Evaluating and Improving the Predictive Power of the Alzheimer's Disease Progression by Introducing Time-Varying Factors

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Overview

Proposal Outline

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- Significance
- Innovation
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- Research Strategy
  - Specific Aim
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Research Question

How can the predictive power of models for Alzheimer's Disease (AD) progression be improved by introducing one or more additional time-varying factors at multiple time points?

Introduction

Background:

- AD is the leading cause of dementia in older adults
- Pathophysiology of AD is complex and involves multiple factors
- Critical need for innovative research methods
- New model with potential to improve accuracy
- Dataset: The Alzheimer's Disease Neuroimaging Initiative (ADNI)

Introduction

Significance:

- More accurate predictions
- Understanding the dynamics of AD progression
- Impact on caregivers and families

Innovation:

- A novel approach to modeling AD progression
- Incorporation of time-varying factors
- Benchmark advanced machine learning techniques against traditional Cox proportional hazards models

Research Plan

1. Data Collection
2. Variable Selection
3. Model Construction and Prediction
4. Model Evaluation and Comparison
5. Analysis and Interpretation
6. Continual Improvement and Future Research

Research Strategy

Specific Aim

To evaluate and improve the predictive power of the Alzheimer's Disease progression by introducing time-varying variables at multiple time points

Hypothesis

We hypothesize that introducing time-varying variables into predictive models will improve the prediction of Alzheimer's Disease progression compared to models with only time-constant variables.

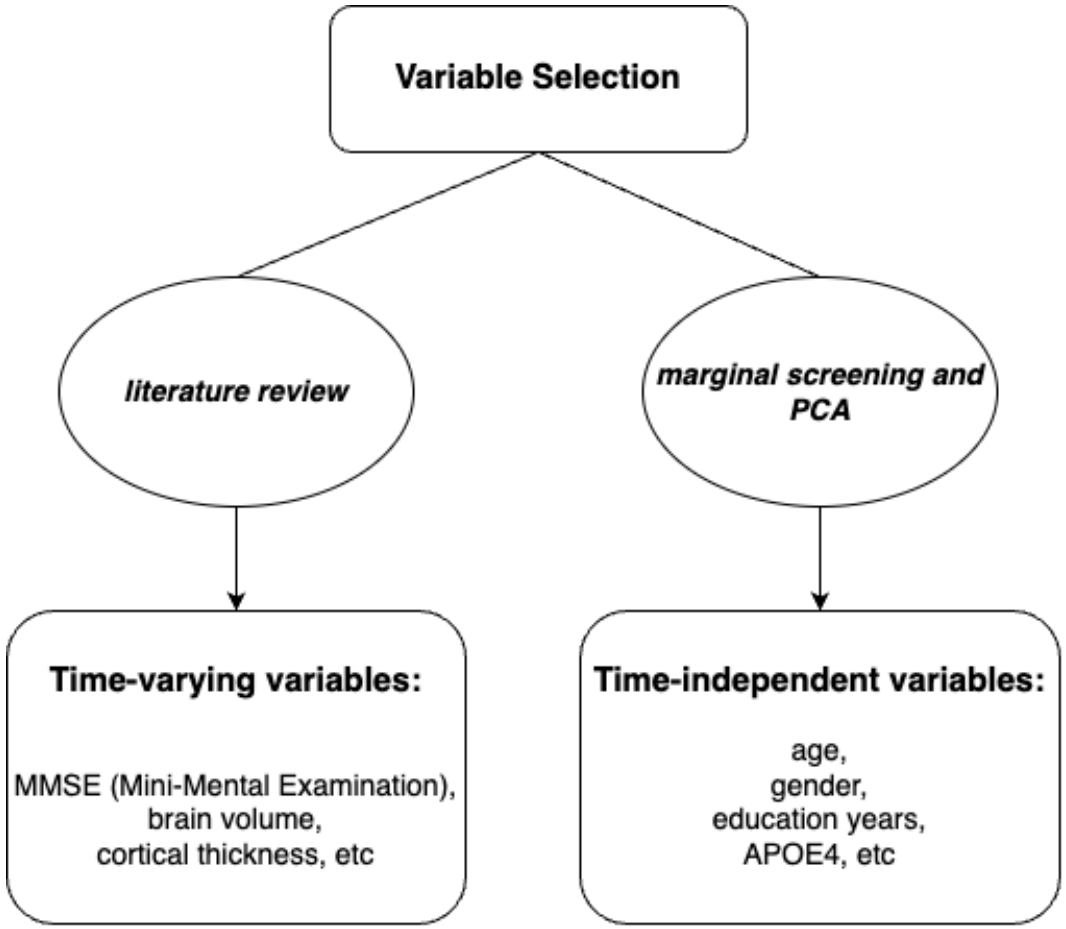
Research Strategy

Two innovations:

1. Time-varying variables
   - Cognitive Scores: MMSE (Mini-Mental State Examination)
   - Biomarkers: brain volume, cortical thickness, etc.
2. Landmark Analysis
   a method constructing a nested set of datasets at 'landmark' times and fitting a survival model at each time point.

Experimental Approach

- **Data Collection**
  ADNI data: The Alzheimer's Disease Neuroimaging Initiative.
- **Variable Selection**



Experimental Approach

- **Statistical Modeling and Analysis:**
  - Landmark analysis to periodically select cohorts of patients
  - Random survival forests for each "landmark" time
- **Competing method:** Cox proportional hazards model that treat time-varying covariates as time-constant variable
- **Model Validation:** Cross-validation, Performance metrics, such as concordance index (C-index)

Interpretation of Potential results

Should the hypothesis be confirmed would:

- signify a notable improvement over the traditional method
- provide insights into the progression of Alzheimer's Disease
- offer a more accurate and holistic assessment of AD risk over time
- potentially inform more personalized treatment approaches
- provide snapshots of the disease progression at various stages, revealing critical windows for therapeutic intervention
- more details will be included in the refinement

Potential Problems and Alternatives

- Problem: may not fully capture the disease's dynamics
  Alternative: alternative machine learning approach - deep learning
- Problem: poor data quality or missing data
  Alternative: sensitivity analyses
- Problem: overfitting
  Alternative: alternative approaches - penalized regression models

References

- Li, Kan, and Sheng Luo. "Dynamic prediction of Alzheimer's disease progression using features of multiple longitudinal outcomes and time-to-event data." Statistics in medicine vol. 38,24 (2019): 4804-4818. doi:10.1002/sim.8334
- Shu Jiang, Yijun Xie, Graham A. Colditz, Functional Ensemble Survival Tree: Dynamic Prediction of Alzheimer's Disease Progression Accommodating Multiple Time-Varying Covariates, Journal of the Royal Statistical Society Series C: Applied Statistics, Volume 70, Issue 1, January 2021, Pages 66–79, https://doi.org/10.1111/rssc.12449

Thanks for listening!

Q&A