

LONGITUDINAL MODELING OF RANK-BASED GLOBAL OUTCOME

Maomao Ding, Jing Ning*, Xuming He, Anne-Marie Wills and
Ruosha Li*

*Rice University, University of Texas MD Anderson Cancer Center,
Washington University in St. Louis,
Massachusetts General Hospital and
University of Texas Health Science Center at Houston*

Abstract: Many chronic diseases exhibit multifaceted symptoms that cannot be comprehensively characterized by one outcome. To address this, researchers often adopt a global outcome to combine information from multiple individual outcomes. The global rank-sum facilitates robust integration of multiple outcomes and has been applied in many clinical studies. We consider longitudinal settings and devise a global percentile outcome for depicting patients' time-varying global disease burden. We develop useful regression strategies for the longitudinal global percentile outcome based on a flexible regression framework of the monotonic index model. Posing minimal restrictions, we propose a maximum rank correlation type estimator and show that it entails desirable asymptotic properties. The methods are also extended to accommodate the common missing at random dropout scenarios. We propose a computationally stable and efficient procedure for parameter estimation, as well as a perturbation scheme for consistent variance estimation. Numerical studies show that our method performs well under realistic settings. We apply the proposed method to data from a Parkinson's disease clinical trial to examine risk factors associated with elevated global disease burden and accelerated disease progression.

Key words and phrases: Global percentile outcome, longitudinal data, maximum rank correlation, monotonic index model, Parkinson's disease.

1. Introduction

Definition of the primary outcome plays a central role in biomedical studies. For many diseases with complex symptoms and multi-dimensional deteriorations, however, there is no single outcome that is comprehensive enough to capture all important aspects of the disease. In these situations, researchers often construct a global outcome that combines information from multiple individual outcomes. For example, the NIH Exploratory Trials in Parkinson's Disease (NET-PD) Long-term Study-1 (LS-1) was a multi-center, double-blind, placebo-controlled,

*Corresponding author. E-mail: (Ning) jning@mdanderson.org; (Li) ruosha.li@uth.tmc.edu