

Causal mediation analysis with a repeatedly measured mediator and a time-to-event response

Susanne Strohmaier^{1,2}, Kjetil Røysland², Rune Hoff², Terje R. Pedersen³, Odd O. Aalen²

1) Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School, Boston, USA

2) Oslo Center for Biostatistics and Epidemiology, Oslo, Norway

3) Oslo University Hospital-Ullevål, University of Oslo, Oslo, Norway

Important questions within the fields of social sciences, epidemiology as well as clinical trial research involve the challenge of decomposing the effect of an intervention into direct and indirect effects working through a defined mediator, thereby aiming for a better understanding of the underlying mechanisms.

For the case of a single and multiple mediators measured at a single point in time, researchers have established theoretical properties and developed practical tools for the analysis of a broad class of mediator and outcome models. However, data structures are often more complex than the described scenarios. Especially when it comes to clinical survival trials, usually collection of time-to-event data goes hand in hand with the collection of information on other internal time-dependent covariates, but this potentially useful information is hardly ever used.

We present dynamic path analysis, a method that allows to investigate how mediation processes develop over time by integrating more of the routinely collected data. Additionally, we suggest definitions of direct, indirect and total effects for this particular setting involving a time-to-event outcome and a repeatedly measured mediator that allow for a causal interpretation without making explicit use of the counterfactual framework.