Adaptive Functioning in Angelman Syndrome: Insights from Statistical Modeling

Julia Zhang, RTI International

Modeling person ability scores in rare disease natural history studies presents several methodological challenges, including nonlinear developmental trajectories, heterogeneous variance, and floor and ceiling effects. This presentation describes a modeling framework developed to address these challenges using data from a large, multi-site longitudinal study of individuals with Angelman syndrome (AS).

AS is a rare neurogenetic condition characterized by severe to profound intellectual disability, minimal speech, and motor impairments. We focus on modeling adaptive functioning over age, using Vineland-3 Growth Scale Value scores across multiple subdomains. To capture the complex structure of these data, we evaluated and compared a series of candidate models and selected an approach that balances interpretability with statistical rigor while accommodating key features of the data, including nonlinearity and heteroscedasticity.

We present the model development process, including comparison of alternative specifications, and highlight how the selected framework captures distinct developmental trajectories across molecular subtypes of AS. Results demonstrate meaningful differences in patterns of adaptive functioning by subtype and illustrate how model choice influences substantive conclusions. We conclude with practical recommendations for modeling longitudinal person ability scores in rare disease contexts, with implications for study design, analysis, and interpretation.

Novel Influence Diagnostics in Multistate Models for Breast Cancer

Valeria Leiva, Department of Public Health, Universidad de los Andes, Chile

Multistate models were developed to model survival data where several midpoints and endpoints are of interest; and they have been particular succesful in modeling dynamics of cancer. As in any statistical model, identification of influential observations is an essential task, as they can significantly affect the validity of infered parameters and conclusions drawn from the data. The local influence approach is a set of methods designed to detect the effect of small perturbations of the model or data on the inference, allowing for deeper data analysis. In this paper, we derive local influence methods for multistate models and illustrate their use with a breast cancer dataset. In particular, we develop and implement local influence diagnostic techniques based on a suitable estimation equation. For simplicity, we restrict our consideration to the Multistate Proportional Hazards model, using different case-weight perturbation strategies.

Goodness-of-fit test for the Dirichlet distribution

Sucharitha Dodamgodage, Clarkson University

The Dirichlet distribution is the first choice for modeling compositional data like microbiome profiles, yet the literature lacks a rigorous goodness-of-fit (GoF) framework to validate its assumptions. Existing methodologies face computational barriers and lack documented performance for dimensions $d > 2$. This study evaluates the implementation, test size, and Power of standard Empirical Distribution Function (EDF) tests, specifically Kolmogorov-Smirnov (KS), Anderson-Darling (AD), and Cramér-von Mises (CvM), alongside a novel Parametric Bootstrap Chi-square (PB-CS) test. Implementing EDF tests for the Dirichlet distribution introduces two major hurdles: the absence of a closed-form distribution function for $d > 2$ and the mathematical ambiguity of ranking multivariate observations. To bypass the closed-form limitation, we propose a two-step transformation using Beta decomposition and the Rosenblatt transformation to map $(d-1)$-dimensional unit simplex data into a $(d-1)$-dimensional unit hypercube. Furthermore, we demonstrate that the frequency-based PB-CS test completely bypasses the multivariate ranking problem. To adapt it for continuous data, we introduce an extended Doane's rule for bin selection paired with a quasirandom binning strategy using Sobol sequences and Voronoi partitioning. Extensive simulations show that while EDF methods thrive in lower dimensions, the PB-CS framework delivers superior or comparable omparable performance as dimensionality increases.

A Bayesian Exploration of Bimodal Fertility Patterns Using Lifetime Densities.

Shambhavi Singh, University of Petroleum and Energy Studies, Dehradun, Uttarakhand, India.

The work explores mixtures of three lifetime densities, viz., normal, Weibull, and generalized gamma densities, to capture fertility patterns characterized by hump- or bimodal-shaped behavior, an intriguing trend that researchers have observed over the last two to three decades. It harnesses the Bayesian framework to achieve a comprehensive posterior analysis. The Metropolis algorithm was used with a carefully selected candidate-generating density to produce posterior samples for each case. Numerical illustrations have been conducted using unabridged real-life data. Ultimately, the proposed models were compared to identify the most suitable model, ensuring compatibility with the available data. This work is inspired by previous studies that have largely overlooked the use of more flexible lifetime models in analyzing fertility patterns of this nature, prompting us to incorporate them into our analysis.