The YODA Project
Research Proposal Review

The following page contains the final YODA Project review approving this proposal.

The YODA Project
Research Proposal Review - Final
(Protocol #: 2019-4078)

Reviewers:

- ☒ Nihar Desai
- ☐ Cary Gross
- ☐ Harlan Krumholz
- ☒ Richard Lehman
- ☒ Joseph Ross

Review Questions:	**Decision:**
1. Is the scientific purpose of the research proposal clearly described?	Yes
2. Will request create or materially enhance generalizable scientific and/or medical knowledge to inform science and public health?	Yes
3. Can the proposed research be reasonably addressed using the requested data?	Yes, or it's highly likely
4. Recommendation for this data request:	Approve

Comments:

It is still somewhat unclear to me how the proposed algorithm will be validated. However, as an exploratory analysis this seems to be a worthwhile exercise, and it flags up an important issue for debate.

The YODA Project
Research Proposal Review

Revisions were requested during review of this proposal.
The following pages contain the original YODA Project review and the original submitted proposal.

The Yale University Open Data Access (YODA) Project
Yale University Center for Outcomes Research and Evaluation (CORE)
1 Church Street, Suite 200, New Haven, CT 06510

The YODA Project
Research Proposal Review - Revisions Requested
(Protocol #: 2019-4078)

Reviewers:

- ☒ Nihar Desai
- ☐ Cary Gross
- ☐ Harlan Krumholz
- ☒ Richard Lehman
- ☒ Joseph Ross

Review Questions:	**Decision:**
1. Is the scientific purpose of the research proposal clearly described?	No
2. Will request create or materially enhance generalizable scientific and/or medical knowledge to inform science and public health?	Yes
3. Can the proposed research be reasonably addressed using the requested data?	Yes, or it's highly likely
4. Recommendation for this data request:	Not Approve

Comments:

1. This is an interesting study to better understand the use of PANSS in patients. The proposal could be strengthened if the investigators pre-specified the algorithm based on “expert opinion”. It seems as if the investigators are simply comparing/correlating different components of the total and component scores of the PSP, PANSS and Clinical Global Rating of severity (CGI-s). However, more clarity would be useful. And it would be helpful for the investigators to pre-specify what threshold will be used to identify inconsistencies across ratings.

2. The authors refer to definitions and expert consensus recommendations but they are not included. This proposal would benefit from some additional details on the analytic plan; "outcomes" and statistical considerations.

Principal Investigator

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General Information

Key Personnel (in addition to PI):
First Name: Jonathan
Last name: Rabinowitz
Degree: PhD
Primary Affiliation: Bar Ilan Univerity
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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?: Colleague

Conflict of Interest

https://yoda.yale.edu/system/files/yoda_project_coi_form_for_data_requestors_2019.docx

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. NCT00111189 - R092670PSY3001 - A Randomized Double-blind Placebo-controlled Parallel Group Study Evaluating Paliperidone Palmitate in the Prevention of Recurrence in Patients With Schizophrenia. Placebo Consists of 20% Intralipid (200 mg/mL) Injectable Emulsion
2. NCT01529515 - R092670PSY3012 - A Randomized, Multicenter, Double-Blind, Relapse Prevention Study of Paliperidone Palmitate 3 Month Formulation for the Treatment of Subjects With Schizophrenia
3. NCT01193153 - R092670SCA3004 - A Randomized, Double-Blind, Placebo-Controlled, Parellel-Group Study of Paliperidone Palmitate Evaluating Time to Relapse in Subjects With Schizoaffective Disorder

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 Personal and Social Performance (PSP) scale

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. The International Society for CNS Clinical Trials and Methodology convened an expert working-group that assembled consistency/inconsistency flags for the Personal and Social Performance Scale 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 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. Objective: To determine the relevance of continuity checks to data from the Personal and Social Performance Scale (PSP). Study Design: International Society for CNS Clinical Trials and Methodology convened an expert Working Group that assembled consistency/inconsistency flags for the Personal and Social Performance Scale (PSP). Participants: Data sets are being requested from sponsors who conducted clinical trials that used the PSP and the PANSS. Main outcome measure: 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. The International Society for Central Nervous System (CNS) Clinical Trials and Methodology (ISCTM) expert Working Group focusing on improving consistency in measurement has been 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” of the working group and then testing it in data sets. Recommendations have been published for Positive and Negative Syndrome Scale (PANSS) (Rabinowitz, Schooler, et al 2017) and Montgomery-Asberg Depression Rating Scale (MADRS) (Rabinowitz, Schooler et al, 2019).
The current focus is the Personal and Social Performance (PSP).

Specific Aims of the Project:

Apply algorithm developed based on expert opinion to detect scoring inconsistencies in the use of the Personal and Social Performance scale. Algorithm to be applied to data sets from various clinical trials. Recommendations based on this work to be published.

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 PSP domain and total scores, PANSS item level data, Clinical Global Rating of severity (CGI-s) data by visit with sequential subject identifiers.
Please note that I do not need patient demographic, psychiatric history, or safety data nor subject id numbers.

Main Outcome Measure and how it will be categorized/defined for your study:

Frequency of occurrence of potential scoring inconsistency based on expert consensus derived inconsistency flags.

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

There is no independent variable for this project. Potential scoring inconsistencies are defined based on the inconsistency flags developed by the expert working group of the International Society for CNS Clinical Trials and Methodology.

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

N/A

Statistical Analysis Plan:

New variables identifying inconsistencies in a given rating will be added to the data set. Each flag will be a new variable. Using descriptive analysis, the data will be analyzed to examine the frequency with which each of the the potential inconsistencies occurs.
Software Used:
R
Project Timeline:

Once I obtain data sets I will apply consistency flags to the data sets. Data management and analysis are anticipated to take 4 months. The descriptive analysis emanating from this work will be included in a manuscript presenting the consistency flags . I anticipate the production of a manuscript for publication within 12 months.

Dissemination Plan:

As previously done for the PANSS (Rabinowitz,et al, 2017) and MADRS (Rabinowitz et al, 2019) the goal is to produce a journal manuscript presenting the inconsistency flags for the PSP, the frequency of their occurrence in available data and recommendations. Target journal: Schizophrenia Research.

Bibliography:

Rabinowitz J, Schooler NR, Anderson A, et al. Consistency checks to improve measurement with the Positive and Negative Syndrome Scale (PANSS). Schizophr Res. 2017;190:74–76. doi:10.1016/j.schres.2017.03.017

Rabinowitz J, Schooler NR, Brown B, Dalsgaard M, Engelhardt N, Friedberger G, et al. Consistency checks to improve measurement with the Montgomery-Asberg Depression Rating Scale (MADRS). J Affect Disord. 2019;256:143-7. https://doi.org/10.1016/j.jad.2019.05.077