Introduction to Biostatistics (BIOS:4120)
Breheny

Assignment 13
Due: No due date

1. To illustrate how multiple comparisons can produce significant associations with no clinical plausibility, Canadian investigators conducted a study of the association between astrological signs and common reasons for hospitalization. They tested 24 such associations.

   (a) How many statistically significant findings (*i.e.*, with $p < 0.05$) would you expect the investigators to discover in their study?

   (b) If we apply the Bonferroni correction, what number should we compare our p-values to in order to maintain a 5% overall probability of making a single type I error?

   (c) The study obtained two "significant" findings: individuals born under Leo had a higher probability of gastrointestinal hemorrhage ($p = 0.0447$), while Sagittarians had a higher probability of humerus fracture ($p = 0.0123$) compared to all other signs combined. Are these findings statistically significant in light of the multiple comparisons that the investigators performed?

2. German researchers carried out a study of two different treatments for heart attacks in a randomized trial involving 421 patients suffering from acute myocardial infarctions. They performed hypothesis tests for 15 different cardiac outcomes.

   (a) In order to keep the overall probability of making a type I error at 5%, what significance level should they test each individual hypothesis at?

   (b) The hypothesis test for the most important outcome, mortality, was $p = .0095$. Is this statistically significant according to the cutoff you defined in part (a)?

   (c) Of the 15 hypotheses, 4 (including the test for mortality mentioned above) were significant at the level $\alpha = .01$. What is the false discovery rate associated with this α level?

   (d) The investigators conclude that there is a statistically significant difference in the mortality rates of the two treatments. Comment on whether this statement is or is not justified in light of the multiple comparisons that they have made. In particular, state whether you agree with their conclusion.

3. From 1974 to 1984, the Mayo Clinic conducted a randomized, placebo-controlled clinical trial of the drug penicillamine on patients with primary biliary cirrhosis of the liver. Their data is available from our course website and contains three variables:

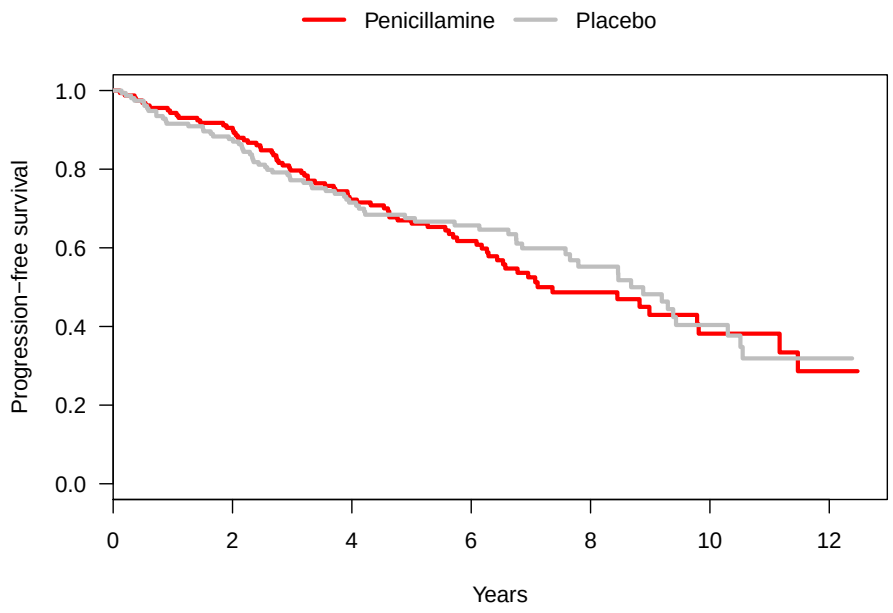
   - Time: the time until either censoring, death, or transplant. Measured in years.
   - Status: what happened at the end of the patient's time on study. Either the patient's failure time was censored (0), the patient required a liver transplant (1), or the patient died (2).
   - Group: whether the patient received penicillamine or placebo.

   The outcome of interest was the time until the patient either died or required a liver transplant (*i.e.*, the time until the death of the liver). All of the questions on this assignment concern this data set.

(a) The table below lists a portion of the data for the penicillamine group, sorted by survival time. The table starts somewhere in the middle of the observed failure times, after 20 patients' livers had already failed. Fill in the rest of the table.

Therapy	Time (Days)	Death/Transplant	$n(t)$	$\hat{S}(T)$
	...			
Penicillamine	799	Yes	139	.873
Penicillamine	824	Yes		
Penicillamine	839	No		
Penicillamine	877	Yes		
Penicillamine	901	Yes		
Penicillamine	904	Yes		
	...			

(b) The Kaplan-Meier curves for this study are given below.



(i) What are the estimated 5-year survival rates for patients on penicillamine and placebo, respectively?

(ii) What are the median survival times for patients on penicillamine and placebo, respectively?

(c) If there were truly no difference between the groups, there would be a 73% chance of seeing a difference as large or larger than the one in the above figure. What procedure that we discussed in class could be used to calculate that "73%" number?

(d) Provide a one-sentence summary of the conclusions of this study.