Preferences of the Opioid Use Disorder Patient:
Clinical Trial Methodologies and COVID19 Mitigations that Motivate Participation

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ABSTRACT

Introduction: The need to conduct clinical trials for the treatment of opioid use disorder (OUD) cannot be overemphasized, as 128 people die each day in the US from opioid overdose and this death toll has been increasing per year (CDC, 2020). However, one crucial aspect hindering trial conduct and data quality is poor subject retention, and research suggests OUD studies have significantly high dropouts (O'Connor et al., 2020). While no research could be located assessing OUD patients' specific preferences on trial design and conduct strategies, including during the COVID19 pandemic, exploring these factors is arguably an essential step toward enhancing these participants' study retention (Costello, 2016). **Methods:** Eighty-two patients diagnosed with OUD and seeking an OUD clinical trial completed (before study screening) a 10-point Likert 45-item questionnaire on perspective of methodological, site operational, and COVID19 mitigation approaches that would motivate them to participate in an OUD trial. **Results:** Highlighted preferences that strongly motivate participation included shorter visit durations, free transportation, knowing they are helping to bring new treatment to market, and obtaining mental health care. Surprisingly, no significant preferences were reported for inpatient vs outpatient studies or visit frequencies. Patients strongly preferred onsite than remote visits during COVID19. No significant demographic differences were found, except African-American patients significantly desired the Consent Form being explained before study participation as compared to Caucasian patients. **Conclusions:** The poster will discuss how OUD patient reported preferences regarding trial design and site operations (particularly respective of the COVID19 pandemic) can positively influence subject retention.

INTRODUCTION

- The Opioid Use Disorder (OUD) pandemic is well documented. The OUD amassment has resulted in nearly 450,000 American deaths from 1999-2018 (CDC, 2011) and 128 people presently die per day from an overdose (CDC, 2020). Globally in 2016, 27 million people suffered from OUD (WHO, 2018), with OUD increasing 47% since 1990 (Deganhardt et al., 2018).
- The opioid crisis demands clinical trials focus on OUD treatments. However, issues related to OUD participant retention, a critical component to trial data quality, could not be located after a thorough review of the literature. Data on subject dropouts is essential because poor retention has several negative clinical trial implications, including longer study durations, costlier trials, lower likelihood of statistical power for both the study and the validity of the results, morale of study site staff, and potential termination of the trial which could bring less prospective interventions to those suffering from an OUD (Sullivan, 2004). What we do know about retention in this area solely comes from OUD related work, such as OUD treatment dropouts which has been shown to be significantly high at approximately 57% (O'Connor et al., 2020) and Gehling et al.'s (2011) 19 study meta-analysis of patients with chronic pain due to osteoarthritis which indicated that these participants have a significantly increased dropout rate.
- Understanding subjects' clinical trial preferences across various trial factors is a fundamental step toward enhancing retention (Costello, 2016; Gul & Ali, 2010; Northrup et al., 2017; Page & Persch, 2013; Sullivan, 2004). Given that no data could be found specifically on these issues among OUD patients, the current investigation surveyed OUD patients seeking to enroll into an OUD clinical trial and their desire for several trial design and operational variables that would motivate them to participate in an OUD treatment clinical trial.
- Similar to the dearth of data on OUD patients' clinical trial preferences, no empirical work could be found on participants' clinical trial methodology propensities respective of the current COVID19 pandemic. However, these matters were routinely solicited by sponsors and CROs to research sites across the US during several industry meetings conducted since the onset of the pandemic 's profound industry impact in March 2020. As such, the current study assessed COVID19 related design scenario preferences as well from OUD patients.

METHODS

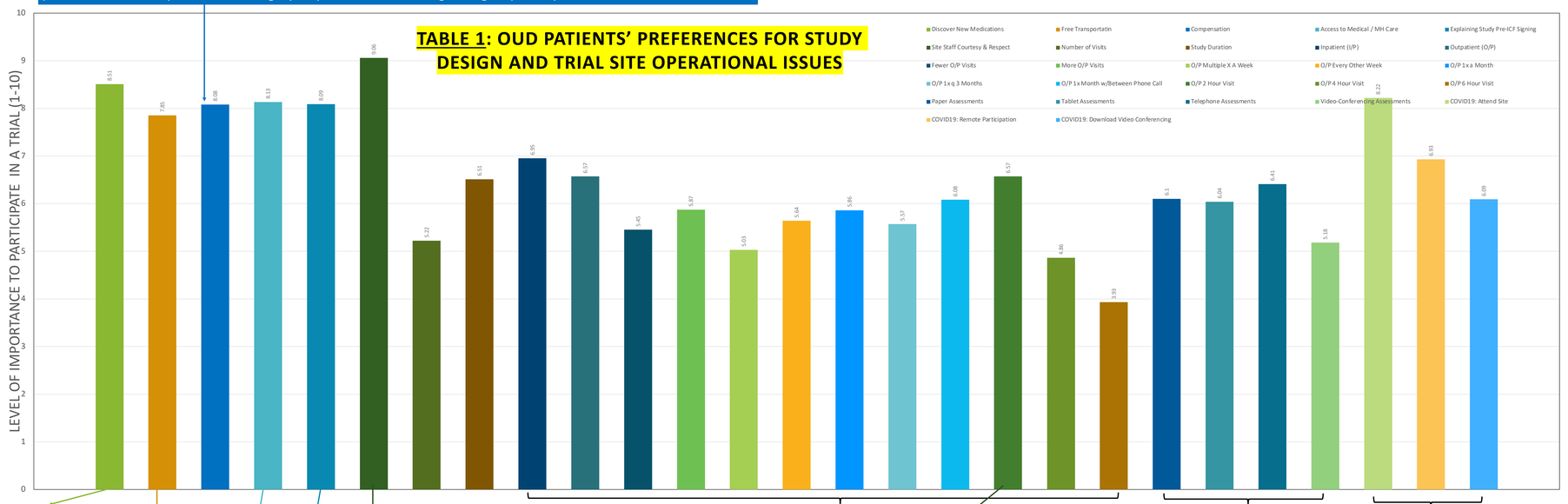
- This study was conducted from May-August, 2020 at an East coast US research site where OUD clinical trials were being conducted.
- Through the site's database and advertisements, individuals who reported using an opioid substance and expressed interest in joining an OUD treatment clinical trial were psychiatrically evaluated by qualified clinicians through education and experience.
- Only patients diagnosed with primary OUD via the DSM-5 (APA, 2013) were included in the current data results.
- Before signing consent for any OUD clinical trial, the diagnosed OUD patients completed a seven-page Research Participant Preferences Survey (RPPS) which asked about their preferences on various research design and site operational matters on a 10-point Likert scale. Open ended questions were also queried. Age, gender, and race were also collected.

RESULTS

- Out of the 82 OUD patients who completed the RPPS, their demographics were:
  - 49 males (60%)
  - 33 females (40%)
  - Mean age was 40 (range from 21-65)
  - 37 identified as White (45%)
  - 36 African-American (44%)
  - 7 Latino (17%)
  - 1 Asian (.01%)
- 70 (85%) of the responders had never been in a clinical trial, while 8 (10%) had participated in only one trial. These data are understandable since the enrolling site OUD studies at the time the survey was being completed by patients needed to have current rather than previous opioid abusers. Current study data should be interpreted in this context and may present as a study limitation .
- Results of patient preferences on study design and site are shown in **Table 1** with particular DISCUSSION points articulated inoperational matters the colored boxes respective of the data bar graph.
- Significant differences across variables are noted in green highlight.

Substantial thought by the sponsor and CRO should go into how much compensation the OUD subject is provided as this is perceived as highly important for their agreeing to participate in a trial.

TABLE 1: OUD PATIENTS' PREFERENCES FOR STUDY DESIGN AND TRIAL SITE OPERATIONAL ISSUES



Given this high level of importance reported by OUD patients, when such subjects struggle to stay in the OUD treatment/withdrawal trial, which research has corroborated (Milligan et al., 2004; O'Connor et al., 2020), it may be beneficial to remind the subjects they are participating in a study to discover new treatments.

Although a majority of the OUD patients completing this survey were recruited from arguably harsh / dangerous urban areas, it is important to note that these patients ranked staff courtesy and respect toward them as the highest motivation for their trial participation, and as such, site staff need to be mindful of this during their interactions with OUD study subjects.

OUD patients did not seem to feel particularly motivated to participate in a study because of the trial's length, visit numbers (fewer vs more), inpatient vs outpatient, or even visit frequency. What they did seem to care more about is how long they needed to be on site for outpatient studies. They significantly preferred shorter visits (2 hours; Median=7, M=6.52, SD=2.99), followed by 4 hour visits (Median=5, M=4.86, SD=2.99), and lastly, 6 hour study visits (Median=4, M=3.93, SD=3.02), $X^{2(2)}=46.79$, $p<0.001$.

- As such, it would behoove OUD study participation and seemingly retention if study designers insert just enough trial procedures and assessments so as not to prolong study visits.
- This findings is also good news for the efforts implemented to reduce the placebo effect, as research and experts (Alphs et al., 2012; Taiminen et al., 1996) alike have asserted there is a strong chance of enhanced placebo response with the longer study subject stays on site. This is because the subject is conceivably being provided more clinical care and attention the longer he/she stays on site and such site responsiveness can booster the placebo-assigned participant's subjective feelings (i.e., feel better).

OUD patients did not seem to have a preference for being assessed via paper, computer/tablet, telephone, or video-conferencing (e.g., Skype, Facetime, Zoom, etc.). All of these evaluation procedures were about equally valuable to the patients, including whether those assessment modes were administered by the site clinician or self-report. However, it should be stressed that 85% of the current study responders had never participated in a study and thus are not directly aware of the pros and cons to each of these evaluation methods. Nonetheless, these data are important as they tell us a sponsor or CROs need not stress or be concerned about selecting one mode over another if the point of implementing any of these assessment administration methods is to help enhance participant enrollment into their trial.

The OUD responders had a clear sequential preference for coming into the research site (Median=9, M=8.22, SD=2.02) during the COVID19 pandemic as opposed to having all study procedures done at their home, a non-site location (such as for lab draws), or via their downloading a video-conferencing platform (Median=7, M=6.51 [derived from combining all outside site procedure preferences], SD=2.60), $z=-4.89$, $p<0.001$. We believe these data are important because since COVID19 escalated in the US, sponsors and CROs have asked sites, in order to organize and prepare new and ongoing trials, what subjects prefer pertaining to these procedures. These data can be applied to OUD trials. We also surveyed other CNS study indication patients and are currently analyzing these data.

Sites should provide free transportation as this factor seems to be deemed highly helpful for OUD patients' motivation to enroll into trials.

OUD patients reported having access to mental health care professionals as essential to their agreeing to join a trial. This is understandable because it has been our experience that the site clinicians are trained and skilled in discussing with the patients their study participation and through research rapport encouraging them to continue their study participation.

One of the few significant differences found among the preference factors and the demographic variables, the results indicated that African-American (Median=10, M=8.82, SD=1.99) OUD patients felt substantially motivated to participate in an OUD trial, compared to their Caucasian counterparts (Median=8, M=7.66, SD=2.71), if the Consent Form was further explained by the site staff (Coordinator) beyond their reading of the Consent ($t=-2.00$, $p=0.048$). It has been well documented (Corbie et al., 2002;) that the African-American community has valid mistrust of clinical trials (e.g., Tuskegee experiments) and so perhaps connecting with another person who explains the nuances of the trial helps reduce the African-American patients' participation anxiety.

STUDY LIMITATIONS

- In addition to the limitation of generalizability (given that the survey was completed at only one research site in the US), a primary limitation to the current study is that a majority of the OUD patients (85%) had never participated in a clinical trial. It would have been interesting to explore if more experienced trial patients perceived certain variables, such as having site staff further explain the Consent Form, as important as it was for the de novo patients. Alternatively, we may have found that other factors, including number of study visits or visit frequencies, could have been deemed more important by patients who had increased trial familiarity. The RPPS also queried patients about their reasons for discontinuing previous clinical trials but this could not be validly explored given the low number of subjects who had not been in a clinical trial, and those in our sample that were in a previous trial were only in one trial.

References provided upon request to ecohen@hritrials.com

Poster presented at the Annual International/Canadian Society of Addiction Medicine, November 2020, Virtual Meeting