Chapter 5A

(AST305) Lifetime Data Analysis I

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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

Review: Location–scale and Log-location–scale distributions

Location–scale distributions

- A random variable Y is said to follow a **location–scale distribution** with location parameter $u \in \mathbb{R}$ and scale parameter $b > 0$ if its survivor function can be written as

$$S_Y(y; u, b) = P(Y > y) = S_0\left(\frac{y-u}{b}\right), \qquad -\infty < y < \infty,$$

where $S_0(\cdot)$ is a fixed **standard survivor function**.

- The corresponding probability density function is

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

where

$$f_0(z) = -\frac{d}{dz} S_0(z).$$

Standardization

- Define the standardized variable

$$Z = \frac{Y - u}{b}.$$

- Then Z has survivor function $S_0(z)$ and density $f_0(z)$.
- Thus, all members of the location–scale family are obtained by shifting and rescaling a single standard distribution.

Examples

- Common examples of location–scale distributions for Y include
  - normal,
  - logistic,
  - extreme-value (Gumbel).
- These distributions are particularly important because they lead to flexible parametric models for lifetime data after log transformation.

Log-location–scale distributions

- Let $T > 0$ denote a lifetime random variable and define

$$Y = \log T.$$

- If Y follows a location–scale distribution with parameters (u, b), then T is said to follow a **log-location–scale distribution**.

Survivor function of T

- For $t > 0$,

$$\begin{aligned} S_T(t; u, b) &= P(T > t) \\ &= P(\log T > \log t) \\ &= S_0\left(\frac{\log t - u}{b}\right). \end{aligned}$$

  It is often convenient to re-parameterize the model by defining

$$\alpha = e^u, \qquad \beta = 1/b,$$

  so that

$$\frac{\log t - u}{b} = \beta \log\left(\frac{t}{\alpha}\right).$$

- Define

$$S_0^\star(w) = S_0(\log w), \qquad w > 0.$$

- Then the survivor function of T can be written as

$$S_T(t; \alpha, \beta) = S_0^\star\left[(t/\alpha)^\beta\right].$$

Interpretation of parameters

- $\alpha > 0$ is a **scale parameter** on the original time scale.
- $\beta > 0$ is a **shape parameter** controlling the hazard behavior.
- $u = \log \alpha$ and $b = 1/\beta$ are often more convenient for likelihood-based inference.

Common log-location–scale models

Distribution of $Y = \log T$	Distribution of T
Extreme-value	Weibull
Logistic	Log-logistic
Normal	Log-normal

Subsection 2

5.1 Inference for location-scale distributions

Likelihood based methods

The goal is to estimate the parameters (u, b) or (α, β)

For likelihood-based inference, estimating (u, b) (or equivalently $(u, \log b)$) has several advantages:

- the log-likelihood is typically closer to quadratic;
- normal approximations for $(\hat{u}, \hat{b})$ tend to be more accurate;
- numerical optimization is more stable;
- most statistical software (e.g., `survreg()` in R) uses the $(u, \log b)$ parameterization.

In the following sections, likelihood-based inference procedures are developed using the (u, b) parameterization, with results later transformed to (α, β) for interpretation on the original time scale.

Likelihood function

- Suppose we observe a possibly right-censored sample

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

where t_i is the observed time and $\delta_i = 1$ indicates a failure while $\delta_i = 0$ indicates right censoring.

- Define

$$y_i = \log t_i \quad \text{and} \quad z_i = \frac{y_i - u}{b}.$$

Likelihood function

- For a log-location–scale model with standard survivor function $S_0(\cdot)$ and density $f_0(\cdot)$, the likelihood function is

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

- The corresponding log-likelihood function is

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

where $r = \sum_{i=1}^{n} \delta_i$ is the total number of failures.

Score functions

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

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

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

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

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

Hessian matrix

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

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

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

- The maximum likelihood estimator (MLE) of (u, b) is defined as

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

- Under regularity conditions, the asymptotic covariance matrix of $(\hat{u}, \hat{b})'$ can be estimated by the inverse of the observed information matrix evaluated at the MLEs:

$$\text{Var}\begin{pmatrix} \hat{u} \\ \hat{b} \end{pmatrix} \approx \hat{V} = \left[I(\hat{u}, \hat{b}) \right]^{-1},$$

- 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

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

Likelihood ratio test based CI

- 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

LRT-based CI for the location parameter u

To test the null hypothesis $H_0 : u = u_0$, the likelihood ratio test statistic is

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

where

$$(\hat{u}, \hat{b})' = \arg\max_{(u,b)' \in \Theta} \ell(u, b), \qquad \text{(unrestricted MLEs)},$$
$$\tilde{b}(u_0) = \arg\max_{b \in \Theta} \ell(u_0, b), \qquad \text{(MLE under } H_0\text{)}.$$

LRT-based CI for the location parameter u

- Under H_0,

$$\Lambda_1(u_0) \xrightarrow{d} \chi^2_{(1)}.$$

- An approximate two-sided $100(1-p)\%$ confidence interval for u is given by the set of values u_0 such that

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

LRT-based CI for the location parameter u

Homework

- Derive the likelihood ratio test–based confidence interval for the scale parameter b.

Quantiles and their confidence intervals

Quantiles of log-lifetime

- The pth quantile of the log-lifetime variable Y satisfies

$$P(Y \leq y_p) = p.$$

- Equivalently,

$$S_0\Big(\frac{y_p - u}{b}\Big) = 1 - p,$$

which implies

$$y_p = u + bw_p, \qquad w_p = S_0^{-1}(1-p) = F_0^{-1}(p).$$

Quantiles and their confidence intervals

Wald-type CI for y_p

An estimator of y_p is

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

Using the delta method, its standard error is

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

The pivotal quantity

$$Z_p = \frac{\hat{y}_p - y_p}{se(\hat{y}_p)}$$

is approximately standard normal, leading to a $100(1-q)\%$ confidence interval

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

Quantiles and their confidence intervals

LRT-based CI for quantiles

The pth quantile can be expressed as

$$y_p = u + w_p b.$$

To obtain an LRT-based confidence interval for y_p, consider the null hypothesis

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

The likelihood ratio statistic is

$$\Lambda(y_{p_0}) = 2\ell(\hat{u}, \hat{b}) - 2\ell(\tilde{u}, \tilde{b}), \tag{1}$$

where $(\tilde{u}, \tilde{b})$ are the MLEs under H_0.

Quantiles and their confidence intervals

Steps to compute $(\tilde{u}, \tilde{b})$

1. Under H_0, $u = y_{p_0} - w_p b$.
2. Obtain
$$\tilde{b} = \arg\max_{b \in \Theta} \ell(y_{p_0} - w_p b,\, b).$$
3. Set
$$\tilde{u} = y_{p_0} - w_p \tilde{b}.$$

An approximate $100(1-q)\%$ confidence interval for y_p is given by the set of y_{p_0} values satisfying
$$\Lambda(y_{p_0}) \leq \chi^2_{(1),\, 1-q}.$$

Quantiles and their confidence intervals

- The general likelihood results developed above apply to all log-location–scale models.
- In the following sections, these results are specialized to particular distributions, beginning with the extreme-value and Weibull models.

Subsection 3

5.2 Weibull and extreme-value distributions

5.2 Weibull and extreme-value distributions

- The pdf of Weibull distribution

$$f(t;\alpha,\beta) = \frac{\beta}{\alpha}\left(\frac{t}{\alpha}\right)^{\beta-1}\exp\left[-(t/\alpha)^{\beta}\right] \quad (2)$$

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

5.2 Weibull and extreme-value distributions

- The pdf of extreme-value distribution

$$f(y; u, b) = \frac{1}{b}\ \exp\left[(y-u)/b\right]\ \exp\left[-\, e^{(y-u)/b}\right] \tag{3}$$

$$= \frac{1}{b}\, f_0\Big(\frac{y-u}{b}\Big) \tag{4}$$

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

- 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**

$$\ell(u, b) = -r \log b + \sum_{i=1}^{n} \left(\delta_i z_i - e^{z_i} \right) \tag{5}$$

  - $r = \sum_i \delta_i$
- 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** $(\hat{u},\hat{b})'$

$$
\hat{V} = \left[I(\hat{u},\hat{b})\right]^{-1} \tag{9}
$$

Covariance matrix

- MLEs of α and β (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)

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

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

$$\hat{u} \pm z_{1-p/2}\; se(\hat{u})$$

$$\hat{b} \pm z_{1-p/2}\; se(\hat{b})$$

$$\hat{b} \exp\left[\pm z_{1-p/2}\; se(\log \hat{b})\right]$$

CI for (u, b) (LRT based)

- Log-likelihood function corresponding to $H_0 : b = b_0$ is (from Equation 5)

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

- 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 pth quantile of $Y \sim EV(u, b)$

$$S(y_p) = S_0\left(\frac{y_0 - u}{b}\right) = (1 - p) \tag{10}$$

$$\exp\left[-\exp\left(\frac{y_p - u}{b}\right)\right] = (1 - p) \tag{11}$$

$$\frac{y_p - u}{b} = \log\left[-\log(1 - p)\right] = S_0^{-1}(1 - p) = w_p \tag{12}$$

$$y_p = u + w_p\, b \tag{13}$$

CI for quantiles

CI for quantiles (Wald)

- The estimate of pth quantile

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

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

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

- 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 31)

- 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 ψ

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

- 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

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

  - where $(\tilde{u}, \tilde{b})$ are the MLEs under H_0

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

$$f(y; u, b) = \frac{1}{b} \exp\left[(y-u)/b - e^{(y-u)/b}\right] \tag{14}$$

$$S(y; u, b) = \exp\left[-e^{(y-u)/b}\right] \tag{15}$$

- Log-likelihood function

$$\ell_{ev}(u, b) = \log \prod_{i=1}^{n} \left[f(y_i; u, b)\right]^{\delta_i} \left[S(y_i; u, b)\right]^{1-\delta_i} \tag{16}$$

- 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()`

```
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 (α, β) (6MP group)

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

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

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

CIs of (α, β) (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 (α, β) (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 $(\hat{u}, \hat{b})$

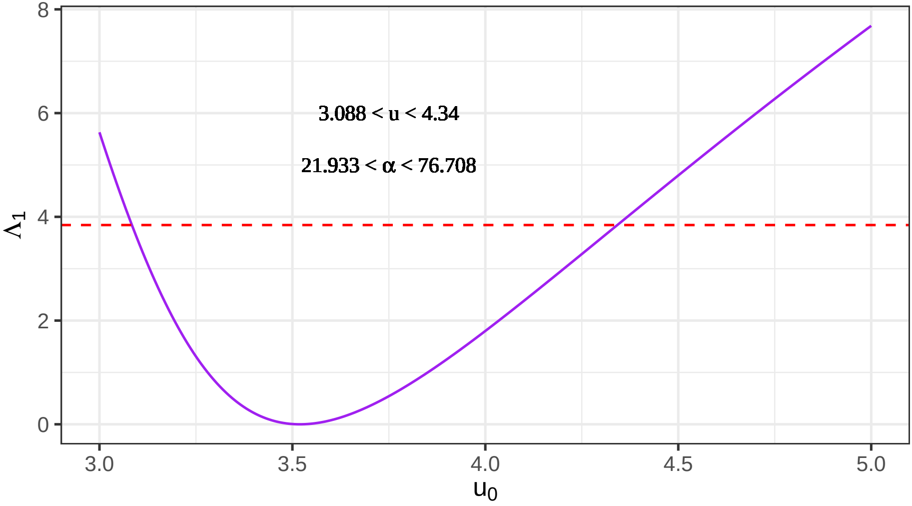
$$\begin{aligned} \hat{u} \pm z_{.975}\, se(\hat{u}) &= 2.984 \text{ to } 4.055 \\ \hat{\alpha} \pm z_{.975}\, se(\hat{\alpha}) &= \exp(2.984) \text{ to } \exp(4.055) \\ &= 19.76 \text{ to } 57.698 \end{aligned}$$

- 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 (α, β) (6MP group)

- Using the method described in Section 46, we obtain the LRT-based CIs for u and b



CIs of (α, β) (6MP group)

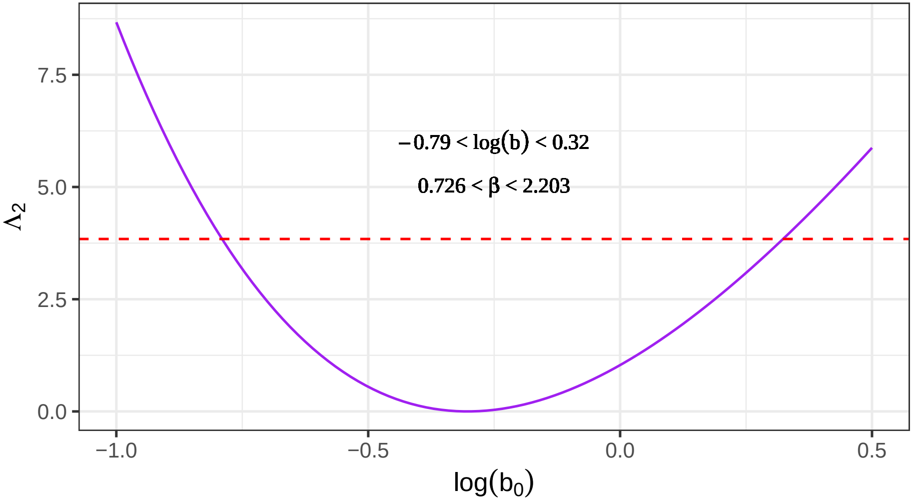


Figure 2: Plot of LRT statistic against different null values b_0 and 95% confidence interval for $\log b$ and β

CIs of (α, β) (6MP group)

Table 3: 95% confidence intervals for α and β by different methods

parameter	method	6-MP
α	Wald $(\hat{\alpha})$	(15.674, 51.856)
NA	Wald $(\hat{u})$	(19.76, 57.698)
NA	LRT	(21.933, 76.708)
β	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

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

Model fit with the data of placebo group

```r
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 4: 95% confidence intervals for α and β by different methods

parameter	method	6-MP	Placebo
α	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)
β	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 pth 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 49 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 5: 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

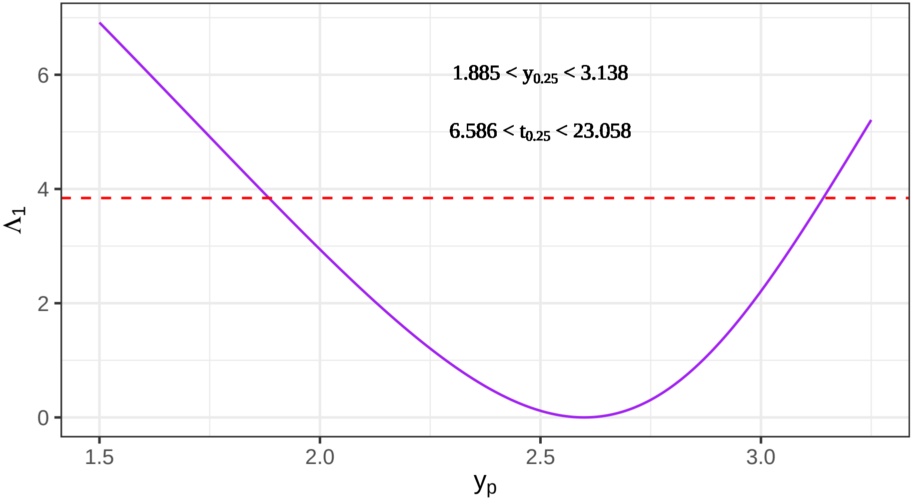


Figure 3: Plot of LRT statistic against different null values y_{p_0} and 95% confidence interval for $y_{.25}$ and $t_{.25}$ (6-MP group)

Quantiles and their CIs

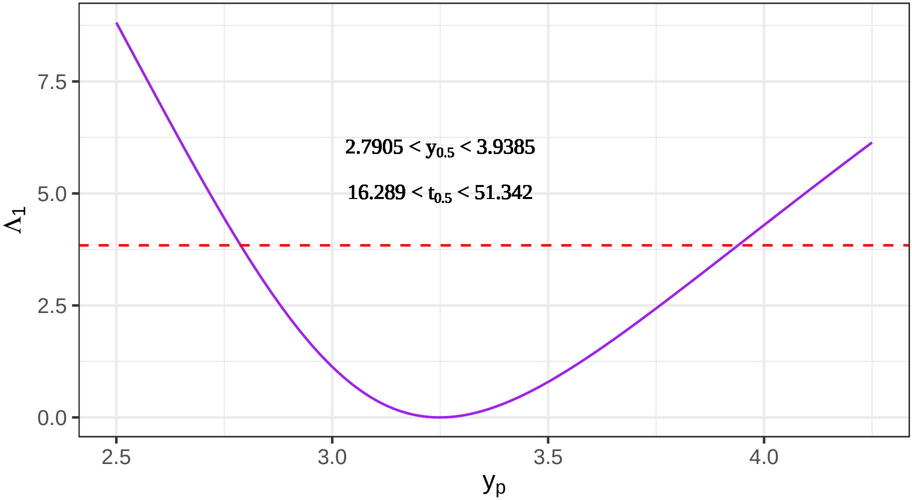


Figure 4: Plot of LRT statistic against different null values y_{p_0} and 95% confidence interval for $y_{.5}$ and $t_{.5}$ (6-MP group)

Quantiles and their CIs

Table 6: 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 7: 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
α	33.765	9.482
β	1.354	1.370

Survivor function

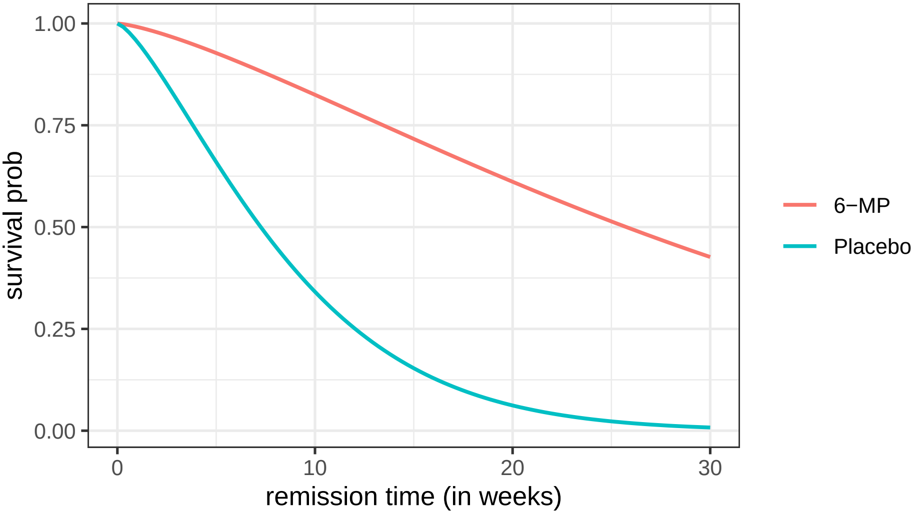


Figure 5: Comparison survival probabilities of between two treatment groups

Survivor function

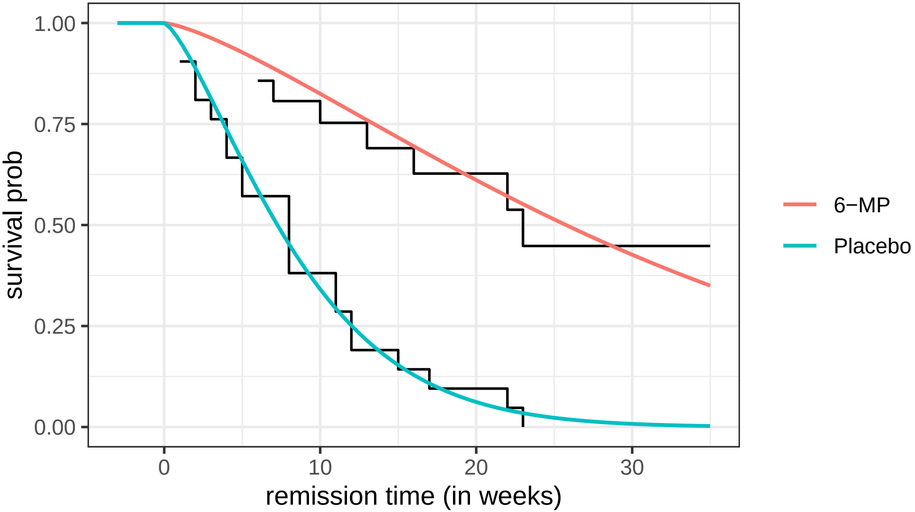


Figure 6: Comparison of parametric (Weibull) and non-parametric (step-function) estimates of survivor function using remission time data

Survivor function

Homework

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