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

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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 (PsA).

Design: Meta-analysis.

Data sources and eligibility criteria: PubMed, Web of Science, Cochrane Library, CNKI, WanFang, and VIP databases were searched to collect randomized controlled trials (RCTs), which were conducted to evaluate the effect of bDMARDs in treatment of patients with PsA and reported QoL-related outcomes, from inception to November 2020.

Data extraction and synthesis: Outcomes about Health Assessment Questionnaire Disability Index (HAQ-DI), Dermatology Life Quality Index (DLQI), physical component summary (PCS) and mental component summary (MCS) of the Short Form 36 (SF-36), EuroQol Visual Analogue Scale (EQ-VAS), Psoriasis Area Severity Index (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 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 outcomes. Against methotrexate (MTX) and tofacitinib, bDMARDs showed no statistically significant advantages or even significant disadvantages. Similar results 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. 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.

Conclusions: Compared with placebo, bDMARDs taken by patients with PsA appear to significantly improve the QoL. Compared with other therapeutic agents, more studies

are still 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

- The effects of bDMARDs on QoL among patients with PsA have not been previously studied. Therefore, the results of this meta-analysis can inform evidence-based decision-making in clinical practice.
- Subgroup analyses with the 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.
- Because most of the included RCTs were multi-center studies, subgroup analysis on the basis of countries and regions was not conduct to evaluate the effects of bDMARDs on the QoL of different races patients.
- The follow-up period for all included studies didn't exceed 24 weeks, so that the long-term effects can't be assessed.

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 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" 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 "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 articles as an additional search. Researches were limited to RCTs published in English and Chinese. The complete electronic search strategy for PubMed is provided in 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, ≥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. Twenty RCTs have reported the effects of bDMARDs on HAQ Disability Index (HAQ-DI), 20 RCTs on SF-36 PCS, 16 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, 1 RCT on DAPSA, 7 RCTs on the proportion of participants achieving 50% improvement from baseline in PASI (PASI 50), 2 RCTs on PASI 70, 23 RCTs on PASI 75, 20 RCTs on PASI 90, 7 RCTs on PASI 100 and 1 RCT on PASI score. Among them, HAQ-DI, DLQI, PsAQoL, DAPSA, and PASI scores are negative outcomes, 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 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 HAQ-DI (MD=-0.22; 95% CI, -0.25, -0.18; P <0.00001; I^2: 100%), DLQI (MD=-4.36; 95% CI, -5.76, -2.96; P <0.00001; I^2: 99%), and improve SF-36 PCS (MD=3.89; 95% CI, 3.44, 4.34; P <0.00001; I^2: 99%), SF-36 MCS (MD=1.82; 95% CI, 1.24, 2.40; P <0.00001; I^2: 98%), EQ-VAS (MD=5.27; 95% CI, 1.21, 9.34; P <0.00001; I^2: 99%), PASI 50 (RR=4.09; 95% CI, 2.71, 6.16; P <0.00001; I^2: 82%), PASI 75 (RR=4.73; 95% CI, 3.77, 5.95; P <0.00001; I^2: 84%), PASI 90 (RR=5.44; 95% CI, 4.30, 6.89; P <0.00001; I^2: 66%), PASI 100 (RR=9.11; 95% CI, 6.75, 12.31; P <0.00001; I^2: 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 trials	Effect model	Effect size	95% CI	I^2 (%)	P-value

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 outcomes						
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

Outcomes	Pre-sensitivity analysis			Upper & lower of effect size	Post-sensitivity analysis		
	Number of trials	Pooled estimates	95% CI		Pooled estimates	95% CI	Excluded trials
HAQ-DI	20	-0.22	-0.25, -0.18	Upper	-0.19	-0.23, -0.15	Mease PJ 2000
				Lower	-0.25	-0.28, -0.21	NCT00265096 (GO-REVEAL)
SF-36 PCS	20	3.89	3.44, 4.34	Upper	4.12	3.67, 4.56	NCT01877668 (OPAL Broaden)
				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)
				Lower	1.70	1.11, 2.29	NCT00265096 (GO-REVEAL)
EQ-VAS	3	5.27	1.21, 9.34	Upper	9.66	5.34, 13.98	NCT01877668 (OPAL Broaden)
				Lower	3.71	-0.58, 7.99	NCT02181673 (GO-VIBRANT)
DLQI	8	-4.36	-5.76, -2.96	Upper	-3.50	-5.00, -2.00	NCT01392326 (FUTURE 1)

				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)
				Lower	3.30	2.29, 4.78	NCT00265096 (GO-REVEAL)
PASI 75	23	4.73	3.77, 5.95	Upper	5.10	4.26, 6.09	NCT01877668 (OPAL Broaden)
				Lower	4.50	3.60, 5.62	NCT00265096 (GO-REVEAL)
PASI 90	20	5.44	4.30, 6.89	Upper	5.84	4.39, 7.78	NCT02404350 (FUTURE 5)
				Lower	5.13	4.06, 6.50	NCT01392326 (FUTURE 1)

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.

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

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

4. Discussion

This meta-analysis focused on the effects of bDMARDs on QoL in patients with 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 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 (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 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 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 PCS, 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 methotrexate.

Looking specifically at the subgroup of bDMARDs vs. placebo, variety of bDMARDs and duration of treatment were probable sources of heterogeneity. Infliximab, golimumab, adalimumab, and ixekizumab had no significant difference

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 the PASI score of patients in infliximab plus MTX group was significantly lower than 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 controlled trial.

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.

Contributors YQL substantially contributed to the conception and design of the research, and the acquisition, analysis and interpretation of data; involved in drafting 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;

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

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Competing Interests None declared.

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.

Ethics approval Neither ethics approval nor participant consent was required as this study was based solely on the summary results of previously published articles. Individual patient data were not obtained or accessed.

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

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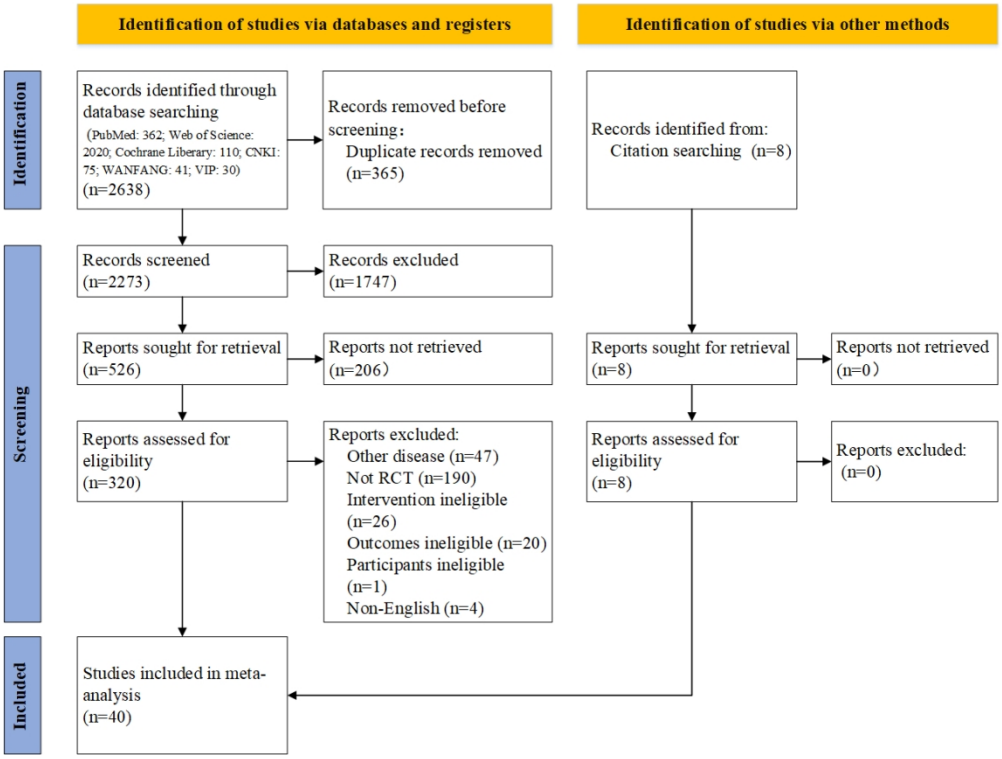

Figure 1 Flowchart of the study selection. RCT, randomized controlled trial.

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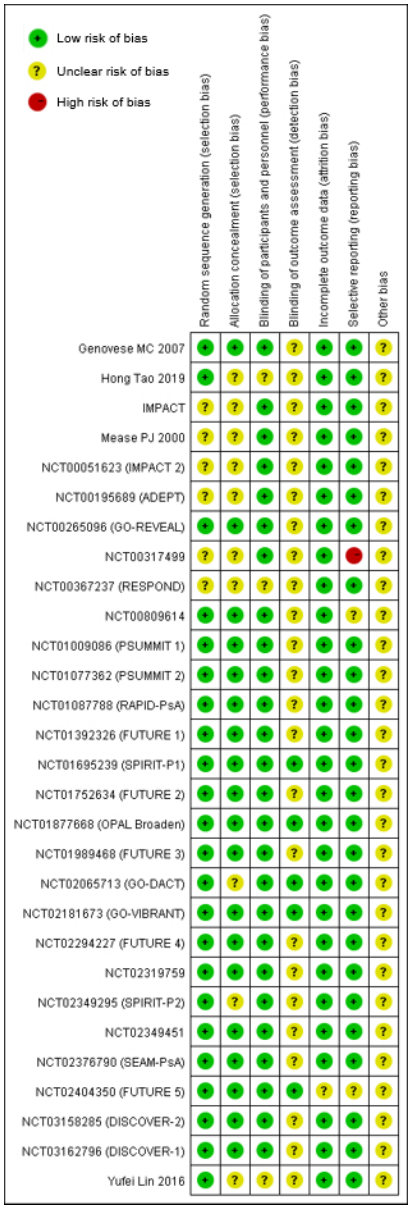

Figure 2 Quality assessment of included RCTs using Cochrane's risk of bias tool, RCT, randomized controlled trial.

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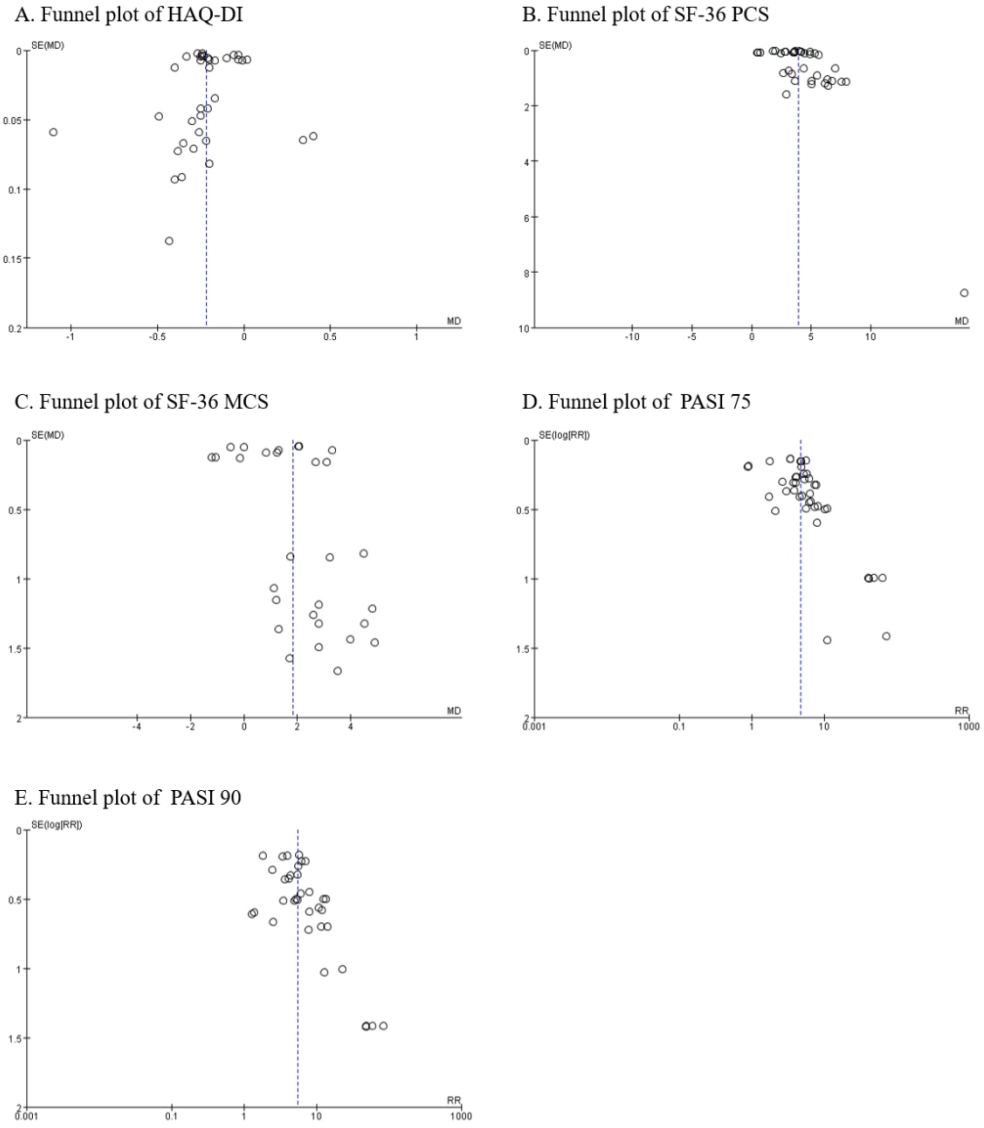

Figure 3 Funnel plots of HAQ-DI, SF-36 PCS, SF-36 MCS, PASI 75, and PASI 90. HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36; PASI 75/90, the proportion of participants achieving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

197x227mm (150 x 150 DPI)

Content

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-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 [26]	Adalimumab 40 mg SC q2w	51 (56.9)	50.4±11.0	7.2±7.0	12 weeks	①②③⑤
	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	3.56±1.29	24 weeks	⑩⑫
	MTX 15.36±1.69 mg q1w	33 (54.55)	35.94±6.25	3.82±1.28		
IMPACT [28]	Infliximab 5 mg/kg at weeks 0, 2, 6, 14	52 (57.7)	45.7±11.1	11.7±9.8	16 weeks	⑪
	Placebo	52 (57.7)	45.2±9.7	11.0±6.6		
Mease PJ 2000 [29]	Etanercept 25 mg SC BIW	30 (53)	46.0*	9.0*	12 weeks	①⑪
	Placebo	30 (60)	43.5*	9.5*		
NCT00051623 (IMPACT 2) [30,31,32]	Infliximab 5 mg/kg IV at weeks 0, 2, 6, 14, 22	100 (71)	47.1±12.8	8.4±7.2	24 weeks	①②③
	Placebo	100 (51)	46.5±11.3	7.5±7.8		⑨⑪⑫
NCT00195689 (ADEPT) [33,34,35]	Adalimumab 40 mg SC at weeks 0, 2, 4, then q4w	151 (56.3)	48.6±12.5	9.8±8.3	24 weeks	①②③⑤
	Placebo	162 (54.9)	49.2±11.1	9.2±8.7		⑨⑪⑫⑬
NCT00265096 (GO-REVEAL) [36,37]	Golimumab 50 mg SC q4w	146 (61)	45.7±10.7	7.2±6.8	24 weeks	①②③
	Golimumab 100 mg SC q4w	146 (59)	48.2±10.9	7.7±7.8		⑨⑪⑫
	Placebo	113 (61)	47.0±10.6	7.6±7.9		
NCT00317499 [38]	Etanercept 25 mg SC BIW	101 (57)	47.6	9	24 weeks	⑨⑪
	Placebo	104 (45)	47.3	9.2		
NCT00367237 (RESPOND) [39]	Infliximab 5 mg/kg at weeks 0, 2, 6, 14 + MTX	56 (48.2)	40.1±12.3	2.8±2.6	16 weeks	①⑪⑫
	MTX 15 mg q1w	54 (61.1)	42.3±10.5	3.7±2.7		
NCT00809614 [40]	Secukinumab 10 mg/kg SC on days 1, 22	28 (32)	46.7±11.3	6.3±6.8	24 weeks	②
	Placebo	14 (43)	47.6±8.1	5.4±3.8		

NCT01009086 (PSUMMIT 1) [41]	Ustekinumab 45 mg SC at weeks 0,2, then q12w	205 (51.7)	48.0 (39.0-55.0)*	3.4(-1.2-9.2)*	24 weeks	①②③⑤⑪
	Ustekinumab 90 mg SC at weeks 0,2, then q12w	204 (56.9)	47.0 (38.5-54.0)*	4.9(-1.7-8.3)*		
	Placebo	206 (52.4)	48.0 (39.0-57.0)*	3.6(-1.0-9.7)*		
NCT01077362 (PSUMMIT 2) [42]	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	①②③⑤⑪⑫
	Ustekinumab 90 mg at weeks 0, 4, then q12w	105 (46.7)	48.0(41.0-57.0)*	4.5(-2.7-10.3)*		
	Placebo	104 (49.0)	48.0(38.5-56.0)*	5.5 (-2.3-12.2)*		
NCT01087788 (RAPID-PsA) [43,44]	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 200 mg q2w	138 (46.4)	48.2±12.3	9.6±8.5	24 weeks	①②③⑤⑦⑨⑪⑫
	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 400 mg q4w	135 (45.9)	47.1±10.8	8.1±8.3		
	Placebo	136 (41.9)	47.3±11.1	7.9±7.7		
NCT01392326 (FUTURE 1) [45,46]	Secukinumab 75 mg/kg IV at weeks 2, 4, then 75 mg SC q4w	202 (41.6)	48.8±12.2	---	24 weeks	①②③⑤⑦⑪⑫
	Secukinumab 75 mg/kg IV at weeks 2, 4, then 150 mg SC q4w	202 (47.5)	49.6±11.8	---		
	Placebo	202 (47.5)	48.5±11.2	---		
NCT01695239 (SPIRIT-P1) [47,48]	Ixekizumab 80 mg SC q2w	107 (42.1)	49.1±10.1	6.2±6.4	24 weeks	①②③⑤⑥⑪⑫⑬
	Ixekizumab 80 mg SC q4w	103 (46.6)	49.8±12.6	7.2±8.0		
	Adalimumab 40 mg SC q2w	101 (50.5)	48.6±12.4	6.2±7.5		
	Placebo	106(45.3)	50.6±12.3	6.5±6.9		
NCT01752634 (FUTURE 2) [49]	Secukinumab 300 mg SC q1w to week 4 then q4w	100 (51)	46.9±12.6	---	24 weeks	①②⑪⑫
	Secukinumab 150 mg SC q1w to week 4 then q4w	100 (55)	46.5±11.7	---		
	Secukinumab 75mg SC q1w to week 4 then q4w	99 (47)	48.6±11.4	---		
	Placebo	98 (41)	49.9±12.5	---		

NCT01877668 (OPAL Broaden) [50][51]	Adalimumab 40 mg SC q2w	106 (53)	47.4±11.3	5.7±5.3	3 months	①②③⑥
	Tofacitinib 5 mg orally BID	107 (47)	49.4±12.6	7.1±8.2		⑪
	Tofacitinib 10 mg orally BID	104 (40)	46.9±12.4	5.4±5.8		
	Placebo	105 (47)	47.7±12.3	6.4±6.4		
NCT01989468 (FUTURE 3) [52]	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
	Secukinumab 150 mg SC at weeks 1, 2, 3, 4, then q4w	138 (44.2)	50.1±11.7	7.7±8.5		
	Placebo	137 (43.1)	50.1±12.6	6.6±6.9		
NCT02065713 (GO-DACT) [53]	Golimumab 50 mg SC q4w + MTX	21 (81.0)	46.2 (15.5)*	3.8 (6.7)*	24 weeks	⑨⑩⑫
	MTX 15 mg orally q1w and increased 5 mg q4w until 25 mg q1w	22 (87.0)	44.1 (24.6)*	4.3 (6.1)*		
NCT02181673 (GO-VIBRANT) [54,55]	Golimumab 2 mg/kg IV at weeks 0, 4, then q8w	241 (50.6)	45.7±11.3	6.1±6.0	24 weeks	①②③⑤
	Placebo	239 (53.1)	46.7±12.5	5.0±5.9		⑥⑪⑫⑬
NCT02294227 (FUTURE 4) [56]	Secukinumab 150 mg SC q4w LD	114 (41.2)	48.3±12.2	5.6±7.3	16 weeks	②⑪⑫
	Secukinumab 150 mg SC q4w no-LD	113 (45.1)	50.4±11.8	5.7±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	6.9±7.2		⑪⑫⑬
NCT02349295 (SPIRIT-P2) [58]	Ixekizumab 80 mg SC q4w	122 (52)	52.6±13.6	11.0±9.6	24 weeks	①②③
	Ixekizumab 80 mg SC q2w	123 (41)	51.7±11.9	9.9±7.4		⑪⑫⑬
	Placebo	118 (47)	51.5±10.4	9.2±7.3		
NCT02349451 [59]	Adalimumab 40 mg SC q1w	72 (54.2)	50.5±12.0	8.4±9.2	12 weeks	⑪⑫
	Placebo	24 (50.0)	50.5±12.0	7.6±7.2		
NCT02376790 (SEAM-PsA) [60,61]	Etanercept 50 mg SC q1w	284 (53.2)	48.5±13.5	3.1±6.0	24 weeks	①②③④
	Etanercept 50 mg SC + MTX orally q1w	283 (50.9)	48.1±12.7	3.0±6.0		⑧

	MTX 20 mg orally q1w	284 (43.7)	48.7±13.1	3.6±6.8		
NCT02404350 (FUTURE 5) [62]	Secukinumab 300 mg SC q4w LD	222 (48.6)	48.9±12.8	6.1±8.3	16 weeks	⑪⑫
	Secukinumab 150 mg SC q4w LD	220 (50.5)	48.4±12.9	6.7±7.1		
	Secukinumab 150 mg SC q4w no-LD	222 (54.1)	48.8±11.8	6.2±6.1		
	Placebo	332 (48.5)	49.0±12.1	6.8±7.6		
NCT03158285 (DISCOVER-2) [63]	Guselkumab 100mg SC at weeks 0,4, then q4w	245 (58)	45.9±11.5	5.5±5.9	24 weeks	①②③
	Guselkumab 100mg SC at weeks 0,4, then q8w	248 (52)	44.9±11.9	5.1±5.5		⑪⑫⑬
	Placebo	246 (48)	46.3±11.7	5.8±5.6		
NCT03162796 (DISCOVER-1) [64]	Guselkumab 100 mg SC q4w	128 (52)	47.4±11.6	6.6±6.3	24 weeks	①②③
	Guselkumab 100 mg SC at weeks 0, 4, then q8w	127 (54)	48.9±11.5	6.4±5.9		⑪⑫⑬
	Placebo	126 (48)	49.0±11.1	7.2±7.6		
Yufei Lin 2016 [65]	Infliximab 5mg /kg IV at weeks 0,2,6,12 + MTX	42 (61.90)	44.01±10.33	3.62±2.11	24 weeks	⑭
	MTX 7.5-15 mg orally q1w and increased to 15-25 mg q1w	42 (66.67)	43.59±10.29	3.71±2.12		

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; ⑥EQ-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; ⑩PASI 70, the proportion of participants achieving 70% improvement from baseline in Psoriasis Area Severity Index; ⑪PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index; ⑫PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index; ⑬PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; ⑭PASI score, Psoriasis Area Severity Index score.

* Data are reported as median (IQR);

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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
bDMARDs	**HAQ-DI**					
vs. Placebo	Total	31	-0.24	-0.27, -0.21	99	< 0.00001
	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	< 0.00001
	IL-17i	11	-0.22	-0.27, -0.16	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	4	-0.20*	-0.22, -0.19	21	< 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
	Secukinumab	7	-0.17	-0.23, -0.11	99	< 0.00001
	Ixekizumab	4	-0.32	-0.46, -0.18	98	< 0.00001
	Duration of PsA					
	< 6 years	7	-0.23	-0.26, -0.21	95	< 0.00001
	6-9 years	14	-0.19	-0.26, -0.13	99	< 0.00001
	≥ 9 years	5	-0.46	-0.65, -0.28	99	< 0.00001
	Unclear	5	-0.18	-0.25, -0.11	99	< 0.00001
	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	< 0.00001
	SF-36 PCS					
	Total	33	4.22	3.82, 4.61	99	< 0.00001
	Category of bDMARD					
	TNFi	10	5.75	4.35, 7.14	88	< 0.00001
	IL-12/23i	9	4.06	3.66, 4.46	96	< 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	4	4.47	2.50, 6.44	79	< 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
	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	9	3.37	2.97, 3.77	97	< 0.00001
	6-9 years	15	4.87	3.76, 5.99	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					
< 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					
< 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	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

	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
	≥ 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+ MTX vs. MTX	HAQ-DI	2	-0.22	-0.58, 0.14	86	0.23
	SF-36 PCS	1	2.00	1.90, 2.10	---	< 0.00001
	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.

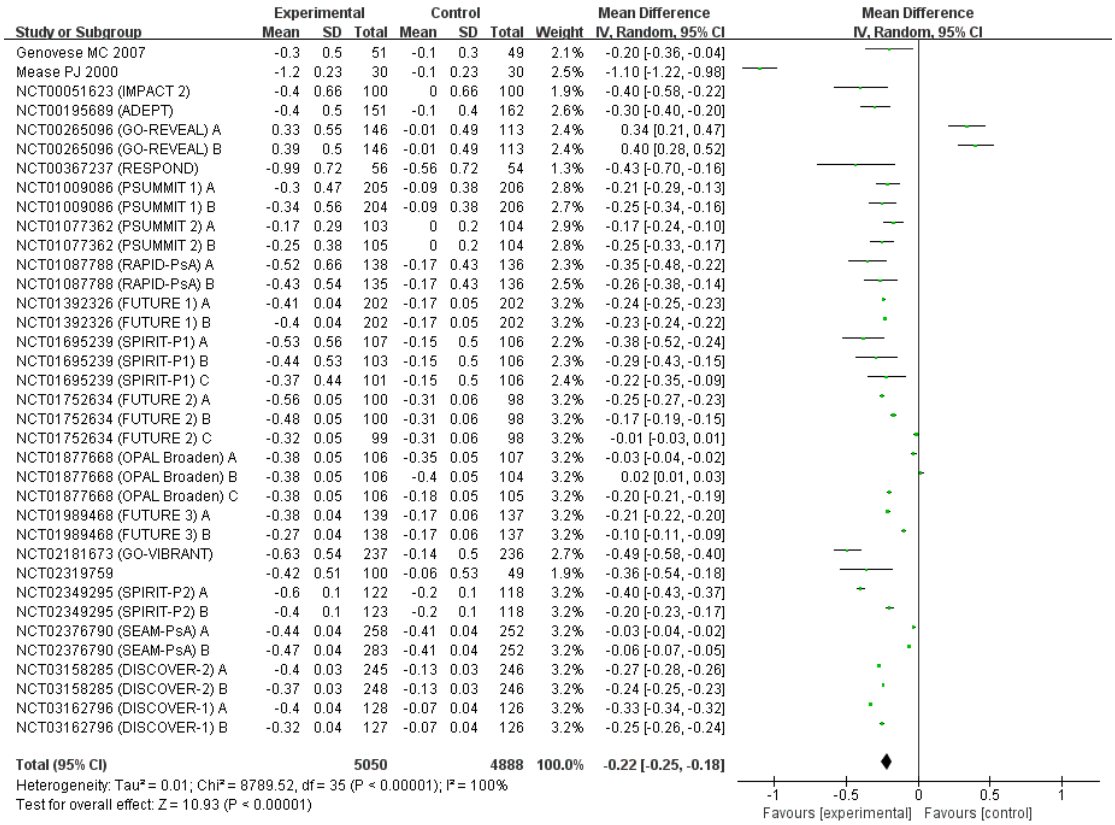


Figure S2. Forest plot of SF-36 PCS. SF-36 PCS, physical component summary of the Short Form 36.

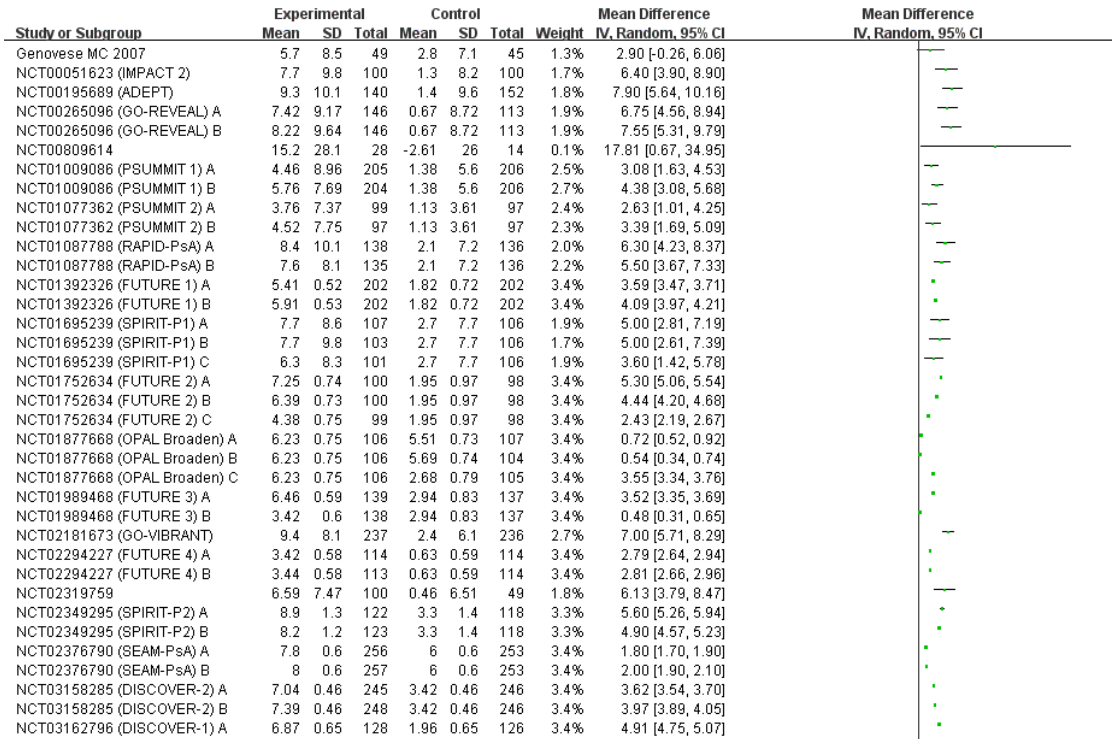


Figure S3. Forest plot of SF-36 MCS. SF-36 MCS, mental component summary of the Short Form 36.

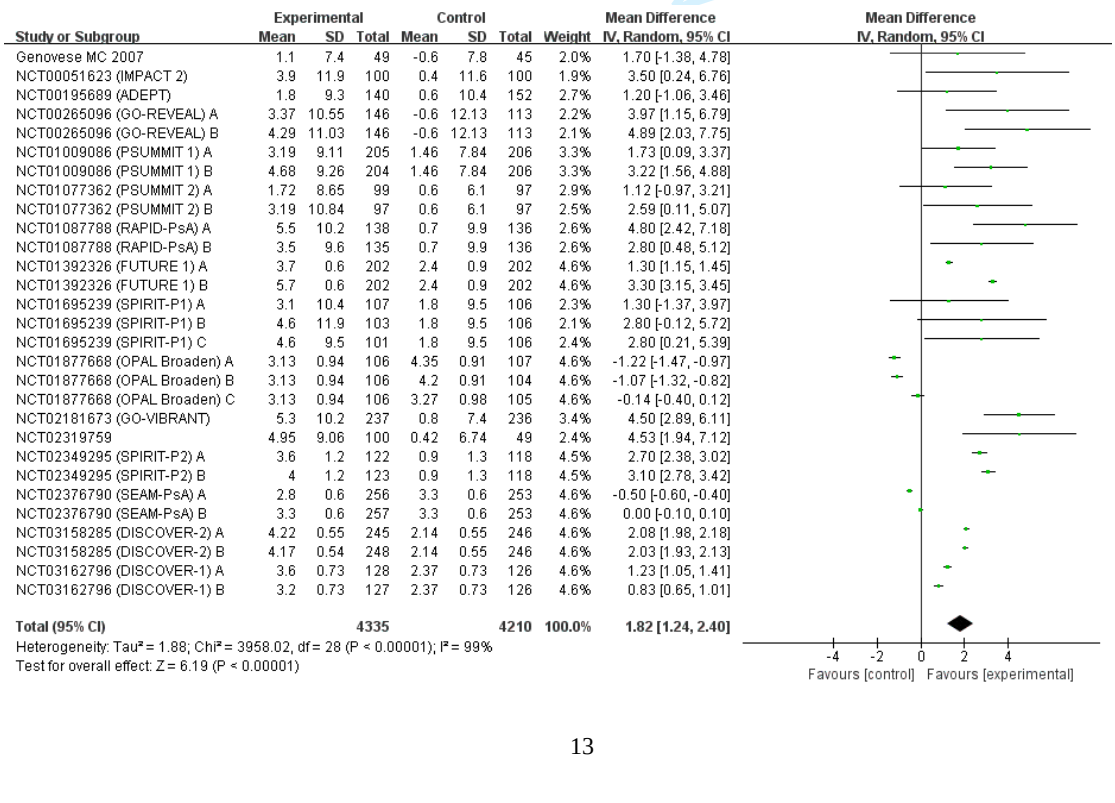


Figure S4. Forest plot of DLQI. DLQI, Dermatology Life Quality Index.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference 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: Tau² = 6.63; Chi² = 954.91, df = 13 (P < 0.00001); I² = 99%
Test for overall effect: Z = 6.09 (P < 0.00001)

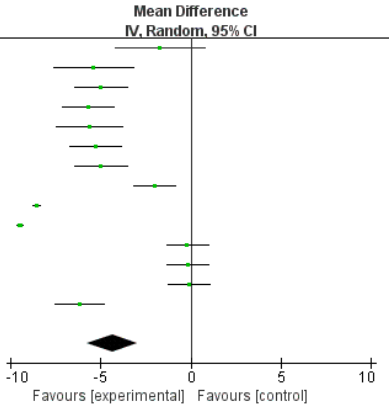


Figure S5. Forest plot of EQ-VAS. EQ-VAS, EuroQol Visual Analogue Scale.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference 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 = 619.38, df = 6 (P < 0.00001); I² = 99%
Test for overall effect: Z = 2.54 (P = 0.01)

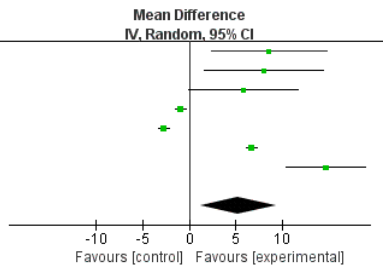


Figure S6. Forest plot of PASI 50. PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index.

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio 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: Tau² = 0.31; Chi² = 45.41, df = 8 (P < 0.00001); I² = 82%
Test for overall effect: Z = 6.72 (P < 0.00001)

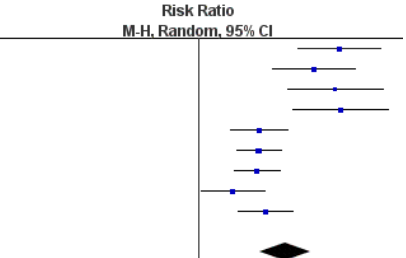
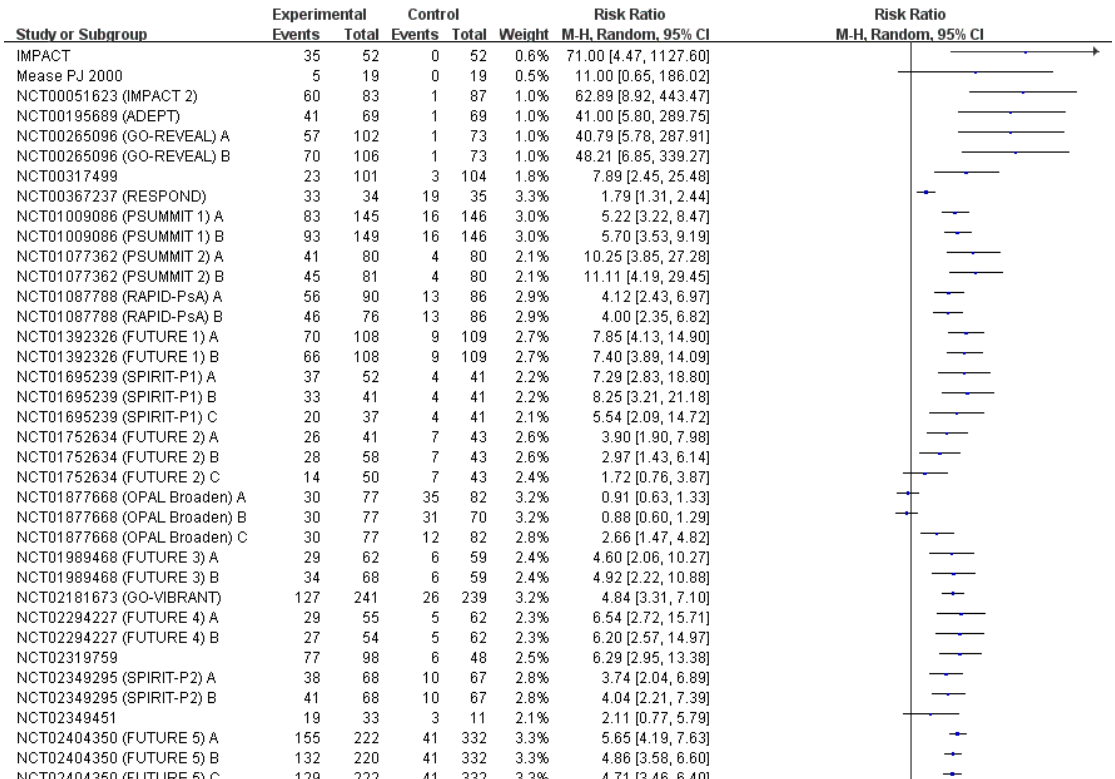


Figure S7. Forest plot of PASI 75. PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index.



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
IMPACT	35	52	0	52	0.6%	71.00 [4.47, 1127.60]
Mease PJ 2000	5	19	0	19	0.5%	11.00 [0.65, 186.02]
NCT00051623 (IMPACT 2)	60	83	1	87	1.0%	62.89 [8.92, 443.47]
NCT00195689 (ADEPT)	41	69	1	69	1.0%	41.00 [5.80, 289.75]
NCT00265096 (GO-REVEAL) A	57	102	1	73	1.0%	40.79 [5.78, 287.91]
NCT00265096 (GO-REVEAL) B	70	106	1	73	1.0%	48.21 [6.85, 339.27]
NCT00317499	23	101	3	104	1.8%	7.89 [2.45, 25.48]
NCT00367237 (RESPOND)	33	34	19	35	3.3%	1.79 [1.31, 2.44]
NCT01009086 (PSUMMIT 1) A	83	145	16	146	3.0%	5.22 [3.22, 8.47]
NCT01009086 (PSUMMIT 1) B	93	149	16	146	3.0%	5.70 [3.53, 9.19]
NCT01077362 (PSUMMIT 2) A	41	80	4	80	2.1%	10.25 [3.85, 27.28]
NCT01077362 (PSUMMIT 2) B	45	81	4	80	2.1%	11.11 [4.19, 29.45]
NCT01087788 (RAPID-PsA) A	56	90	13	86	2.9%	4.12 [2.43, 6.97]
NCT01087788 (RAPID-PsA) B	46	76	13	86	2.9%	4.00 [2.35, 6.82]
NCT01392326 (FUTURE 1) A	70	108	9	109	2.7%	7.85 [4.13, 14.90]
NCT01392326 (FUTURE 1) B	66	108	9	109	2.7%	7.40 [3.89, 14.09]
NCT01695239 (SPIRIT-P1) A	37	52	4	41	2.2%	7.29 [2.83, 18.80]
NCT01695239 (SPIRIT-P1) B	33	41	4	41	2.2%	8.25 [3.21, 21.18]
NCT01695239 (SPIRIT-P1) C	20	37	4	41	2.1%	5.54 [2.09, 14.72]
NCT01752634 (FUTURE 2) A	26	41	7	43	2.6%	3.90 [1.90, 7.98]
NCT01752634 (FUTURE 2) B	28	58	7	43	2.6%	2.97 [1.43, 6.14]
NCT01752634 (FUTURE 2) C	14	50	7	43	2.4%	1.72 [0.76, 3.87]
NCT01877668 (OPAL Broaden) A	30	77	35	82	3.2%	0.91 [0.63, 1.33]
NCT01877668 (OPAL Broaden) B	30	77	31	70	3.2%	0.88 [0.60, 1.29]
NCT01877668 (OPAL Broaden) C	30	77	12	82	2.8%	2.66 [1.47, 4.82]
NCT01989468 (FUTURE 3) A	29	62	6	59	2.4%	4.60 [2.06, 10.27]
NCT01989468 (FUTURE 3) B	34	68	6	59	2.4%	4.92 [2.22, 10.88]
NCT02181673 (GO-VIBRANT)	127	241	26	239	3.2%	4.84 [3.31, 7.10]
NCT02294227 (FUTURE 4) A	29	55	5	62	2.3%	6.54 [2.72, 15.71]
NCT02294227 (FUTURE 4) B	27	54	5	62	2.3%	6.20 [2.57, 14.97]
NCT02319759	77	98	6	48	2.5%	6.29 [2.95, 13.38]
NCT02349295 (SPIRIT-P2) A	38	68	10	67	2.8%	3.74 [2.04, 6.89]
NCT02349295 (SPIRIT-P2) B	41	68	10	67	2.8%	4.04 [2.21, 7.39]
NCT02349451	19	33	3	11	2.1%	2.11 [0.77, 5.79]
NCT02404350 (FUTURE 5) A	155	222	41	332	3.3%	5.65 [4.19, 7.63]
NCT02404350 (FUTURE 5) B	132	220	41	332	3.3%	4.86 [3.58, 6.60]
NCT02404350 (FUTURE 5) C	129	222	41	332	3.3%	4.71 [3.46, 6.40]
NCT03158285 (DISCOVER-2) A	144	184	42	183	3.3%	3.41 [2.59, 4.49]
NCT03158285 (DISCOVER-2) B	139	176	42	183	3.3%	3.44 [2.61, 4.54]
NCT03162796 (DISCOVER-1) A	77	89	11	78	2.9%	6.13 [3.53, 10.67]
NCT03162796 (DISCOVER-1) B	62	82	11	78	2.9%	5.36 [3.06, 9.40]
Total (95% CI)		**3855**		**4032**	**100.0%**	**4.73 [3.77, 5.95]**
Total events	2331		527			

Heterogeneity: Tau² = 0.39; Chi² = 248.01, df = 40 (P < 0.00001); I² = 84%
Test for overall effect: Z = 13.34 (P < 0.00001)

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

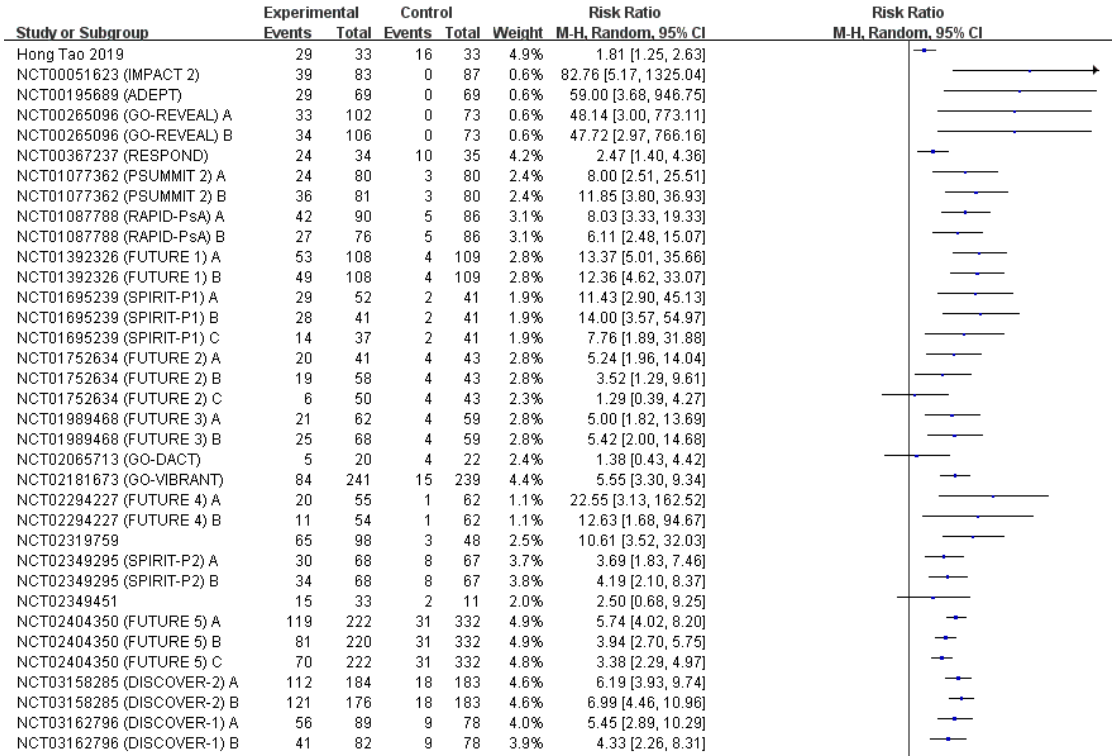
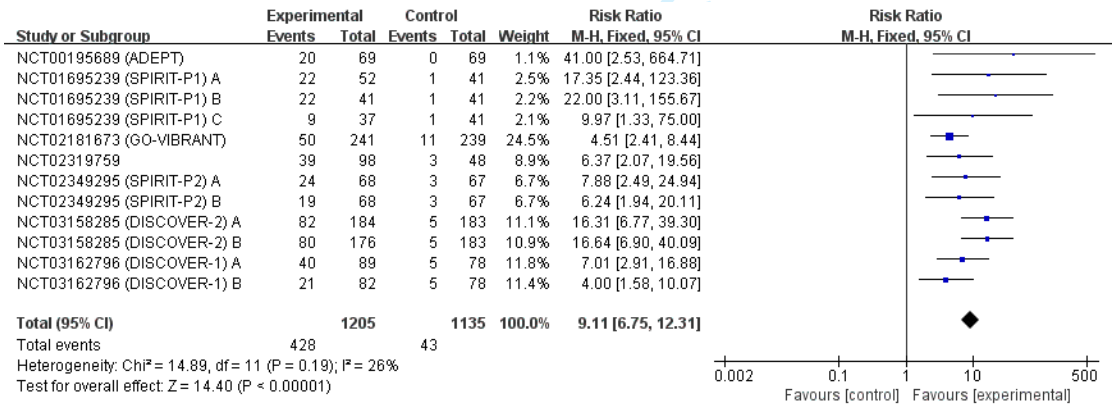


Figure S9. Forest plot of PASI 100. PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index.



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	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			
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			
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 identify 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 report, 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 outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used 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 performed, describe the 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 analyses conducted to assess robustness of the synthesized results.	Page7/line12-13

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	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			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page7/line26-28 and Page 8/line1-13
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	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
	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			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page11/line8-28 and Page12/line1-18
	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/line19-27
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page14/line8-9
Competing interests	26	Declare any competing interests of review authors.	Page14/line11
Availability of data, code and 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/line22-24

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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Word Count 3197.

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 (PsA).

Design: Meta-analysis.

Data sources and eligibility criteria: PubMed, Web of Science, Cochrane Library, CNKI, WanFang, and VIP databases were searched to collect randomized controlled trials (RCTs), which were conducted to evaluate the effect of bDMARDs in treatment of patients with PsA and reported QoL-related outcomes, from inception to November 2020 and updated on 19 February 2022.

Data extraction and synthesis: Outcomes about Health Assessment Questionnaire Disability Index (HAQ-DI), Dermatology Life Quality Index (DLQI), physical component summary (PCS) and mental component summary (MCS) of the Short Form 36 (SF-36), EuroQol Visual Analogue Scale (EQ-VAS), Psoriasis Area Severity Index (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 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 outcomes. Against methotrexate (MTX) and tofacitinib, bDMARDs showed no statistically significant advantages or significant disadvantages. Similar results 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. tofacitinib, bDMARDs vs. MTX, were -0.21 (MD, 95% CI, -0.23, -0.18), -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.

Conclusions: Compared with placebo, bDMARDs taken by patients with PsA appear to significantly improve the QoL. Compared with other therapeutic agents, more studies

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 disease-modifying 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 "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 the reference citation sections of eligible articles as an additional level of searching. Research articles were limited to those regarding RCTs that were published in English or Chinese. The complete electronic search strategy for PubMed is provided in 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

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; I^2: 100%), DLQI (MD=-4.36; 95% CI, -5.76, -2.96; P <0.00001; I^2: 99%), and improve SF-36 PCS (MD=3.76; 95% CI, 3.42, 4.10; P <0.00001; I^2: 99%), SF-36 MCS (MD=1.76; 95% CI, 1.27, 2.25; P <0.00001; I^2: 99%), EQ-VAS (MD=5.27; 95% CI, 1.21, 9.34; P <0.00001; I^2: 99%), PASI 50 (RR=4.09; 95% CI, 2.71, 6.16; P <0.00001; I^2: 82%), PASI 75 (RR=4.72; 95% CI, 3.87, 5.75; P <0.00001; I^2: 81%), PASI 90 (RR=5.73; 95% CI, 4.73, 6.95; P <0.00001; I^2: 59%), PASI 100 (RR=9.57; 95% CI, 7.38, 12.43; P <0.00001; I^2: 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 outcomes						
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 outcomes						
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.

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

Outcomes	Pre-sensitivity analysis			Upper & lower of effect size	Post-sensitivity analysis		
	Number of trials	Pooled estimates	95% CI		Pooled estimates	95% CI	Excluded trials
HAQ-DI	25	-0.19	-0.22, -0.17	Upper	-0.18	-0.20, -0.15	Mease PJ 2000
				Lower	-0.21	-0.24, -0.19	NCT00265096 (GO-REVEAL)
SF-36 PCS	23	3.76	3.42, 4.10	Upper	3.96	3.63, 4.28	NCT01877668 (OPAL Broaden)
				Lower	3.65	3.31, 4.00	NCT02349295 (SPIRIT-P2)
SF-36 MCS	18	1.76	1.27, 2.25	Upper	2.12	1.62, 2.61	NCT01877668 (OPAL Broaden)
				Lower	1.65	1.14, 2.16	NCT02349295 (SPIRIT-P2)
EQ-VAS	3	5.27	1.21, 9.34	Upper	9.66	5.34, 13.98	NCT01877668 (OPAL Broaden)
				Lower	3.71	-0.58, 7.99	NCT02181673 (GO-VIBRANT)
DLQI	8	-4.36	-5.76, -2.96	Upper	-3.50	-5.00, -2.00	NCT01392326 (FUTURE 1)
				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)
				Lower	3.30	2.29, 4.78	NCT00265096 (GO-REVEAL)
PASI 75	27	4.72	3.87, 5.75	Upper	5.01	4.30, 5.83	NCT01877668 (OPAL Broaden)
				Lower	4.54	3.74, 5.51	NCT00265096 (GO-REVEAL)
PASI 90	26	5.73	4.73, 6.95	Upper	6.19*	5.53, 6.93	Hong Tao 2019
				Lower	5.50	4.54, 6.67	NCT01392326 (FUTURE 1)

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.

* 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 placebo, but bDMARDs plus MTX compared with MTX, bDMARDs compared with tofacitinib, and bDMARDs compared with MTX had no obvious advantages or 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 respectively -0.21 (MD, 95% CI, -0.23, -0.18), -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). The detailed results of the subgroup analysis are 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 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, -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 (MD=1.76; 95% CI, 1.27, 2.25; > 1.33)[76-78], and DLQI (MD=-4.36; 95% CI, -5.76, -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

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 methotrexate.

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.

Taken together, the quantitative analysis results of the effects of bDMARDs on the QoL of PsA patients is robust.

The patients who took 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]. However, our meta-analysis showed an improvement in terms of SF-36 MCS, which was inconsistent with the results reported by Lemos LL et al. [23]. This variance could be attributed to the differences in search strategies and inclusion criteria. For example, the study of Lemos LL et al. considered the effects of TNFi rather than 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 countries and regions to evaluate the effects of bDMARDs on the QoL of patients from 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 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.

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.

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

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.

Contributors YQL substantially contributed to the conception and design of the research, and the acquisition, analysis and interpretation of data; was involved in drafting the manuscript and revising it critically for important intellectual content; ZJD substantially contributed to the acquisition, analysis and interpretation of data; was involved in drafting the manuscript and revising it critically for important intellectual content; YL substantially contributed to the conception and design of the research; was involved in revising the manuscript critically for important intellectual content; FC substantially contributed to the conception and design of the research, and the acquisition, analysis and interpretation of data; involved in revising the manuscript critically for important intellectual content. All authors gave their approval for the manuscript to be submitted in BMJ Open and agreed to be accountable for all aspects of the work.

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

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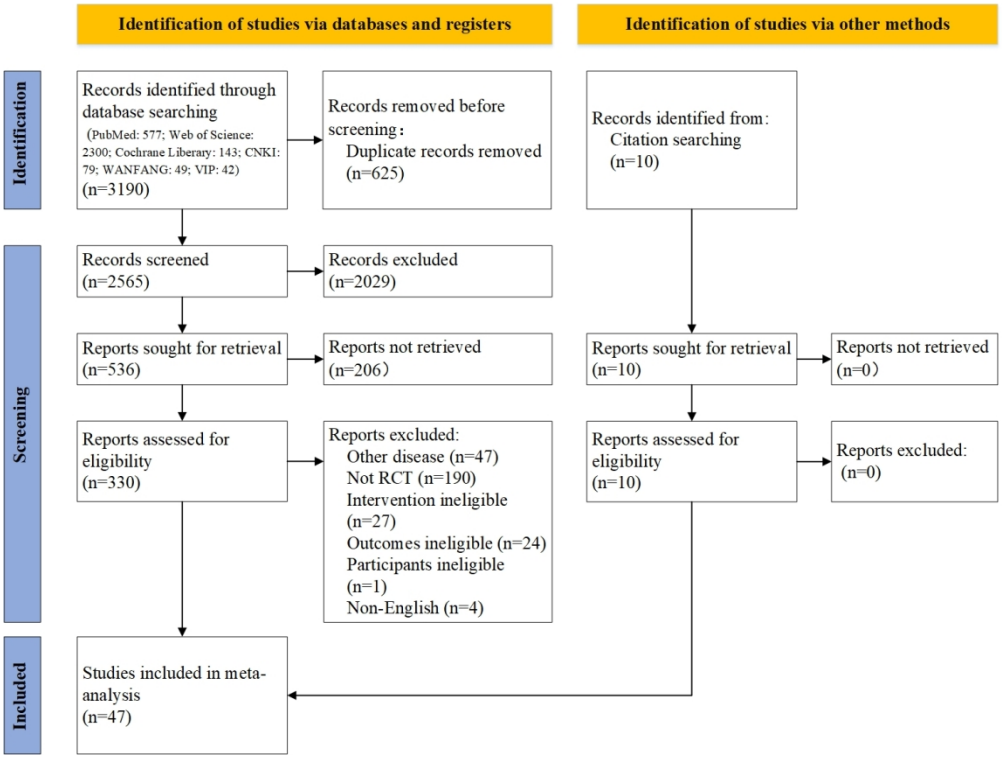

Figure 1 Flowchart of the study selection. RCT, randomized controlled trial.

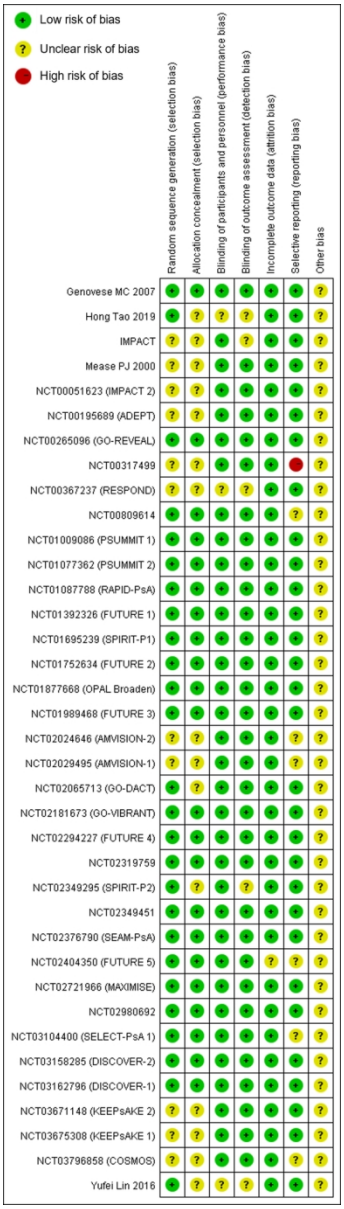

Figure 2 Quality assessment of included RCTs using Cochrane's risk of bias tool, RCT, randomized controlled trial.

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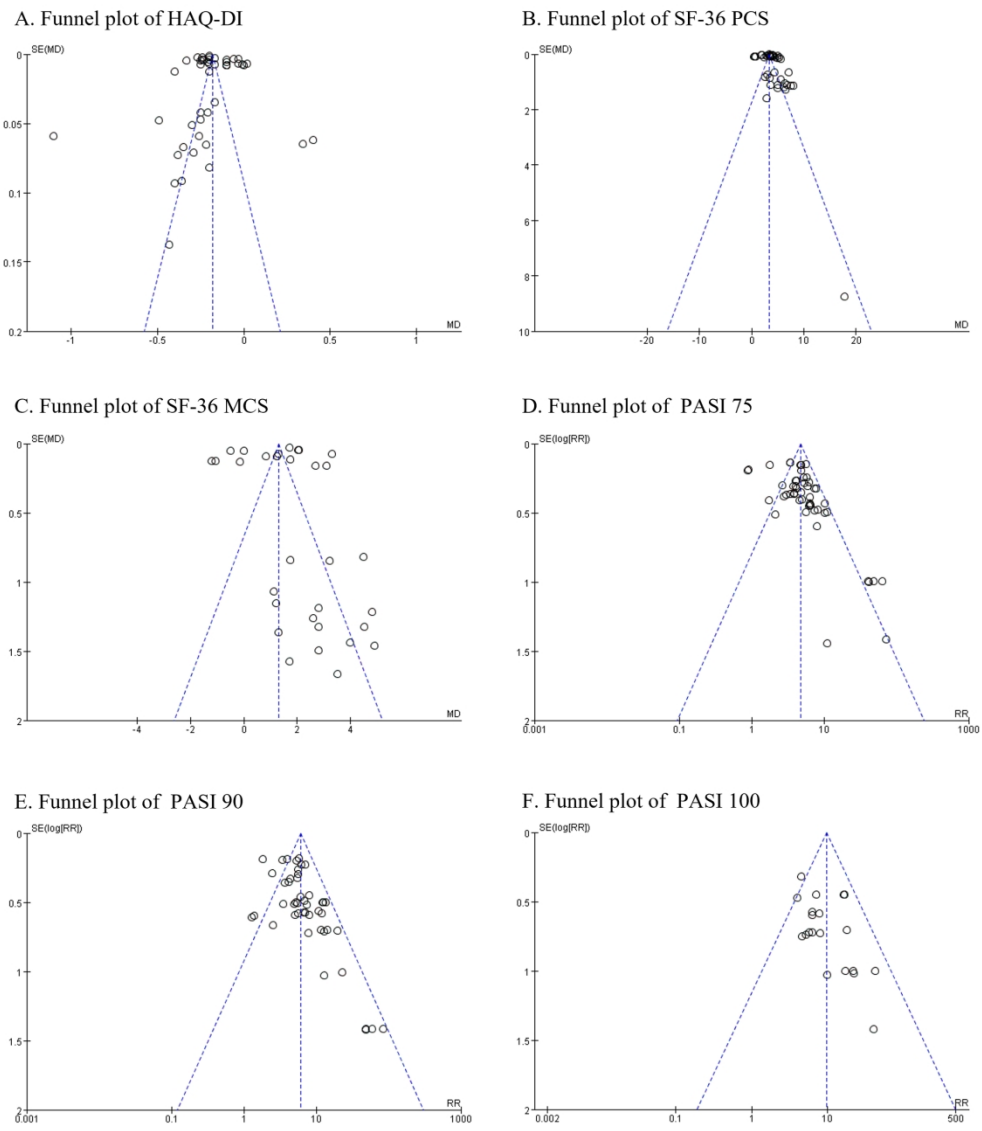

Figure 3 Funnel plots of HAQ-DI, SF-36 PCS, SF-36 MCS, PASI 75, PASI 90 and PASI 100. HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, physical component summary of the Short Form 36; SF-36 MCS, mental component summary of the Short Form 36; PASI 75/90/100, the proportion of participants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

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Content

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-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 [26]	Adalimumab 40 mg SC q2w	51 (56.9)	50.4±11.0	7.2±7.0	12 weeks	①②③⑤
	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	3.56±1.29	24 weeks	⑩⑫
	MTX 15.36±1.69 mg q1w	33 (54.55)	35.94±6.25	3.52±1.28		
IMPACT [28]	Infliximab 5 mg/kg at weeks 0, 2, 6, 14	52 (57.7)	45.7±11.1	11.7±9.8	16 weeks	⑪
	Placebo	52 (57.7)	45.2±9.7	11.0±6.6		
Mease PJ 2000 [29]	Etanercept 25 mg SC BIW	30 (53)	46.0*	7.0*	12 weeks	①⑪
	Placebo	30 (60)	43.5*	9.5*		
NCT00051623 (IMPACT 2)[30,31,32]	Infliximab 5 mg/kg IV at weeks 0, 2, 6, 14, 22	100 (71)	47.1±12.8	8.4±7.2	24 weeks	①②③
	Placebo	100 (51)	46.5±11.3	7.5±7.8		⑨⑪⑫
NCT00195689 (ADEPT)[33,34,35]	Adalimumab 40 mg SC at weeks 0, 2, 4, then q4w	151 (56.3)	48.6±12.5	9.8±8.3	24 weeks	①②③⑤
	Placebo	162 (54.9)	49.2±11.1	9.2±8.7		⑨⑪⑫⑬
NCT00265096 (GO-REVEAL) [36,37]	Golimumab 50 mg SC q4w	146 (61)	45.7±10.7	7.4±6.8	24 weeks	①②③
	Golimumab 100 mg SC q4w	146 (59)	48.2±10.9	7.1±7.8		⑨⑪⑫
	Placebo	113 (61)	47.0±10.6	7.6±7.9		
NCT00317499 [38]	Etanercept 25 mg SC BIW	101 (57)	47.6	9	24 weeks	⑨⑪
	Placebo	104 (45)	47.3	9.2		
NCT00367237 (RESPOND) [39]	Infliximab 5 mg/kg at weeks 0, 2, 6, 14 + MTX	56 (48.2)	40.1±12.3	2.8±2.6	16 weeks	①⑪⑫
	MTX 15 mg q1w	54 (61.1)	42.3±10.5	3.7±2.7		
NCT00809614 [40]	Secukinumab 10 mg/kg SC on days 1, 22	28 (32)	46.7±11.3	6.3±6.8	24 weeks	②
	Placebo	14 (43)	47.6±8.1	5.4±3.8		

NCT01009086 (PSUMMIT 1) [41]	Ustekinumab 45 mg SC at weeks 0,2, then q12w	205 (51.7)	48.0 (39.0-55.0)*	3.4(-1.2-9.2)*	24 weeks	①②③⑤
	Ustekinumab 90 mg SC at weeks 0,2, then q12w	204 (56.9)	47.0 (38.5-54.0)*	4.9(-1.7-8.3)*		⑪
	Placebo	206 (52.4)	48.0 (39.0-57.0)*	3.6(-1.0-9.7)*		
NCT01077362 (PSUMMIT 2) [42]	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
	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 (RAPID-PsA) [43,44]	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 200 mg q2w	138 (46.4)	48.2±12.3	6.6±8.5	24 weeks	①②③⑤ ⑦⑨⑪⑫
	Certolizumab pegol 400 mg SC at weeks 0, 2, 4 + 400 mg q4w	135 (45.9)	47.1±10.8	8.1±8.3		
	Placebo	136 (41.9)	47.3±11.1	4.9±7.7		
NCT01392326 (FUTURE 1) [45,46]	Secukinumab 75 mg/kg IV at weeks 2, 4, then 75 mg SC q4w	202 (41.6)	48.8±12.2	---	24 weeks	①②③⑤ ⑦⑪⑫
	Secukinumab 75 mg/kg IV at weeks 2, 4, then 150 mg SC q4w	202 (47.5)	49.6±11.8	---		
	Placebo	202 (47.5)	48.5±11.2	---		
NCT01695239 (SPIRIT-P1) [47,48]	Ixekizumab 80 mg SC q2w	107 (42.1)	49.1±10.1	6.2±6.4	24 weeks	①②③⑤ ⑥⑪⑫⑬
	Ixekizumab 80 mg SC q4w	103 (46.6)	49.8±12.6	7.2±8.0		
	Adalimumab 40 mg SC q2w	101 (50.5)	48.6±12.4	6.9±7.5		
	Placebo	106(45.3)	50.6±12.3	6.3±6.9		
NCT01752634 (FUTURE 2) [49]	Secukinumab 300 mg SC q1w to week 4 then q4w	100 (51)	46.9±12.6	---	24 weeks	①②⑪⑫
	Secukinumab 150 mg SC q1w to week 4 then q4w	100 (55)	46.5±11.7	---		
	Secukinumab 75mg SC q1w to week 4 then q4w	99 (47)	48.6±11.4	---		
	Placebo	98 (41)	49.9±12.5	---		

NCT01877668 (OPAL Broaden) [50][51]	Adalimumab 40 mg SC q2w	106 (53)	47.4±11.3	57.7±5.3	3 months	①②③⑥
	Tofacitinib 5 mg orally BID	107 (47)	49.4±12.6	71.2±8.2		⑪
	Tofacitinib 10 mg orally BID	104 (40)	46.9±12.4	59.4±5.8		
	Placebo	105 (47)	47.7±12.3	62.4±6.4		
NCT01989468 (FUTURE 3) [52]	Secukinumab 300 mg SC at weeks 1, 2, 3, 4, then q4w	139 (48.2)	49.3±12.9	83.3±9.2	24 weeks	①②⑪⑫
	Secukinumab 150 mg SC at weeks 1, 2, 3, 4, then q4w	138 (44.2)	50.1±11.7	77.7±8.5		
	Placebo	137 (43.1)	50.1±12.6	68.6±6.9		
NCT02024646 (AMVISION-2) [53]	Brodalumab 140mg SC q2w	160 (50.0)	47.4±12.8	69.5±7.4	24 weeks	⑪⑫⑬
	Brodalumab 210mg SC q2w	163 (48.5)	47.0±12.6	69.4±7.7		
	Placebo	161 (47.2)	48.3±13.0	71.1±7.5		
NCT02029495 (AMVISION-1) [53]	Brodalumab 140mg SC q2w	158 (49.4)	49.9±12.8	83.1±8.1	24 weeks	⑪⑫⑬
	Brodalumab 210mg SC q2w	159 (56.0)	49.1±12.2	93.4±9.3		
	Placebo	161 (50.3)	48.1±11.8	83.2±8.2		
NCT02065713 (GO-DACT) [54]	Golimumab 50 mg SC q4w + MTX	21 (81.0)	46.2 (15.5)*	3.3 (6.7)*	24 weeks	⑨⑩⑫
	MTX 15 mg orally q1w and increased 5 mg q4w until 25 mg q1w	22 (87.0)	44.1 (24.6)*	4.1 (6.1)*		
NCT02181673 (GO-VIBRANT) [55,56]	Golimumab 2 mg/kg IV at weeks 0, 4, then q8w	241 (50.6)	45.7±11.3	62.2±6.0	24 weeks	①②③⑤
	Placebo	239 (53.1)	46.7±12.5	58.3±5.9		⑥⑪⑫⑬
NCT02294227 (FUTURE 4) [57]	Secukinumab 150 mg SC q4w LD	114 (41.2)	48.3±12.2	55.6±7.3	16 weeks	②⑪⑫
	Secukinumab 150 mg SC q4w no-LD	113 (45.1)	50.4±11.8	57.7±7.7		
	Placebo	114 (39.5)	48.5±12.2	60.9±7.6		
NCT02319759 [58]	Guselkumab 100 mg SC at weeks 0, 4, then q8w	100 (52)	47.4±12.8	71.0±7.2	24 weeks	①②③⑨
	Placebo	49 (49)	44.2±12.4	69.9±7.2		⑪⑫⑬
NCT02349295	Ixekizumab 80 mg SC q4w	122 (52)	52.6±13.6	160.0±9.6	24 weeks	①②③

(SPIRIT-P2) [59]	Ixekizumab 80 mg SC q2w	123 (41)	51.7±11.9	9.3±7.4		⑪⑫⑬
	Placebo	118 (47)	51.5±10.4	9.2±7.3		
NCT02349451 [60]	Adalimumab 40 mg SC q1w	72 (54.2)	50.5±12.0	8.4±9.2	12 weeks	⑪⑫
	Placebo	24 (50.0)	50.5±12.0	7.6±7.2		
NCT02376790	Etanercept 50 mg SC q1w	284 (53.2)	48.5±13.5	3.1±6.0	24 weeks	①②③④
(SEAM-PsA) [61,62]	Etanercept 50 mg SC + MTX orally q1w	283 (50.9)	48.1±12.7	3.0±6.0		⑧
	MTX 20 mg orally q1w	284 (43.7)	48.7±13.1	3.6±6.8		
NCT02404350	Secukinumab 300 mg SC q4w LD	222 (48.6)	48.9±12.8	6.4±8.3	16 weeks	⑪⑫
(FUTURE 5) [63]	Secukinumab 150 mg SC q4w LD	220 (50.5)	48.4±12.9	6.3±7.1		
	Secukinumab 150 mg SC q4w no-LD	222 (54.1)	48.8±11.8	6.3±6.1		
	Placebo	332 (48.5)	49.0±12.1	6.3±7.6		
NCT02721966	Secukinumab 300 mg SC at weeks 1, 2, 3, 4, then q4w	167 (46.1)	46.2±12.3	---	12 weeks	①
(MAXIMISE) [64]	Secukinumab 150 mg SC at weeks 1, 2, 3, 4, then q4w	165 (49.1)	46.9±11.5	---		
	Placebo	166 (53.0)	46.6±11.5	---		
NCT02980692 [65]	Tildrakizumab 200 mg SC q4w	78 (41.0)	50.1±13.3	7.1±8.5	24 weeks	①⑧
	Tildrakizumab 200 mg SC q12w	79 (53.2)	49.3±11.2	6.3±7.2		⑪⑫⑬
	Tildrakizumab 100 mg SC q12w	77 (39.0)	49.2±11.9	7.1±6.6		
	Tildrakizumab 20 mg SC q12w	78 (47.4)	47.2±13.4	6.1±6.7		
	Placebo	79 (44.3)	48.1±13.3	6.2±6.1		
NCT03104400	Adalimumab 40 mg SC q2w	429 (48.3)	51.4±12.0	5.1±7.1	24 weeks	①②③
(SELECT-PsA 1) [66]	Placebo	423 (50.1)	50.4±12.2	6.1±7.0		
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) [67]	Guselkumab 100mg SC at weeks 0,4, then q8w	248 (52)	44.9±11.9	5.1±5.5		⑪⑫⑬
	Placebo	246 (48)	46.3±11.7	5.8±5.6		

NCT03162796	Guselkumab 100 mg SC q4w	128 (52)	47.4±11.6	6.6±6.3	24 weeks	①②③
(DISCOVER-1) [68]	Guselkumab 100 mg SC at weeks 0, 4, then q8w	127 (54)	48.9±11.5	6.4±5.9		⑪⑫⑬
	Placebo	126 (48)	49.0±11.1	7.2±7.6		
NCT03671148	Risankizumab 150mg SC at weeks 0, 4, 16	224 (44.6)	53 (23–84)	8.2±8.2	24 weeks	①②⑫
(KEEPsAKE 2) [69]	Placebo	219 (45.2)	52 (24-83)	8.2±8.3		
NCT03675308	Risankizumab 150mg SC at weeks 0, 4, 16	483 (52.2)	52 (20–85)	7.1±7.0	24 weeks	①②⑫
(KEEPsAKE 1) [71]	Placebo	481 (48.6)	52 (22–79)	7.1±7.7		
NCT03796858	Guselkumab 100 mg SC at weeks 0, 4, then q8w	189 (46)	49±12	8.3±7.8	24 weeks	③⑪⑫
(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	42 (61.90)	44.01±10.33	3.62±2.11	24 weeks	⑭
	MTX 7.5-15 mg orally q1w and increased to 15-25 mg q1w	42 (66.67)	43.59±10.29	3.71±2.12		

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; ⑥EQ-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; ⑩PASI 70, the proportion of participants achieving 70% improvement from baseline in Psoriasis Area Severity Index; ⑪PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index; ⑫PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index; ⑬PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index; ⑭PASI score, Psoriasis Area Severity Index score.

* 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					
< 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					
Total	27	2.11	1.76, 2.46	97	< 0.00001
Category of bDMARD					
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					
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	< 0.00001
Guselkumab	6	1.66	1.22, 2.10	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	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					
< 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	28	6.10*	5.31, 7.00	23	< 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	37	7.04*	6.14, 8.08	14	< 0.00001
bDMARDs+ MTX vs. MTX	HAQ-DI	2	-0.22	-0.58, 0.14	86	0.23
	SF-36 PCS	1	2.00	1.90, 2.10	---	< 0.00001
	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 vs. Tofacitinib	HAQ-DI	2	-0.01	-0.05, 0.04	96	0.84
	SF-36 PCS	2	0.63*	0.49, 0.77	36	< 0.00001
	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 vs. MTX	HAQ-DI	1	-0.03	-0.04, -0.02	---	< 0.00001
	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.

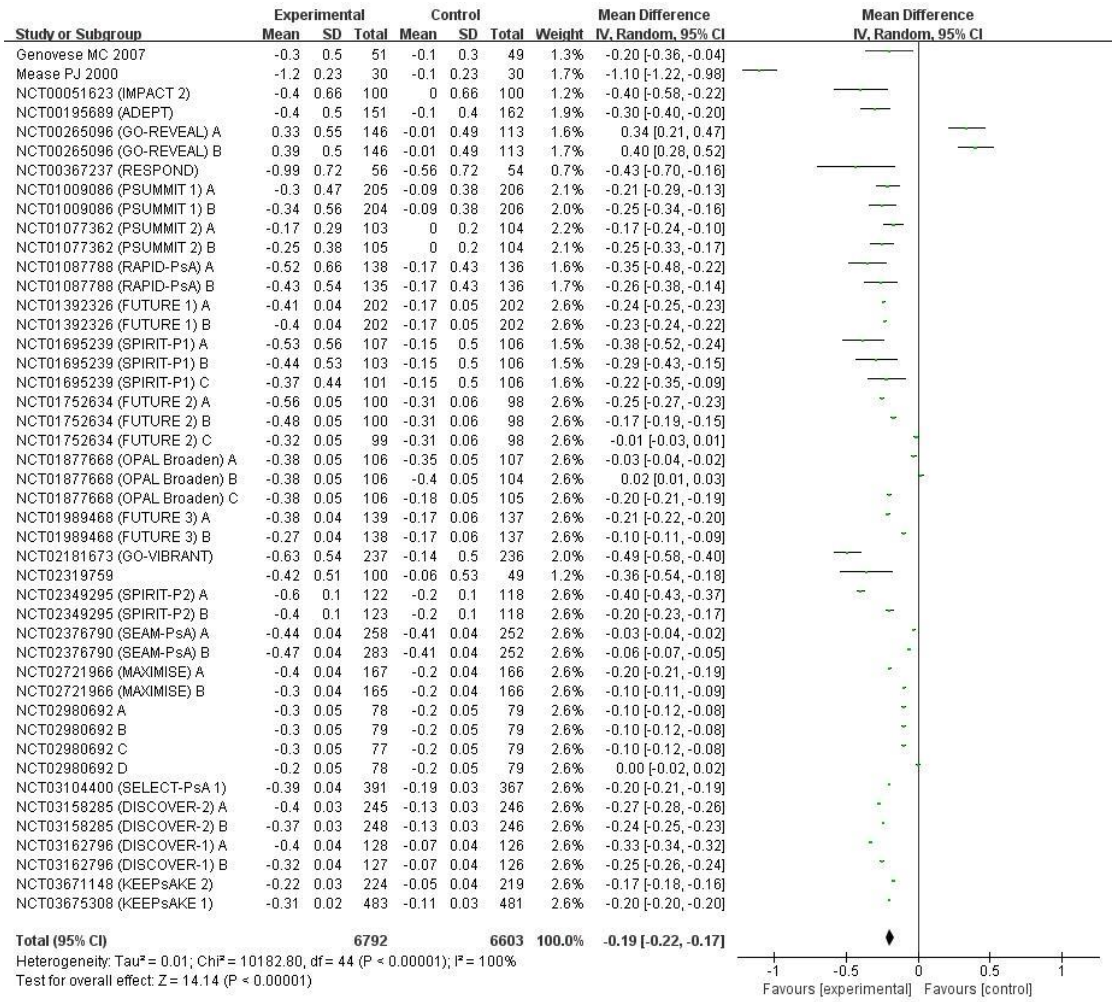


Figure S2. Forest plot of SF-36 PCS. SF-36 PCS, physical component summary of the Short Form 36.

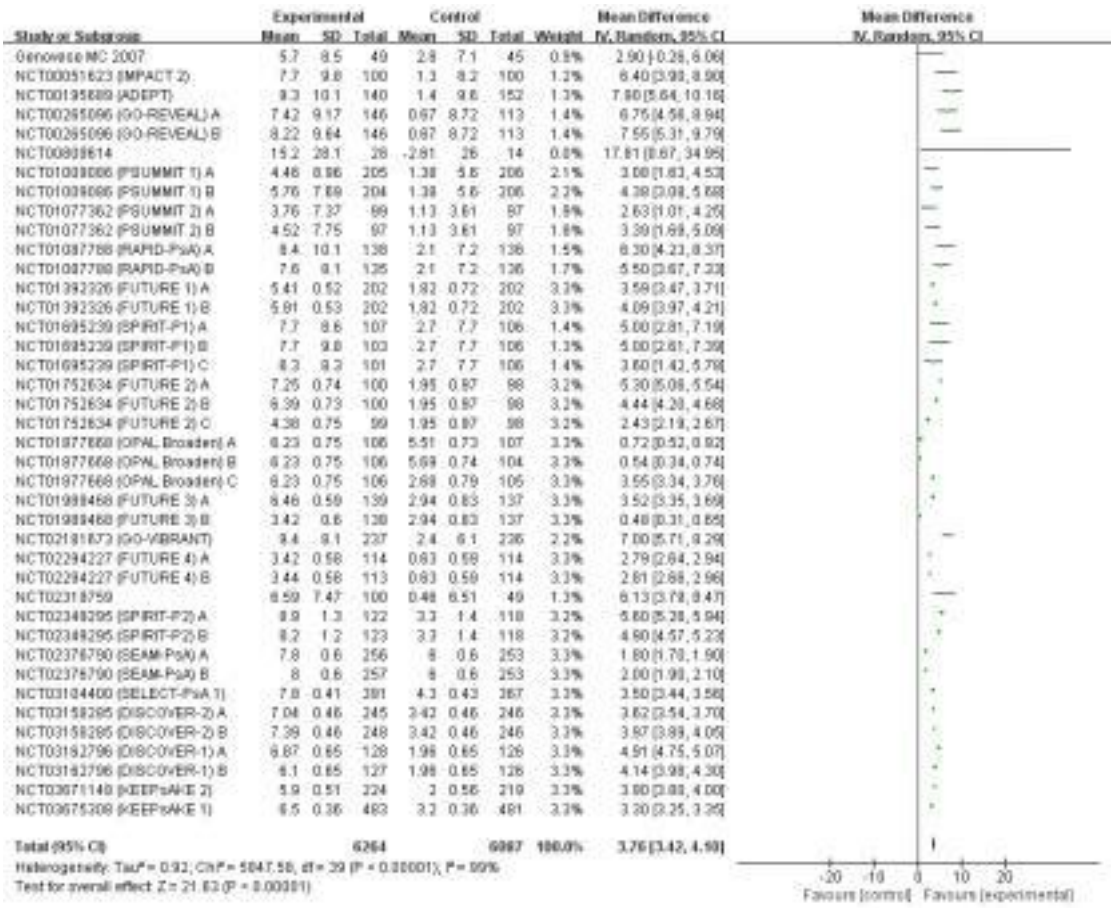


Figure S3. Forest plot of SF-36 MCS. SF-36 MCS, mental component summary of the Short Form 36.

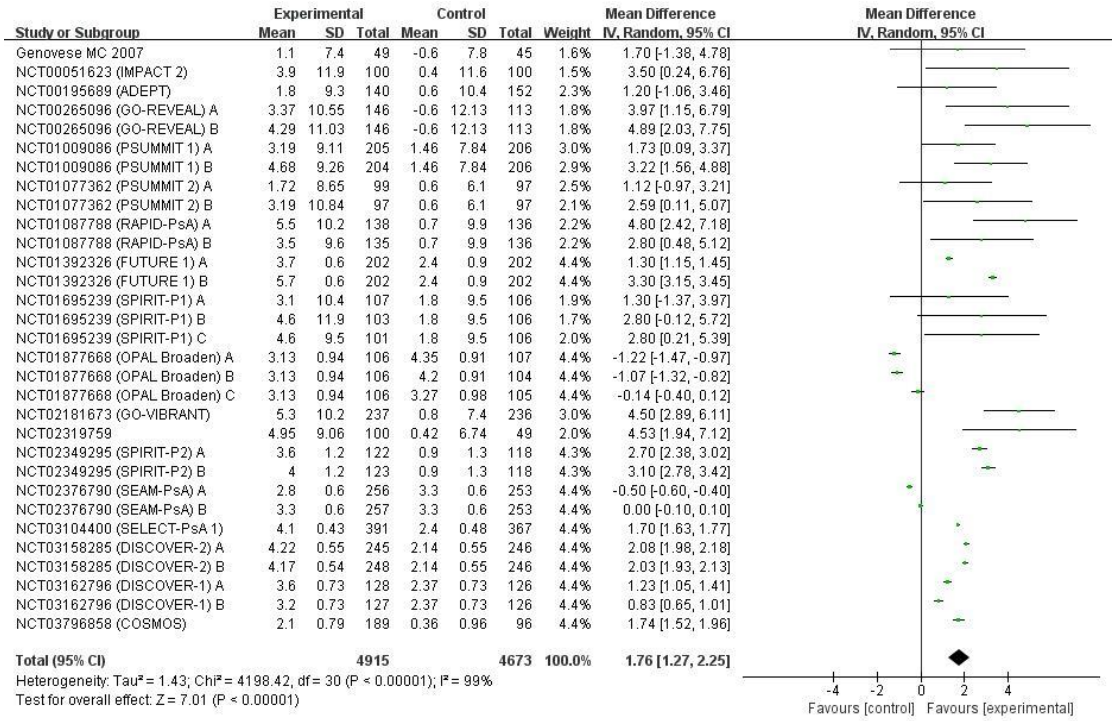


Figure S4. Forest plot of EQ-VAS. EQ-VAS, EuroQol Visual Analogue Scale.

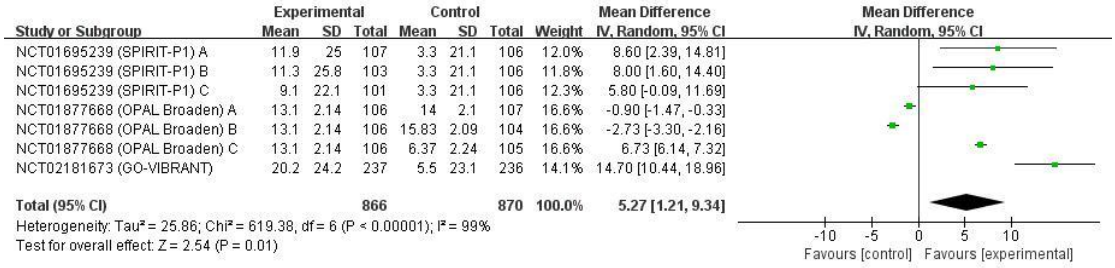


Figure S5. Forest plot of DLQI. DLQI, Dermatology Life Quality Index.

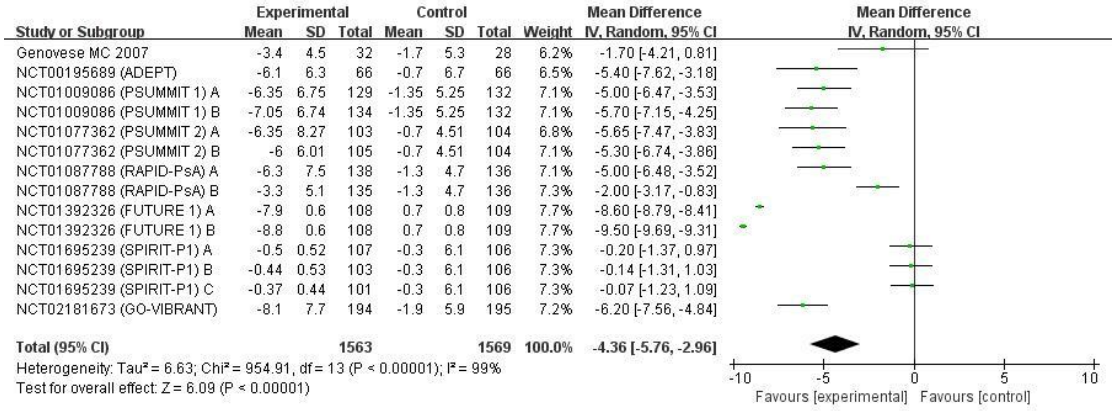


Figure S6. Forest plot of PASI 50. PASI 50, the proportion of participants achieving 50% improvement from baseline in Psoriasis Area Severity Index.

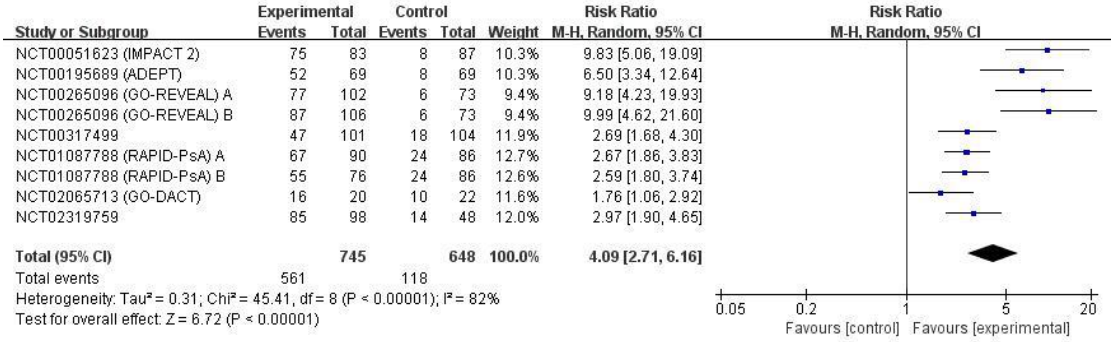


Figure S7. Forest plot of PASI 75. PASI 75, the proportion of participants achieving 75% improvement from baseline in Psoriasis Area Severity Index.

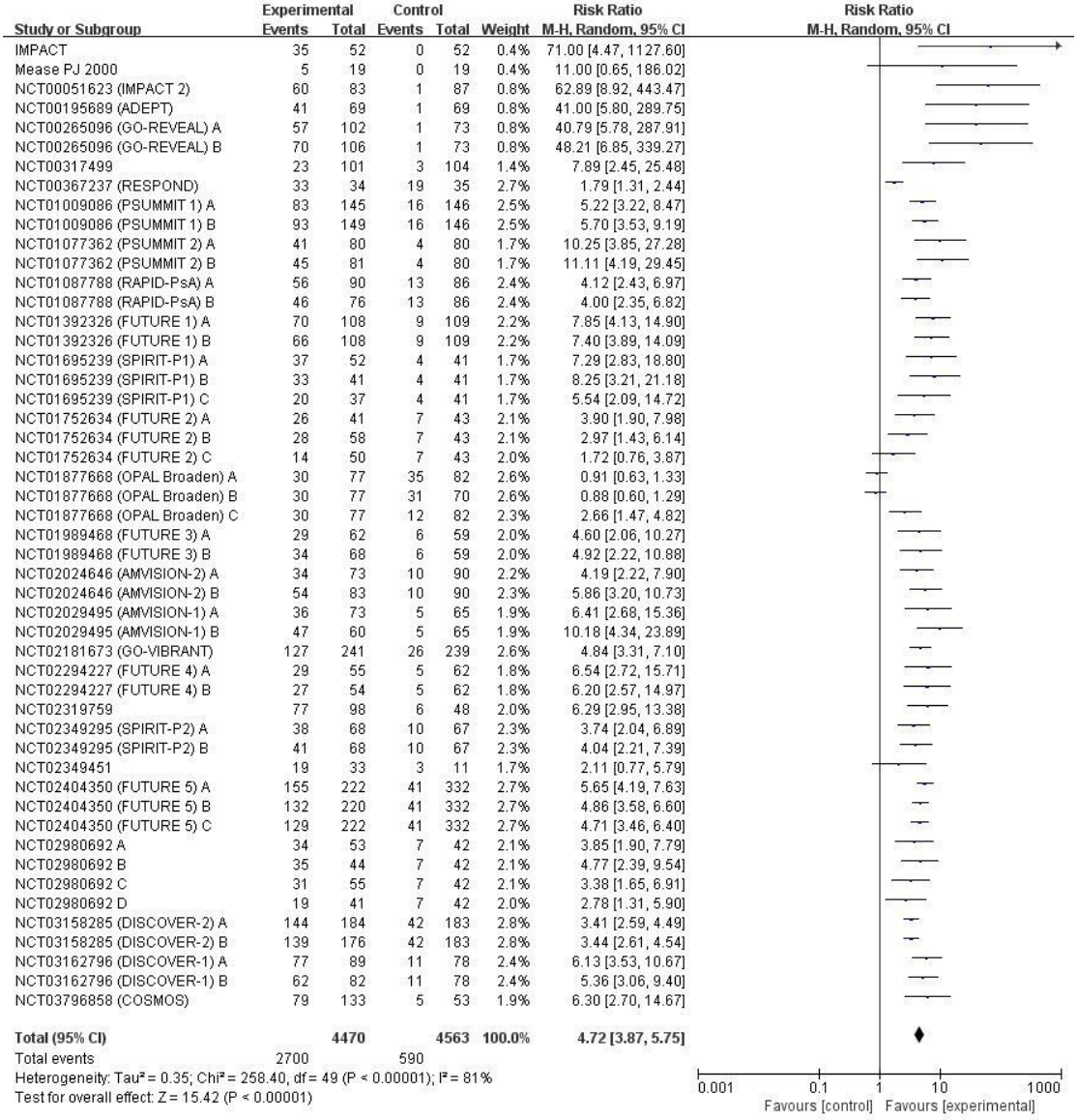


Figure S8. Forest plot of PASI 90. PASI 90, the proportion of participants achieving 90% improvement from baseline in Psoriasis Area Severity Index.

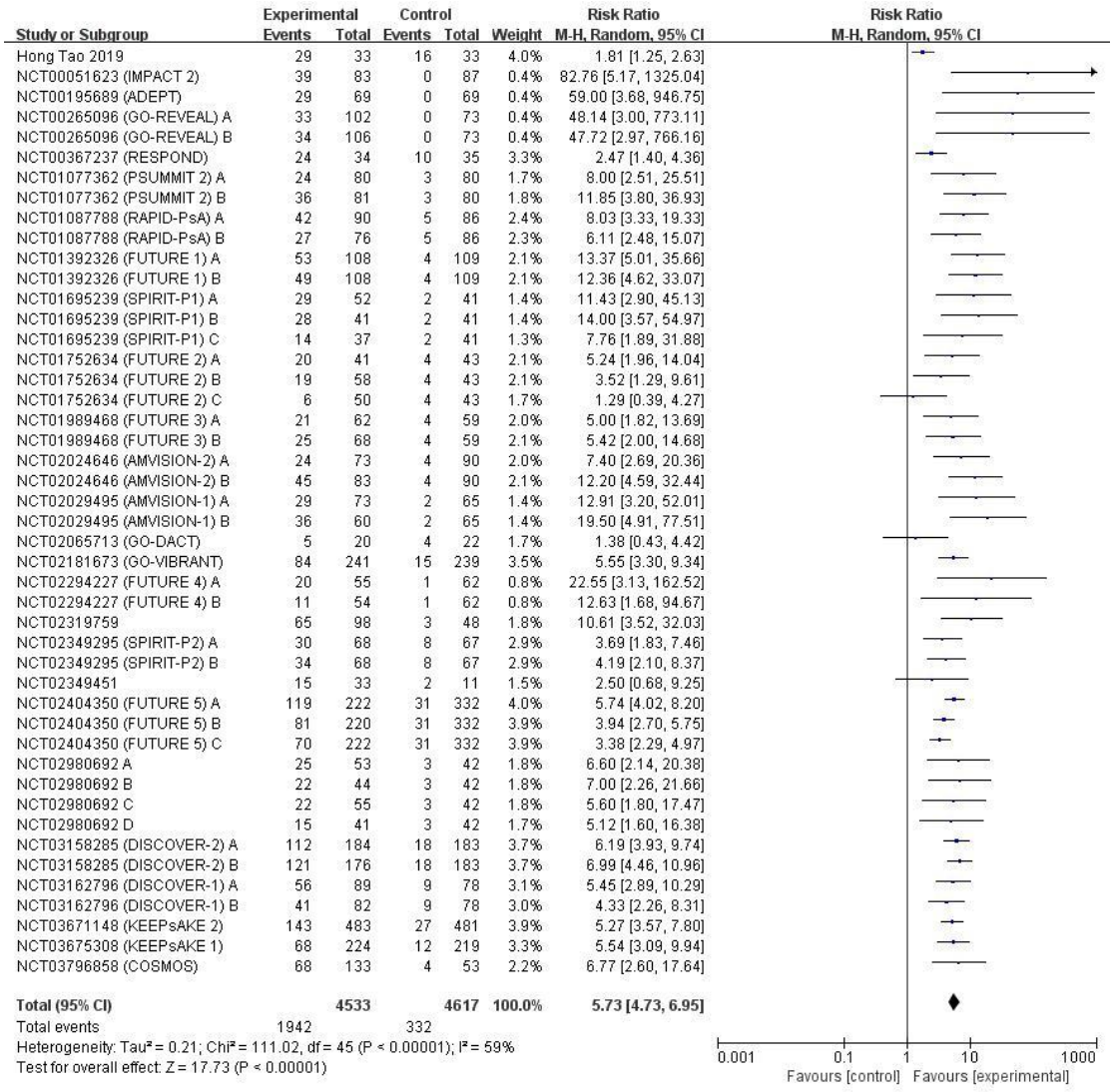
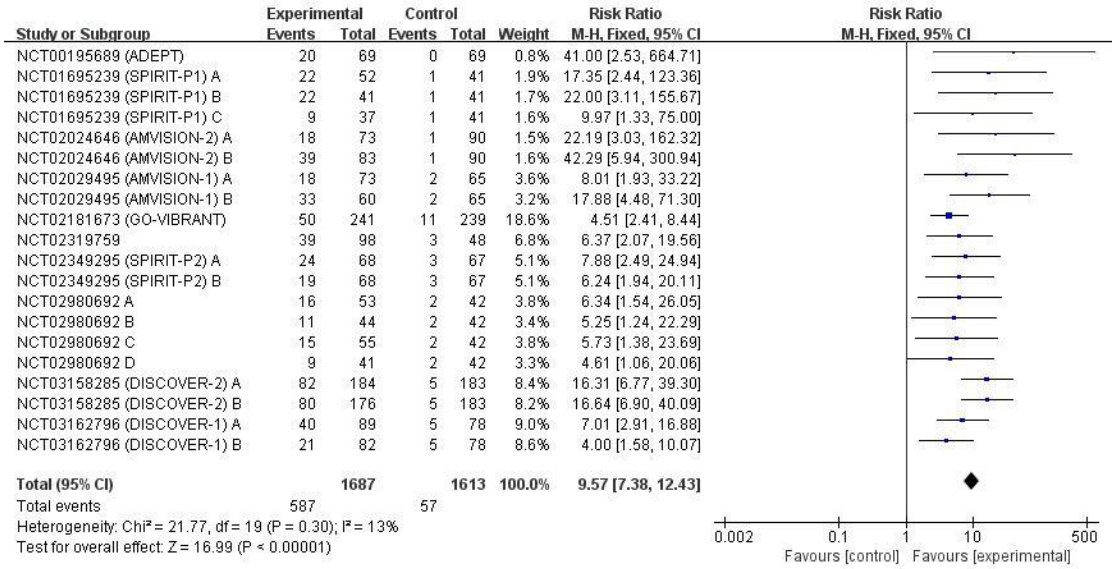


Figure S9. Forest plot of PASI 100. PASI 100, the proportion of participants achieving 100% improvement from baseline in Psoriasis Area Severity Index.



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	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			
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			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page6/line7-18
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page5/line15-17
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/line1-5
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/line7-8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, 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/line20-21
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page6/line21-23
	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/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 many reviewers assessed 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 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 performed, describe the 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, meta-regression).	Page7/line14-24
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page7/line13-14

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	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/line23-24
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page7/line6-8
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page7/line27-28 and Page 8/line1-14
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	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/line16-27
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Supplementary table S3
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page9/line8-15
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
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 1
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page11/line18-28, Page12/line1-28 and Page 13/line1-15
	23b	Discuss any limitations of the evidence included in the review.	Page13/line16-25
	23c	Discuss any limitations of the review processes used.	N/A
	23d	Discuss implications of the results for practice, policy, and future research.	Page14/line1-2
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page14/line28 and Page15/line1
Competing interests	26	Declare any competing interests of review authors.	Page15/line3
Availability of data, code and 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.	Page15/line14-16

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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