Presentation 25-04

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Models

- Joint model for (S_0, T_0, S_1, 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

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

model	loglik	copula_par0	copula_par1	kendall0	kendall1	spea
normal (ord)	-4185.41	0.91	0.95	0.72	0.79	
Clayton (ord)	-4113.97	5.84	8.71	0.74	0.81	
Frank (ord)	-4119.60	14.20	18.64	0.75	0.80	
gumbel (ord)	-4172.09	3.78	4.82	0.74	0.79	

|	model	loglik	copula_par0	copula_par1	kendall0	kendall1	s
5	normal	-4177.76	0.93	0.97	0.77	0.83	
6	Clayton	-4132.61	7.81	12.19	0.80	0.86	
7	Frank	-4132.84	18.61	24.00	0.80	0.84	
8	gumbel (ord)	-4135.12	4.68	6.14	0.79		

Goodness of Fit: Marginal Survival Functions

- model based: red; KM-estimate: black
- good marginal fit
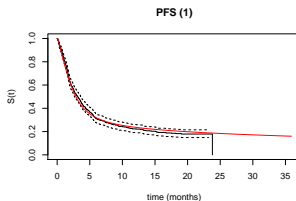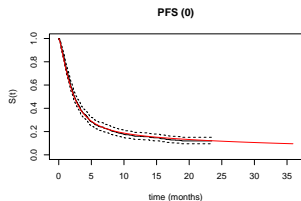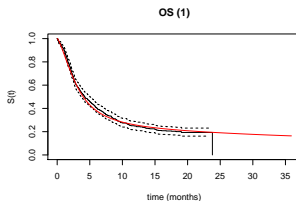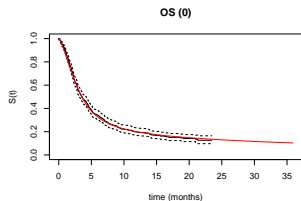
Goodness of Fit: Association

- 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
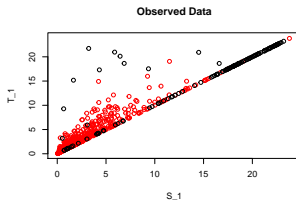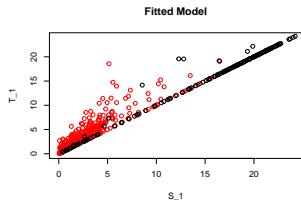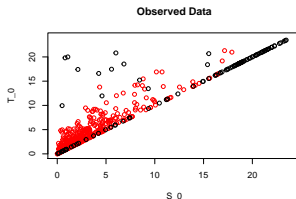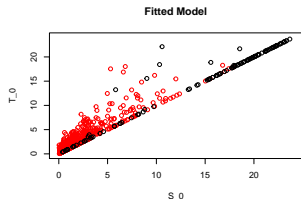
Goodness of Fit: Association (no time orderings)

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

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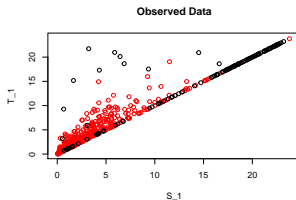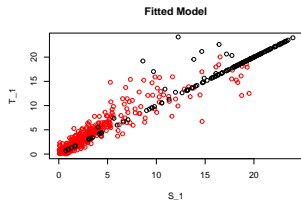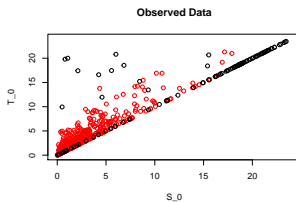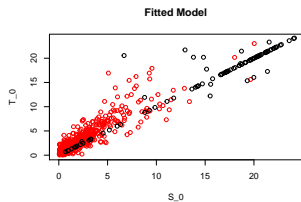
- Individual causal effect:
  - $\Delta S = S_1 - S_0$ and $\Delta T = T_1 - T_0$
- Three measures for Individual Causal Association (ICA):

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

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

$$\rho_{ICC} = 1 - e^{-2 \cdot I(\Delta S, \Delta T)}$$

Surrogacy Measures: Sensitivity Analysis

- Sample copula parameters for c_{23}, $c_{13;2}$, $c_{24;3}$ and $c_{14;23}$
- Parameters should be positive for Clayton copula
- In gaussian copula: unidentifiable correlations sampled from uniform distribution
    - not possible anymore
- Sample from $U(0, \max(\hat{\theta}_{c_{12}}, \hat{\theta}_{c_{34}}))$
    - reasonable that unidentifiable associations are weaker than observable
- Clayton copula only models positive association
    - also sample rotation parameter $(0, 90, 180, 270)$ (with equal probability)
- With estimated parameters and sampled unidentifiable parameters
    - distribution of (S_0, S_1, T_0, T_1) determined
    - Measures of surrogacy can be computed

UHASSELT
KNOWLEDGE IN ACTION

Surrogacy Measures: Sensitivity Analysis (Results)

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