Interpretation of effect estimates in competing risks survival models: A simulated analysis of organ-specific progression-free survival in a randomised phase III cancer trial

Subject Category: Survival Data Analyses

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In survival analyses, competing risks are encountered where the subjects under study are at risk for more than one mutually exclusive failure event [1]. Competing risks are often analysed using either cause-specific or subdistribution (cumulative incidence) proportional hazards models. Cause-specific hazards model the rate of occurrence of an event, whereas subdistribution hazards model the risk of failure of a specific event. Results of competing risks analyses are being presented more frequently in the medical literature, but the difference in the interpretation of various estimates, compared to standard Cox hazard ratios, is rarely considered.

We apply a simulated data set to show that the effect of liver-targeted treatment on the event of interest (progression inside the liver) can be influenced by competing events (progression outside the liver and death). The simulation involves different scenarios showing how censoring, the number of patients per treatment group and the number of occurrences of each event influence the treatment effect estimate of each event from both cause-specific and subdistribution hazards models.

We conclude that, to better understand the effect of prognostic factors on survival, it is important to estimate and report effect estimates for both the event of interest and each competing risk, using both cause-specific and subdistribution hazards models. Having demonstrated that effect estimates for competing events are interrelated, we intend to study the statistical feasibility of meta-analysing hazard ratios derived from competing risks models and their interpretation.

[1] Jason P. Fine, Robert J. Gray; A Proportional Hazards Model for the Subdistribution of a Competing Risk; *Journal of the American Statistical Association* 1999; Vol. 94, No. 446, page 496- 509