Quality of Systematic Reviews with Network Meta-Analyses on JAK Inhibitors in the Treatment of Rheumatoid Arthritis: Application of the AMSTAR 2 Scale

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OBJECTIVE

This study aimed to evaluate the methodological quality of systematic reviews with network meta-analysis assessing the efficacy and/or safety of JAK inhibitors in rheumatoid arthritis, using AMSTAR 2.

INTRODUCTION

Systematic reviews (SRs) with network meta-analyses (NMAs) play a fundamental role in synthesizing evidence, allowing both direct and indirect comparisons of therapeutic interventions. JAK inhibitors have been widely evaluated in SRs with NMAs due to their emerging role in rheumatoid arthritis (RA) management.

However, the reliability of these reviews depends on methodological rigor. The AMSTAR 2 tool provides a critical appraisal framework to identify potential flaws that may compromise evidence-based practice.

METHODS

A literature search was conducted in PubMed (last update: June 2025) following Cochrane and PRISMA guidelines. Included SRs with NMAs on JAK inhibitors in RA, assessing efficacy and/or safety, with full text in English or Portuguese. Excluded narrative reviews, editorials, letters, to the editor and commentaries, SRs without NMA, duplicates, and reviews focused exclusively on a single JAK inhibitor. Three independent reviewers screened studies and assessed quality using AMSTAR 2 (16 items, 7 critical). Compliance per domain was summarized descriptively.

RESULTS

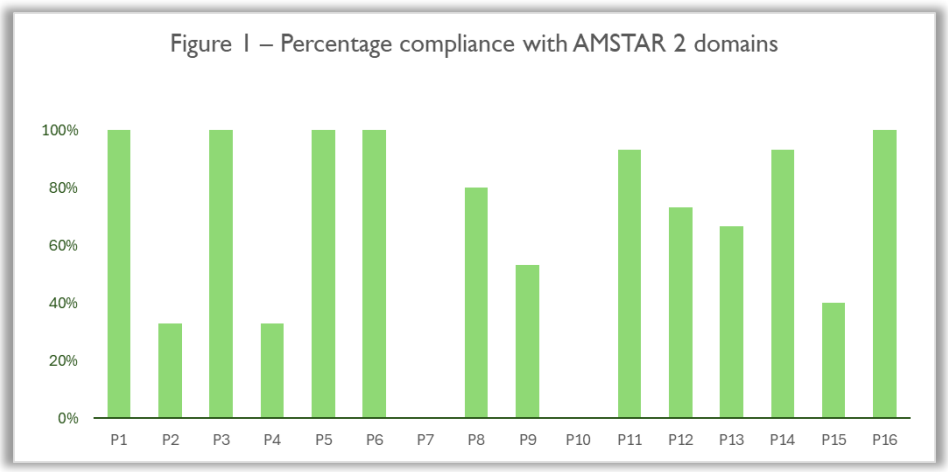
✓ The PubMed search retrieved 69 records; 15 SRs with NMAs met eligibility criteria (5 efficacy, 5 safety, 5 both). Methodological quality was assessed with AMSTAR 2 by three independent reviewers.

Overall Compliance with AMSTAR 2 Criteria

Structural domains showed high compliance (PICO question, study design, duplicate selection, conflicts of interest: 100%).

In contrast, transparency-related domains revealed major weaknesses: protocol registration (33%), detailed search strategy (33%), publication bias (40%), justification for study exclusions (0%), and reporting of funding sources (0%).

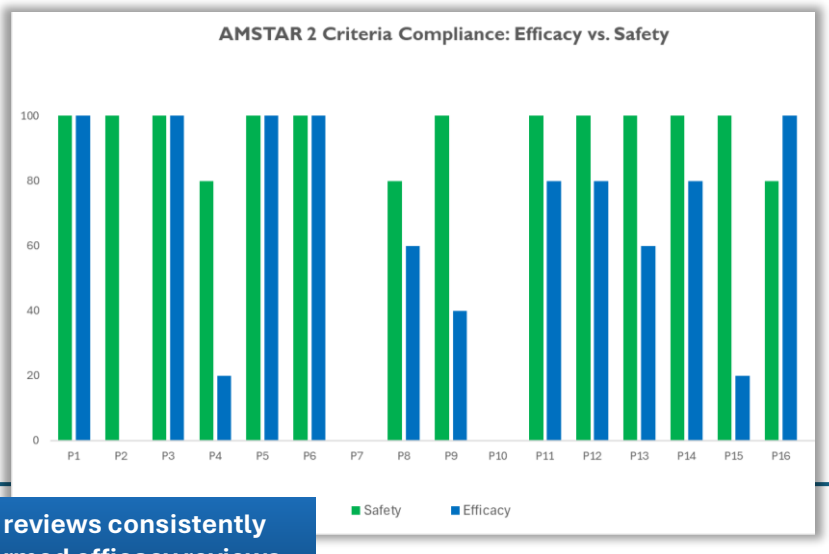
Figure 1 – Percentage compliance with AMSTAR 2 domains



High compliance in structural domains, but major gaps in transparency and reproducibility.

Comparison Between Efficacy and Safety Reviews

Safety-focused reviews achieved higher methodological quality. All reported protocol registration, comprehensive search strategies, risk of bias assessment, and publication bias. Efficacy-focused reviews showed low compliance in these domains, while mixed reviews had inconsistent performance, combining strengths (e.g., PICO, duplicate extraction) with major flaws (no protocol, no bias assessment).



Safety reviews consistently outperformed efficacy reviews, especially in critical domains.

✓ **Despite good compliance in structural domains, all reviews presented at least one critical methodological flaw, raising concerns about the reliability of their conclusions for clinical and regulatory decision-making.**

CONCLUSIONS

Safety-focused reviews showed higher methodological quality, while efficacy and mixed reviews were weaker and inconsistent, with persistent gaps in transparency and reproducibility. These shortcomings undermine the reliability of NMAs for clinical and regulatory decisions, reinforcing the need for more consistent and rigorous methodologies to ensure trustworthy evidence.

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CLEVIDENCE

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