ISCTM
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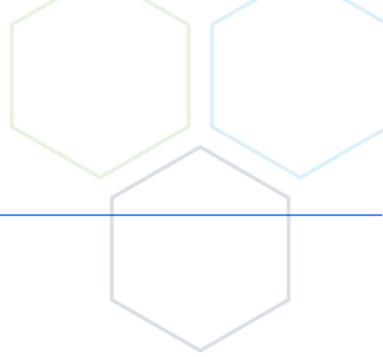
PARTICIPANT RETENTION AND STUDY BURDEN:
A WORTHY SUBJECT

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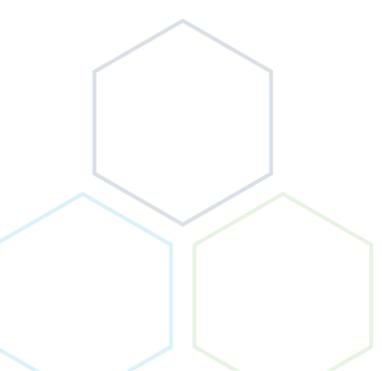**HRI** A division of Apex Innovative Sciences

Disclosures – Elan Cohen, PHD – February 2022

The Dr. Cohen has no conflicts of interest or bias in the contents of this presentation.

Dr. Cohen is a current employee of Hassman Research Institute, an independent research site that conducts investigator-initiated and industry-sponsored pharmaceutical trials.

The Problem

- The dropout rate post-randomization within CNS (psychiatric) clinical trials approximates to 30% (Cohen et al., 2021). Specifically, for example:

  - ➢ Psychosis trials: dropout ranges from 33% (Wahlbeck et al., 2001), 48% (Kemmlet et al. 2005), and even exceeding 50% (Martin et al., 2006)

  - ➢ MDD studies: dropout ranges from 21% to 49% (Kahn et al., 2000; Rutherford et al., 2010; Torous et al., 2020)

  - ➢ Lurie & Levine's (2010) meta-analysis of PTSD trials found an average withdrawal rate of 30%

  - ➢ Separate ADHD and anxiety disorder placebo-controlled clinical trials have noted poor participant completion rates: 33% for ADHD (Sutherland et al., 2012), 24% for GAD (Gommoll et al., 2015), and 42% for OCD (Foa et al., 2005)
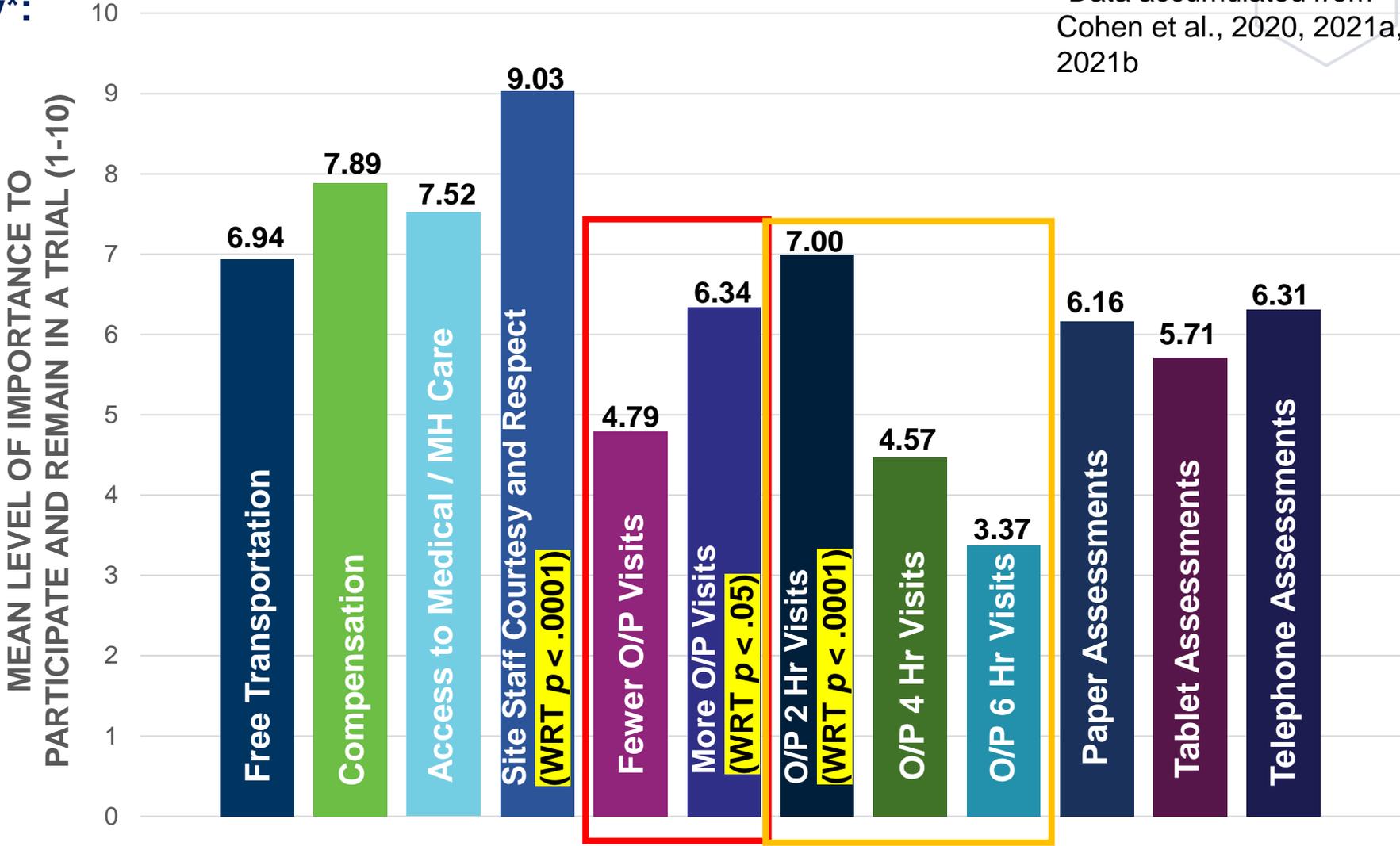
The Problem (Con't)

- Participant early withdrawal is problematic as it leads to:

  - ➢ Missing data

  - ➢ Costly delays in study completion (Costello, 2016; Ross et al., 1999)

  - ➢ Potential premature trial termination (Gul & Ali, 2010)

  - ➢ Negative research site moral (Sullivan, 2004)

  - ➢ Questionable validity of the findings (Gul & Ali, 2010; Kadam et al., 2016; Levine et al., 2015)

  - ➢ Statistical measures aimed to fix poor subject accrual have also been noted as bias (Rabinowitz & Davidov, 2008)

CNS and Opioid Use Disorder Participant Key Study Procedure Preferences

Study Program I Methodology*:

- 343 patients diagnosed with Schizophrenia, MDD, or OUD

- Participants completed at Prescreen a 7-page, 10-point Likert Scale, 45-item, 5-minute Research Participant Preferences Survey (RPPS)

- Mean number of trials previously participated was 2.68 – responders had enough previous trial experience to complete survey

- <mark>Wilcoxon ranked test (WRT) was performed</mark>

*Data accumulated from Cohen et al., 2020, 2021a, 2021b

Chart — MEAN LEVEL OF IMPORTANCE TO PARTICIPATE AND REMAIN IN A TRIAL (1-10):

Category	Value
Free Transportation	6.94
Compensation	7.89
Access to Medical / MH Care	7.52
Site Staff Courtesy and Respect	9.03
Fewer O/P Visits (WRT *p* <.0001)	4.79
More O/P Visits (WRT *p* <.05)	6.34
O/P 2 Hr Visits (WRT *p* <.0001)	7.00
O/P 4 Hr Visits	4.57
O/P 6 Hr Visits	3.37
Paper Assessments	6.16
Tablet Assessments	5.71
Telephone Assessments	6.31

# And What Do Actual Study Data Tell Us About Participant Burden

Study Program II Methodology:

- Cohen et al. (2021) examined 176 completed outpatient MDD, ADHD, GAD, PTSD, and OCD clinical trials (2312 randomized participants)

- Studies conducted at 6 US sites

- Examined placebo-controlled, open-label, and extension trials

- Pearson analyses performed

- Dropouts operationalized as participants withdrawing post-baseline

  - ➤ (a) obtained from Closeout Report Forms submitted to IRBs and sponsors

  - ➤ (b) directly due to participant decisions or factors (e.g., lost to follow-up and withdrew consent) rather than matters out of their control (e.g., investigator discretion due to labs and adverse events)
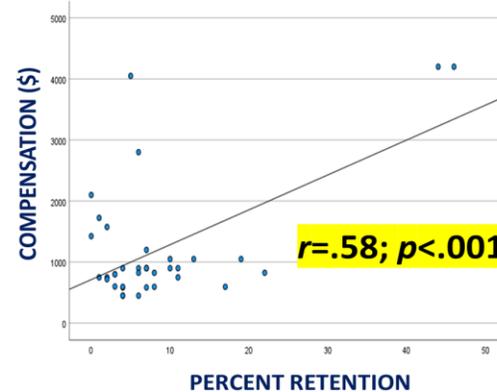
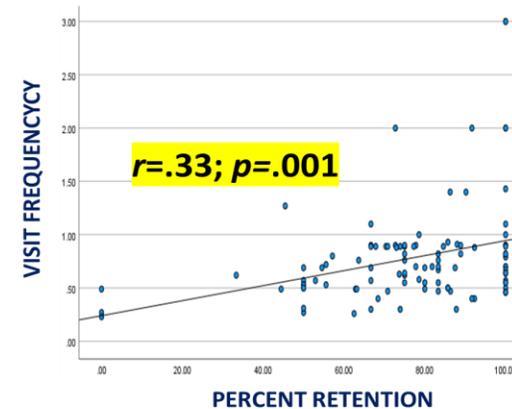**Figure 1: Correlation Between Participant Retention and Study Duration**

$r=-.36; p<.001$
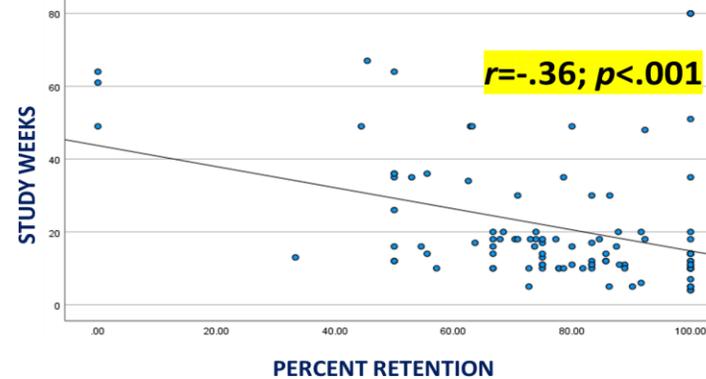
Figure 2: Correlation Between Participant Retention and Number of Study Scales
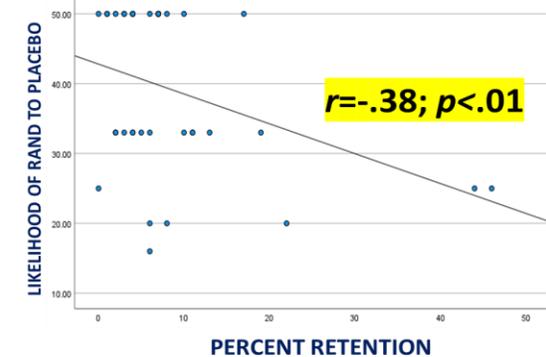
$r=-.39; p=.02$
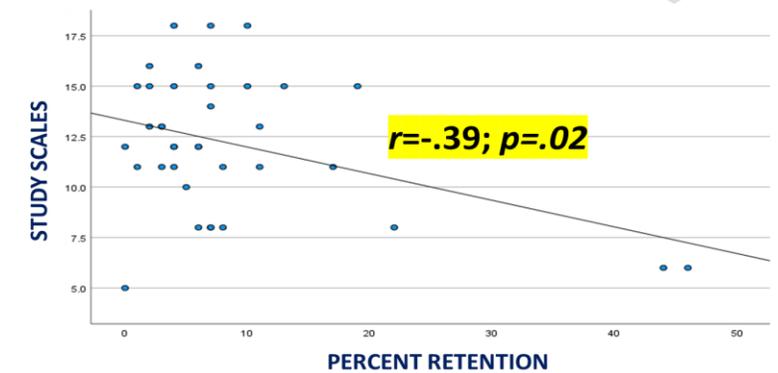
Figure 3: Correlation Between Participants Retention and Study Compensation

$r=.58; p<.001$

Figure 4: Correlation Between Participant Retention and Visit Frequency

$r=.33; p=.001$

Figure 5: Correlation Between Participant Retention and Likelihood of Randomization to Placebo

$r=-.38; p<.01$

Further Recommendations to Reduce Participant Burden

Single sign on and password management

Typing on tablet

Camera / Audio setup and use

Implement platform update remotely

IT Support
- Knowledgeable
- Access to tablet
- Responsive!

TABLETS

Stylus pen that writes legibly

Not routinely shutting down or freezing

Further Recommendations to Reduce Participant Study Burden (Con't):
eCOA (ePROS, eICFs, eDiaries, Wearables, Apps, etc.

- User-friendly and intuitive

  ➤ CRO or Sponsor representative should take device home to use (don't just practice with it in the vendor's office)

- Ask if vendor engaged in pre-test (User Requirement Specifications) on actual patients with the targeted protocol indication

- Setup time

  ➤ E.g., ALZ participants and informants (generally speaking – technology for them is burdensome)

La-La Land

Real World

Example feedback from a participant with Schizophrenia:
"I keep trying to use this. Hate it! Too confusing. I'm done! You keep saying I didn't take my medication but I do all the time. Stop telling me I didn't use it."

Further Recommendations to Reduce Participant Study Burden (Con't): eCOA (ePROS, eICFs, eDiaries, Wearables, Apps, etc.

- Resetting device per visit needs to be streamlined

- Data that gets continuously saved

  - ➢ E.g., Prevents parent from calling site saying they keep having to re-enter information

- Participant / Informant needs to be compensated for their time working on device

- App that does not deplete cell data time

- Provide participant with smart device / cell phone

- Odor resilient

- Comfortable

- Not conspicuous (confidentiality)

Further Recommendations to Reduce Participant Study Burden (Con't):

- Ensure timed assessments and procedures are logistically / operationally feasible

  - E.g., EEG setup time or travel time to MRI facility is incompatible with expected next timed assessment or lab procedure

- Study Restrictions

  - Food

  - Smoking

  - Medication (Ativan)

BOTTOM LINE:

ASK SITES THEIR PERSPECTIVE
WHILE DEVELOPING THE PROTOCOL AND VENDOR SEARCHING

Questions to Discuss

1. Is there any feedback on the recommendations provided in this presentation – any concerns (feasibility) with such suggestions?

2. Any recommendations on how sites can work with sponsors / protocol developers to explore leveraging the numbers of scales in a study and participant burden?

3. Any other thoughts on how we can use technology, as we can all agree on its importance in clinical trial data capturing, while also minimizing site stress and participant burden?

4. How do we balance participant compensation to accurately reflect their duration onsite per study visit procedures, while also avoiding enrolling "professional patients"?