# Chapter 5A

## (AST405) Lifetime data analysis

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# Lecture Outline

1. 5. Inference Procedures for Log-location-scale Distributions
   - 5.1 Inference for location-scale distributions
   - 5.2 Weibull and extreme-value distributions

Section 1

# 5. Inference Procedures for Log-location-scale Distributions

Subsection 1

## 5.1 Inference for location-scale distributions

# 5.1 Inference for location-scale distributions

- Location-scale distributions have survivor function of the form

$$S(y; u, b) = S_0\left(\frac{y-u}{b}\right) \quad -\infty < y < \infty \tag{1}$$

$$-\infty < u < \infty \ \text{ and } \ b > 0$$

- Log-lifetime $Y = \log T$ has a location-scale distribution with survivor function of the form Equation 1

# 5.1 Inference for location-scale distributions

- Lifetime variable $T$ has a log-location-scale distribution with the survivor function

$$S_T(t;\alpha,\beta) = S_0\left(\frac{\log t - u}{b}\right) = S_0^\star\left[(t/\alpha)^\beta\right] \tag{2}$$

  - $S_0^\star(w) = S_0(\log w)$ for $w > 0$
  - $u = \log \alpha$
  - $b = (1/\beta)$

# 5.1 Inference for location-scale distributions

- Lifetime and log-lifetime distributions
  - exponential, Weibull, log-logistic, log-normal, etc.
  - extreme-value, logistic, normal, etc.

# Likelihood based methods

- Goal is to estimate the parameters $(u, b)$ or $(\alpha, \beta)$
- Some advantages of estimating $(u, b)$
  - Log-likelihood function for $(u, b)$ is more closer to quadratic than that for $(\alpha, \beta)$
  - Large sample normal approximations for $(\hat{u}, \hat{b})$ tend to be more accurate that those for $(\hat{\alpha}, \hat{\beta})$
- A better choice of parameters for obtaining MLEs and implementing normal approximations is $(u, \log b)$, which is used by most statistical software

# Likelihood function

- For a censored sample

$$\{(t_i, \delta_i),\ i = 1, \ldots, n\},$$

the likelihood function

$$L(u, b) = \prod_{i=1}^{n} \left[ \frac{1}{b} f_0\left( \frac{y_i - u}{b} \right) \right]^{\delta_i} \left[ S_0\left( \frac{y_i - u}{b} \right) \right]^{1-\delta_i} \qquad (3)$$

  - $y_i = \log t_i$
  - $f_0(z) = -dS_0(z)/dz \ \rightarrow$ pdf

# Likelihood function

- The standardized variable

$$z_i = \frac{y_i - u}{b}$$

- The likelihood function

$$L(u, b) = \prod_{i=1}^{n} \left[ \frac{1}{b} f_0(z_i) \right]^{\delta_i} \left[ S_0(z_i) \right]^{1-\delta_i} \tag{4}$$

# Likelihood function

- The corresponding log-likelihood function

$$
\begin{aligned}
\ell(u,b) &= -r\log b + \sum_{i=1}^{n}\Big[\delta_i \log f_0(z_i) + (1-\delta_i)\log S_0(z_i)\Big] \\
&= -r\log b + \sum_{i=1}^{n}\ell_i(z_i,\delta_i) \qquad (5)
\end{aligned}
$$

  - $r = \sum_{i=1}^{n}\delta_i$

# Score functions

$$
\begin{aligned}
\ell(u,b) &= -r\log b + \sum_{i=1}^{n} \ell_i(z_i,\delta_i) \\
&= -r\log b + \sum_{i=1}^{n} \Big[\delta_i \log f_0(z_i) + (1-\delta_i)\log S_0(z_i)\Big]
\end{aligned}
$$

$$
\begin{aligned}
\frac{\partial \ell(u,b)}{\partial u} &= \sum_{i=1}^{n} \frac{\partial \ell_i(z_i,\delta_i)}{\partial z_i} \times \frac{\partial z_i}{\partial u} \\
&= \sum_{i=1}^{n} \frac{\partial \ell_i(z_i,\delta_i)}{\partial z_i} \times \left(\frac{-1}{b}\right) \\
&= -\frac{1}{b}\sum_{i=1}^{n} \left[\delta_i \frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\frac{\partial \log S_0(z_i)}{\partial z_i}\right]
\end{aligned}
$$

# Score functions

$$\ell(u,b) = -r\log b + \sum_{i=1}^{n}\left[\delta_i \log f_0(z_i) + (1-\delta_i)\log S_0(z_i)\right]$$

$$\begin{aligned}
\frac{\partial \ell(u,b)}{\partial b} &= -\frac{r}{b} + \sum_{i=1}^{n} \frac{\partial \ell_i(z_i,\delta_i)}{\partial z_i} \times \frac{\partial z_i}{\partial b} \\
&= -\frac{r}{b} + \sum_{i=1}^{n} \frac{\partial \ell_i(z_i,\delta_i)}{\partial z_i} \times \left(\frac{-z_i}{b}\right) \\
&= -\frac{r}{b} - \frac{1}{b}\sum_{i=1}^{n} z_i\left[\delta_i \frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\frac{\partial \log S_0(z_i)}{\partial z_i}\right]
\end{aligned}$$

# Hessian matrix

$$\frac{\partial \ell(u,b)}{\partial u} = -\frac{1}{b} \sum_{i=1}^{n} \left[ \delta_i \, \frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i) \, \frac{\partial \log S_0(z_i)}{\partial z_i} \right]$$

$$\begin{aligned} \frac{\partial^2 \ell(u,b)}{\partial u^2} &= \frac{\partial}{\partial u}\left[\frac{\partial \ell(u,b)}{\partial u}\right] \\ &= \frac{1}{b^2} \sum_{i=1}^{n} \left[ \delta_i \, \frac{\partial^2 \log f_0(z_i)}{\partial z_i^2} + (1-\delta_i) \, \frac{\partial^2 \log S_0(z_i)}{\partial z_i^2} \right] \end{aligned}$$

# Hessian matrix

$$\frac{\partial \ell(u,b)}{\partial b} = -\frac{r}{b} - \frac{1}{b}\sum_{i=1}^{n} z_i \left[\delta_i \,\frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\,\frac{\partial \log S_0(z_i)}{\partial z_i}\right]$$

$$\begin{aligned}\frac{\partial^2 \ell(u,b)}{\partial b^2} = \frac{r}{b^2} &+ \frac{2}{b^2}\sum_{i=1}^{n} z_i \left[\delta_i \,\frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\,\frac{\partial \log S_0(z_i)}{\partial z_i}\right] \\ &+ \frac{1}{b^2}\sum_{i=1}^{n} z_i^2 \left[\delta_i \,\frac{\partial^2 \log f_0(z_i)}{\partial z_i^2} + (1-\delta_i)\,\frac{\partial^2 \log S_0(z_i)}{\partial z_i^2}\right]\end{aligned}$$

# Hessian matrix

$$\frac{\partial \ell(u,b)}{\partial u} = -\frac{1}{b}\sum_{i=1}^{n}\left[\delta_i \frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\frac{\partial \log S_0(z_i)}{\partial z_i}\right]$$

$$\frac{\partial^2 \ell(u,b)}{\partial u\,\partial b} = \frac{1}{b^2}\sum_{i=1}^{n}\left[\delta_i \frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\frac{\partial \log S_0(z_i)}{\partial z_i}\right] + \frac{1}{b^2}\sum_{i=1}^{n} z_i\left[\delta_i \frac{\partial^2 \log f_0(z_i)}{\partial z_i^2} + (1-\delta_i)\frac{\partial^2 \log S_0(z_i)}{\partial z_i^2}\right]$$

# Score function and information matrix

$$U(u, b) = \begin{bmatrix} \frac{\partial \ell(u,b)}{\partial u} \\ \frac{\partial \ell(u,b)}{\partial b} \end{bmatrix}$$

$$I(u, b) = -H(u, b) = -\begin{bmatrix} \frac{\partial^2 \ell(u,b)}{\partial u^2} & \frac{\partial^2 \ell(u,b)}{\partial u \, \partial b} \\ \frac{\partial^2 \ell(u,b)}{\partial b \, \partial u} & \frac{\partial^2 \ell(u,b)}{\partial b^2} \end{bmatrix}$$

# Statistical inference

- MLE

$$(\hat{u}, \hat{b})' = \arg\max_{(u,b)' \in \Theta} \ell(u, b)$$

- Variance-covariance matrix

$$\text{var}(\hat{u}, \hat{b}) = \left[I(\hat{u}, \hat{b})\right]^{-1} = \hat{V}$$

- Sampling distribution

$$\begin{pmatrix} \hat{u} \\ \hat{b} \end{pmatrix} \sim \mathcal{N}_2 \left( \begin{bmatrix} u \\ b \end{bmatrix}, \left[I(\hat{u}, \hat{b})\right]^{-1} \right)$$

# Wald type CIs

- For a large $n$, $(\hat{u}, \hat{b})'$ follows a bivariate normal distribution with mean $(u, b)'$ and variance matrix $\hat{V}$
- Standard error of $\hat{u}$ and $\hat{b}$ can be obtained from the diagonal elements of $\hat{V}$
$$se(\hat{u}) = \hat{V}_{11}^{1/2} \text{ and } se(\hat{b}) = \hat{V}_{22}^{1/2}$$

# Wald type CIs

- Following pivotal quantities follow standard normal distributions

$$Z_1 = \frac{\hat{u} - u}{se(\hat{u})}, \qquad Z_2 = \frac{\hat{b} - b}{se(\hat{b})}, \qquad Z_2' = \frac{\log \hat{b} - \log b}{se(\log \hat{b})}$$

  - $se(\log \hat{b}) = se(\hat{b})/\hat{b}$

- $(1-p)100\%$ confidence intervals

$$\hat{u} \pm z_{1-p/2}\, se(\hat{u})$$
$$\hat{b} \pm z_{1-p/2}\, se(\hat{b})$$
$$\hat{b} \exp\{\pm z_{1-p/2}\, se(\log \hat{b})\}$$

# Quantiles

- $p$th quantile of log lifetime $Y$

$$
\begin{aligned}
P(Y \leq y_p) = p \;\Rightarrow\; S_0\Big(\frac{y_p - u}{b}\Big) &= 1 - p \\
\frac{y_p - u}{b} &= S_0^{-1}(1-p) \\
y_p &= u + bw_p
\end{aligned}
$$

  - $w_p = S_0^{-1}(1-p) = F_0^{-1}(p) \rightarrow p$th quantile of $S_0(z)$, the standardize distribution

# Quantiles

- Estimate of $p$th quantile and the corresponding standard error

$$\hat{y}_p = \hat{u} + \hat{b} w_p$$

$$se(\hat{y}_p) = \sqrt{\hat{V}_{11} + w_p^2 \hat{V}_{22} + 2 w_p \hat{V}_{12}}$$

- Pivotal quantity

$$Z_p = \frac{\hat{y}_p - y_p}{se(\hat{y}_p)} \sim \mathcal{N}(0,1)$$

- $(1-q)100\%$ confidence interval for $y_p$

$$\hat{y}_p \pm z_{1-q/2}\, se(\hat{y}_p)$$

# Likelihood ratio procedures

- Normal approximation based confidence intervals could be inaccurate for small samples
- An alternative to normal approximation, bootstrap simulations can be used to estimate the distributions of pivots
- All these methods can perform poorly in small samples with heavy censoring
- Implementation of likelihood ratio based confidence intervals is relatively complicated, but LRT based CI often performs better in small and medium-size samples

# Likelihood ratio procedures

- To test the hypothesis $H_0 : u = u_0$, the following likelihood ratio test statistic can be used

$$\Lambda_1(u_0) = 2\ell(\hat{u}, \hat{b}) - 2\ell(u_0, \tilde{b}(u_0))$$

- MLEs

$$(\hat{u}, \hat{b})' = \arg\max_{(u,b)' \in \Theta} \ell(u, b) \quad \text{unrestricted}$$

$$\tilde{b}(u_0) = \arg\max_{b \in \Theta_1} \ell(u_0, b) \quad \text{under } H_0$$

# Likelihood ratio procedures

- Under $H_0 : u = u_0$, asymptotically $\Lambda_1(u_0) \sim \chi^2_{(1)}$
  - Approximate two-sided $(1-p)100\%$ confidence interval for $u$ can be obtained as the set of values of $u_0$ for which

$$\Lambda_1(u_0) \leq \chi^2_{(1),1-p}$$

# Likelihood ratio procedures

## Homework - 1

- Obtain the expression of likelihood ratio test statistic based confidence interval for the scale parameter $b$

# Likelihood ratio procedures

- The $p$th quantile of location-scale distribution can be expressed as

$$y_p = u + w_p b, \;\; where \;\; w_p = S_0^{-1}(1-p)$$

- To obtain confidence intervals for a quantile, consider the null hypothesis

$$H_0 : y_p = y_{p_0}$$

- The corresponding likelihood ratio test statistic

$$\Lambda(y_{p_0}) = 2\ell(\hat{u}, \hat{b}) - 2\ell(\tilde{u}, \tilde{b}) \tag{6}$$

# Likelihood ratio procedures

## Steps

- The estimates $\hat{u}$ and $\hat{b}$ are MLEs under $H_1$

$$(\hat{u}, \hat{b})' = \arg\,\max_{(u,b)' \in \Theta} \ell(u, b)$$

- Steps to obtain MLEs $\tilde{u}$ and $\tilde{b}$, under $H_0 : y_p = y_{p_0}$
  1. Under $H_0$, $y_{p_0} = u + w_p b \;\Rightarrow\; u = y_{p_0} - b w_p$
  2. $\tilde{b} = \arg\,\max_{b \in \Theta} \ell(y_{p_0} - w_p b, b)$
  3. $\tilde{u} = y_{p_0} - w_p \tilde{b}$
- $(1 - q)100\%$ Confidence interval for $y_p$ can be obtained from the set of $y_{p_0}$ values such that

$$\Lambda(y_{p_0}) \leq \chi^2_{(1),1-q}$$

# Likelihood ratio procedures

- To obtain confidence interval for $S(y_0)$, consider the null hypothesis

$$H_0 : S(y_0) = s_0$$

- The same likelihood ratio statistic Equation 6 can be used to test the hypothesis

$$\Lambda(s_0) = 2\ell(\hat{u}, \hat{b}) - 2\ell(\tilde{u}, \tilde{b})$$

# Likelihood ratio procedures

## Steps

- Steps for obtaining MLEs $\tilde{u}$ and $\tilde{b}$ under $H_0$
  1. Under $H_0 : S(y_0) = s_0$

$$S(y_0) = S_0\left(\frac{y_0 - u}{b}\right) = s_0 \;\; \Rightarrow \;\; u = y_0 - S_0^{-1}(s_0)b$$

  2. $\tilde{b} = \arg\max_{b\in\Theta} \ell(y_0 - S_0^{-1}(s_0)b, b)$
  3. $\tilde{u} = y_0 - S_0^{-1}(s_0)\tilde{b}$
- The $(1-p)100\%$ confidence interval for $S(y_0)$ can be defined as the set of $s_0$ values such that

$$\Lambda(s_0) \leq \chi^2_{(1),1-p} \tag{7}$$

# Likelihood ratio procedures

- The likelihood ratio procedure can provide quite accurate confidence intervals when the number of failures is about 20 or more
- Two-sided intervals perform better than one-sided intervals as the former giving more closer to nominal coverage than the other

Subsection 2

## 5.2 Weibull and extreme-value distributions

# 5.2 Weibull and extreme-value distributions

- The pdf of Weibull distribution

$$f(t;\alpha,\beta) = \frac{\beta}{\alpha}\left(\frac{t}{\alpha}\right)^{\beta-1}\exp\left[-(t/\alpha)^{\beta}\right] \tag{8}$$

  - $\alpha > 0$ and $\beta > 0$ are scale and shape parameters, respectively

# 5.2 Weibull and extreme-value distributions

- The pdf of extreme-value distribution

$$f(y; u, b) = \frac{1}{b}\ \exp\left[(y-u)/b\right]\ \exp\left[-e^{(y-u)/b}\right] \tag{9}$$

$$= \frac{1}{b}\, f_0\left(\frac{y-u}{b}\right) \tag{10}$$

  - $u = \log \alpha$
  - $b = (1/\beta)$

- Extreme-value distribution is used to make inferences about Weibull distribution

# Likelihood based inference procedures

- Censored sample

$$\{(t_i, \delta_i),\ i = 1, \dots, n\}$$

- Define

$$y_i = \log t_i \ \text{ and } \ z_i = (y_i - u)/b$$

# Likelihood based inference procedures

- General expression of likelihood function

$$\ell(u,b) = -r\log b + \sum_{i=1}^{n}\left[\delta_i \log f_0(z_i) + (1-\delta_i)\log S_0(z_i)\right]$$

- For extreme-value distribution

$$S_0(z) = \exp(-e^z)$$
$$f_0(z) = -\frac{d}{dz}S_0(z) = \exp(z - e^z)$$

# Likelihood based inference procedures

$$\ell(u,b) = -r\log b + \sum_{i=1}^{n}\left[\delta_i \log f_0(z_i) + (1-\delta_i)\log S_0(z_i)\right]$$

- **Log-likelihood function for EV distribution**

$$\ell(u,b) = -r\log b + \sum_{i=1}^{n}\left(\delta_i z_i - e^{z_i}\right) \tag{11}$$

  - $r = \sum_i \delta_i$
- This log-likelihood function $\ell(u,b)$ is easily maximized to give $\hat{u}, \hat{b}$ (using software)

# Score functions

- *The general expression for location-scale family* can also help us find the expressions for the first (and also second) derivatives of $\ell(u, b)$.
- General expressions

$$\frac{\partial \ell(u,b)}{\partial u} = -\frac{1}{b}\sum_{i=1}^{n}\left[\delta_i \frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\frac{\partial \log S_0(z_i)}{\partial z_i}\right]$$

$$\frac{\partial \ell(u,b)}{\partial b} = -\frac{r}{b} - \frac{1}{b}\sum_{i=1}^{n} z_i\left[\delta_i \frac{\partial \log f_0(z_i)}{\partial z_i} + (1-\delta_i)\frac{\partial \log S_0(z_i)}{\partial z_i}\right]$$

# Score functions

- For extreme-value distribution

$$\frac{\partial \log f_0(z)}{\partial z} = \frac{\partial}{\partial z} \log\{\exp(z - e^z)\} = 1 - e^z$$

$$\frac{\partial \log S_0(z)}{\partial z} = \frac{\partial}{\partial z} \log\{\exp(-e^z)\} = -e^z$$

- These gives straightforward expressions for the first and second derivatives of $\ell(u, b)$, which can be used to find MLEs, $\hat{u}, \hat{b}$

# Hessian matrix

## Hessian matrix

- Hessian matrix at MLEs $\hat{u}$ and $\hat{b}$

$$H(\hat{u},\hat{b}) = -\frac{1}{\hat{b}^2}\begin{bmatrix} r & \sum_{i=1}^{n}\hat{z}_i e^{\hat{z}_i} \\ \sum_{i=1}^{n}\hat{z}_i e^{\hat{z}_i} & r+\sum_{i=1}^{n}\hat{z}_i^2 e^{\hat{z}_i}\end{bmatrix}$$

## Proof

- For extreme-value distribution

$$\frac{\partial^2 \ell(u,b)}{\partial u^2} = \frac{1}{b^2}\sum_{i=1}^{n}\left[\delta_i \frac{\partial^2 \log f_0(z_i)}{\partial z_i^2} + (1-\delta_i)\frac{\partial^2 \log S_0(z_i)}{\partial z_i^2}\right] = -\frac{1}{b^2}\sum_{i=1}^{n} e^{z}$$

where

$$\frac{\partial^2 \log f_0(z)}{\partial z^2} = \frac{\partial}{\partial z}\{1-e^z\} = -e^z = \frac{\partial^2 \log S_0(z)}{\partial z^2}$$

# Covariance matrix

- Observed information matrix at MLEs $\hat{u}$ and $\hat{b}$

$$
\begin{aligned}
I(\hat{u},\hat{b}) &= -H(\hat{u},\hat{b}) \\
&= \frac{1}{\hat{b}^2}\begin{bmatrix} r & \sum_{i=1}^{n} \hat{z}_i e^{\hat{z}_i} \\ \sum_{i=1}^{n} \hat{z}_i e^{\hat{z}_i} & r + \sum_{i=1}^{n} \hat{z}_i^2 e^{\hat{z}_i} \end{bmatrix}
\end{aligned}
$$

- **Covariance matrix of** $(\hat{u},\hat{b})'$

$$
\hat{V} = \left[I(\hat{u},\hat{b})\right]^{-1} \tag{15}
$$

# Covariance matrix

- MLEs of $\alpha$ and $\beta$ (Weibull model parameters)

$$\hat{\alpha} = e^{\hat{u}} \text{ and } \hat{\beta} = 1/\hat{b}$$

- Covariance matrix of $(\hat{\alpha}, \hat{\beta})'$ (using multivariate delta method)

$$\operatorname{var}(\hat{\alpha}, \hat{\beta}) = G\,\hat{V}\,G'$$

where

$$G = \begin{bmatrix} \frac{\partial g_1(u,b)}{du} & \frac{\partial g_1(u,b)}{\partial b} \\ \frac{\partial g_2(u,b)}{\partial u} & \frac{\partial g_2(u,b)}{\partial b} \end{bmatrix} = \begin{bmatrix} e^{\hat{u}} & 0 \\ 0 & -\frac{1}{\hat{b}^2} \end{bmatrix}$$

  - $\alpha = g_1(u, b) = e^u$
  - $\beta = g_2(u, b) = (1/b)$

# Covariance matrix

- Wald-type statistics based $100(1-p)\%$ CI for $u$ and $b$

$$
\begin{aligned}
&\hat{u} \pm z_{1-p/2}\, se(\hat{u}) \\
&\hat{b} \pm z_{1-p/2}\, se(\hat{b}) \\
&\hat{b} \exp\left[\pm z_{1-p/2}\, se(\log \hat{b})\right]
\end{aligned}
$$

# CI for $(u, b)$ (LRT based)

- Log-likelihood function corresponding to $H_0 : b = b_0$ is (from Equation 11)

$$\ell(u, b_0) = -r \log b_0 + \sum_{i=1}^{n} \left[ \delta_i \left( \frac{y_i - u}{b_0} \right) - e^{(y_i - u)/b_0} \right]$$

- MLE of $u$ under $H_0 : b = b_0$

$$\left. \frac{\partial \ell(u, b_0)}{\partial u} \right|_{u = \tilde{u}} = 0 \;\Rightarrow\; -\frac{1}{b_0} \left[ r - \sum_{i=1}^{n} e^{(y_i - \tilde{u})/b_0} \right] = 0$$

$$\Rightarrow\; \tilde{u}(b_0) = b_0 \log \left[ \frac{1}{r} \sum_{i=1}^{n} e^{y_i / b_0} \right]$$

# CI for $(u, b)$ (LRT based)

- LRT statistics

$$\Lambda(b_0) = 2\ell(\hat{u}, \hat{b}) - 2\ell(\tilde{u}(b_0), b_0)$$

- $100(1-p)\%$ CI for $b$ is defined by the set of $b_0$ values such that

$$\Lambda_1(b_0) \leq \chi^2_{(1),1-p}$$

- Similarly, confidence interval for $u$ can be obtained using the corresponding LRT statistics (Homework)

# CI for quantiles

- The $p$th quantile of $Y \sim EV(u, b)$

$$S(y_p) = S_0\Big(\frac{y_0 - u}{b}\Big) = (1 - p) \tag{16}$$

$$\exp\Big[-\exp\Big(\frac{y_p - u}{b}\Big)\Big] = (1 - p) \tag{17}$$

$$\frac{y_p - u}{b} = \log\big[-\log(1 - p)\big] = S_0^{-1}(1 - p) = w_p \tag{18}$$

$$y_p = u + w_p\, b \tag{19}$$

# CI for quantiles

## CI for quantiles (Wald)

- The estimate of $p$th quantile

$$\hat{y}_p = \hat{u} + w_p \hat{b}$$

- Standard error of $\hat{y}_p$ (using the multivariate delta method)

$$\mathrm{var}(\hat{y}_p) = \begin{bmatrix} 1 & w_p \end{bmatrix} \hat{V} \begin{bmatrix} 1 \\ w_p \end{bmatrix} = \hat{V}_{11} + \hat{V}_{22} w_p^2 + 2\hat{V}_{12} w_p$$

- Large sample based $100(1-q)\%$ confidence interval for $y_p$

$$\hat{y}_p \pm z_{1-q/2}\, se(\hat{y}_p)$$

- **Find the $100(1-q)\%$ confidence interval for $t_p$**

# CI for quantiles

## CI for quantiles (LRT)

- To obtain LRT statistic based confidence interval for the quantile $y_p$, consider the following null hypothesis

$$H_0 : y_p = y_{p_0}$$

- The corresponding LRT statistic

$$\Lambda(y_{p_0}) = 2\ell(\hat{u}, \hat{b}) - 2\ell(\tilde{u}, \tilde{b})$$

  - The procedure of obtaining parameter estimates $\tilde{u}$ and $\tilde{b}$ (under $H_0$) is explained in Section 28)

- LRT statistic based $(1-q)100\%$ confidence interval for $y_p$ can be obtained from the set of $y_{p_0}$ values such that

$$\Lambda(y_{p_0}) \leq \chi^2_{(1),1-q}$$

# CI for $S(\cdot)$ (Wald)

- To obtain confidence interval for survival probability

$$S(y_0) = S_0\Big(\frac{y_0 - u}{b}\Big) = \exp\Big[-\exp\Big(\frac{y_0 - u}{b}\Big)\Big]$$

- We can defined

$$\psi = S_0^{-1}\Big(S(y_0)\Big) = \log\big[-\log\big(S(y_0)\big)\big] = \frac{y_0 - u}{b}$$

- MLE and SE

$$\hat{\psi} = \frac{y_0 - \hat{u}}{\hat{b}}$$

$$\text{var}(\hat{\psi}) = a'\hat{V}a = \begin{bmatrix} -1/\hat{b} & -\hat{\psi}/b \end{bmatrix} \begin{bmatrix} \hat{V}_{11} & \hat{V}_{12} \\ \hat{V}_{21} & \hat{V}_{22} \end{bmatrix} \begin{bmatrix} -1/\hat{b} \\ -\hat{\psi}/b \end{bmatrix}$$

# CI for $S(\cdot)$ (Wald)

- $(1-p)100\%$ CI for $\psi$

$$\hat{\psi} - se(\hat{\psi})\, z_{1-p2} < \psi \leq \hat{\psi} + se(\hat{\psi})\, z_{1-p/2}$$
$$L < \psi \leq U$$

- Confidence interval for $S(y_0)$

$$L < \log\left[-\log\left(S(y_0)\right)\right] \leq U$$
$$\exp\left[-\exp(U)\right] < S(y_0) \leq \exp\left[-\exp(L)\right]$$

# CI for $S(\cdot)$ (LRT)

- Consider the null hypothesis $H_0 : S(y_0) = s_0$, where

$$S(y_0) = \exp\left[ -\exp\left( \frac{y_0 - u}{b} \right) \right]$$

- The $(1-p)100\%$ confidence interval for $S(y_0)$ can be defined as the set of $s_0$ values such that $\Lambda(s_0) \leq \chi^2_{(1),1-p}$, where

$$\Lambda(s_0) = 2\ell(\hat{u}, \hat{b}) - 2\ell(\tilde{u}, \tilde{b})$$

  - The procedure of obtaining parameter estimates $\tilde{u}$ and $\tilde{b}$ (under $H_0$) is explained in Section 30)

## Example 5.2.1:

- Leukemia remission time data were given in Example 1.1.7 and used as an example for the non-parametric methods (e.g. Kaplan-Meier method) described in Chapter 3
- Two groups of patients (6MP and placebo), each group has 21 patients, were followed up to observed either remission or censoring times (in weeks)

# Example 5.2.1:

## Remission time data

```
glimpse(gehan65)
```

```
Rows: 42
Columns: 3
$ time   <dbl> 6, 6, 6, 6, 7, 9, 10, 10, 11, 13, 16, 17, 19, 20, 22
$ status <dbl> 1, 1, 1, 0, 1, 0, 1, 0, 0, 1, 1, 0, 0, 0, 1, 1, 0, 0
$ drug   <chr> "6-MP", "6-MP", "6-MP", "6-MP", "6-MP", "6-MP", "6-MI
```

| drug | status | n |
|---|---|---|
| 6-MP | 0 | 12 |
| 6-MP | 1 | 9 |
| placebo | 1 | 21 |

- Each group has 21 subjects, and all subjects of the placebo group were failed (end of remission) and drug group (6MP) has 12 censored times

# Example 5.2.1:

- Two separate Weibull distributions are assumed for the failure times of two treatment groups, e.g.
  - 6MP group:
  $$T \sim \text{Weibull}(\alpha_1, \beta_1),\ Y = \log T \sim EV(u_1, b_1)$$
  - Placebo group:
  $$T \sim \text{Weibull}(\alpha_2, \beta_2),\ Y = \log T \sim EV(u_2, b_2)$$
- *Objectives*: Drawing inference about the parameters

# Example 5.2.1:

- Observed data

$$\{(t_i, \delta_i), i = 1, \dots, n\}$$

- Log-likelihood function

$$\ell(\alpha, \beta) = \sum_{i=1}^{n} \left[\delta_i \log f(t_i; \alpha, \beta) + (1 - \delta_i) \log S(t_i; \alpha, \beta)\right]$$

- MLEs

$$(\hat{\alpha}, \hat{\beta})' = \arg\ \max_{(\alpha,\beta)' \in \Theta} \ell(\alpha, \beta)$$

# Example 5.2.1:

## Analysis of remission time data (Extreme-value distribution)

- Define $y = \log t$ and corresponding probability density and survivor function

$$f(y; u, b) = \frac{1}{b} \exp\left[(y-u)/b - e^{(y-u)/b}\right] \tag{20}$$

$$S(y; u, b) = \exp\left[- e^{(y-u)/b}\right] \tag{21}$$

- Log-likelihood function

$$\ell_{ev}(u, b) = \log \prod_{i=1}^{n} \left[f(y_i; u, b)\right]^{\delta_i} \left[S(y_i; u, b)\right]^{1-\delta_i} \tag{22}$$

- MLEs

$$(\hat{u}, \hat{b})' = \arg\, \max_{(u,b)' \in \Theta} \ell_{ev}(u, b)$$

# `survreg` function

- R function `survreg()` can also be used to fit distributions of log-location-scale family, its syntax is similar to the syntax of `survfit()`

```r
survreg(formula, data, dist)
```

- In `formula`, response is a `Surv` object, e.g. to model the variables `time` and `status`

$$\texttt{formula = Surv(time, status)} \sim 1$$

- Lifetime or log-lifetime distributions can be passed to `survreg` by the argument `dist`

# `survreg` function

- Available lifetime or log-lifetime distributions include "weibull", "exponential", "gaussian", "logistic", "lognormal", "loglogistic", "extreme"

- The `time` argument of `Surv` function is either a lifetime or a log-lifetime depending on whether the mentioned `dist` is a lifetime (e.g. "weibull") or a log-lifetime (e.g. "extreme")

$$\text{weibull} \rightarrow \texttt{formula = Surv(time, status)} \sim 1$$

$$\text{extreme} \rightarrow \texttt{formula = Surv(log(time), status)} \sim 1$$

# survreg function

## Data for the treatment (6MP) group

```
d6mp <- gehan65 |>
   filter(drug == "6-MP")
glimpse(d6mp)
```

```
Rows: 21
Columns: 3
$ time   <dbl> 6, 6, 6, 6, 7, 9, 10, 10, 11, 13, 16, 17, 19, 20, 22
$ status <dbl> 1, 1, 1, 0, 1, 0, 1, 0, 0, 1, 1, 0, 0, 0, 1, 1, 0, 0
$ drug   <chr> "6-MP", "6-MP", "6-MP", "6-MP", "6-MP", "6-MP", "6-MI
```

# survreg function

## Analysis of the treatment group using survreg function

```
w_sreg_6mp <- survreg(Surv(time, status) ~ 1,
                      data = d6mp, dist = "weibull")
```

```
ev_sreg_6mp <- survreg(Surv(log(time), status) ~ 1,
                       data = d6mp, dist = "extreme")
```

# survreg function

## Extreme-value distribution

- *Estimates of model parameters* $u$ and $\log b$

```r
broom::tidy(ev_sreg_6mp)
```

```
# A tibble: 2 x 5
  term        estimate std.error statistic  p.value
  <chr>          <dbl>     <dbl>     <dbl>    <dbl>
1 (Intercept)    3.52      0.273     12.9  6.28e-38
2 Log(scale)    -0.303     0.278     -1.09 2.77e- 1
```

# survreg function

- *Variance-covariance matrix* of $(\hat{u}, \log \hat{b})$

```
vcov(ev_sreg_6mp)
```

```
            (Intercept) Log(scale)
(Intercept)  0.07473057 0.03305811
Log(scale)   0.03305811 0.07750538
```

# `survreg` function

## Analysis of remission time data using `survreg` function

- The `survreg()` function returns estimates of $(u, \log b)'$ and corresponding variance matrix
- For making inference about Weibull distribution, followings are required
  1. estimate of $(u, b)'$ and the corresponding variance matrix
  2. estimate of $(\alpha, \beta)'$ and the corresponding variance matrix
- It is important to understand the methods to obtain estimates and the corresponding variance of $(u, b)'$ and $(\alpha, \beta)'$ from the estimates and the corresponding variance of $(u, \log b)'$

# `survreg` function

## Homework

- Obtain the variance-covarince matrix of $(\hat{\alpha}, \hat{\beta})'$ and $(\hat{u}, \hat{b})'$

# CIs of $(\alpha, \beta)$ (6MP group)

- 95% CI using the sampling distribution of $(\hat{\alpha}, \hat{\beta})$

$$\begin{aligned} \hat{\alpha} \pm z_{.975}\, se(\hat{\alpha}) &= 33.765 \pm (1.96)(9.23) \\ &= 15.674 \text{ to } 51.856 \\ \hat{\beta} \pm z_{.975}\, se(\hat{\beta}) &= 1.354 \pm (1.96)(0.377) \\ &= 0.615 \text{ to } 2.092 \end{aligned}$$

# CIs of $(\alpha, \beta)$ (6MP group)

- 95% CI using the sampling distribution of $(\hat{u}, \log \hat{b})$

$$\begin{aligned}
\hat{u} \pm z_{.975}\, se(\hat{u}) &= 2.984 \text{ to } 4.055 \\
\hat{\alpha} \pm z_{.975}\, se(\hat{\alpha}) &= \exp(2.984) \text{ to } \exp(4.055) \\
&= 19.76 \text{ to } 57.698
\end{aligned}$$

  - Similarly

$$\begin{aligned}
\log \hat{b} \pm z_{.975}\, se(\log \hat{b}) &= -0.849 \text{ to } 0.243 \\
\hat{\beta} \pm z_{.975}\, se(\hat{\beta}) &= 1/\exp(0.243) \text{ to } 1/\exp(-0.849) \\
&= 0.784 \text{ to } 2.336
\end{aligned}$$

# CIs of $(\alpha, \beta)$ (6MP group)

(Obtain the variance matrix of $(\hat{u}, \hat{b})$ using the sampling distribution of $(\hat{u}, \log \hat{b})'$)

- 95% CI using the sampling distribution of $(\hat{u}, \hat{b})$

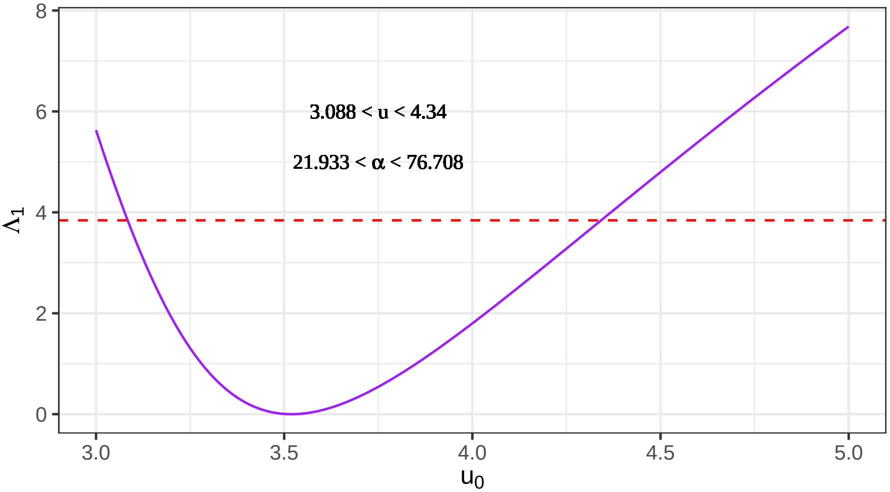
$$\begin{aligned}
\hat{u} \pm z_{.975}\, se(\hat{u}) &= 2.984 \text{ to } 4.055 \\
\hat{\alpha} \pm z_{.975}\, se(\hat{\alpha}) &= \exp(2.984) \text{ to } \exp(4.055) \\
&= 19.76 \text{ to } 57.698
\end{aligned}$$

- Similarly

$$\begin{aligned}
\hat{b} \pm z_{.975}\, se(\hat{b}) &= 0.336 \text{ to } 1.142 \\
\hat{\beta} \pm z_{.975}\, se(\hat{\beta}) &= 1/1.142 \text{ to } 1/0.336 \\
&= 0.876 \text{ to } 2.979
\end{aligned}$$

# CIs of $(\alpha, \beta)$ (6MP group)

- Using the method described in Section 44, we obtain the LRT-based CIs for $u$ and $b$



# CIs of $(\alpha, \beta)$ (6MP group)

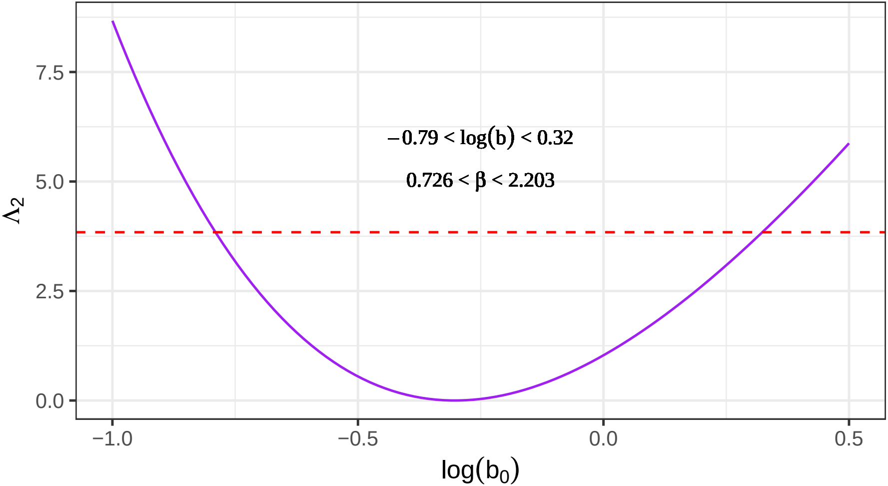



Figure 2: Plot of LRT statistic against different null values $b_0$ and 95% confidence interval for $\log b$ and $\beta$

# CIs of $(\alpha, \beta)$ (6MP group)

Table 2: 95% confidence intervals for $\alpha$ and $\beta$ by different methods

| parameter | method | 6-MP |
|---|---|---|
| $\alpha$ | Wald $(\hat{\alpha})$ | (15.674, 51.856) |
| NA | Wald $(\hat{u})$ | (19.76, 57.698) |
| NA | LRT | (21.933, 76.708) |
| $\beta$ | Wald $(\hat{\beta})$ | (0.615, 2.092) |
| NA | Wald $(\log \hat{b})$ | (0.784, 2.336) |
| NA | Wald $(\hat{b})$ | (0.876, 2.979) |
| NA | LRT | (0.726, 2.203) |

# Analyses for Placebo group

```
dplacebo <- gehan65 %>%
  filter(drug == "placebo")
```

Model fit with the data of placebo group

```
w_sreg_p <- survreg(Surv(time, status) ~ 1,
                    data = dplacebo, dist = "weibull")
```

# Analyses for Placebo group

Estimates of model parameters

```
broom::tidy(w_sreg_p)
```

```
# A tibble: 2 x 5
  term        estimate std.error statistic  p.value
  <chr>          <dbl>     <dbl>     <dbl>    <dbl>
1 (Intercept)    2.25      0.168     13.4  5.72e-41
2 Log(scale)    -0.315     0.174     -1.82 6.94e- 2
```

# Analyses for Placebo group

Table 3: 95% confidence intervals for $\alpha$ and $\beta$ by different methods

| parameter | method | 6-MP | Placebo |
|---|---|---|---|
| $\alpha$ | Wald ($\hat{\alpha}$) | (15.674, 51.856) | (6.363, 12.601) |
| NA | Wald ($\hat{u}$) | (19.76, 57.698) | (6.824, 13.175) |
| NA | LRT | (21.933, 76.708) | (6.659, 13.25) |
| $\beta$ | Wald ($\hat{\beta}$) | (0.615, 2.092) | (0.904, 1.837) |
| NA | Wald ($\log \hat{b}$) | (0.784, 2.336) | (0.975, 1.926) |
| NA | Wald ($\hat{b}$) | (0.876, 2.979) | (1.023, 2.077) |
| NA | LRT | (0.726, 2.203) | (0.951, 1.868) |

# Quantiles and their CIs

- Estimate of $p$th quantile

$$\hat{y}_p = \hat{u} + \hat{b} w_p$$

  - $w_p = \log[-\log(1-p)]$
  - $\hat{u} = 3.519$ and $\hat{b} = 0.739$ (for treatment group)

- Wald-type CI (see Section 47 for detail)

$$\hat{y}_p \pm se(\hat{y}_p) z_{1-q/2}$$

- Note the estimate of $\hat{y}_p$ depends on the estimate of $\hat{u}$ and $\hat{b}$, and the corresponding variance matrix
  - `survreg()` returns estimate and variance matrix for $\hat{u}$ and $\log \hat{b}$

# Quantiles and their CIs

Table 4: 95% confidence intervals for different quantiles of treatment group (6-MP)

| $p$ | $w_p$ | $\hat{y}_p$ | $se(\hat{y}_p)$ | lower | upper |
|---|---|---|---|---|---|
| 0.25 | -1.246 | 2.599 | 0.655 | 3.726 | 48.559 |
| 0.50 | -0.367 | 3.249 | 0.264 | 15.357 | 43.225 |
| 0.75 | 0.327 | 3.761 | 0.395 | 19.822 | 93.241 |

# Quantiles and their CIs

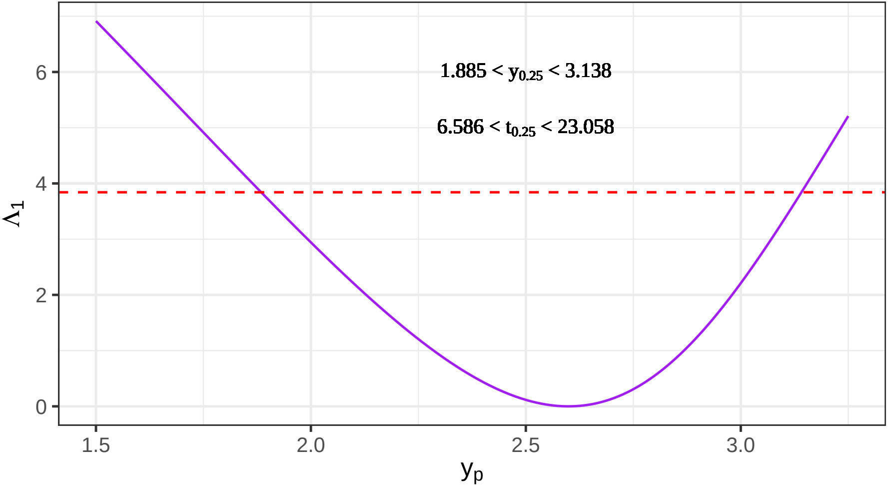



Figure 3: Plot of LRT statistic against different null values $y_{p_0}$ and 95% confidence interval for $y_{.25}$ and $t_{.25}$ (6-MP group)

# Quantiles and their CIs

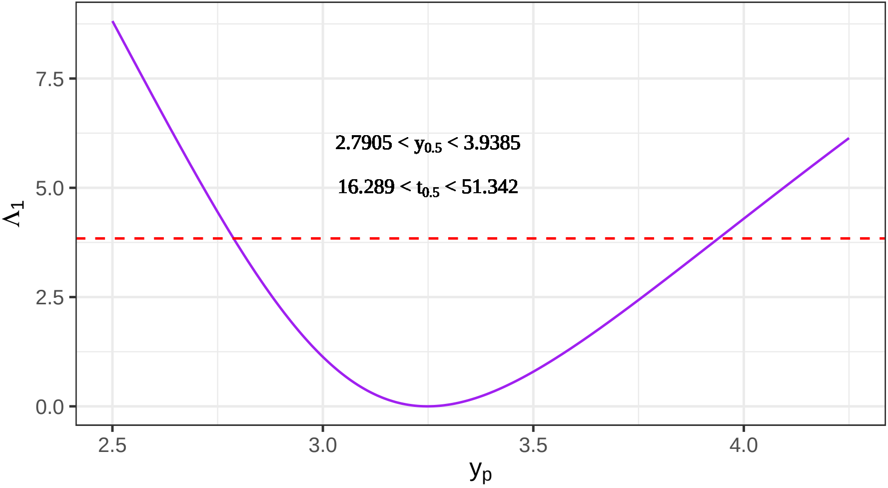



Figure 4: Plot of LRT statistic against different null values $y_{p_0}$ and 95% confidence interval for $y_{.5}$ and $t_{.5}$ (6-MP group)

# Quantiles and their CIs

Table 5: 95% confidence intervals of different quantiles using Wald and LRT method (6-MP group)

| $p$ | lower | upper | lower | upper |
|---|---|---|---|---|
| 0.25 | 3.726 | 48.559 | 6.586 | 23.058 |
| 0.50 | 15.357 | 43.225 | 16.289 | 51.342 |
| 0.75 | 19.822 | 93.241 | 27.522 | 112.730 |

# Quantiles and their CIs

Table 6: 95% confidence intervals for different quantiles using Wald and LRT method (placebo group)

| $p$ | lower | upper | lower | upper |
|---|---|---|---|---|
| 0.25 | 1.362 | 10.707 | 2.031 | 5.927 |
| 0.50 | 4.499 | 11.708 | 5.755 | 9.488 |
| 0.75 | 8.592 | 16.863 | 8.873 | 16.996 |

# Survivor function

- For Weibull distribution, the expression of survivor function

$$S(t; \alpha, \beta) = \exp\big(-(t/\alpha)^{\beta}\big)$$

- Estimated survivor function

$$S(t; \hat{\alpha}, \hat{\beta}) = \exp\big(-(t/\hat{\alpha})^{\hat{\beta}}\big)$$

| par | 6-MP | placebo |
|---|---:|---:|
| $\alpha$ | 33.765 | 9.482 |
| $\beta$ | 1.354 | 1.370 |

# Survivor function

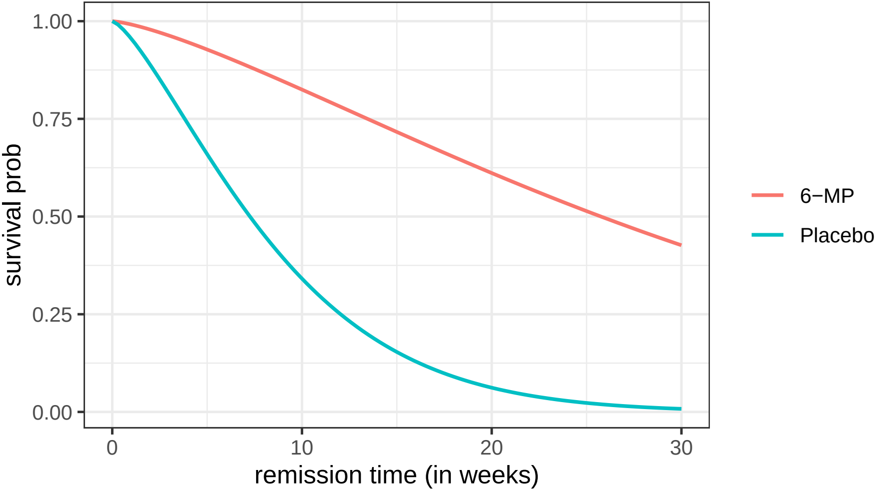



Figure 5: Comparison survival probabilities of between two treatment groups

# Survivor function

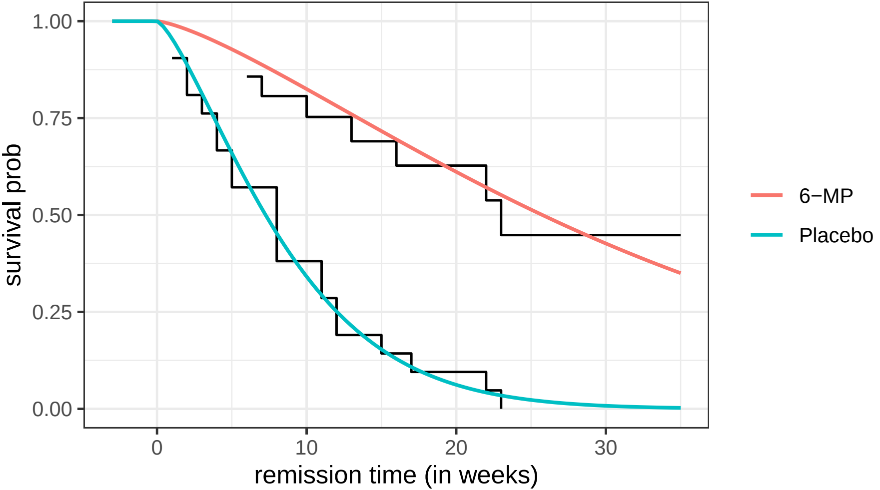



Figure 6: Comparison of parametric (Weibull) and non-parametric (step-function) estimates of survivor function using remission time data

# Survivor function

## Homework

- Obtain Wald and LRT statistics based confidence interval for the survival probability $S(10)$