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

Alvaro Muñoz*, Johns Hopkins University
Alison G Abraham, Johns Hopkins University
Matthew Matheson, Johns Hopkins University
Nikolas Wada, Johns Hopkins University

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 $\lambda_1^*(t)/\lambda_2(t) \equiv a_1$ 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.

* Presenting author