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Qualitative and Psychometric Validation of Myelofibrosis Symptom Assessment Form Version 4.0, a Harmonized Patient-Reported Outcome Measure

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OBJECTIVES

- To evaluate the understanding, relevance, and recall period of the MFSAF v4.0 using cognitive interviews, including both concept elicitation (CE) and cognitive debriefing (CD)
- To evaluate the psychometric properties of the MFSAF v4.0 with an independent sample of adult patients with MF in the United States (US) and the United Kingdom (UK)

CONCLUSIONS

The MFSAF v4.0 Total Symptom Score (TSS) has sufficient reliability and validity to be used in clinical trials to support labelling claims in the MF population
Results from this study supports other published literature on the psychometric properties of the MFSAF v4.0

Interview analysis supports content validity for the MFSAF v4.0

Psychometric analysis demonstrates high levels of internal consistency reliability, test-retest reliability, and construct validity, including convergent and divergent validity, with selected reference measures

Although there is heterogeneity within the patient experience of MF symptoms, the MFSAF v4.0 assesses the most common and burdensome symptoms in the MF target population

Next Steps

- Patients described cognitive complaints as an important concept that can be perceived as both symptom or an impact, but also is tied closely to the fatigue MF patients experience. Future research could further explore how cognitive symptoms and impacts are defined in MF patients
- Further validation of the MFSAF v4.0 TSS in larger and more diverse samples (e.g., multi-country clinical trials) or with combination agents for assessing the ability to detect change should be explored

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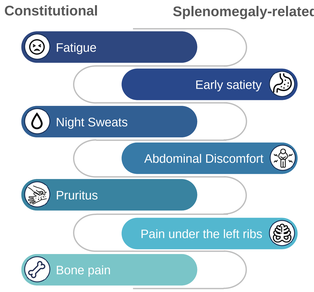
Elektra Papadopoulos, Avijeet Chopra, Kavita Sail, and Kristina Fitzgerald are employees of AbbVie and may own AbbVie stock or stock options

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INTRODUCTION

- Myelofibrosis (MF) is a rare myeloproliferative malignancy affecting approximately 1 in every 100,000 person-years[1] in the US, with 90% of patients diagnosed after the age of 40 years[2]
- Symptoms of MF may be constitutional or related to splenomegaly. Reduction in MF symptom burden is important to patients with MF and a key goal in clinical trials for new therapeutics
- Myelofibrosis Symptom Assessment Form (MFSAF) v2.0 was developed to assess symptom improvement with ruxolitinib based on prior MF symptom assessment forms and US Food and Drug Administration's feedback[3,4]
- Myelofibrosis Symptom Assessment Form (MFSAF) v4.0 is a harmonized, consensus-based patient-reported outcome (PRO) measure developed by C-Path's PRO Consortium's MF Working Group to assess symptom burden in MF[5]
- MFSAF v4.0 focuses on 7 core symptoms of MF each assessed on an 11-point Numeric Rating Scale from 0 (absent) to 10 (worst imaginable)[5]
  - It is scored as a Total Symptom Score (TSS) from 0 (no symptoms) to 70 (worst symptoms). This study used the MFSAF v4.0 24-hour recall format[5]

MFSAF v4.0 symptoms[5]



METHODS

- This study was an observational, mixed-methods study consisting of both qualitative cognitive interviews and quantitative questionnaire

Study Overview

	Qualitative Cognitive Interview (N = 17)	Online Survey (N = 38)
Rationale/ Objective	• Concept elicitation to establish content validity • Debrief instructions, item concept, response scale and options, and recall period of the MFSAF	• Non interventional study that included two timepoints, a baseline and a 2-week follow-up
Study population	• US patients with clinician-confirmed MF • Intermediate-1, Intermediate-2 or High-risk MF • Currently experiencing at least 2 symptoms related to MF	• US and UK patients with clinician-confirmed MF • Intermediate-1, Intermediate-2 or High-risk MF • Currently experiencing at least 2 symptoms related to MF
Data source	• Interview Transcript	• Time 1 and Time 2 survey
Analysis	• Comprehensiveness (content validity) of the MFSAF v4.0 with regard to symptoms of MF using thematic analysis • Understanding, relevance, and suitability of the MFSAF v4.0 • Appropriateness of the response options and recall period	• The psychometric measurement properties of the MFSAF v4.0 were evaluated. Item-level analyses included: quality of completion, item performance and distribution, inter-item and item-total correlations • The validity and reliability of the MFSAF v4.0 TSS were assessed and estimates of interpretability of thresholds were conducted using distribution-based methods

Note: Following their interviews, all 17 participants completed the online survey as well.

RESULTS

Sample

- Participants were 59.6 years old on average, mostly female (53.8%) and White (94.1%)

Concept Elicitation

- CE interviews confirmed the MF experience in this study was consistent with previous literature
- Fatigue was confirmed as an important aspect in the daily MF patient experience

Cognitive Debriefing

- The MFSAF v4.0 instructions were easy to understand
- The 7 items of the MFSAF v4.0 were well-understood (100%)
- Relevance of items varied (60-100%) depending on participants' personal MF experience
- Participants confirmed the recall period was suitable and the response options were appropriate (100%)
- No changes were recommended for the measure

Quantitative

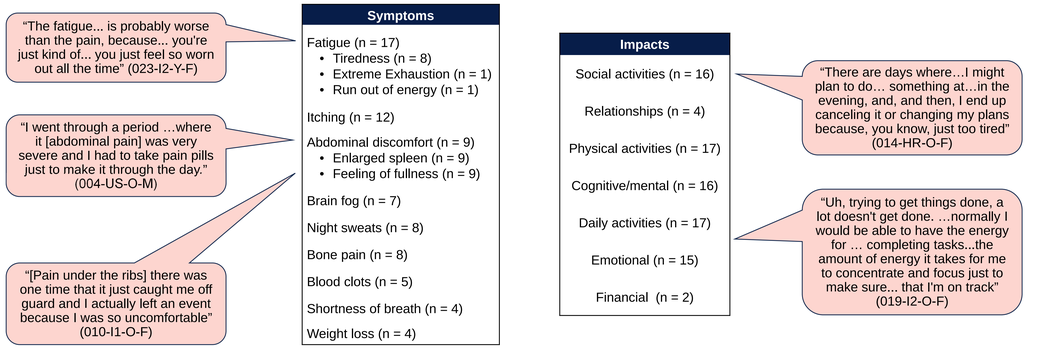
- All participants (100%) completed every item and a TSS was used for analysis
- Ceiling, where more participants than expected did not suffer from these symptoms of MF, may be due to the heterogeneity of the condition
- Inter-item and item-total correlations suggest a single overall construct
- Strong internal consistency and test-retest reliability were observed
- Overall results support convergent / divergent and known groups validity of the MFSAF v4.0 TSS
- As distribution-based methods provide the lower- bound estimates of meaningful change for MWPC and MID, a change of at least 4.5 to 5.5 may be considered above measurement error

Study Population

Parameter	Response	Interview Population (N = 17)	Online Survey Population (N = 39)
Diagnosis, n (%)	Primary MF	9 (52.9%)	15 (38.5%)
	Secondary MF	7 (41.2%)	21 (53.8%)
	Diagnosed, but unsure	1 (5.9%)	3 (7.7%)
MF risk stratification, n (%)	Intermediate-1	6 (35.3%)	14 (35.9%)
	Intermediate-2	9 (52.9%)	14 (35.9%)
	High-risk MF	1 (5.9%)	5 (12.8%)
	Unsure	1 (5.9%)	6 (15.4%)
Current MF symptoms[1] at enrollment, n (%)	Fatigue	16 (94.1%)	37 (94.9%)
	Night sweats	9 (52.9%)	17 (43.6%)
	Itching	8 (47.1%)	14 (35.9%)
	Abdominal discomfort (bloating, pressure)	12 (70.6%)	25 (64.1%)
	Pain under ribs on left side	5 (29.4%)	11 (28.2%)
	Feeling of fullness	9 (52.9%)	20 (51.3%)

[1] Participants selected yes/no on the screening survey to indicate if they were currently experiencing the listed symptoms.

Patient-reported Symptoms and Impacts from Concept Elicitation Interviews



Psychometric Evaluation of MFSAF v4.0 TSS

Parameter	Prespecified Thresholds	Online Survey (N = 38 at Time 1; N = 37 at Time 2)
Distribution of scores	≥ 25% of responses in relevant categories used to indicate ceiling and floor effects	• No floor effects were found • Four items had ceiling effects: Item 2 (Night sweats), Item 3 (Itching), Item 5 (Pain under the left side of the ribs), and Item 7 (Bone pain)
Internal consistency reliability	≥ 0.70	Cronbach's alpha = 0.827
Test-retest reliability	≥ 0.70	• TRP1 (n = 4); TRP 2 (n = 30); TRP3 (n = 22): ICC = 0.846-0.855
Convergent/ divergent validity	Cohen's guidelines for coefficients: small (< 0.3), moderate (≥ 0.30 to < 0.50), large (≥ 0.50 to < 0.7), and very large (≥ 0.7)	• MSAS-SF: Physical Symptoms Subscale (0.690); Global Distress Index (0.551) • SF-12 v2: Small correlations: GH, MH, MCS; Moderate correlations: VT, SF, RE, Large correlations: PF, RP, BP, PCS • PGI-S: Overall MF Symptoms (0.774); Fatigue due to MF (0.625)
Known-groups validity	Monotonic pattern across categories and effect size ≥ 0.50	Low (n = 14): LS Means (SE): 16.86 (3.04); Effect size = — Moderate (n = 14): LS Means (SE): 19.79 (3.04); Effect size = 0.263 High (n = 5): LS Means (SE): 25.00 (5.09); Effect size = 0.393
Distribution-based MID	Lower-bound estimates for both within-patient MWPCs and between-group MIDs	0.2 SD = 2.22; 0.5 SD = 5.55 ; 0.8 SD = 8.88 SEM = 4.62

Abbreviations

CE = concept elicitation; LS = least squares; MF = myelofibrosis; MFSAF = Myelofibrosis Symptom Assessment Form; MID = meaningful important difference; MPN-SAF = Myeloproliferative Neoplasm Symptom Assessment Form; MSAS-SF = Memorial Symptom Assessment Scale – Short Form; MWPC = meaningful within-patient change; PRO = patient reported outcome; SD = standard deviation; SE = standard error; SEM = standard error of measurement; TRP = test-retest population; TSS = total symptom score

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