

### Kelompok 3 Model Survival

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#### Bab 2 Nomor 3

The time to death (in days) following a kidney transplant follows a log logistic distribution with  $\alpha = 1.5$  and  $\lambda = 0.01$

(a) Find the 50, 100, and 150 day survival probabilities for kidney transplantation in patients

⇒ Akan dicari probabilitas survival 50, 100, 150 hari pada pasien transplantasi ginjal  
Diketahui bahwa data berdistribusi log logistic dist. dengan  $\alpha = 1.5$  dan  $\lambda = 0.01$   
Maka fungsi survivalnya

$$S(x) = \frac{1}{1 + \lambda x^\alpha} = \frac{1}{1 + (0.01)(x)^{1.5}}$$

Untuk  $x = 50$

$$S(50) = \frac{1}{1 + (0.01)(50)^{1.5}} = \frac{1}{4.5355339} \approx 0.22048$$

Untuk  $x = 100$

$$S(100) = \frac{1}{1 + (0.01)(100)^{1.5}} = \frac{1}{10} \approx 0.09091$$

Untuk  $x = 150$

$$S(150) = \frac{1}{1 + (0.01)(150)^{1.5}} = \frac{1}{19.371173} \approx 0.05162$$

∴ Probabilitas pasien dapat survive dalam 50 hari adalah 0.22048, 100 hari adalah 0.09091, dan 150 hari adalah 0.05162

(b) Find the median death following a kidney transplant

⇒ Akan dicari median waktu kematian transplantasi ginjal

Karena median adalah kuantil tengah maka  $p = \frac{1}{2} = 0.5$

$$x_p = \left[ \frac{p}{\lambda(1-p)} \right]^{1/\alpha}$$

$$x_{1/2} = \left[ \frac{0.5}{0.01(1-0.5)} \right]^{1/1.5} = \left[ \frac{0.5}{0.005} \right]^{1/1.5} = (100)^{1/1.5} \approx 21.5443 = 21.5$$

∴ Median waktu kematian pasien transplantasi ginjal adalah 21,5 hari

(c) 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.

⇒ Akan ditunjukkan bahwa nilai hazard akan naik kemudian turun. Lalu akan dicari saat nilai berapa fungsi hazard berubah dan naik kemudian turun.

Seperti yang diketahui bahwa fungsi hazard pada log logistic distribution akan naik saat  $\alpha > 1$  hingga nilai maksimum pada  $[(\alpha - 1)/\lambda]^{1/\alpha}$  dan kemudian turun menuju nol tak hingga.

Akan ditunjukkan:

$$h(x) = \frac{\alpha x^{\alpha-1} \lambda}{1 + \lambda x^\alpha} = \frac{1.5 \cdot x^{0.5} \cdot 0.01}{1 + (0.01 \cdot x^{1.5})} = \frac{0.015 \cdot x^{0.5}}{1 + (0.01 \cdot x^{1.5})}$$

Untuk  $x = 1$

$$h(1) = \frac{0.015 \cdot 1^{0.5}}{1 + (0.01 \cdot 1^{1.5})} \approx 0.1485$$

Untuk  $x = 5$

$$h(5) = \frac{0,015 \cdot 5^{0,5}}{1 + (0,01 \cdot 5^{1,5})} \approx 0,3016$$

Dari  $x = 1$  ke  $x = 5$  terjadi peningkatan nilai fungsi hazard

Untuk  $x = 10$

$$h(10) = \frac{0,015 \cdot 10^{0,5}}{1 + (0,01 \cdot 10^{1,5})} \approx 0,3603$$

Dari  $x = 5$  ke  $x = 10$  terjadi peningkatan nilai fungsi hazard

Untuk  $x = 20$

$$h(20) = \frac{0,015 \cdot 20^{0,5}}{1 + (0,01 \cdot 20^{1,5})} \approx 0,03541$$

Dari  $x = 10$  ke  $x = 20$  terjadi penurunan nilai fungsi hazard

Untuk  $x = 50$

$$h(50) = \frac{0,015 \cdot 50^{0,5}}{1 + (0,01 \cdot 50^{1,5})} \approx 0,02338$$

Dari  $x = 20$  ke  $x = 50$  terjadi penurunan nilai fungsi hazard

Maka terlihat bahwa nilai fungsi hazard mulanya akan naik sampai nilai tertentu kemudian akan turun menuju nol tak hingga.

Sehingga kita dapat mencari titik balik atau nilai di mana fungsi hazard akan berubah dari naik kemudian turun

$$x = [(a-1) / \lambda]^{1/a}$$

$$= [(1,5 - 1) / 0,01]^{1/1,5}$$

$$= (0,5 / 0,01)^{1/1,5} = (50)^{\frac{1}{1,5}} \approx 13,57209 = 13,572$$

$\therefore$  Terlihat bahwa fungsi hazard awalnya akan naik sampai titik tertentu yaitu pada  $x = 13,572$  kemudian akan turun menuju nol tak hingga pada pasien transplantasi ginjal

(d) Find the mean time to death

$\Rightarrow$  Akan dicari rata-rata waktu kematian

$$E(x) = \frac{\pi \csc(\pi/a)}{a \lambda^{1/a}} = \frac{\pi \csc(\pi/1,5)}{1,5 \cdot 0,01^{1/1,5}} \approx 52,10283 = 52,1$$

$\therefore$  Rata-rata waktu kematian pasien transplantasi ginjal adalah 52,1 hari.

### Bab 3 Nomor 2

A large number of disease-free individuals were enrolled in a study beginning January 1, 1970, and were followed for 30 years to assess the age at which they developed breast cancer.

Individuals had clinical exams every 3 years after enrollment. For four selected individuals described below, discuss in detail, the types of censoring and truncation that are represented

(a) A healthy individual, enrolled in the study at age 30, never developed breast cancer during the study

↳ Penyensoran Kanan Tipe I pada usia 60 tahun atau 30 tahun studi

(b) A healthy individual, enrolled in the study at age 40, was diagnosed with breast cancer at the fifth exam after enrollment (i.e., the disease start sometime between 12 dan 15 years after enrollment)

↳ Penyensoran Interval pada usia  $(52, 55]$  atau 12-15 tahun studi

(c) A healthy individual, enrolled in the study at age 50, died from a cause unrelated to the disease (i.e., not diagnosed with breast cancer at any time during the study) at age 61

↳ Penyensoran random dan pemancungan kiri pada usia 61 tahun atau 11 tahun studi.

(d) An individual, enrolled in the study at age 42, moved away from the community at age 55 and was never diagnosed with breast cancer during the period of obs.

↳ Penyensoran random dan pemancungan kiri pada usia 55 atau 13 tahun studi

(e) Confining ur attention to four individuals described above, write down the likelihood for this portion of the study

⇒ likelihood yang digunakan berdasarkan 4 kasus tsb adalah likelihood data terpencung kiri dengan  $x$  merupakan usia enrollment pada studi

$$x := \{30, 40, 50, 42\}$$



### Bab 3 Nomor 7

To estimate the distribution of the ages at which postmenopausal women develop breast cancer, a sample of eight 50-year-old women were given yearly mammograms for a period of 10 years. At each exam, the presence or absence of a tumor was recorded. In the study, no tumors were detected by the women by self-examination between the scheduled yearly exams, so all that is known about the onset time of breast cancer is that it occurs between examinations. For four of the eight women, breast cancer was not detected during the 10 year study period. The age at onset of breast cancer for the eight subjects was in the following intervals:

(55, 56], (56, 59], (59, 60], (60, 61],  $\geq 60$ ,  $\geq 60$ ,  $\geq 60$ ,  $\geq 60$

(a) What type of censoring or truncation is represented in this sample?

⇒ Pada kasus tersebut terbagi menjadi dua tipe.

1. 4 wanita lanjut usia yang terkena kanker payudara merupakan data tersensor interval karena terdeteksi pada interval waktu (tahun)
2. 4 wanita lanjut usia yang tidak terkena kanker payudara merupakan data tersensor kanan tipe I

(b) Assuming that the age at which breast cancer develops follows a Weibull distributions with parameters  $\lambda$  and  $\alpha$ , construct the likelihood function

⇒ Akan dicari fungsi likelihoodnya

1. 4 wanita lanjut usia dg penyensoran interval

$$L(x; \alpha, \lambda) = \prod_{i \in D} f(x_i) \prod_{j \in V} [S(L_j) - S(R_j)]$$

$$\text{ket: } D = \{d \mid d = n - v\}$$

$v$  = objek tersensor interval  
 $n$  = ukuran sampel

$S(L_j)$  : Survival kiri

$S(R_j)$  : Survival kanan

2. 4 wanita lanjut usia dg penyensoran kanan

$$L(x; \alpha, \lambda) = \prod_{i \in D} f(x_i) \prod_{r \in C} S(r)$$

$$\text{ket: } D = \{d \mid d = n - r\}$$

$n$  = ukuran sampel

$r$  = objek tersensor kanan

$S(r)$  : Survival tersensor kanan

Maka Likelihood untuk

$$L(x; \alpha, \lambda) = \prod_{i \in D} f(x_i) \prod_{j \in V} [S(L_j) - S(R_j)] \prod_{r \in C} S(r)$$

Survival function dari Weibull Dist

$$S(x) = \exp[-\lambda x^\alpha]$$

$$= \prod_{i \in D} f(x_i) \cdot (S(55) - S(56)) \cdot (S(58) - S(59))$$

$$(S(52) - S(53)) \cdot (S(59) - S(60)) \cdot [S(60)]^4$$

$$\therefore L(x; \alpha, \lambda) = \prod_{i \in D} f(x_i) \cdot (\exp(-\lambda 55^\alpha) - \exp(-\lambda 56^\alpha)) \cdot (\exp(-\lambda 58^\alpha) - \exp(-\lambda 59^\alpha))$$

$$(\exp(-\lambda 52^\alpha) - \exp(-\lambda 53^\alpha)) \cdot (\exp(-\lambda 59^\alpha) - \exp(-\lambda 60^\alpha)) \cdot$$

$$(\exp(-\lambda 60^\alpha))^4$$

2.10) A model used in the construction of life tables is a piecewise-constant hazard rate model. Here the time axis is divided into  $k$  intervals,  $[t_{i-1}, t_i)$ ,  $i=1, \dots, k$ , with  $t_0=0$  and  $t_k=\infty$ . The hazard rate on the  $i$ th interval is a constant value,  $\theta_i$ ; that is

$$h(x) = \begin{cases} \theta_1 & , 0 \leq x < t_1 \\ \theta_2 & , t_1 \leq x < t_2 \\ \vdots & \\ \theta_{k-1} & , t_{k-2} \leq x < t_{k-1} \\ \theta_k & , x \geq t_{k-1} \end{cases}$$

a) Find the survival function for this model

Alasan dicari  $S(x)$

$$h(x) = -\frac{d}{dx} [\ln(S(x))]$$

$$\Leftrightarrow H(x) = -\ln(S(x))$$

$$\Leftrightarrow -H(x) = \ln(S(x))$$

$$\Leftrightarrow e^{-H(x)} = S(x)$$

Alasan dicari  $H(x)$  terdahulu

• Untuk  $0 \leq x < t_1$

$$H(x) = \int_0^x h(u) du = \int_0^x \theta_1 du = \theta_1 x$$

• Untuk  $t_1 \leq x < t_2$

$$\begin{aligned} H(x) &= \int_0^{t_1} h(u) du + \int_{t_1}^x h(u) du \\ &= \theta_1 t_1 + \int_{t_1}^x \theta_2 du = \theta_1 t_1 + \theta_2 (x - t_1) \end{aligned}$$

Terlihat untuk interval lainnya akan memiliki pola  $\theta_1 t_1 + \theta_2 (x - t_1) + \dots + \theta_k (x - t_{k-1})$ . Sehingga  $H(x)$ :

$$H(x) = \begin{cases} \theta_1 x & , 0 \leq x < t_1 \\ \theta_1 t_1 + \theta_2 (x - t_1) & , t_1 \leq x < t_2 \\ \vdots & \\ \theta_1 t_1 + \theta_2 (x - t_1) + \dots + \theta_{k-1} (x - t_{k-2}) & , t_{k-2} \leq x < t_{k-1} \\ \theta_1 t_1 + \theta_2 (x - t_1) + \dots + \theta_k (x - t_{k-1}) & , x \geq t_{k-1} \end{cases}$$

∴ Sehingga fungsi survival dari model di atas adalah

$$S(x) = \begin{cases} e^{-[\theta_1 x]} & 0 \leq x < \tau_1 \\ e^{-[\theta_1 \tau_1 + \theta_2 (x - \tau_1)]} & \tau_1 \leq x < \tau_2 \\ \vdots & \vdots \\ e^{-[\theta_1 \tau_1 + \theta_2 (x - \tau_1) + \dots + \theta_{k-1} (x - \tau_{k-2})]} & \tau_{k-2} \leq x < \tau_{k-1} \\ e^{-[\theta_1 \tau_1 + \theta_2 (x - \tau_1) + \dots + \theta_k (x - \tau_{k-1})]} & x \geq \tau_{k-1} \end{cases}$$

b). Find the mean residual-life Function

Akan dicari  $mrl(x)$

$$mrl(x) = \int_x^\infty \frac{S(u)}{S(x)} du$$

• Untuk  $0 \leq x < \tau_1$

$$mrl(\tau_1) = \int_x^\infty \frac{e^{-[\theta_1 u]}}{e^{-[\theta_1 x]}} du = \frac{-e^{-[\theta_1 u]}}{\theta_1 e^{-[\theta_1 x]}} \Big|_x^\infty = 0 + \frac{e^{-[\theta_1 x]}}{\theta_1 e^{-[\theta_1 x]}} = \frac{1}{\theta_1}$$

• Untuk  $\tau_1 \leq x < \tau_2$

$$mrl(\tau_2) = \int_x^\infty \frac{e^{-[\theta_1 \tau_1 + \theta_2 (u - \tau_1)]}}{e^{-[\theta_1 \tau_1 + \theta_2 (x - \tau_1)]}} du = \frac{-e^{-[\theta_1 \tau_1 + \theta_2 (u - \tau_1)]}}{\theta_2 e^{-[\theta_1 \tau_1 + \theta_2 (x - \tau_1)]}} \Big|_x^\infty \\ = 0 + \frac{\theta_2 e^{-[\theta_1 \tau_1 + \theta_2 (x - \tau_1)]}}{e^{-[\theta_1 \tau_1 + \theta_2 (x - \tau_1)]}} = \frac{1}{\theta_2}$$

∴ Terlihat untuk interval lainnya akan memiliki pola  $\frac{1}{\theta_k}$ , Sehingga  $mrl(x)$ :

$$mrl(x) = \begin{cases} 1/\theta_1 & 0 \leq x < \tau_1 \\ 1/\theta_2 & \tau_1 \leq x < \tau_2 \\ \vdots & \vdots \\ 1/\theta_{k-1} & \tau_{k-2} \leq x < \tau_{k-1} \\ 1/\theta_k & x \geq \tau_{k-1} \end{cases}$$

c). Find the median residual-life Function

Karena hazard rate dari model adalah konstan, dapat digunakan rumus berikut

$$M_{eRL}(x) = x + \frac{S(x)}{h(x)}$$

∴ maka fungsi median residual life dan model adalah

$$M_{eRL}(x) = \begin{cases} x + \frac{e^{-[\theta_1 x]}}{\theta_1} & , 0 \leq x < \tau_1 \\ x + \frac{e^{-[\theta_1 x + \theta_2(x - \tau_1)]}}{\theta_2} & , \tau_1 \leq x < \tau_2 \\ \vdots & \\ x + \frac{e^{-[\theta_1 x + \theta_2(x - \tau_1) + \dots + \theta_{k-1}(x - \tau_{k-2})]}}{\theta_{k-1}} & , \tau_{k-2} \leq x < \tau_{k-1} \\ x + \frac{e^{-[\theta_1 x + \theta_2(x - \tau_1) + \dots + \theta_k(x - \tau_{k-1})]}}{\theta_k} & , x \geq \tau_{k-1} \end{cases}$$

2.17 Suppose that the mean residual life of a continuous survival time  $X$  is given by  $ML(x) = x + 10$ .

a. Find the mean of  $X$

b. Find  $h(x)$

c. Find  $S(x)$

$$a. \mu = E(X) = mrl(0) = 0 + 10 = 10$$

$$\therefore \mu = 10$$

$$\begin{aligned} b. h(x) &= f \cdot \frac{\left( \frac{d}{dx} mrl(x) + 1 \right)}{mrl(x)} \\ &= \frac{\frac{d}{dx} (x + 10) + 1}{mrl(x)} \\ &= \frac{1 + 1}{x + 10} \\ &= \frac{2}{x + 10} \end{aligned}$$

$$\therefore h(x) = \frac{2}{x + 10}$$

$$\begin{aligned} c. S(x) &= \prod_x f(t) dt \\ &= \exp \left[ - \int_0^x h(u) du \right] \\ &= \exp \left[ - \int_0^x \frac{2}{u + 10} du \right] \\ &= \exp \left[ -2 \ln(u + 10) \Big|_0^x \right] \\ &= \exp \left[ -2 (\ln(x + 10) - \ln(10)) \right] \\ &= \exp \left[ -\ln(x + 10)^2 + \ln 10^2 \right] \\ &= \exp \left[ \ln \left( \frac{100}{(x + 10)^2} \right) \right] \end{aligned}$$

$$\therefore S(x) = \ln \left( \frac{100}{(x + 10)^2} \right)$$



- 3.6 The following data consists of the times to relapse and the times to death following relapse of 10 bone marrow transplant patients. In the sample patients 4 and 6 were alive in relapse at the end of the study and patients 7–10 were alive, free of relapse at the end of the study. Suppose the time to relapse had an exponential distribution with hazard rate  $\lambda$  and the time to death in relapse had a Weibull distribution with parameters  $\theta$  and  $\alpha$ .

Patient	Relapse Time (months)	Death Time (months)
1	5	11
2	8	12
3	12	15
4	24	33 <sup>+</sup>
5	32	45
6	17	28 <sup>+</sup>
7	16 <sup>+</sup>	16 <sup>+</sup>
8	17 <sup>+</sup>	17 <sup>+</sup>
9	19 <sup>+</sup>	19 <sup>+</sup>
10	30 <sup>+</sup>	30 <sup>+</sup>

<sup>+</sup> Censored observation

- Construct the likelihood for the relapse rate  $\lambda$ .
- Construct a likelihood for the parameters  $\theta$  and  $\alpha$ .
- Suppose we were only allowed to observe a patients death time if the patient relapsed. Construct the likelihood for  $\theta$  and  $\alpha$  based on this truncated sample, and compare it to the results in (b).

#### a. Relapse time berdistribusi eksponensial

Fungsi likelihood untuk distribusi eksponensial

$$L = \lambda^n \exp(-\lambda \sum t_i) \quad n = \text{banyak event terjadi}$$

$\sum t_i$  : total waktu tiap individu

Diketahui,  $n = 6$

$$\sum t_i = \sum_{i=1}^n x_i = 180$$

$$\text{Maka } L = \lambda^6 \exp(-\lambda(180))$$

$$\therefore L = \lambda^6 \exp(-180\lambda)$$

#### b. Death time berdistribusi weibull & tersensor kanan

Likelihood tersensor kanan

$$L = \prod f(x_i) \prod S(c_i)$$

Yang diperlukan distribusi weibull memiliki

$$f(x) = \lambda \cdot \alpha \cdot x^{\alpha-1}$$

$$S(x) = \exp[-\lambda x^\alpha]$$

maka likelihood-nya menjadi

$$\begin{aligned}
 L &= f(x_1) \cdot f(x_2) \cdot f(x_3) \cdot S(x_4) \cdot f(x_5) \cdot S(x_6) \cdot S(x_7) \cdot S(x_8) \cdot S(x_9) \cdot S(x_{10}) \\
 &= (\alpha \theta \cdot 11^{\alpha-1} \exp(-\theta \cdot 11^{\alpha})) \cdot (\alpha \theta \cdot 12^{\alpha-1} \exp(-\theta \cdot 12^{\alpha})) \cdot (\alpha \theta \cdot 15^{\alpha-1} \exp(-\theta \cdot 15^{\alpha})) \cdot \exp(-\theta \cdot 33^{\alpha}) \cdot (\alpha \theta \cdot 45^{\alpha-1} \exp(-\theta \cdot 45^{\alpha})) \\
 &\quad \exp(-\theta \cdot 28^{\alpha}) \cdot \exp(-\theta \cdot 16^{\alpha}) \cdot \exp(-\theta \cdot 17^{\alpha}) \cdot \exp(-\theta \cdot 19^{\alpha}) \cdot \exp(-\theta \cdot 30^{\alpha}) \\
 &= 2^9 \cdot \theta^9 \cdot (11 \cdot 12 \cdot 15 \cdot 45)^{\alpha-1} \cdot \exp(-\theta (11^{\alpha} + 12^{\alpha} + 15^{\alpha} + 33^{\alpha} + 45^{\alpha} + 28^{\alpha} + 16^{\alpha} + 17^{\alpha} + 19^{\alpha} + 30^{\alpha}))
 \end{aligned}$$

c. Jika kita hanya mengobservasi death time dengan syarat relapse terjadi, kita memperoleh data hanya hingga pasien ke-6.

fungsi likelihood-nya

$$\begin{aligned}
 L &= f(x_1) \cdot f(x_2) \cdot f(x_3) \cdot S(x_4) \cdot f(x_5) \cdot S(x_6) \\
 &= (f \theta \cdot 11^{\alpha-1} \exp(-\theta \cdot 11^{\alpha})) (\alpha \theta \cdot 12^{\alpha-1} \exp(-\theta \cdot 12^{\alpha})) \cdot (\alpha \theta \cdot 15^{\alpha-1} \exp(-\theta \cdot 15^{\alpha})) \cdot \exp(-\theta \cdot 33^{\alpha}) \cdot (\alpha \theta \cdot 45^{\alpha-1} \exp(-\theta \cdot 45^{\alpha})) \\
 &\quad \exp(-\theta \cdot 28^{\alpha}) \\
 &= \alpha^6 \cdot \theta^6 \cdot (11 \cdot 12 \cdot 15 \cdot 45)^{\alpha-1} \cdot \exp(-\theta (11^{\alpha} + 12^{\alpha} + 15^{\alpha} + 33^{\alpha} + 45^{\alpha} + 28^{\alpha}))
 \end{aligned}$$