Statistics 262: Intermediate Biostatistics

Modelling Hazard: Parametric Models

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Today’s class

- Hazard rates (yes, again).
- Parametric models: accelerated failure models.
- Likelihood.
- Diagnostics.
Hazard Rates & Densities

\[ f(t)dt = P(t \leq T < t + dt). \]

\[ h(t)dt = P(t \leq T < t + dt | T > t) = \frac{f(t)dt}{S(t)} \]

Both model instantaneous probability of failure at time \( t \), but hazard is conditional on surviving up to time \( t \).
Conceptually, it can be easier to model hazard than density.

Hazard incorporates “what-ifs”: “If you survive up to 100 days, then the probability you will fail within a day is $\sim h(100)$.”

Density does not: “The probability you will fail on the 101-st day is $\sim f(100)$.”
Log-logistic
Accelerated failure model

Log-linear model \( W_i = \log Z_i, \ Var(W_i) = \sigma^2: \)

\[
\log T_i = \beta_0 + \sum_{j=1}^{p} X_{i,j} \beta_j + W_i
\]
Accelerated failure model

- Survival function:

\[ S(t|\beta, X) = S_Z \left( \exp \left( \beta_0 + \sum_{j=1}^{p} X_{ij} \beta_j \right) t \right). \]

- Hazard rate:

\[ h(t|\beta, X) = \exp \left( \beta_0 + \sum_{j=1}^{p} \beta_j X_j \right) \times h_Z \left( \exp \left( \beta_0 + \sum_{j=1}^{p} \beta_j X_j \right) t \right). \]
Accelerated failure model

“Accelerated” refers to the fact that increase in linear predictor “accelerates” your position along the hazard curve.

All variables have the same shape of hazard function, $h_Z$.

Covariates act multiplicatively in front of hazard and on the time scale.
Likelihood of model

\[ L(\beta, \sigma|(t_i, \delta_i), 1 \leq i \leq n) \]
\[
\propto \prod_{i=1}^{n} (1 - F(t_i|\beta, \sigma))^{1-\delta_i} f(t_i|\beta, \sigma)\delta_i.
\]

Only difference with this and Kaplan-Meier is that \( F \) is a parametric model so likelihood is actually a function of parameters \( \beta, \sigma \).

Maximization is carried out numerically.
Interpretation of coefficients

- Coefficient $\beta_j$ affects median (or any other quantile of) survival time.
- Specifically,

$$e^{\beta_j} = \frac{t_{50}(X_1, \ldots, X_j + 1, \ldots, X_p)}{t_{50}(X_1, \ldots, X_j, \ldots, X_p)} = TR((X_1, \ldots, X_j + 1, \ldots, X_p), (X_1, \ldots, X_j + 1, \ldots, X_p))$$

- Another reason why it is called “accelerated” failure: i.e. for every cigarette you smoke, your median survival time goes down by a factor $e^{\beta_{cigarette}}$. 
Fisher information

Unlike linear models there is no explicit formula for variance / covariance of parameter estimates \((\hat{\beta}, \hat{\sigma})\).

\[
\hat{V}ar(\hat{\sigma}, \hat{\beta}) = \left( -\frac{\partial^2 \log L}{\partial \sigma \partial \beta} \right)^{-1}
\]

Generic way to estimate variance/covariance of MLE estimates. Obeys “delta rule.”
Example: variance of sample mean

- If $\sigma^2$ is known

$$-\log L(\mu|Z_1, \ldots, Z_n) \sim \frac{1}{2\sigma^2} (\|Z\|^2 - 2n\bar{Z}\mu + n\mu^2)$$

- Second derivative gives:

$$-\frac{\partial^2}{\partial\mu^2} \log L(\mu|Z_1, \ldots, Z_n) = \frac{n}{\sigma^2}.$$

- “Inverse” yields

$$\widehat{\text{Var}}(\bar{Z}) = \frac{\hat{\sigma}^2}{n}.$$
Residual diagnostics: Cox-Snell

- Like regression models, to assess goodness of fit, we use residuals.

- Parametric model imposes a (cumulative) hazard function \( H(t, X, \beta) \). Leads to Cox-Snell residuals (similar to “QQplot”)

\[
    r_i = H(t_i, X_i, \hat{\beta}).
\]

- If model is correct, the collection \((r_i, \delta_i)_{1 \leq i \leq n}\) should be like a sample from a censored \( \text{Exp}(1) \) sample. Plot of \( r_i \) vs. Nelson-Aalen estimator should be linear with slope 1.
Residual diagnostics: martingale

\[ M_i = \delta_i - r_i. \]

Martingale residuals can be used to see relation between \( j \)-th covariate and hazard by plotting \((X_{ij}, r_i)\) and using “lowess” or other smoother.

Residuals are motivated the Cox model, and definitions are basically identical. We’ll revisit them later.
We will look at many models:
- Exponential: only drug.
- Weibull: only drug.
- Weibull: drug + age.
- Lognormal: drug + age.
- Loglogistic: drug + age.
Exponential vs. Weibull

- Exponential is special case of Weibull with $\alpha = 1$.
- Can test if exponential is appropriate by testing $\alpha = 1$ or not.
Cox-snell: exponential

The diagram shows a plot comparing model hazard against estimated hazard. The x-axis represents the model hazard, ranging from 0.0 to 3.0, while the y-axis represents the estimated hazard, also ranging from 0.0 to 3.0.

The plot includes a linear trend line in blue, which appears to align with the estimated hazard values. The data points are scattered above and below the trend line, indicating variability in the estimated hazard values compared to the model predictions.
Cox-snell: Weibull

Estimated hazard vs Model hazard

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Martingale: Weibull