Competing Risks in Analysis of NASH Trial Outcomes

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Limitations of Current Trials

- Frequent presence of co-morbidities
- May significantly impact outcomes
- May be different in populations studied:
  - Cardiovascular in NAFLD
  - Liver disease in NASH, dependent on stage of liver disease
- Competing risk analysis:
  - Survival analysis that aims to correctly estimate marginal probability of an event in the presence of competing events
- Traditional methods (Kaplan Meier product-limit method) not designed to accommodate:
  - Competing nature of multiple causes to the same
  - May produce inaccurate estimates when analyzing the marginal probability for cause-specific events
- In the presence of competing risks, the Kaplan-Meier estimate upward biases the estimation of incidenc
  - Treats competing events as censored and removing censored observations from the risk sets in subsequent time points

Proposed Solutions To Assess Competing Events

- Understand competing events versus competing risks
- Cumulative Incidence Function (CIF):
  - Estimates the marginal probability of a certain event as a function of its cause-specific probability and overall survival probability.
  - probability of experiencing the primary event conditioned upon not experiencing either event (primary or competing) until that time. Given this, the CIF appropriately calculates incidence by correctly handling competing events, instead of just censoring them
- Hybridizes the idea of product-limit approach and the idea of competing causal pathways,
- Provides a more interpretable estimate for the survival of multiple competing events for a group of subjects including:
  - A non-parametric method which involves the use of a modified Chi-squared test to compare CIF curves between groups,
  - A parametric approach which model the CIF based on a subdistribution hazard function.