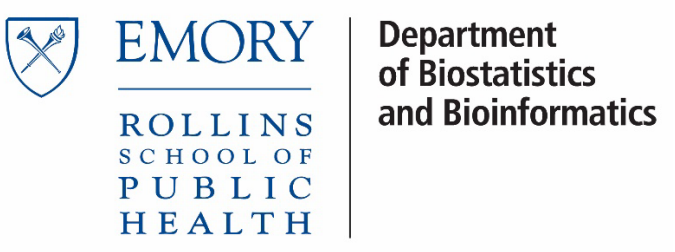

BIOS 522: Survival Analysis Methods

Activity 12:

Competing risks

This week, we defined the concept of competing risks in time-to-event data. We introduced analytical approaches for estimating cause-specific hazard functions.

Problem 1. Hodgkin's disease mortality

In Ng et al. (2002), the purpose of the study is to estimate overall and cause-specific mortality in patients under 50 treated for early-stage Hodgkin's disease. The investigators assess the relationship between baseline, prognostic risk factors and survival using a Cox proportional hazards model. Age- and sex-specific incidence rates from the National Center for Health Statistics are used to characterize absolute excess risk (AR) for Hodgkin's patients as compared to the general population. The investigators used a competing risks approach to study the competing causes of death over time.

(a) Examine Figure 1. Report the estimated 15-year overall survival in this population. How was this estimated?

Estimated overall survival at 15 years is 84% (95% CI: 81%, 86%). This was estimated by standard Kaplan-Meier methods using the endpoint of death by any cause.

(b) Examine Figure 2. Investigators consider competing causes of death, including Hodgkin's disease, second malignancy (new cancer that occurs in an individual as a result of previous treatment with radiation or chemotherapy), cardiac/pulmonary disease, infection, and other causes. The plot displays the cumulative incidence functions for each cause. (*For some reason, the plot does not have color. The legend sorts the groups by frequency*.)

What is the leading cause of mortality in the first 15 years after treatment? What is the leading cause of mortality 20 years after treatment? If these causes are not the same, why does this change?

In the first 15 years, the primary cause of death is Hodgkin's disease. After 15 years, there are no additional deaths attributed to Hodgkin's disease, so the curve stabilizes (flat). Over time, deaths attributed to secondary malignancy increase, including beyond 15 years. At around 18 years, the cumulative probability of death due to second malignancy is higher than the cumulative probability of death due to Hodgkin's disease. Thus, when considering long-term outcomes for patients with Hodgkin's disease, secondary malignancies are an important cause of death.

(c) Describe how we can use Figure 2 to estimate the overall 15-year survival probability in this population.

If we add up the cause-specific cumulative incidence functions for the five causes, this is equal to the cumulative distribution function for overall mortality $F(t)$ at $t = 15$.

$$F_1(t) + F_2(t) + F_3(t) + F_4(t) + F_5(t) = F(t)$$

Eyeballing the plot at $t = 15$:

$$0.06 + 0.05 + 0.02 + 0.02 + 0.01 = 0.16$$

Thus, the survival probability at $t = 15$ is $S(t) = 1 - F(t) = 1 - 0.16 = 0.84$ or 84%. This is consistent with the first paragraph of the RESULTS (last sentence) that states that the 15-year KM survival estimate for all patients was 84%.