Estimating Long-Term Disease Trajectories from Short-Term Data

https://neurodegenerationresearch.eu/survey/estimating-long-term-disease-trajectories-from-short-term-data/

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Country

USA

Title of project or programme

Estimating Long-Term Disease Trajectories from Short-Term Data

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,487,095.41

Start date of award

01/02/2016

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s clinical trial design is predominantly

guided by fragmented analyses on short-term data from pre- specified groups. We conceive these groups by cross-sectional examination of the distribution of assessments. We then characterize longitudinal changes in these groups to calculate power and sample size. This approach is effective in establishing practical inclusion criteria for staging trials, but the resuting criteria may be unnecessarily course. Novel analytical methods that capture the full continuum of the disease will make more efficient use of multivariate longitudinal data, allow more sophisticated and inclusive inclusion criteria, and provide new insights into optimal populations tailored to specific interventions. A better understanding of the long-term continuum of disease dynamics will allow us to discover gaps in our current understanding and provide a comprehensive, data-driven approach to designing clinical trials. Analytic methods to support this new approach to AD clinical trial design are underdeveloped and technically challenging. We will develop, implement, and interpret novel statistical methods to accurately and efficiently characterize the long-term dynamics of Alzheimer's disease markers from preclinical to dementia. We will apply our statistical methods to existing short-term biomarker datasets to optimize Alzheimer's clinical trial design and improve personalized prognostic predictions. This project will have a substantial impact on our progress with Alzheimer's by more accurately characterizing long-term disease dynamics; identifying risk factors and ideal clinical trial populations and outcome measures; and providing personalized prognostic predictions. Specific Aim 1: To Develop an Analytic Framework for Modeling Long-Term AD Dynamics. We will develop a novel hierarchical Bayesian latent variable model to discern long-term multivariate disease trajectories from short-term sampled data. The base model will be extended to model sampling variation, disease heterogeneity, and complex network mediation structure using Dynamic Bayesian Belief Nets. Specific Aim 2: To Develop Optimized Clinical Trial Study Designs and Personalized Prognoses. The models developed under Aim 1 will be leveraged to determine the optimal combinations of study population and outcome measure for specific mechanistic biomarker effects, and to obtain personalized predictions of disease course and therapeutic benefit. We will develop and validate the machinery necessary to use our models to make relevant clinical trial and personalized prognostic predictions. Specific Aim 3: To Develop Software and Web Application. Computer software implementing the methods developed in Aims 1-2 will be developed and distributed as a free R package. We will build an interactive web application so that clinicians and clinical trialists can explore, visualize, and interrogate our analysis results to predict prognoses and simulate clinical trial scenarios. The application will enable clinical trialists to optimize their trial designs based on our model and their prior knowledge of their intervention's biomarker effects.

Lay Summary

PUBLIC HEALTH RELEVANCE: We will develop, implement, and interpret novel statistical methods to accurately and efficiently characterize the long-term dynamics of Alzheimer's disease markers from preclinical to dementia. We will apply our statistical methods to existing short-term biomarker datasets to optimize Alzheimer's clinical trial design so that we can more quickly determine which drugs work and also provide personalized prognostic predictions for patients. This project will have a substantial impact on our progress with Alzheimer's by more accurately characterizing long-term disease dynamics; identifying risk factors and ideal clinical trial populations and outcome measures; and providing personalized prognostic predictions.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A