CAUSAL ANALYSES OF CENSORED SURVIVAL DATA WITH TIME-VARYING TREATMENT

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ITT analyses compare groups of patients solely defined by which arm of an experiment they were randomized. Complier average causal estimates (CACE) compare the arms in the subset of patients (compliers) who would have received the randomized treatment however they were randomized. It is the effect of treatment rather than the effect of randomisation. We develop a CACE for failure time data where the standard treatment arm can start experimental treatment at any time, but the experimental arm receives treatment at once. In this setting the groups of compliers gets smaller over time, as the patients in the standard arm start the experimental treatment.

We define switch time as the time U that a patient would start experimental treatment if randomised to the standard arm. We assume the exclusion restriction, that the event hazard in all patients with switch time U; at times t $\geq U$; is the same in both arms. The CACE is the ratio between arms of the hazards at time t in patients with a switch time $U > t$: We assume that censoring is independent of all failure and switch times.

If a previously compliant patient fails at time T; then all we know is $U > T$: Subsequently we do not know the number of compliant patients at risk when estimating hazards at times greater than T: Hence the CACE is not fully identified. We present extrema of pointestimates of time-dependent CACE hazard ratios and then show how a variety of further assumptions can improve identifiability.