8.4 *Regression:* Cox Proportional Hazards Model

Suppose we wish to model the hazard function $h(t)$ for a population, in terms of explanatory variables – or **covariates** – $X_1, X_2, X_3, \ldots, X_m$. That is,

$$h(t) = h(t; X_1, X_2, X_3, \ldots, X_m),$$

so that all the individuals corresponding to one set of covariate values have a different hazard function from all the individuals corresponding to some other set of covariate values.

Assume initially that h has the general form $h(t) = h_0(t)\ C(X_1, X_2, X_3, \ldots, X_m)$.

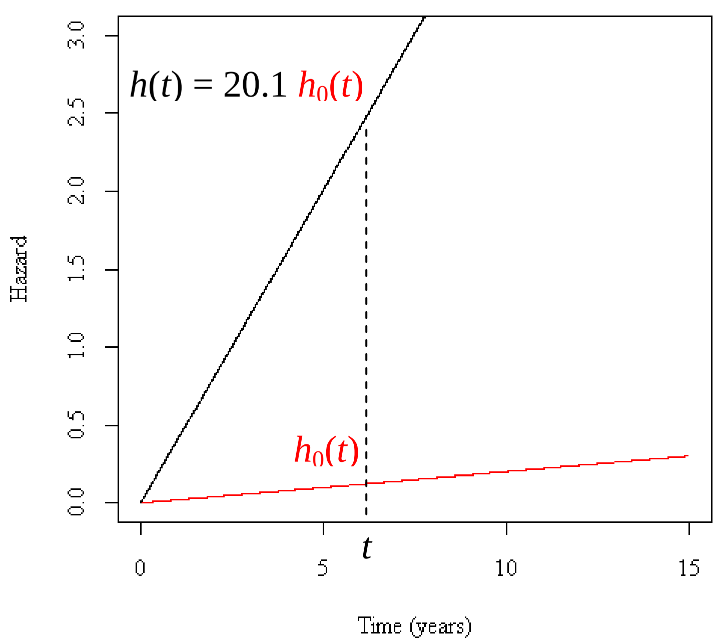
Example: In a population of 50-year-old males, X_1 = smoking status (0 = No, 1 = Yes), X_2 = # pounds overweight, X_3 = # hours of exercise per week. Consider

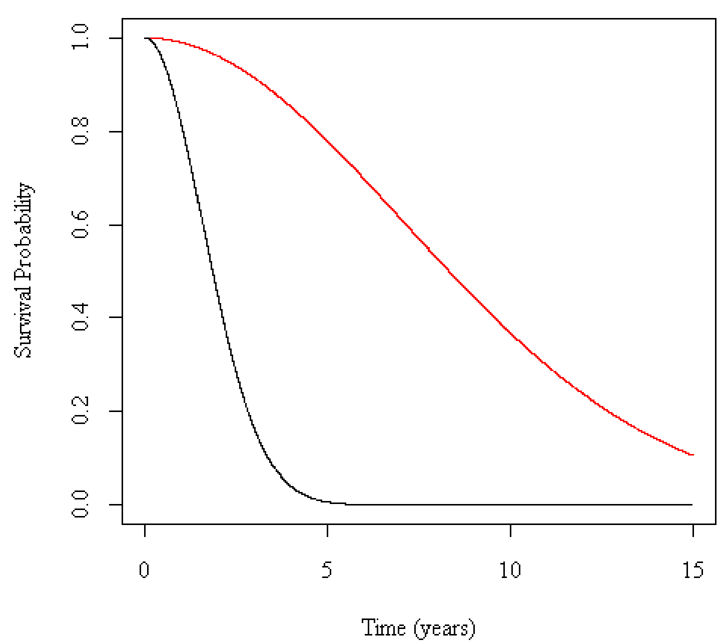
$$h(t) = .02\, t\ e^{X_1 + 0.3X_2 - 0.5X_3}.$$

If $X_1 = 0$, $X_2 = 0$, $X_3 = 0$, then $h_0(t) = .02\, t$. This is the **baseline hazard**. (Therefore, the corresponding survival function is $S_0(t) = e^{-.01\, t^2}$. Why?)

If $X_1 = 1$, $X_2 = 10$ lbs, $X_3 = 2$ hrs/wk, then $h(t) = .02\, t\, e^3 = .02\, t\, (20.1) = .402\, t$. (Therefore, the corresponding survival function is $S(t) = e^{-.201\, t^2}$. Why?)

Thus, the proportion of hazards $\dfrac{h(t)}{h_0(t)} = e^3$ (= 20.1), i.e., constant for all time t.





Furthermore, notice that this hazard function can be written as…

$$h(t) \;=\; .02\,t\;\; (e^{X_1})\,(e^{0.3X_2})\,(e^{-0.5X_3}).$$

Hence, with all other covariates being equal, we have the following properties.

- If X_1 is changed from 0 to 1, then the net effect is that of *multiplying* the hazard function by a constant factor of $e^1 \approx 2.72$. Similarly,
- If X_2 is increased to $X_2 + 1$, then the net effect is that of *multiplying* the hazard function by a constant factor of $e^{0.3} \approx 1.35$. And finally,
- If X_3 is increased to $X_3 + 1$, then the net effect is that of *multiplying* the hazard function by a constant factor of $e^{-0.5} \approx 0.61$. (Note that this is less than 1, i.e., beneficial to survival.)

In general, the hazard function given by the form

$$\boxed{h(t) \;=\; h_0(t)\; e^{\beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_m X_m}}$$

where h_0(t) is the **baseline hazard** function, is called the **Cox Proportional Hazards Model**, and can be rewritten as the equivalent linear regression problem:

$$\boxed{\ln\left(\frac{h(t)}{h_0(t)}\right) \;=\; \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_m X_m}$$

The "constant proportions" assumption is empirically verifiable. Once again, the regression coefficients are computationally intensive, and best left to a computer.

<u>*Comment*</u>: There are many practical extensions of the methods in this section, including techniques for hazards modeling when the "constant proportions" assumption is violated, when the covariates $X_1, X_2, X_3, \ldots, X_m$ are **time-dependent**, i.e.,

$$\ln\left(\frac{h(t)}{h_0(t)}\right) \;=\; \beta_1 X_1(t) + \beta_2 X_2(t) + \ldots + \beta_m X_m(t),$$

when patients continue to be recruited after the study begins, etc. Survival Analysis remains a very open area of active research.