**Project Title:** Examining the Natural History of ADHD in a Clinical Setting: The Problem of Missing Data

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**Background**:

Attention Deficit-Hyperactivity Disorder (ADHD) is a condition that is characterized by persistent patterns of inattention and/or hyperactivity-impulsivity that impair functioning or development (APA 2013). ADHD is the most common psychiatric disorder of childhood, affecting 8-10% of school-age children (Polanczyk et al .2014). As a neurodevelopmental condition, ADHD frequently onsets in childhood and symptoms often persist throughout the lifespan. ADHD is associated with significant social, academic, occupational, and functional impairment (Getahun et al 2013; Elia et al. 2008; Mordre et al. 2011; Fredriksen et al. 2014). The economic impact of ADHD is substantial. It is estimated ADHD costs the US between $143 and $266 billion per year (Matza et al., 2005)

Despite these outcomes, there is a limited understanding of the course or trajectory of ADHD. Predictors of severity and clinical presentation (e.g. psychiatric comorbidities, executive and adaptive functions) are also not fully understood. Most studies that examine the natural history of ADHD use self- or caregiver-reported data, which is subject to numerous biases. As a result, there is a considerable dearth of longitudinal studies among clinical populations using deeply phenotyped samples.

The Department of Neuropsychology at the Kennedy Krieger Institute is one of the largest outpatient psychological assessment facilities in the United States. On average, the department sees 2,700 youth, ages 3-25 years of age, per year. Roughly 60% of these individuals have ADHD. The department captures a wealth of information during the clinical visits, from parent ratings to diagnosis to a host of psychological and neuropsychological assessments. Since this clinical data has been in existence since 2005, it is very long (N>25,000) and wide (multi-informant, multi-method information).

However, there is one critical limitation of this dataset: most youth are only evaluated once. In fact, only 15% of initial evaluations are reevaluated. Reasons for lack of follow-up are numerous (e.g., insurance-related issues, youth aging out into adulthood, issues with caregiver follow-up, geographic location, difficultly getting a new referral, questionable diagnostic presentation, etc.) and unknown. To understand the trajectories and predictors of ADHD symptomatology, the accuracy and representativeness of our clinical sample must be fully understood.

**Problem Statement**: We aim to examine the clinical course of ADHD who received evaluation at a large, urban pediatric hospital. A secondary objective is to identify predictors of symptom severity and complexity. Both of these findings have important implications for treatment. However, we do not know if there are systematic differences between those who do and do not return for evaluation. Understanding the nature of potential biases, and how the findings change in the presence of various methods that account for selection, holds important implications. Clinically, identifying populations who are lost to follow-up will help inform our understanding about children who do not thorough monitoring of their cognition. This is important since many recommendations (e.g., about educational, behavioral, and pharmacological treatment) are made after the initial evaluation. Second, empirical knowledge of ADHD, including its course, outcomes, and risk factors, is needed to advance personalized care.

**Aim 1:** To understand the demographic and clinical differences between youth with ADHD who do and do not return for follow-up.

**Aim 2:** To examine 2a) changes in ADHD symptomatology, and 2b) predictors of symptom change, among youth with ADHD who return for follow-up.

**Aim 3:** To 3a) evaluate the performance of various methods in managing missing data. To 3b) understand how the findings change in Aim 2 (using complete case analysis) when modern methods for missing data are employed.

**Data Set Identification:**

The data set is comprised of all clinical data collected for patients seen for evaluation within the Neuropsychology Department at the Kennedy Krieger Institute since 2005. This includes demographic information collected on patients at the point of initial registration (e.g., age, race/ethnicity, geographic location, insurance-type, guarantor) with the hospital, clinical history information and symptom ratings provided by caregivers (e.g., behavior problems, medical issues), and clinical point of care data (e.g., standardized, neuropsychological assessment of inhibition and inattention).

Demographic information is available for roughly 20,000 unique patient visits. Previsit history information and ratings is available for around 8,000 patients. Considerable variability exists in sample sizes for clinical point of care data, as specific tests are chosen and administered only when clinically indicated for a particular patient. For instance, the Beery Buktenica Developmental Test of Visual Motor Integration, 6th Edition (VMI-6) is one of the most commonly administered tests with over 10,000 unique administrations. On the other hand, the Wechsler Intelligence Scales for Children, 5th Edition, a very commonly administered IQ test, is available on half of that figure (N~ 5,000). Behavior Assessment System for Children, a measure of internalizing (e.g., anxiety, depression) and externalizing (e.g., oppositionality, conduct issues) problems, is available for 1800 unique patient visits. We hope the students at JHU BME will help us understand the natural history of ADHD while appreciating the selection that arises when only a proportion of our clinical population is reevaluated.

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**Other Supporting Information:**

Please see citations for work based upon these datasets.

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