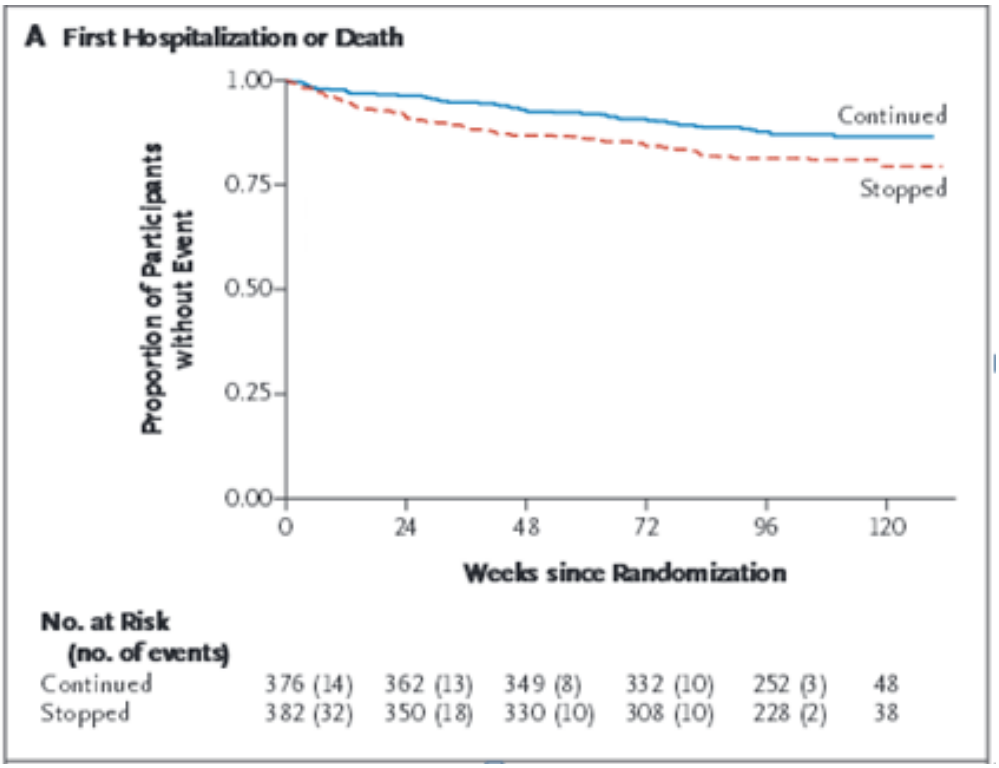
Self-Evaluation Problems
Class 7
Answer Key

A study[1] compared outcomes between HIV-infected children *randomly assigned* to either **continue** or **stop** prophylaxis therapy after receiving at least 96 weeks of anti-retroviral therapy. Below are the **Kaplan-Meier survival curve estimates** ($\hat{S}(t)$) of time after randomization to *either* first hospitalization or death for the two groups.



1. Approximately what is the estimated proportion of children in the "**Stopped**" group who had been either hospitalized or had died ***within*** 24 weeks after randomization into the study? (*Circle only one response*).

   a) 10% = 1- estimated S(24) = 1-0.90
   b) 90%
   c) 2%
   d) 98%
   e) 25%.

[1] Bwakura-Dangarembiz M, et al. A Randomized Trial of Prolonged Co-trimoxazole in HIV-Infected Children in Africa (2014). *New England Journal of Medicine* 370 (1):41-53.

2. The p-value given by the **log rank test** comparing the two survival curves is 0.007. Assuming a significance level (alpha) of 0.05, one can conclude that the observed differences in the Kaplan-Meier curves between the two groups are: (*Circle only one response*).

   a) *Relatively likely* if there is **no difference** in survival over the study follow-up period (at the population level) for the two randomization groups.
   b) *Relatively likely* if there is a scientifically important difference in survival over the study follow-up period (at the population level) for the two randomization groups.
   c) *Relatively unlikely* if there is no difference in survival over the study follow-up period (at the population level) for the two randomization groups.

      The null hypothesis for the log rank test is Ho: Overall survival is the same by group. A p-value=0.007 would lead us to reject Ho and suggests that, if the null hypothesis is true, then the probability of observing the data that we observed by chance alone is very low (7 out of 1000 times).

   d) *Relatively unlikely* if there is a scientifically important difference in survival over the study follow-up period (at the population level) for the two randomization groups.
   e) Reflecting a 0.7% chance that the null hypothesis of no survival difference is true.

3. What can be inferred about the **estimated hazard ratio (HR)** of first hospitalization or death for the children randomized to the "**Continued**" group compared to children randomized to the "**Stopped**" group? (*Circle only one response*).
   a) HR =0
   b) HR = 1
   c) HR > 1
   d) **HR < 1**

   We can see from the figure that the survival estimates over time are higher in the "Continued" group than the "Stopped" group. This means that the hazard of the event is lower in the "Continued" group as compared to the "Stopped" group and, thus, we can infer that the relative hazard (hazard ratio) will be less than one.

   e) It is not possible to estimate this from the information given.

4. Three-hundred seventy-six (376) children were randomized to the "**Continued**" group, and 48 (13%) children were still at risk of hospitalization or death at 120 weeks. However, the corresponding Kaplan-Meier curve estimate at 120 weeks for this group is approximately 90%. How can this have happened? (*Circle only one response*).

   a) Some of the observations in the "Continued" group were censored prior to 120 weeks.
   IF there had been no censoring, then the cumulative probability of survival beyond 120 would have been 48/376 or 13%. With censoring, the number at risk at each time an event occurs may vary. This can result in a Kaplan-Meier estimate that differs substantially from what the estimated survival curve would have been if censored observations were actually events (i.e. no censoring). From the figure on page 1, we can see that there is quite a bit of censoring: 9 patients were censored between 48 and 72 weeks, 70 patients were censored between 72 and 96 weeks, and 201 patients were censored between 96 and 120 weeks.

   b) The researchers estimated the Kaplan-Meier curve using only the data on patients who were hospitalized or died during the 120 weeks after randomization.
   c) The researchers estimated the Kaplan-Meier curve using only the data on patients who were not censored during the 120 weeks after randomization.
   d) The Kaplan-Meier estimate at 120 weeks is the risk of surviving beyond 120 weeks among only those who were at risk of having the event at 120 weeks.
   e) The hazard of hospitalization or death for the children in the "Continued" group was assumed to be constant over time.

5. How does the Kaplan-Meier approach to estimating the survival function utilize information from censored observations? (*Circle only one response*).

   a) It drops all censored observations from the sample before the curve is estimated.
   b) It uses the censored observations when considering who is "at risk" of an event at each given time in the follow-up period.
   The Kaplan-Meier approach utilizes the information regarding time at risk of an event for a censoring observation up through the time at which the observation is censored. After the censoring time, the observation no longer contributes to the estimate.
   c) It treats the censoring times as event times.
   d) It treats the event times as censoring times.
   e) It assumes that all censored observations have the event by the end of follow-up.

