

A new internet-based tool for reporting and analysing patient-reported outcomes and the feasibility of repeated data collection from patients with myeloproliferative neoplasms

Nana Brochmann¹ · Ann-Dorthe Zwisler² · Mette Kjerholt¹ · Esben Meulengracht Flachs³ · Hans Carl Hasselbalch¹ · Christen Lykkegaard Andersen¹

Accepted: 31 August 2015
© Springer International Publishing Switzerland 2015

Abstract

Purpose An Internet-based tool for reporting and analysing patient-reported outcomes (PROs) has been developed. The tool enables merging PROs with blood test results and allows for computation of treatment responses. Data may be visualized by graphical analysis and may be exported for downstream statistical processing. The aim of this study was to investigate, whether patients with myeloproliferative neoplasms (MPNs) were willing and able to use the tool and fill out questionnaires regularly.

Methods Participants were recruited from the outpatient clinic at the Department of Haematology, Roskilde University Hospital, Denmark. Validated questionnaires that were used were European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, Myeloproliferative Neoplasm Symptom Assessment Form, Brief Fatigue Inventory and Short Form 36 Health Survey. Questionnaires were filled out ≥ 6 months online or on paper according to participant preference. Regularity of questionnaire submission was investigated, and participant acceptance was evaluated by focus-group interviews.

Results Of 135 invited patients, 118 (87 %) accepted participation. One hundred and seven participants (91 %) preferred to use the Internet-based tool. Of the 118 enrolled participants, 104 (88 %) submitted PROs regularly ≥ 6 months. The focus-group interviews revealed that the Internet-based tool was well accepted.

Conclusion The Internet-based approach and regular collection of PROs are well accepted with a high participation rate, persistency and adherence in a population of MPN patients. The plasticity of the platform allows for adaptation to patients with other medical conditions.

Keywords Patient-reported outcomes · Health-related quality of life · Regular collection of patient-reported outcomes · Internet-based tool · Feasibility study · Myeloproliferative neoplasm

Abbreviations

MPN	Myeloproliferative neoplasm
CML	Chronic myeloid leukaemia
ET	Essential thrombocythemia
PV	Polycythaemia vera
MF	Myelofibrosis
AML	Acute myeloid leukaemia
JAK2	Janus Kinase 2
EORTC QLQ C-30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30
MPN-SAF	Myeloproliferative Neoplasm Symptom Assessment Form
MPN-SAF QoL	Answer to the question “What is your overall quality of life?” in the questionnaire MPN-SAF
MPN-SAF TSS	Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score

✉ Nana Brochmann
nmor@regionsjaelland.dk

¹ Department of Haematology, Roskilde University Hospital, Koegevej 7-13, 4000 Roskilde, Denmark

² National Centre for Rehabilitation and Palliation, University of Southern Denmark, and Odense University Hospital, Oester Farimagsgade 5A, 1353 Copenhagen, Denmark

³ National Institute of Public Health, University of Southern Denmark, Oester Farimagsgade 5A, 1353 Copenhagen, Denmark

BFI	Brief Fatigue Inventory
SF-36	Short Form 36 Health Survey
CCI	Charlson comorbidity index

Introduction

Patient centeredness is a fundamental component in the optimal treatment of and care for patients with chronic diseases or otherwise prolonged disease courses [1]. Because of often heterogeneous symptoms with variable impact on health-related quality of life (HRQoL), it is important to measure patient-reported outcomes (PROs) to assess the status of the disease and thereby prescribe the most appropriate and accurate prevention, medical treatment, rehabilitation and care for the individual patient [2].

For cancer patients, HRQoL can be a predictor of treatment efficacy, and studies have found that HRQoL, physical well-being, pain and mood are predictive of survival [3, 4]. Thus, HRQoL and symptoms are important PROs for cancer patients.

Myeloproliferative neoplasms (MPNs) are heterogeneous haematological diseases with a chronic disease course. These diseases are traditionally divided into two groups: (1) chronic myeloid leukaemia (CML) carrying the Philadelphia chromosome, and (2) MPNs without the Philadelphia chromosome, essential thrombocythemia (ET), polycythaemia vera (PV) and myelofibrosis (MF). The diseases are all caused by an acquired damage to bone marrow stem cells and are characterized by overproduction of blood cells: in CML leucocytes, in ET primarily platelets, in PV primarily red cells but also very often leucocytes and platelets (pancytosis). MF is characterized by bone marrow fibrosis, which ultimately may result in a decreased production of blood cells (pancytopenia). To compensate for this shortage, blood cells are produced in other organs, particularly in the spleen, giving rise to splenomegaly, which may be massive. ET may develop into PV, and PV may develop into MF because of disease progression [5]. The diseases can also transform into acute myeloid leukaemia (AML). All three disease entities are associated with a decreased lifespan that is most pronounced in patients with MF who have an average post-diagnosis survival of 7 years [6]. If patients develop AML, survival is only a few months [6]. MPN patients may be cured through bone marrow transplantation, but unfortunately this possibility only exists for a minority of younger patients. However, new targeted medical treatments are expected to result in complete haematological and major molecular remissions in a large proportion of patients including, e.g. Janus Kinase 2 (JAK2)—inhibitors and interferon-alpha 2 for patients with ET and PV if treatment is instituted from the time of diagnosis [6]. Hypermetabolic

symptoms are common including fatigue, fever/sweats and weight loss. Many patients are suffering from cardiovascular and thromboembolic complications, and in the advanced myelofibrosis stage common complications include bleeding and infections as well [7–12]. Clinical presentation and symptoms depend on MPN subtype. In general, ET patients have the fewest symptoms, while PV and MF patients experience the greatest symptom burden [13, 14]. HRQoL is reduced to varying degrees for MPN patients depending on whether the disease is stable or accelerated [14, 15]. Because the symptom burden and thereby decreased HRQoL are troublesome to many MPN patients, alleviating the symptom burden is an important treatment objective.

Since symptom burden displays a marked fluctuation during the disease course of these neoplasms, assessment of symptoms and HRQoL may be efficient to follow MPN patients carefully in order to clarify the disease status and to achieve a more complete and integrated signature of the patient's health—and life situation. A lack of knowledge exists in regard to fluctuations in symptoms and HRQoL over time and the association among symptoms, HRQoL and blood parameters for disease activity. Furthermore, collecting PROs in a hospital setting (outpatient clinic, clinical trials, etc.) is a resource-intensive procedure that involves various healthcare professionals. Known challenges are low adherence and difficulties in establishing reproducible procedures between departments. Therefore, a new Internet-based tool for reporting PROs, merging PROs with blood test results and analysing PROs was developed.

The aim of this study was to investigate whether a population of MPN patients was willing and able to use the new Internet-based tool and fill out questionnaires regularly. We aimed to investigate whether there was a difference of response rates in different MPN subtypes and whether an association existed between the questionnaire response rates, symptom burden and HRQoL for the different MPN subtypes. Finally, we aimed to investigate whether there was a difference in demographic characteristics, MPN subtype and the connection to the hospital between the following groups: (1) enrolled participants and patients who declined to participate, (2) participants who filled out questionnaires online and those who filled out on paper and (3) participants continuously enrolled until the end of follow-up and participants who discontinued.

Methods

A new Internet-based tool

Department of Haematology, Roskilde Hospital, Denmark, and Danish Telemedicine A/S have in cooperation

developed an Internet-based tool that may easily capture and assess PROs. The tool enables swift merging of PROs and blood test results. It may be used in clinical practice and clinical trials. The plasticity of the platform allows for adaptation to patients with other medical conditions.

Patient perspective

Tutorial, access and content

A paper tutorial is handed out to each patient before the questionnaire collection starts; the tutorial informs how the tool works. Depending on the patient's preference, an SMS and/or email request with a password and an encrypted link to a secure server (described below) is dispatched when it is time to complete the questionnaires. If a questionnaire is not submitted on day 1, a reminder is dispatched on day 2. The Internet-based approach enables the patient to complete questionnaires in various places, e.g. at home or on holiday. The encrypted site that the patient logs into consists of a start page, a page for each questionnaire and a final page. On the start page, the patient is asked to enter the password and his Danish civil registration number. The civil registration number is a personal identification number registered in the Danish Civil Registration System. The patient receives a new password prior to each collection. The patient presses the login field on the screen in order to login.

PRO collection

Questionnaires are completed and submitted one at a time. All questions in a given questionnaire are mandatory in order to minimize missing data. A pop-up window will inform the patient if questions have not been answered. The final page contains a text box in which the healthcare professional may thank the patient for completing the questionnaires and give additional relevant information. After completing the questionnaires, the patient cannot review the answers. For patients who want to use paper and pencil, questionnaires with prespecified dates are handed out in the outpatient clinic and collected during the subsequent visit. A healthcare professional manually enters these data.

Healthcare professional perspective

Tutorial, access and content

A tutorial is available to the healthcare professional on the login page and as a paper tutorial handout. The tutorial provides a detailed description of how to use the tool. A username and password are required to login. After logging

in, the site contains four pages: patients, calendar, statistics and messages.

Calendar for PRO collection

It is possible to select a predetermined combination of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) [16] and the disease-specific questionnaire Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF) [17] co-administered with the symptom-specific questionnaire Brief Fatigue Inventory (BFI) [17] and the generic questionnaire Short Form 36 Health Survey (SF-36) [18]; it is also possible to select these questionnaires individually. MPN-SAF Total Symptom Score (MPN-SAF TSS) is an abbreviated symptom score developed from MPN-SAF and BFI [9], and this score is presented together with answers to the MPN-SAF. The MPN-SAF was translated from English to Danish according to guidelines prior to the development of the Internet-based tool [19]. The collection start date and end date may be entered, and if no choices are made, the questionnaire collection starts immediately and continues indefinitely. After having chosen which questionnaires are to be used, the healthcare professional defines the interval with which they have to be dispatched. The choices are: once, once a week, once a month and every 3 months. The system automatically displays on the message page when an SMS and/or email with a request to fill out the questionnaire has been dispatched.

Different calendar colour codes signify whether a particular questionnaire is queued for sending, has been filled out or has not been filled out by the patient as requested. It is possible to see how many questionnaires an individual patient has not filled out. The patients filling out least frequently are shown at the top (Fig. 1).

Blood test results and treatment response

Blood test results are automatically imported into the system immediately after analysis in any Danish laboratory. PROs, blood test results and clinical data are merged so that treatment responses, incorporated into the system according to internationally accepted response criteria, may be calculated for individual patients.

Graphical presentation and interpretation of data

PROs may be presented graphically as a function of time and as relative to other variables. A prespecified summary page for individual patients is presented to the healthcare professional. This summary page depicts an overview of common symptoms for MPN patients, HRQoL and

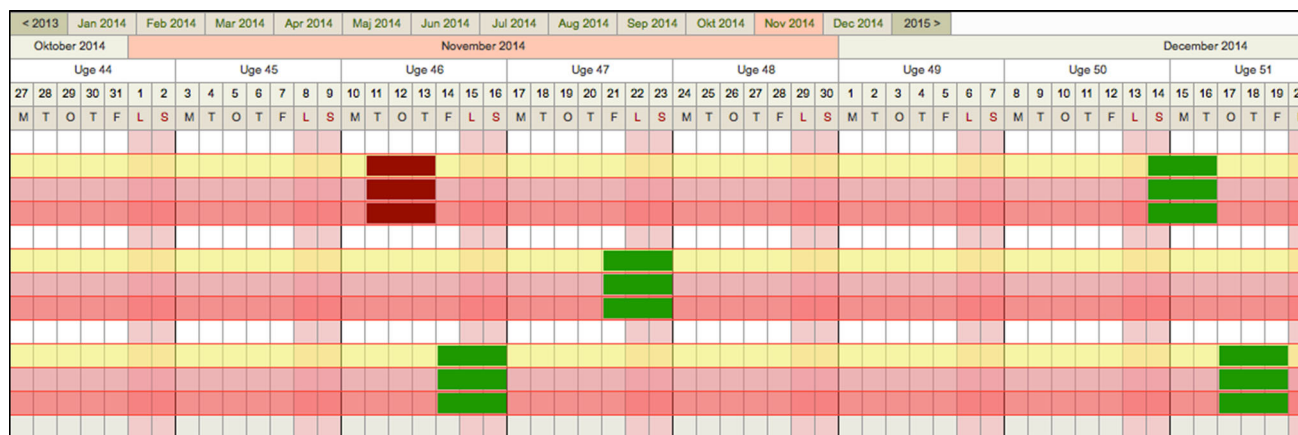


Fig. 1 Calendar for PRO collection in the Internet-based tool. A group of three *horizontal coloured rows* signifies one patient. Each of the three *coloured horizontal rows* within a group signifies a single questionnaire (at the *top* MPN-SAF, in the *middle* EORTC QLQ C-30 and at the *bottom* SF-36). The *colour codes* covering 3 days indicate the opening period for each questionnaire (*blue* indicates the questionnaire is queued for sending, *green* indicates the questionnaire has been completed, *red* indicates the questionnaire has not been

completed as requested). The *colour codes* covering the time span between the opening period for each questionnaire indicates the response rate (*green* indicates that all questionnaires have been submitted, *yellow* indicates that one questionnaire has not been submitted, *light red* indicates that two questionnaires have not been submitted and *strongly red* indicates that at least three questionnaires have not been submitted)

selected SF-36 scores in four systems of coordinates, thus ensuring a fast presentation of PROs. The first system of coordinates presents the answer to the question “What is your overall quality of life?” from the questionnaire MPN-SAF (MPN-SAF QoL) and MPN-SAF TSS (Fig. 2). The second system of coordinates presents fatigue, night sweat, fever and weight loss and the third system of coordinates presents abdominal pain, bone pain and itching. The fourth system of coordinates presents the scores general health, mental health, physical functioning and social functioning from SF-36. The associations between PROs, blood values and treatment responses may be graphically investigated by choice. An export function enables data to be delivered for downstream statistical software.

Data security

Encryption ensures complete control of patient-sensitive data. Data are securely stored at data facilities in Copenhagen, Denmark. Data security complies with the rules established by the Danish Health Authorities and the Danish Data Protection Agency.

Feasibility studies

The feasibility of use of the new Internet-based tool and regular collection of PROs has been investigated through mixed method analysis. One hypothesis posits that the population of MPN patients is willing and able to fill out questionnaires online. Another hypothesis posits that the

population of MPN patients is willing and able to fill out questionnaires regularly.

Quantitative study

Participants

The participants were recruited from the outpatient clinic at the Department of Haematology, Roskilde University Hospital, Denmark. The inclusion criterion was a MPN diagnosis of ET, PV, MF, CML or MPN that was unclassified according to international diagnostic criteria [20, 21] and otherwise independent of treatment strategy. Palliative care was an exclusion criterion. The participants were enrolled from 1 April 2012 to 30 June 2013. The follow-up period ended on 31 December 2013.

Questionnaires

Four validated questionnaires were used in the study: (1) EORTC QLQ-C30 version 3.0, (2) MPN-SAF, (3) BFI and (4) SF-36 version 2.0. Additionally, MPN-SAF TSS was used in the study.

Collection of questionnaires

The participants were asked to fill out the questionnaires at home once a month. They had the opportunity to choose between filling out the questionnaires online or on paper.

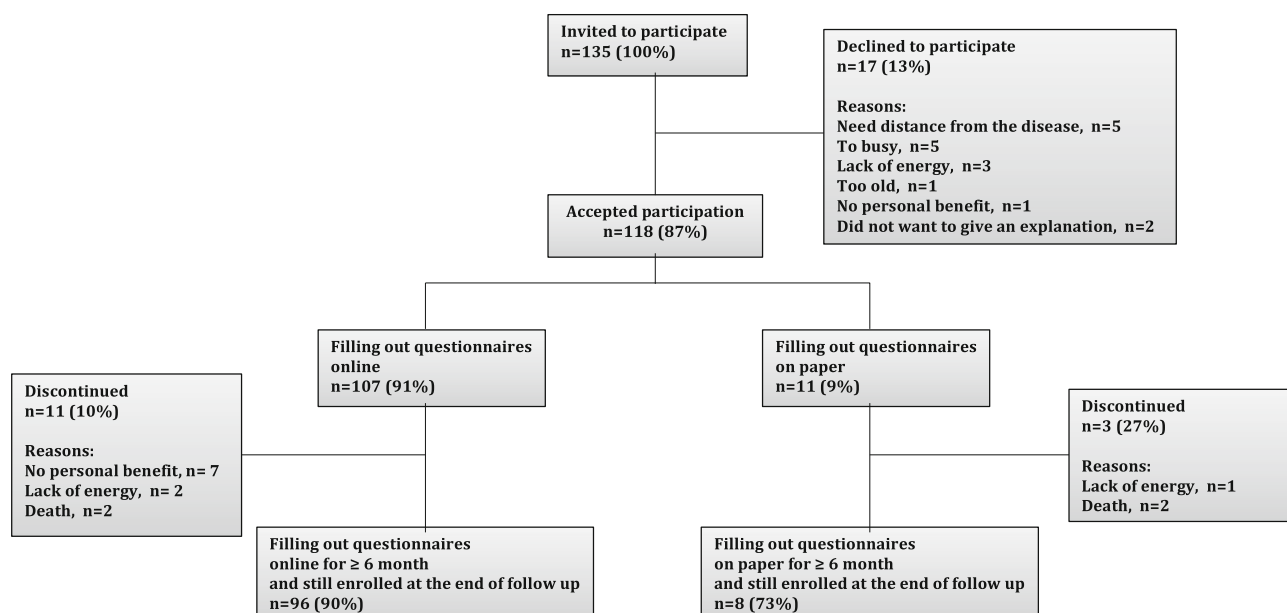


Fig. 3 Flow chart for participation, declining participation and discontinuation of participation

Focus-group interviews

The focus-group interviews were carried out on 18 June 2013. The purpose was to test the hypothesis. A deductive approach was used [23, 24]. The interviews were semi-structured. An interview guide and a structured analysis matrix were developed. Thus, the participants were asked to share their thoughts about the number of questions and the three questionnaires that were repeated each month, to determine whether they found any questions inappropriate and whether they had any technical difficulties in using the Internet-based tool. The participants were asked to share all of their preinterview considerations about the study and all that came to mind during the interview. Furthermore, the purpose was to uncover different thoughts and perspectives on the subject as a whole and to explore the issues that were important to the participants by letting them interact and have room to make any comment as well as ask questions [25]. The duration of each interview was approximately 1.5 h. The interviews were recorded on tape and then transcribed. The answers were listed according to the questions. Analysis was performed on answers to the questions and on further comments from the participants [23].

Results

Quantitative study

Participants

Of the 135 patients who were invited to participate, 118 (87 %) accepted. Seventeen patients (13 %) declined to

participate; the most frequent reasons for declining were the need for distance from the disease (5 patients) and a lack of time (5 patients) (Fig. 3).

Of the 118 enrolled participants, 107 (91 %) preferred to fill out questionnaires online and 11 (9 %) preferred to fill out questionnaires on paper. Participants who preferred to fill out questionnaires on paper were significantly older (71 vs. 61 years old, $p < 0.01$) compared with participants who filled out the questionnaires online (Table 1). One hundred and four participants (88 %) were enrolled in the study for ≥ 6 months and were still enrolled at the end of follow-up. The participants who discontinued were more often living alone (57 % vs. 17 %, $p < 0.01$) and had fewer visits in the outpatient clinic ($n = 4$ vs. $n = 9$, $p < 0.01$) compared with participants who participated ≥ 6 months and were still enrolled at the end of follow-up.

Response rates, symptom burden and QoL

The subgroups of participants with PV and MF had the highest mean symptom burden measured by MPN-SAF TSS and the lowest HRQoL measured by MPN-SAF QoL during the follow-up period. The subgroups of participants with ET and CML had the lowest mean symptom burden and the highest HRQoL. The difference between the four MPN subgroups was significant ($p < 0.01$) (Table 2). The subgroups of participants with PV and MF submitted questionnaires more often than the subgroups of participants with ET and CML. The difference in response rates between the four MPN subgroups was not significant.

Table 1 Differences between groups in demographics, MPN subtype, comorbidity score and connection to hospital

	Declined to participate	Accepted participation	<i>p</i> values for differences	Filling out questionnaires online	Filling out questionnaires on paper	<i>p</i> values for differences	Discontinuation	Filling out questionnaires for >6 month and still enrolled at end of follow-up	<i>p</i> values for differences
Participants (<i>n</i>)	17	118		107	11		14	104	
Age (mean, SD)	62 ± 14	62 ± 12	<i>p</i> = 0.64*	61 ± 12	71 ± 12	<i>p</i> < 0.01*	67 ± 17	61 ± 11	<i>p</i> = 0.08*
<i>Sex (n)</i>									
Female	12 (71 %)	63 (53 %)	<i>p</i> = 0.17**	58 (54 %)	5 (45 %)	<i>p</i> = 0.84**	8 (57 %)	55 (53 %)	<i>p</i> = 0.55**
Male	5 (29 %)	55 (47 %)		49 (46 %)	6 (55 %)		6 (43 %)	49 (47 %)	
<i>Living arrangement (n)</i>									
Living alone	1 (6 %)	26 (22 %)	<i>p</i> = 0.09***	22 (21 %)	4 (36 %)	<i>p</i> = 0.47***	8 (57 %)	18 (17 %)	<i>p</i> < 0.01***
Living with others	16 (94 %)	92 (78 %)		85 (79 %)	7 (64 %)		6 (43 %)	86 (83 %)	
<i>Parenthood (n)</i>									
Yes		107 (91 %)		98 (92 %)	9 (82 %)	<i>p</i> = 0.15***	12 (86 %)	95 (91 %)	<i>p</i> = 0.31***
No		11 (9 %)		9 (8 %)	2 (18 %)		2 (14 %)	9 (9 %)	
<i>Education (n)</i>									
Basic school	6 (35 %)	24 (20 %)	<i>p</i> = 0.14***	18 (17 %)	6 (55 %)	<i>p</i> = 0.39***	6 (42 %)	17 (15 %)	<i>p</i> = 0.33***
Upper secondary or vocational school	5 (29 %)	61 (52 %)		57 (53 %)	4 (36 %)		5 (36 %)	57 (54 %)	
Higher education	6 (35 %)	33 (28 %)		32 (30 %)	1 (9 %)		3 (35 %)	30 (29 %)	
<i>MPN subtype (n)</i>									
ET	4 (24 %)	27 (23 %)	<i>p</i> = 0.77***	27 (25 %)	0	<i>p</i> = 0.94***	4 (29 %)	23 (24 %)	<i>p</i> = 0.41***
PV	5 (29 %)	44 (37 %)		40 (37 %)	4 (36 %)		2 (14 %)	38 (39 %)	
MF	2 (12 %)	21 (18 %)		18 (17 %)	3 (27 %)		3 (21 %)	16 (17 %)	
CML	5 (29 %)	24 (20 %)		20 (19 %)	4 (36 %)		5 (36 %)	17 (18 %)	
MPN unclassified	1 (6 %)	2 (2 %)		2 (2 %)	0		0	2 (2 %)	
Charlson comorbidity index (mean, SD)	1 ± 1	1 ± 1	<i>p</i> = 0.15***	1 ± 1	1 ± 1	<i>p</i> = 0.34***	1 ± 1	1 ± 1	<i>p</i> = 0.47***
Visits in haematological outpatient clinic (<i>n</i>) (mean, SD)		9 ± 7		9 ± 7	7 ± 3	<i>p</i> = 0.27***	4 ± 4	9 ± 7	<i>p</i> < 0.01***
Hospitalizations (<i>n</i>) (mean, SD)		1 ± 1		1 ± 1	1 ± 2	<i>p</i> = 0.50***	1 ± 1	1 ± 1	<i>p</i> = 0.84***

* adjusted for sex; ** adjusted for age; *** adjusted for sex and age

Table 2 Questionnaire response rate, MPN-SAF Total Symptom Score and QoL

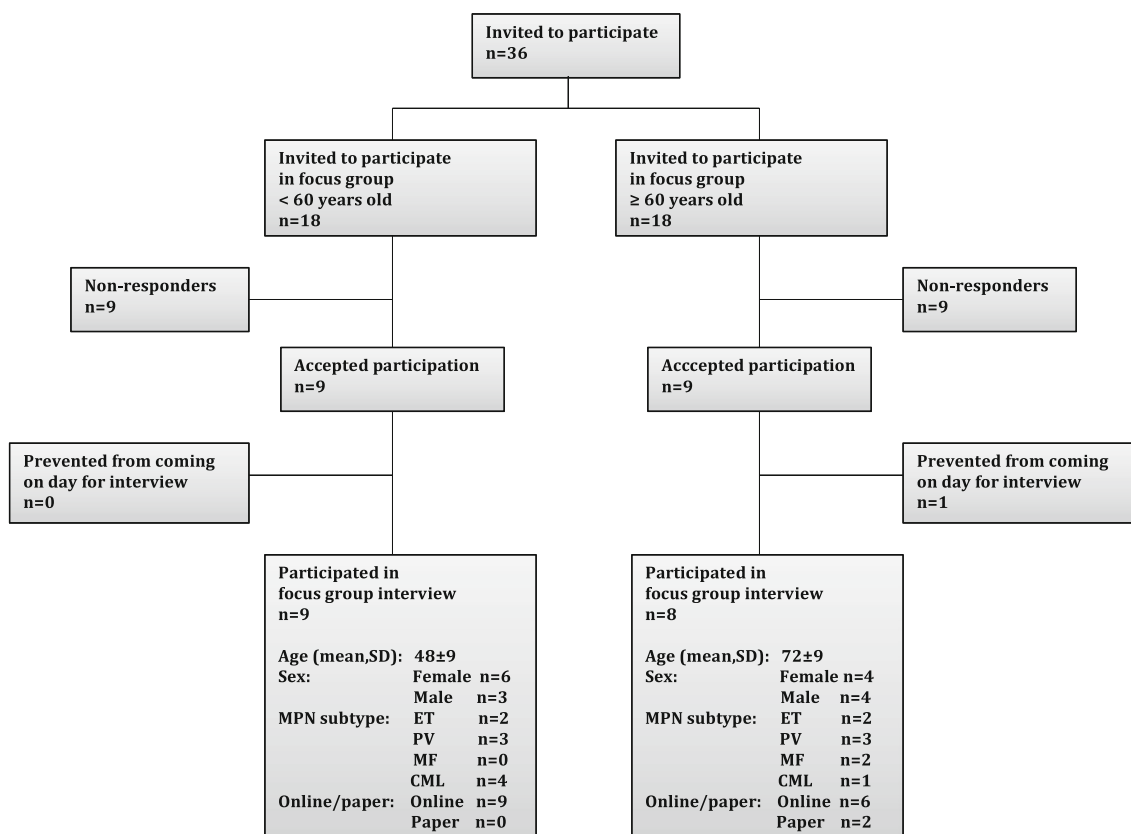
Participants	PV (<i>n</i> = 42)	MF (<i>n</i> = 18)	ET (<i>n</i> = 23)	CML (<i>n</i> = 19)	<i>p</i> value for difference
<i>Questionnaire response rate</i>					
Responded every time	<i>n</i> = 21 (50 %)	<i>n</i> = 7 (39 %)	<i>n</i> = 8 (35 %)	<i>n</i> = 5 (26 %)	<i>p</i> = 0.32
Failed to respond once or twice	<i>n</i> = 14 (33 %)	<i>n</i> = 9 (50 %)	<i>n</i> = 8 (35 %)	<i>n</i> = 7 (37 %)	
Failed to respond >three times	<i>n</i> = 7 (17 %)	<i>n</i> = 2 (11 %)	<i>n</i> = 7 (30 %)	<i>n</i> = 7 (37 %)	
MPN-SAF TSS (mean, SD)	22 ± 19	23 ± 20	20 ± 17	18 ± 16	<i>p</i> < 0.01
MPN-SAF QoL (mean, SD)	3 ± 2	4 ± 2	3 ± 2	2 ± 2	<i>p</i> < 0.01

Differences in response rate for the MPN subgroups were investigated as “responded every time” and “failed to respond once or twice” in contrast with “failed to respond \geq three times”

MPN-SAF TSS is an abbreviated symptom score developed from the questionnaires MPN-SAF and BFI. The nine most clinically relevant symptoms from MPN-SAF and the one most clinically relevant symptom from BFI form MPN-SAF TSS. The participants rated on a 0–10 scale. 0 meant the symptom was absent and 10 meant the symptom was worst imaginable. Thus, the MPN-SAF TSS has a 0–100 scale

MPN-SAF QoL is the answer to the question “What is your overall quality of life?” from the questionnaire MPN-SAF. The participants rated on a 0–10 scale. 0 meant QoL was as good as it could be and 10 meant QoL was as bad as it could be

Because only two participants had a diagnosis of MPN unclassified, these participants were not included in the calculations

**Fig. 4** Flow chart for participation and characteristics of participants in focus groups

Qualitative study

Participants and focus-group composition

Eighteen participants ≥ 60 years old from the population in the quantitative study were invited to participate; nine were

non-responders and nine accepted participation in the focus-group interview (Fig. 4). One participant was unable to participate on the day of the interview because of hospitalization. Eighteen participants < 60 years old were invited to participate; nine were non-responders and nine

Table 3 Answers to the questions and further comments from the participants in two focus-group interviews

	Participants <60 years old in one focus group	Participants >60 years old in another focus group
“How do you think about the number of questions?”	“You get used to it” “Many” “It is good, that you ask the same questions in different ways in case we give the wrong answers”	“I think it is just the right number of questions” (online) “It is important to answer the questions, I think. Some questions seem alike” (online)
“How do you think about asking you the same questions every month?”	“It works fine” “I think it is reassuring in a way” “It is fine” “You just wait for the questionnaires to show up” “One could say that by asking the questions every month, you keep track of the patient’s situation”	“I think it is a good idea. It may not help us, but it may help others” (online)
“Do you find any questions inappropriate?”	“No”	“No” (online, paper) “One of the questions you do not need to answer, right?” (paper)
“Have you experienced technical problems?”	“No”	“No” (online)
Further comments from the participants	“I felt the progression in my disease before the doctors realized it. Before they could read it in the blood values” “I miss a box, where I can write symptoms, you do not ask for in the questionnaires”	“I forget to tell everything to the doctor at the consultation” (online) “I use 45 min to find a parking place, and when I finally reach to the doctor, I feel different than at home” (paper) “My son fills out the questionnaires for me” (online) “I need 5 min to fill out the questionnaires” (online) “I need 10 min” (online) “I need 15–20 min to fill out the questionnaires” (paper) “I need 30 min to fill out the questionnaires” (online) “At the end of the questionnaires it should be possible to write further comments” (paper)

In the focus group with participants <60 years old everyone filled out questionnaires online

Distribution of participants filling out questionnaires online and on paper is written in the parentheses next to the answers in the focus group with participants ≥ 60 years old

accepted participation in the focus-group interview. All were able to participate on the day of the interview. In the group of participants <60 years old, all filled out questionnaires online. In the group of participants ≥ 60 years old, six filled out questionnaires online and two on paper.

Focus-group interviews

All participants assessed the total amount of questions in the questionnaires as acceptable (Table 3). However, one participant rated the number of questions as “many”. They assessed it as acceptable to fill out the questionnaires once a month. One participant mentioned that she made use of the option to leave some questions unanswered on the paper version of the questionnaires. Participants using the

Internet-based tool had not thought of the fact that they did not have the opportunity to leave questions unanswered. No one had technical problems using the Internet-based tool. Most of the participants used 10–20 min to complete the four questionnaires. This applied to both participants who filled out questionnaires online and those who filled out questionnaires on paper as well as the ones <60 years old and the ones ≥ 60 years old. One participant mentioned her visual impairment and explained that her son read the questions aloud from the questionnaires. Then she gave her answers and her son filled out the questionnaires online. There was agreement among the participants that the opportunity to complete the questionnaires at home ensured time and calmness to consider what to answer. There was agreement that it would have been appropriate

to have the opportunity to write a free text for healthcare professionals if the questionnaires did not sufficiently cover current symptoms and health difficulties.

Discussion

To our knowledge, the developed Internet-based tool is the first to enable merging PROs with blood test results and allowing for computation of the treatment response [26–29]. The merging feature brings a new perspective to assessing PROs, describing the extent to which the disease activity read in blood test results and the disease activity read in PROs are linked and thereby providing a robust platform for assessment of response to treatment. Furthermore, to our knowledge the graphical data visualization solution including both a predetermined PRO summary page and the option to visualize selected PROs is a new feature [26–29].

We believe the response rate in the feasibility study was high. The MPN population was willing and able to fill out questionnaires online and to do this regularly. PV and MF participants filled out questionnaires more frequently and had the highest symptom burden and the lowest HRQoL compared with ET and CML participants. It seems reasonable that the more symptoms a patient experiences, the more it may make sense for the patient to communicate the symptoms to healthcare professionals. Importantly, the response regularity advocates that the participants with the highest symptom burden were able to complete the questionnaires frequently. Regardless, we generally have to be cognizant of only asking the patients to submit PROs that are essential for treatment response evaluations that clarify the needs that can be met by healthcare professionals or that otherwise contribute to an optimal situation for the individual patient. The Internet-based tool and the questionnaires were well accepted by the participants in the focus-group interviews. We will meet the desire from the focus-group participants for a write-in free text area for healthcare professionals if the questionnaires do not sufficiently cover the current symptoms and health difficulties of the patients.

All questions in a given questionnaire were mandatory to minimize missing data. When filling out questionnaires on paper, questions may be missed or deliberately skipped. One may argue that it should be possible to skip questions online as well. One participant mentioned that her son filled out the questionnaires due to impaired vision. This demonstrates a dilemma; it is valuable that patients who are unable to fill out PROs themselves are supported by their relatives, but PROs filled out by relatives may be influenced by the relatives' opinions. The Internet-based

tool does not allow the patient to review the submitted PROs because we speculate that a patient may be influenced by earlier submitted PROs.

In this study, the number of participants was relatively small, and we had to consider this when evaluating the differences between groups. The participants filling out questionnaires online received a reminder if the questionnaires were not submitted on day 1. The participants filling out questionnaires on paper did not receive a reminder. The reminder feature (and lack thereof) may have influenced the response rate. This study focused on a single centre, and some participants knew the researchers behind the study, which may have motivated them to participate and fill out questionnaires frequently [30].

We believe that PROs support healthcare professionals in decision-making and in understanding the patient's condition as a whole [1–4]. PROs may reduce misinterpretation by the healthcare professional. Regular collection of PROs may reduce recall bias. Healthcare professionals can receive a larger amount of PROs, more frequently from the patient by asking for submission from home instead of exclusively reporting PROs at visits in the outpatient clinic.

The organizational experiences and experiences from healthcare professionals using the Internet-based tool capturing PROs from MPN patients in the haematological outpatient clinic at Roskilde Hospital, Denmark, will be investigated in the future. The results from the ongoing longitudinal study of symptoms and HRQoL among MPN patients in the outpatient clinic at Roskilde Hospital, Denmark, will follow.

Conclusion

An Internet-based tool for reporting and analysing PROs has been developed for use in clinical practice and clinical trials. The tool was initially developed for MPN patients. A feasibility study revealed that the Internet-based approach and regular collection of PROs was well accepted with a high participation rate, persistency and adaptation in a MPN population. We conclude that the new Internet-based approach and regular collection of PROs suit the MPN population. The platform will allow for adaptation to patients with other medical conditions.

Acknowledgments We thank the participants in this study. The Health Science Research Foundation Of Region Zealand, The Illum Foundation, Einar Willumsen's Memorial Foundation, The Frimodt-Heineke Foundation, Master Carpenter Axel Kastrop-Nielsen and wife Eva Kastrop-Nielsens Foundation and Anders Hasselbalch's Foundation For Combating Leukaemia supported this work. HH, ADZ, CLA and NB provided the study's conception and design. CLA and Danish Telemedicine A/S developed the Internet-based tool. NB pilot-tested the Internet-based tool. NB collected data for the quantitative study. ADZ and NB analysed the quantitative study. MK and

NB conducted and analysed the focus-group interviews. EMF provided the statistical analysis. NB drafted the manuscript. ADZ participated significantly in drafting the manuscript. CLA participated in drafting the manuscript. HH revised the manuscript critically for scientific content. All authors participated in the revision and final approval of the manuscript.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interest.

Ethical standards The Danish Data Protection Agency (SN-6-2012) and The National Committee on Health Research Ethics (SJ-288) approved the study. The participants were informed that participation was voluntary. Written informed consent was obtained in the quantitative study.

References

- Snyder, C. F., Wu, A. W., Miller, R. S., Jensen, R. E., Bantug, E. T., & Wolff, A. C. (2011). The Role of Informatics in Promoting Patient-Centered Care. *Cancer Journal*, *17*(4), 211–218.
- Novik, A., Salek, S., & Ionova, T. (2012). Patient-reported outcomes in patients with hematological disorders: Conceptual issues. In A. Novik, S. Salek, & T. Ionova (Eds.), *Guidelines patient-reported outcomes in hematology* (pp. 19–22). Genoa: Forum service editore.
- Coates, A., Porzsolt, F., & Osoba, D. (1997). Quality of life in oncology practice: Prognostic value of EORTC QLQ-C30 scores in patients with advanced malignancy. *European Journal of Cancer*, *33*(7), 1025–1030.
- Coates, A., Thomson, D., McLeod, G. R., Hersey, P., Gill, P. G., Olver, I. N., et al. (1993). Prognostic value of quality of life scores in a trial of chemotherapy with or without interferon in patients with metastatic malignant melanoma. *European Journal of Cancer*, *29A*(12), 1731–1734.
- Skov, V., Thomassen, M., Riley, C. H., Jensen, M. K., Bjerrum, O. W., Kruse, T. A., et al. (2012). Gene expression profiling with the principal component analysis depicts the biological continuum from essential thrombocythemia over polycythemia vera to myelofibrosis. *Experimental Hematology*, *40*(9), 771–780.
- Scherber, R. M., Geyer, H. L., & Mesa, R. A. (2014). Quality of life in MPN comes of age as a therapeutic target. *Current Hematologic Malignancy Reports*, *9*(4), 324–330.
- Geyer, H. L., Emanuel, R. M., Dueck, A. C., Kiladjian, J. J., Xiao, Z., Slot, S., et al. (2014). Distinct clustering of symptomatic burden amongst myeloproliferative neoplasm patients: Retrospective assessment in 1470 patients. *Blood*, *123*(24), 3803–3810.
- Mesa, R. A., Niblack, J., Wadleigh, M., Verstovsek, S., Camoriano, J., Barnes, S., et al. (2007). The Burden of Fatigue and Quality of Life in Myeloproliferative Disorders (MPDs): An International Internet-based Survey of 1179 MPD Patients. *Cancer*, *109*(1), 68–76.
- Emanuel, R. M., Dueck, A. C., Geyer, H. L., Kiladjian, J. J., Slot, S., Zweegman, S., et al. (2012). Myeloproliferative neoplasm (MPN) symptom assessment form total symptom score: prospective international assessment of an abbreviated symptom burden scoring system among patients with MPNs. *Journal of Clinical Oncology*, *30*(33), 4098–4103.
- Cella, D., Nowinski, C. J., & Frankfurt, O. (2014). The impact of symptom burden on patient quality of life in chronic myeloid leukemia. *Oncology*, *87*(3), 133–147.
- McMahon, B., & Stein, B. L. (2013). Thrombotic and bleeding complications in classical myeloproliferative neoplasms. *Seminars in Thrombosis and Hemostasis*, *39*(1), 101–111.
- Hasselbalch, H. C. (2014). Perspectives on the impact of JAK-inhibitor therapy upon inflammation-mediated comorbidities in myelofibrosis and related neoplasms. *Expert Review of Hematology*, *7*(2), 203–216.
- Abelsson, J., Andréasson, B., Samuelsson, J., Hultcrantz, M., Ejerblad, E., Johansson, B., et al. (2013). Patients with polycythemia vera have worst impairment of quality of life among patients with newly diagnosed myeloproliferative neoplasms. *Leukaemia & Lymphoma*, *54*(10), 2226–2230.
- Trask, P., Cella, D., Powell, C., Reisman, A., Whiteley, J., & Kelly, V. (2013). Health-related quality of life in chronic myeloid leukemia. *Leukemia Research*, *37*(1), 9–13.
- Johansson, P., Mesa, R. A., Scherber, R., Abelsson, J., Samuelsson, J., Birgegaard, G., et al. (2012). Association between quality of life and clinical parameters in patients with myeloproliferative neoplasms. *Leukaemia & Lymphoma*, *53*(3), 441–444.
- European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30. <http://groups.eortc.be/qol/eortc-qlq-c30>. Last assessed June 2015.
- Scherber, R., Dueck, A. C., Johansson, P., Barbui, T., Barosi, G., Vannucchi, A. M., et al. (2011). The Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF): International Prospective Validation and Reliability Trial in 402 patients. *Blood*, *118*(2), 401–408.
- Short Form 36 Health Survey. <http://www.sf-36.org/tools/SF36.shtml>. Last assessed June 2015.
- European Organisation for Research and Treatment of Cancer Questionnaire Translation Manual. <http://groups.eortc.be/qol/manuals>. Last assessed June 2015.
- Barbui, T., Barosi, G., Birgegaard, G., Cervantes, F., Finazzi, G., Griesshammer, M., et al. (2011). Philadelphia-negative classical myeloproliferative neoplasms: critical concepts and management recommendations from European LeukemiaNet. *Journal of Clinical Oncology*, *29*(6), 761–770.
- Jabbour, E., & Kantarjian, H. (2012). Chronic myeloid leukemia: 2012 update on diagnosis, monitoring, and management. *American Journal of Hematology*, *87*(11), 1037–1045.
- Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases*, *40*(5), 373–383.
- Satu, E., & Kyngäs, H. (2008). The qualitative content analysis process. *Journal of Advanced Nursing*, *62*(1), 107–115.
- Catanzaro, M. (1988). Using qualitative analytical techniques. In N. F. Woods & M. Catanzaro (Eds.), *Nursing research: Theory and practice*. C.V. Mosby: St Louis, MO.
- Kitzinger, J. (1995). Introducing focus groups. *BMJ*, *311*(7000), 299–302.
- Jensen, R. E., Snyder, C. F., Abernethy, A. P., Basch, E., Potosky, A. L., Roberts, A. C., et al. (2014). Review of electronic patient-reported outcomes systems used in cancer clinical care. *Journal of Oncology Practice*, *10*(4), e215–e222.
- Bush, N., Donaldson, G., Moinspour, C., Haberman, M., Milliken, D., Markle, V., et al. (2005). Development, feasibility and compliance of a web-based system for very frequent QOL and symptom home self-assessment after hematopoietic stem cell transplantation. *Quality of Life Research*, *14*(1), 77–93.
- Bliven, B. D., Kaufman, S. E., & Spertus, J. A. (2001). Electronic collection of health-related quality of life data: Validity, time benefits, and patient preference. *Quality of Life Research*, *10*(1), 15–22.

-
29. Hjollund, N. H. I., Larsen, L. P., Biering, K., Johnsen, S. P., Riiskjær, E., & Schougaard, L. M. (2014). Use of patient-reported outcome (PRO) measures at group and patient Levels: Experiences from the generic integrated PRO system, WestChronic. *Interactive Journal of Medical Research*,. doi:[10.2196/ijmr.2885](https://doi.org/10.2196/ijmr.2885).
30. Reeve, B. B., Wyrwich, K. W., Wu, A. W., Velikova, G., Terwee, C. B., Snyder, C. F., et al. (2013). ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. *Quality of Life Research*, 22(8), 1889–1905.