Facilitating User Accessibility to Regulatory-Endorsed Drug Development Tools for Alzheimer Disease (AD)

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Background

• The Critical Path for Alzheimer’s Disease (CPAD) consortium is a public-private partnership founded by the Critical Path Institute (C-Path), which facilitates the development of quantitative solutions accelerate Alzheimer’s drug development.
• CPAD provides the precompetitive infrastructure for data and knowledge sharing, allowing CPAD to standardize and integrate patient level data to develop the proposed quantitative solutions (Figure 1)

Figure 1: Construct for data sharing and development of quantitative solutions for AD drug development

Objectives

The objectives of this effort are aimed at addressing the challenges to making the CTS tools widely accessible and efficient:
• Develop user-friendly CTS tools via graphical user interfaces, to optimize the design of clinical trials in mild-to-moderate AD and predementia
• Provide streamlined access to the tools
• To develop real-time solutions for the efficient computational application of CTS tools that are accessible to all members of drug development teams and regulators

Methods

• Both CTS tools (mild-to-moderate AD and predementia) are based on a drug-disease-trial model with parameters estimated from clinical data (Figure 2)

Figure 2: Model structure underlying the CTS tools

Results

Mild-to-moderate AD CTS Graphical User Interface (GUI) (Figure 3)
• A fully-functional GUI was developed in Rshiny (QR code [4]) for the mild-to-moderate AD CTS tool using the CPAD database (N = 4,726 individuals) to describe the longitudinal trajectories of ADASCog11 scores
• The GUI allows users to simulate patient populations including choices for enrichment: baseline MMSE scores, sex, number of APOE-e4 alleles, and concomitant medication use
• The GUI provides trial simulations for treatment and placebo groups for a user-chosen disease modification rate for both parallel and delayed-start clinical trial designs
• It allows users to perform power calculations for specific enrichment criteria to help define various trial designs including parallel and delayed-start designs

Figure 3: GUI for the mild-to-moderate AD CTS tool

Predementia CTS Graphical User Interface (Figure 4)
• A fully-functional GUI was developed in Rshiny (QR code [5]) for the pre-dementia CTS tool using ADNI data (N = 702 individuals) to simulate the longitudinal trajectories of CDR-SB
• The GUI allows users to simulate patient populations including choices for enrichment: baseline MMSE scores, sex, number of APOE-e4 alleles, and hippocampal volume
• It allows users to perform power calculations for specific enrichment criteria to help inform parallel trial design

Figure 4: GUI for the mild-to-moderate AD CTS tool

Envisioned Outcome

The long-term goal of this effort is to provide a framework for end-to-end quantitative solutions to accelerate drug development across the AD continuum. The evolution of completed work has been:
• Framing of key drug development needs in the AD disease continuum within the pre-competitive environment provided by CPAD
• Acquisition of patient-level data from multiple partner organizations
• Development of quantitative tools built upon acquired data
• Development of efficient user accessible platforms to make the tools widely available

The envisioned outcome is to provide training on the developed platforms while refining the underlying models with newly acquired data

References

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