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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, China National Knowledge Infrastructure, WanFang and VIP databases were searched to collect randomised controlled trials (RCTs), which were conducted to evaluate the effect of bDMARDs in the 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, physical component summary and mental component summary of the Short Form 36, EuroQol Visual Analogue Scale, 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 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 versus placebo, bDMARDs+MTX versus MTX, bDMARDs versus tofacitinib and bDMARDs versus MTX were −0.21 (MD, 95% CI, −0.23 to −0.18), −0.22 (MD, 95% CI, −0.58 to 0.14), −0.01 (MD, 95% CI, −0.05 to 0.04) and −0.03 (MD, 95% CI, −0.04 to −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.

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 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 first, then category of bDMARDs, variety of bDMARDs, duration of PsA.
- Meta-analysis was not performed for the outcomes reported in less than 3 randomised controlled trials (RCTs), and funnel charts were 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 was 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.

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 *et al* analysed the 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 *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 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] Among these questionnaires, the higher scores of SF-36 and EQ-5D indicate higher levels of QoL, 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 tumour necrosis factor inhibitors (TNFi, eg, etanercept, infliximab, adalimumab, golimumab, certolizumab pegol), interleukin-17 inhibitors (IL-17i, eg, ustekinumab, guselkumab, risankizumab) and interleukin-12/23 inhibitors (IL-12/23i, eg, secukinumab, ixekizumab, brodalumab).[1 20] Ruyssen-Witrand *et al*,[21] Lu *et al*[22] and Lemos *et al*[23] studied the efficacy and safety of bDMARDs in treating PsA, and found that the physical summarised component of SF-36 Score was improved, HAQ Score and PASI Score were decreased, but the change of mental summarised component 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 randomised 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.

MATERIALS AND METHODS

Search strategy and study selection

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.[24] To identify RCTs reporting the effects of bDMARDs on QoL, two independent authors (YqL and ZD) electronically conducted the searches in PubMed, Web of Science, the Cochrane Library, China National Knowledge Infrastructure, 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 studies, the 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 online supplemental table S1.

Inclusion and exclusion criteria

Studies were independently selected by two authors (YqL and ZD), and they achieved good agreement (κ=0.942). Studies were included if they met the following inclusion criteria: (1) the trial was a human study conducted on patients with PsA; (2) 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; (3) the study provided appropriate data (means and 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.

Data extraction and quality assessment

Two authors (YqL and ZD) independently extracted data from each selected RCT 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 ZD) 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: randomisation generation, allocation concealment, blinding of participants and outcome assessment, incomplete outcome data, 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.

Data synthesis and statistical analysis

All statistical analyses were conducted using Review Manager V.5.3 software (Cochrane Collaboration, Copenhagen, Denmark) and STATA software V.16.0 (Stata Corp, College Station, Texas, USA). 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 was used for analyses. Otherwise, heterogeneity was assumed, the random effects model was used to analyse and its source should be further determined by sensitivity

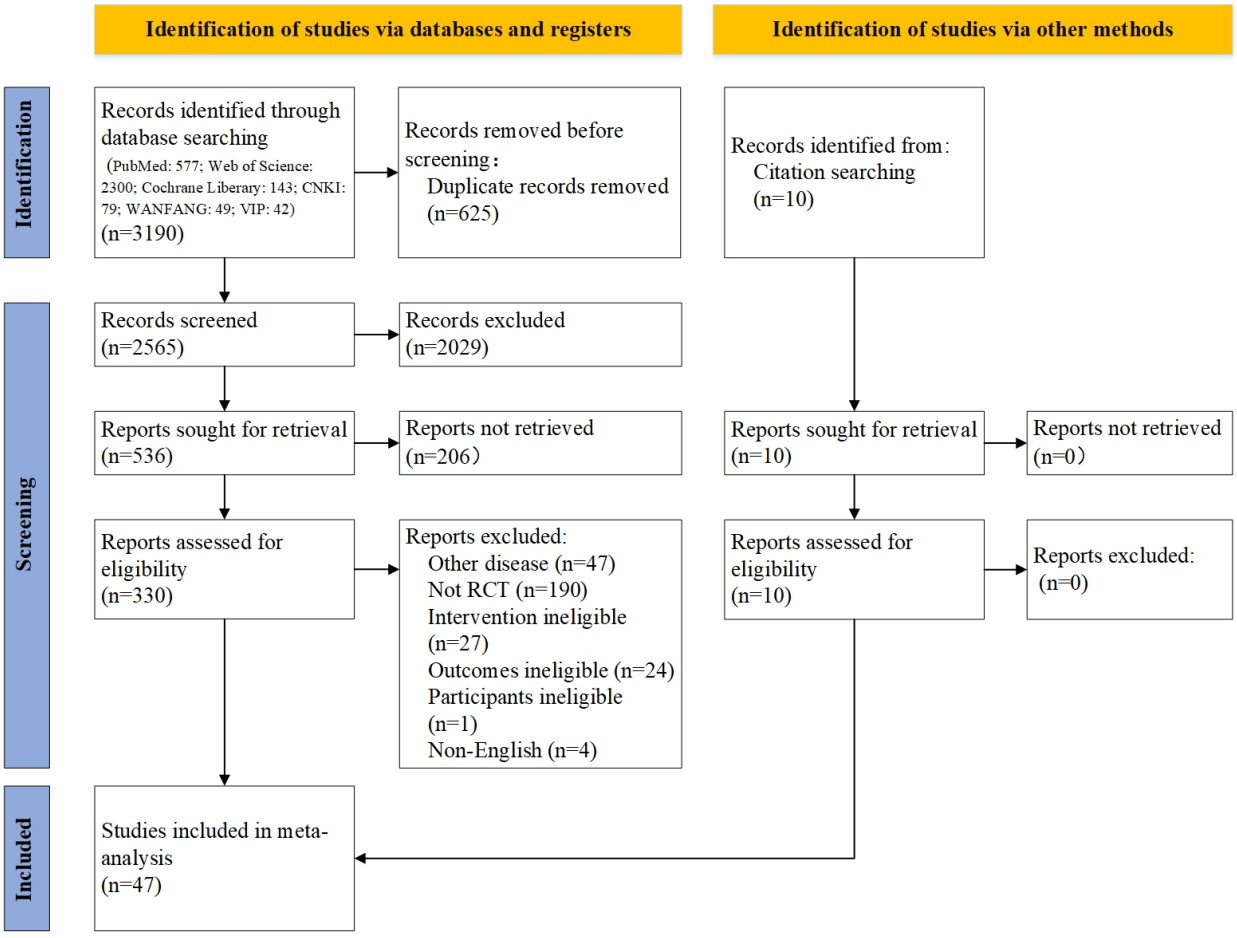

Figure 1 Flowchart of the study selection. RCT, randomised controlled trial.

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 were probably the biggest cause of heterogeneity. Then, each subgroup was analysed 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, was used to determine any possible publication bias.

RESULTS

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. Overall, 25 RCTs have reported the effects of bDMARDs on HAQ Disability Index (HAQ-DI), 23 RCTs on SF-36 physical component summary (PCS), 18 RCTs on SF-36 mental component summary (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 the opposite. The detailed characteristics of selected RCTs are summarised in online supplemental 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 three RCTs.

Main outcomes

Forest plots demonstrating the effects of bDMARDs on QoL are provided in online supplemental figures S1–S9. The pooled effect sizes of all outcomes are summarised in

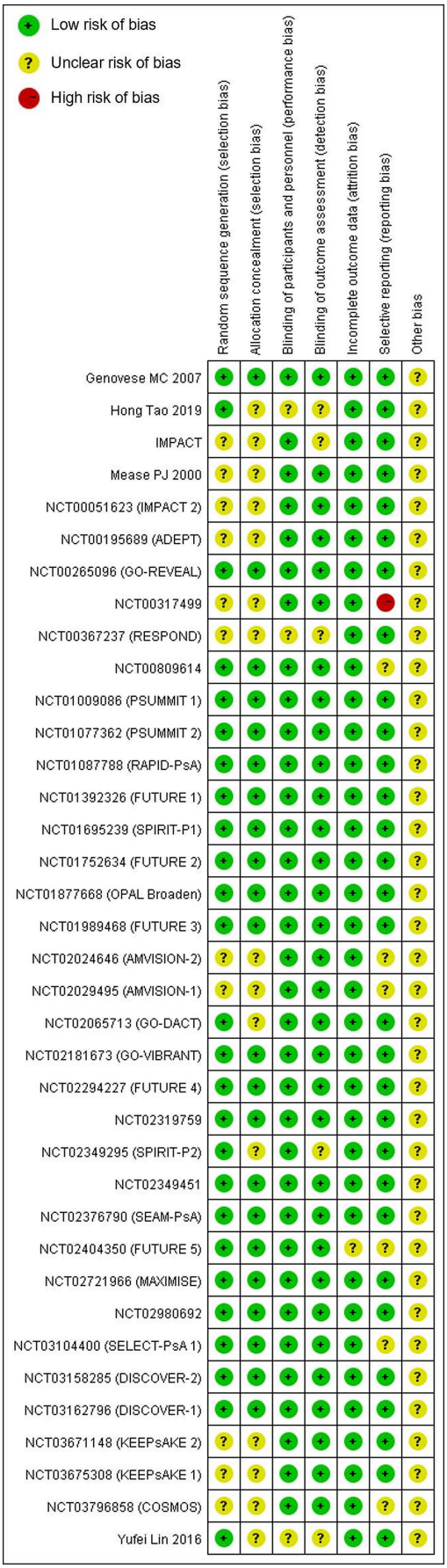

Figure 2 Quality assessment of included randomised controlled trials using Cochrane's risk-of-bias tool.

table 1. The results show that bDMARDs taken by patients with PsA can significantly decrease HAQ-DI (MD=−0.19; 95% CI, −0.22 to −0.17; p<0.00001; I^2: 100%), DLQI (MD=−4.36; 95% CI, −5.76 to −2.96; p<0.00001; I^2: 99%) and improve SF-36 PCS (MD=3.76; 95% CI, 3.42 to 4.10; p<0.00001; I^2: 99%), SF-36 MCS (MD=1.76; 95% CI, 1.27 to 2.25; p<0.00001; I^2: 99%), EQ-VAS (MD=5.27; 95% CI, 1.21 to 9.34; p<0.00001; I^2: 99%), PASI 50 (RR=4.09; 95% CI, 2.71 to 6.16; p<0.00001; I^2: 82%), PASI 75 (RR=4.72; 95% CI, 3.87 to 5.75; p<0.00001; I^2: 81%), PASI 90 (RR=5.73; 95% CI, 4.73 to 6.95; p<0.00001; I^2: 59%), PASI 100 (RR=9.57; 95% CI, 7.38 to 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.

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 Tao *et al*[27], the heterogeneity of PASI 90 decreased from 59% to 41%. After excluding NCT02181673 (GO-VIBRANT), postsensitivity pooled MD for EQ-VAS was 3.71 (95% CI, −0.58 to 7.99), which differed from presensitivity significantly. No statistically significant difference was found between presensitivity and postsensitivity 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.

Subgroup analysis

Following subgroup analyses, heterogeneity was changed among some of the strata of subgroups. Regarding the subgroup of bDMARDs versus placebo, there was a significant difference between presubgroup and post-subgroup analysis for HAQ-DI in strata of golimumab (MD=0.08; 95% CI, −0.53 to 0.69), SF-36 MCS in strata of adalimumab (MD=1.24; 95% CI, −0.11 to 2.59) and strata of <24 weeks (MD=−0.13; 95% CI, −0.39 to 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 versus MTX, HAQ-DI, SF-36 MCS, EQ-VAS and PASI 75 in the subgroup of bDMARDs versus tofacitinib, SF-36 MCS in the subgroup of bDMARDs versus MTX. In general, bDMARDs had obvious advantages in improving the QoL of PsA compared with placebo, but bDMARDs+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 versus placebo, bDMARDs+MTX versus MTX, bDMARDs versus tofacitinib and bDMARDs versus MTX were −0.21 (MD, 95% CI, −0.23 to −0.18), −0.22 (MD, 95% CI, −0.58 to 0.14), −0.01 (MD, 95% CI, −0.05 to 0.04) and −0.03 (MD, 95% CI, −0.04 to −0.02), respectively. The detailed results of the

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 to −0.17	100	<0.00001
SF-36 PCS	23	RE	3.76	3.42 to 4.10	99	<0.00001
SF-36 MCS	18	RE	1.76	1.27 to 2.25	99	<0.00001
EQ-VAS	3	RE	5.27	1.21 to 9.34	99	0.01
Secondary outcomes						
DLQI	8	RE	−4.36	−5.76 to −2.96	99	<0.00001
PASI 50	7	RE	4.09	2.71 to 6.16	82	<0.00001
PASI 75	27	RE	4.72	3.87 to 5.75	81	<0.00001
PASI 90	26	RE	5.73	4.73 to 6.95	59	<0.00001
PASI 100	10	FE	9.57	7.38 to 12.43	13	<0.00001

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

subgroup analysis are presented in online supplemental table S3.

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.

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 nine outcomes, it was found that bDMARDs could effectively improve the QoL of patients with PsA. By reviewing the studies on minimal clinically important differences 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 to −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 to 4.10; >2.1),[75–78] SF-36 MCS (MD=1.76; 95% CI, 1.27 to 2.25; >1.33),[76–78] and DLQI (MD=−4.36; 95% CI, −5.76 to −2.96; <−2.24),[79] but not for EQ-VAS (MD=5.27; 95% CI, 1.21 to 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 MTX, 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 MTX.

Looking specifically at the subgroup of bDMARDs versus placebo, the 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 the treatment <24 weeks, which might indicate that long-term use of bDMARDs can improve the QoL of patients.

In this meta-analysis, quantitative analysis was not performed on the outcomes that were reported in less than three 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, Tao *et al*[27] found that infliximab+MTX got more significant improvement than MTX, while NCT02065713 (GO-DACT)[54] found that golimumab+MTX had no difference from MTX. Additionally, Tao *et al*[27] found that the PASI Score of patients in the infliximab+MTX group was

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

Outcomes	Presensitivity analysis			Upper and lower of effect size	Postsensitivity analysis		
	Number of trials	Pooled estimates	95% CI		Pooled estimates	95% CI	Excluded trials
HAQ-DI	25	−0.19	−0.22 to −0.17	Upper	−0.18	−0.20 to −0.15	Mease *et al*[29]
				Lower	−0.21	−0.24 to −0.19	NCT00265096 (GO-REVEAL)
SF-36 PCS	23	3.76	3.42 to 4.10	Upper	3.96	3.63 to 4.28	NCT01877668 (OPAL Broaden)
				Lower	3.65	3.31 to 4.00	NCT02349295 (SPIRIT-P2)
SF-36 MCS	18	1.76	1.27 to 2.25	Upper	2.12	1.62 to 2.61	NCT01877668 (OPAL Broaden)
				Lower	1.65	1.14 to 2.16	NCT02349295 (SPIRIT-P2)
EQ-VAS	3	5.27	1.21 to 9.34	Upper	9.66	5.34 to 13.98	NCT01877668 (OPAL Broaden)
				Lower	3.71	−0.58 to 7.99	NCT02181673 (GO-VIBRANT)
DLQI	8	−4.36	−5.76 to −2.96	Upper	−3.50	−5.00 to −2.00	NCT01392326 (FUTURE 1)
				Lower	−5.67	−6.71 to −4.62	NCT01695239 (SPIRIT-P1)
PASI 50	7	4.09	2.71 to 6.16	Upper	4.83	2.75 to 8.49	NCT01087788 (RAPID-PsA)
				Lower	3.30	2.29 to 4.78	NCT00265096 (GO-REVEAL)
PASI 75	27	4.72	3.87 to 5.75	Upper	5.01	4.30 to 5.83	NCT01877668 (OPAL Broaden)
				Lower	4.54	3.74 to 5.51	NCT00265096 (GO-REVEAL)
PASI 90	26	5.73	4.73 to 6.95	Upper	6.19*	5.53 to 6.93	Tao *et al*[27]
				Lower	5.50	4.54 to 6.67	NCT01392326 (FUTURE 1)

*Fixed effect.
PASI 50/75/90, the proportion of participants achieving 50%/75%/90% improvement from baseline in Psoriasis Area Severity Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol Visual Analogue Scale; HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 MCS, mental component summary of the Short Form 36; SF-36 PCS, physical component summary of the Short Form 36; QoL, quality of life; RCTs, randomised controlled trials.

significantly lower than that in the MTX group. Taken together, the quantitative analysis results of the effects of bDMARDs on the QoL of patients with PsA are robust.

The patients who took bDMARDs showed an improvement in terms 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 *et al*.[23] This variance could be attributed to the differences in search strategies and inclusion criteria. For example, the study of Lemos *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 analysed the effects of bDMARDs on the QoL of patients with PsA, and quantitatively analysed 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 multicentre studies. It was difficult to conduct subgroup analysis based on countries and regions to evaluate the effects of bDMARDs on the

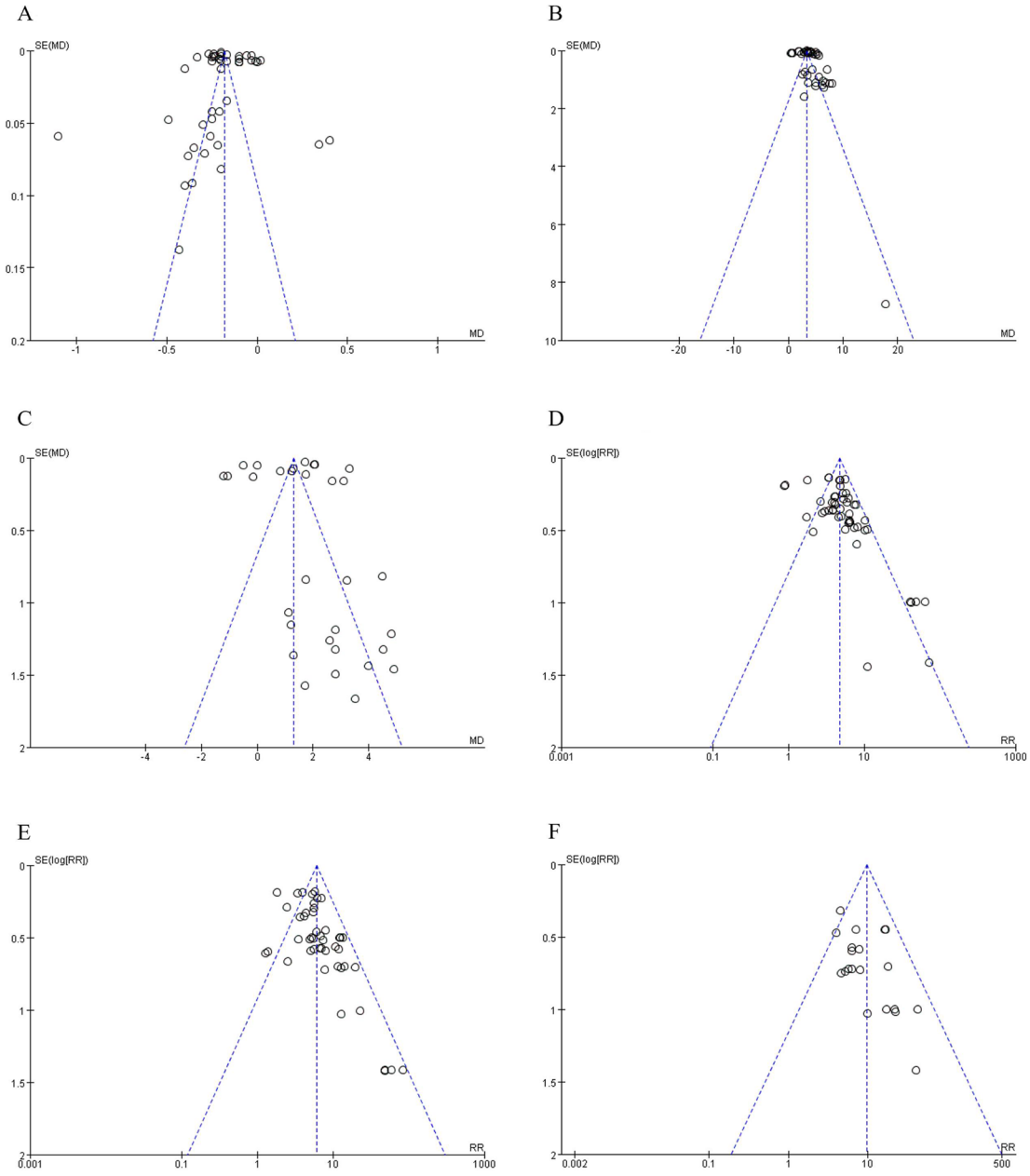

Figure 3 Funnel plots of (A) HAQ-DI, (B) SF-36 PCS, (C) SF-36 MCS, (D) PASI 75, (E) PASI 90 and (F) PASI 100. HAQ-DI, Health Assessment Questionnaire Disability Index; PASI 75/90/100, the proportion of participants achieving 75%/90%/100% improvement from baseline in Psoriasis Area Severity Index; SF-36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

QoL of patients from different races and backgrounds. Third, the follow-up period for all included studies did not exceed 24 weeks, so the long-term effects were unable to be assessed. Thus, more studies that 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 patients with PsA.

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.

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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. ZD 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, the guarantor of the manuscript, 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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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 applicable.

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Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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REFERENCES

1 Singh JA, Guyatt G, Ogdie A, *et al*. Special article: 2018 American College of Rheumatology/National psoriasis Foundation guideline for the treatment of psoriatic arthritis. *Arthritis Rheumatol* 2019;71:5–32.
2 Mease PJ, Gladman DD, Papp KA, *et al*. Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. *J Am Acad Dermatol* 2013;69:729–35.
3 Kavanaugh A, Helliwell P, Ritchlin CT. Psoriatic arthritis and burden of disease: patient perspectives from the population-based multinational assessment of psoriasis and psoriatic arthritis (MAPP) survey. *Rheumatol Ther* 2016;3:91–102.
4 Scotti L, Franchi M, Marchesoni A, *et al*. Prevalence and incidence of psoriatic arthritis: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2018;48:28–34.
5 Giannelli A. A review for physician assistants and nurse practitioners on the considerations for diagnosing and treating psoriatic arthritis. *Rheumatol Ther* 2019;6:5–21.
6 Rosen CF, Mussani F, Chandran V, *et al*. Patients with psoriatic arthritis have worse quality of life than those with psoriasis alone. *Rheumatology* 2012;51:571–6.
7 Salaffi F, Carotti M, Gasparini S, *et al*. The health-related quality of life in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a comparison with a selected sample of healthy people. *Health Qual Life Outcomes* 2009;7:25.
8 Mease PJ. Assessing the impact of psoriatic arthritis on patient function and quality of life: lessons learned from other rheumatologic conditions. *Semin Arthritis Rheum* 2009;38:320–35.
9 McKenna SP, Doward LC, Whalley D, *et al*. Development of the PsAQoL: a quality of life instrument specific to psoriatic arthritis. *Ann Rheum Dis* 2004;63:162–9.
10 Xia P, Lu C, Wang Y. Introduction of quality of life scale for psoriatic arthritis and its international application. *Chinese Journal of Rheumatology* 2015;19:701–4. (Chinese).
11 Busija L, Pausenberger E, Haines TP, *et al*. Adult measures of general health and health-related quality of life: medical outcomes study short form 36-item (SF-36) and short form 12-Item (SF-12) health surveys, Nottingham health profile (NHP), sickness impact profile (SIP), medical outcomes study short form 6D (SF-6D), health Utilities index mark 3 (HUI3), quality of well-being scale (QWB), and assessment of quality of life (AQoL). *Arthritis Care Res* 2011;63 Suppl 11:S383–412.
12 Bruce B, Fries JF. The Stanford health assessment questionnaire: dimensions and practical applications. *Health Qual Life Outcomes* 2003;1:20.
13 Balestroni G, Bertolotti G. [EuroQol-5D (EQ-5D): an instrument for measuring quality of life]. *Monaldi Arch Chest Dis* 2012;78:155–9.
14 Mease PJ. Measures of psoriatic arthritis: tender and swollen joint assessment, psoriasis area and severity index (PASI), nail psoriasis severity index (NAPSI), modified nail psoriasis severity index (mNAPSI), Mander/Newcastle Enthesitis index (Mei), Leeds Enthesitis index (LEI), spondyloarthritis research Consortium of Canada (SPARCC), Maastricht ankylosing spondylitis Enthesis score (MASES), Leeds Dactylitis index (LDI), patient global for psoriatic arthritis, dermatology life quality index (DLQI), psoriatic arthritis quality of life (PsAQOL), functional assessment of chronic illness Therapy-Fatigue (FACIT-F), psoriatic arthritis response criteria (PsARC), psoriatic arthritis joint activity index (PsAJAI), disease activity in psoriatic arthritis (DAPSA), and composite psoriatic disease activity index (CPDAI). *Arthritis Care Res* 2011;63 Suppl 11:S64–85.
15 Lewis VJ, Finlay AY. Two decades experience of the psoriasis disability index. *Dermatology* 2005;210:261–8.
16 Prinsen CAC, Lindeboom R, Sprangers MAG, *et al*. Health-Related quality of life assessment in dermatology: interpretation of Skindex-29 scores using patient-based anchors. *J Invest Dermatol* 2010;130:1318–22.
17 Simons N, Degboé Y, Barnetche T, *et al*. Biological DMARD efficacy in psoriatic arthritis: a systematic literature review and meta-analysis on articular, enthesitis, dactylitis, skin and functional outcomes. *Clin Exp Rheumatol* 2020;38:508–15.
18 Cawson MR, Mitchell SA, Knight C, *et al*. Systematic review, network meta-analysis and economic evaluation of biological therapy for the management of active psoriatic arthritis. *BMC Musculoskelet Disord* 2014;15:26.
19 Gossec L, Baraliakos X, Kerschbaumer A, *et al*. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann Rheum Dis* 2020;79:700–12.
20 Kamata M, Tada Y. Efficacy and safety of biologics for psoriasis and psoriatic arthritis and their impact on comorbidities: a literature review. *Int J Mol Sci* 2020;21:1690.
21 Ruyssen-Witrand A, Perry R, Watkins C, *et al*. Efficacy and safety of biologics in psoriatic arthritis: a systematic literature review and network meta-analysis. *RMD Open* 2020;6:e001117.
22 Lu C, Wallace BI, Waljee AK, *et al*. Comparative efficacy and safety of targeted DMARDs for active psoriatic arthritis during induction therapy: a systematic review and network meta-analysis. *Semin Arthritis Rheum* 2019;49:381–8.
23 Lemos LLP, de Oliveira Costa J, Almeida AM, *et al*. Treatment of psoriatic arthritis with anti-TNF agents: a systematic review and meta-analysis of efficacy, effectiveness and safety. *Rheumatol Int* 2014;34:1345–60.
24 Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
25 Higgins JPT, Thomas J, Chandler J. Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). *Cochrane*, 2021. Available: www.training.cochrane.org/handbook
26 Genovese MC, Mease PJ, Thomson GTD, *et al*. Safety and efficacy of adalimumab in treatment of patients with psoriatic arthritis who had failed disease modifying antirheumatic drug therapy. *J Rheumatol* 2007;34:1040–50.
27 Tao H, Zheng J, Ye Q. Effect of infliximab combined with methotrexate on serum alkaline phosphatase levels in patients with psoriatic arthritis and its curative effect. *Chinese Journal of Immunology* 2019;35:98–101. (Chinese).
28 Antoni CE, Kavanaugh A, Kirkham B, *et al*. Sustained benefits of infliximab therapy for dermatologic and articular manifestations of psoriatic arthritis: results from the infliximab multinational psoriatic arthritis controlled trial (impact). *Arthritis Rheum* 2005;52:1227–36.
29 Mease PJ, Goffe BS, Metz J, *et al*. Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial. *Lancet* 2000;356:385–90.
30 Kavanaugh A, Krueger GG, Beutler A, *et al*. Infliximab maintains a high degree of clinical response in patients with active psoriatic arthritis through 1 year of treatment: results from the impact 2 trial. *Ann Rheum Dis* 2007;66:498–505.

31 Kavanaugh A, Antoni C, Krueger GG, *et al*. Infliximab improves health related quality of life and physical function in patients with psoriatic arthritis. *Ann Rheum Dis* 2006;65:471–7.
32 Antoni C, Krueger GG, de Vlam K, *et al*. Infliximab improves signs and symptoms of psoriatic arthritis: results of the impact 2 trial. *Ann Rheum Dis* 2005;64:1150–7.
33 Mease PJ, Gladman DD, Ritchlin CT, *et al*. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2005;52:3279–89.
34 Gladman DD, Mease PJ, Cifaldi MA, *et al*. Adalimumab improves joint-related and skin-related functional impairment in patients with psoriatic arthritis: patient-reported outcomes of the adalimumab effectiveness in psoriatic arthritis trial. *Ann Rheum Dis* 2007;66:163–8.
35 Gladman DD, Mease PJ, Ritchlin CT, *et al*. Adalimumab for long-term treatment of psoriatic arthritis: forty-eight week data from the adalimumab effectiveness in psoriatic arthritis trial. *Arthritis Rheum* 2007;56:476–88.
36 Kavanaugh A, McInnes I, Mease P, *et al*. Golimumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four-week efficacy and safety results of a randomized, placebo-controlled study. *Arthritis Rheum* 2009;60:976–86.
37 Kavanaugh A, McInnes IB, Krueger GG, *et al*. Patient-Reported outcomes and the association with clinical response in patients with active psoriatic arthritis treated with golimumab: findings through 2 years of a phase III, multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Care Res* 2013;65:1666–73.
38 Mease PJ, Kivitz AJ, Burch FX, *et al*. Etanercept treatment of psoriatic arthritis: safety, efficacy, and effect on disease progression. *Arthritis Rheum* 2004;50:2264–72.
39 Baranauskaite A, Raffayová H, Kungurov NV, *et al*. Infliximab plus methotrexate is superior to methotrexate alone in the treatment of psoriatic arthritis in methotrexate-naive patients: the respond study. *Ann Rheum Dis* 2012;71:541–8.
40 McInnes IB, Sieper J, Braun J, *et al*. Efficacy and safety of secukinumab, a fully human anti-interleukin-17A monoclonal antibody, in patients with moderate-to-severe psoriatic arthritis: a 24-week, randomised, double-blind, placebo-controlled, phase II proof-of-concept trial. *Ann Rheum Dis* 2014;73:349–56.
41 McInnes IB, Kavanaugh A, Gottlieb AB, *et al*. Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial. *Lancet* 2013;382:780–9.
42 Ritchlin C, Rahman P, Kavanaugh A, *et al*. Efficacy and safety of the anti-IL-12/23 p40 monoclonal antibody, ustekinumab, in patients with active psoriatic arthritis despite conventional non-biological and biological anti-tumour necrosis factor therapy: 6-month and 1-year results of the phase 3, multicentre, double-blind, placebo-controlled, randomised PSUMMIT 2 trial. *Ann Rheum Dis* 2014;73:990–9.
43 Gladman D, Fleischmann R, Coteur G, *et al*. Effect of certolizumab pegol on multiple facets of psoriatic arthritis as reported by patients: 24-week patient-reported outcome results of a phase III, multicenter study. *Arthritis Care Res* 2014;66:1085–92.
44 Mease PJ, Fleischmann R, Deodhar AA, *et al*. Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a phase 3 double-blind randomised placebo-controlled study (RAPID-PsA). *Ann Rheum Dis* 2014;73:48–55.
45 Mease PJ, McInnes IB, Kirkham B, *et al*. Secukinumab inhibition of interleukin-17A in patients with psoriatic arthritis. *N Engl J Med* 2015;373:1329–39.
46 Strand V, Mease P, Gossec L, *et al*. Secukinumab improves patient-reported outcomes in subjects with active psoriatic arthritis: results from a randomised phase III trial (future 1). *Ann Rheum Dis* 2017;76:203–7.
47 Mease PJ, van der Heijde D, Ritchlin CT, *et al*. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. *Ann Rheum Dis* 2017;76:79–87.
48 Gottlieb AB, Strand V, Kishimoto M, *et al*. Ixekizumab improves patient-reported outcomes up to 52 weeks in bDMARD-naïve patients with active psoriatic arthritis (SPIRIT-P1). *Rheumatology* 2018;57:1777–88.
49 McInnes IB, Mease PJ, Kirkham B, *et al*. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (future 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2015;386:1137–46.
50 Mease P, Hall S, FitzGerald O, *et al*. Tofacitinib or adalimumab versus placebo for psoriatic arthritis. *N Engl J Med* 2017;377:1537–50.
51 Strand V, de Vlam K, Covarrubias-Cobos JA, *et al*. Tofacitinib or adalimumab versus placebo: patient-reported outcomes from opal Broaden-a phase III study of active psoriatic arthritis in patients with an inadequate response to conventional synthetic disease-modifying antirheumatic drugs. *RMD Open* 2019;5:e000806.
52 Nash P, Mease PJ, McInnes IB, *et al*. Efficacy and safety of secukinumab administration by autoinjector in patients with psoriatic arthritis: results from a randomized, placebo-controlled trial (future 3). *Arthritis Res Ther* 2018;20:47.
53 Mease PJ, Helliwell PS, Hjuler KF, *et al*. Brodalumab in psoriatic arthritis: results from the randomised phase III AMVISION-1 and AMVISION-2 trials. *Ann Rheum Dis* 2021;80:185–93.
54 Vieira-Sousa E, Alves P, Rodrigues AM, *et al*. GO-DACT: a phase 3B randomised, double-blind, placebo-controlled trial of golimumab plus methotrexate (MTX) versus placebo plus MTX in improving DACTylitis in MTX-naive patients with psoriatic arthritis. *Ann Rheum Dis* 2020;79:490–8.
55 Kavanaugh A, Husni ME, Harrison DD, *et al*. Safety and efficacy of intravenous golimumab in patients with active psoriatic arthritis: results through week twenty-four of the GO-VIBRANT study. *Arthritis Rheumatol* 2017;69:2151–61.
56 Husni ME, Kavanaugh A, Chan EKH, *et al*. Effects of intravenous golimumab on health-related quality of life in patients with psoriatic arthritis: 24-week results of the GO-VIBRANT trial. *Value Health* 2020;23:1286–91.
57 Kivitz AJ, Nash P, Tahir H, *et al*. Efficacy and Safety of Subcutaneous Secukinumab 150 mg with or Without Loading Regimen in Psoriatic Arthritis: Results from the FUTURE 4 Study. *Rheumatol Ther* 2019;6:393–407.
58 Deodhar A, Gottlieb AB, Boehncke W-H, *et al*. Efficacy and safety of guselkumab in patients with active psoriatic arthritis: a randomised, double-blind, placebo-controlled, phase 2 study. *Lancet* 2018;391:2213–24.
59 Nash P, Kirkham B, Okada M, *et al*. Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. *Lancet* 2017;389:2317–27.
60 Mease PJ, Genovese MC, Weinblatt ME, *et al*. Phase II study of ABT-122, a tumor necrosis factor- and Interleukin-17A-Targeted dual variable domain immunoglobulin, in patients with psoriatic arthritis with an inadequate response to methotrexate. *Arthritis Rheumatol* 2018;70:1778–89.
61 Mease PJ, Gladman DD, Collier DH, *et al*. Etanercept and methotrexate as monotherapy or in combination for psoriatic arthritis: primary results from a randomized, controlled phase III trial. *Arthritis Rheumatol* 2019;71:1112–24.
62 Coates LC, Merola JF, Mease PJ, *et al*. Performance of composite measures used in a trial of etanercept and methotrexate as monotherapy or in combination in psoriatic arthritis. *Rheumatology* 2021;60:1137–47.
63 Mease P, van der Heijde D, Landewé R, *et al*. Secukinumab improves active psoriatic arthritis symptoms and inhibits radiographic progression: primary results from the randomised, double-blind, phase III future 5 study. *Ann Rheum Dis* 2018;77:890–7.
64 Baraliakos X, Gossec L, Pournara E, *et al*. Secukinumab in patients with psoriatic arthritis and axial manifestations: results from the double-blind, randomised, phase 3 maximise trial. *Ann Rheum Dis* 2021;80:582–90.
65 Mease PJ, Chohan S, Fructuoso FJG, *et al*. Efficacy and safety of tildrakizumab in patients with active psoriatic arthritis: results of a randomised, double-blind, placebo-controlled, multiple-dose, 52-week phase IIb study. *Ann Rheum Dis* 2021;80:1147–57.
66 Strand V, Mease PJ, Soriano ER, *et al*. Improvement in patient-reported outcomes in patients with psoriatic arthritis treated with Upadacitinib versus placebo or adalimumab: results from SELECT-PsA 1. *Rheumatol Ther* 2021;8:1789–808.
67 Mease PJ, Rahman P, Gottlieb AB, *et al*. Guselkumab in biologic-naive patients with active psoriatic arthritis (DISCOVER-2): a double-blind, randomised, placebo-controlled phase 3 trial. *Lancet* 2020;395:1126–36.
68 Deodhar A, Helliwell PS, Boehncke W-H, *et al*. Guselkumab in patients with active psoriatic arthritis who were biologic-naive or had previously received TNFα inhibitor treatment (DISCOVER-1): a double-blind, randomised, placebo-controlled phase 3 trial. *Lancet* 2020;395:1115–25.
69 Östör A, Van den Bosch F, Papp K, *et al*. Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the

randomised, double-blind, phase 3 KEEPsAKE 2 trial. *Ann Rheum Dis* 2022;81:351–8.
70 Kristensen LE, Keiserman M, Papp K, *et al*. Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised, double-blind, phase 3 KEEPsAKE 1 trial. *Ann Rheum Dis* 2022;81:225–31.
71 Coates LC, Gossec L, Theander E, *et al*. Efficacy and safety of guselkumab in patients with active psoriatic arthritis who are inadequate responders to tumour necrosis factor inhibitors: results through one year of a phase IIIB, randomised, controlled study (Cosmos). *Ann Rheum Dis* 2022;81:359–69.
72 Lin Y. Clinical efficacy of infliximab combined with methotrexate in the treatment of psoriatic arthritis. *Heilongjiang Medicine and Pharmacy* 2016;39:113–4. (Chinese).
73 Mease PJ, Woolley JM, Bitman B, *et al*. Minimally important difference of health assessment questionnaire in psoriatic arthritis: relating thresholds of improvement in functional ability to patient-rated importance and satisfaction. *J Rheumatol* 2011;38:2461–5.
74 Kwok T, Pope JE. Minimally important difference for patient-reported outcomes in psoriatic arthritis: health assessment questionnaire and pain, fatigue, and global visual analog scales. *J Rheumatol* 2010;37:1024–8.
75 Carreon LY, Glassman SD, Campbell MJ, *et al*. Neck disability index, short form-36 physical component summary, and pain scales for neck and arm pain: the minimum clinically important difference and substantial clinical benefit after cervical spine fusion. *Spine J* 2010;10:469–74.
76 Sekhon S, Pope J, *et al*, Canadian Scleroderma Research Group. The minimally important difference in clinical practice for patient-centered outcomes including health assessment questionnaire, fatigue, pain, sleep, global visual analog scale, and SF-36 in scleroderma. *J Rheumatol* 2010;37:591–8.
77 Witt S, Krauss E, Barbero MAN, *et al*. Psychometric properties and minimal important differences of SF-36 in idiopathic pulmonary fibrosis. *Respir Res* 2019;20:47.
78 Colangelo KJ, Pope JE, Peschken C. The minimally important difference for patient reported outcomes in systemic lupus erythematosus including the HAQ-DI, pain, fatigue, and SF-36. *J Rheumatol* 2009;36:2231–7.
79 Basra MKA, Salek MS, Camilleri L, *et al*. Determining the minimal clinically important difference and responsiveness of the dermatology life quality index (DLQI): further data. *Dermatology* 2015;230:27–33.
80 Hu X, Jing M, Zhang M, *et al*. Responsiveness and minimal clinically important difference of the EQ-5D-5L in cervical intraepithelial neoplasia: a longitudinal study. *Health Qual Life Outcomes* 2020;18:324.
81 Chen P, Lin K-C, Liing R-J, *et al*. Validity, responsiveness, and minimal clinically important difference of EQ-5D-5L in stroke patients undergoing rehabilitation. *Qual Life Res* 2016;25:1585–96.
82 Zanini A, Aiello M, Adamo D, *et al*. Estimation of minimal clinically important difference in EQ-5D visual analog scale score after pulmonary rehabilitation in subjects with COPD. *Respir Care* 2015;60:88–95.
83 Nolan CM, Longworth L, Lord J, *et al*. The EQ-5D-5L health status questionnaire in COPD: validity, responsiveness and minimum important difference. *Thorax* 2016;71:493–500.