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Perceived Burden of Completion of Patient-Reported Outcome Measures in Clinical Trials: Results of a Preliminary Study

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Abstract

Background: Understanding the perceived burden of clinical trial participation is an important element of patient-centric trial design and conduct.

Methods: We report the results of a study to gain preliminary insights into the perceived burden associated with patient-reported outcome (PRO) data collection among a sample (n = 61) of volunteers from the general population including people with various health conditions resulting in chronic pain.

Results: Participants identified morning completion as more burdensome than completion of PRO measures in the evening. Weekly completion was perceived as less burdensome than daily, and twice-a-day more burdensome than once-a-day.

Conclusion: Our results, while not generalizable in isolation, provide a valuable starting point to understand the complex construct of subject burden. This preliminary work is intended to be a catalyst for more in-depth research to better understand and predict burden and acceptable burden thresholds in clinical trials. Understanding subject burden is a vital component of human subject research that will be valuable in helping to inform future clinical trial designs.

Keywords

subject burden, patient-reported outcome, patient-reported outcome measure, PRO, PROMs

Background

Fundamental to all ethical clinical research is the protection of human subjects. A component of this is to ensure that any clinical research study aims to minimize the burden placed on study participants.[1] Both perceived benefit and perceived burden influence subject recruitment and retention in clinical trials.[2] At a high level, the dimensions of benefit and burden have been suggested to encompass physical, psychological, economic, familial, and social components.[2]

Burden of participation in a clinical trial is a holistic composite of multiple factors that include the direct risk of participation, including treatment side effects and adverse events, and aspects of inconvenience such as study duration; location, frequency, and duration of clinic visits; the invasiveness of clinical procedures; the frequency and route of administration of medication; and the requirements to collect and record data outside clinic visits—such as completion of patient-reported outcome measures (PROMs) and the use of wearable devices in nonclinic or field-based settings (eg, subject's home, school, or workplace).

While it is unknown how the burden of individual study elements contributes to the overall perception of study burden, it is valuable to begin by assessing burden associated with certain study elements as we strive to make trial participation more convenient and patient-centric. The focus of this preliminary work is on the length and frequency of PROM completion.

The collection of PRO data is increasingly a component of clinical trials and typically involves the self-completion of PROMs at clinic visits or remotely by study subjects. Completion is sometimes performed on paper or via an electronic medium such as a smartphone or tablet computer. The perceived burden of regular PROM completion in clinical trials is currently poorly understood, and yet this knowledge may be valuable to inform future study design. Minimizing subject

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burden is also one of the strategies suggested to reduce missing data,[3] where missing PRO data create challenges for data analysis and can compromise the interpretability and value of study findings.

In this study, we collected preliminary ratings of perceived burden in PROM completion by a sample of participants taking part in a larger PROM equivalence study.

Methods

Participants based in the UK aged 18 years or older, at least 50% of whom had a chronic health condition resulting in pain, were invited to participate in this single-center, single-visit study. Sample diversity was sought with respect to age, sex, and education level. Participants provided written informed consent to participate.

The subject burden evaluation was included as a component of a larger measurement equivalence study in which participants were requested to complete a PROM on 3 occasions on paper and different electronic modes of administration during the same clinic visit, each administration separated by a short washout period. On completion of the main study tasks, participants were asked if they would be willing to complete a questionnaire that sought their opinions on the perceived burden of completing questionnaires as part of a clinical trial.

The subject burden questionnaire took approximately 5 minutes to complete and was completed in paper format. The burden questionnaire explained the use of PROMs in clinical trials and explained that questionnaires used in clinical trials often take the same form as the PROM featured in the equivalence study. In completing the burden questionnaire, participants were asked to assume that they have been invited to complete health questionnaires within a clinical trial for a 3-month time period. The burden questionnaire asked participants

- whether they had participated in a clinical trial previously;
- to rate their perceived burden of PROM completion every morning, every evening, every morning and evening, or weekly for different length PROMs for a period of 3 months (using an 11-point numeric rating scale where 0 represented "not at all a burden" and 10 represented "an extreme burden");
- to select 3 factors that most contribute to the burden of completing PROMs in clinical trials, from a list of options; and
- to provide any additional factors contributing to PROM completion burden.

Subject burden questionnaire data were reported using summary statistics, and differences in burden scores between morning, evening, and morning and evening completion were assessed using the Wilcoxon signed ranks test using IBM SPSS Statistics for Windows, version 26 (IBM Corp, Armonk, NY).[4]

Table 1. Baseline Participant Demographics (N = 61).[a]

Variable	
Age	
Range	18-77
Mean (SD)	49.5 (15.8)
Sex	
Female	48 (78.7)
Male	13 (21.3)
Racial group	
Black	2 (3.3)
Asian	5 (8.2)
White	54 (88.5)
Education	
Left school with no qualifications	2 (3.3)
GCSE or equivalent	8 (13.1)
A Level or equivalent	8 (13.1)
College/technical college	11 (18.0)
University: Undergraduate level	20 (32.8)
University: Postgraduate level	12 (19.7)
Disease indication	
No known significant health problems	30 (49.2)
Cancer pain	1 (1.6)
Endometriosis	1 (1.6)
Fibromyalgia	2 (3.3)
Joint / back pain	5 (8.2)
Migraine	2 (3.3)
Multiple sclerosis	4 (6.6)
Osteoarthritis	4 (6.6)
Rheumatoid arthritis	5 (8.2)
Other	7 (11.5)

Abbreviation: GCSE, General Certificate of Secondary Education.
[a]Values are n (%) unless otherwise noted.

Results

Sixty-one participants aged 18 to 77 years (mean = 49.5; SD = 15.8 years) were enrolled in the study, and all completed the subject burden questionnaire. Seventy-nine percent (48/61) were female. Most participants (54/61, 88/5%) were white, with a further 5 participants (8.2%) Asian and 2 participants (3.3%) black. Over half of the participants (32/61, 52.5%) had completed either an undergraduate or postgraduate degree, with 11 participants (18.0%) attending college/technical college. Almost half of the participants were healthy volunteers (30/61). The remaining participants suffered from a range of conditions resulting in chronic pain, including joint and back pain (5/61), multiple sclerosis (4/61), osteoarthritis (4/61), and rheumatoid arthritis (5/61) among other conditions (Table 1). Nineteen participants (31.1%) had previously participated in a clinical trial.

Perceived burden scores increased with the length of time for PROM completion (Table 2, Figure 1). The same length of daily questionnaire was perceived as significantly less burdensome when completed in the evening in comparison to the morning based on the Wilcoxon signed ranks test (Table 3). For example, on the 0 to 10 scale (where 0 represented "Not at all a burden" and 10 represented "An extreme burden"),

Table 2. PROM Completion Burden Ratings.

Variable	PROM completion burden rating (0 = not at all a burden to 10 = extreme burden)		
	Range	Median	Mean (SD)
Morning completion for 3 mo			
1-min questionnaire	0-10	0	1.3 (2.5)
2-min questionnaire	0-10	0	1.5 (2.5)
5-min questionnaire	0-10	3	3.1 (2.7)
10-min questionnaire	0-10	5	4.9 (2.8)
15-min questionnaire	0-10	7	6.5 (2.9)
20-min questionnaire	0-10	9	7.8 (2.9)
Evening completion for 3 mo			
1-min questionnaire	0-10	0	1.1 (2.4)
2-min questionnaire	0-10	0	1.2 (2.3)
5-min questionnaire	0-10	1	2.1 (2.4)
10-min questionnaire	0-10	4	3.8 (2.6)
15-min questionnaire	0-10	5	5.3 (3.0)
20-min questionnaire	0-10	7	6.5 (3.1)
Morning and evening completion for 3 mo			
1-min questionnaire	0-10	0	2.1 (3.0)
2-min questionnaire	0-10	0	2.4 (2.9)
5-min questionnaire	0-10	3	3.9 (3.1)
10-min questionnaire	0-10	5	5.6 (3.0)
15-min questionnaire	0-10	7	7.1 (2.9)
20-min questionnaire	0-10	9	7.9 (2.9)
Once-a-week completion for 3 mo			
5-min questionnaire	0-10	0	0.8 (1.7)
10-min questionnaire	0-10	0	1.0 (1.8)
15-min questionnaire	0-10	2	1.8 (2.1)
20-min questionnaire	0-10	2	2.7 (2.6)
25-min questionnaire	0-10	4	4.0 (2.9)
30-min questionnaire	0-10	5	4.9 (3.2)

Abbreviation: PROM, patient-reported outcome measure.

median scores for completion of a 5-minute daily PROM were 3 for morning completion, compared to 1 for evening completion (Table 2). In all cases, burden scores for twice-a-day (morning and evening) completion were higher than morning only completion, and statistically significant for all completion times except for the longest time assessed—20 minutes (Table 3). In addition, evening completion was considered significantly less burdensome in comparison to morning only and twice-a-day (morning and evening) completion (Table 3).

Weekly completion was considered least burdensome, with median burden scores not exceeding 5 at the longest completion time of 30 minutes, and median scores of 2 or less for 20-minute and lower completion times (Table 2).

The difference in mean burden scores between participants suffering from chronic pain conditions (n = 31) and healthy volunteers (n = 30) was explored visually (Figure 2). In general, higher perceived burden scores were recorded more frequently among the participants with chronic pain conditions compared to healthy volunteers.

When asked to select the 3 factors that most contribute to the burden of PROM completion, completion time and frequency were the most commonly reported—both by 41 participants (67.2%). The number of weeks of completion was identified as a burden factor by 27 participants (44.3%). Feeling unwell or anxious at the time of PROM completion was identified as an important contributor to burden by 22 participants (36.1%). Six participants (9.8%) identified that completion of a PROM on a smartphone or tablet would add burden; and 4 participants (6.6%) identified completion on paper as adding to PROM burden (Table 4).

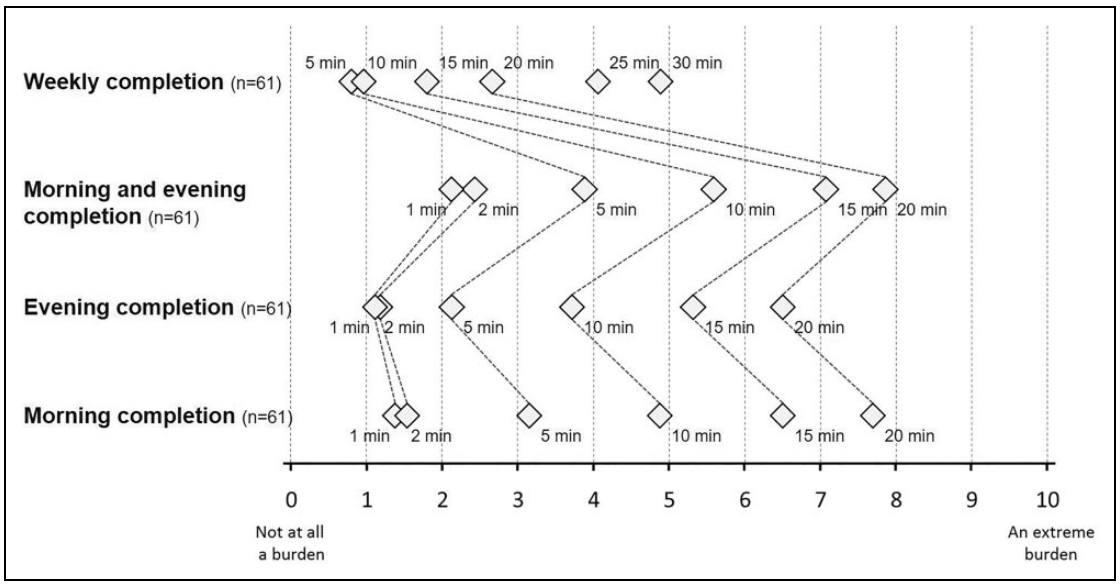

Figure 1. Mean perceived burden scores by completion time.

Table 3. Statistical Analysis of Differences in Burden Scores Between Morning, Evening, and Morning and Evening PROM Completion.

	Am vs pm		Am vs (am and pm)		Pm vs (am and pm)	
Completion Time (min)	Mean Difference (SD)	*P*	Mean Difference (SD)	*P*	Mean Difference (SD)	*P*
1	0.25 (0.79)	.015	-0.80 (1.45)	<.001	−1.05 (1.63)	<.001
2	0.34 (0.98)	.008	−0.90 (1.54)	<.001	−1.25 (1.71)	<.001
5	1.03 (1.96)	<.001	−0.82 (1.62)	.001	−1.85 (2.18)	<.001
10	1.15 (2.17)	<.001	−0.72 (1.78)	.002	−1.87 (2.03)	<.001
15	1.26 (2.03)	<.001	−0.52 (1.53)	.009	−1.79 (1.92)	<.001
20	1.23 (2.16)	<.001	−0.13 (1.73)	.092	−1.36 (1.95)	<.001

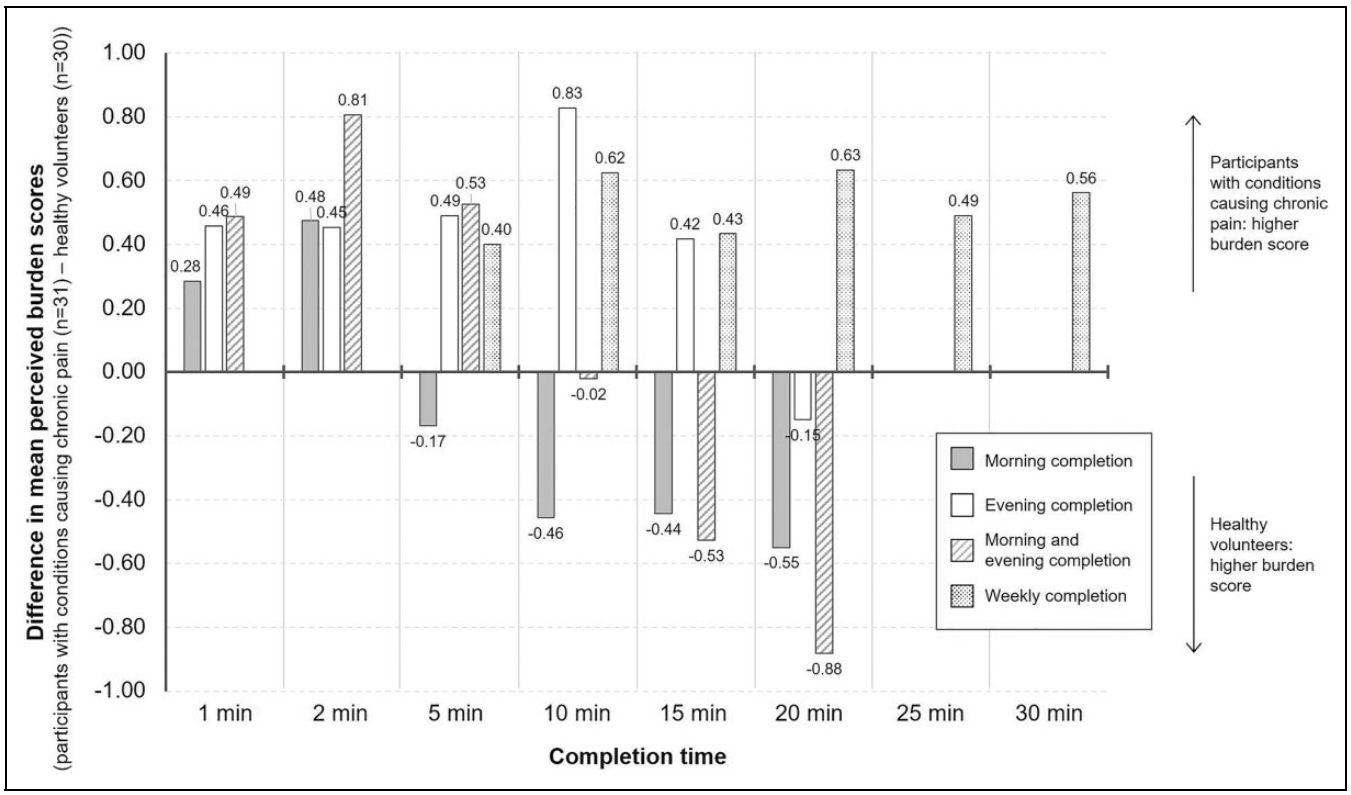

Figure 2. Difference in perceived burden in PROM completion between participants suffering from conditions causing chronic pain and healthy volunteers. PROM, patient-reported outcome measure.

When asked to identify any additional factors that impact the burden of completing health questionnaires regularly as part of a clinical trial (in addition to those rated in the earlier question), 18 (30%) participants provided no answer and 28 (46%) participants reported they could not identify any additional burden factor. Factors identified by the remaining participants included fatigue (2 [3%] participants), unavailability due to holidays (3 [5%] participants), restrictions imposed by completion time windows (5 [8%] participants), instrument terminology or design (5 [8%] participants), forgetting to complete the PROM on time (5 [8%] participants), being inadequately compensated for completion (3 [5%] participants), and technology concerns such as slow Internet or needing to use voice-activated software (2 [3%] participants]) (Table 5).

Discussion and Conclusions

This study aimed to provide preliminary information regarding the perceived burden associated with PROM collection in clinical trials. In isolation, our results provide a starting point to begin to understand this complex construct. This study sample considered evening completion less burdensome than morning completion when PROM completion times were identical and twice-daily completion more burdensome than once a day. If we were to assign an arbitrary median burden score of 4 as an acceptable threshold, we might conclude that the following completion times would be acceptable: 5 minutes for morning completion, 10 minutes for evening completion, 5 minutes for morning and evening completion, and 25 minutes for weekly completion.

Table 4. Factors Important in PROM Completion Burden (N = 61).

Factor	n (%)
The time I would need to complete the questionnaires	41 (67.2)
How often I would need to complete the questionnaires	41 (67.2)
The number of weeks I will need to continue completing the questionnaire for	27 (44.3)
If I am feeling unwell or anxious at the time I am asked to complete the questionnaire	22 (36.1)
The questions are difficult to understand or use terms I don't understand	19 (31.1)
The number of questions I need to answer each time	17 (27.9)
The questionnaires have to be completed on a smartphone or tablet	6 (9.8)
The questionnaires have to be completed on paper	4 (6.6)
I am asked to complete the questionnaires without any help	2 (3.3)

Table 5. Additional Burden Factors Reported by Participants (N = 61).

Factor	n (%)
Not answered	18 (30)
Answered	43 (70)
No additional factor	28 (46)
Fatigue	2 (3)
Holidays or breaks	3 (5)
Prescribed completion times (time windows)	5 (8)
Questionnaire terminology / design	5 (8)
Forgetfulness	5 (8)
Compensation for completion	3 (5)
Technology concerns	2 (3)

However, while our study provides interesting preliminary data in this area, generalization of these results to inform trial design is more problematic. Actual study burden is a multifaceted construct, and we do not understand the impact of individual components to the overall perceived burden of trial participation. In addition, while our study included both participants with conditions resulting in chronic pain and those with no known significant health problems, the burden of any aspect of trial participation is highly dependent on the specific patient population studied. Visual inspection of the mean burden scores reported in our study indicated that higher scores were reported more frequently among the participants with chronic pain conditions compared to healthy volunteers. While not a conclusion from the data in this study, the impact of the disease indication can affect the burden PROM completion places on an individual. Palliative care patients, for example, may feel less able to complete PROMs that are not used to inform or adjust their individual treatment. Participants less engaged with the study aims and objectives, and less attached to the value their data may bring to others with the same condition, may have a lower threshold for any burden associated with PROM completion.

A further limitation of our study was the lack of validation of the burden questionnaire developed to obtain the preliminary data reported. While aimed at assessing simple constructs related to the frequency and duration of completion, and other aspects of subject burden associated with PROM completion, we did not independently assess whether participants interpreted the individual burden questionnaire items in the ways intended. However, the results of the study show good face validity, which provides some support that the burden questionnaire is associated with reasonable measurement properties.

While this study has provided some confirmation that completion duration, frequency, and patient population, may be important factors in PROM completion burden, these preliminary data do not support definitive recommendations. More valuable would be the collection of perceived burden measures during study design, such as using the Perceived Research Burden Assessment (PeRBA) instrument,[1] or during clinical trial conduct using study-specific probes. Conducting trial exit interviews among subjects exiting the trial may also allow for in-depth examination of the subject's experience completing PROMs during the trial and factors that influence perceptions of burden as well as compliance with PROM completion. Such data, collected in a standardized manner using a burden assessment questionnaire, may begin to provide a comprehensive picture when applied across a collection of clinical trials.

While it is possible that the complex measurement administrations required by the main equivalence study may affect the perceived burden in PROM completion among the participants, the measure studied in the equivalence study was a very short PROM containing only 6 items, and so we believe that the potential for completion fatigue affecting the perceived burden scores reported is minimal.

Understanding participant burden is an essential factor in the design of patient-centric trials and in encouraging patient recruitment and retention. It could also help limit the quantity of missing data and contribute to data quality overall. Our study is intended to be an initial contribution to this understanding; more in-depth research is encouraged to better comprehend and predict burden and acceptable burden thresholds in clinical trials.

Declaration of Conflicting Interests

Ms Eremenco reports nonfinancial support from CRF Health, Inc, grants from AbbVie, grants from Amgen, grants from Shire, from Gilead Sciences, grants from ERT Inc, non-financial support from Janssen, grants from Bracket, grants from Pfizer, grants from iCardiac, outside the submitted work. Mr Bodart reports personal fees from Biomedical Systems, during the conduct of the study; personal fees from Biomedical Systems, outside the submitted work. Ms Flood reports other from Icon, during the conduct of the study.

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Ethical Approval

The study was approved by the Salus Institutional Review Board, Austin, Texas.

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