Copula Modeling for Clinical Trials

Nathan T. James, ScM

Dept. of Biostatistics, Vanderbilt University

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Introduction

- Ordinal Cumulative Probability Model (CPM)
  - $G[P(Y \leq y_i|X)] = \alpha_i - \beta^T X$
  - y_i - ordered, continuous outcome
  - X - matrix of covariates
  - $G(\cdot)$ - link function

Why use a Bayesian CPM with a **continuous** outcome?

- Invariant to monotonic transformation of outcome
- Directly model full conditional CDF
- Handles any ordered outcome including mixed discrete/continuous distributions (e.g., continuous outcome with lower limit of detection)
- Inference using posterior probabilities

- α_i estimate posterior CDF for $X = 0$
- β measure association between X and distribution of Y; interpretation depends on link function
- Mean and quantiles calculated from posterior distribution of full conditional CDF using single model

Placeholder

Image

- Implemented using `brms` and `rstanarm`; both call `Rstan`
- Different parameterizations; using default priors `rstanarm` more accurate in simulations
- Model convergence depends on package and link function

- `brms` needs to compile C++ code, `rstanarm` pre-compiled
- Major differences in computation time based on link function
- For datasets up to ~ 1000 distinct y values computation time is approximately linear for both packages; for larger datasets compute time increases at a faster rate for `brms`

- With moderate sample size, reasonably robust to misspecification of link function
- Uncertainty in link function can be accounted for using a mixture of links

Contact
email: nathan.t.james AT vanderbilt.edu
web: ntjames.com
twitter: @nalhsyjones