

Research Use Statement for Application for Genomic Data from NIAGADS

Please limit to 2,200 characters max. The statement should include the following components:

- Objectives of the proposed research;
- Study design;
- Analysis plan, including the phenotypic characteristics that will be evaluated in association with genetic variants

Integrated predictive risk models using multimodal imaging and genetics

The objective of this study is to develop and evaluate predictive models of disease progression and risk to assist patients and clinicians in care decisions. To achieve this goal, we plan to leverage algorithms built from MRI (Data provided by NACC), genetics, and other phenotypic data. With this rich information, we test the feasibility of and design tools aimed at improving the (1) differentiation of an individual patient's risk, (2) assisting clinicians in directing patients to optimal clinical care, and (3) providing personalized, actionable risk information.

Specifically, we have trained models utilizing features derived from non-contrast MRI and from genotyping data along with demographics (age and gender) and risk factors such as medications, sleep, glucose measurements, diabetes, head injury, bmi, vitals, labs, exercise, diet, alcohol, and tobacco use. One key aspect of our work will be to use state-of-the-art algorithms, including neural networks which require large longitudinal datasets, and hence we would like to have access to as much of the overlapping cohort with NACC as possible.

We will subset the data into cognitively healthy/normal, mild cognitive impairment, and dementia. We also plan to utilize cognitive testing results along with further subtyping of mild cognitive impairment into late and early stage and dementia into Vascular Dementia, Alzheimer's disease to gain further insights into the ability of integrating imaging and genetics for risk stratification.

Non-Technical Summary for Application for Genomic Data from NIAGADS

Investigators will provide a non-technical summary of their proposed research. If the project is approved, this statement will be publicly available for lay audiences to read the purpose and objectives of the research. Please limit to 1,100 characters.

The goal of this work is to provide risk information that empowers individuals in management of their health and assists in improving clinical outcomes via more accurate, personalized risk information. Current models for predicting onset of dementia rely primarily on data from a single modality. However, it is necessary to

include multiple modalities including imaging, genetics, and clinical biomarkers to fully assess an individual's risk. Furthermore, accurate prediction requires assessing imaging features beyond a single structure, genotyping beyond a single SNP, and further investigation into mitigating risk factors. Based on our studies of multimodal models, we expect integrated algorithms will yield a more accurate prediction of dementia and cognitive decline as well as provide insights that will assist individuals in reducing their risk and improving outcomes.