

Advancing Health through Clinical Records Research

Funded Projects

The Harvard Catalyst Biomedical Informatics Program sponsored this pilot grant opportunity to support efforts to secure patient-level data based on results obtained during the Harvard Catalyst Shared Health Research Information Network (SHRINE) query <u>prize opportunity</u> awarded in June 2012. This recent funding program was open only to <u>winners</u> of the past prize opportunity.

Four pilot grants were awarded in amounts of up to \$50,000 for each one-year project.

Funding decisions for the Advancing Health through Clinical Records Research pilot grants were announced in October of 2012.

Hyperplasticity in Autism Spectrum Disorders Confers Protection from Alzheimer's

Principal Investigator: Lindsay Oberman, PhD, Beth Israel Deaconess Medical Center

Co-Investigator: Alvaro Pascual-Leone, MD, PhD, Beth Israel Deaconess Medical Center

Autism Spectrum Disorders (ASD) currently affects approximately 1% of the population necessitating a better understanding of the currently enigmatic etiology of these disorders. Recent data suggests that patients with ASD have a dysfunction in brain plasticity (specifically an excessive amount of plasticity). Plasticity is essential to the establishment and maintenance of brain circuitry, however, too much plasticity may lead to instability of structural connections and compromising of functional systems necessary for cognition and behavior. Multiple lines of evidence suggest that plasticity declines throughout the age-span and may underlie age-related cognitive decline. We hypothesize that individuals whose cortex begins as relatively "hyperplastic" (such as seen in ASD) should then be relatively protected from age-related cognitive decline (which we suggest is related to a reduction in plasticity). Based on this hypothesis we conducted a SHRINE Query of patients over 65 with comorbid ASD and dementia. Results supported our claim finding <10 patients. Our ability to verify diagnoses, however, is limited by what information is present in the patient's medical record. Thus, in the current proposal we seek to validate our SHRINE findings by directly evaluating the presence of behavioral and neuroimaging markers for dementia in patients over 65 with ASD (as compared to both patients with Schizophrenia and a healthy control group). If we see differences in the presence of these markers between the groups in this pilot study, multicenter, longitudinal studies would need to be conducted. Additionally, future translational studies could explore the genetic and neuropathological basis of these differences.

In Utero Antidepressant Exposure and Autism Risk

Principal Investigator: Roy Perlis, MD, MSc, Massachusetts General Hospital

Co-Investigators: Roscoe Brady, MD, PhD, Beth Israel Deaconess Medical Center

Sek Won Kong, MD, Boston Children's Hospital

Jordan Smoller, MD, ScD, Massachusetts General Hospital

In utero exposure to antidepressants was recently associated with increased risk for autism in an analysis of a large health care claims database. This result is consistent with twin studies indicating greater concordance for autism among dizygotic twins compared to non-twin siblings, likely pointing to shared in utero risk. The need to clarify the risk posed by antidepressants is acute, as it has profound public health implications for decision-making by women with depression who become pregnant.

The proposed study will utilize electronic health record (EHR) data from patients in the Partners Healthcare system as well as Beth Israel Deaconess Medical Center and Children's Hospital Boston based on SHRINE and i2b2 queries. Children age 4-12 with a diagnosis of autism will be identified from ICD-9 codes. A matched (2:1) cohort of children with a diagnosis of ADHD will be identified, along with a matched (4:1) control cohort of children receiving routine pediatric care. Using Massachusetts state birth certificate data, these children will then be securely matched with mothers. Maternal EHR data will then be used to characterize sociodemographic status, medical and psychiatric illness, and medication treatment during pregnancy, augmenting available birth certificate data. Logistic regression will be used to compare exposures between groups.

This study will provide essential pilot data for larger-scale investigation, and facilitate cross-institution collaboration and development of early-career investigators at the CHB and BIDMC sites. It builds on the extensive experience of the investigators in the use of bioinformatics tools to characterize neuropsychiatric disorders.

Characterizing the Rise in Precocious Puberty 2001-2009

Principal Investigator: Lisa Topor, MD, MMSc, Boston Children's Hospital

Co-Investigators: Amy Fleischman, MD, MMSc, Boston Children's Hospital

Natalie Shaw, MD, MMSc, Massachusetts General Hospital

Early puberty is rising, as documented through recent population studies. It is also a frequent topic of discussion by the media. In additional to psychological concerns, forms early puberty are associated with increased risk of insulin resistance and type 2 diabetes mellitus (T2DM). The etiology of the rising rates of precocious puberty is unclear, though increased weight gain during infancy and childhood obesity are recognized risk factors in girls.

SHRINE queries revealed a 5-fold increase in annual visits for precocious puberty in affiliated hospitals between 2001-09. The rise was seen in both genders. More than 1000 of these children were \leq 5 years old at the time of evaluation. In the last 3 years of our search, 14% of children with precocious puberty were diagnosed as overweight or obese. Co-morbidities were also seen, with insulin resistance in 27 children and mood disorders in 181 children seen for early puberty.

Next steps include identifying factors associated with the rise in precocious puberty, as well as risk factors for associated co-morbidities. We will identify the prevalence of overweight and obesity in children with precocious puberty using body mass index. Using a case-control design we will identify risk factors for co-morbidities such as insulin resistance, T2DM, anxiety, and depression. As early pubertal development may be a biomarker for future disease risk in some children, we hope to be able to identify those most at-risk for development of future co-morbidities to develop medical and psychosocial interventions to reduce the burden of disease.

A Multi-institutional Collaboration to Develop Algorithms for Identifying Patient Diagnoses in Support of Clinical Care and Translational Research

Principal Investigator: Adam Wright, PhD, Brigham and Women's Hospital

Co-Investigators: Michael Hassett, MD, MPH, Dana-Farber Cancer Institute

Kenneth Mandl, MD, MPH, Boston Children's Hospital Charles Safran, MD, Beth Israel Deaconess Medical Center

David Ting, MD, Massachusetts General Hospital

An accurate and up-to-date patient problem list is essential for safe, high quality care; however, research has shown that problem lists are often inaccurate, incomplete, and poorly maintained. In a prior study at BWH, we developed a set of rules to infer patient problems and created alerts in our EHR to notify clinicians when their patients had potential gaps on their problem list, resulting in a three-fold increase in problem list utilization. Initial queries in SHRINE suggest that similar gaps can be found at other Catalyst institutions. We have assembled a team of researchers from BWH, MGH, DFCI, BIDMC and CHB to study problem list usage at these

sites, with a focus on three specific aims to 1) assess problem list completeness at the Catalyst member sites, 2) validate our existing problem inference rules and 3) improve and expand our rules. Our research will focus on five conditions: diabetes, acute lymphoblastic and chronic myelogenous leukemias (ALL and CML), sickle cell disease and myasthenia gravis. At the conclusion of this work, we would have fully validated inference rules for the five conditions as well as details on their performance according to standard metrics. In future work, we plan to build on these results (and on our multi-institutional collaboration) to apply for an R01 in order to test the rules we develop at the sites in our consortium, as well as to explore new applications of our inference rules, including enhanced EHR-based phenotyping for genomic studies.