Title: UK Results from the Myeloproliferative Neoplasms (MPN) Landmark Survey on the symptom, emotional and economic burden of MPNs.

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Myelofibrosis (MF), polycythaemia vera (PV), and essential thrombocythemia (ET) are associated with a considerable disease burden and a reduced quality of life (QoL) (Emanuel et al., 2012; Mesa et al., 2016). MPN patients experience many symptoms, with fatigue one of the most severe (Abelsson et al., 2013; Johansson et al., 2012; Scherber et al., 2011). Few studies explore how symptom burden affects the work productivity and daily activities of patients (Mesa et al., 2016). We previously conducted a survey, the 'US MPN Landmark Survey', reporting a substantial reduction in QoL and work productivity suggesting a reduction of symptom burden may improve QoL and productivity of MPN patients, as previous studies have suggested that QoL and overall symptom burden can differ between countries, we conducted the Landmark Survey in 6 countries outside the US (Harrison et al., 2017). Here we present the first UK-specific analysis of the survey data exploring the impact of the overall symptom burden experienced by MPN patients.

The methodology used was a cross-sectional survey of MPN patients and treating physicians conducted in 2016 in Australia, Canada, Germany, Italy, Japan and the UK. Physician and patient surveys were not linked and explored: physician-patient relationship, disease management/treatment attitudes, treatment and treatment goals and the economic, emotional and physical burden of the disease. Work productivity, absenteeism, presenteeism and activity impairment were measured using the Work Productivity and Activity Impairment Index (Reilly et al., 1993). Each domain was measured on a 0-100% scale with a higher percentage indicating a greater amount of impairment.

Data were stratified by overall symptom severity, calculated by combining the number of symptoms and their associated severity for each patient. This was used to allocate patients into quartiles (Q1 = lowest symptoms burden; Q4 = highest symptom burden) at a global level (**Table 1**).

To be eligible, patients required a diagnosis of MF, PV, or ET , ≥ 18 years of age and not participating in a clinical trial. Patients were recruited in the UK via their managing physician following routine consultations or via a patient organization, MPN Voice. All respondent data are anonymised with analysis presented at an aggregated level.

All analyses presented are descriptive in nature with relevant descriptive statistics reported. Confidence intervals are presented for numeric outcomes (i.e. means) and for patient reported impact ratings. No formal hypothesis testing was performed.

Overall, 286 patients (45 MF, 78 PV, 163 ET) and 31 physicians completed the survey in the UK. Respondent demographics are presented in table 1. UK physicians reported a numerically higher number of patients under their care than the rest of the world (ROW) (UK vs ROW; 26.58 vs 13.66 MF, 49.84 vs 19.81 PV, 52.45 vs 20.02 ET respectively) and mostly agreed with the statement '*There is not enough time during the appointment to discuss all of the symptoms a patient is experiencing*' (74% agreed in UK vs 54% agreed in ROW) (**Table 1**).

Over 98% of patients experienced symptoms in the previous 12 months. Almost half of Q3&4 patients agreed with the statement '*MPN symptoms reduce my life quality*' (49% "agree strongly"). However, 40% of Q1&2 patients stated they "Somewhat agree" with the statement (**Table 1**).

Q3&4 patients reported a higher emotional burden in that more patients reported they experienced each emotional burden more 'frequently' than those in Q1&2. This burden was particularly marked when interfering in the patients' family/social life (Q3&4 57% vs Q1&2 24%) and interfering in patients' sex life (Q3&4 58% vs Q1&2 22%) (**Fig. 1**).

A third of patients in Q3&4 reported reducing their hours at work compared with Q1&2 patients (34% vs 16%), voluntarily terminating a job (17% vs 7%) or going on disability allowance (12% vs 1%) (**Fig. 1**). A higher overall work impairment, absenteeism (missing work due to condition), presenteeism (working whilst sick) and activity impairment was reported by Q3&4 patients compared to Q1&2 patients (48.6% vs 21.7%, 13% vs 1.9%, 41.3% vs 20.4% and 49.9% vs 21.8%, respectively) (**Fig. 1**).

Our data demonstrates that UK MPN patients experience a high disease burden. This burden was higher than ROW (Harrison et al., 2017). The stratification of patients into symptom severity quartiles was conducted at a global level with UK patients disproportionately represented in higher symptom burden group. Patients reported that 'MPN symptoms reduce my life quality' regardless of their overall symptom burden, suggesting a significant impact QoL in the lower burden groups. High emotional burden was noted with patients 'frequently' experiencing anxiety, worry and frustration, and impact on family and social life suggesting that the burden could be felt further afield than the patient directly.

Impact on patients' work productivity and activity impairment was high and demonstrated a greater societal burden of MPNs with Q3&4 patients associated with a higher burden across all facets. It is possible that financial burdens associated with work related stress increases emotional and symptom burden associated with MPNs. Whilst further research would need to be conducted to confirm this relationship, the assumption is supported by data demonstrating that patients with high symptom burden also experience a higher emotional and work/financial burden. The development of improved treatments and management strategies aimed at improving the symptom burden patients experience will assist in alleviating this burden.

UK physicians felt there was not enough time in appointments to address all symptoms more so than ROW. To help mitigate this, patient support structures are needed, such as adopting telemedicine to collect symptom feedback prior to appointments. The high impact of symptom burden proves to be a challenge for both the clinical and patient community. Both groups require further support from the wider stakeholder community. Such strategies would also be complimentary to the patient support structures mentioned above (i.e. telephone clinics, remote symptom monitoring via mobile apps) and have previously demonstrated to be of a benefit in previous trials across various disease areas, including haematological cancers (Breen et al., 2015).

Disclosures

Ali: *Novartis*: consultancy, honoraria, expenses for travel and accommodations. **Harrison:** *Novartis:* consultancy, honoraria, expenses for travel and accommodations, research funding, speakers bureau; *Shire:* honoraria, speakers bureau; *Gilead:* honoraria, speakers bureau; *Baxalta:* consultancy, honoraria, speakers bureau; *Incyte:* honoraria, speakers bureau. **Mead:** *Novartis:* consultancy, honoraria, expenses for travel and accommodations, research funding, speakers bureau; **Taylor -Stokes:** *Adelphi Real World:* employment. **Waller:** *Adelphi Real World:* employment.

Authorship

All authors must fulfil the following three criteria:

• Substantial contributions to research design, or the acquisition, analysis or interpretation of data,

• Drafting the paper or revising it critically, and • Approval of the submitted and final versions. In the Acknowledgments section of the paper all authors, must indicate their specific contributions to the work described in the manuscript. Some examples include

X performed the research

All authors designed the research survey

John Waller analysed the data

John Waller wrote the paper

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Tables

Table 1: Respondent demographics and clinical characteristics

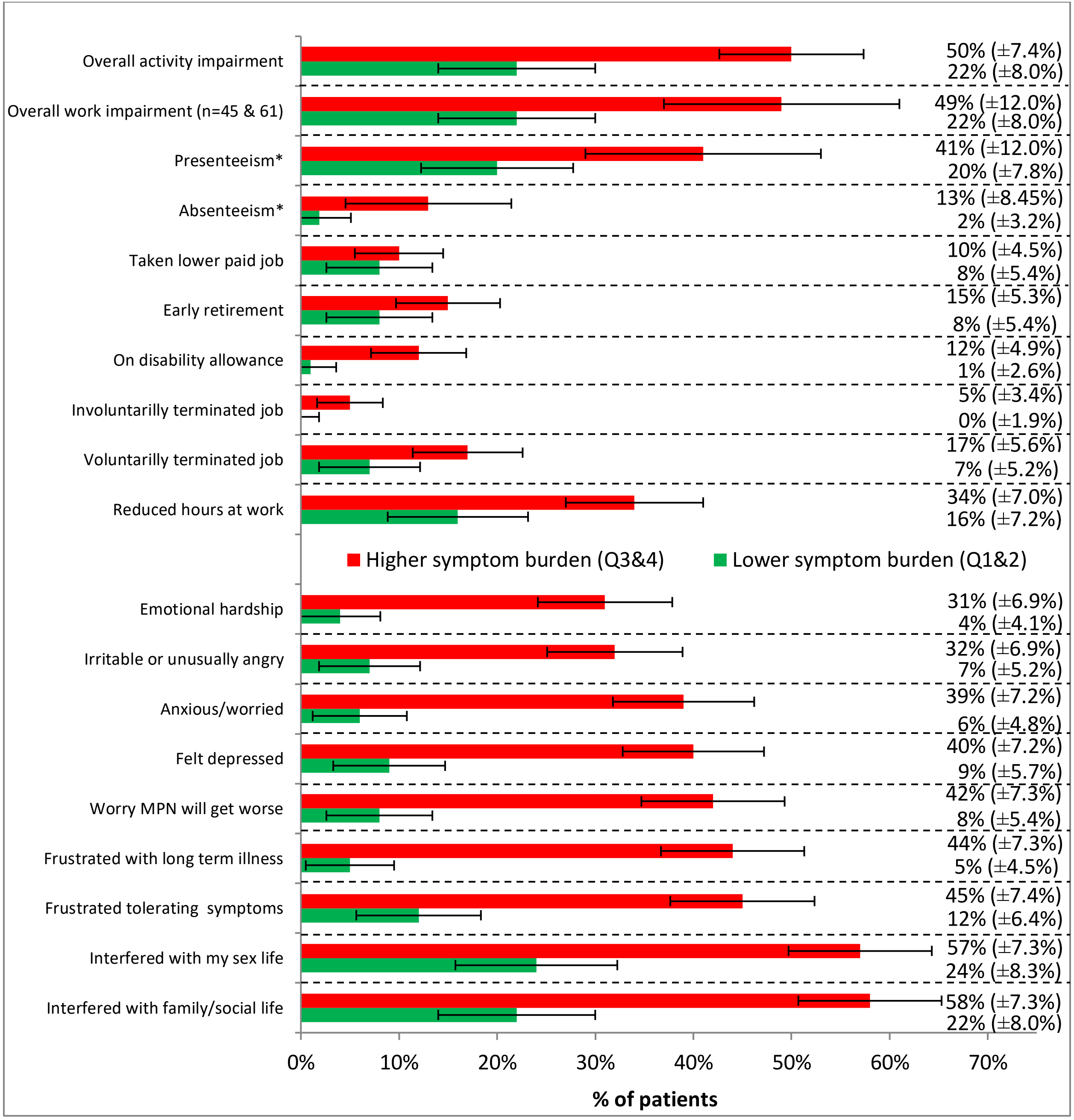
PATIENT DATA			
Overall sample, n	*MF*	45	
	PV	78	
	ET	163	
Overall symptom burden, % (n)	*Lower quartile (Q1)*	14 (39)	
	2nd quartile (Q2)	23 (62)	
	3rd quartile (Q3)	28 (76)	
	Upper quartile (Q4)	35 (97)	
		(Q1&Q2) (n=101)	**(Q3&Q4) (n=173)**
Mean age in years (±CI)		57.0 (±4.54)	55.4 (±3.82)
Gender, % (n)	Male	42 (42)	34 (58)
	Female	58 (59)	66 (115)
Current state of health, % (n)	*Excellent*	12 (12)	1 (2)
	Very good	28 (28)	12 (20)
	Good	51 (52)	32 (55)
	Fair	9 (9)	40 (69)
	Poor	-	15 (26)
	Very poor	-	1 (1)
Impact of symptoms on QoL by severity, % (n)	*Agree strongly*	7 (7)	49 (85)
	Somewhat agree	47 (47)	40 (69)
	Somewhat disagree	23 (23)	6 (10)
	Strongly disagree	24 (24)	5 (9)
PHYSICIAN DATA			
Specialty, % (n)	*Haematology-Oncology*	35 (11)	
	Haematology	65 (20)	
Primary setting, % (n)	*University/Teaching hospital*	71 (22)	
	Regional/Community hospital	29 (9)	
		UK (n=31)	**ROW (n=188)**
Mean number of patients currently under care (±CI)	*MF patients*	26.58 (±16.4)	13.66 (±6.4)
	PV patients	49.84 (±26.4)	19.81 (±6.8)
	ET patients	52.45 (±28.7)	20.02 (±7.44)
Is there enough appointment time, % (n)	Yes	74 (23)	54 (101)
	No	26 (8)	46 (87)

Questions asked of physicians: How many of your patients with MPN are: a) currently under your care, b) under your care in the past 12 months and c) newly diagnosed in the past 12 months. Based on your experience with your MPN patients, how much do you agree with the following statements?

** Patients only eligible if symptoms experienced in past 12 months.*

Question: Please indicate whether you agree strongly, agree somewhat, disagree somewhat or disagree strongly with the statement: 'MPN symptoms reduce my life quality'.

Figure 1: Patient reported impact ratings (where only ‘frequently’ is shown) stratified by their quartile classification for overall symptom severity



Confidence intervals representative of 95% confidence.

**n = 45 and 61 for lower symptom burden group and higher symptom burden group respectively.*