

# BMJ Open 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.

## 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.<sup>1–3</sup> Scotti *et al* analysed the results of 28 studies and found that

## 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.

the prevalence and incidence rates of PsA are respectively 133 per 100 000 subjects and 83 per 100 000 person-years.<sup>4</sup> PsA develops in up to 30% of patients with psoriasis.<sup>5</sup> Rosen *et al* reported that the QoL of patients with PsA is significantly lower than that of patients with psoriasis.<sup>6</sup> 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).<sup>7–10</sup> Among these questionnaires, the higher scores of SF-36 and EQ-5D indicate higher levels of QoL, while others are the opposite.<sup>11–16</sup>

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.<sup>17 18</sup> The bDMARDs are widely recommended by management guidelines,<sup>1 19</sup> 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).<sup>1 20</sup> Ruysse-Witrand *et al*,<sup>21</sup> Lu *et al*<sup>22</sup> and Lemos *et al*<sup>23</sup> 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.<sup>24</sup> 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 Database, 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

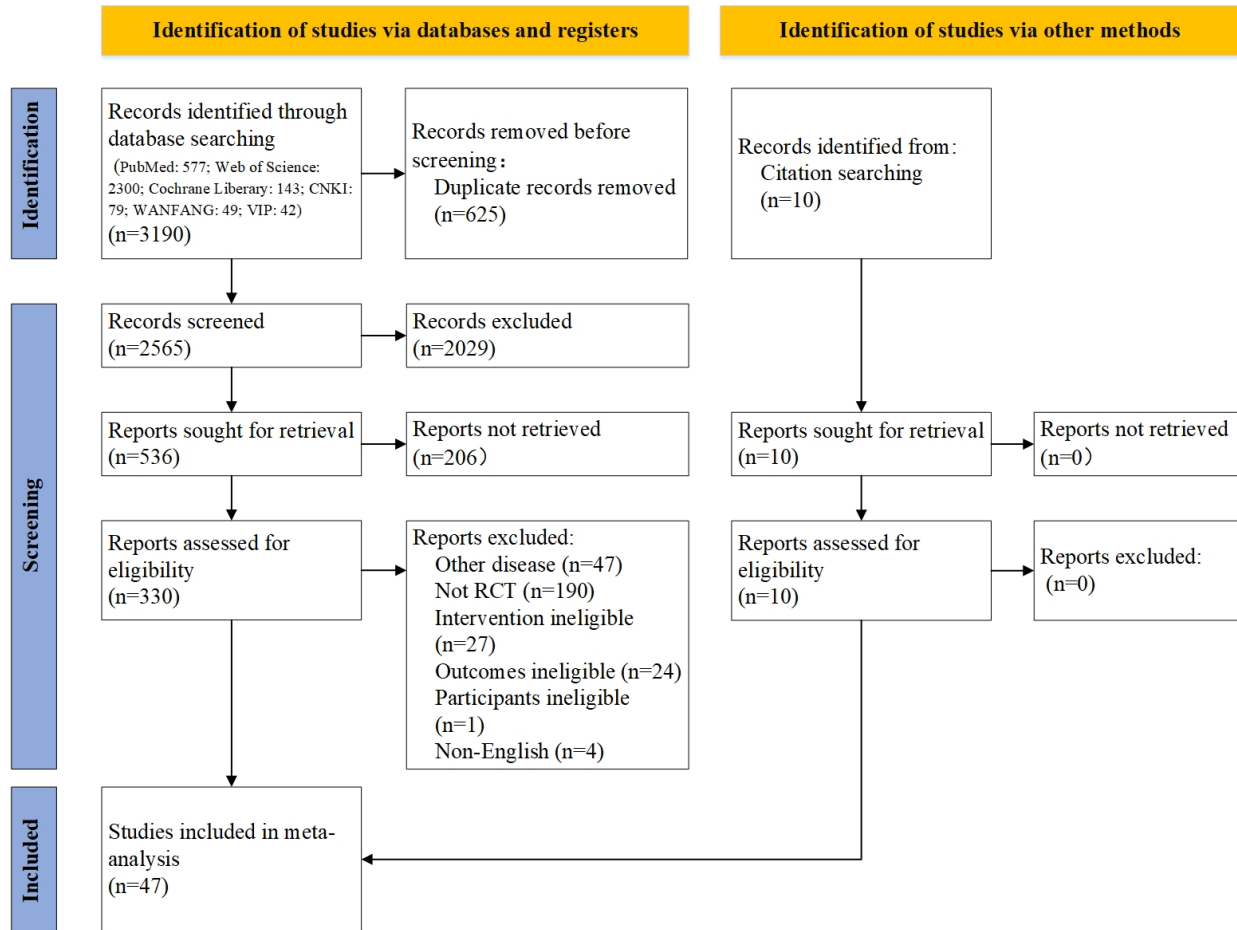
Studies were independently selected by two authors (YqL and ZD), and they achieved good agreement ( $\kappa=0.942$ ). Studies were included if they met the following inclusion criteria: (1) the trial was a human study conducted on patients with PsA; (2) the experimental group was treated with bDMARDs 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 ( $\kappa=0.959$ ). 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 ( $\kappa=0.853$ ).<sup>25</sup> 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  $\chi^2$ -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<sup>26–72</sup> (37 RCTs

reported) were ultimately included in the meta-analysis. There was a total of 14 115 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



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Genovese MC 2007	+	+	+	+	+	+	?
Hong Tao 2019	+	?	?	?	+	+	?
IMPACT	?	?	+	?	+	+	?
Mease PJ 2000	?	?	+	+	+	+	?
NCT00051623 (IMPACT 2)	?	?	+	+	+	+	?
NCT00195689 (ADEPT)	?	?	+	+	+	+	?
NCT00265096 (GO-REVEAL)	+	+	+	+	+	+	?
NCT00317499	?	?	+	+	+	+	?
NCT00367237 (RESPOND)	?	?	?	?	+	+	?
NCT00809614	+	+	+	+	+	?	?
NCT01009086 (PSUMMIT 1)	+	+	+	+	+	+	?
NCT01077362 (PSUMMIT 2)	+	+	+	+	+	+	?
NCT01087788 (RAPID-PsA)	+	+	+	+	+	+	?
NCT01392326 (FUTURE 1)	+	+	+	+	+	+	?
NCT01695239 (SPIRIT-P1)	+	+	+	+	+	+	?
NCT01752634 (FUTURE 2)	+	+	+	+	+	+	?
NCT01877668 (OPAL Broaden)	+	+	+	+	+	+	?
NCT01989468 (FUTURE 3)	+	+	+	+	+	+	?
NCT02024646 (AMVISION-2)	?	?	+	+	+	?	?
NCT02029495 (AMVISION-1)	?	?	+	+	+	?	?
NCT02065713 (GO-DACT)	+	?	+	+	+	+	?
NCT02181673 (GO-VIBRANT)	+	+	+	+	+	+	?
NCT02294227 (FUTURE 4)	+	+	+	+	+	+	?
NCT02319759	+	+	+	+	+	+	?
NCT02349295 (SPIRIT-P2)	+	?	+	?	+	+	?
NCT02349451	+	+	+	+	+	+	?
NCT02376790 (SEAM-PsA)	+	+	+	+	+	+	?
NCT02404350 (FUTURE 5)	+	+	+	+	?	?	?
NCT02721966 (MAXIMISE)	+	+	+	+	+	+	?
NCT02980692	+	+	+	+	+	+	?
NCT03104400 (SELECT-PsA 1)	+	+	+	+	+	?	?
NCT03158285 (DISCOVER-2)	+	+	+	+	+	+	?
NCT03162796 (DISCOVER-1)	+	+	+	+	+	+	?
NCT03671148 (KEEPsAKE 2)	?	?	+	+	+	+	?
NCT03675308 (KEEPsAKE 1)	?	?	+	+	+	+	?
NCT03796858 (COSMOS)	?	?	+	+	+	?	?
Yufei Lin 2016	+	?	?	?	+	+	?

**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<sup>2</sup>: 100%), DLQI (MD=-4.36; 95% CI, -5.76 to -2.96; p<0.00001; I<sup>2</sup>: 99%) and improve SF-36 PCS (MD=3.76; 95% CI, 3.42 to 4.10; p<0.00001; I<sup>2</sup>: 99%), SF-36 MCS (MD=1.76; 95% CI, 1.27 to 2.25; p<0.00001; I<sup>2</sup>: 99%), EQ-VAS (MD=5.27; 95% CI, 1.21 to 9.34; p<0.00001; I<sup>2</sup>: 99%), PASI 50 (RR=4.09; 95% CI, 2.71 to 6.16; p<0.00001; I<sup>2</sup>: 82%), PASI 75 (RR=4.72; 95% CI, 3.87 to 5.75; p<0.00001; I<sup>2</sup>: 81%), PASI 90 (RR=5.73; 95% CI, 4.73 to 6.95; p<0.00001; I<sup>2</sup>: 59%), PASI 100 (RR=9.57; 95% CI, 7.38 to 12.43; p<0.00001; I<sup>2</sup>: 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*<sup>27</sup>, 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 <sup>2</sup> (%)	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).<sup>73 74</sup> Similar results were found for SF-36 PCS (MD=3.76; 95% CI, 3.42 to 4.10; >2.1),<sup>75-78</sup> SF-36 MCS (MD=1.76; 95% CI, 1.27 to 2.25; >1.33),<sup>76-78</sup> and DLQI (MD=-4.36; 95% CI, -5.76 to -2.96; <-2.24),<sup>79</sup> but not for EQ-VAS (MD=5.27; 95% CI, 1.21 to 9.34, <5.35).<sup>80-83</sup>

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),<sup>61 62</sup> etanercept or plus MTX could decrease DAPSA and improve SF-36 Score compared with MTX, but without statistical significance. The result of NCT02980692<sup>65</sup> showed that tildrakizumab could decrease DAPSA compared with placebo without statistical significance. The results of NCT01087788 (RAPID-PsA)<sup>43 44</sup> and NCT01392326 (FUTURE 1)<sup>45 46</sup> showed that certolizumab pegol and secukinumab could significantly decrease PsAQoL compared with placebo. As for PASI 70, Tao *et al*<sup>27</sup> found that infliximab+MTX got more significant improvement than MTX, while NCT02065713 (GO-DACT)<sup>54</sup> found that golimumab+MTX had no difference from MTX. Additionally, Tao *et al*<sup>27</sup> 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 <i>et al</i> <sup>29</sup>
				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 <i>et al</i> <sup>27</sup>
				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.

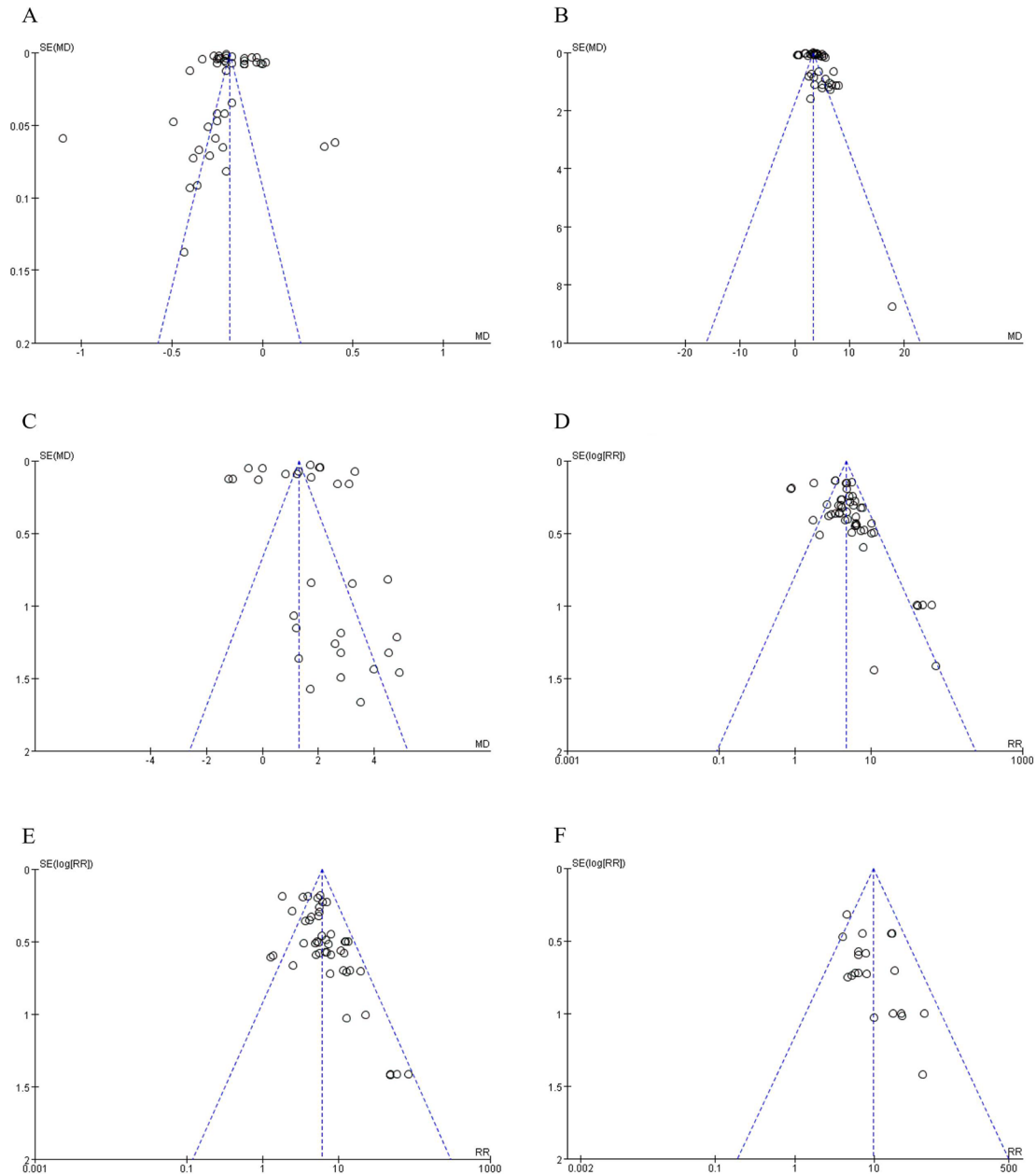
significantly lower than that in the MTX group. Taken together, the quantitative analysis results of the effects of bDMARDs on the QoL of patients with PsA are robust.

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.<sup>21–23</sup> However, our meta-analysis showed an improvement in terms of SF-36 MCS, which was inconsistent with the results reported by Lemos *et al*.<sup>23</sup> 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.<sup>23</sup> The articles included in that study concerned not only RCTs but also observational studies.<sup>23</sup> 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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