

*BIOS 522: Survival Analysis Methods*

**Activity 6:**

**Interpreting the Cox model**

*This week, we interpreted hazard ratios for binary, categorical, and continuous covariates. We extended the allowable shapes by transformations, splines, and interactions. We defined global and local hypothesis tests for the Cox model and constructed confidence intervals for hazard ratios.*

Problem 1. Calculating hazard ratios

Using data from the ACTG 320 trial described in the Week 3 R Tutorial, we fit the following Cox proportional hazards model:

where if the participant receives indinavir (0 otherwise), is the participant’s baseline Karnofsky score, and is the participant’s baseline CD4 cell count (cells/mm3). Karnofsky score measures health and functional impairment, with patients having scores of 70 (most impairment), 80, 90, or 100 (no impairment). The outcome is new AIDS-defining event or death.

We fit the model with partial likelihood. We obtain the following coefficients:

|  |  |  |
| --- | --- | --- |
| **Covariate** | **Coefficient** | **Exp(Coefficient)** |
| Treatment |  |  |
| Karnofsky score = 80 |  |  |
| Karnofsky score = 90 |  |  |
| Karnofsky score = 100 |  |  |
| CD4 |  |  |

Using the coefficients in the table above, calculate the estimated hazard ratio comparing each of the following sets of populations.

1. Participants with tx = 1, Karnofsky score = 100, CD4 = 50 *vs.*

Participants with tx = 1, Karnofsky score = 70, CD4 = 50.

1. Participants with tx = 1, Karnofsky score = 70, CD4 = 70 *vs.*

Participants with tx = 1, Karnofsky score = 70, CD4 = 50.

1. Participants with tx = 1, Karnofsky score = 100, CD4 = 50 *vs.*

Participants with tx = 1, Karnofsky score = 80, CD4 = 50.

1. Participants with tx = 1, Karnofsky score = 90, CD4 = 50 *vs.*

Participants with tx = 0, Karnofsky score = 70, CD4 = 50.

Problem 2. Calculating test statistics

Consider the leukemia data set in the R survival package. The dataset summarizes survival in 23 patients with Acute Myelogeneous Leukemia. The clinical question was whether the standard course of chemotherapy should be extended (“maintenance”) for additional cycles.

We are interested in testing the null hypothesis that maintenance has no impact on survival. We fit two models:

* A model with no covariates. It has log likelihood -.
* A model with a single binary covariate for maintenance. It has MPLE  , variance of   , and log likelihood -41.03

1. Calculate a Wald test statistic for .
2. Calculate a likelihood ratio test statistic for .
3. For this model with only a single binary covariate, describe how we might calculate a score test statistic for .