Copula Modeling for Clinical Trials Notation

d	Number of outcomes of interest
Y_j	Random variable for outcome $j = 1, \ldots, d$
y_j	Observed value of random variable Y_j
$F_j(y_j)$	Distribution function of random variable $Y_j \rightarrow$ Converts from data to probabilities
$F_j^{-1}(q)$	Quantile function of random variable $Y_j \rightarrow$ Converts from probabilities to data
γ_j	Parameters for distribution function F_j
Probability integral transform	$F_1(Y_1) = U \sim Unif(0,1) \rightarrow$ Convert between Y_1 and uniform random variable U
$H(y_1, \ldots, y_d)$	Multivariate distribution function
$C(u_1, \ldots, u_d)$	Copula (distribution) function
θ	Parameters for copula C
τ	Kendall's rank correlation coefficient
Gumbel copula	$C(u_1, u_2) = \exp[-((-\log u_1)^\theta + (-\log u_2)^\theta)^{1/\theta}]$
Clayton copula	$C(u_1, u_2) = \max[u_1^{-\theta} + u_2^{-\theta} - 1, 0]^{-1/\theta}$
Normal copula	$C(u_1, u_2) = \Phi_2(\Phi^{-1}(u_1), \Phi^{-1}(u_2)\|\rho)$
$\Phi_2(\cdot, \cdot\|\rho)$	Bivariate standard normal distribution function with correlation coefficient ρ
Φ	Standard normal distribution function
Φ^{-1}	Standard normal quantile function
Independence copula	$\Pi(u_1, \ldots, u_d) = \prod_{j=1}^d u_j$
Copula lower bound	$M(u_1, \ldots, u_d) = \min\{u_1, \ldots, u_d\}$
Copula upper bound	$W(u_1, \ldots, u_d) = \max\{\sum_{j=1}^d u_j - d + 1, 0\}$
$c(u_1, \ldots, u_d)$	copula density
$f_j(y_j)$	marginal density
Log-likelihood with continuous margins	$\ell(\gamma_1, \ldots, \gamma_d, \theta) = \sum_{i=1}^n \{\log c_\theta(F_1(y_{i1}; \gamma_1), \ldots, F_d(y_{id}; \gamma_d)) + \sum_{j=1}^d \log f_j(y_{ij}; \gamma_j)\}$

Benefit-Risk Analysis (Costa and Drury 2018) Notation

n	Total sample size
i	Index for i^{th} subject
t	Placebo ($t = 1$) or active ($t = 2$) intervention group
$x_i = (x_{i1}, x_{i2})$	Treatment indicator vector for subject i; $x_{it} = 1$ for treatment t, 0 otherwise
$y_i = (y_{i1}, y_{i2})$	Bivariate response for subject i
y_{i1}	Continuous efficacy outcome, assumed to be normal with mean μ_t and variance σ_t^2
y_{i2}	Binary adverse event outcome, assumed to be Bernoulli with parameter p_t
Efficacy model	$y_{i1} \sim Normal(\mu_t, \sigma_t) \quad \mu_t = x_{i1}\beta_{11} + x_{i2}\beta_{12} \quad \sigma_t = x_{i1}s_1 + x_{i2}s_2$
Safety model	$y_{i2} \sim Bernoulli(p_t) \quad \Phi^{-1}(p_i) = x_{i1}\beta_{21} + x_{i2}\beta_{22}$
Dependence model	$H_{\theta_t}(y_{i1}, y_{i2}) = C_{\theta_t}^{Norm}(F_1(y_{i1}; \mu_t, \sigma_t), F_2(y_{i2}; p_t)) \quad \theta_t = x_{i1}\omega_1 + x_{i2}\omega_2$
β_{jt}	Effect parameters for marginal models
s_t	Dispersion parameters for efficacy model
ω_t	Copula dependency parameters
θ_t	Poly-serial correlation between the normal efficacy outcome and the latent normal distribution underlying the binary safety outcome
$\rho_t = \theta_t \cdot \frac{\phi[\Phi^{-1}(p_t)]}{\sqrt{p_t(1-p_t)}}$	Pearson correlation between normal efficacy outcome and binary safety outcome