Characterizing the humanistic burden of anemia associated with myelofibrosis through patient-reported outcomes: findings from a systematic literature review

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INTRODUCTION

Anemia is a hallmark clinical feature of myelofibrosis (MF), common at diagnosis and increasingly prevalent with disease progression. It is associated with reduced survival, poorer health-related quality of life (HRQoL), fatigue, and impaired physical functioning. Although JAK inhibitors are standard in MF treatment, they may worsen anemia and inadequately address anemia-related symptoms, while also influencing HRQoL assessments through effects on other MF symptoms.[1-3] Transfusion dependence associated with anemia may further increase burden and impair daily functioning.[3] There remains significant unmet need for therapies that effectively address MF-associated anemia and reduce the associated burden.

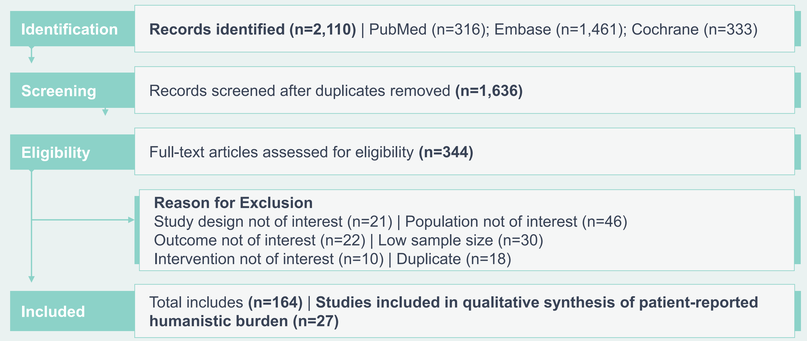
AIM

This systematic literature review (SLR) aimed to characterize the epidemiological, clinical, economic, and humanistic burden of anemia of MF, and the current analysis specifically summarizes the humanistic burden of anemia focused on patient-reported outcome (PRO) evidence.

METHODS

- This SLR followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist and identified English-language peer-reviewed manuscripts (2021–26) and conference abstracts (2024–26) from PubMed, Embase, and Cochrane CENTRAL (Figure 1)
- Eligible studies reported epidemiologic, clinical, economic, or humanistic outcomes, with the current analysis focused on PROs. Titles/abstracts and full texts were screened through dual independent review, and findings were synthesized qualitatively

Figure 1. *PRISMA Flow Diagram of Study Selection*



CONCLUSIONS

- These findings show that anemia in MF is associated with a substantial, multi-dimensional humanistic burden
- Across studies, greater anemia severity and transfusion dependence were linked to worse PROs, while Hgb improvement and transfusion independence were associated with meaningful HRQoL increases
- Clinically, anemia emerges as a key independent driver of functional impairment in MF, underscoring the need to prioritize its management alongside other symptoms of the disease
- Evidence gaps remain regarding the full impact of anemia in MF on patients' daily functioning and real-world activities, indicating that the anemia-specific burden is not yet fully understood and characterized in the literature
- Prospective studies are needed to better characterize the relationships between Hgb, transfusion status, and disease-specific PROs in MF
- Given the high humanistic burden of anemia in MF, newer therapies are needed to address anemia in patients with MF

RESULTS

Most evidence originated from interventional studies of current and emerging MF therapies

- This SLR identified 164 included studies, of which 27 reported humanistic outcomes and are the focus of this synthesis[2-28]
- Across 27 included studies, evidence was derived predominantly from randomized/interventional clinical trials and post hoc analyses (n=19), supplemented by real-world observational studies (n=4) and surveys/interviews (n=4)
- Studies most commonly evaluated JAK inhibitor–based regimens, including momelotinib (n=8), ruxolitinib (n=8), and pacritinib (n=2), alongside investigational therapies, such as elritercept (n=2), luspatercept (n=2), and pelabresib (n=1)

Evidence on anemia-related humanistic burden was largely derived from symptom-focused assessments, with limited use of broader HRQoL measures

- PRO assessment was primarily **conducted using symptom-focused instruments, specifically MPN-SAF and MF-SAF**. These tools predominantly evaluate disease-related symptoms, including fatigue, inactivity, abdominal discomfort, and early satiety
- Patient-reported global impression of change scales, such as PGIC, were used less frequently, and evidence from formal multi-domain HRQoL and generic PRO measures, including EORTC QLQ-C30, FACT-An, FACT-Lym, FACIT-Fatigue, PROMIS Physical Function/SF-10b, EQ-5D, and EQ-5D VAS, was limited (Figure 2)

Across studies, anemia in MF was associated with substantial and persistent patient-reported burden, while Hgb improvement and TI were linked to better HRQoL and symptom outcomes

- **EQ-5D-5L VAS** scores increased by 11.8 points among patients with Hgb improvement ≥2 g/dL versus 5.7 points among those without these Hgb improvements at Week 24, indicating a meaningful incremental benefit in perceived health[23]
- **Cancer-specific HRQoL measures (EORTC QLQ-C30 and FACT-An)** showed modest improvements with treatment in patients with anemia, with 36.2% achieving improved global HRQoL on the EORTC QLQ-C30[9]
- **Physical functioning (PROMIS SF-10b)** remained impaired, with low response rates (~5-15%) at Week 24.[9] In contrast, **PGIC** consistently showed greater patient-reported improvement among patients with Hgb improvement (Figure 3)[23]
- Among treated patients with a mean Hgb increase ≥1.5 g/dL, 83% showed a “meaningful improvement” in their **FACT-An Anemia Subscale** and 66% in the **Fatigue Subscale** scores. Higher Hgb levels (≥10 g/dL) were associated with better FACT-An outcomes[19]
- Across studies, **FACIT-Fatigue** scores indicated a substantial fatigue burden among patients with MF-associated anemia. In one study, patients with high-risk MF and Hgb <10 g/dL reported worse fatigue (mean FACIT-F = 28.1) than the broader MF population (31.7)[17]
- In patients with anemia who were TD at baseline, **FACT-Lym TS symptom response** at Week 24 was significantly higher in those without new/worsening anemia compared to patients with new/worsening anemia (44.4% vs 31.1%; p = 0.04). It was also numerically higher at Week 48 (37.5% vs 25.8%), though not statistically significant (p = 0.15)[20]

Figure 2. *Frequency of PRO Instruments Across Included Studies**

***Note**: PRO instruments are not mutually exclusive; individual studies may have reported outcomes using more than 1 instrument*

#FACT/ includes FACT-Lym, FACT-An, and -Fatigue

Figure 3. *PGIC Improvement or Worsening at Week 24 by Hgb Increase Threshold[23]*

Pooled analysis of the Phase 3 SIMPLIFY-1 and SIMPLIFY-2 trials of momelotinib versus ruxolitinib in myelofibrosis (n=215 evaluable for PGIC at Week 24). Values represent the proportion of patients reporting PGIC improvement or worsening by Hgb increase threshold

Key findings suggest modest symptom improvement in patients with MF and anemia; however, persistent symptom burden remains despite treatment with current/investigational therapies (JAKi, BETi, activin inhibitors/TGF-β inhibitors, androgens)

- **Among patients with MF and anemia, TSS50 response rates varied widely (0-84.6%) despite treatment,** reflecting heterogeneity in populations and treatments[2,4-13]
- Across current therapies, **the median TSS50 response rates in patients with MF and anemia** were modest across studies, ranging from **21% (MPN-SAF)**[2,7,11-13] **to 25% (MF-SAF),**[4,6,8-10] and the absolute **mean changes in TSS ranged from −3.9 to −11.5 points at 24 weeks**[5]
- Despite treatment, clinically meaningful **improvement in MF-SAF disease-related fatigue was achieved by only 18.5% of patients at Week 24**[9]

Anemia and transfusion dependence impose a significant burden on the patients’ ADL and HRQoL, with patients noting that anemia improvement was very important to them

- Patient-reported data highlight substantial real-world impact, with **anemia affecting daily activities, physical functioning, cognition, and emotional health** (Figure 4, Figure 5)[3,25]
- Most patients (81%) reported that improvement in anemia was **highly important**[3]
- Among transfusion-dependent patients, additional burdens included: **time-consuming transfusions (42%), transfusion-related anxiety (37%), and limited symptom relief despite transfusions (21%)**[18]

Figure 4. *Average Impact of Anemia on Daily Activities[25]*

Note: Values represent average reported impact of anemia across daily life domains by DIPSS risk group. Scale: 1–5 (1 = not at all; 5 = a lot)

Figure 5. *Proportion of Patients Reporting Anemia-Related Burden Across Domains[3]*

Data are derived from a multinational, cross-sectional online survey. Survey items and response options were developed based on findings from a targeted literature review and qualitative concept elicitation interviews

Abbreviations: ADL = activities of daily living; BETi = bromodomain and extra-terminal inhibitor; CENTRAL = Cochrane Central Register of Controlled Trials; DIPSS = Dynamic International Prognostic Scoring System; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EQ-5D = EuroQol 5-Dimension; EQ-5D-5L = EuroQoL 5-Dimension 5-Level; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy – Fatigue; FACT-An = Functional Assessment of Cancer Therapy–Anemia; Hgb = hemoglobin; HRQoL = health-related quality of life; JAKi = Janus kinase inhibitor; MF = myelofibrosis; MF-SAF = Myelofibrosis Symptom Assessment Form; MPN-SAF = Myeloproliferative Neoplasm Symptom Assessment Form; PGIC = Patient Global Impression of Change; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PRO = patient-reported outcome; PROMIS SF-10b = Patient-Reported Outcomes Measurement Information System Short Form 10b; SLR = systematic literature review; TD = transfusion dependent; TI = transfusion independent; TGF-β = transforming growth factor beta; TSS = total symptom score; TSS50 = ≥50% reduction in total symptom score; VAS = visual analogue scale

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