

Survival Data Analysis (BIOS 7210)  
Breheny

Assignment 5  
Due: Thursday, October 8

1. One of the earliest randomized clinical trials of a chemotherapeutic agent was conducted across 11 American hospitals, and involved children with acute leukemia that experienced a complete or partial remission (i.e, all/most of the signs of the disease had disappeared) of their leukemia following treatment with the drug prednisone. The trial was conducted by matching pairs of patients at a given hospital by remission status (complete or partial) and randomizing within the pair to either a 6-MP or placebo. Patients were followed until their leukemia returned (relapse) or until the end of the study. This data is available on the course website ([Freireich1963](#)).

Another use of the stratified log-rank test we derived in class is that it can be applied to paired data like this. Analyze this data using a paired log-rank test. Provide the expected/observed counts, the  $p$ -value, and a brief conclusion regarding whether the drug is effective or not.

2. In class, we derived score, Wald, and likelihood ratio test approaches for the exponential distribution and applied them to the Pike et al. (1966) rat data. As we did in class, use years as the unit of time (the data is provided in days).
  - (a) Provide confidence intervals for  $\lambda$  based on the score, Wald, and likelihood ratio approaches.
  - (b) Consider the transformation  $\gamma = \log \lambda$ . What is the score function with respect to  $\gamma$ ?
  - (c) What is the information with respect to  $\gamma$ ? Comment on how this differs from the information with respect to  $\lambda$ .
  - (d) Provide score, Wald, and likelihood ratio confidence intervals for  $\gamma$ .
  - (e) Transform the intervals from (d) to yield confidence intervals for  $\lambda$ ; how do they compare with the intervals in (a)?
  - (f) Test the hypothesis that  $\gamma = 0$  (i.e., that  $\lambda = 1$ ) using the score and Wald approaches. How do the results compare with the  $p$ -values we obtained in class?
  - (g) Consider the transformation  $\alpha = \lambda^{1/3}$ . Plot the log-likelihood as a function of  $\alpha$ , along with the Wald approximation. Comment on the accuracy of the Wald approach's Taylor series approximation compared to the plot on slide 25 of the September 29 notes.
  - (h) Provide score, Wald, and likelihood ratio confidence intervals for  $\alpha$ .
  - (i) Transform the intervals from (h) to yield confidence intervals for  $\lambda$ ; how do they compare with the intervals in (a) and (e)?
  - (j) Test the hypothesis that  $\alpha = 1$  (i.e., that  $\lambda = 1$ ) using the score and Wald approaches. How do the results compare with the  $p$ -values we obtained in class and those from (f)?