BNP for semi-competing risks

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A Bayesian Nonparametric Approach for Evaluating the Effect of Treatment in Randomized Trials with Semi-Competing Risks

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(Submitted on 20 Mar 2019)

We develop a Bayesian nonparametric (BNP) approach to evaluate the effect of treatment in a randomized trial where a nonterminal event may be censored by a terminal event, but not vice versa (i.e., semi-competing risks). Based on the idea of principal stratification, we define a novel estimand for the causal effect of treatment on the non-terminal event. We introduce identification assumptions, indexed by a sensitivity parameter, and show how to draw inference using our BNP approach. We conduct a simulation study and illustrate our methodology using data from a brain cancer trial.

Subjects: **Methodology (stat.ME)**

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Submission history

From: Yanxun Xu [view email]

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Bivariate sub-distribution: together G^z & V^z define

$$\widetilde{F}_x^1(s,t) = p(P^1 \leq s, D^1 \leq t, P^1 \leq D^1 \mid x)$$

$s \leq t$, and same for $\widetilde{F}_x^0$.

Random prob measures, will use working model $F_x^1(s,t)$

– & $F_x^0(s,t)$ imply $\widetilde{F}_x^1$ & $\widetilde{F}_x^0$.
DDP mix of normals.

Assumption 1. Treatment is randomized: $Z \perp (P^z, D^z, C, x)$, $z = 0, 1$ (and $0 < p(Z = 1) < 1$).

This obviously holds by design in randomized trials as considered here.

Ass 2. Non-informative censoring: $C \perp (P^z, D^z)$ $z = 0, 1$ and $p(C > P^z, C > D^z) \mid x) > 0, \forall x$

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Quantity of interest: Odds of progression

$$\tau_{\boldsymbol{x}}(u) = \frac{\int_{P^1<u} \int_{D^0 \geq u} \int_{D^1 \geq u} dV_1(P^1 \mid D^1, \boldsymbol{x}) \, dG_{\boldsymbol{x}}(D^0, D^1)}{\int_{P^0<u} \int_{D^0 \geq u} \int_{D^1 \geq u} dV_0(P^0 \mid D^1), \boldsymbol{x} \, dG_{\boldsymbol{x}}(D^0, D^1)}$$

Ass 3. Copula: F^0 and F_1 are linked with a normal copula.

$\Phi \quad = $ standard normal c.d.f and

$\Phi_{2,\rho} =$ bivariate normal with correlation ρ.

$$G(D^0, D^1;\ \rho) = \Phi_{2,\rho}\left[\Phi^{-1}\{G_0(D^0)\}, \Phi^{-1}\{G_1(D^1)\}\right]$$

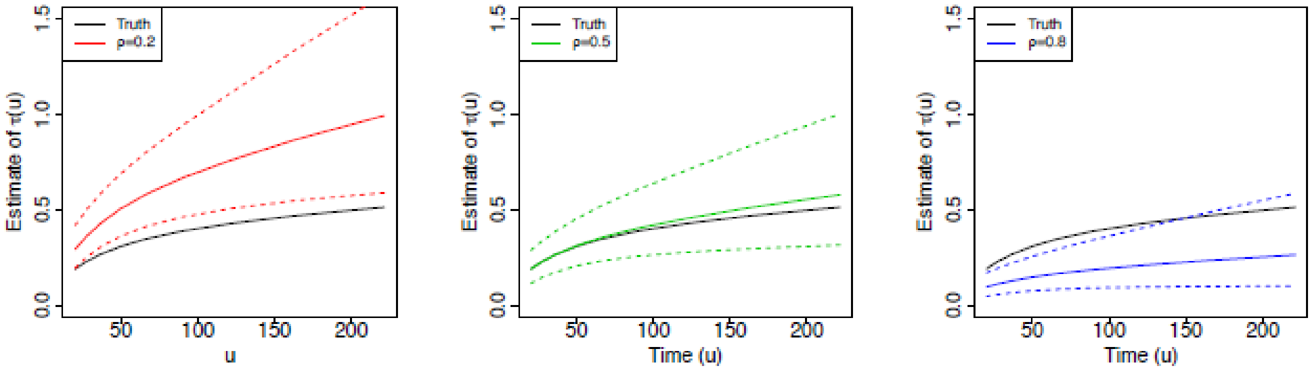
- for fixed , G is identified since G 0 and G 1 are identified
- ρ is not identifiable – ρ is a sensitivity par

?

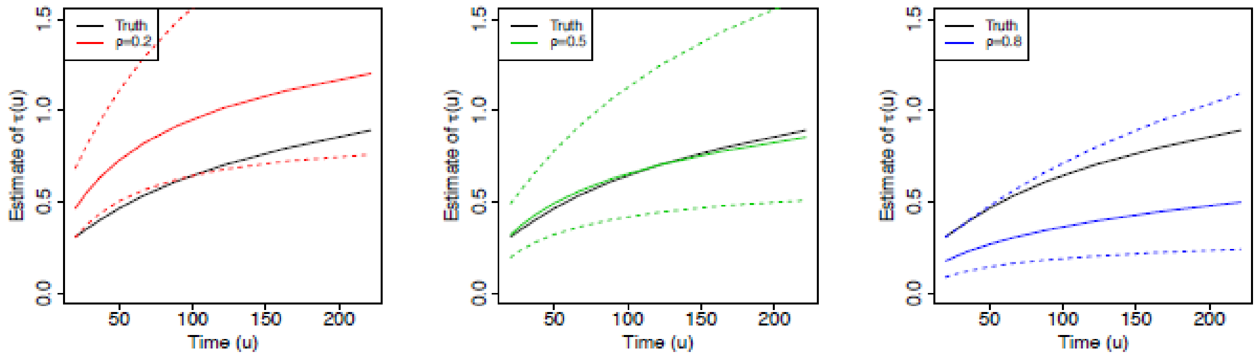
Assumption 4: $P^z \perp D^{1-z} \mid D^z, x,\ z = 0, 1$

allows copula to extend to P^z.

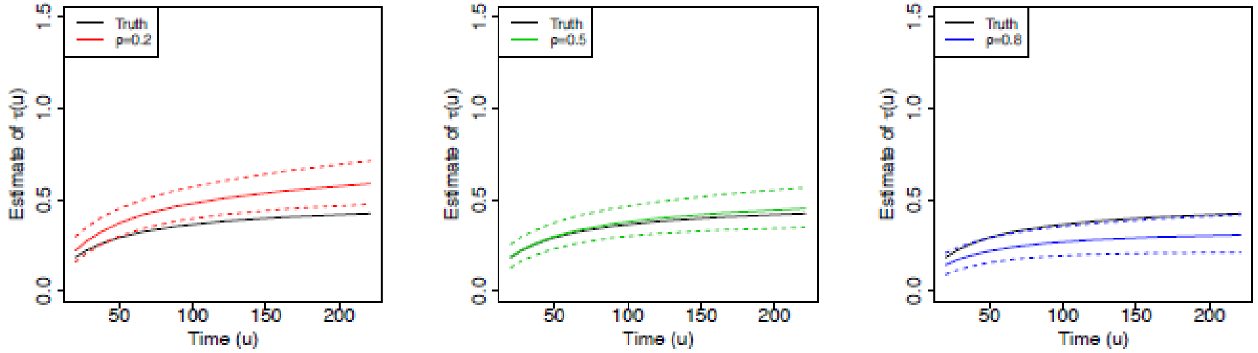
Scenario 1



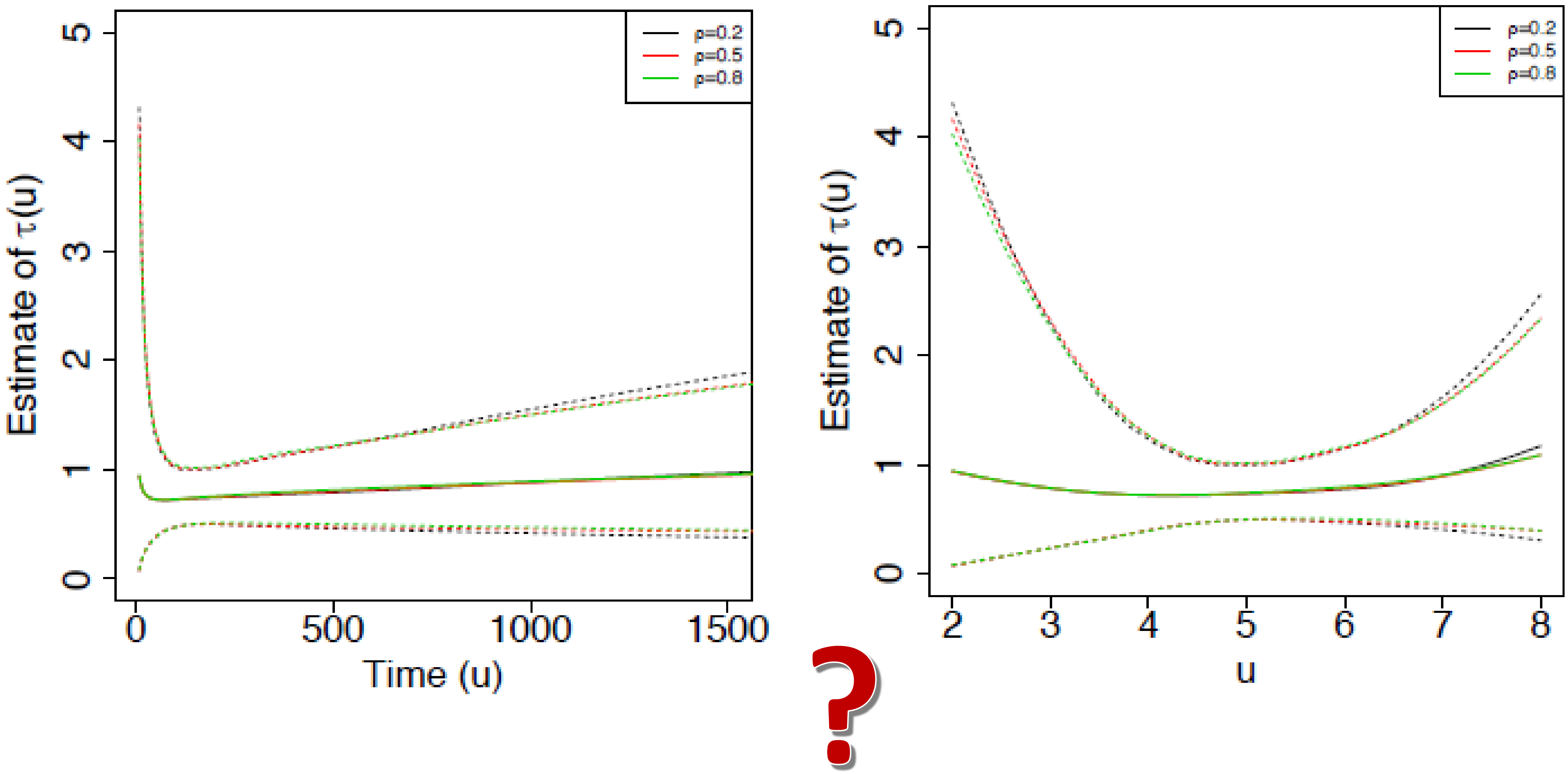
Scenario 2



Scenario 3



ρ_0?



Estimate of τ(u)
Time (u)
ρ=0.2
ρ=0.5
ρ=0.8
0
500
1000
1500
0
1
2
3
4
5
Estimate of τ(u)
u
ρ=0.2
ρ=0.5
ρ=0.8
2
3
4
5
6
7
8
0
1
2
3
4
5

Quantity of interest:

Conditional ? Odds of progression

$$\tau_{\boldsymbol{x}}(u) = \frac{\int_{P^1<u}\int_{D^0\geq u}\int_{D^1\geq u} dV_1(P^1 \mid D^1, \boldsymbol{x})\; dG_{\boldsymbol{x}}(D^0, D^1)}{\int_{P^0<u}\int_{D^0\geq u}\int_{D^1\geq u} dV_0(P^0 \mid D^1), \boldsymbol{x}\; dG_{\boldsymbol{x}}(D^0, D^1)}$$

$$\tau(u) = \frac{\int_{\boldsymbol{x}}\int_{s<u}\int_{v\geqslant u}\int_{t\geqslant u} dV_{\boldsymbol{x}}^1(s|t)dG_{\boldsymbol{x}}(v,t)dK(\boldsymbol{x})}{\int_{\boldsymbol{x}}\int_{s<u}\int_{v\geqslant u}\int_{t\geqslant u} dV_{\boldsymbol{x}}^0(s|t)dG_{\boldsymbol{x}}(v,t)dK(\boldsymbol{x})}$$

The model: Joint distribution for V=(P,D)

$$dH_{\boldsymbol{x}}(\boldsymbol{v}) = \sum_h w_h \phi\left(\boldsymbol{v}; \boldsymbol{\theta}_h(\boldsymbol{x}), \boldsymbol{\Sigma}\right) d\boldsymbol{v}$$

?

O’Bayes

Objective?