

Original Research Article

Errors in answering migraine patient-reported outcome measure questions: patients consider training necessary in clinical trials

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Received: 10 June 2019

Accepted: 26 June 2019

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ABSTRACT

Background: In migraine clinical trials, patients' understanding of the terminology used in patient-reported outcome (PRO) measures is important as variability in completing PRO measures can reduce the power to detect treatment efficacy. This study examines patients' understanding of how to complete PRO measures in the absence of training, if minimal training can improve the accuracy of answering PRO items, and patients' opinion on the necessity of training and their preference for the method of training.

Methods: Participants reporting a diagnosis of migraine completed online surveys. Participants were given scenarios of how to report headache days and pain severity. Respondents were asked about their opinions on the necessity of training, and their preference for the method of training. In a second study, participants were given a hypothetical scenario on how to report pain severity before and after a short training.

Results: The majority of participants had different criteria to interpret PRO questions and provided incorrect answers to our scenarios. In the second study, with minimal training, errors were reduced by 7.5%. Over 90% of participants viewed educational materials and training as necessary and preferred electronic modes of training with the ability to review training materials as needed for the duration of the trial.

Conclusions: Patient training may improve data quality and inter-rater reliability in clinical trials. Electronic interactive training could be used as an approach to reduce inconsistencies in PRO measures and improve data quality.

Keywords: Patient-reported outcome, Study participant training, Migraine

INTRODUCTION

In clinical trials assessing the treatment efficacy of migraines, patient-reported outcomes (PROs) are often the primary endpoints. These endpoints include headache days and pain severity and are often recorded in daily diaries.¹ Inconsistencies can arise when patients do not have an understanding of the terminology or instrument scale. As a result, variability in completing these PRO measures can reduce the power to detect treatment efficacy. One of the objectives of this study is to examine patients' understanding of how to complete PRO measures.

Migraine, a chronic neurovascular disorder, is characterized by severe headache that usually presents with throbbing, unilateral pain, nausea, and sensitivity to light and/or sound. Migraines can last from 4 to 72 hours and can be exacerbated by physical activities. The prevalence of migraine in adults in the United States and worldwide is estimated to be 11-15%, while the prevalence in children and adolescents is 5%.^{2,3} Migraine headache are one of the leading causes of outpatient and emergency department visits and disability according to the Global Burden of Disease Study 2013 Collaborators.⁴

Clinical trials for migraine often use changes in the duration and/ or frequency of migraine headaches as primary or secondary endpoints, along with symptoms including nausea, photophobia, and phonophobia. However, without training, patients may not always define days with a headache in the same way. For example, a patient may count a day as a 24 hour period. That patient is likely to report a headache that begins at 8:00 pm in the evening and lasts through 8:00 am the next morning, as one headache day. On the other hand, a patient who counts a day based on the 24 hour clock may count the same headache duration as a headache that lasted two days. Inconsistent and unreliable headache-day interpretations pose a significant risk towards the quality of data collection and may compromise the results of the clinical trials. In this study, we examined migraine patients' understanding of how to count a headache day to determine if there are variability in their determination of a headache day.

Another endpoint in migraine trials is reporting pain severity. However, patients may interpret the question in a variety of ways. For example, a question that asks patients to rate their pain severity in the last day could be interpreted as average pain over the whole day, pain at the time they are responding to the question, or pain at its worst for the day. If data are unreliable, due to variability resulting from subject interpretation errors, results will be unreliable.

Accordingly, regulatory agencies recommend patient training to improve data quality and minimize inconsistencies in clinical trials. The FDA PRO Guidance and the European Medicines Agency's reflection paper specify that training and instructions be given to patients for self-administered PROs.⁶ However, patients' opinion regarding the necessity of the training and their preference for the method of training has rarely been explored.

The current two studies were undertaken to help determine (1) whether in the absence of training or instruction, people would use the same criteria to interpret questions about headache days and pain severity; (2) if even minimal training or instructions can improve the accuracy of answering PRO items, and (3) examine patients' opinion on the necessity of training and their preference for the method of training.

METHODS

Study 1

Study participants were recruited via an online patient recruitment resource and reported being diagnosed with a history of migraine. Participants completed the questionnaire via an online survey and provided their responses in a multiple choice format. Demographic data including age, gender, education, income, as well as whether they have ever participated in clinical trials were

also collected. Respondents were able enter a raffle for a \$100 gift card.

To assess participants' understanding of how to count and report headache days, they were given the following scenario of an overnight headache: "If you were participating in a clinical trial that asked you to report how many days you had a headache in a week and you had a headache from 8:00 pm Sunday night to 8:00 am Monday morning" and asked "does it count as 1 or 2 days with a headache?" They were provided the following response options:

- 1 day. The sum of hours that I had a headache is fewer than 24.
- 2 days. I had a headache on Sunday and Monday (correct answer).
- It depends on how bad my headache was at each occurrence. I would need more information to answer this question.
- How to count this depends on many factors and I do not have enough information to answer this question.

To examine participants' understanding of how to report pain severity, respondents were asked the following question: "If you were participating in a clinical trial that asked you to report how severe your pain was on a daily basis, you should report?" Respondents were given the following response options:

- Average the pain you had throughout the day and report the average.
- The pain level that you are experiencing when you record the pain rating.
- The pain level at its worst point (correct answer).

To evaluate participants' opinions regarding the necessity of training, preferred training material format, and importance of accessibility of the training for the duration of the trial, participants were asked the following questions:

- "If you were participating in a clinical trial, do you think it would help to be provided educational materials and training on your role in it, what to expect and the purpose of the clinical trial?"
- "If you were participating in a clinical trial and educational information and training was provided to you on your role and what to expect in a clinical trial, which format would you most prefer to take the training?"
- "If you were participating in a clinical trial and educational information and training was provided to you about your role and what to expect in a clinical trial, is it important to you to have access to this training at any time during the trial, so you could refresh on it?"

Participants were also asked how they would handle questions that may arise when completing a PRO

measures during a clinical trial with the following question: “If you participated in a clinical trial and the doctor asked you to complete a questionnaire every day for 6 months and you had questions about how to respond to a particular question, what would you do?”

Study 2

To examine whether training would improve the accuracy of responses, a second group of study participants were recruited via an online patient recruitment resource. Participants who reported being diagnosed with a history of migraine completed an online survey and provided their responses in a multiple choice format. Demographic data were also collected in this second study.

Participants were given the following scenario and asked to select answers to the situational questions.

“You are participating in a clinical trial that asks you to rate your pain by selecting the one number that best describes your pain at its worst in the last 24 hours (0=no pain, 10=worst pain you can imagine). If your pain changed throughout the day (9 in the morning, 5 at noon, 1 in the evening when you’re completing your report), you should report.” Respondents were given the following response options:

- 1
- 5
- 9 (correct answer)

Participants were then presented with minimal training information, which consisted of the following: “When reporting your worst pain was on a daily basis, you should rate how severe your pain was at its worst point during the day. You should not average your pain over the day or report your pain level at the moment you are answering, but rather consider your pain level at its highest point that day.” Participants were presented with the same scenario and question.

RESULTS

Study 1

Demographics

74 participants reported being diagnosed with migraines and completed the survey questions. The average age of participants was 42.7, with a standard deviation of 14.4 (Table 1). Age ranged from 16 years to 80 years. 90.5% of participants were female and 9.5% were male. The majority of participants (54.1%) reported that the highest level of education attained were a technical degree or some college. 1.4% of participants attained some high school, 14.9% high school degrees or GED, 18.9% college degrees, and 10.8% advance degrees. 23.3% of participants reported a household income of below \$20,000, 38.4% reported income of \$20,000-49,000,

30.1% reported a household income of \$50,000-99,000, and 8.2% reported \$100,000 or above.

Table 1: Demographics for study 1 and study 2.

	Study 1 (n=74)		Study 2 (n=120)	
Gender	Count	%	Count	%
Female	67	90.5	109	90.8
Male	7	9.5	11	9.2
Age	Mean (SD)	Range	Mean (SD)	Range
	42.7 (14.4)	16-80	41.3 (13.6)	18-72

Accuracy in answering PRO items

In recording headache days, only 20.3% of participants answered the question correctly by selecting “2 days. I had a headache on Sunday and Monday”. The majority of respondents (60.8%) selected “1 day. The sum of hours that I had a headache is fewer than”. 17.9% of respondents either chose “It depends on how bad my headache was at each occurrence. I would need more information to answer this question”, or “How to count this depends on many factors and I do not have enough information to answer this question”. In regards to prior experience in clinical trials, 20.3% of participants reported they had participated in clinical trials before. Of those participants, only 20.0% answered the question correctly.

In reporting pain severity, more people chose the wrong answer by selecting “Average the pain you had throughout the day and report the average,” (44.6%) or “the pain level that you are experiencing when you record the pain rating” (13.5%). 41.9% people of respondents answered correctly and chose “The pain level at its worst point” (Figure 2). Respondents with prior participation in clinical trials performed better on this item, 60.0% selected the correct response.

When participants were asked what they would do should they have questions about how to complete a particular study question, 58.1% stated they would ask the trial doctor, while 32.4% reported they would look up information online or in reference materials. 9.5% indicated they would read the question a couple of times and try to pick the best answer.

Training preferences

93.2% of participants considered educational materials and patient training necessities in clinical trials, with 71.2% of participants reporting that they were “definitely needed” and 21.9% stating that they were “somewhat needed”. 5.5% and 1.4% of participants indicated that training was “not necessary” and did “not want any educational information or training”, respectively.

With respect to the mode of the training, 62.2% of participants indicated that they preferred to complete electronic interactive training videos, with 40.5%

choosing to watch on the training on the internet and 21.6% choosing to view it on mobile electronic devices such as smartphones and tablets (Figure 4). On the other hand, 33.8% of participants preferred having paper guides to take home. 4.1% of participants stated that they “would not want any educational information or training”.

87.8% of participants also believed that having access to the training material, in order to refresh on the information, for the duration of the trial to be “definitely needed” or “somewhat needed” (51.4% and 36.5%, respectively). 12.2% of participants indicated that training was “not necessary”.

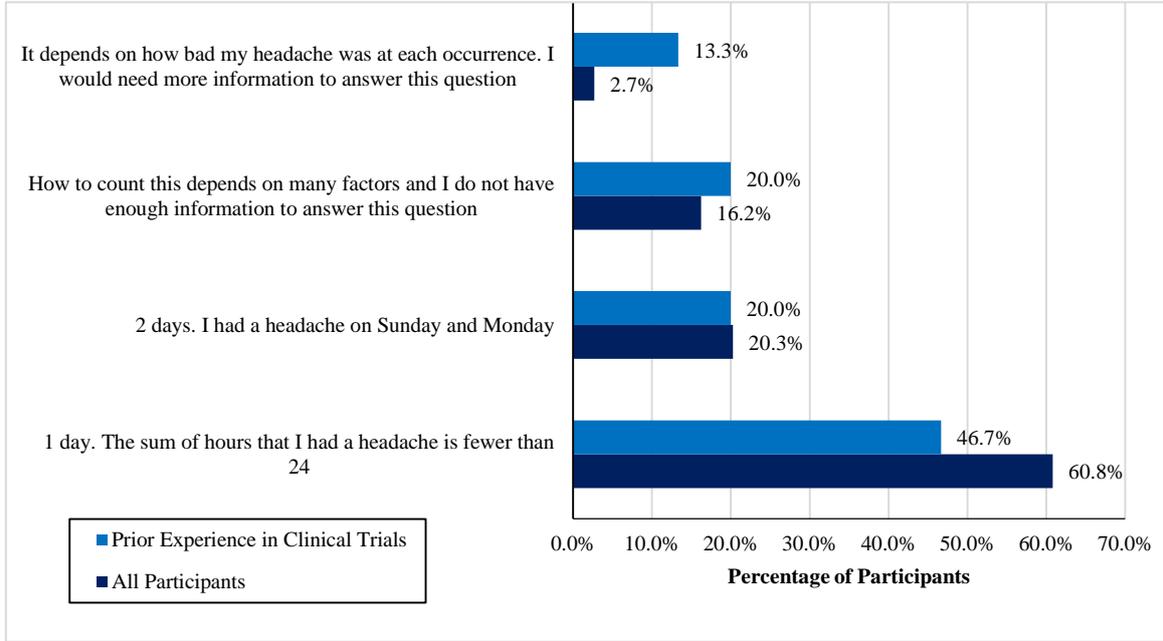


Figure 1: Counting and reporting headache days.

Percentage of participants who chose the correct response “2 days”. Comparison between participants who had prior participation in a clinical trial and participants who did not.

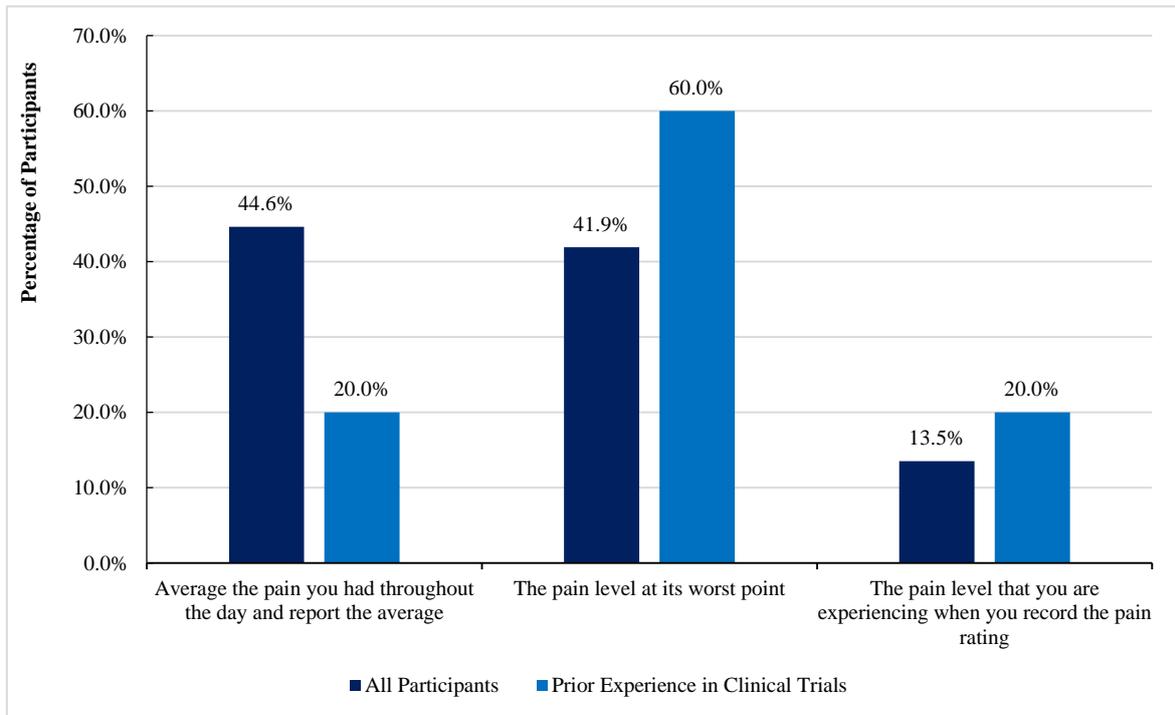


Figure 2: Reporting pain severity.

Percentage of participants who chose the correct response “Pain level at its worst point”. Comparison between participants who had prior participation in a clinical trial and participants who did not.

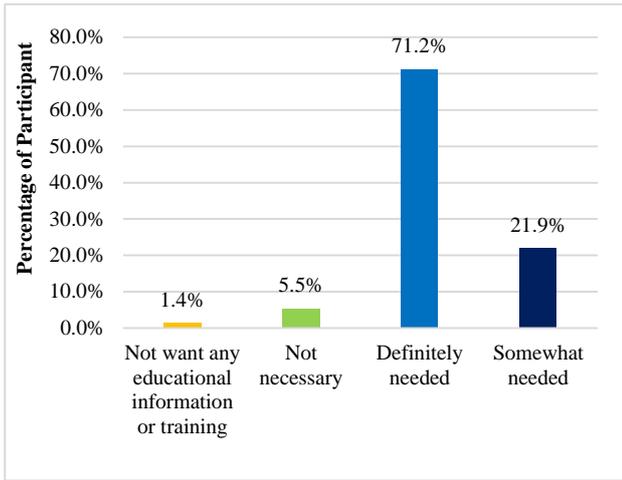


Figure 3: Participant’s opinion on the necessity of educational materials and training in clinical trials.

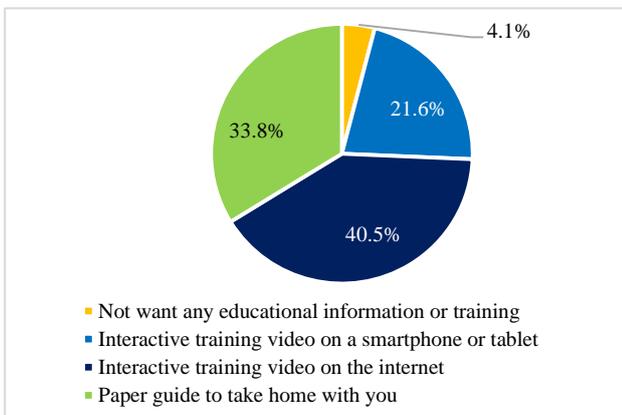


Figure 4: Participants’ preference for mode of training.

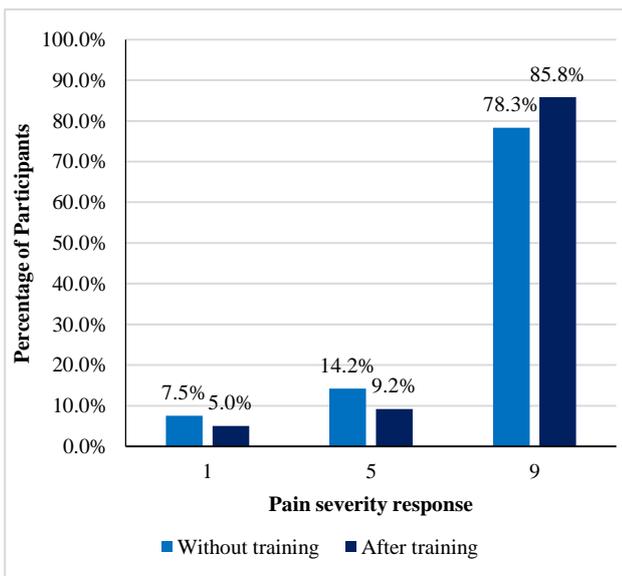


Figure 5: Accuracy in reporting pain severity before and after reading training instructions.
Percentage of participants who chose the correct response “9”.

Study 2

Demographics:

120 respondents with migraines participated in Study 2 and completed the survey questions. The average age of participants was 41.3, with a standard deviation of 13.6 (Table 1). Age ranged from 18 years to 72 years. 90.8% of participants were female and 9.2% were male. The majority of participants (53.3%) reported that the highest level of education attained were a technical degree or some college. 1.7% of participants attained some high school, 19.2% high school degrees or GED, 22.5% college degrees, and 3.3% advance degrees. 35.0% of participants reported a household income of below \$20,000, 40.8% reported income of \$20,000-49,000, 16.7% reported a household income of \$50,000-99,000, and 7.5% reported \$100,000 or above.

Accuracy in answering PRO items without and with training:

In reporting pain severity without training, 78.3% of the participants selected option 9 to indicate their worst pain severity (Figure 5). On the other hand, a total of 21.7% selected incorrect responses. After the respondents were given training information, 85.8% selected option 9, while 14.2% selected incorrect responses. This shows a reduction in incorrect response after the minimal training information.

DISCUSSION

Findings from our two studies suggest that participants, without training or instruction, use different criteria to interpret PRO questions such as reporting headache day and pain severity. When presented with a hypothetical overnight headache scenario, respondents in this study provided a diverse range of answers among the possible choices, indicating that participants were not clear on how to count and report headache days. Without training or guidance on the definition of a “headache-day” or “day”, almost 80% of the respondents provided incorrect answers. Participants who had prior participation or experience in a clinical trial did not perform better on the question. When reporting pain severity, more than half of the respondents selected the incorrect response. Those with prior clinical trial experience performed slightly better with 60% choosing the correct answer.

Such diversified interpretations in how to answer PROs items may pose a risk to the quality of clinical outcome data collection. When patients with migraine enroll in clinical trials that involve headache-day counts, the need to determine if they had a headache on a given day, or reporting headache pain severity, many patients may report in a similar pattern to those who participated in our study.

Our findings also suggest that when patients encounter unclear situations or have questions during a clinical trial, they may not consult the site staff who are equipped to provide study participants with consistent and accurate answers. Instead, almost half of the participants would either try to find information on their own or guess the correct answer. This behavior could further lead to poor data quality if the patients were not properly trained and encountered such unclear scenarios during a migraine trial.

Finding from our second study suggests that even with minimal training or instructions, training can improve the accuracy of answering PRO items. Prior to training, 21.7% of participants selected incorrect responses. After the respondents were given minimal training information, incorrect responses were reduced by 7.5%.

Patients' opinion on the necessity of training and their preference for the method of training has rarely been explored. Our findings indicate that the vast majority of participants, over 90%, considered educational materials and patient training to be an integral part of clinical trial participation. With respect to the mode of training, the majority of participants preferred electronic interactive training videos, choosing to either watch the training on the internet or on mobile electronic devices such as smartphones and tablets. Furthermore, over 80% of participants believed that it was necessary to have access to the training materials during the trial, in order to refresh on the information.

CONCLUSION

The results from our studies are in line with regulatory agencies' recommendations. The FDA PRO Guidance⁵ and the EMA reflection paper specify that training and instructions be given to patients for self-administered PROs.⁶ Despite the limitations of our study, for example, the relatively small sample size, descriptive nature of the study, and that we did not deploy a full electronic interactive training, our study still suggested a necessity for training study participant to ameliorate the risk of compromised data quality. In all, patient training may improve data quality and inter-rater reliability in clinical trials. Electronic interactive training could be used as an approach to reduce inconsistencies in PRO measures and improve data quality

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Ly JJ, Yamamoto RT, Dallabrida SM. Errors in answering migraine patient-reported outcome measure questions: patients consider training necessary in clinical trials. *Int J Clin Trials* 2019;6(3): 69-74.