

## Original Research Article

# Measurement of equivalence using a patient-reported daily pain diary across three smartphone devices

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**Received:** 16 September 2019

**Revised:** 03 October 2019

**Accepted:** 05 October 2019

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## ABSTRACT

**Background:** Patient-reported outcomes play an essential role in evaluating the results of clinical trials. As technological advances are made throughout the industry, pharmaceutical sponsors' ability to collect field-based patient data has greatly increased. Recently, many clinical trials are utilizing varying modes of data capture in order to enable maximum flexibility. Given the regulatory concern over the equivalence of mixed modes of administration, the need to research the use of varying devices is essential.

**Methods:** This study reviewed three handheld smartphone devices for conceptual equivalence and conducted usability for standard questions used in a daily pain diary. Out of ten participants, 7 were females and 3 were males with age ranging from 27-70 years, diagnosed with chronic pain or fibromyalgia, completed the same pain diary on three different smartphone devices.

**Results:** Overall, participants reported no differences between these three smartphone devices and found the presentation of the diary content to be similar, if not identical, on all three devices.

**Conclusions:** Device type had no impact on the presentation of the diary content or participants' understanding of the diary questions.

**Keywords:** Equivalence, Electronic data capture, Patient-reported outcomes, Clinical outcome assessments, Bring your own device

## INTRODUCTION

Within the past few decades, patient-reported outcomes (PRO) data collection has made a significant shift in the pharmaceutical industry from paper-based assessments to electronic patient reported outcomes (ePRO). Electronic data capture has many advantages over traditional paper-based PROs as patients can complete questionnaires outside of the clinic and report on their symptoms of a daily basis. From a regulatory perspective, the US Food and Drug Administration (FDA) has reported that electronic data capture is now the preferred method of data collection with improved integrity and accuracy of the data over paper data collection.<sup>1</sup>

Most clinical trials historically have collected ePRO data through provisioned devices, in which all participants utilize the same smartphone or handheld device. However, more flexibility in the types of devices used for data collection is needed as the number of global sites in a clinical trial have increased with varying electronic device regulations for different countries. One of the key regulatory and scientific concerns of implementing varying modes of data collection in clinical trials raised by both the FDA and the ISPOR PRO mixed modes good research practices task force is the importance of demonstrating measurement of equivalence between the varying devices collecting ePRO data.<sup>1,2</sup> The FDA stresses the importance of demonstrating that regardless of the ePRO being modified for various devices that the

data which is captured must be equivalent.<sup>3</sup> As such, the purpose of this study is to evaluate conceptual equivalence and conduct usability testing among three handheld devices for the purposes of clinical trial data capture.

## **METHODS**

The equivalency study asked participants (n=10) to complete a daily pain diary (based on diaries typically used for clinical trials) as if they were participating in a clinical trial. Interviews were held at the eResearch Technology (ERT) office (500 Rutherford Ave, Boston MA 02129) from November 6<sup>th</sup> to 17<sup>th</sup> 2017. They completed the questionnaire on each of the following smartphone devices sequentially: Google Nexus N5 (Android OS: 4.4, 4.95-inch screen), the Samsung E5 (Android OS: 4.44, 5.0-inch screen), and the BlueBird SF550 (Android OS: 5.1, 5.5-inch screen). The order of device presentation to participants was randomized. Interviews were then conducted using a semi-structured interview guide to obtain feedback on the questionnaire in each device format. The interviews were audio recorded, transcribed verbatim, coded, and analyzed. Demographic information, including age, gender, education, income, familiarity using smartphones were also collected.

### **Ethics**

Before the study commenced, the study, including recruitment materials and study documents, was reviewed and approved by an Independent Review Board on October 25, 2017.

### **Recruitment**

Following IRB approval, participants were recruited via advertisements in the local newspaper. Interested participants contacted study personnel via phone; and were screened for eligibility and scheduled their study appointment.

### **Inclusion criteria**

All of the participants met the following inclusion criteria at the time of screening: participants were 18 years or older; participants provided a signed consent form and indicated an understanding of the study objectives and study procedures and a willingness to participate in the study; participants had the ability to read and comprehend surveys in English; participants provided documentation from a doctor or other health professional that they were diagnosed with chronic pain or fibromyalgia.

### **Exclusion criteria**

Participants did not qualify for the study if they met any of the following exclusion criteria: participants reported being diagnosed with any of the following: traumatic

brain injury, dementia, schizophrenia, psychoses, with current symptoms; alcohol or drug dependence, with current symptoms. Participants currently participating in a clinical trial or investigational drug trial; participants who are employees or relatives of the study site.

### **Sample size**

Previous research suggests that a minimum of three and a maximum of twenty participants is appropriate for a qualitative usability and conceptual equivalence study, depending on study complexity and length of the diary (i.e., number of items/concepts).<sup>5</sup> The general consensus is that five participants will uncover 80% of the issues that should arise and that seven or more participants would be an optimal number.<sup>6</sup> Recruitment for this study targeted ten adult participants who reported a diagnosis of chronic pain or fibromyalgia, as ten participants are the industry standard for diaries of this nature and the daily pain diary used in this study contained a small number of items (five in total).

### **Interviews**

Before conducting interviews, the research team created a semi-structured interview guide for the pain diary to identify any challenging aspects of the interview and highlight the most important questions to address in order to answer the research questions. Semi-structured interviews were conducted by study personnel who underwent National Institutes of Health Human Participant Protection training, as well as training for participant interviews, improving inter-rater reliability and reporting. The interviews were conducted in a private room to ensure participant confidentiality.

### **Questionnaires**

The daily pain diary consists of five screens in total. The daily pain diary interview guide prompted participants to review and comment on all screens in the following order:

#### *Worst pain severity (0-10 numerical rating scale)*

Select the number below that best describes your worst pain in the past 24 hours:

0=No pain; 10=Pain as bad as you can imagine

#### *Worst pain severity (0-100 visual analog scale)*

Select the number that best describes your worst pain in the past 24 hours:

0=No pain; 100=Pain as bad as you can imagine

#### *Worst pain severity (verbal description scale)*

In the past 24 hours, how would you rate your worst pain?

(None, A little, A lot, As bad as I can imagine)

#### *Medication selection*

What medication did you take to treat your pain in the past 24 hours?

(Ibuprofen, acetaminophen, naproxen, excedrin, other, none)

#### *Medication amount*

How many/much of the following medication did you take? [Selected medication name]

(Number pad entry)

The answer options vary by item, but all involve the selection of an answer and clicking “next” at the bottom of the screen to confirm the answer and to advance to the following screen. If “next” is selected without an answer having been chosen, the answer options are highlighted and the participant is again prompted to select a response before advancing.

#### **Procedures**

Interviews were conducted to determine if participants understood the diary in a conceptually equivalent fashion when presented on the three smartphone devices. After each participant was identified, screened, and provided written consent, they were shown to a private room for interview by a trained interviewer. The interviewer introduced herself/himself, gave an overview of the objectives of the interview and what to expect, and secured additional verbal consent from the participant to have the interview audio recorded. The participant completed a demographic and health information form. The interviewer then turned on the audio recorder and allowed the participant to complete the diary, on each device sequentially, without assistance from the interviewer as if they were participating in a clinical trial. The device order was randomized amongst the participants. Following completion of the questionnaire on the first device, they were instructed to complete the same diary, on the second device, and then the third. After participants completed the diary on all three devices independently, the interview began. A semi-structured interview guide was used. The guide included yes-or-no as well as open-ended questions to collect qualitative data from the participant’s perspective for each of the nine screens in the questionnaire, and allowing for both structured and spontaneous feedback from each participant during the interview.

The interviewer presented each diary item to the subject on the first device and asked:

- Can you tell me in your own words, what this item is asking about?
- Can you describe any thoughts you had about deciding what to do next?

Then, the item was presented to participants on all three devices, side-by-side, and was asked the following questions:

- When you look at the way this screen looks in these three formats, is there anything among the three versions that might affect how you think about the information? Or what you understand the information to mean?
- Is there anything among the three versions that might affect the answer you would choose? (if yes, please describe).

Following the participant’s responses, the devices were advanced by the interviewer to the subsequent item, and the interviewer would repeat the series of four questions with the subject for the following item. This process continued for all screens in the diary for a comprehensive assessment of each questionnaire’s equivalency between the three smartphone devices. Upon completion, each participant was compensated with a \$100 gift card.

#### **Qualitative data analysis**

Audio recordings of the interviews were transcribed verbatim and anonymized by removing identifying information such as first and last names. Transcripts were manually coded in Microsoft Excel® based on the study objectives and an interview guide. Each transcript was considered a unit of analysis, and data from all transcripts were aggregated following coding. Once aggregated, researchers reviewed all of the coded transcripts and prepared them for analysis by grouping like responses together.

## **RESULTS**

#### **Study population: demographic information**

Demographic information for participants reporting a diagnosis of chronic pain (and/or fibromyalgia) is presented in Table 1. Seven participants were female, and three were male. Participant ages ranged from 27-70 years old (median=61). Half of the participants (5) reported an annual household income of less than \$20,000. Seven participants had received some college education, a technical degree, or an associate’s degree; 2 participants had a college degree, and 2 participants had completed high school or received a GED. Two participants were employed part-time, two reported being on disability, four were retired, and one reported being currently unemployed.

**Table 1: Participant demographic information (n=10).**

Variable	N
<b>Gender</b>	
Female	7
Male	3
<b>Age (years)</b>	
20-29	1
30-39	0
40-49	0
50-59	4
60-70	5
<b>Education</b>	
High school graduate	2
Some college or technical degree	3
College degree	3
Advanced degree	1
Did not respond	1
<b>Household Income</b>	
Less than \$20,000	5
Between \$20,000 and \$49,999	2
Between \$50,000 and \$99,999	1
Did not respond	2
<b>Occupational Status</b>	
Employed part-time	2
Employed full-time	1
Retired	4
On disability	2
Unemployed	1

**Table 2: Participant experience with technology (n=10).**

Experience	N
<b>Do you have internet access at home?</b>	
Yes	8
No	1
Did not respond	1
<b>If yes, what kind of devices do you use to access the internet? (Select all that apply)</b>	
Laptop or desktop computer	5/8
Tablet computer	3/8
Smartphone	5/8
<b>Do you own a smartphone?</b>	
Yes	6/10
No	4/10
<b>If yes, what kind?</b>	
Apple	1/6
Android	5/6
<b>How frequently do you use it?</b>	
Daily	5/6
Less frequently	1/6
<b>What activities do you use your smartphone to do? (Select all that apply)</b>	
Making phone calls	6/6
Web browsing	4/6
Text messaging	4/6
Email	4/6
Taking/viewing photos	3/6
Listening to music	4/6
Other apps (games, lifestyle, travel, social media)	2/6

### Experience with technology

Each participant self-reported their experience with different technologies and is presented in Table 2. A majority of participants (8) did have internet access at home, with five accessing the internet at home via a laptop or desktop computer, three via a tablet, and five via their smartphones. The majority of participants (6) reported owning a smartphone that was either Apple (1) or Android (5).

### Conceptual equivalence

The findings from our interviews of ten participants, comparing the daily pain diary on the three smartphone devices are summarized in Table 3 below.

**Table 3: Conceptual equivalency testing of the daily pain diary (n=10).**

Interviewer question	Yes	No
<b>Pain numerical rating scale</b>		
Is there anything among the three versions that would affect how you think about the question?	0/10	10/10
Is there anything among the three versions that would affect the answer you would choose?	0/10	10/10
<b>Pain visual analog scale</b>		
Is there anything among the three versions that would affect how you think about the question?	0/10	10/10
Is there anything among the three versions that would affect the answer you would choose?	0/10	10/10
<b>Pain verbal description scale</b>		
Is there anything among the three versions that would affect how you think about the question?	0/10	10/10
Is there anything among the three versions that would affect the answer you would choose?	0/10	10/10
<b>Medication selection</b>		
Is there anything among the three versions that would affect how you think about the question?	0/10	10/10
Is there anything among the three versions that would affect the answer you would choose?	0/10	10/10
<b>Medication amount</b>		
Is there anything among the three versions that would affect how you think about the question?	0/10	10/10
Is there anything among the three versions that would affect the answer you would choose?	0/10	10/10

All participants found the items to be conceptually equivalent to the three devices. We found no reports of a

subject’s understanding to vary among the three formats, and all participants reported that 100% of their answers would have been the same, regardless of which device they were using. This held true for each of the three items in the daily pain diary. Participants offered these representative responses when asked if there were any differences among the three devices that would affect their understanding of, or response to, each diary item:

- Worst pain numerical rating scale
  - “They’re all saying the same thing.”
  - “No, my answer was the same for all three.”
  - “It’s not like they’re asking me different questions. They’re all the same.”
- Worst pain visual analog scale
  - “No, it was pretty much the same.”
  - “Everything says the exact same thing.”
  - “No, my answer was the same.”
- Worst pain verbal description scale
  - “Nope, cause they’re asking me the same thing in all questions. None of them are different.”
  - “No, it would not. How I think or affect the answer.”
  - “No. They look the same.”
- Medication selection
  - “They’re all the same questions.”
  - “No, I thought the same thing.”
- Medication amount
  - “No. Very, very clear. I kind of like that.”
  - “No, I thought the same thing in all three.”

In sum, all participants reported an equivalent conceptual understanding of the Daily Pain Diary content on the three devices. Additional spontaneous feedback offered by the participants during the interview alluded to the fact that they were using a device like this for the first time. Overall, there were no cases of a subject identifying anything among the three versions that would affect their understanding of the information or the answer they would select. In all cases, they reported no difference in their understanding of the diary content and indicated an equivalent experience using the Daily Pain Diary on the three devices.

### Usability testing

Following the evaluation of the pain diary on the three formats, participants were asked about their overall experience reading and using the devices. Participants had a range of experience levels with technology; some

owned a personal smartphone and computer, and some used neither with any regularity (Table 2). Regardless of experience, participants universally reported that the questionnaires on the three devices were easy to use and easy to read.

- Were the devices easy or difficult to read?
  - Easy: 10/10
  - Difficult: 0/10
  - Sample participant quotes:
    - “Very easy, yes.”
    - “It was easy to read.”
- Were the devices easy or difficult to use?
  - Easy: 9/9
  - Difficult: 0/9
  - Sample participant quotes:
    - “I think it was very easy.”
    - “It wasn’t difficult.”

## DISCUSSION

This study explored conceptual equivalence and conducted usability testing among three handheld devices. Participants reported an overall conceptual equivalence among all three of the handheld devices, each reporting that the device itself would not influence how they would think about or answer a given question within the questionnaire. This included the diary items displaying an NRS or VAS on the handheld devices. Participant’s feedback consistently reflected the similarity of their overall experience between the three devices. They specifically reported that although the devices and screens were different, this would not change their thought process or responses to the questions.

Additionally, when participants were asked about the usability of the three devices participants universally reported that the questionnaires on the three devices were easy to use and easy to read. Given the consistent feedback from participants that their experiences with the three devices were similar (if not identical), and that the type of device amongst these three would not alter their understanding or responses in any way, these devices could be used interchangeably in new or ongoing clinical trials.

### *Implications for bring your own device and future directions*

Historically, the majority of field-based ePROs are collected through device provisioned studies, in which all participants utilize the same locked down device. Although provisioned devices have advantages and enables maximum control for clinical researchers in trials, there is the potential for maximizing flexibility and

an ability to eliminate patients having to carry and maintain an additional device to their personal devices.<sup>4</sup>

The bring your own device (BYOD) approach allows patients to respond to daily symptom diaries and study questionnaires on their personal mobile device. As owning a smartphone is the norm for many research patients today, there can be a convenience and familiarity with completing clinical trial assessments on their own device rather than having to carry an extra device with them on a daily basis. The majority of patients prefer digital collection and BYOD gives patients the option to use the device of their choice.<sup>5</sup> Other advantages for utilizing the BYOD approach are reducing study start-up timelines (no need to ship devices) and reducing site burden (sites do not need to store the devices or manage the replacement of devices).<sup>7</sup>

There are number aspects to consider before determining if BYOD is a suitable alternative. As we know, one of the key regulatory and scientific concerns of implementing varying modes of data collection in clinical trials raised by both the FDA and the ISPOR PRO Mixed Modes Good Research Practices Task Force is the importance of demonstrating measurement of equivalence between the varying devices collecting ePRO data.<sup>1,2</sup> Our findings demonstrated the measurement of equivalence for ePRO data collected on Google Nexus N5, the Samsung E5, and the BlueBird SF550.

In addition, there are many privacy, security and operational concerns to pay close attention to, such as data transfer security, lost or stolen devices, internet availability, device ownership, design and support to consider prior to deciding if a BYOD approach is appropriate for a clinical trial.<sup>2,8</sup>

## CONCLUSION

Findings from this study support the use of different but similar smartphones to capture ePRO data to provide more flexibility in global clinical trials. The results are also in line with regulatory agencies that emphasized the importance of demonstrating equivalence between the varying devices collecting ePRO data. We acknowledge that one of the limitations of this study is that all handheld devices were using an Android Operating System. Although the operating system was the same on all devices, the make, model and screen sizes varied: 4.95-inch, 5.0-inch and 5.5-inch screen.

*Funding: eResearch Technology (ERT)*

*Conflict of interest: None declared*

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

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**Cite this article as:** Conrad E, Gary S, Khurana L, Otero T, Ly J, Dallabrida S. Measurement of equivalence using a patient-reported daily pain diary across three smartphone devices. *Int J Clin Trials* 2019;6(4):154-60.