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General Information

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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.

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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

Associated Trial(s): NCT00866996 - A Multi-center Randomized Parallel Group Study Evaluating Treatment Outcomes of Concerta (Extended Release Methylphenidate) and Strattera (Atomoxetine) in Children With Attention-deficit/Hyperactivity 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

Applications of Item Response Theory to Clinical ADHD Research: Analysis of the Psychometric Properties of the ADHDRS-IV

Narrative Summary:
Rating scales serve as a necessary tool for clinicians who wish to determine presence and severity of ADHD symptoms. Therefore, accurate measurement of symptomatology is essential. Item response theory (IRT), a latent variable model, presents an opportunity to improve the way we measure baseline clinical symptoms of ADHD. This study aims to evaluate the psychometric properties of the ADHDRS-IV in a large, combined baseline sample of children and adolescents using IRT. The results are predicted to identify a more concise and presumably more sensitive change index which could have research and clinical value both in diagnosis and in treatment assessment.

Scientific Abstract:
Background: Item response theory (IRT), a latent variable model, presents an opportunity to improve the way we measure and evaluate baseline clinical symptoms of ADHD.
Objective: This study aims to evaluate the psychometric properties of the ADHDRS-IV and to determine if these estimates differ by age or gender in a large, combined baseline sample of children and adolescents using IRT.
Study Design: This study will employ a cross-sectional, pooled, multi-level analysis of baseline ADHDRS-IV items. Data will be pooled from a number of investigators in order to create a large sample of participants for the proposed analysis.
Participants: Participants include all children ages 6 to 17 who were rated using the ADHDRS-IV by a trained clinician.
Main Outcome: IRT item parameter estimates of the ADHDRS-IV will be the main outcomes of the study. Estimates will better inform our understanding of symptoms of ADHD and their respective utility in diagnosis.
Measure(s): The ADHDRS-IV will be evaluated in this study. Characteristics of the scale will be compared on key demographic variables including age and gender.
Statistical Analysis: Item response theory will be used to model the psychometric properties of the ADHDRS-IV. A multilevel item factor model will allow the investigator to model the nested nature of the data.

Brief Project Background and Statement of Project Significance:
Attention-deficit/hyperactivity disorder (ADHD) is an externalizing behavioral disorder that affects between 5 and 10 percent of youth (Polanczyk, Silva de Lima, Biederman, & Rohde, 2007). A number of rating scales exist for the purpose of measuring symptoms of ADHD for children and adolescents including the CPRS (Conners, Sitarenios, Parker, & Epstein, 1998), SNAP-IV (Swanson, 1992), and the ADHDRS-IV (DuPaul, Anastopoulos, Power, Reid, Ikeda, & McGoey, 1998). Rating scales serve as a necessary tool for clinicians who wish to determine presence and severity of ADHD symptoms, in addition to monitoring response to treatment (Conners, 1997). Because the best method for detecting the effectiveness of a treatment is through perceived changes in symptoms, accurate measurement of symptomatology is essential. However, as advances in quantitative methodology have improved measurement in domains such as physical functioning, emotional distress, and pain, clinical research in ADHD has lagged behind.

Item response theory (IRT), a latent variable model, presents an opportunity to improve the way we measure

baseline clinical symptoms of ADHD and treatment response. Successful IRT modeling of rating scales by the Patient-Reported Outcomes Measurement Information System (PROMIS) Cooperative Group and NIH has led to the development of reliable short forms that can be compared on the same scale to longer established measures of a number of constructs. PROMIS investigators now boast the efficiency, flexibility and precision of items that can be combined in a number of ways to measure constructs of interest (Cella et al., 2010). To maximize the potential of IRT application in ADHD measurement, we must also capitalize on the increasing availability of data previously collected by investigators and companies that have a stake in the advancement of research and treatment.

However, latent variable models such as IRT with many model parameters require big samples for stable and precise estimation. The last few years are making it increasingly possible to take advantage of the availability of data. Now, many samples exist and can be combined to both improve our measurement and understanding of symptoms and to identify targeted treatment approaches.

This study will use IRT to evaluate the psychometric properties of the ADHDRS-IV in a large, combined baseline sample of children and adolescents. The results of this IRT analysis are predicted to identify a more concise and presumably more sensitive change index which could have research and clinical value in diagnosis and treatment assessment. In addition, greater measurement precision may lead to a reduction in the number of patients required to find significant effect in a clinical trial while holding constant statistical power.

Specific Aims of the Project:
Psychometric properties of the ADHDRS-IV collected at intake will be evaluated using IRT. More specifically, this study aims to (1) use IRT to confirm the pre-treatment multidimensional structure of the 18 ADHDRS-IV items in children and adolescents (2) evaluate the item parameters of the IRT model including discrimination, thresholds, and the unique information provided by items at intake to determine the unique contribution of each item to the construct of ADHD as a whole (3) determine if a short form for ADHD may be developed through closer examination of IRT item parameter estimates and (4) determine if gender or age effect IRT item parameters, which would inform our understanding of ADHD.

What is the purpose of the analysis being proposed? Please select all that apply. Participant-level data meta-analysis
Participant-level data meta-analysis will pool data from YODA Project with other additional data sources

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:
A baseline sample of children and adolescents who were rated using the ADHDRS-IV are needed to estimate the IRT model. It is important that this sample reflects the population of interest, in this case youth who may possess symptoms of ADHD. We want a high degree of precision in our estimates of this clinically more severe sample. For this reason, baseline demographic and ADHDRS-IV data is requested from Janssen study NCT00866996, titled “A Multi-center Randomized Parallel Group Study Evaluating Treatment Outcomes of Concerta (Extended Release Methylphenidate) and Strattera (Atomoxetine) in Children with Attention-deficit/Hyperactivity Disorder.”

Baseline samples have also been requested from studies listed on Clinical Study Data Request (clinicalstudydatarequest.com) and Shire Pharmaceuticals. A very large sample is required to produce stable model parameter estimates in IRT for the ADHDRS-IV and therefore these baseline samples will be combined for analysis. Screening or baseline item-level ADHDRS-IV data for all 6 to 17 year-old study participants will be used. There are no other inclusion/exclusion criteria for participants to be included in the analysis.

Main Outcome Measure and how it will be categorized/defined for your study:
The ADHDRS-IV will be used as the main outcome measure for this study. The IRT model will include all items of the ADHDRS-IV, and parameter estimates will be generated for each item. Primarily the specific item parameter estimates will be evaluated and discussed.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:
In the primary model, there will be no independent variables as the purpose is to fit the general IRT model. However, during sub-group analysis, age and gender will serve as grouping variables in separate models. Children ages 7 to 11 will be grouped and children ages 12 to 17 will be grouped. A decision regarding how to group by age

was made based on literature presented regarding the statistically significant increase in inattention symptoms for children over the age of 11 (Bussing et al., 2008) and the general decrease in symptoms of hyperactivity/impulsivity as children age (Lahey, Pelham, Loney, Lee, & Willcutt, 2005), in the late pre-pubertal period of development. Gender will be evaluated as any differences in item parameter estimates between males and females.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:
The requested studies were all multi-site trials and data was collected across the U.S. The varying prevalence and treatment rates across the U.S. (CDC, 2010) support the need to model the baseline data within a multilevel framework to account for site differences of ADHDRS-IV baseline ratings. A multilevel item factor model will allow the investigator to model the nested nature of the data, where study participants (level-1 units) were nested within sites (level-2 units). Therefore, site will be used as another variable of interest.

Statistical Analysis Plan:
Item response theory will be used to model the psychometric properties of the ADHDRS-IV including item discrimination, thresholds, and the unique information about the latent trait of ADHD provided by the 18 items. Specifically, a graded response, unidimensional model (Samejima, 1969; Embretson & Reise, 2000) for symptoms of inattention and hyperactivity/impulsivity will be modeled separately as supported by literature. A multilevel item factor model will allow the investigator to model the nested nature of the data.

Models will likely be estimated in flexMIRT (Cai, 2013) using maximum marginal likelihood via the Bock-Aitkin EM algorithm (Bock & Aitkin, 1981), which will also handle missing data. The use of flexMIRT is necessary due to the complexity of the IRT model (e.g. multiple group, multilevel). Several indices of model fit will be reported to assess the fit of the model. Due the possibility of many response patterns (4^9) and a sparse contingency table, the M2 statistic will be reported (Cai & Hansen, 2013). Root mean square error of approximation (RMSEA; Steiger & Lind, 1980) will also be reported in addition to marginal fit (chi-square) and LD (chi-square) statistics for further evaluation and discussion of model fit.

Sub-group differences across gender and age will be explored using differential item functioning using a multi-step Wald chi-square procedure (Woods, Cai, & Wang, 2013; Langer, 2008; Cai et al., 2011). In addition, DIF may also be computed within and between sites for the ADHDRS-IV items. To control the inflated error rate caused by multiple DIF comparisons, the false discovery rate procedure (Benjamini & Hochberg, 1995) will be us

Project Timeline:
The project will start as soon as data, or decisions regarding data, have been received. Analyses will be completed within three months following receipt of data. The dissertation will be drafted by the end of the 2015 calendar year, and available on ProQuest in the first few months of 2016. A manuscript will then be drafted by March of 2016 and submitted for publication by June 2016.

Dissemination Plan:
The purpose of these analyses is primarily for dissertation research which will be completed by March of 2016. Publication of results will occur by June 2016, and will be submitted to journals such as Psychological Medicine, Journal of Attention Disorders, and Psychological Assessment.

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