

# Copula Modeling for Clinical Trials

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December 14, 2018

# 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

- ▶  $\alpha_i$  estimate posterior CDF for  $X = 0$
- ▶  $\beta$  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



- ▶ 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  $\sim 1000$  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

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