

Janus Kinase Inhibitors for Myeloproliferative Neoplasms: A Systematic Review Meta-Analysis of Efficacy and Safety

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INTRODUCTION

MPNs (Polycythemia Vera, Essential Thrombocytopenia, Myelofibrosis) are chronic hematologic malignancies driven by dysregulated JAK-STAT signaling. JAK inhibitors have transformed management.

OBJECTIVE

To evaluate the efficacy and safety of JAKi versus placebo/BAT across MPN subtypes via systematic review and meta-analysis.

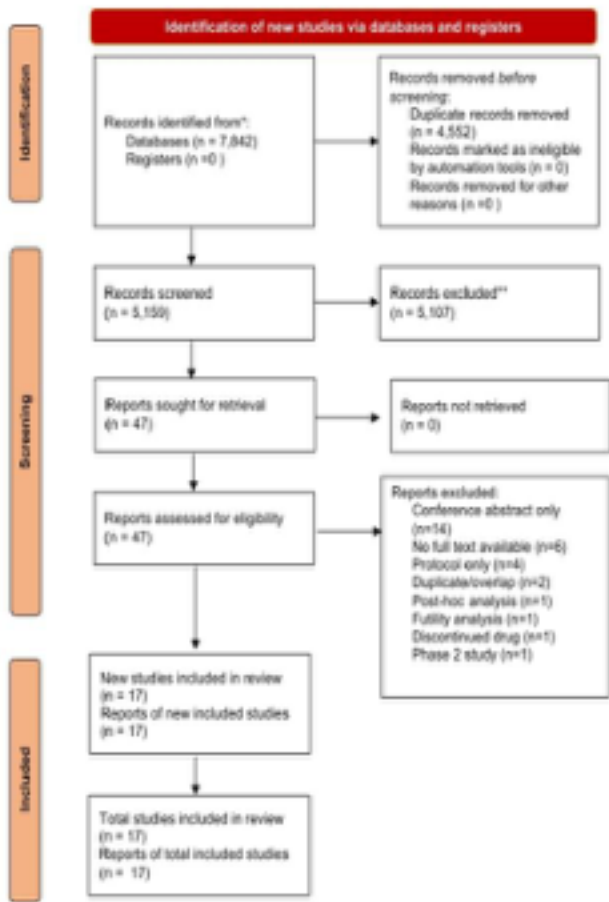
METHODS

Data Sources; PubMed, Scopus, Embase, and ClinicalTrials.gov from inception through December 31, 2026

Eligibility Criteria: Randomized controlled trials (RCTs) evaluating JAKi in adults with WHO-defined MPNs.

Statistical Analysis: Pooled risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using random-effects models. Risk of bias was assessed using Cochrane ROB-2 tool, and heterogeneity was quantified using I² statistics.

PICO DIAGRAM



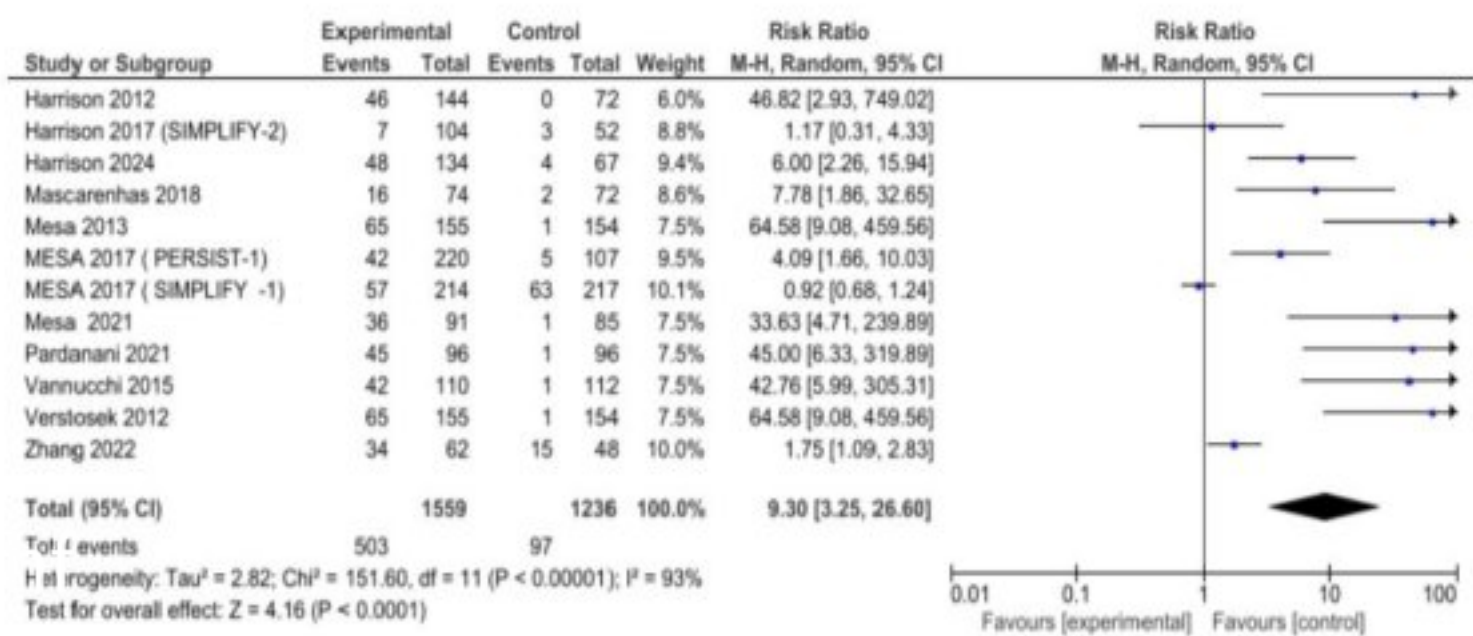
PRIMARY RESULTS

- Spleen Volume Reduction (SVR35):** JAK inhibitors significantly reduced spleen volume compared to controls (RR: 9.30, 95% CI 3.25–26.60, I²=93%).
- Total Symptom Score (TSS≥50%):** JAK inhibitors demonstrated meaningful symptom improvement (RR: 3.16, 95% CI 1.83–5.44, I²=91%).

POOLED ANALYSIS

Outcome	Studies (n)	Effect size (RR) [95% CI]	p-value	I ² (%)
SVR35 (Spleen Volume Reduction)	11	9.30 [3.25, 26.60]	<0.00001	93%
TSS50 (Total Symptom Score Reduction)	14	3.16 [1.83, 5.44]	<0.00001	91%
Transfusion Independence	4	1.58 [1.09, 2.31]	0.02	27%
Serious Adverse Events	7	1.67 [1.32, 2.12]	<0.0001	44%
Discontinuation due to AEs	12	1.83 [1.29, 2.58]	0.0007	19%

FOREST PLOTS



- Transfusion Independence:** Significantly superior with JAK inhibitors (RR: 1.58, 95% CI 1.09–2.31, I²=27%).
- Serious Adverse Events (AEs):** Markedly increased with JAK inhibitors (RR: 1.67, 95% CI 1.32–2.12, I²=44%, P<0.0001).
- Treatment Discontinuation due to AEs:** Significantly higher with JAK inhibitors (RR: 1.83, 95% CI 1.28–2.58, I²=19%, P=0.0007).
- Anemia and Dose Reductions:** Sensitivity analyses revealed significantly higher rates with JAK inhibitors after excluding outliers.

Outcome	Overall Certainty (GRADE)
SVR35 (Spleen Volume Reduction)	VERY LOW
TSS50 (Total Symptom Score Reduction)	VERY LOW
Serious Adverse Events	MODERATE
Discontinuation due to AEs	MODERATE

CONCLUSION

This comprehensive meta-analysis demonstrates that JAK inhibitors significantly improve spleen response, symptoms, and transfusion independence in MPNs, but increase severe adverse events, discontinuation, and anemia, emphasizing individualized risk-benefit stratification and proactive toxicity management for optimized treatment.