Thursday 25 July 2024

09:00-12:30 Mini Symposium 2 (Room 2)

STRengthening Analytical Thinking for Observational Studies (STRATOS) initiative – recent progress and foci for the future

Organizers: Willi Sauerbrei and Els Goetghebeur in collaboration with the STRATOS Steering Group

Causal inference moving forward – embracing joint (dis)appearances

Els Goetghebeur and Saskia le Cessie for TG7 (https://stratos-initiative.org/en/group_7)

Since its start, TG7 has presented estimands as a needed focus for any causal effect estimation. `What are we actually estimating' is surprisingly often absent from applied publications [2023, Lancet Oncol., DOI10.1016/S1470-2045(23)00110-9]. It is not straightforwardly derived, however, from how we estimate our target but also depends on what plausible causal assumptions we make a priori. From the various principled answers developed in a setting with sequential point exposures and subsequent continuous outcome, we are now moving to guidance on more complex outcomes. These include right censored survival times and repeated outcome measures while patients are alive. Other intercurrent events may then appear. Already in randomized trials there is much controversy about what constitutes a meaningful causal effect in that case. These issues and much more play in observational studies, for which many causal methods were first developed. We elaborate in this talk on ongoing and planned work, which looks to collaborate with other topic groups next. We are working on the following:

1. To clarify various causal estimands and estimators we have introduced counterfactual cross world simulations for continuous outcomes as a learning tool. We are finalizing a similar plasmode like effort, starting from an observed case study, for right censored survival outcomes.

2. In the context of the European IMI-SISAQOL project (sisaqol-imi.org) we collaborate with a large consortium to develop guidance for causal effect analysis in (late stage) oncology trials. There, quality of life while alive, as well as survival must be jointly evaluated, often in single arm studies. We define relevant and feasible estimands in that setting and develop corresponding estimators.

3. As a rule, we value causal effects in terms of this joint outcome. While intercurrent events can sometimes be handled by defining composite or (not too) hypothetical outcomes, evaluating treatment policy and outcomes until death is often preferred. When implementing analyses for the joint outcome, many analysis choices must be made. We explain how issues inherent to (single arm) trials as well as cohorts can be more rigorously approached by causal inference methods to allow for target effect estimation under transparent assumptions.

In this talk we describe pitfalls and progress made. We refer to a forthcoming collaboration with TG1 to further analysis in the presence of common missing data patterns in our setting. We look forward to discussions in Thessaloniki and further cross topics work.