Non-proportionality of Sub-hazards in the Competing Events Framework

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Abstract

For the purpose of determining the effect of an exposure on the frequency and timing of two competing events (1 and 2), methods are widely available to semi-parametrically model the sub-hazards $\lambda_i(t)$ in unexposed and $\lambda_i^*(t)$ in exposed for *i*= 1,2 of the cumulative incidences as proportional and to test whether $\lambda_1^*(t)/\lambda_1(t) \equiv a_1$ and $\lambda_2^*(t)/\lambda_2(t) \equiv a_2$ are different from 1. We show that a_1 and a_2 are tethered by $(1-\pi)^{a_1} = 1-(\pi)^{a_2}$ where $\pi =$ P(type 1 event | unexposed); and, that they are independent of the timing of the competing events. Failure to include the tethering relationship when proportionality is not fulfilled, often results in estimates of a_1 and a_2 being on the same side of 1 which is inadmissible. Even if the tethering relationship is incorporated, inappropriate characterization of true relative non-proportional sub-hazards may persists. Since proportionality of the sub-hazards rarely holds in real data, the default analytical approach should be to allow for the relative sub-hazards to depend on time. Using data from a nationwide cohort study of children with kidney disease, we show how the allowance of time dependency of the relative sub-hazards is an informative approach.

Keywords: Competing risks; Non-proportional sub-hazards; Tethering.

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