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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?: External grants or funds are being used to support this research.

Project Funding Source: Signant Health will provide funding for statistical analyses

How did you learn about the YODA Project?: Other

Conflict of Interest

https://yoda.yale.edu/system/files/youngstrom_coi_nov_24_2020.pdf
https://yoda.yale.edu/system/files/busner_coi_nov_25_2020.pdf
https://yoda.yale.edu/system/files/findling_form_for_yoda_and_joan_busner_revised_dec_8.pdf
https://yoda.yale.edu/system/files/daniel_yoda_coi_disclosure_updated_dec_9_2020.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. [NCT01009047 - R076477PSZ3003 - A Randomized, Multicenter, Double-Blind, Active-Controlled, Flexible-Dose, Parallel-Group Study of the Efficacy and Safety of Prolonged Release Paliperidone for the Treatment of Symptoms of Schizophrenia in Adolescent Subjects, 12 to 17 Years of Age](#)
2. [NCT00518323 - R076477PSZ3001 - A Randomized, Multicenter, Double-Blind, Weight-Based, Fixed-Dose, Parallel-Group, Placebo-Controlled Study of the Efficacy and Safety of Extended Release Paliperidone for the Treatment of Schizophrenia in Adolescent Subjects, 12 to 17 Years of Age](#)

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

Research Proposal

Project Title

Validation of a shortened PANSS for use in clinical trials of adolescent schizophrenia.

Narrative Summary:

The 30 item PANSS scale is the gold standard efficacy measure in adult schizophrenia trials. Because of a lack of validated measures in youth, it has also been used in adolescent schizophrenia trials. The scale is long and burdensome for adolescents and their parents. There have been statistical attempts to reduce the number of items to reduce burden in adult trials. Our group is exploring a reduced item scale for use with adolescents. We have looked at an NIMH dataset that did not have a placebo control. We would like to examine the data sets requested to determine the fit with our initial findings and to see if the reduced item PANSS will show discrimination of drug from placebo.

Scientific Abstract:

Background: The 30 item PANSS scale is the gold standard efficacy measure in adult schizophrenia trials. Because of a lack of validated measures in youth, it has also been used in adolescent schizophrenia trials. The scale is difficult to administer and burdensome for adolescents and their parents. There have been statistical attempts to reduce the number of items to reduce burden in adult trials. Our group is exploring 2 reduced item scales for use with youth. We have looked at an NIMH dataset that did not have a placebo control. We would like to examine the paliperidone data sets requested to determine if our preliminary findings hold up and to see if the reduced item PANSS would show discrimination of drug from placebo. **Objective:** The goal of the project is to develop and validate a short form of the PANSS. **Design:** Psychometric analyses. **Participants:** All randomized subjects. **Main Outcome Measures:** PANSS individual items, CGI-S/I by treatment and visit. **Statistical Analysis:** PANSS item data will be used in psychometric analyses (factor analysis, item response theory analysis) to examine item functioning and develop a candidate short form. Following the methods implemented in our previous development of short forms we will evaluate factor structure, item characteristics, internal consistency, and convergent and discriminant validity (using clinical and demographic characteristics and CGI-S/CGI-I scores as criteria). The PANSS item data from follow-up visits will be used to evaluate retest stability of the short form (in the placebo arm) as well as treatment sensitivity.

Brief Project Background and Statement of Project Significance:

The 30 item PANSS is a long and burdensome scale, even in the adult patients for whom it was designed. For children and adolescents the scale is well known to pose a challenge for the patients, the parents, and the clinicians and researchers administering it. The research and clinical field would be advanced by a shortened scale that retained the ability to assess severity and treatment changes over time. Our group is comprised of leaders in adolescent psychopharmacology trials, application of the PANSS to adolescents in clinical trials, and item analysis statistics. A brief listing of relevant publications is provided at the end of the proposal as requested.

Specific Aims of the Project:

The goal of the project is to develop and validate a short form of the Positive and Negative Symptoms Scale, a widely used interview to assess psychotic symptoms. The PANSS was designed for adults not children, and takes a substantial amount of interview time. A short form that concentrated on the most helpful items would reduce burden for participants, as well as training and administration costs for researchers. A short form also would be helpful in clinical applications. The data needed for the project will be the PANSS items at baseline and each study visit, as well as treatment assignment, demographic and clinical characteristics including comorbid diagnoses, and CGI-S/I scores. PANSS item data will be used in psychometric analyses (factor analysis, item response theory analysis) to examine item functioning and develop a candidate short form. We will evaluate factor structure, item characteristics, internal consistency, convergent and discriminant validity (using the comorbid diagnoses, clinical and demographic characteristics, and CGI scores as criteria). PANSS item data from follow-up visits will be used to evaluate retest stability of the short form (in the placebo arm) as well as treatment sensitivity.

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

Summary-level data meta-analysis pooling data from YODA Project with other additional data sources
Research on clinical trial methods
Other

Research Methods

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

All randomized subjects from the two requested paliperidone trials. All randomized subjects from the NIMH TEOSS study (Treatment of Early Onset Schizophrenia Spectrum Disorders) -- NDA #2143.

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

individual item PANSS scores

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

Treatment assignment, Visit

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

Age at baseline, comorbid diagnoses at baseline, CGI-S at each visit, CGI-I at all post-baseline visits

Statistical Analysis Plan:

PANSS item data will be used in psychometric analyses (factor analysis, item response theory analysis) to examine item functioning and develop and assess candidate short forms. We will evaluate factor structure, item characteristics, internal consistency, convergent and discriminant validity (using the comorbid diagnoses, clinical and demographic characteristics, and CGI scores as criteria). PANSS item data from follow-up visits will be used to evaluate retest stability of the short form (in the placebo arm) as well as treatment sensitivity. 2 candidate forms we developed in earlier analyses of a non-placebo-controlled adolescent schizophrenia NIMH data set will be examined for fit with data from the placebo-controlled paliperidone data we are herein requesting.

Software Used:

R

Project Timeline:

12 months should be sufficient for us to access, analyze, and present results for presentation at scientific conferences. A manuscript draft ready for submission should be available within this timeframe as well. Our specific plan is to complete the bulk of the data analysis in time for a June, 2021 submission to AACAP (for presentation in October); additional data analyses would be done by August, 2021, in time for submission to ACNP (for presentation, December, 2021). We plan to have a manuscript submitted by end of December, 2021.

Dissemination Plan:

We plan to disseminate the findings at scientific conferences of relevance to the child psychopharmacology field such as ASCP, APA, AACAP and ACNP. We plan to generate manuscripts for publication in journals of relevance to clinicians and researchers in childhood psychosis and psychopharmacology. Preliminary findings from our NIMH dataset were presented this year at ASCP and will be presented in December at ACNP.

Bibliography:

Busner, J., Youngstrom, E.A., Daniel, D.G., Findling, R.L. Toward development of an abbreviated PANSS for pediatric trials: New analyses of PANSS TEOSS data. Accepted for presentation at the American College of Neuropsychopharmacology Annual Meeting, Dec. 5., 2020.

Busner, J., Youngstrom, E.A., Daniel, D.G., Findling, R.L. Toward development of an abbreviated PANSS for pediatric trials: Secondary analyses of TEOSS and other psychopharmacologic data sets. Presented as poster at the American Society of Clinical Psychopharmacology (ASCP), formerly NCDEU, Annual Meeting, Miami, FL., May 25-29, 2020

Salcedo, S., Rizvi, S. H., Freeman, L. K., Youngstrom, J. K., Findling, R. L., & Youngstrom, E. A. (2018). Diagnostic efficiency of the CBCL thought problems and DSM-oriented psychotic symptoms scales for pediatric psychotic symptoms. *Eur Child Adolesc Psychiatry*. <https://doi.org/10.1007/s00787-018-1140-1>

Youngstrom, E. A., Frazier, T. W., Findling, R. L., & Calabrese, J. R. (2008). Developing a ten item short form of the Parent General Behavior Inventory to assess for juvenile mania and hypomania. *Journal of Clinical Psychiatry*, 69, 831-839. <https://doi.org/10.4088/JCP.v69n0517>

Youngstrom, E. A., Murray, G., Johnson, S. L., & Findling, R. L. (2013). The 7 Up 7 Down Inventory: A 14-item measure of manic and depressive tendencies carved from the General Behavior Inventory. *Psychological Assessment*, 25, 1377-1383. <https://doi.org/10.1037/a0033975>

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