Twitter Thread by Jessica G. Young





@Iplaywithgerms This paper gives documentation on software (with causal reasoning, assumptions reviewed in appendix) for a parametric approach to estimating either "total effects" or "controlled direct effects" with competing events and time-varying

<u>@JuliaLMarcus</u> <u>@Iplaywithgerms</u> Total effects capture paths by which treatment affects competing event (e.g. protective total effect of lifesaving treatment on dementia may be wholly/partially due to effect on survival). Controlled direct effects do not capture these paths

<u>@JuliaLMarcus</u> <u>@Iplaywithgerms</u> More detailed reasoning on the difference and tradeoffs between total and controlled direct effects and causal reasoning in the point treatment context provided here along with description of some estimators and code.

https://t.co/uRQcU1NqJd

<u>@JuliaLMarcus</u> <u>@Iplaywithgerms</u> If you are familiar with more robust approaches like IPW or even better TMLE for time-varying treatment, these are trivially adapted to go after the controlled direct effect by simply treating competing events like loss to follow-up (censoring). e.g. see https://t.co/kew3HltAev

<u>@JuliaLMarcus</u> <u>@Iplaywithgerms</u> Examples of IPW estimation of the total effect of a time-varying treatment described in Appendix D of this paper:

https://t.co/RNhcgTBMkb

And here

https://t.co/rMWmwFBWwV

Others in reference lists of above papers.

@JuliaLMarcus @Iplaywithgerms As discussed here

https://t.co/uRQcU1NqJd

even when treatment is time-fixed, hazard ratios (whether cause-specific or subdistribution) do not quantify causal effects (even when counterfactual contrasts) except in special circumstances that will not hold in most studies

<u>@JuliaLMarcus</u> <u>@Iplaywithgerms</u> These circumstances can fail even when the study is a perfectly executed trial (no loss to follow-up, perfect adherence to the treatment assignment) and even when the treatment does not affect the competing event.

<u>@JuliaLMarcus</u> <u>@Iplaywithgerms</u> More recent work on the separable effects provides notions of mechanism in this setting that, unlike controlled direct effects (effects under eliminating competing events), have real-world, clinical relevance. This does not accommodate t-v treatments (yet, in the works).

<u>@JuliaLMarcus</u> <u>@Iplaywithgerms</u> Here are some papers on the separable effects for point treatments (Epidemiology commentary forthcoming focused on fertility trials that is less technical):

https://t.co/35OJDe8dD6 https://t.co/O08FNqPWWb https://t.co/wKCrltvNhT