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Problem Set 1 | **Stat 245**

2.3 The time to death (in days) following a kidney transplant follows a log logistic distribution with $\alpha = 1.5$ and $\lambda = .01$.

- Find the 50,000 and 150 day survival probabilities for kidney transplantation in patients.
- Find the median time to death following kidney transplant.
- Show that the hazard rate is initially increasing and, then, decreasing over time. Find the time at which the hazard rate changes from increasing to decreasing.
- Find the mean time to death.

Solution

- Let X be the time to death (in days) following a kidney transplant. Then $X \sim \text{log logistic}(\alpha = 1.5, \lambda = .01)$, and from Table 2.2 (reference book) the survival function for X is given by

$$S(x) = \frac{1}{1 + \lambda x^\alpha} = \frac{1}{1 + .01x^{1.5}}.$$

So for $X = 50,000$, we have

$$S(50,000) = \frac{1}{1 + .01(50,000)^{1.5}} = .00000894$$

and finally for $X = 150$, the survival probability is

$$S(150) = \frac{1}{1 + .01(150)^{1.5}} = .0516.$$

- The median time to death following kidney transplant is,

$$\begin{aligned} S(x) &= P(X > x) = .5 \\ &= \frac{1}{1 + .01x^{1.5}} = .5 \\ \Rightarrow .01x^{1.5} &= \frac{1}{.5} - 1 \\ \Rightarrow x^{1.5} &= \frac{1}{.01} \\ \Rightarrow x &= 100^{\frac{1}{1.5}} = 21.54 \end{aligned}$$

- The hazard rate of X from Table 2.2, is given by

$$h(x) = \frac{\alpha x^{\alpha-1} \lambda}{1 + \lambda x^\alpha} = \frac{1.5x^{1.5-1} \cdot .01}{1 + .01x^{1.5}}$$

If we were to plot this, we have something like in Figure 1.

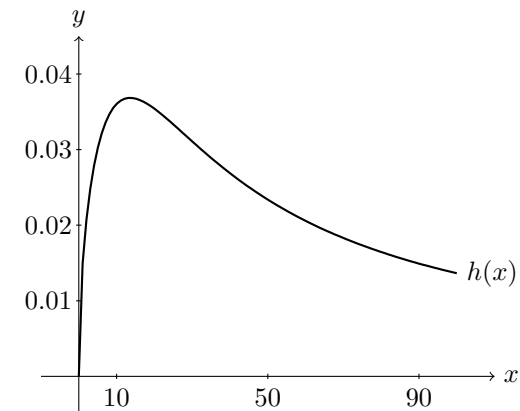


Figure 1: Plot of the hazard function of the Log Logistic(1.5, .01).

And indeed the function increases at first and then at some point in x it starts to decrease. To answer the problem mathematically, we need to apply first differentiation with respect to x to obtain the gradient

of the function $h(x)$. That is,

$$\begin{aligned}\frac{d h(x)}{d x} &= \frac{d}{d x} \frac{.015x^{.5}}{1 + .01x^{1.5}} = \frac{.0075(1 + .01x^{1.5})x^{-.5} - .015^2 x}{(1 + .01x^{1.5})^2} \\ &= \frac{.0075x^{-.5} + .000075x - .015^2 x}{(1 + .01x^{1.5})^2} \\ &= \frac{.0075x^{-.5} - .00015x}{(1 + .01x^{1.5})^2}\end{aligned}$$

Now we compute for the stationary point by setting the derivative to 0, i.e.

$$\begin{aligned}\frac{d h(x)}{d x} &= \frac{.0075x^{-.5} - .00015x}{(1 + .01x^{1.5})^2} = 0 \\ \Rightarrow .0075x^{-.5} - .00015x &= 0 \\ \Rightarrow .00015x &= .0075x^{-.5} \\ \Rightarrow x^{3/2} &= \frac{.0075}{.00015} \\ \Rightarrow x &= 50^{2/3} = 13.57208808.\end{aligned}$$

Hence, the time at which the hazard rate changes from increasing to decreasing is at $x = 50^{2/3}$ (the stationary point). Using this point, consider any time point x' such that $x' \neq x$, then we have the following criterion:

- if $\forall x' : x' < x$ and $h'(x') > 0 \Rightarrow h(x') \uparrow$ (is increasing).
- if $\forall x' : x' > x$ and $h'(x') < 0 \Rightarrow h(x') \downarrow$ (is decreasing).

Suppose $x' = 13.5$ i.e. $x' < x$ then

$$h'(x') = 7.25 \times 10^{-6} > 0, \text{ implies } h(x') \uparrow \forall x' < x, x' \in [0, x].$$

Now if $x' = 13.58$ i.e. $x' > x$ then

$$h'(x') = -7.91 \times 10^{-7}, \text{ implies } h(x') \downarrow \forall x' > x, x' \in (x, 100].$$

Therefore, the hazard function initially increasing and, then, decreasing over time. Figure 2 shows the plot of the gradient of the hazard function.

- (d) The mean time to death is

$$\frac{\pi \csc(\pi/\alpha)}{\alpha \lambda^{1/\alpha}} = \frac{\pi \csc(\pi/1.5)}{1.5(.01)^{1/1.5}} = 52.103$$

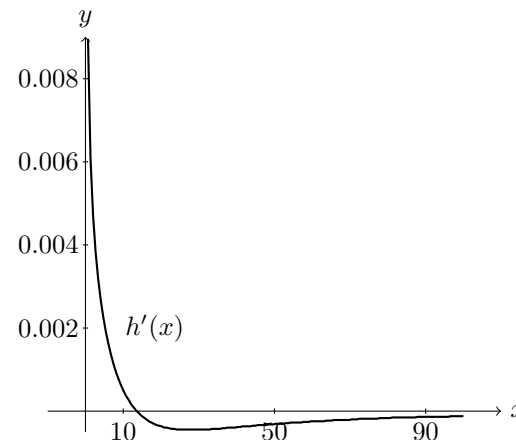


Figure 2: Gradient of the hazard function of the Log Logistic(1.5, .01).

2.5 A model for lifetimes, with a bathtub-shaped hazard rate, is the exponential power distribution with survival function $S(x) = \exp\{1 - \exp[(\lambda x)^\alpha]\}$.

- (a) If $\alpha = .5$ show that the hazard rate has a bathtub shape and find the time at which the hazard rate changes from decreasing to increasing.
- (b) If $\alpha = 2$, show that the hazard rate of x is monotone increasing.

Solution

- (a) The hazard rate for exponential power distribution is given by

$$h(x) = \alpha \lambda^\alpha x^{\alpha-1} \exp\{-(\lambda x)^\alpha\}.$$

Plotting the hazard rate given $\alpha = .5$ for values of $\lambda = \{.05, .07, .09, .11\}$, we something like in Figure 3. To find the time at which the hazard rate changes from decreasing to increasing, we need to apply differentiation on the hazard function and solve for the stationary point.

Figure 4 is the gradient of the hazard function, and mathematically we obtain these functions as follows:

$$\begin{aligned}\frac{d h(x)}{d x} &= \frac{d}{d x} \frac{\alpha \lambda^\alpha x^{\alpha-1}}{\exp[-(\lambda x)^\alpha]} \\ &= \frac{\exp[-(\lambda x)^\alpha] \alpha \lambda^\alpha (\alpha - 1) x^{\alpha-2} - \alpha \lambda^\alpha x^{\alpha-1} \exp[-(\lambda x)^\alpha] (-\lambda^\alpha \alpha x^{\alpha-1})}{\exp[-2(\lambda x)^\alpha]}\end{aligned}$$

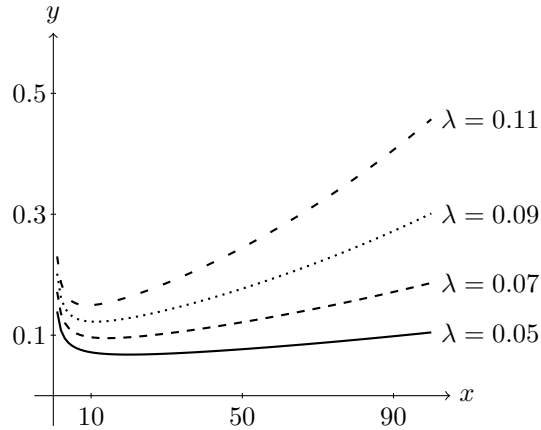


Figure 3: Hazard function of Exponential Power distribution for $\alpha = .5$ and different values of λ .

From this, we solve for the stationary point by setting the equation above to 0, i.e.

$$\begin{aligned} \frac{\exp[-(\lambda x)^\alpha] \alpha \lambda^\alpha (\alpha - 1) x^{\alpha-2}}{\exp[-2(\lambda x)^\alpha]} - \frac{\alpha \lambda^\alpha x^{\alpha-1} \exp[-(\lambda x)^\alpha] (-\lambda^\alpha \alpha x^{\alpha-1})}{\exp[-2(\lambda x)^\alpha]} &= 0 \\ \exp[-(\lambda x)^\alpha] \alpha \lambda^\alpha (\alpha - 1) x^{\alpha-2} - \alpha \lambda^\alpha x^{\alpha-1} \exp[-(\lambda x)^\alpha] (-\lambda^\alpha \alpha x^{\alpha-1}) &= 0 \\ \exp[-(\lambda x)^\alpha] \alpha \lambda^\alpha (\alpha - 1) x^{\alpha-2} &= \alpha \lambda^\alpha x^{\alpha-1} \exp[-(\lambda x)^\alpha] (-\lambda^\alpha \alpha x^{\alpha-1}) \\ (\alpha - 1) x^{\alpha-2} &= x^{\alpha-1} (-\lambda^\alpha \alpha x^{\alpha-1}) \\ (\alpha - 1) x^{\alpha-2} &= -x^{2\alpha-2} (\lambda^\alpha \alpha) \\ \frac{x^{2\alpha-2}}{x^{\alpha-2}} &= \frac{-(\alpha - 1)}{\lambda^\alpha \alpha} \\ x^\alpha &= \frac{-(\alpha - 1)}{\lambda^\alpha \alpha} \\ x &= \left[\frac{-(\alpha - 1)}{\lambda^\alpha \alpha} \right]^{\frac{1}{\alpha}} \end{aligned}$$

Hence, the time at which the hazard rate changes from decreasing to increasing is at $x = \left[\frac{.5}{.5\lambda^{.5}} \right]^2$. So for different values of λ , Table 1 lists the critical points:

- (b) Graphically, consider Figure 5, the plot of the hazard function for $\alpha = 2$.

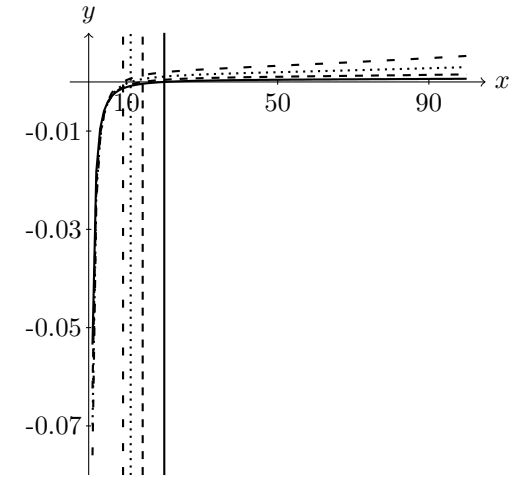


Figure 4: Gradient of the hazard function of exponential power distribution for $\alpha = .5$ and different values of λ along with the vertical lines that correspond to the stationary point of each λ .

λ	Critical Points
.05	20.000
.07	14.286
.09	11.111
.11	9.091

Table 1: Critical points for different values of λ .

From part (a), the derivative of the hazard function is,

$$\begin{aligned} \frac{dh(x)}{dx} &= \frac{d}{dx} \frac{\alpha \lambda^\alpha x^{\alpha-1}}{\exp[-(\lambda x)^\alpha]} \\ &= \frac{\exp[-(\lambda x)^\alpha] \alpha \lambda^\alpha (\alpha - 1) x^{\alpha-2} - \alpha \lambda^\alpha x^{\alpha-1} \exp[-(\lambda x)^\alpha] (-\lambda^\alpha \alpha x^{\alpha-1})}{\exp[-2(\lambda x)^\alpha]} \\ &= \frac{\exp[-(\lambda x)^\alpha] \alpha \lambda^\alpha (\alpha - 1) x^{\alpha-2}}{\exp[-2(\lambda x)^\alpha]} + \frac{\alpha \lambda^\alpha x^{\alpha-1} \exp[-(\lambda x)^\alpha] (\lambda^\alpha \alpha x^{\alpha-1})}{\exp[-2(\lambda x)^\alpha]} \\ &= \exp[(\lambda x)^\alpha] \alpha \lambda^\alpha (\alpha - 1) x^{\alpha-2} + \alpha \lambda^\alpha x^{\alpha-1} (\lambda^\alpha \alpha x^{\alpha-1}) \exp[(\lambda x)^\alpha] \\ &= \exp[(\lambda x)^\alpha] \alpha \lambda^\alpha x^{\alpha-2} [\alpha - 1 + \alpha \lambda^\alpha x^\alpha] \end{aligned}$$

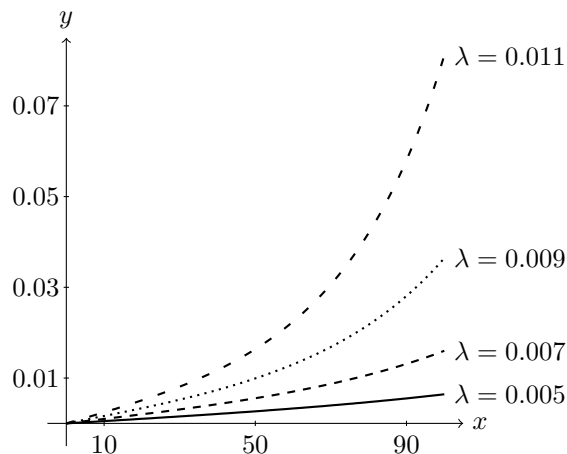


Figure 5: Hazard function of Exponential Power distribution for $\alpha = 2$ and different values of λ .

If $\alpha = 2$, then

$$h'(x) = \frac{d h(x)}{d x} = \frac{d}{d x} \frac{\alpha \lambda^\alpha x^{\alpha-1}}{\exp[-(\lambda x)^\alpha]} = 2\lambda^2 [1 + 2\lambda^2 x^2] \exp[(\lambda x)^2].$$

So that $\forall x, h'(x) > 0$, implying that $h(x)$ is monotone increasing.

2.10 In some applications, a third parameter, called a guarantee time, is included in the models discussed in this chapter. This parameter G is the smallest time at which a failure could occur. The survival function of the three-parameter Weibull distribution is given by

$$S(x) = \begin{cases} 1 & \text{if } x < G \\ \exp[-\lambda(x - G)^\alpha] & \text{if } x \geq G \end{cases}$$

- Find the hazard rate and the density function of the three-parameter Weibull distribution.
- Suppose that the survival time X follows a three-parameter Weibull distribution with $\alpha = 1, \lambda = .0075$ and $G = 100$. Find the mean and the median lifetimes.

Solution

- We compute for the density function first, consider the following

$$P(X > x) = S(x) = \begin{cases} 1 & \text{if } x < G \\ \exp[-\lambda(x - G)^\alpha] & \text{if } x \geq G \end{cases}.$$

Then the cumulative distribution function of X is,

$$F(x) = 1 - P(X > x) = 1 - S(x) = \begin{cases} 0 & \text{if } x < G \\ 1 - \exp[-\lambda(x - G)^\alpha] & \text{if } x \geq G \end{cases}.$$

So that the probability density function is given by,

$$f(x) = \frac{d}{d x} F(x) = \begin{cases} 0 & \text{if } x < G \\ \lambda \alpha (x - G)^{\alpha-1} \exp[-\lambda(x - G)^\alpha] & \text{if } x \geq G \end{cases}.$$

Therefore, the hazard rate is

$$h(x) = \frac{f(x)}{S(x)} = \begin{cases} 0 & \text{if } x < G \\ \lambda \alpha (x - G)^{\alpha-1} & \text{if } x \geq G \end{cases}.$$

- The mean life time is obtain as follows:

$$\begin{aligned} \mu &= \int_0^\infty S(t) dt = G + \int_G^\infty S(t) dt \\ &= G + \int_G^\infty \exp[-\lambda(t - G)^\alpha] dt \\ &= 100 + \int_{100}^\infty \exp[-.0075(t - 100)] dt \\ &= 100 + \exp[.75] \int_{100}^\infty \exp[-.0075t] dt \\ \text{let } u &= -.0075t, \text{ then } -\frac{du}{.0075} = dt \\ \text{if } t &= 100, u = -.75; \\ &= 100 - \frac{\exp[.75]}{.0075} \int_{-.75}^{-\infty} \exp[u] du \\ &= 100 + \frac{\exp[.75]}{.0075} (\exp[-.75]) \\ &= 100 + 133.33 = 233.33 \end{aligned}$$

And for the median denoting it as \tilde{x} , in order to justify the guarantee time, G , we expect $\tilde{x} \geq G$. So that,

$$\begin{aligned}
 S(\tilde{x}) &= P(X > \tilde{x}) = .5 \\
 \exp[-\lambda(\tilde{x} - G)^\alpha] &= .5 \\
 \exp[-.0075(\tilde{x} - 100)] &= .5 \\
 \exp[-.0075\tilde{x}] \exp[.75] &= .5 \\
 \exp[-.0075\tilde{x}] &= \frac{.5}{\exp[.75]} \\
 -.0075\tilde{x} &= \log \left[\frac{.5}{\exp[.75]} \right] \\
 \tilde{x} &= \frac{1.44315}{.0075} = 192.4196
 \end{aligned}$$

2.15 Based on data reported to the International Bone Marrow Transplant Registry, the survival function for a person given an HLA - identical sibling transplant for refractory multiple myeloma is given by

x Months Post Transplant	$S(x)$ Survival Probability
$0 \leq x < 6$	1.00
$6 \leq x < 12$	0.55
$12 \leq x < 18$	0.43
$18 \leq x < 24$	0.34
$24 \leq x < 30$	0.30
$30 \leq x < 36$	0.25
$36 \leq x < 42$	0.18
$42 \leq x < 48$	0.10
$48 \leq x < 54$	0.06
$x \geq 54$	0

- Find the probability mass function for the time to death for a refractory multiple myeloma bone marrow transplant patient.
- Find the hazard rate of X .
- Find the mean residual life at 12, 24, and 36 months post transplant.
- Find the median residual life at 12, 24, and 36 months.

Solution

- Let X be the time to death for a refractory multiple myeloma bone marrow transplant patient. The plot of the survival function is shown

in Figure 6.

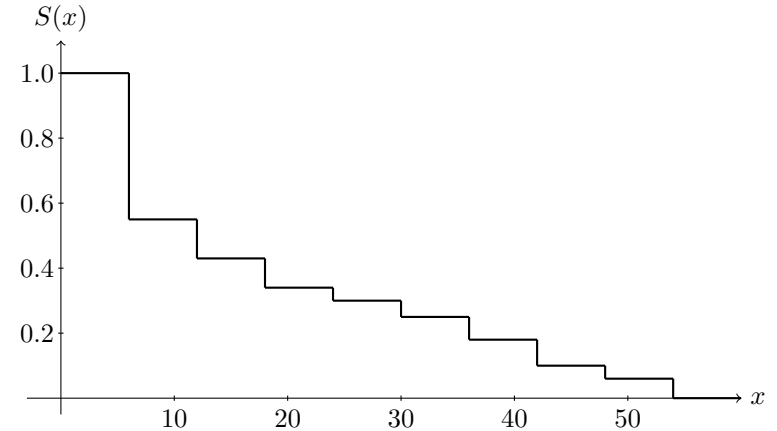


Figure 6: Survival function of the time to death for a refractory multiple myeloma bone marrow transplant patient.

So that the PMF is obtain as follows:

$$p(x_j) = S(x_{j-1}) - S(x_j) = \begin{cases} 0.45, & 6 \leq x < 12 \\ 0.12, & 12 \leq x < 18 \\ 0.09, & 18 \leq x < 24 \\ 0.04, & 24 \leq x < 30 \\ 0.05, & 30 \leq x < 36 \\ 0.07, & 36 \leq x < 42 \\ 0.08, & 42 \leq x < 48 \\ 0.04, & 48 \leq x < 54 \\ 0.06, & x \geq 54 \\ 0, & \text{otherwise} \end{cases}$$

Figure 7 shows the pmf of X .

- The hazard rate is computed using the following equation:

$$h(x_j) = \frac{P(X = x_j)}{P(X \geq x_j)} = \frac{p(x_j)}{S(x_{j-1})}$$

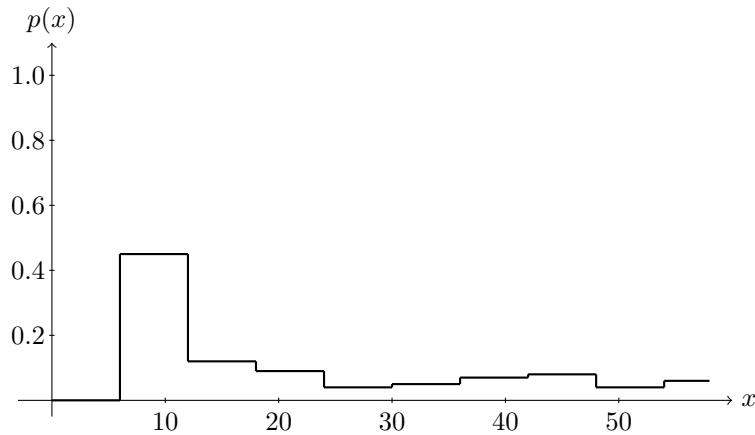


Figure 7: Probability mass function of the time to death for a refractory multiple myeloma bone marrow transplant patient.

From part (a), we have

$$h(x) = \begin{cases} 0.00, & 0 \leq x < 6 \\ 0.82, & 7 \leq x < 12 \\ 0.28, & 13 \leq x < 18 \\ 0.26, & 19 \leq x < 24 \\ 0.13, & 25 \leq x < 30 \\ 0.20, & 31 \leq x < 36 \\ 0.39, & 37 \leq x < 42 \\ 0.80, & 43 \leq x < 48 \\ 0.67, & 49 \leq x < 54 \\ 0, & \text{otherwise} \end{cases} \quad \begin{cases} 0.45, & x = 6 \\ 0.22, & x = 12 \\ 0.21, & x = 18 \\ 0.12, & x = 24 \\ 0.17, & x = 30 \\ 0.28, & x = 36 \\ 0.44, & x = 42 \\ 0.40, & x = 48 \\ 1, & x = 54 \end{cases}$$

Figure 8 is the plot of the hazard rate,

- (c) Analogous to continuous case, the mean residual lifetime is the area under the step function divided by the survival probability of x . i.e.

$$\text{mrl}(x) = \frac{(x_{i+1} - x)S(x_i) + \sum_{j \geq i+1} (x_{j+1} - x_j)S(x_j)}{S(x)}, \quad x_i \leq x < x_{i+1}.$$

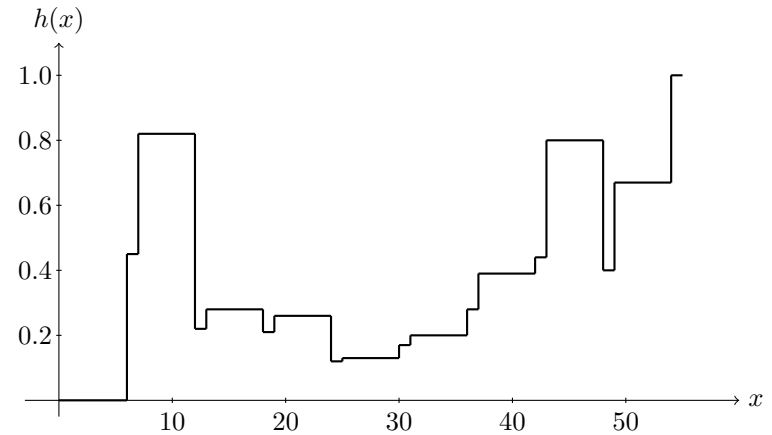


Figure 8: Hazard function of the time to death for a refractory multiple myeloma bone marrow transplant patient.

So that,

$$\begin{aligned} \text{mrl}(12) &= \frac{(13 - 12).43 + (14 - 13).43 + \cdots + (54 - 53).06}{.43} \\ &= \frac{6 \times .43}{.43} + \frac{6 \times .34}{.43} + \frac{6 \times .3}{.43} + \cdots + \frac{6 \times .06}{.43} + 0 \\ &= 23.163 \end{aligned}$$

$$\begin{aligned} \text{mrl}(24) &= \frac{(25 - 24).3 + (26 - 25).3 + \cdots + (54 - 53).06}{.3} \\ &= \frac{6 \times .3}{.3} + \frac{6 \times .25}{.3} + \frac{6 \times .18}{.3} + \cdots + \frac{6 \times .06}{.3} + 0 \\ &= 17.800 \end{aligned}$$

$$\begin{aligned} \text{mrl}(36) &= \frac{(37 - 36).18 + (38 - 37).18 + \cdots + (54 - 53).06}{.18} \\ &= \frac{6 \times .18}{.18} + \frac{6 \times .1}{.18} + \frac{6 \times .06}{.18} + 0 \\ &= 11.333 \end{aligned}$$

- (d) The median residual lifetime is simply the 50th percentile of the remaining lifetime, for brevity we'll denote this as $\text{medrl}(x)$. Hence, using the probability mass function obtained in part (a) excluding the first case which is $p(x_j) = .45$, $6 \leq x_j < 12$. The median residual lifetime at 12th month is $\text{medrl}(12) = \frac{54-12}{2} = 21$. To

verify this, we'll add the probabilities from $x = 13$ th month to $x = 13 + \text{medrl}(12) = 34$ th month, i.e.

$$\begin{aligned} S(x_{.50}) &= \frac{P(12 < x < 18) + P(18 \leq x < 24) + \cdots + P(30 \leq x \leq 34)}{1 - P(6 \leq x < 12) - P(X = 12)} \\ &= \frac{.12 \left(\frac{5}{6}\right) + .09 + .04 + .05 \left(\frac{5}{6}\right)}{1 - .45 - .12 \left(\frac{1}{6}\right)} = .5126 \end{aligned}$$

For 24th month, using the same procedure above, the median residual is 15, but summing up the probabilities from $x = 25$ th to $x = 25 + 15 = 39$ th month will not equal to .5 or closer. Instead, we have to consider 17 as the median percentile, i.e. $\text{medrl}(24) = 17$, since the sum of probabilities from $x = 25$ th to $x = 25 + \text{medrl}(24) = 25 + 17 = 42$ th month is

$$\begin{aligned} S(x_{.50}) &= \frac{P(24 < x < 30) + P(30 \leq x < 36) + P(36 \leq x \leq 42)}{1 - P(6 \leq x < 12) - \cdots - P(X = 24)} \\ &= \frac{.04 \left(\frac{5}{6}\right) + .05 + .07 + .08 \left(\frac{1}{6}\right)}{1 - .45 - .12 - .09 - .04 \left(\frac{1}{6}\right)} = .5 \end{aligned}$$

For 36th month, $\text{medrl}(36) = \frac{54-36}{2} = 9$, so that the sum of the probabilities from $x = 36$ th to $x = 36 + \text{medrl}(36) = 45$.

$$\begin{aligned} S(x_{.50}) &= \frac{P(36 < x < 42) + P(42 \leq x \leq 45)}{1 - P(6 \leq x < 12) - P(12 \leq x < 18) - \cdots - P(30 \leq x < 36)} \\ &= \frac{.07 \left(\frac{5}{6}\right) + .08 \left(\frac{4}{6}\right)}{1 - .45 - .12 - .09 - .04 - .05 - .07 \left(\frac{1}{6}\right)} = .469 \end{aligned}$$

Not exactly, but close to .5 already, if we consider median residual to be 10, we would obtain .5245, so the estimate for $\text{medrl}(36)$ is between 9 and 10, but close to 10.

2.18 Given a covariate Z , suppose that the log survival time Y follows linear model with a logistic error distribution, that is,

$$Y = \ln(X) = \mu + \beta Z + \sigma W \quad \text{where the pdf of } W \text{ is given by}$$

$$f(w) = \frac{e^w}{(1 + e^w)^2}, \quad -\infty < w < \infty.$$

- (a) For an individual with covariate Z , find the conditional survival function of the survival time X , given Z , namely, $S(x|Z)$.
- (b) The odds that an individual will die prior to time x is expressed by $[1 - S(x|Z)]/S(x|Z)$. Compute the odds of death prior to time x for this model.

- (c) Consider two individuals with different covariate values. Show that, for any time x , the ratio of their odds of death is independent of x . The log logistic regression model is the only model with this property.

Solution

(a)

$$\begin{aligned} S(x|Z) &= P(X > x|Z) = P(Y > \ln x|Z) \\ &= P(\mu + \beta Z + \sigma W > \ln x) \\ &= P(\sigma W > \ln x - \mu - \beta Z) \\ &= P\left(W > \frac{\ln x - \mu - \beta Z}{\sigma}\right) \\ &= \int_{\frac{\ln x - \mu - \beta Z}{\sigma}}^{\infty} \frac{e^w}{(1 + e^w)^2} dw \end{aligned}$$

let $u = 1 + e^w$, then $du = e^w dw$. And if $w = \frac{\ln x - \mu - \beta Z}{\sigma}$, then $u = 1 + \exp\left[\frac{\ln x - \mu - \beta Z}{\sigma}\right]$.

$$\begin{aligned} S(x|Z) &= P(X > x|Z) = P(Y > \ln x|Z) \\ &= \int_{1 + \exp\left[\frac{\ln x - \mu - \beta Z}{\sigma}\right]}^{\infty} \frac{1}{u^2} du \\ &= -\frac{1}{u} \Big|_{1 + \exp\left[\frac{\ln x - \mu - \beta Z}{\sigma}\right]}^{\infty} = \frac{1}{1 + \exp\left[\frac{\ln x - \mu - \beta Z}{\sigma}\right]} \\ &= \frac{1}{1 + x^{\frac{1}{\sigma}} \exp[-(\mu + \beta Z)]} \end{aligned}$$

- (b) Let's denote the odds that an individual will die prior to time x given the covariate Z as $\text{odds}(x|Z)$, then

$$\begin{aligned} \text{odds}(x|Z) &= \frac{1 - S(x|Z)}{S(x|Z)} = \frac{1}{S(x|Z)} - 1 \\ &= 1 + x^{\frac{1}{\sigma}} \exp[-(\mu + \beta Z)] - 1 \\ &= x^{\frac{1}{\sigma}} \exp[-(\mu + \beta Z)] \end{aligned}$$

- (c) Let $Z = z_1$ and $Z = z_2$ denote the covariate values of two individuals, of course $z_1 \neq z_2$. Then the ratio of their odds is

$$\frac{\text{odds}(x|z_1)}{\text{odds}(x|z_2)} = \frac{x^{\frac{1}{\sigma}} \exp[-(\mu + \beta z_1)]}{x^{\frac{1}{\sigma}} \exp[-(\mu + \beta z_2)]} = \frac{\exp[-(\mu + \beta z_1)]}{\exp[-(\mu + \beta z_2)]}.$$

Which is pretty obvious from part (b) already.