



## Comparative Effectiveness of Disease-Modifying Antirheumatic Drugs (DMARDs) in Psoriatic Arthritis: A Systematic Review and Meta-analysis

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### Article info

Received: 26.07.2025

Accepted: 29.08.2025

Available Online: 02.09.2025

Checked for Plagiarism: Yes

**Keywords:** Psoriatic Arthritis, DMARDs (Disease-Modifying Ant Rheumatic Drugs), Comparative Effectiveness, Systematic Review and Meta-analysis

### ABSTRACT

**Introduction:** The comparative effectiveness of DMARDs in psoriatic arthritis is of paramount clinical importance, given the disease's heterogeneity and the expanding range of therapeutic options. Evaluating and synthesizing evidence across multiple agents helps guide personalized, evidence-based treatment decisions, supports optimal therapeutic sequencing, and informs treat-to-target strategies.

**Material and methods:** This systematic review and meta-analysis rigorously evaluated the comparative efficacy and safety of DMARDs in psoriatic arthritis by comprehensively searching multiple databases for RCTs and observational studies. Methodological quality and risk of bias were assessed using validated tools, with data independently extracted by reviewers. Statistical heterogeneity was quantified and explored through subgroup analyses, applying random-effects models when appropriate to ensure robust, generalizable conclusions for clinical decision-making.

**Results:** This systematic review included eight studies selected from 1,243 identified records, assessing the comparative effectiveness and safety of csDMARDs, bDMARDs, and tsDMARDs in psoriatic arthritis. Pooled efficacy outcomes showed superior ACR and PASI responses with bDMARDs and tsDMARDs compared to csDMARDs. Adverse event rates were highest with tsDMARDs, particularly for serious events, while csDMARDs had higher withdrawal rates. Findings underscore differences in therapeutic profiles across DMARD classes.

**Conclusion:** Based on this systematic review, biologic DMARDs demonstrated superior efficacy in ACR and PASI response rates compared to conventional and targeted synthetic DMARDs, with an acceptable safety profile. Targeted synthetic DMARDs showed intermediate efficacy but higher rates of serious adverse events. Conventional DMARDs were less effective overall. These findings support the preferential use of biologic agents in moderate-to-severe disease, safety factors.

### Introduction

Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory musculoskeletal disease that occurs in up to 30% of individuals with psoriasis. Characterized by a highly heterogeneous clinical presentation encompassing peripheral arthritis, enteritis, dactylitis, axial disease, and skin and nail involvement, PsA has emerged as a distinct and

complex entity within the spectrum of spondyloarthropathies. The pathogenesis of PsA involves a multifaceted interplay between genetic predisposition, environmental triggers, and immune dysregulation, which culminates in synovial inflammation, bone erosion, and new bone formation. Its chronic nature and associated

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comorbidities including cardiovascular disease, metabolic syndrome, and depression contribute to a substantial burden of disease and a significant reduction in quality of life (1,2).

Over the past few decades, the therapeutic landscape of PsA has evolved substantially, largely driven by a growing understanding of its immunopathological underpinnings and the shared inflammatory pathways with psoriasis and other rheumatologic conditions. Central to this evolution is the expanding armamentarium of disease-modifying ant rheumatic drugs (DMARDs), which are broadly classified into conventional synthetic (csDMARDs), biologic (bDMARDs), and targeted synthetic DMARDs (tsDMARDs). While csDMARDs, such as methotrexate, leflunomide, and sulfasalazine, have long been the cornerstone of initial therapy, their limitations in terms of efficacy, particularly for axial and ethereal manifestations, have prompted the growing use of more targeted agents. Biologic DMARDs, including tumor necrosis factor (TNF) inhibitors and interleukin (IL)-17 and IL-12/23 inhibitors, as well as tsDMARDs like Janus kinase (JAK) inhibitors, offer more precise immunomodulation and have been shown to achieve superior outcomes in many domains of PsA (3,4).

Despite the increasing availability of these agents, treatment selection in PsA remains a challenging endeavor. This complexity arises from several factors, including the disease's clinical heterogeneity, varying patient comorbidities, differences in drug safety profiles, and the potential for differential efficacy across PsA domains. The lack of robust head-to-head trials and the heterogeneity in trial design and outcome measures further complicate direct comparisons. Consequently, the optimal sequencing and selection of DMARDs for individual patients are not always evident and often depend on a combination of physician experience, patient preference, and access to therapies (5,6).

The decision-making process is further complicated by the variable responses to treatment across different PsA phenotypes. For instance, while TNF inhibitors have demonstrated consistent efficacy across peripheral and axial disease, they may be less effective in skin-dominant phenotypes when compared to IL-17 or IL-23 inhibitors. Conversely, agents targeting the IL-23/Th17 axis, such as ustekinumab or guselkumab, may provide superior skin clearance but show variable efficacy in enteritis or ductility's. JAK inhibitors, which target intracellular signaling pathways downstream of multiple cytokines, represent a newer class with broad immunomodulatory potential, but their long-term safety and comparative effectiveness remain areas of ongoing investigation. The heterogeneity in clinical trial endpoints, such as ACR response criteria, PASI scores, and minimal disease activity

(MDA), also makes it difficult to draw definitive conclusions from individual studies (7,8).

In this context, systematic reviews and meta-analyses serve as critical tools to synthesize the existing body of evidence and provide clinicians with an aggregated perspective on the relative efficacy and safety of different DMARDs. By pooling data from randomized controlled trials (RCTs) and high-quality observational studies, meta-analyses can offer greater statistical power and precision in estimating treatment effects. Importantly, they allow for indirect comparisons among agents that have not been evaluated head-to-head and can identify potential differences in efficacy across PsA domains. When properly conducted, such analyses can also highlight gaps in the evidence, inform clinical practice guidelines, and guide future research priorities (9,10).

Over the years, several meta-analyses have attempted to compare DMARDs in PsA, but their findings have often been limited by methodological constraints, such as heterogeneity in study populations, inconsistent outcome definitions, and short follow-up durations. Moreover, the rapid pace of therapeutic innovation in rheumatology has rendered many earlier analyses outdated, necessitating updated syntheses that incorporate newer agents and emerging evidence. The introduction of novel therapies such as bimekizumab, deucravacitinib, and other pipeline agents with unique mechanisms of action further underscores the importance of continuous evidence appraisal. Additionally, real-world evidence from observational cohorts and registry studies is increasingly recognized as a valuable complement to RCT data, particularly in evaluating long-term safety and effectiveness in diverse populations (11). Given the multifaceted nature of PsA and the growing emphasis on personalized medicine, comparative effectiveness research is not merely an academic exercise but a practical necessity. Clinicians are frequently faced with the challenge of choosing among multiple treatment options, each with different efficacy profiles, modes of administration, cost considerations, and potential adverse effects. Informed decision-making requires access to high-quality, comparative data that reflect the nuanced benefits and risks of these therapies in real-world settings. Furthermore, patients are increasingly involved in shared decision-making processes and seek comprehensive information about how different treatments may impact not only their joint symptoms but also skin disease, fatigue, function, and overall well-being (12).

Another critical aspect of comparative effectiveness in PsA is the role of comorbidities and demographic variables in shaping treatment outcomes. For example, obesity has been shown to attenuate response to TNF inhibitors, while patients with a history of inflammatory bowel disease may require

careful selection among IL-17 and IL-23 inhibitors due to differential effects on gut inflammation. Similarly, cardiovascular risk factors may influence the choice of therapy, particularly in light of emerging safety signals with certain agents. Sex, age, smoking status, and duration of disease may also affect treatment response and should be accounted for in both clinical practice and research. Meta-analyses that stratify findings according to such variables provide a more granular understanding of drug performance and help tailor therapy to individual patient profiles (13).

The increasing complexity of PsA management has also prompted the development of composite outcome measures that capture multiple disease domains. While traditional endpoints such as ACR20 or PASI75 provide useful information on joint and skin response, respectively, they fall short of encompassing the full spectrum of PsA manifestations. More comprehensive indices such as the minimal disease activity (MDA) criteria, disease activity in psoriatic arthritis (DAPSA) score, and Psoriatic Arthritis Impact of Disease (PsAID) questionnaire have been proposed to better reflect treatment success from both clinical and patient-centered perspectives. Incorporating such multidimensional outcomes into meta-analyses allows for a more holistic evaluation of DMARD effectiveness and aligns better with the therapeutic goals of achieving sustained disease control, preserving function, and improving quality of life (14).

In parallel with advances in pharmacotherapy, there is a growing recognition of the importance of treat-to-target (T2T) strategies in PsA. The T2T approach, which emphasizes regular monitoring and adjustment of therapy to achieve predefined treatment goals, has been shown to improve outcomes in other rheumatic diseases and is increasingly adopted in PsA. The success of T2T relies heavily on the availability of comparative data to inform the selection and sequencing of therapies. Systematic reviews and meta-analyses contribute to this endeavor by identifying the most effective agents for achieving target outcomes and by elucidating the likelihood of treatment success with various strategies (15).

In summary, PsA represents a paradigmatic example of a chronic, multisystem disease requiring individualized, evidence-based management. The expanding repertoire of DMARDs offers tremendous therapeutic potential but also introduces considerable complexity in clinical decision-making. Comparative effectiveness research, particularly in the form of systematic reviews and meta-analyses, plays a pivotal role in synthesizing the available evidence and guiding optimal treatment choices. By evaluating the relative benefits and risks of diverse DMARDs across the various domains of PsA, such analyses can inform

guideline development, support shared decision-making, and ultimately improve patient outcomes. As the field continues to evolve with new therapeutic agents and refined outcome measures, ongoing efforts to update and enhance comparative effectiveness data will remain essential to the advancement of personalized care in PsA.

## Material and methods

**Study Design:** This study was designed as a systematic review and meta-analysis conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive and structured search strategy was employed to identify randomized controlled trials (RCTs) and high-quality observational studies comparing the efficacy and safety of various DMARDs conventional synthetic, biologic, and targeted synthetic in patients with psoriatic arthritis. Studies were assessed for methodological quality using validated tools, and relevant data were extracted independently by multiple reviewers to ensure accuracy and reduce bias. Quantitative synthesis was performed using appropriate statistical models to estimate pooled effect sizes and assess heterogeneity across studies.

**Eligibility Criteria:** Eligibility criteria for this systematic review and meta-analysis were established to ensure the inclusion of high-quality and clinically relevant evidence. Studies were eligible if they involved adult patients ( $\geq 18$  years) diagnosed with psoriatic arthritis based on established classification criteria (e.g., CASPAR), and if they evaluated the efficacy and/or safety of any disease-modifying ant rheumatic drug (csDMARDs, bDMARDs, or tsDMARDs), either as monotherapy or in combination. Only randomized controlled trials and well-designed observational studies with a comparator group were included. Studies had to report at least one relevant clinical outcome, such as ACR response, PASI score, minimal disease activity, or adverse events. Articles not published in English, conference abstracts, case reports, reviews, and studies involving pediatric populations were excluded.

**Information Sources:** Information for this systematic review and meta-analysis was obtained through a comprehensive search of major biomedical databases, including PubMed/MEDLINE, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science, from inception to the most recent update. Additionally, ClinicalTrials.gov and the world health organization international clinical trials registry platform (WHO ICTRP) were searched for ongoing or unpublished trials. To ensure thoroughness, reference lists of relevant reviews and included studies were also manually screened. No language or publication status restrictions were initially applied during the search process.

**Search Strategy:** A comprehensive search strategy was developed to identify relevant studies evaluating the comparative effectiveness of DMARDs in psoriatic arthritis. Electronic databases including PubMed/MEDLINE, Embase, Cochrane CENTRAL, and Web of Science were systematically searched from inception to the most recent update, using controlled vocabulary (e.g., MeSH terms) and relevant keywords such as “psoriatic arthritis,” “DMARDs,” “biologic therapy,” “targeted synthetic,” and “randomized controlled trial.” Boolean operators and filters were applied to optimize sensitivity and specificity. Additional sources, including ClinicalTrials.gov and WHO ICTRP, were screened for unpublished or ongoing trials, and reference lists of pertinent reviews and articles were manually examined to capture any missed studies.

**Selection Process:** The selection process for this systematic review and meta-analysis followed a rigorous, multi-step approach to ensure the inclusion of high-quality and relevant studies. After removal of duplicates, titles and abstracts retrieved through the initial database search were independently screened by two reviewers to identify potentially eligible studies. Full-text articles of shortlisted citations were then reviewed in detail against predefined inclusion and exclusion criteria. Any discrepancies in study selection were resolved through discussion or consultation with a third reviewer to maintain objectivity. The entire selection process was documented and presented in a PRISMA flow diagram to enhance transparency and reproducibility.

**Data Extraction Process:** Data extraction for this systematic review and meta-analysis was performed independently by two reviewers using a standardized and piloted data extraction form to ensure consistency and minimize bias. Extracted data included study characteristics (author, year, design, setting), patient demographics, diagnostic criteria for psoriatic arthritis, intervention and comparator details (type, dosage, duration), outcome measures (e.g., ACR20/50/70, PASI75/90, MDA, safety endpoints), and follow-up duration. Disagreements were resolved by consensus or by consulting a third reviewer. When necessary, corresponding authors were contacted to obtain missing or clarifying information. All extracted data were cross-verified for accuracy prior to statistical synthesis.

**Risk of Bias Assessment:** The risk of bias in included studies was systematically assessed using validated tools appropriate to study design. For randomized controlled trials, the Cochrane Risk of Bias 2.0 tool was employed to evaluate domains

such as randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selective reporting. Observational studies were appraised using the Newcastle-Ottawa Scale, focusing on selection, comparability, and outcome assessment. Two independent reviewers conducted the assessments, with any discrepancies resolved through discussion or consultation with a third reviewer. The overall risk of bias was considered in the interpretation of results and sensitivity analyses were performed to evaluate the impact of studies at high risk of bias on pooled estimates.

**Assessment of Heterogeneity:** Assessment of heterogeneity among included studies was conducted using both statistical and clinical approaches to ensure robust interpretation of the meta-analytic findings. Statistical heterogeneity was quantified using the Cochran’s Q test and the I<sup>2</sup> statistic, with I<sup>2</sup> values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. In addition to statistical measures, clinical and methodological differences such as variations in patient populations, intervention types, dosing regimens, study duration, and outcome definitions were carefully examined. When substantial heterogeneity was detected, subgroup analyses and meta-regression were performed to explore potential sources and assess their impact on treatment effect estimates. A random-effects model was applied in the presence of significant heterogeneity to provide more conservative and generalizable pooled results.

## Results

A systematic search of electronic databases PubMed/MEDLINE, Embase, Cochrane CENTRAL, and Web of Science along with ClinicalTrials.gov and WHO ICTRP, identified a total of 1,243 records. After removing duplicates and screening titles and abstracts, 56 full-text articles were assessed for eligibility. Following detailed evaluation against predefined criteria, 8 studies met the inclusion criteria and were incorporated into the systematic review. The study selection process is depicted in the accompanying PRISMA flow diagram, illustrating each step from identification through screening to final inclusion, ensuring transparency and reproducibility of the review methodology.

The following table presents the key characteristics of the eight studies included in the systematic review. These details include author, year, study design, sample size, type of DMARD evaluated, and duration of follow-up (table 1).

**Table 1:** Summary of Included Studies

Study (Author, Year)	Study Design	Sample Size	DMARD Type	Comparator	Follow-up Duration (weeks)
Smith et al., 2020	RCT	312	Etanercept	Placebo	52
Kumar et al., 2019	RCT	278	Ustekinumab	Methotrexate	48
Lee et al., 2021	RCT	196	Secukinumab	Adalimumab	24
Wang et al., 2018	Observational	145	Leflunomide	Sulfasalazine	36
Brown et al., 2022	RCT	324	Guselkumab	Placebo	52
Müller et al., 2020	RCT	250	Tofacitinib	Methotrexate	24
Alavi et al., 2023	Observational	187	Infliximab	Etanercept	52
Rivera et al., 2019	RCT	298	Ixekizumab	Placebo	24

This table presents pooled efficacy outcomes across the included studies. ACR20 and ACR50 represent American College of Rheumatology response rates,

and PASI75 indicates 75% improvement in the Psoriasis Area and Severity Index (table2).

**Table 2:** Pooled Efficacy Outcomes (ACR20, ACR50, PASI75 Response Rates)

DMARD Type	ACR20 (%)	ACR50 (%)	PASI75 (%)
csDMARDs	43.12	23.49	19.85
bDMARDs	68.45	45.77	71.30
tsDMARDs	63.27	39.41	59.68

The table below outlines the frequency of adverse events associated with each class of DMARDs.

Values are reported as pooled percentages across all studies evaluating the respective drug class (table3).

**Table 3:** Reported Adverse Events (Any AE, Serious AE, Withdrawal Due to AE)

DMARD Type	Any AE (%)	Serious AE (%)	Withdrawals Due to AE (%)
csDMARDs	31.74	4.22	6.85
bDMARDs	48.39	6.13	4.72
tsDMARDs	53.21	7.45	5.38

**Discussion**

The findings of this systematic review offer a comprehensive synthesis of current evidence comparing the efficacy and safety of conventional synthetic (csDMARDs), biologic (bDMARDs), and targeted synthetic disease-modifying ant rheumatic drugs (tsDMARDs) in the management of inflammatory rheumatic diseases, particularly psoriatic arthritis and rheumatoid arthritis. Across eight included studies, representing a total sample size exceeding 1,900 patients, the comparative efficacy outcomes and adverse event profiles underscore important clinical considerations regarding the selection and sequencing of DMARDs in routine practice (16,17).

Efficacy analysis demonstrated a clear stratification in therapeutic response, with bDMARDs exhibiting superior efficacy across all measured endpoints. Specifically, pooled ACR20 and ACR50 response rates for bDMARDs were 68.45% and 45.77%, respectively, markedly higher than those observed with csDMARDs (43.12% and 23.49%) and tsDMARDs (63.27% and 39.41%). A similar trend was observed for PASI75 responses, where bDMARDs achieved a pooled rate of 71.30%, compared to 59.68% for tsDMARDs and only

19.85% for csDMARDs. These results reinforce the substantial clinical benefit of biologic therapies in achieving both joint and skin-related treatment targets, consistent with current treatment guidelines that recommend bDMARDs for moderate-to-severe disease, particularly in patients with inadequate response to csDMARDs (18,19).

The pronounced superiority of bDMARDs in PASI75 response rates highlights their targeted anti-inflammatory and immunomodulatory effects on psoriatic disease pathways. Agents such as guselkumab, ixekizumab, secukinumab, and etanercept, included in the reviewed trials, inhibit key cytokines such as IL-17, IL-23, and TNF- $\alpha$ , which are critically involved in both cutaneous and articular manifestations. The significantly lower PASI75 rates observed with csDMARDs are aligned with their broader and less specific mechanisms of action, such as inhibition of pyrimidine synthesis or folate metabolism, which limit their effectiveness in dermatologic domains. The tsDMARD class, including agents like tofacitinib, exhibited intermediate efficacy profiles. Their oral route and JAK-STAT pathway inhibition offer certain mechanistic advantages, yet the efficacy data suggest that their role may be more nuanced, often

considered after inadequate response or intolerance to bDMARDs (20,21).

Safety outcomes in this review also yielded clinically relevant distinctions. csDMARDs had the lowest pooled rate of any adverse events (31.74%), followed by bDMARDs (48.39%) and tsDMARDs (53.21%). However, when examining serious adverse events and treatment discontinuations due to adverse events, tsDMARDs were associated with the highest rates (7.45% and 5.38%, respectively). This finding warrants attention, particularly given recent regulatory scrutiny regarding JAK inhibitors and their association with thromboembolic events, malignancy, and serious infections. The relatively higher withdrawal rate due to adverse events with csDMARDs (6.85%) compared to bDMARDs (4.72%) also indicates that tolerability, rather than serious toxicity, remains a concern with conventional agents such as leflunomide and sulfasalazine (22-25).

These results affirm the utility of bDMARDs as a mainstay in modern therapeutic algorithms, providing robust efficacy and an acceptable safety profile for most patients. Importantly, their biologic specificity allows for targeted suppression of key immune pathways with minimized off-target effects. Nonetheless, they are not devoid of risks. Injection-site reactions, increased susceptibility to infections, and immunogenicity-related loss of efficacy are well-documented concerns. Furthermore, cost and access remain significant barriers in many health systems, underscoring the need for individualized treatment strategies based on disease phenotype, comorbidity profile, and patient preferences (26,27). On the other hand, tsDMARDs such as tofacitinib offer practical advantages, particularly their oral administration and rapid onset of action. However, their higher risk of serious adverse events and regulatory warnings necessitate a cautious approach, particularly in patients with cardiovascular risk factors or a history of malignancy. Future real-world data and head-to-head comparisons with bDMARDs will be essential in delineating their optimal positioning in the treatment landscape. Additionally, long-term pharmacovigilance studies are needed to better characterize safety signals that may not be fully captured in randomized controlled trials (28,29).

While csDMARDs remain foundational in early disease management and are widely used due to their affordability and long-standing familiarity, their modest efficacy and tolerability limitations suggest they may be best utilized in combination regimens or in patients with milder disease phenotypes. Notably, their inclusion as comparators in several of the included trials allowed for a baseline reference of therapeutic gain achieved with newer agents. For example, in studies comparing methotrexate with ustekinumab and tofacitinib, both newer agents outperformed methotrexate across key

endpoints, supporting the trend toward favoring advanced therapies when appropriate (30).

The diversity of study designs within the included literature also deserves consideration. While the majority were randomized controlled trials, two studies were observational, introducing potential bias due to confounding and heterogeneity in treatment exposure. However, the inclusion of real-world data adds valuable insight into the external validity of clinical trial findings, especially in heterogeneous populations not typically enrolled in RCTs. The follow-up durations ranged from 24 to 52 weeks, providing a meaningful but temporally limited view of long-term outcomes. Chronic conditions such as psoriatic arthritis and rheumatoid arthritis require sustained control, and future studies should incorporate longer-term follow-up to assess durability of response and long-term safety.

Methodologically, the systematic search employed in this review was robust, encompassing multiple high-yield databases and clinical trial registries, thereby minimizing publication bias and maximizing comprehensiveness. The transparent documentation of study selection using a PRISMA flow diagram further enhances reproducibility and methodological rigor. Nevertheless, heterogeneity in patient populations, outcome definitions, and follow-up intervals across studies may have influenced pooled estimates. Although meta-analytic techniques were not applied due to the limited number of studies and potential clinical heterogeneity, narrative synthesis allowed for contextual interpretation of findings.

Overall, the results of this systematic review provide a compelling rationale for favoring bDMARDs as the most efficacious treatment class for inflammatory rheumatic diseases, with tsDMARDs offering a viable alternative in select patient populations. csDMARDs, while less potent, remain valuable in initial treatment and as comparators in clinical trials. Treatment decisions should be guided by a combination of clinical response, risk tolerance, patient values, and access considerations. As the therapeutic armamentarium continues to expand, precision medicine approaches integrating biomarkers, pharmacogenomics, and real-world data will be pivotal in optimizing outcomes.

Moreover, head-to-head trials directly comparing bDMARDs and tsDMARDs remain sparse, limiting the granularity of current evidence in distinguishing among newer therapies. Existing studies such as those evaluating secukinumab versus adalimumab or tofacitinib versus methotrexate offer partial insights, yet broader comparative effectiveness data are essential to inform therapeutic sequencing and switching strategies. Additionally, combination therapy, particularly involving csDMARDs with bDMARDs or tsDMARDs, is a common clinical practice but underrepresented in randomized data. Future research should explore combination

regimens to determine additive or synergistic effects and their impact on long-term disease control, functional outcomes, and healthcare resource utilization.

Patient-centered outcomes, including quality of life, fatigue, and work productivity, were not uniformly reported in the included studies, representing a gap in the current literature. These outcomes are particularly relevant in chronic, disabling conditions and should be integrated as core endpoints in future trials. Likewise, stratified analyses based on disease subtype, comorbidity burden, and prior treatment exposure would allow for a more tailored understanding of therapeutic benefit.

In conclusion, this systematic review underscores the superior efficacy of bDMARDs in achieving clinical remission and skin clearance in patients with inflammatory arthritis, with tsDMARDs emerging as a promising but risk-sensitive alternative. While csDMARDs maintain a role in early and adjunctive treatment, their limited efficacy and tolerability warrant judicious use. Clinicians must balance therapeutic benefit with potential adverse events, cost implications, and patient-specific factors to make informed, individualized treatment decisions. The evolving landscape of DMARD therapy holds great promise, but ongoing research and vigilance are necessary to fully harness its potential while ensuring patient safety and long-term disease control.

### Conclusion

Based on this systematic review, biologic DMARDs demonstrated superior efficacy in ACR and PASI response rates compared to conventional and targeted synthetic DMARDs, with an acceptable safety profile. Targeted synthetic DMARDs showed intermediate efficacy but higher rates of serious adverse events. Conventional DMARDs were less effective overall. These findings support the preferential use of biologic agents in moderate-to-severe disease, with treatment individualized based on efficacy, safety, and patient-specific factors.

### Disclosure Statement

No potential conflict of interest reported by the authors.

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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