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General Information

Key Personnel (in addition to PI):
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Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.
How did you learn about the YODA Project?: Scientific Publication

Conflict of Interest

https://yoda.yale.edu/system/files/consent_form_yoda_cmai.pdf

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT00249158 - RIS-AUS-5/CR006010 - Risperidone in the Treatment of Behavioural and Psychological Signs and Symptoms in Dementia (BPSSD): a Multicentre, Double-blind, Placebo-controlled Parallel-group Trial
2. NCT00249145 - RIS-INT-24/CR006046 - Risperidone in the Treatment of Behavioral Disturbances in Demented Patients: an International, Multicenter, Placebo-controlled, Double-blind, Parallel-group Trial Using Haloperidol as Internal Reference
3. NCT00253123 - RIS-USA-63/CR006022 - A Randomized, Double-Blind, Placebo-Controlled Study of Risperidone for Treatment of Behavioral Disturbances in Subjects With Dementia

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Consistency checks to improve measurement with the Cohen Mansfield Agitation Inventory (CMAI)

Narrative Summary:

Symptom manifestations in studies of psychiatric disorders can be subtle. Small imprecisions in measurement can lead to over- or under-estimation of change. One strategy to improve measurement is to conduct logical consistency checks within and across measures. I have assembled consistency/inconsistency flags for the CMAI for the purpose of improving the quality of measurement when using this scale. Flags will be applied to assessments derived from clinical trials to help understand how often various potential scoring inconsistencies occur.

Scientific Abstract:

Background: Symptom manifestations can be subtle. Small imprecisions in measurement can lead to over- or under-estimation of change. One strategy to improve measurement is to conduct logical consistency checks between item responses (i.e., cross-sectionally) and across test administrations (i.e., longitudinally) of rating scales, bearing in mind that some degree of inconsistency is to be expected due to subject-based variability. Objective: Test consistency flags for the CMAI on clinical trial data. Study Design: Potential scoring inconsistency flags were derived based on logical analysis of scoring guidelines eliciting expert opinion and my published factor analysis (Rabinowitz et al, 2004) of the CMAI. Participants: Data sets are being requested from sponsors who conducted clinical trials that used the CMAI. Main outcome measure: The primary outcome measure is the frequency with which each of the potential scoring inconsistencies("flags") occurs. Secondary outcome is the frequency with which CMAI administrations have multiple inconsistencies. Frequency with which each of the potential scoring inconsistencies occurs. Statistical analysis: Descriptive analysis of frequency of occurrence of each of the potential scoring inconsistencies. Trials or investigators will not be identified in the reporting of the results.

Brief Project Background and Statement of Project Significance:

Symptom manifestations in schizophrenia can be subtle. Small imprecisions in measurement can lead to over- or under-estimation of change. One strategy to improve measurement is to conduct logical consistency checks between item responses (i.e., cross-sectionally) and across test administrations (i.e., longitudinally) of rating scales, bearing in mind that some degree of inconsistency is to be expected due to subject-based variability. As part of my research which focuses on improving measurement methods in clinical trials, I have been actively involved on improving consistency in measurement specifically, developing algorithms for flags to identify possible errors in use of rating scales widely used in our field. The model includes developing an algorithm based on the “expert opinion” and then testing it in data sets. I have published recommended consistency checks/flags for Positive and Negative Syndrome Scale (PANSS)
(Rabinowitz and Rabinowitz, 2021; Rabinowitz et al., 2017), the Personal and Social Performance (PSP) scale (Rabinowitz et al., 2021), the Montgomery-Asberg Depression Rating Scale (MADRS)(Rabinowitz et al., 2019) and the Hamilton Rating Scale for Depression (HAM-D) (Rabinowitz et al., 2022). The value of this approach of flagging inconsistencies on improving signal detection has recently been demonstrated (Opler et al., 2021).

Specific Aims of the Project:

Apply algorithm developed based on expert opinion to detect scoring inconsistencies in the use of the Cohen Mansfield Agitation Inventory (CMAI). Algorithm to be applied to data sets from various clinical trials. Recommendations based on this work to be published.

What is your Study Design?:

Methodological research

What is the purpose of the analysis being proposed? Please select all that apply.

Research on clinical trial methods

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

Data on all subjects with available data on CMAI (Cohen Mansfield Agitation Inventory). We are requesting CMAI item level data and where available CGI-s data. All data by visit with sequential subject identifiers. Please note that we do not need patient demographic, psychiatric history, or safety data.

Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:

The primary outcome measure is the frequency with which each of the potential scoring inconsistencies("flags") occurs. Secondary outcome is the frequency with which CMAI administrations have multiple inconsistencies. Flags are included as an attachment to this request.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

The main independent variable will be the item level scores on the CMAI which will be used to create and test the consistency flags.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

The data will be analyzed descriptively to examine the frequency with which the potential inconsistencies occur. Software Used: R

Statistical Analysis Plan:

The frequency with which each of the expert-derived logical consistency flags occurred in the clinical trial data will be assessed. Then, using the norms that we derived from the trials, we will apply all of the following empirically based checks of outlier rating administrations: (1) Underuse of a value (e.g., rarely choosing a score of 4), (2) Overuse of a value; (3) Disproportionate use of even or odd response choices; (4) “Long-string,” using the same response on several consecutive items--the assumption is that careless raters may choose the same response option to many questions in a row and that attentive raters will not use the same response option for large numbers of consecutive items; (5) Inter-item standard deviation which checks for random patterns of response within a CMAI administration as measured by how much an individual administration strays from its own midpoint across the CMAI items, and (6) Outlier response choices on multiple items as measured by the Mahalanobis distance that shows when an individual is on the outskirts of the multivariate distribution formed by responses to all items. Outliers were predefined as administrations that were in the top or bottom 2.5 percent of one or more of the measures, or 5% on only one side for skewed items where lower 2.5% does not exist (to approximate a p-value of .05). To identify the outlier cutting points for overuse or underuse of values, disproportionate use of odd/even values, longest consecutive use of same response choice in each YMRS administration, and intra-item standard deviation and multivariate outliers (Mahalanobis distance), I will examine the frequency distributions for each of these measures.
A final round of analyses will evaluate the overlap in flagging by outlier-pattern and expert-derived flags in the clinical trial samples. In addition a final round of analysis will focus on determining how these flags would perform in a sample of administrations completed in a random fashion to simulate what one might find in the case of careless/inattentive subjects or raters. To accomplish this, I will generate a “simulated random” dataset using Monte Carlo methods
such that responses were uniformly distributed for each item, without regard to the values of other items. Multivariate outliers will be detected using Mahalanobis distance. Longest consecutive use of values with the same

response will be examined using the code for detecting long-string responding. Intra-item standard deviation which shows how much each CMAI administration strays from its midpoint across the CMAI items will be computed as per Marjanovic et al (2015) as the standard deviation of responses across the items for an individual CMAI administration. All analyses will be conducted in R version 4.1.3 and using the package 'careless' (Yentes, 2021).
Software Used:
RStudio

Project Timeline:

Consistency flags have been assembled. Once data has been obtained I will apply the flags to the data sets. Data management and analysis are anticipated to take 5 months. We anticipate producing a manuscript for publication within 12 months.

Dissemination Plan:

As we have previously done for the Positive and Negative Syndrome Scale (PANSS) (Rabinowitz and Rabinowitz, 2021; Rabinowitz et al., 2017), the Personal and Social Performance (PSP) scale (Rabinowitz et al., 2021), the Montgomery-Asberg Depression Rating Scale (MADRS)(Rabinowitz et al., 2019) and the Hamilton Rating Scale for Depression (HAM-D) (Rabinowitz et al., 2022) I anticipate producing a journal manuscript presenting the inconsistency flags for the CMAI, the frequency of their occurrence in available data and recommendations. Target journal: Journal for Prevention of Alzheimer's Disease

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Supplementary Material:

https://yoda.yale.edu/sites/default/files/rabinowitz_cmai_flags_yoda_proposal.docx