CNS PATIENTS PREFER TO HAVE TRAINING THAT IS ELECTRONIC, INTERACTIVE AND READILY AVAILABLE WHEN PARTICIPATING IN A CLINICAL TRIAL

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BACKGROUND

Patient-reported outcome (PRO) refers to any reports that come directly from a patient about a health condition or its treatment without interpretations of clinicians or others[1]. They serve as critical methods to determine the treatment's efficacy and/or safety in many clinical trials. They pose an irreplaceable position in evaluating the impact of new medications and treatments on patient functioning and well-being, especially for non-observable events, or observable events that are assessed on a daily basis[2,3].

PROs collected as endpoints in clinical trials often require patients to report symptom severity, frequency, or intensity, or the impact of symptoms on quality of life. PROs can be easily affected by variances in human interpretation of measurement parameters and judgment bias[4]. It is generally accepted that to have statistical validity and reliability, the variability in PROs should be reduced to ensure data quality. In particular, patient training has been considered as a key and high-ranking component to improve the PRO data quality by global regulatory agencies as well as scientific and educational organizations, including FDA, EMA and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). For example, The Clinical Trial Quality Control section within the PRO Guidance from FDA specifies: "The quality of a clinical trial can be optimized at the design stage by specifying in the protocol procedures to minimize inconsistencies in trial conduct. We recommend a standardized order by which PRO and other clinical assessments are administered. Other examples of standardized instructions and processes that are recommended by the FDA include: Training and instructions to patients for self-administered PRO instruments"[5]. Similar recommendations can also be found in EMA instructions, as stipulated in the 2010 EMA Reflection Paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials: "The individual (investigator site staff, study subjects, caregivers or others) capturing the data need to have documented training in the correct use of the instrument and the electronic data capture document."[6]

More and more studies have demonstrated the superiority of electronic devices in capturing quality PRO data. Perhaps one of the most influential one was the compliance comparison done by Stone et. al in 2003[7]. In the study, the authors examined compliance of paper and electronic diaries in chronic pain patients. They implemented a photosensor in the paper diary book to track the actual opening time and length of diary opening. The results revealed an astounding discrepancy between the compliance reported by participating patients and that tracked by the photosensor. Meanwhile, patients who were assigned to electronic diary group showed an actual compliance rate as high as 94%, suggesting a compliance enhancement feature of electronic diary. Furthermore, Gwaltney et. al demonstrated the equivalence between paper- and electronically-administered PROs[8]. Taken together, electronic diary is equivalent to paper diary, while having a compliance- and data quality-enhancing feature.

CNS is a therapeutic area that relies heavily on PROs. PROs are commonly used as the primary or key secondary endpoints in trials for CNS diseases, particularly in migraine, epilepsy and major psychiatric disorders[2,9,10]. While scientists, educational communities and regulatory agencies have all come to a common appreciation of patient training as a key and high-ranking component to ensure the quality of PRO data capturing and ultimately the success of clinical trials, and that electronic PRO data capturing provides an advantageous way of enhancing data quality. It remains largely unknown whether CNS patients have the interest in receiving training, or what format they would prefer to be trained. In this study, we designed a survey questionnaire to examine CNS patients' opinions on these topics.

METHODS

240 participants reported at least one CNS-related disease, including addiction, anxiety disorder, bipolar disorder, depression, obsessive-compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), schizophrenia, Alzheimer's disease, epilepsy/seizure, migraine, multiple sclerosis, amyotrophic lateral sclerosis (ALS), Parkinson's disease and stroke. Participants were recruited via the Clinical Connection website (https://www.clinicalconnection.com), an online patient recruitment resource.

Patients were first asked to select their age, gender, education level and household income. Then they were asked to select their CNS disease indications from a drop down list. Multiple-entries were allowed.

In order to understand patients' opinions regarding the necessity of training during clinical trials, their preferred training material format and the importance of training accessibility, participants were asked 3 questions:

1. "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?"
2. "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?" and
3. "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?"

In each question, patients were asked to select 1 answer out of 4 choices. We analyzed the selections of the participants for of each question. Non respondents were excluded from analysis.

RESULTS

- The average age of participants was 46, with youngest participant age 16 and oldest participant age 80 and a standard deviation (STD) of 15.2.
- 79.6% participants were female (n=191) and 20.4% were male (n=49).
- Most participants reported a highest education level of "High school graduate/GED" or "Some college/Technical degree/AA/AS" (83.3%, n=170).
- 58 patients reported a household income of below 20k (24.3%), 84 reported income of 20-49k (35.1%). 73 patients reported a household income of 50-99k (30.5%) and 24 reported 100k or above (10.0%).
- Depression was the most reported CNS disease among all participants (148 entries). Following depression, anxiety disorder (108 entries), migraine (78 entries), addiction (39 entries) and bipolar disorder (33 entries) were also among the most prevalent indications.
- 220 participants responded to the first question (Figure 2). 94.5% (208 patients) considered educational materials and training "definitely needed" (75%, 165 patients) or "somewhat needed" (19.5%, 43 patients).
- 221 participants responded to the second question (Figure 3). 98.3% (217 patients) reported that they would be interested in some form of training. Specifically, 68.8% (152 patients) reported that they prefer interactive training videos provided on mobile electronic devices or the internet (28.6% or 63 patients, 40.5% or 89 patients, respectively). An additional 29.5% (65 patients) reported a preference of training materials delivered in the form of paper guidance.
- Among the 221 patients who responded to the third question (Figure 4), 87.8% (194 patients) considered it "definitely necessary" (57.0%, 126 patients) or "somewhat necessary" (30.8%, 68 patients) to have access and to refresh training at any time during the trial.

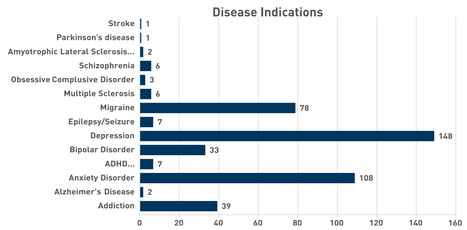

Figure 1. Distribution of CNS diseases among the surveyed patients.

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?

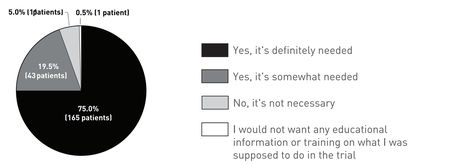

Figure 2. Patients' response regarding whether educational materials and training are needed, data shown in percentage of total respondents.

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?

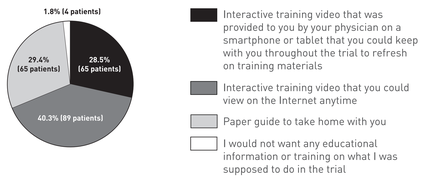

Figure 3. Participants' preferred way of training material and delivery format, data shown as percentage of total respondents.

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?

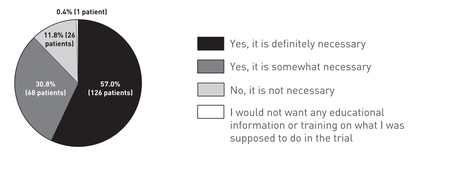

Figure 4. Patients' opinions regarding the importance of training material accessibility, data shown as percentage of respondents.

CONCLUSION

- The vast majority of respondents consider educational materials and training important and requisite for clinical trial participation.
- Most respondents prefer electronic means of training, as well as the ability to readily refresh on training materials. Such a mechanism can be addressed in the form of interactive training videos on the trial device, such as an eCOA handheld or tablet device, where such materials can be accessed offline at any time.
- Patient and/or caregiver training could be used as an approach to improve data quality and increase signal-to-noise ratio during CNS clinical trial data collection processes.
- The use of eCOA handheld or tablet devices may also be an effective mechanism to enhance patient engagement during CNS clinical trials
- Such findings of patient preferences are also in line with regulatory guidance from FDA, EMA & ISPOR regarding PROs and mechanisms for optimizing the quality of clinical trial data.

DISCLOSURES

The authors are employees of ERT.

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