristics of selected RCTs are summarized in supplementary table S2. The methodological quality assessment of RCTs based on the Cochrane Collaboration risk of bias tool is shown in figure 2. Meta-analysis was not performed for the outcomes reported in less than 3 RCTs.

3.2 Main outcomes

Forest plots demonstrating the effects of bDMARDs on QoL are provided in supplementary figure S1-S9. The pooled effect sizes of all outcomes are summarized in table 1. The results show that bDMARDs taken by patients with PsA can significantly decrease HAQ-DI (MD=-0.19; 95% CI, -0.22, -0.17; *P* <0.00001; *P*: 100%), DLQI (MD=-4.36; 95% CI, -5.76, -2.96; *P* <0.00001; *P*: 99%), and improve SF-36 PCS (MD=3.76; 95% CI, 3.42, 4.10; *P* <0.00001; *P*: 99%), SF-36 MCS (MD=1.76; 95% CI, 1.27, 2.25; *P* <0.00001; *P*: 99%), EQ-VAS (MD=5.27; 95% CI, 1.21, 9.34; *P* <0.00001; *P*: 99%), PASI 50 (RR=4.09; 95% CI, 2.71, 6.16; *P* <0.00001; *P*: 82%), PASI 75 (RR=4.72; 95% CI, 3.87, 5.75; *P* <0.00001; *P*: 81%), PASI 90 (RR=5.73; 95% CI, 4.73, 6.95; *P* <0.00001; *P*: 59%), PASI 100 (RR=9.57; 95% CI, 7.38, 12.43; *P* <0.00001; *P*: 13%). The changes in all outcomes mean that the bDMARDs can effectively improve the QoL of patients with PsA.

Table 1 Meta-analysis of RCTs that examined the effects of bDMARDs on QoL

Outcomes	Number of trials	Effect model	Effect size	95% CI	I ² (%)	P-value
Primary outcome	es					
HAQ-DI	25	RE	-0.19	-0.22, -0.17	100	< 0.00001
SF-36 PCS	23	RE	3.76	3.42, 4.10	99	< 0.00001
SF-36 MCS	18	RE	1.76	1.27, 2.25	99	< 0.00001
EQ-VAS	3	RE	5.27	1.21, 9.34	99	0.01
Secondary outco	mes					
DLQI	8	RE	-4.36	-5.76, -2.96	99	< 0.00001
PASI 50	7	RE	4.09	2.71, 6.16	82	< 0.00001
PASI 75	27	RE	4.72	3.87, 5.75	81	< 0.00001
PASI 90	26	RE	5.73	4.73, 6.95	59	< 0.00001
PASI 100	10	FE	9.57	7.38, 12.43	13	< 0.00001

HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36, DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; PASI 50/75/90/100, the proportion of participants achieving 50%/75%/90%/100% improvement from baseline in Psoriasis Area Severity Index; FE, fixed-effects model; RE, random-effects model.

3.3 Sensitivity analysis

With the exclusion of any single study, the heterogeneity did not change materially in terms of any outcomes except PASI 90. After excluding Hong Tao et al. 2019, the heterogeneity of PASI 90 decreased from 59% to 41%. After excluding NCT02181673 (GO-VIBRANT), post-sensitivity pooled MD for EQ-VAS was 3.71 (95% CI: -0.58, 7.99), which differed from pre-sensitivity significantly. No statistically significant difference was found between pre- and post-sensitivity pooled MDs or RRs for HAQ-DI, SF-36 PCS, SF-36 MCS, DLQI, PASI 50, PASI 75, and PASI 90. The detailed results of sensitivity analyses are presented in table 2.

1 Table 2 Sensitivity analysis of RCTs that examined the effects of bDMARDs on QoL

5 — 6		Pre	-sensitivity a	nalysis	Upper &	Post-sensitivity analysis				
7 8	Outcomes	Number of trials	Pooled estimates	95% CI	lower of effect size	Pooled estimates	95% CI	Excluded trials		
9 — 10 H	IAQ-DI	25	-0.19	-0.22, -0.17	Upper	-0.18	-0.20, -0.15	Mease PJ 2000		
11					Lower	-0.21	-0.24, -0.19	NCT00265096 (GO-REVEAL)		
12 S	F-36 PCS	23	3.76	3.42, 4.10	Upper	3.96	3.63, 4.28	NCT01877668 (OPAL Broaden)		
14					Lower	3.65	3.31, 4.00	NCT02349295 (SPIRIT-P2)		
	F-36 MCS	18	1.76	1.27, 2.25	Upper	2.12	1.62, 2.61	NCT01877668 (OPAL Broaden)		
16 17					Lower	1.65	1.14, 2.16	NCT02349295 (SPIRIT-P2)		
18 E	Q-VAS	3	5.27	1.21, 9.34	Upper	9.66	5.34, 13.98	NCT01877668 (OPAL Broaden)		
19					Lower	3.71	-0.58, 7.99	NCT02181673 (GO-VIBRANT)		
20— 21 D	DLQI	8	-4.36	-5.76, -2.96	Upper	-3.50	-5.00, -2.00	NCT01392326 (FUTURE 1)		
22					Lower	-5.67	-6.71, -4.62	NCT01695239 (SPIRIT-P1)		
23 24 P	ASI 50	7	4.09	2.71, 6.16	Upper	4.83	2.75, 8.49	NCT01087788 (RAPID-PsA)		
2 4 25					Lower	3.30	2.29, 4.78	NCT00265096 (GO-REVEAL)		
26 P	ASI 75	27	4.72	3.87, 5.75	Upper	5.01	4.30, 5.83	NCT01877668 (OPAL Broaden)		
27 28					Lower	4.54	3.74, 5.51	NCT00265096 (GO-REVEAL)		
	ASI 90	26	5.73	4.73, 6.95	Upper	6.19*	5.53, 6.93	Hong Tao 2019		
30 31—					Lower	5.50	4.54, 6.67	NCT01392326 (FUTURE 1)		

- 2 HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component
- 3 summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36;
- 4 DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; PASI 50/75/90,
- 5 the proportion of participants achieving 50%/75%/90% improvement from baseline in Psoriasis
- 6 Area Severity Index.
- 7 * fixed effect

3.4 subgroup analysis

Following subgroup analyses, heterogeneity was changed among some of the strata of subgroups. Regarding the subgroup of bDMARDs vs. placebo, there was a significant difference between pre- and post-subgroup analysis for HAQ-DI in strata of golimumab (MD=0.08; 95% CI, -0.53, 0.69), SF-36 MCS in strata of adalimumab (MD=1.24; 95% CI, -0.11, 2.59) and strata of < 24 weeks (MD=-0.13; 95% CI, -0.39, 0.13), DLQI in strata of adalimumab, ixekizumab, 6-9 years and < 24 weeks. Similar results were found for HAQ-DI and SF-36 MCS in the subgroup of bDMARDs+MTX vs. MTX, HAQ-DI, SF-36 MCS, EQ-VAS, and PASI 75 in the subgroup of bDMARDs vs. tofacitinib, SF-36 MCS in the subgroup of bDMARDs vs. MTX. In general,

- bDMARDs had obvious advantages in improving the QoL of PsA compared with
- 2 placebo, but bDMARDs plus MTX compared with MTX, bDMARDs compared with
- 3 tofacitinib, and bDMARDs compared with MTX had no obvious advantages or
- 4 disadvantages in improving the QoL of PsA. Taking the outcome of HAQ-DI as an
- 5 example, the results of the subgroups of bDMARDs vs. placebo, bDMARDs+MTX vs.
- 6 MTX, bDMARDs vs. tofacitinib, bDMARDs vs. MTX, were respectively -0.21 (MD,
- 7 95% CI, -0.23, -0.18), -0.22 (MD, 95% CI, -0.58, 0.14), -0.01(MD, 95% CI, -0.05, 0.04),
- 8 -0.03 (MD, 95% CI, -0.04, -0.02). The detailed results of the subgroup analysis are
- 9 presented in supplementary table S3.

3.5 Publication bias

- Since the funnel chart requires a certain amount of literature, this part of the study
- was limited to outcomes that included at least 10 RCTs. As presented in figure 3, there
- was potential publication bias detected for the outcomes including HAQ-DI, SF-36 PCS,
- SF-36 MCS, PASI 75, PASI 90, and PASI 100. The P-value calculated by Egger's test
- based on these outcomes also suggested the presence of publication bias, which can
- likely be attributed to unpublished studies with negative findings.

4. Discussion

- This meta-analysis focused on the effects of bDMARDs on QoL in patients with
- 19 PsA, involving a total of 29 RCTs and 9720 participants. Through the quantitative
- analysis of 9 outcomes, it was found that bDMARDs could effectively improve the QoL
- of patients with PsA. By reviewing the studies on minimal clinically important
- differences (MCID) related to PsA on PubMed and comparing the minimal results of
- concerned outcomes, it was found that the decrease of HAQ-DI (MD=-0.19; 95% CI, -
- 24 0.22, -0.17) was a probable clinically meaningful effect (< -0.131) [73-74]. Similar results
- were found for SF-36 PCS (MD=3.76; 95% CI, 3.42, 4.10; > 2.1) [75-78], SF-36 MCS
- 26 (MD=1.76; 95% CI, 1.27, 2.25; > 1.33)^[76-78], and DLOI (MD=-4.36; 95% CI, -5.76, -
- 27 2.96; < -2.24) [79], but not for EQ-VAS (MD=5.27; 95% CI, 1.21, 9.34, < 5.35) [80-83].
- Since the medicines in experimental and control groups had large differences in

methotrexate.

the effects on QoL, subgroup analysis was conducted according to the experimental groups and control groups. The results showed that there was obvious dissimilarity in subgroups of bDMARDs compared with placebo, tofacitinib, and methotrexate, concerning HAQ-DI, SF-36 MCS, EQ-VAS, and PASI 75. The bDMARDs had a significant effect on improving the QoL compared with placebo, but more experimental data were required to confirm the effects of bDMARDs compared with tofacitinib and

Looking specifically at the subgroup of bDMARDs vs. placebo, variety of bDMARDs and duration of treatment were probable sources of heterogeneity. Golimumab, adalimumab, and ixekizumab had no significant difference from placebo concerning one or two of HAQ-DI, SF-36 MCS, and DLQI, which might be due to the efficacy of these bDMARDs that cannot be reflected on the change of QoL. The bDMARDs had no significant difference from placebo in the subgroup of duration of treatment < 24 weeks, which might indicate that long-term use of bDMARDs can improve the QoL of patients.

In this meta study, quantitative analysis was not performed on the outcomes that were reported in less than 3 RCTs, including SF-36 score, PsAQoL, DAPSA, PASI 70, and PASI score. According to NCT02376790 (SEAM-PsA) [61-62], etanercept or plus MTX could decrease DAPSA and improve SF-36 score compared with MTX, but without statistical significance. The result of NCT02980692[65] showed that tildrakizumab could decrease DAPSA compared with placebo without statistical significance. The results of NCT01087788 (RAPID-PsA) [43-44] and NCT01392326 (FUTURE 1) [45-46] showed that certolizumab pegol and secukinumab could significantly decrease PsAQoL compared with placebo. As for PASI 70, Hong Tao et al. [27] found that infliximab plus MTX got more significant improvement than MTX, while NCT02065713 (GO-DACT)[54] found that golimumab plus MTX had no difference form MTX. Additionally, Hong Tao et al. [27] found that the PASI score of patients in infliximab plus MTX group was significantly lower than that in MTX group.

- 1 Taken together, the quantitative analysis results of the effects of bDMARDs on the QoL
- 2 of PsA patients is robust.
- The patients who took bDMARDs showed an improvement in term of SF-36 PCS,
- 4 EQ-VAS, PASI 50, and PASI 90, which was consistent with the results of previous
- 5 studies [21-23]. However, our meta-analysis showed an improvement in terms of SF-36
- 6 MCS, which was inconsistent with the results reported by Lemos LL et al. [23]. This
- 7 variance could be attributed to the differences in search strategies and inclusion criteria.
- 8 For example, the study of Lemos LL et al. considered the effects of TNFi rather than
- 9 bDMARDs.^[23] The articles included in that study concerned not only RCTs, but also
- observational studies.^[23] Additionally, the new trials that appeared after August 2013
- were included in our study and could not have been reviewed by them. Furthermore,
- this meta-analysis comprehensively and specifically analyzed the effects of bDMARDs
- on the QoL of patients with PsA, and quantitatively analyzed some other outcomes that
- were not studied before, including HAQ-DI and DLQI. The results of this meta-analysis
- might be used to support the evidence-based clinical application of bDMARDs.
- However, there were several limitations of this meta-analysis. First, all the
- included studies were published only in English or Chinese, and the results of Egger's
- test indicated the presence of some publication bias. Second, most of the included RCTs
- were multi-center studies. It was difficult to conduct subgroup analysis based on
- 20 countries and regions to evaluate the effects of bDMARDs on the QoL of patients from
- 21 different races and backgrounds. Third, the follow-up period for all included studies
- didn't exceed 24 weeks, so the long-term effects were unable to be assessed. Thus, more
- studies which include longer follow-up periods of using bDMARDs in the treatment of
- 24 PsA are required in the future to confirm the long-term effect of bDMARDs on the QoL
- of PsA patients.

5. Conclusions

- In summary, this meta-analysis demonstrated that the use of bDMARDs by
- patients with PsA appeared to significantly improve the QoL compared with a placebo.

1 To compare bDMARDs with other therapeutic agents, more extensive studies are still

required to confirm the effect of single and combined bDMARDs.

- **Figure 1** Flowchart of the study selection. RCT, randomized controlled trial.
- 5 Figure 2 Quality assessment of included RCTs using Cochrane's risk of bias tool, RCT, randomized
- 6 controlled trial.
- Figure 3 Funnel plots of HAQ-DI, SF-36 PCS, SF-36 MCS, PASI 75, PASI 90 and PASI 100.
- 8 HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component
- 9 summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36;
- PASI 75/90/100, the proportion of participants achieving 75%/90%/100% improvement from
- baseline in Psoriasis Area Severity Index.

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- 9 Index (MEI), Leeds Enthesitis Index (LEI), Spondyloarthritis Research
- 10 Consortium of Canada (SPARCC), Maastricht Ankylosing Spondylitis Enthesis
- Score (MASES), Leeds Dactylitis Index (LDI), Patient Global for Psoriatic
- 12 Arthritis, Dermatology Life Quality Index (DLQI), Psoriatic Arthritis Quality of
- 13 Life (PsAQOL), Functional Assessment of Chronic Illness Therapy-Fatigue
- 14 (FACIT-F), Psoriatic Arthritis Response Criteria (PsARC), Psoriatic Arthritis Joint
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- 11 (DLQI): further data. *Dermatology* 2015;230:27-33.
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- *Qual Life Res* 2016;25:1585-1596.
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- difference in EQ-5D visual analog scale score after pulmonary rehabilitation in
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- in COPD: validity, responsiveness and minimum important difference. *Thorax*
- 23 2016;71:493-500.

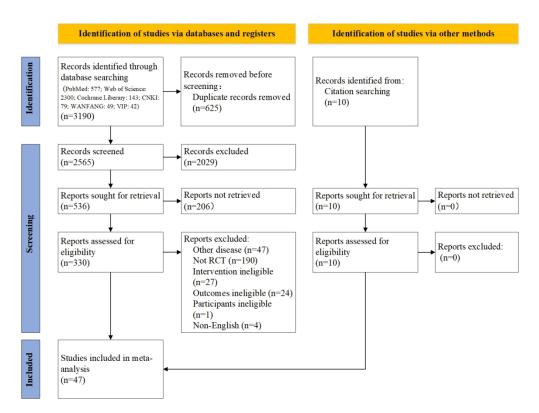


Figure 1 Flowchart of the study selection. RCT, randomized controlled trial.

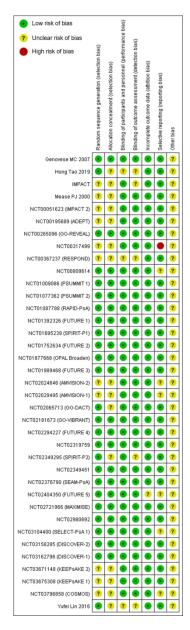


Figure 2 Quality assessment of included RCTs using Cochrane's risk of bias tool, RCT, randomized controlled trial.

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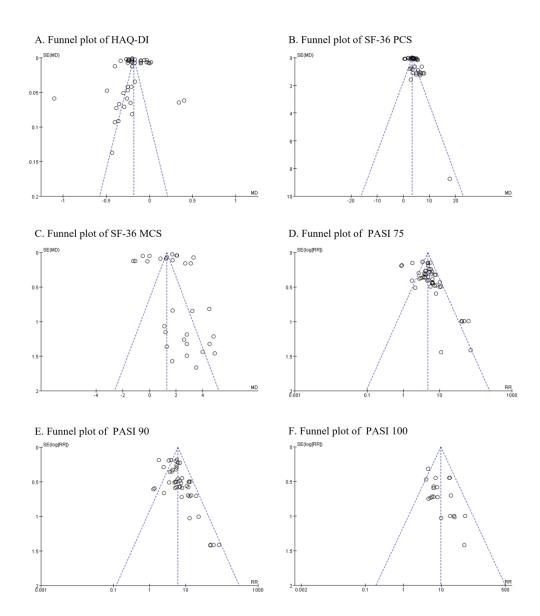


Figure 3 Funnel plots of HAQ-DI, SF-36 PCS, SF-36 MCS, PASI 75, PASI 90 and PASI 100. HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36; PASI 75/90/100, the proportion of participants achieving 75%/90%/100% improvement from baseline in Psoriasis Area Severity Index.

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Conten

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Table S1. Full electronic search strategy of PubMed

#1 "arthritis, psoriatic" [MeSH Terms] #2 "etanercept" [Title/Abstract] OR "infliximab" [Title/Abstract] OR "adalimumab" [Title/Abstract] OR "golimumab"[Title/Abstract] OR "certolizumab"[Title/Abstract] OR "ustekinumab"[Title/Abstract] OR "guselkumab"[Title/Abstract] OR "risankizumab"[Title/Abstract] OR "tildrakizumab"[Title/Abstract] OR "secukinumab"[Title/Abstract] OR "ixekizumab"[Title/Abstract] OR "brodalumab"[Title/Abstract] OR "tumor necrosis factor inhibitor"[Title/Abstract] OR "TNFi"[Title/Abstract] OR "IL-12/23i"[Title/Abstract] OR "interleukin-"interleukin-12/23 inhibitor"[Title/Abstract] OR "IL-17i"[Title/Abstract] OR inhibitor"[Title/Abstract] OR "biologic"[Title/Abstract] #3 "health-related quality of life" [All Fields] OR "HRQoL" [All Fields] OR "Dermatology Life Quality Index"[All Fields] OR "DLQI"[All Fields] OR "disease activity index for psoriatic arthritis" [All Fields] OR "DAPSA" [All Fields] OR "psoriasis area and severity index" [All Fields] OR "PASI" [All Fields] OR "short form-36" [All Fields] OR "SF-36" [All Fields] OR "health assessment questionnaire" [All Fields] OR "HAQ" [All Fields] OR "Nottingham Health Profile"[All Fields] OR "NHP"[All Fields] OR "EuroQol-5D"[All Fields] OR "EQ-5D"[All Fields] OR "psoriasis disability index" [All Fields] OR "PDI" [All Fields] OR "Skindex-29" [All Fields] OR "Skindex-17"[All Fields] OR "quality of life"[All Fields] OR "PsAQoL"[All Fields]

#4 #1 AND #2 AND #3

Table S2. Characteristics of included studies

Trial name[Ref.]	Treatment arms and doses	Sample size (male, %)	Age, years	Duration of PsÆ, years	Duration of treatment	Presented outcomes
Genovese MC 2007	Adalimumab 40 mg SC q2w	51 (56.9)	50.4±11.0	78±7.0	12 weeks	1235
[26]	Placebo	49 (51.0)	47.7±11.3	.⊙ 7 .⊉ ±7.0		
Hong Tao 2019 [27]	Infliximab 3mg /kg IV at weeks 0,2,6,14,22,24 +MTX MTX 15.36±1.69 mg q1w	33 (57.58) 33 (54.55)	35.63±6.12 35.94±6.25	3.55±1.29 3.52±1.28	24 weeks	1012
IMPACT ^[28]	Infliximab 5 mg/kg at weeks 0, 2, 6, 14 Placebo	52 (57.7) 52 (57.7)	45.7±11.1 45.2±9.7	ä. 11 5 7±9.8 11 5 0±6.6	16 weeks	11)
Mease PJ 2000 [29]	Etanercept 25 mg SC BIW Placebo	30 (53) 30 (60)	46.0* 43.5*	59.0* 59.5*	12 weeks	1111
NCT00051623	Infliximab 5 mg/kg IV at weeks 0, 2, 6, 14, 22	100 (71)	47.1±12.8	88±7.2	24 weeks	123
(IMPACT 2)[30,31,32]	Placebo	100 (51)	46.5±11.3	7 ≒ ±7.8		91112
NCT00195689	Adalimumab 40 mg SC at weeks 0, 2, 4, then q4w	151 (56.3)	48.6±12.5	9 <mark>8</mark> ±8.3	24 weeks	1235
(ADEPT)[33,34,35]	Placebo	162 (54.9)	49.2±11.1	9 ₹ ±8.7		9(1)(12(13)
NCT00265096 (GO-	Golimumab 50 mg SC q4w	146 (61)	45.7±10.7	7 <u>\$</u> ±6.8	24 weeks	123
REVEAL) [36,37]	Golimumab 100 mg SC q4w Placebo	146 (59) 113 (61)	48.2±10.9 47.0±10.6	≟: 7∄±7.8 76±7.9		91112
NCT00317499 ^[38]	Etanercept 25 mg SC BIW Placebo	101 (57) 104 (45)	47.6 47.3	7,6±7.9 7,6±7.9 by 9.2	24 weeks	911
NCT00367237	Infliximab 5 mg/kg at weeks 0, 2, 6, 14 + MTX	56 (48.2)	40.1±12.3	2 <u>8</u> ±2.6	16 weeks	1111
(RESPOND) [39]	MTX 15 mg q1w	54 (61.1)	42.3±10.5	3 2 ±2.7		
NCT00809614 ^[40]	Secukinumab 10 mg/kg SC on days 1, 22 Placebo	28 (32) 14 (43)	46.7±11.3 47.6±8.1	6 8 ±6.8 5 2 ±3.8	24 weeks	2

	BM.	J Open		3/bmjope		
				6/bmjopen-2021-05849		
NCT01009086	Ustekinumab 45 mg SC at weeks 0,2, then q12w	205 (51.7)	48.0 (39.0-55.0)*	3.4 2.2-9.2)*	24 weeks	1235
(PSUMMIT 1) ^[41]	Ustekinumab 90 mg SC at weeks 0,2, then q12w Placebo	204 (56.9) 206 (52.4)	47.0 (38.5-54.0)* 48.0 (39.0-57.0)*	4.9(1.7-8.3)* 3.6(1.0-9.7)*		11)
NCT01077362	Ustekinumab 45 mg at weeks 0, 4, then q12w	103 (46.6)	49.0(40.0-56.0)*	5.3(2.3-12.2)*	24 weeks	1235
(PSUMMIT 2) ^[42]	Ustekinumab 90 mg at weeks 0, 4, then q12w Placebo	105 (46.7) 104 (49.0)	48.0(41.0-57.0)* 48.0(38.5-56.0)*	Ñ 4.5(ᡶ.7-10.3)* 5.5 ② .3-12.2)*		1112
NCT01087788	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 200	138 (46.4)	48.2±12.3	\$6±8.5	24 weeks	1235
(RAPID-PsA) [43,44]	mg q2w Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 400	135 (45.9)	47.1±10.8	ф ф 1±8.3		791112
	mg q4w Placebo	136 (41.9)	47.3±11.1	http: 5 9±7.7		
NCT01392326	Secukinumab 75 mg/kg IV at weeks 2, 4, then 75 mg	202 (41.6)	48.8±12.2		24 weeks	1235
(FUTURE 1) ^[45,46]	SC q4w Secukinumab 75 mg/kg IV at weeks 2, 4, then 150 mg	202 (47.5)	49.6±11.8	 		71112
	SC q4w Placebo	202 (47.5)	48.5±11.2	m/ or		
NCT01695239	Ixekizumab 80 mg SC q2w	107 (42.1)	49.1 ± 10.1	—————————————————————————————————————	24 weeks	1235
(SPIRIT-P1) [47,48]	Ixekizumab 80 mg SC q4w Adalimumab 40 mg SC q2w	103 (46.6) 101 (50.5)	49.8 ± 12.6 48.6 ± 12.4	7:2±8.0 69:±7.5	24 Weeks	6111213
	Placebo	106(45.3)	50.6 ± 12.3	623±6.9		
NCT01752634	Secukinumab 300 mg SC q1w to week 4 then q4w	100 (51)	46.9±12.6	guest.	24 weeks	121112
(FUTURE 2) ^[49]	Secukinumab 150 mg SC q1w to week 4 then q4w Secukinumab 75mg SC q1w to week 4 then q4w	100 (55) 99 (47)	46.5±11.7 48.6±11.4	st. Protected		
	Placebo	98 (41)	49.9±12.5	<u> </u>		

	ВМЈ	5/bmjopen				
				3. 6/bmjopen-2021-058497 5		
NCT01877668	Adalimumab 40 mg SC q2w	106 (53)	47.4 ± 11.3	53±5.3	3 months	1236
(OPAL Broaden)	Tofacitinib 5 mg orally BID	107 (47)	49.4 ± 12.6	$7\frac{3}{18} \pm 8.2$		11)
[50][51]	Tofacitinib 10 mg orally BID	104 (40)	46.9 ± 12.4	5₫±5.8		
	Placebo	105 (47)	47.7 ± 12.3	6 ≥ ±6.4		
NCT01989468	Secukinumab 300 mg SC at weeks 1, 2, 3, 4, then q4w	139 (48.2)	49.3±12.9	8 <u>.3</u> ±9.2	24 weeks	12112
(FUTURE 3) ^[52]	Secukinumab 150 mg SC at weeks 1, 2, 3, 4, then q4w Placebo	138 (44.2) 137 (43.1)	50.1±11.7 50.1±12.6	O 7 <u>≤</u> 7±8.5 © 6±6.9		
NCT02024646	Brodalumab 140mg SC q2w	160 (50.0)	47.4±12.8	&5±7.4	24 weeks	11)12)13
(AMVISION-2) ^[53]	Brodalumab 210mg SC q2w Placebo	163 (48.5) 161 (47.2)	47.0±12.6 48.3±13.0	ਰੋ 624±7.7 7 <u>2</u> 1±7.5		
NCT02029495	Brodalumab 140mg SC q2w	158 (49.4)	49.9±12.8	851±8.1	24 weeks	111213
(AMVISION-1) [53]	Brodalumab 210mg SC q2w Placebo	159 (56.0) 161 (50.3)	49.1±12.2 48.1±11.8	954±9.3 852±8.2		
NCT02065713 (GO-	Golimumab 50 mg SC q4w + MTX	21 (81.0)	46.2 (15.5)*	3.8 (6.7)*	24 weeks	91012
DACT) ^[54]	MTX 15 mg orally q1w and increased 5 mg q4w until 25 mg q1w	22 (87.0)	44.1 (24.6)*	4. 2 (6.1)*		
NCT02181673 (GO-	Golimumab 2 mg/kg IV at weeks 0, 4, then q8w	241 (50.6)	45.7 ± 11.3	6 <u>2</u> ±6.0	24 weeks	1235
VIBRANT) [55,56]	Placebo	239 (53.1)	46.7 ± 12.5	5.93±5.9		6 (1)(12(13)
NCT02294227	Secukinumab 150 mg SC q4w LD	114 (41.2)	48.3±12.2	556±7.3	16 weeks	21112
(FUTURE 4) ^[57]	Secukinumab 150 mg SC q4w no-LD Placebo	113 (45.1) 114 (39.5)	50.4±11.8 48.5±12.2	\$7±7.7 \$9±7.6		
NCT02319759 ^[58]	Guselkumab 100 mg SC at weeks 0, 4, then q8w Placebo	100 (52) 49 (49)	47.4±12.8 44.2±12.4	9±7.2 7±0±7.2 6€9±7.2	24 weeks	1239
NCT02349295	Ixekizumab 80 mg SC q4w	122 (52)	52.6±13.6	1 ₫ .0±9.6	24 weeks	123
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NCT03162796	Guselkumab 100 mg SC q4w	128 (52)	47.4±11.6	65±6.3	24 weeks	123
(DISCOVER-1) [68]	Guselkumab 100 mg SC at weeks 0, 4, then q8w Placebo	127 (54) 126 (48)	48.9±11.5 49.0±11.1	634±5.9 7€2±7.6		11/12/13
NCT03671148	Risankizumab 150mg SC at weeks 0, 4, 16	224 (44.6)	53 (23–84)	852±8.2	24 weeks	1212
(KEEPsAKE 2) [69]	Placebo	219 (45.2)	52 (24-83)	8 <u>.2</u> ±8.3		
NCT03675308	Risankizumab 150mg SC at weeks 0, 4, 16	483 (52.2)	52 (20–85)	<i>7</i> €1±7.0	24 weeks	1212
(KEEPsAKE 1) [71]	Placebo	481 (48.6)	52 (22–79)	7 <u>⊊</u> i±7.7		
NCT03796858	Guselkumab 100 mg SC at weeks 0, 4, then q8w	189 (46)	49±12	8 ± ±7.8	24 weeks	3(1)(12)
(COSMOS)	Placebo	96 (54)	49±12	8\$\\\7\±7.2		
Yufei Lin 2016 ^[72]	Infliximab 5mg /kg IV at weeks 0,2,6,12 + MTX MTX 7.5-15 mg orally q1w and increased to 15-25 mg	42 (61.90) 42 (66.67)	44.01±10.33 43.59±10.29	3.52±2.11 3.51±2.12	24 weeks	14)
	q1w			njop		
				O		

MTX: methotrexate; IV: intravenous; SC: subcutaneous; qXw: once every X weeks; BID: twice daily; BIW: twice weekly LD: loading dose; ---: not reported; 1 HAQ-DI, Health Assessment Questionnaire Disability Index; 2SF-36 PCS, physical component summary of the Short Form 36; 3SF-36 MCS, mental component summary of the Short Form 36; 4SF-36 score, the Short Form 36 score; 5DLQI, Dermatology Life Quality Index; 6EQSVAS, EuroQol Visual Analogue Scale;

(7) PsAQoL, Psoriasis Arthritis Quality of Life; (8) DAPSA, Disease Activity for Psoriatic Arthritis; (9) PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 70, the proportion of participants achieving 70% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; (10) PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area 100% improvement from baseline

^{*} Data are reported as median (IQR);

Table S3. Subgroup analysis of RCTs that examined the effect of bDMARDs on QoL

Groups	Outcomes	K	Effect size	95% CI	I ² (%)	P-value
bDMARDs	HAQ-DI				•	
vs. Placebo	Total	40	-0.21	-0.23, -0.18	99	< 0.00001
	Category of bDMARD					
	TNFi	11	-0.25	-0.31, -0.18	98	< 0.00001
	IL-12/23i	9	-0.23	-0.27, -0.19	99	< 0.00001
	IL-17i	11	-0.17	-0.21, -0.14	99	< 0.00001
	Variety of bDMARD					
	Etanercept	1	-1.10	-1.22, -0.98		< 0.00001
	Infliximab	1	-0.40	-0.58, -0.22		< 0.0001
	Adalimumab	5	-0.20*	-0.20, -0.20	0	< 0.00001
	Golimumab	3	0.08	-0.53, 0.69	99	0.79
	Certolizumab pegol	2	-0.30*	-0.39, -0.21	1	< 0.00001
	Ustekinumab	4	-0.21*	-0.25, -0.17	0	< 0.00001
	Guselkumab	5	-0.27	-0.31, -0.24	98	< 0.00001
	Tildrakizumab	4	-0.07	-0.12, -0.03	97	0.003
	Risankizumab	2	-0.19	-0.21, -0.16	98	< 0.00001
	Secukinumab	9	-0.17	-0.22, -0.12	99	< 0.00001
	Ixekizumab	4	-0.32	-0.46, -0.18	98	< 0.00001
	Duration of PsA					
	< 6 years	8	-0.22	-0.25, -0.20	98	< 0.00001
	6-9 years	20	-0.16	-0.20, -0.13	99	< 0.00001
	≥9 years	5	-0.46	-0.65, -0.28	99	< 0.00001
	Unclear	7	-0.17	-0.23, -0.12	99	< 0.00001
	Duration of treatment					
	< 24 weeks	5	-0.32	-0.40, -0.24	99	< 0.00001
	≥ 24 weeks	35	-0.19	-0.22, -0.17	99	< 0.00001
	SF-36 PCS					
	Total	36	4.04	3.75, 4.32	99	< 0.00001
	Category of bDMARD					
	TNFi	11	4.96	4.37, 5.56	88	< 0.00001
	IL-12/23i	11	3.93	3.58, 4.28	98	< 0.00001
	IL-17i	14	3.78	3.05, 4.50	99	< 0.00001
	Variety of bDMARD					
	Infliximab	1	6.40	3.90, 8.90		< 0.00001
	Adalimumab	5	3.62	3.26, 3.98	73	< 0.00001
	Golimumab	3	7.06*	6.06, 8.05	0	< 0.00001
	Certolizumab pegol	2	5.85*	4.48, 7.22	0	< 0.00001
	Ustekinumab	4	3.47*	2.74, 4.22	6	< 0.00001
	Guselkumab	5	4.22	3.77, 4.67	98	< 0.00001
	Risankizumab	2	3.60	3.01, 4.19	99	< 0.00001
	Secukinumab	10	3.30	2.50, 4.11	99	< 0.00001
	Ixekizumab	4	5.22	4.67, 5.78	64	< 0.00001

Duration of PsA					
< 6 years	10	3.39	3.09, 3.68	97	< 0.00001
6-9 years	17	4.44	3.81, 5.08	99	< 0.00001
≥9 years	4	5.58	4.84, 6.31	79	< 0.00001
Unclear	5	3.97	3.27, 4.67	99	< 0.00001
Duration of treatment	J	3.57	3.27, 1.07		(0.00001
< 24 weeks	4	3.04	2.62, 3.46	92	< 0.00001
≥ 24 weeks	32	4.19	3.88, 4.50	99	< 0.00001
SF-36 MCS	32	1.17	3.00, 1.50		(0.00001
Total	27	2.11	1.76, 2.46	97	< 0.00001
Category of bDMARD		2.11	1.70, 2.10	,	(0.00001
TNFi	11	2.60	1.59, 3.60	95	< 0.00001
IL-12/23i	9	1.75	1.28, 2.22	96	< 0.00001
IL-17i	7	2.37	1.51, 3.23	99	< 0.00001
Variety of bDMARD	,	2.57	1.31, 3.23	77	< 0.00001
Infliximab	1	3.50	0.24, 6.76		0.04
Adalimumab	5	1.24	-0.11, 2.59	98	0.07
Golimumab	3	4.47*	3.22, 5.72	0	< 0.00001
Certolizumab pegol	2	3.78*	2.11, 5.44	28	0.0002
Ustekinumab	4	2.21*	1.27, 3.15	0	< 0.0002
Guselkumab	6	1.66	1.22, 2.10	98	< 0.00001
Secukinumab	2	2.30	0.34, 4.26	100	0.00001
Ixekizumab					
	4	2.89*	2.67, 3.11	32	< 0.00001
Duration of PsA	0	1 57	1 12 2 01	00	× 0.00001
< 6 years	8	1.57	1.13, 2.01	98	< 0.00001
6-9 years	13	2.00	1.49, 2.52	84	< 0.00001
≥ 9 years	4	2.90	2.40, 3.40	61	< 0.00001
Unclear	2	2.30	0.34, 4.26	100	0.02
Duration of treatment		0.404	0.00 0.10	25	0.05
< 24 weeks	2	-0.13*	-0.39, 0.13	27	0.86
≥ 24 weeks	25	2.24	1.91, 2.57	97	< 0.00001
EQ-VAS	_				
Total	5	8.76	5.32, 12.20	71	< 0.00001
Category of bDMARD					
TNFi	3	9.05	3.75, 14.35	85	0.0008
IL-17i	2	8.31*	3.85, 12.77	0	0.0003
Variety of bDMARD					
Adalimumab	2	6.72*	6.13, 7.31	0	< 0.00001
Golimumab	1	14.70	10.44, 18.96		< 0.00001
Ixekizumab	2	8.31*	3.85, 12.77	0	0.0003
Duration of PsA					
< 6 years	1	6.73	6.14, 7.32		< 0.00001
6-9 years	4	9.66	5.34, 13.98	58	< 0.0001
Duration of treatment					

< 24 weeks	1	6.73	6.14, 7.32		< 0.00001
≥ 24 weeks	4	9.66	5.34, 13.98	58	< 0.0001
DLQI					
Total	14	-4.36	-5.76, -2.96	99	< 0.00001
Category of bDMARD					
TNFi	6	-3.38	-5.53, -1.23	92	0.002
IL-12/23i	4	-5.39*	-6.15, -4.63	0	< 0.00001
IL-17i	4	-4.79	-6.81, -2.77	99	< 0.00001
Variety of bDMARD					
Adalimumab	3	-2.31	-5.60, 0.98	89	0.17
Golimumab	1	-6.20	-7.56, -4.84		< 0.00001
Certolizumab pegol	2	-3.46	-6.40, -0.53	90	0.02
Ustekinumab	4	-5.39*	-6.15, -4.63	0	< 0.00001
Secukinumab	2	-9.05	-9.93, -8.17	98	< 0.00001
Ixekizumab	2	-0.17*	-0.99, 0.65	0	0.69
Duration of PsA					
< 6 years	4	-5.39*	-6.15, -4.63	0	< 0.00001
6-9 years	6	-1.70	-3.59, 0.19	92	0.08
≥9 years	2	-5.12*	-6.35, -3.89	0	< 0.00001
Unclear	2	-9.05	-9.93, -8.17	98	< 0.00001
Duration of treatment					
< 24 weeks	1	-1.70	-4.21, 0.81		0.18
≥ 24 weeks	13	-4.53	-5.97, -3.10	99	< 0.00001
PASI 50					
Total	8	4.54	2.98, 6.91	81	< 0.00001
Category of bDMARD					
TNFi	7	4.92	3.00, 8.07	83	< 0.00001
IL-12/23i	1	2.97	1.90, 4.65		< 0.00001
Variety of bDMARD					
Etanercept	1	2.69	1.68, 4.30		< 0.0001
Infliximab	1	9.83	5.06, 19.09		< 0.00001
Adalimumab	1	6.50	3.34, 12.64		< 0.00001
Golimumab	2	9.59	5.55, 16.56	0	< 0.00001
Certolizumab pegol	2	2.63	2.03, 3.40	0	< 0.00001
Guselkumab	1	2.97	1.90, 4.65		< 0.00001
Duration of PsA					
6-9 years	4	6.93	3.33, 14.42	80	< 0.00001
≥9 years	4	3.06	2.20, 4.25	54	< 0.00001
PASI 75					
Total	47	5.29*	4.85, 5.76	45	< 0.00001
Category of bDMARD					
TNFi	13	7.19	4.26, 12.16	74	< 0.00001
IL-12/23i	13	4.95*	4.30, 5.69	49	< 0.00001
IL-17i	21	4.94*	4.36, 5.60	5	< 0.00001

Variety of bDMARD					
Etanercept	2	8.34*	2.83, 24.62	0	0.0001
Infliximab	2	65.64*	13.30, 322.82	0	< 0.00001
Adalimumab	4	4.58	1.72, 12.22	74	0.002
Golimumab	3	18.30	2.23, 149.96	84	0.007
Certolizumab pegol	2	4.06*	2.79, 5.91	0	< 0.00001
Ustekinumab	4	6.50*	4.79, 8.83	2	< 0.00001
Guselkumab	6	4.23*	3.56, 5.02	43	< 0.00001
Tildrakizumab	4	3.70*	2.59, 5.28	0	< 0.00001
Secukinumab	12	5.10*	4.41, 5.89	21	< 0.00001
Ixekizumab	4	5.03*	3.51, 7.22	2	< 0.00001
Brodalumab	4	6.16*	4.32, 8.80	0	< 0.00001
Duration of PsA					
< 6 years	9	4.68	3.57, 6.13	57	< 0.00001
6-9 years	26	5.68*	5.06, 6.38	26	< 0.00001
≥9 years	7	5.92	3.33, 10.51	57	< 0.00001
Unclear	5	4.23	2.43, 7.36	68	< 0.00001
Duration of treatment					
< 24 weeks	9	5.13*	4.37, 6.02	37	< 0.00001
≥ 24 weeks	38	5.34*	4.83, 5.91	48	< 0.00001
PASI 90					
Total	43	6.38*	5.68, 7.16	30	< 0.00001
Category of bDMARD					
TNFi	9	9.45*	6.62, 13.50	49	< 0.00001
IL-12/23i	11	7.47*	5.97, 9.35	0	< 0.00001
IL-17i	23	5.39*	4.66, 6.24	23	< 0.00001
Variety of bDMARD					
Infliximab	1	82.76	5.17, 1325.04		0.002
Adalimumab	3	7.64	1.43, 40.80	65	0.02
Golimumab	3	16.48	2.33, 116.59	65	0.005
Certolizumab pegol	2	7.11*	3.78, 13.36	0	< 0.00001
Ustekinumab	2	9.93*	4.42, 22.34	0	< 0.00001
Guselkumab	6	6.36*	4.96, 8.16	0	< 0.00001
Tildrakizumab	4	6.09*	3.44, 10.76	0	< 0.00001
Risankizumab	2	5.36*	3.87, 7.42	0	< 0.00001
Secukinumab	12	5.12	3.72, 7.03	51	< 0.00001
Ixekizumab	4	5.75*	3.70, 8.93	39	< 0.00001
Brodalumab	4	12.05*	6.80, 21.36	0	< 0.00001
Duration of PsA					
< 6 years	6	7.52*	5.62, 10.07	0	< 0.00001
6-9 years	20	6.10*	5.31, 7.00	23	< 0.00001
	28	0.10	, , , , ,		
≥ 9 years	28 4	5.52	2.83, 10.78	51	< 0.00001
≥ 9 years Unclear					

	< 24 weeks	6	4.60*	3.73, 5.67	44	< 0.00001
	≥ 24 weeks	37	7.04*	6.14, 8.08	14	< 0.00001
bDMARDs+	HAQ-DI	2	-0.22	-0.58, 0.14	86	0.23
MTX vs.	SF-36 PCS	1	2.00	1.90, 2.10		< 0.00001
MTX	SF-36 MCS	1	0.00	-0.10, 0.10		1.00
	PASI 50	1	1.76	1.06, 2.92		0.03
	PASI 75	1	1.79	1.31, 2.44		0.0002
	PASI 90	2	1.97	1.45, 2.70	0	< 0.0001
bDMARDs	HAQ-DI	2	-0.01	-0.05, 0.04	96	0.84
vs.	SF-36 PCS	2	0.63*	0.49, 0.77	36	< 0.00001
Tofacitinib	SF-36 MCS	2	-1.15*	-1.32, -0.97	0	< 0.00001
	EQ-VAS	2	-1.81	-3.61, -0.02	95	0.05
	PASI 75	2	0.90*	0.69, 1.17	0	0.43
bDMARDs	HAQ-DI	1	-0.03	-0.04, -0.02		< 0.00001
vs. MTX	SF-36 PCS	1	1.80	1.70, 1.90		< 0.00001
	SF-36 MCS	1	-0.50	-0.60, -0.40		< 0.00001

bDMARDs, the biological disease-modifying anti-rheumatic drugs; TNFi, the tumor necrosis factor inhibitor; IL-17i, interleukin-17 inhibitor; IL-12/23i, interleukin-12/23 inhibitor; HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36, DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; PASI 50/75/90, the proportion of participants achieving 50%/75%/90% improvement from baseline in Psoriasis Area Severity Index;

K: Number of data reported in included studies;

^{*} fixed effect

Figure S1 Forest plot of HAQ-DI. HAQ-DI, Health Assessment Questionnaire Disability Index.

	Evne	erimen	tal	C	ontrol			Mean Difference	Mean Difference		
Study or Subgroup	Mean			Mean		Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Genovese MC 2007	-0.3	0.5	51	-0.1	0.3	49	1.3%	-0.20 [-0.36, -0.04]			
Mease PJ 2000		0.23	30		0.23	30	1.7%	-1.10 [-1.22, -0.98]			
NCT00051623 (IMPACT 2)	-0.4		100		0.66	100	1.2%	-0.40 [-0.58, -0.22]			
NCT00195689 (ADEPT)	-0.4	0.5	151	-0.1	0.4	162	1.9%	-0.30 [-0.40, -0.20]	N		
NCT00265096 (GO-REVEAL) A	0.33		146	-0.01	0.49	113	1.6%	0.34 [0.21, 0.47]			
NCT00205096 (GO-REVEAL) B	0.33	0.55	146	-0.01	0.49	113	1.7%	0.40 [0.28, 0.52]			
NCT00203030 (GO-REVEAL) B	-0.99		56			54	0.7%	-0.43 [-0.70, -0.16]			
NCT01009086 (PSUMMIT 1) A		0.47	205			206	2.1%	-0.21 [-0.29, -0.13]	_		
NCT01009086 (PSUMMIT 1) B	-0.34			-0.09		206	2.0%	-0.25 [-0.34, -0.16]			
10. 15을 내고 10. 15을 위한 10. 15를 받았다면서 보고 있는데 10. 15를 받았다.			103	-0.09	0.30	104	2.0%		OK SERVI		
NCT01077362 (PSUMMIT 2) A	-0.17		105	0	0.2	104	2.1%	-0.17 [-0.24, -0.10]	4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-4-		
NCT01077362 (PSUMMIT 2) B	-0.25							-0.25 [-0.33, -0.17]			
NCT01087788 (RAPID-PsA) A	-0.52		138			136	1.6%	-0.35 [-0.48, -0.22]	25 35 28		
NCT01087788 (RAPID-PsA) B	-0.43			-0.17		136	1.7%	-0.26 [-0.38, -0.14]	\$400000		
NCT01392326 (FUTURE 1) A	-0.41			-0.17		202	2.6%	-0.24 [-0.25, -0.23]			
NCT01392326 (FUTURE 1) B		0.04		-0.17		202	2.6%	-0.23 [-0.24, -0.22]			
NCT01695239 (SPIRIT-P1) A	-0.53			-0.15	0.5	106	1.5%	-0.38 [-0.52, -0.24]	<u> </u>		
NCT01695239 (SPIRIT-P1) B	-0.44			-0.15	0.5	106	1.5%	-0.29 [-0.43, -0.15]	8-8-8		
NCT01695239 (SPIRIT-P1) C	-0.37			-0.15	0.5	106	1.6%	-0.22 [-0.35, -0.09]			
NCT01752634 (FUTURE 2) A	-0.56			-0.31		98	2.6%	-0.25 [-0.27, -0.23]			
NCT01752634 (FUTURE 2) B		0.05		-0.31	0.06	98	2.6%	-0.17 [-0.19, -0.15]	7		
NCT01752634 (FUTURE 2) C	-0.32			-0.31	0.06	98	2.6%	-0.01 [-0.03, 0.01]	1		
NCT01877668 (OPAL Broaden) A	-0.38		106			107	2.6%	-0.03 [-0.04, -0.02]	~		
NCT01877668 (OPAL Broaden) B	-0.38		106		0.05	104	2.6%	0.02 [0.01, 0.03]	•		
NCT01877668 (OPAL Broaden) C	-0.38			-0.18		105	2.6%	-0.20 [-0.21, -0.19]	7		
NCT01989468 (FUTURE 3) A		0.04	139	-0.17		137	2.6%	-0.21 [-0.22, -0.20]	.5		
NCT01989468 (FUTURE 3) B	-0.27	0.04	138	-0.17	0.06	137	2.6%	-0.10 [-0.11, -0.09]	1		
NCT02181673 (GO-VIBRANT)	-0.63			-0.14	0.5	236	2.0%	-0.49 [-0.58, -0.40]	20-		
NCT02319759	-0.42		100		0.53	49	1.2%	-0.36 [-0.54, -0.18]			
NCT02349295 (SPIRIT-P2) A	-0.6	0.1	122	-0.2	0.1	118	2.6%	-0.40 [-0.43, -0.37]	T		
NCT02349295 (SPIRIT-P2) B	-0.4	0.1	123	-0.2	0.1	118	2.6%	-0.20 [-0.23, -0.17]	- T		
NCT02376790 (SEAM-PsA) A	-0.44	0.04	258	-0.41	0.04	252	2.6%	-0.03 [-0.04, -0.02]	5		
NCT02376790 (SEAM-PsA) B	-0.47	0.04	283	-0.41	0.04	252	2.6%	-0.06 [-0.07, -0.05]			
NCT02721966 (MAXIMISE) A	-0.4	0.04	167	-0.2	0.04	166	2.6%	-0.20 [-0.21, -0.19]	150		
NCT02721966 (MAXIMISE) B	-0.3	0.04	165	-0.2	0.04	166	2.6%	-0.10 [-0.11, -0.09]	<i>a</i>		
NCT02980692 A	-0.3	0.05	78	-0.2	0.05	79	2.6%	-0.10 [-0.12, -0.08]	*		
NCT02980692 B	-0.3	0.05	79	-0.2	0.05	79	2.6%	-0.10 [-0.12, -0.08]	*		
NCT02980692 C	-0.3	0.05	77	-0.2	0.05	79	2.6%	-0.10 [-0.12, -0.08]	*		
NCT02980692 D	-0.2	0.05	78	-0.2	0.05	79	2.6%	0.00 [-0.02, 0.02]	1 ×		
NCT03104400 (SELECT-PsA 1)	-0.39	0.04	391	-0.19	0.03	367	2.6%	-0.20 [-0.21, -0.19]	*		
NCT03158285 (DISCOVER-2) A	-0.4	0.03	245	-0.13	0.03	246	2.6%	-0.27 [-0.28, -0.26]	•		
NCT03158285 (DISCOVER-2) B	-0.37	0.03	248	-0.13	0.03	246	2.6%	-0.24 [-0.25, -0.23]	*		
NCT03162796 (DISCOVER-1) A	-0.4	0.04	128	-0.07	0.04	126	2.6%	-0.33 [-0.34, -0.32]	•		
NCT03162796 (DISCOVER-1) B	-0.32	0.04	127	-0.07	0.04	126	2.6%	-0.25 [-0.26, -0.24]			
NCT03671148 (KEEPsAKE 2)	-0.22	0.03	224	-0.05	0.04	219	2.6%	-0.17 [-0.18, -0.16]	•		
NCT03675308 (KEEPsAKE 1)	-0.31			-0.11		481	2.6%	-0.20 [-0.20, -0.20]			
Total (95% CI)			6792			6603	100.0%	-0.19 [-0.22, -0.17]	•		
Heterogeneity: Tau ² = 0.01; Chi ² = 1	0182.80	df = 4	4 (P < 1	0.00001); 2 = 1	100%			-1 -05 0 05 1		
Test for overall effect: Z = 14.14 (P <	0.00001)							Favours [experimental] Favours [control]		
		3							ravours (experimental) ravours (control)		

Figure S2. Forest plot of SF-36 PCS. SF-36 PCS, physical component summary of the Short Form 36.

		rimer		Control				Mean Difference	Mean Difference	
Study or Subgroup			Total			Total	Wittahi	IV, Bandom, 95% CI	M. Randam, 95% Cl	
Genovese MC 2007	5.7	8.5	49	2.8	7.1	45	0.1%	2.90 0.28, 6.06	-	
NCT00051623 (MPACT 2)	7.2	9.0	100	1.2	82	100	1.7%	6.40 (3.90, 8.90)		
NCT00195889 (ADEPT)	9.3	10.1	140	1.4	3.8	152	1.3%	7.90[5.64, 10.16]		
NCT00295096 (9.0-REVEAL) A	7.42	9.17	345	0.67	8.72	113	1.4%	6.75 (4.56, 9.94)	700	
NCT00265096 (90-REVEAL) 6	8.22	9.64	146	0.67	8.72	113	1.4%	7.55(5.31.9.79)	-	
NCT00888614	152	28.1	28	-2.81	26	. 14	0.0%	17.81 (0.67, 34.95)		
ACTOTOGODOG (PSUMMIT T) A	4.46	0.16	205	1.38	5.5	206	21%	3.00 (1.63, 4.53)	-	
(CTO1009086 (PSUMMIT 1) B	5.76	7.89	204	1.38	5.5	206	2.2%	4.38 (3.08, 5.68)	-	
ICT01077362 (PSUMMIT 2) A			- 99	1.13	3.61	BT	1.5%	2.63(1.01, 4.26)	-	
CT01077362 (PSUMMIT 2) B		7.75	97		3.61	97	1.6%	3.39 (1.69, 5.09)	-	
CT01087788 (RAPID-PSA) A	8.4		138	2.1	7.2	136	1.5%	0.30 [4.23, 0.37]	-	
CT01007780 (PAPID-PsA) B	7.6	0.1	135	2.1	7.2	126	1.7%	550(367,733)	-	
ICT01392326 (FUTURE 1) A	5.41	0.52	202		0.72	202	3.1%	3.59(3.47, 3.71)	(a)	
ICT01392326 (FUTURE 1) B	5.91	0.53	202		0.72	202	3.3%	4.09 [3.97, 4.21]	4	
(CT01695239 (SP/R/T-P1) A	7.3	8.6	107	27		106	1.4%	5.00 (2.81, 7.19)	-	
(CT01695239 (SP#RT-F1) III	7.7	9.0	103	27	1.5	106	1.1%	5.00(2.81,7.39)	-	
(CT01695239 (SPIRIT-P1) C	8.3	9.3	301	27	7.7	106	1.4%	3.60 (1.42, 5.78)		
ICT01752634 (FUTURE 2) A	7.25	0.74	100		0.87	98	3.2%	530 (5.08, 5.54)	100	
CT01752634 (FUTURE 2):8		0.73	100		0.97	98	3.1%	4.44 [4.20, 4.68]	100	
CT01752634 (FUTURE 2) C	4.38		99		0.17	58	3.2%	2.43(2.19, 2.67)	+	
(CTD1977868 (OPAL Broader) A		0.75	106		0.73	107	11%	0.72(0.52, 0.92)		
ICT01977668 (OPAL Broaders B		0.75	106		0.74	104	3.7%	0.54 (0.34, 0.74)		
iCT01977668 (OPAL Broaders C			106		0.79	105	0.3%	3.55 (3.34, 3.76)		
						137			1.00	
ICT01998468 (FUTURE 3) A	8.46	0.59	139		0.83		3.3%	3.52 [3.35, 3.69]	100	
CT01989468 (FUTURE 3) B	3.42	0.6	120		0.83	137	3.3%	0.40 (0.31, 0.85)		
(CT02181873 (GO-VIBRANT)	9.4	9.1	237		6.1	226	2.2%	7.00 (5.71, 9.29)		
(CT02294227 (FUTURE 4) A	3.42		114		0.59	114	3.7%	279 [2.64, 2.94]	12	
ICT02294227 (FUTURE 4) B	3.44	0.58	113		0.50	114	3.1%	2,81 [2.88, 2.96]	A	
ICT02318759	6.59	7.47	100		6.51	49	1.3%	6.13 [3.78, 0.47]	-	
ICT02349295 (SP-RIT-P2) A	0.9	1.3	122	3.3	1.4	310	3.2%	5.80 (5.28, 5.94)		
ICT02349295 (SPIRIT-P2) B	8.2	1.3	123	3.9	1.4	118	3.7%	4.90 (4.57, 5.23)	11.77	
(CT02376780 (SEAM Pol/) A	7.8	0.6	256	- 6		253	3.3%	1.80 (1.70, 1.90)		
(CT02376790 (SEAM-PsA) B	. 8	0.6	257		0.6	253	3.3%	2.00 (1.90, 2.10)	*	
ICT03104400 (SELECT-PsA,1)	7.0	0.41	391		0.43	367	2.2%	3.50 [3.44, 3.58]		
(CT03158295 (DISCOVER-2) A	7.04	0.45	245	2000	0.45	246	2.1%	3.62 (3.54, 3.70)		
ICT03158295 (DISCOVER-2) B	7.39		248		0.46	246	3.3%	3.97 (3.89, 4.05)	1.55	
(CT03182796 (DISCOVER-1) A	6.87	0.66	128	1.98	0.65	126	3.3%	4.91 (4.75, 5.07)		
ICT03142796 (DISCOVER-1) 8	6.3	0.65	127	1.98	0.65	128	3.3%	4.14 (3.98, 4.30)		
CT03071140 PEEPsA(E 2)	5.9	0.51	224	- 2	0.55	210	23%	3 00 (3.00, 4.00)	-	
NCT03675308 (KEEPISAKE 1)	6.5	0.36	483	3.2	0.36	481	3.7%	3 20 (3.25, 3.35)		
Total (95% Ct)			6264			6987	100.0%	3.76 [3.42, 4.50]	9 9 Jan 6	
Haterogeneity TauF = 0.92; ChiF = 5	04T.50, 6	ff = 39	P = 0	000013	P = 36	7%			\$ 10 A A	
est for overall effect Z = 21 63 (P -									-20 -16 0 10 20 Favours (control) Favours (experimental	

Figure S3. Forest plot of SF-36 MCS. SF-36 MCS, mental component summary of the Short Form 36.

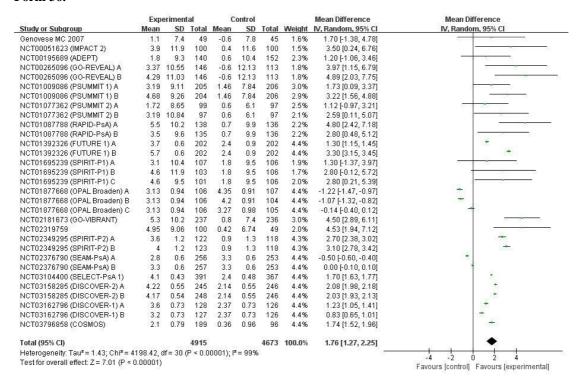


Figure S4. Forest plot of EQ-VAS. EQ-VAS, EuroQol Visual Analogue Scale.

	Expe	rimen	ital	C	ontrol			Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	SD Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
NCT01695239 (SPIRIT-P1) A	11.9	25	107	3.3	21.1	106	12.0%	8.60 [2.39, 14.81]			
NCT01695239 (SPIRIT-P1) B	11.3	25.8	103	3.3	21.1	106	11.8%	8.00 [1.60, 14.40]			
NCT01695239 (SPIRIT-P1) C	9.1	22.1	101	3.3	21.1	106	12.3%	5.80 [-0.09, 11.69]			
NCT01877668 (OPAL Broaden) A	13.1	2.14	106	14	2.1	107	16.6%	-0.90 [-1.47, -0.33]	<u> </u>		
NCT01877668 (OPAL Broaden) B	13.1	2.14	106	15.83	2.09	104	16.6%	-2.73 [-3.30, -2.16]	*		
NCT01877668 (OPAL Broaden) C	13.1	2.14	106	6.37	2.24	105	16.6%	6.73 [6.14, 7.32]	<u>√</u>		
NCT02181673 (GO-VIBRANT)	20.2	24.2	237	5.5	23.1	236	14.1%	14.70 [10.44, 18.96]	-		
Total (95% CI)			866			870	100.0%	5.27 [1.21, 9.34]			
Heterogeneity: Tau ² = 25.86; Chi ² =	619.38, 0	df = 6 (P < 0.0	0001); [² = 99	%		27 28 28 20 			
Test for overall effect: $Z = 2.54$ (P = 0	0.01)								-10 -5 0 5 10 Favours (control) Favours (experimental)		

Figure S5. Forest plot of DLQI. DLQI, Dermatology Life Quality Index.

	Ехре	erimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	1000	Mean	(0/2.0)	Total 28	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Genovese MC 2007	-3.4	4.5		-1.7			6.2%	-1.70 [-4.21, 0.81]	9
NCT00195689 (ADEPT)	-6.1	6.3	66	-0.7	6.7	66	6.5%	-5.40 [-7.62, -3.18]	
NCT01009086 (PSUMMIT 1) A	-6.35	6.75	129	-1.35	5.25	132	7.1%	-5.00 [-6.47, -3.53]	2 7.78 -0.
NCT01009086 (PSUMMIT 1) B	-7.05	6.74	134	-1.35	5.25	132	7.1%	-5.70 [-7.15, -4.25]	
NCT01077362 (PSUMMIT 2) A	-6.35	8.27	103	-0.7	4.51	104	6.8%	-5.65 [-7.47, -3.83]	
NCT01077362 (PSUMMIT 2) B	-6	6.01	105	-0.7	4.51	104	7.1%	-5.30 [-6.74, -3.86]	
NCT01087788 (RAPID-PsA) A	-6.3	7.5	138	-1.3	4.7	136	7.1%	-5.00 [-6.48, -3.52]	- * - -
NCT01087788 (RAPID-PsA) B	-3.3	5.1	135	-1.3	4.7	136	7.3%	-2.00 [-3.17, -0.83]	2 - 2
NCT01392326 (FUTURE 1) A	-7.9	0.6	108	0.7	0.8	109	7.7%	-8.60 [-8.79, -8.41]	*
NCT01392326 (FUTURE 1) B	-8.8	0.6	108	0.7	0.8	109	7.7%	-9.50 [-9.69, -9.31]	•
NCT01695239 (SPIRIT-P1) A	-0.5	0.52	107	-0.3	6.1	106	7.3%	-0.20 [-1.37, 0.97]	- 8 -
NCT01695239 (SPIRIT-P1) B	-0.44	0.53	103	-0.3	6.1	106	7.3%	-0.14 [-1.31, 1.03]	- 1 56
NCT01695239 (SPIRIT-P1) C	-0.37	0.44	101	-0.3	6.1	106	7.3%	-0.07 [-1.23, 1.09]	
NCT02181673 (GO-VIBRANT)	-8.1	7.7	194	-1.9	5.9	195	7.2%	-6.20 [-7.56, -4.84]	-
Total (95% CI)			1563			1569	100.0%	-4.36 [-5.76, -2.96]	•
Heterogeneity: Tau2 = 6.63; Chi2	= 954.91	. df = 1	13 (P <	0.0000	1); 2=	99%		70527 id 52	t- t t t
Test for overall effect: Z = 6.09 (F		2000	8		6511				-10 -5 0 5 1 Favours [experimental] Favours [control]

Figure S6. Forest plot of PASI 50. PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index.

	Experim	ental	Conti	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
NCT00051623 (IMPACT 2)	75	83	8	87	10.3%	9.83 [5.06, 19.09]	
NCT00195689 (ADEPT)	52	69	8	69	10.3%	6.50 [3.34, 12.64]	
NCT00265096 (GO-REVEAL) A	77	102	6	73	9.4%	9.18 [4.23, 19.93]	
NCT00265096 (GO-REVEAL) B	87	106	6	73	9.4%	9.99 [4.62, 21.60]	
NCT00317499	47	101	18	104	11.9%	2.69 [1.68, 4.30]	39 -11-1 2
NCT01087788 (RAPID-PsA) A	67	90	24	86	12.7%	2.67 [1.86, 3.83]	
NCT01087788 (RAPID-PsA) B	55	76	24	86	12.6%	2.59 [1.80, 3.74]	
NCT02065713 (GO-DACT)	16	20	10	22	11.6%	1.76 [1.06, 2.92]	- (- (-
NCT02319759	85	98	14	48	12.0%	2.97 [1.90, 4.65]	2 · · · · · · · · · · · · · · · · · · ·
Total (95% CI)		745		648	100.0%	4.09 [2.71, 6.16]	•
Total events	561		118				
Heterogeneity: Tau2 = 0.31; Chi2:	= 45.41, df	= 8 (P <	0.000013	$ \cdot ^2 = 80$	2%		
Test for overall effect: Z = 6.72 (P	< 0.00001)	10				'	0.05 0.2 1 5 20 Favours [control] Favours [experimental]

Figure S7. Forest plot of PASI 75. PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index.

	Experim	ental	Contr	01		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
MPACT	35	52	0	52	0.4%	71.00 [4.47, 1127.60]	
Mease PJ 2000	5	19	0	19	0.4%	11.00 [0.65, 186.02]	
NCT00051623 (IMPACT 2)	60	83	1	87	0.8%	62.89 [8.92, 443.47]	No. 20
NCT00195689 (ADEPT)	41	69	1	69	0.8%	41.00 [5.80, 289.75]	
ICT00265096 (GO-REVEAL) A	57	102	1	73	0.8%	40.79 [5.78, 287.91]	
ICT00265096 (GO-REVEAL) B	70	106	1	73	0.8%	48.21 [6.85, 339.27]	
VCT00317499	23	101	3	104	1.4%	7.89 [2.45, 25.48]	W - 12-3 0
CT00367237 (RESPOND)	33	34	19	35	2.7%	1.79 [1.31, 2.44]	
VCT01009086 (PSUMMIT 1) A	83	145	16	146	2.5%	5.22 [3.22, 8.47]	-
VCT01009086 (PSUMMIT 1) B	93	149	16	146	2.5%	5.70 [3.53, 9.19]	30-33-2
VCT01077362 (PSUMMIT 2) A	41	80	4	80	1.7%	10.25 [3.85, 27.28]	
ICT01077362 (PSUMMIT 2) B	45	81	4	80	1.7%	11.11 [4.19, 29.45]	N - 22 - 12 - 12
VCT01087788 (RAPID-PsA) A	56	90	13	86	2.4%	4.12 [2.43, 6.97]	
CT01087788 (RAPID-PsA) B	46	76	13	86	2.4%	4.00 [2.35, 6.82]	S
ICT01392326 (FUTURE 1) A	70	108	9	109	2.2%	7.85 [4.13, 14.90]	
ICT01392326 (FUTURE 1) B	66	108	9	109	2.2%	7.40 [3.89, 14.09]	97-05-10-54 57-05-10-54
NCT01695239 (SPIRIT-P1) A	37	52	4	41	1.7%	7.49 [3.69, 14.69]	50,000 mod
NCT01695239 (SPIRIT-P1) B	33	41	4	41	1.7%	8.25 [3.21, 21.18]	22 23 25
ICT01695239 (SPIRIT-P1) C	20	37	4	41	1.7%	5.54 [2.09, 14.72]	50 30 00 50 30 50
ICT01752634 (FUTURE 2) A	26	41	7	43	2.1%	3.90 [1.90, 7.98]	713 - 712 - 12X
ICT01752634 (FUTURE 2) B	28	58	7	43	2.1%	2.97 [1.43, 6.14]	45 40 20
ICT01752634 (FUTURE 2) C	14	50	7	43	2.1%	1.72 [0.76, 3.87]	10. 85 - 69
ICT01752634 (FOTORE 2) C ICT01877668 (OPAL Broaden) A	30	77	35	82	2.6%		0010000-00
[1] [1] [1] [1] [1] [1] [1] [1] [1] [1]	30	77	31	70		0.91 [0.63, 1.33]	100 (0)
VCT01877668 (OPAL Broaden) B	30	77	12	82	2.6%	0.88 [0.60, 1.29]	- 0.000
NCT01877668 (OPAL Broaden) C					2.3%	2.66 [1.47, 4.82]	200 AND 2
ICT01989468 (FUTURE 3) A	29	62	6	59	2.0%	4.60 [2.06, 10.27]	73 - 27 - 32
ICT01989468 (FUTURE 3) B	34	68	6	59	2.0%	4.92 [2.22, 10.88]	00-00-
ICT02024646 (AMVISION-2) A	34	73	10	90	2.2%	4.19 [2.22, 7.90]	02 - F2 - 40.
VCT02024646 (AMVISION-2) B	54	83	10	90	2.3%	5.86 [3.20, 10.73]	22-52-
VCT02029495 (AMVISION-1) A	36	73	5	65	1.9%	6.41 [2.68, 15.36]	8 <u>9</u>
NCT02029495 (AMVISION-1) B	47	60	5	65	1.9%	10.18 [4.34, 23.89]	NS 45 - 30
ICT02181673 (GO-VIBRANT)	127	241	26	239	2.6%	4.84 [3.31, 7.10]	220,000
ICT02294227 (FUTURE 4) A	29	- 55	5	62	1.8%	6.54 [2.72, 15.71]	82 <u>-8</u> -
ICT02294227 (FUTURE 4) B	27	54	5	62	1.8%	6.20 [2.57, 14.97]	8-2
ICT02319759	77	98	6	48	2.0%	6.29 [2.95, 13.38]	10 - 10 - 10 - 10 - 10 - 10 - 10 - 10 -
NCT02349295 (SPIRIT-P2) A	38	68	10	67	2.3%	3.74 [2.04, 6.89]	19 <u>25</u> -0
ICT02349295 (SPIRIT-P2) B	41	68	10	67	2.3%	4.04 [2.21, 7.39]	28-58-
ICT02349451	19	33	3	11	1.7%	2.11 [0.77, 5.79]	84 × 3
ICT02404350 (FUTURE 5) A	155	222	41	332	2.7%	5.65 [4.19, 7.63]	100 m
ICT02404350 (FUTURE 5) B	132	220	41	332	2.7%	4.86 [3.58, 6.60]	3/4/2004
ICT02404350 (FUTURE 5) C	129	222	41	332	2.7%	4.71 [3.46, 6.40]	87 <u>6.</u> 2
ICT02980692 A	34	53	7	42	2.1%	3.85 [1.90, 7.79]	<u> </u>
ICT02980692 B	35	44	7	42	2.1%	4.77 [2.39, 9.54]	38-33-38
ICT02980692 C	31	55	7	42	2.1%	3.38 [1.65, 6.91]	0 -21-0 1
ICT02980692 D	19	41	7	42	2.0%	2.78 [1.31, 5.90]	12-12-30
ICT03158285 (DISCOVER-2) A	144	184	42	183	2.8%	3.41 [2.59, 4.49]	and the second s
ICT03158285 (DISCOVER-2) B	139	176	42	183	2.8%	3.44 [2.61, 4.54]	and the second s
ICT03162796 (DISCOVER-1) A	77	89	11	78	2.4%	6.13 [3.53, 10.67]	30-72-
ICT03162796 (DISCOVER-1) B	62	82	11	78	2.4%	5.36 [3.06, 9.40]	(Andrews)
NCT03796858 (COSMOS)	79	133	5	53	1.9%	6.30 [2.70, 14.67]	R 3 3
otal (95% CI)		4470		4563	100.0%	4.72 [3.87, 5.75]	•
otal events	2700		590				

Figure S8. Forest plot of PASI 90. PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index.

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events				Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Hong Tao 2019	29	33	16	33	4.0%	1.81 [1.25, 2.63]	
NCT00051623 (IMPACT 2)	39	83	0	87	0.4%	82.76 [5.17, 1325.04]	
NCT00195689 (ADEPT)	29	69	0	69	0.4%	59.00 [3.68, 946.75]	30 52
NCT00265096 (GO-REVEAL) A	33	102	0	73	0.4%	48.14 [3.00, 773.11]	
NCT00265096 (GO-REVEAL) B	34	106	0	73	0.4%	47.72 [2.97, 766.16]	V
NCT00367237 (RESPOND)	24	34	10	35	3.3%	2.47 [1.40, 4.36]	-
NCT01077362 (PSUMMIT 2) A	24	80	3	80	1.7%	8.00 [2.51, 25.51]	
NCT01077362 (PSUMMIT 2) B	36	81	3	80	1.8%	11.85 [3.80, 36.93]	
NCT01087788 (RAPID-PsA) A	42	90	5	86	2.4%	8.03 [3.33, 19.33]	
NCT01087788 (RAPID-PsA) B	27	76	5	86	2.3%	6.11 [2.48, 15.07]	
NCT01392326 (FUTURE 1) A	53	108	4	109	2.1%	13.37 [5.01, 35.66]	
NCT01392326 (FUTURE 1) B	49	108	4	109	2.1%	12.36 [4.62, 33.07]	
NCT01695239 (SPIRIT-P1) A	29	52	2	41	1.4%	11.43 [2.90, 45.13]	
NCT01695239 (SPIRIT-P1) B	28	41	2	41	1.4%	14.00 [3.57, 54.97]	65 555 55
	14	37	2	41	1.4%		- 100 - 100
NCT01695239 (SPIRIT-P1) C		302				7.76 [1.89, 31.88]	
NCT01752634 (FUTURE 2) A	20 19	41 58	4	43 43	2.1%	5.24 [1.96, 14.04]	32-22-28
NCT01752634 (FUTURE 2) B			4		2.1%	3.52 [1.29, 9.61]	
NCT01752634 (FUTURE 2) C	6	50	4	43	1.7%	1.29 [0.39, 4.27]	
NCT01989468 (FUTURE 3) A	21	62	4	59	2.0%	5.00 [1.82, 13.69]	
NCT01989468 (FUTURE 3) B	25	68	4	59	2.1%	5.42 [2.00, 14.68]	
NCT02024646 (AMVISION-2) A	24	73	4	90	2.0%	7.40 [2.69, 20.36]	
ICT02024646 (AMVISION-2) B	45	83	4	90	2.1%	12.20 [4.59, 32.44]	10 10 10 10 10 10 10 10 10 10 10 10 10 1
ICT02029495 (AMVISION-1) A	29	73	2	65	1.4%	12.91 [3.20, 52.01]	10 Th - 10
NCT02029495 (AMVISION-1) B	36	60	2	65	1.4%	19.50 [4.91, 77.51]	2 7 - 10 - 1 0
NCT02065713 (GO-DACT)	5	20	4	22	1.7%	1.38 [0.43, 4.42]	
NCT02181673 (GO-VIBRANT)	84	241	15	239	3.5%	5.55 [3.30, 9.34]	
NCT02294227 (FUTURE 4) A	20	55	1	62	0.8%	22.55 [3.13, 162.52]	
NCT02294227 (FUTURE 4) B	11	54	1	62	0.8%	12.63 [1.68, 94.67]	St. 52
NCT02319759	65	98	3	48	1.8%	10.61 [3.52, 32.03]	₩ <u>₩₩₩</u>
NCT02349295 (SPIRIT-P2) A	30	68	8	67	2.9%	3.69 [1.83, 7.46]	<u>−97</u> ⊗
NCT02349295 (SPIRIT-P2) B	34	68	8	67	2.9%	4.19 [2.10, 8.37]	9 9 56 6 6
NCT02349451	15	33	2	11	1.5%	2.50 [0.68, 9.25]	50 St
NCT02404350 (FUTURE 5) A	119	222	31	332	4.0%	5.74 [4.02, 8.20]	
NCT02404350 (FUTURE 5) B	81	220	31	332	3.9%	3.94 [2.70, 5.75]	
NCT02404350 (FUTURE 5) C	70	222	31	332	3.9%	3.38 [2.29, 4.97]	
NCT02980692 A	25	53	3	42	1.8%	6.60 [2.14, 20.38]	5 10 - 10 - 10 4
VCT02980692 B	22	44	3	42	1.8%	7.00 [2.26, 21.66]	100 - 100 -
NCT02980692 C	22	55	3	42	1.8%	5.60 [1.80, 17.47]	(A) 2000 (A)
NCT02980692 D	15	41	3	42	1.7%	5.12 [1.60, 16.38]	
NCT03158285 (DISCOVER-2) A	112	184	18	183	3.7%	6.19 [3.93, 9.74]	
NCT03158285 (DISCOVER-2) B	121	176	18	183	3.7%	6.99 [4.46, 10.96]	
NCT03150203 (DISCOVER-2) B	56	89	9	78	3.1%	5.45 [2.89, 10.29]	
NCT03162796 (DISCOVER-1) B	41	82	9	78	3.0%	4.33 [2.26, 8.31]	No. of the second secon
가장 내 가지 얼마를 하게 한다면 생활하게 하면 가지 않아 하고 그래요?	143	483	27	481	3.9%		100 <u>4</u> -00
NCT03671148 (KEEPsAKE 2)	143		12	219		5.27 [3.57, 7.80]	
NCT03675308 (KEEPsAKE 1) NCT03796858 (COSMOS)	68	133	12	53	3.3% 2.2%	5.54 [3.09, 9.94] 6.77 [2.60, 17.64]	2000 2000 C
40103130000 (COOMOO)	08	133	4	133	2.270	0.77 [2.00, 17.04]	25 - 52 - 55
Fotal (95% CI)		4533		4617	100.0%	5.73 [4.73, 6.95]	•
Total events	1942		332			95 99 XSX	
Heterogeneity: Tau² = 0.21; Chi² =		- 45 /0		13:12-	5000	-	

Figure S9. Forest plot of PASI 100. PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index.

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
NCT00195689 (ADEPT)	20	69	0	69	0.8%	41.00 [2.53, 664.71]	N-1 (N-1)
NCT01695239 (SPIRIT-P1) A	22	52	1	41	1.9%	17.35 [2.44, 123.36]	
NCT01695239 (SPIRIT-P1) B	22	41	1	41	1.7%	22.00 [3.11, 155.67]	€ 61 - 61
NCT01695239 (SPIRIT-P1) C	9	37	1	41	1.6%	9.97 [1.33, 75.00]	15 15 15 15 15 15 15 15 15 15 15 15 15 1
NCT02024646 (AMVISION-2) A	18	73	1	90	1.5%	22.19 [3.03, 162.32]	85 85 88
NCT02024646 (AMVISION-2) B	39	83	1	90	1.6%	42.29 [5.94, 300.94]	
NCT02029495 (AMVISION-1) A	18	73	2	65	3.6%	8.01 [1.93, 33.22]	
NCT02029495 (AMVISION-1) B	33	60	2	65	3.2%	17.88 [4.48, 71.30]	
NCT02181673 (GO-VIBRANT)	50	241	11	239	18.6%	4.51 [2.41, 8.44]	
NCT02319759	39	98	3	48	6.8%	6.37 [2.07, 19.56]	
NCT02349295 (SPIRIT-P2) A	24	68	3	67	5.1%	7.88 [2.49, 24.94]	
NCT02349295 (SPIRIT-P2) B	19	68	3	67	5.1%	6.24 [1.94, 20.11]	
NCT02980692 A	16	53	2	42	3.8%	6.34 [1.54, 26.05]	
NCT02980692 B	11	44	2	42	3.4%	5.25 [1.24, 22.29]	
NCT02980692 C	15	55	2	42	3.8%	5.73 [1.38, 23.69]	
NCT02980692 D	9	41	2	42	3.3%	4.61 [1.06, 20.06]	
NCT03158285 (DISCOVER-2) A	82	184	5	183	8.4%	16.31 [6.77, 39.30]	
NCT03158285 (DISCOVER-2) B	80	176	5	183	8.2%	16.64 [6.90, 40.09]	
NCT03162796 (DISCOVER-1) A	40	89	5	78	9.0%	7.01 [2.91, 16.88]	
NCT03162796 (DISCOVER-1) B	21	82	5	78	8.6%	4.00 [1.58, 10.07]	10 (10 to 10
Total (95% CI)		1687		1613	100.0%	9.57 [7.38, 12.43]	•
Total events	587		57				
Heterogeneity: Chi² = 21.77, df = 1	9 (P = 0.30); $I^2 = 10$	3%				0.002 0.1 1 10 500
Test for overall effect: Z = 16.99 (P	< 0.00001)					0.002 0.1 1 10 50 Favours (control) Favours (experimental)



PRISMA 2020 Checklist

			-20 2	
Section and Topic	Item #	Checklist item	·1-058	Location where item is reporte
TITLE			34.9	
Title	1	Identify the report as a systematic review.	7 0	Page1/line1-2
ABSTRACT			<u></u>	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2 April	Page2/line1-28 and Page3/line?
INTRODUCTION			20	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	22.	Page4/line1-28
			Down	and Page25/line1-2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	loa	Page5/line3-9
METHODS			ded	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	fro	Page6/line7-18
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to Specify the date when each source was last searched or consulted.	identify studies.	Page5/line15-17
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	://bmjop	Page5/line18-2and Page6/line1-5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many rev record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used.		Page6/line7-8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of a in the process.		Page6/line20-2
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which		Page6/line21-23
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding any assumptions made about any missing or unclear information.	ig sources). Describe	Page6/line21-23
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how may each study and whether they worked independently, and if applicable, details of automation tools used in the process		Page6/line23-28
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation	of results.	Page7/line6-8
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study inter and comparing against the planned groups for each synthesis (item #5)).	wention characteristics	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summ conversions.	gry statistics, or data	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	×	N/A
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was per model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.		Page7/line8-13
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis	s, meta-regression).	Page7/line14-2
	13f	Describe any sensitivity arfatyses-conditated to/assess/robbostness lofthecsynthesized results lelines.xhtml		Page7/line13-1



PRISMA 2020 Checklist

Pa	ge 49 of 49		BMJ Open 36/b									
1 2	PRISMA 2020 Checklist											
3	Section and Topic	Item #	Checklist item 27	Location where item is reported								
6	Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases)	Page7/line23-24								
8	Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page7/line6-8								
10	RESULTS		o ri									
10 11 12	Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the remover of studies included in the review, ideally using a flow diagram.	Page7/line27-28 and Page 8/line1-14								
14		16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were executed.	Figure 1								
15 16	Study characteristics	17	Cite each included study and present its characteristics.	Supplementary table S2								
17 18	Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Figure 2								
19 20	Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary figure S1-S9								
21 22 23	Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Supplementary table S2 and Figure 2								
24 25		20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page8/line16-27								
26 27		20c	Present results of all investigations of possible causes of heterogeneity among study results.	Supplementary table S3								
28		20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page9/line8-15								
29 30	Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page11/line11-16 and Figure 3								
32	Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 1								
34	DISCUSSION		Q_									
35 36 37 38	Discussion	23a	Provide a general interpretation of the results in the context of other evidence. Provide a general interpretation of the results in the context of other evidence.	Page11/line18-28 , Page12/line1-28 and Page 13/line1-15								
39		23b	Discuss any limitations of the evidence included in the review.	Page13/line16-25								
40		23c	Discuss any limitations of the review processes used.	N/A								
41		23d	Discuss implications of the results for practice, policy, and future research.	Page14/line1-2								
42	OTHER INFORMA	TION	9 									
43	Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A								
45	protocol	24b	Indicate where the review protocolroanibevacobssed; por/stratestpendoprotocol/wias/abtopre/paried: lines.xhtml	N/A								
46												



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2	PRISMA 2	2020 Checklist	1136/bmjopen-202	
Section and Topic	Item #		21-05	Location where item is reported
5	24c	Describe and explain any amendments to information provided at registration or in the protocol.	3 49.	N/A
6 7 Support 8	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the re-	geiew.	Page14/line28 and Page15/line1
9 Competing 10 interests	26		April	Page15/line3
1 Availability of 12 data, code an 13 other material	nd	Report which of the following are publicly available and where they can be found: template data collection forms; data included studies; data used for all analyses; analytic code; any other materials used in the review.	extracted from	Page15/line14-16
14 15 <i>From:</i> Page 16 10.1136/bmj.n7		e JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for report	ag systematic reviews. BN	//J 2021;372:n71. doi:
17		For more information, visit: http://www.prisma-statement.org/	გ t	
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