

Presentation 25-04

Florian Stijven

25-4-2022

- Joint model for (S_0, S_1, T_0, T_1) : based on D-vine copula
 - with $c_{ab;d}$ (conditional) copula densities

$$\begin{aligned} f_{1234} = & f_1 \cdot f_2 \cdot f_3 \cdot f_4 \\ & \cdot c_{12} \cdot c_{23} \cdot c_{34} \\ & \cdot c_{13;2} \cdot c_{24;3} \\ & \cdot c_{14;23} \end{aligned} \tag{1}$$

- likelihood contributions (for observed data):
 - (S_0, T_0) : $f_{12} = f_1 \cdot f_2 \cdot c_{12}$
 - (S_1, T_1) : $f_{34} = f_3 \cdot f_4 \cdot c_{34}$
- c_{23} , $c_{13;2}$, $c_{24;3}$ and $c_{14;23}$: unidentifiable
 - Part of sensitivity analysis
- Gaussian copula model can also be represented as a D-vine copula

Comparison of Models

- 3 copula models
- For every copula:
 - model with time ordering (ord)
 - model without time ordering

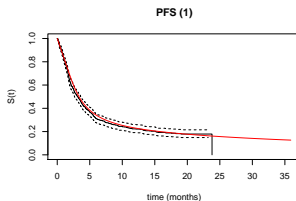
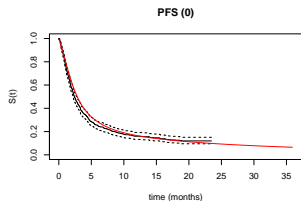
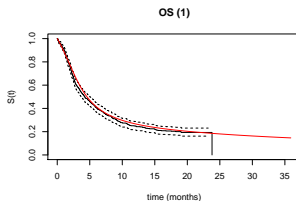
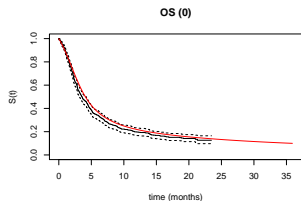
{

| model | loglik | kendall0 | kendall1 | spearman0 | spearman1 |
|---------------|----------|----------|----------|-----------|-----------|
| normal (ord) | -4191.40 | 0.72 | 0.79 | 0.90 | 0.94 |
| Clayton (ord) | -4168.21 | 0.62 | 0.73 | 0.80 | 0.90 |
| Frank (ord) | -4124.94 | 0.74 | 0.80 | 0.92 | 0.95 |

| model | loglik | kendall0 | kendall1 | spearman0 | spearman1 |
|---------|----------|----------|----------|-----------|-----------|
| normal | -4181.75 | 0.78 | 0.83 | 0.93 | 0.96 |
| Clayton | -4287.45 | 0.62 | 0.73 | 0.80 | 0.90 |
| Frank | -4167.10 | 0.78 | 0.85 | 0.94 | 0.97 |

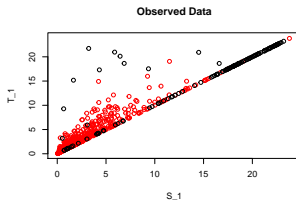
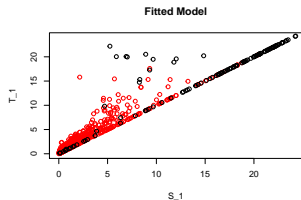
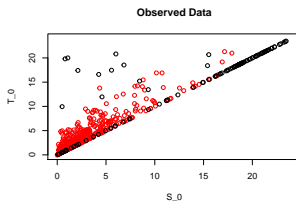
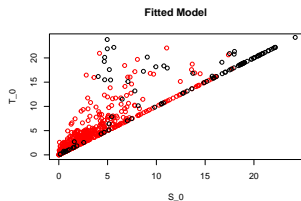
Goodness of Fit: Marginal Survival Functions

- model based: red; KM-estimate: black
- good marginal fit



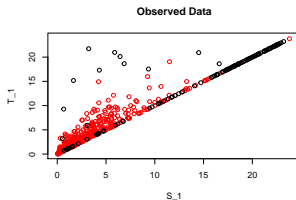
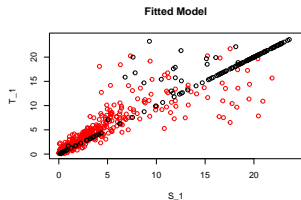
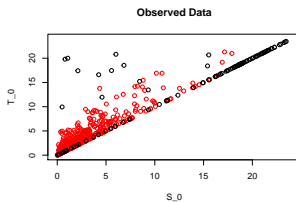
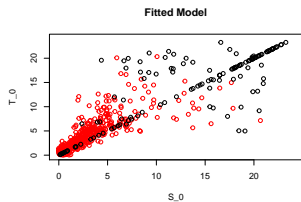
Goodness of Fit: Association

- observed data versus sampled data from fitted model
- Sampled data censored by sampling censoring times
 - Makes sampled and observed data comparable
- red: non-censored; black: censored



Goodness of Fit: Association (no time orderings)

- Frank copula model with no time ordering
 - clearly issue with time ordering (though limited)



- Individual causal effect:
 - $\Delta S = S_1 - S_0$ and $\Delta T = T_1 - T_0$
- Two measures for Individual Causal Association (ICA):

$$\rho_{sp} = \text{cor}(R(\Delta S), R(\Delta T))$$

$$\tau = P((\Delta S_1 - \Delta S_2)(\Delta T_1 - \Delta T_2) > 0) - P((\Delta S_1 - \Delta S_2)(\Delta T_1 - \Delta T_2) < 0)$$

Surrogacy Measures: Sensitivity Analysis

- Sample copula parameters for c_{23} , $c_{13;2}$, $c_{24;3}$ and $c_{14;23}$
- Parameters defined on entire real line for Frank copula
- In gaussian copula: unidentifiable correlations sampled from uniform distribution
 - not possible anymore
- Sample from $U(-1 \cdot \max(\hat{\theta}_{c_{12}}, \hat{\theta}_{c_{34}}), 1 \cdot \max(\hat{\theta}_{c_{12}}, \hat{\theta}_{c_{34}}))$
 - reasonable that unidentifiable associations are weaker than observable
- With estimated parameters and sampled unidentifiable parameters
 - distribution of (S_0, S_1, T_0, T_1) determined
 - Measures of surrogacy can be computed

Surrogacy Measures: Sensitivity Analysis (Results)

- Frank copula model with time orderings: top plots
- Frank copula model without time orderings: bottom plots
- Longer left tail for model without time orderings
 - it “pays off” to take orderings into account

