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Mathematisches Kolloquium

Causal mediation with longitudinal mediator and survival outcome

Sprecher: Prof Dr. Vanessa Didelez
Eingeladen vom Institut für Statistik

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In causal mediation analysis, we are interested in understanding different mechanisms (causal pathways) of a treatment or exposure affecting some outcomes. Often this is formalised in terms of (in)direct causal effects - popular notions of these are based on so-called “nested counterfactuals”. These concepts however run into difficulties of interpretation in the particular context of survival analyses. I will discuss the problem and propose an alternative approach that does not suffer from such shortcomings [1]: this novel approach follows Robins and Richardson [2], where mechanisms need to be specified allowing a separation into the different treatment paths, formalized using an augmented directed acyclic graph (DAG). A number of methods for estimation of these separated effects are investigated. It can be shown that under specific assumptions identification of such alternative mediated effects is possible, resulting in the familiar mediation formula. In continuous time, it can further be shown that for the particular case of combining a linear model for the mediator with an additive hazard model, the familiar “path-tracing” formula can be recovered [3].

For illustration, this is applied to an example of mediated effects of a blood-pressure treatment on time to kidney failure [3]. We investigate intensive versus standard blood-pressure treatment and find that there is little, and not much time-varying, indirect effect via diastolic blood pressure on kidney failure. Hence, other ways of preventing this side effect of intensive blood-pressure treatment might be worth investigated.

The proposed new approach solves a crucial conceptual problem of mediation analysis with a survival outcome and can be extended to competing risks [4]. It is founded in decision theory, avoids genuine counterfactual assumptions and - even in non-survival contexts - constitutes an interesting alternative to the prevailing structural equation models.

References [1] Didelez. Defining causal meditation with a longitudinal mediator and a survival outcome. Lifetime Data Analysis, DOI: 10.1007/s10985-018-9449-0, 2018. [2] Robins, Richardson. Alternative graphical causal models and the identification of direct effects. Causality and psychopathology: Finding the determinants of disorders and their cures, pages 103-158, 2011. [3] Aalen, Stensrud, Didelez, Daniel, Roysland, Strohmaier. Time-dependent mediators in survival analysis: Modelling direct and indirect effects with the additive hazards model. Biometrical Journal. 2019; (Epub 2019 Feb 19). [4] Stensrud, Young, Didelez, Robins, Hernán. Separable effects for causal inference in the presence of competing risks. 2019. arXiv:1901.09472.