CHAPTER - III

3.2

(Developing breast cancer)

(a) Right censoring, left truncation

(b) Interval censoring, left truncation

(c) Competing Risk right censoring, left truncation

(d) Competing Risk right censoring, left truncation

(e) $L \propto \dfrac{S(60)}{S(30)} \times \dfrac{S(52)-S(55)}{S(40)} \times \dfrac{S(61)}{S(51)} \times \dfrac{S(55)}{S(42)}$

3.3. (a) Left censoring at 42 days.

(b) Type-I right censoring

(c) Interval censoring

(d)

(e) $L \propto [1-S(42)]\, S(140)\, [S(84)-S(91)]\, S(37)$

3.5. pdf: $\dfrac{\alpha\lambda x^{\alpha-1}}{[1+\lambda x^{\alpha}]^2}$, $S(x) = \dfrac{1}{1+\lambda x^{\alpha}}$, $h(x) = \dfrac{\alpha\lambda x^{\alpha-1}}{1+\lambda x^{\alpha}}$

Data given: 0.5, 1, 0.75, 0.25−, 1.25−

$L \propto f(0.5) \times f(1) \times f(0.75) \times (1-S(0.25)) \times (1-S(1.25))$

$$L \propto \frac{\alpha\lambda(0.5)^{\alpha-1}}{[1+\lambda.(0.5)^{\alpha}]^2} \times \frac{\alpha\lambda(1)^{\alpha-1}}{[1+\lambda(1)^{\alpha}]^2} \times \frac{\alpha\lambda(0.75)^{\alpha-1}}{[1+\lambda(0.75)^{\alpha}]^2} \times$$

$$\left(1-\frac{1}{1+\lambda.(0.25)^{\alpha}}\right)\left(1-\frac{1}{1+\lambda(1.25)^{\alpha}}\right)$$

3.7 (a) $(55,56] \to$ ~~Right~~ Interval censoring

$(58,59] \to$ Interval Censoring

$(52,53] \to$ " "

$(59,60] \to$ " "

$\geq 60 \to$ Type-I Right censoring

(b) Weibull: $\beta\lambda e^{-\lambda x^{\beta}} \cdot x^{\beta-1}$

$S(x) = e^{-\lambda x^{\beta}}$

$$L \propto \left[e^{-\lambda 55^{\beta}} - e^{-\lambda 56^{\beta}}\right]\left[e^{-\lambda 58^{\beta}} - e^{-\lambda 59^{\beta}}\right]$$

$$\left[e^{-\lambda 52^{\beta}} - e^{-\lambda 53^{\beta}}\right]\left[e^{-\lambda 59^{\beta}} - e^{-\lambda 60^{\beta}}\right]$$

$$\times\left(e^{-\lambda 60^{\beta}}\right)^4$$

3.6 (a) $L \propto f(5).f(8).f(12).f(24).f(32).f(17).S(16).S(17).S(19).S(30)$

Relapse rate follows exp. with hazard rate λ.

$$L \propto \lambda e^{-5\lambda}.\lambda.e^{-8\lambda}.\lambda e^{-12\lambda}.\lambda e^{-24\lambda}.\lambda e^{-32\lambda}.\lambda e^{-17\lambda}.e^{-16\lambda}.$$

$$e^{-17\lambda}.e^{-19\lambda}.e^{-30\lambda}$$

(b)

$L \propto f(11) \cdot f(12) \cdot f(15) \cdot S(33) \cdot f(45) \cdot S(28) \cdot S(16) \cdot S(17) \cdot S(19) \cdot S(30)$

(c) The patient death time is observed only when the patient relapsed.

Therefore, the death times are truncated at relapse times.

$$L \propto \frac{f(11)}{S(5)} \times \frac{f(12)}{S(8)} \times \frac{f(15)}{S(12)} \times \frac{S(33)}{S(24)} \times \frac{f(45)}{S(32)} \times \frac{S(28)}{S(17)}$$

3.4 Time to relapse dist. is exponential with hazard rate λ.

$f(x, \lambda) = \lambda e^{-\lambda x}$

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

Censored : $\{32+, 34+, 32+, 25+, 11+, 20+, 19+, 17+, 35+, 9+, 16+, 10+\}$

Rest : $\{10, 7, 23, 22, 6, 16, 6, 6, 13\}$

$L \propto \lambda^{12} \cdot e^{-\lambda(109)} \cdot e^{-\lambda(318)}$

$\log L = 12 \log \lambda - 109\lambda - 318\lambda$

$\frac{\partial(\log L)}{\partial \lambda} = \frac{12}{\lambda} - 427 = 0 \Rightarrow \lambda = \frac{12}{427}$

3.8 $X \sim Exp(\lambda)$

$C \sim Exp(\theta)$

$T = \min(X, C)$

$\delta = 1$, if $X \le C$

$= 0$, if $X > C$

(a) $P(\delta=1) = P(X \le C)$

$$= \int_0^\infty P[X \le c \mid X = x] \cdot f_X(x)\,dx$$

$$= \int_0^\infty S_c(x) f_X(x)\,dx \quad = \int_0^\infty e^{-\theta x} \cdot \lambda e^{-\lambda x}\,dx$$

$$= \lambda \int_0^\infty e^{-(\lambda+\theta)x}\,dx = \boxed{\frac{\lambda}{\lambda+\theta}}$$

(c) $P(\delta=1, T>t) = P(\delta=1) \cdot P(T>t)$ [To prove]

$$\frac{\lambda}{\lambda+\theta} \qquad e^{-(\lambda+\theta)t}$$

$$P(\delta=1, T>t) = P(X \le c, \min(X,c) > t)$$

$$= \cancel{P(X \le c)}\ P(X \le c, X > t)$$

$$= P(t < X < c)$$

$$= \int_t^\infty P(X < c)\, f(x)\,dx$$

$$= \int_t^\infty e^{-\theta x} \cdot \lambda e^{-\lambda x}\,dx. \quad = \lambda \int_t^\infty e^{-(\lambda+\theta)x}\,dx$$

$$= \lambda \left[\frac{e^{-(\lambda+\theta)x}}{-(\lambda+\theta)}\right]_t^\infty = \boxed{\frac{\lambda}{\lambda+\theta} \cdot e^{-(\lambda+\theta)t}} = P(\delta=1)\, P(T>t)$$

3

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ONE-SAMPLE TEST

Null hypothesis : $H_0 : h(t) = h_0(t)$ for all $0 < t \leq \tau$

NA estimate of the cum. hazard function $H(t)$ is

$$\tilde{H}(t) = \sum_{t_i \leq t} \frac{d_i}{Y(t_i)}$$

d_i :- no. of events at the observed event times $t_1, \dots, t_D$

$Y(t_i)$:- no. of individuals under study just prior to the observed event time t_i.

Estimate of hazard rate $h(t)$ is $\hat{h}(t_i) = \frac{d_i}{Y(t_i)}$

Under null hypothesis, exp. hazard rate at t_i is $h_0(t_i)$

→ We shall compare the weighted differences b/w the observed and expected hazard rates to test the null hypothesis.

Let $W(t)$:- weight function

$W(t) = 0$ whenever $Y(t) = 0$

Test Statistic : $Z(\tau) = O(\tau) - E(\tau) = \sum_{i=1}^{D} W(t_i) \cdot \frac{d_i}{Y(t_i)} - \int_0^\tau W(s) h_0(s) ds$.

Sample variance $= V(Z(\tau)) = \int_0^\tau W^2(s) \cdot \frac{h_0(s)}{Y(s)} ds$

For large sample, $\frac{Z^2(\tau)}{V(Z(\tau))} \sim \chi^2_{(1)}$ $\left[\frac{Z(\tau)}{V(Z(\tau))}\right] \sim N(0,1)$

ONE SAMPLE LOG RANK TEST

$W(t) = Y(t)$

$\therefore\ O(\tau) = \sum_{i=1}^{D} W(t_i) \cdot \frac{d_i}{Y(t_i)} = \sum_{i=1}^{D} d_i$

$E(\tau) = Var(Z(\tau)) = \sum_{j=1}^{N} [H_0(T_j) - H_0(L_j)]$, where

$H_0(t)$:- cum. hazard under null hypothesis

T_j :- time of study for the j^{th} patient, $j = 1(1)n$

L_j :- entry time for the j^{th} patient, $j = 1(1)n$

For large sample, $\frac{Z^2(\tau)}{Var(Z(\tau))} \sim \chi^2_{(1)}$

$Z(\tau) = 9 - 5.378 = 3.622$

$\Sigma d_i = 9$

$Var(Z(\tau)) =$

$\therefore\ \frac{(3.622)^2}{5.378} = 2.439 \sim \chi^2_1$

0.118

5.378

0.118

Ex 7.1

Gender	d_i	L_j	T_j	$S_0(L_j)$	$S_0(T_j)$	$H_0(T_j) - H_0(L_j)$
F	1	66	74	~~0.74131~~ 0.85169	~~0.56238~~ 0.72716	0.16
F	1	60	76	~~0.837~~ 0.90756	0.68387	0.28
F	1	70	77	0.79839	0.66014	0.19
F	1	71	81	0.78420	0.54997	0.35
M	1	50	59	~~0.95575~~ 0.91148	~~0.91455~~ 0.84299	~~0.008~~ 0.08
M	1	60	66	~~0.90756~~ 0.83135	~~0.85169~~ 0.74131	0.11
M	1	51	69	~~0.95273~~ 0.90639	~~0.81324~~ 0.68339	0.28
M	1	69	71	~~0.81324~~ 0.68339	~~0.78420~~ 0.63865	~~0.007~~ 0.07
M	1	58	71	~~0.72096~~ 0.85370	~~0.78420~~ 0.63865	0.29
F	0	50	68	0.95575	0.82702	0.14
F	0	55	72	0.93713	0.76522	0.20
F	0	56	60	0.93222	0.90756	~~0.003~~ 0.03
F	0	45	55	0.96694	0.93713	~~0.003~~ 0.03
F	0	48	57	0.96091	0.95273	0.008
F	0	44	55	0.96862	0.93713	0.03
F	0	33	57	0.98005	0.95273	0.03 / 2.278
F	0	44	50	0.96862	0.95575	0.01
F	0	60	70	0.90756	0.79839	0.13
F	0	55	60	0.93713	0.90756	0.03
F	0	60	72	0.90756	0.76522	0.17
F	0	77	80	0.66014	0.57991	0.13
F	0	70	75	0.79839	0.70619	0.12
F	0	66	70	0.85169	0.79839	0.06
F	0	59	63	0.91455	0.86275	0.04
F	0	62	63	0.89169	0.86275	0.01
M	0	53	68	~~0.94568~~ 0.89480	~~0.82778~~ 0.70383	0.24
M	0	55	62	0.88068	0.80511	0.09
M	0	56	63	0.87250	0.79052	0.10
M	0	45	57	0.93161	0.90639	0.03
M	0	48	61	0.92050	0.81873	0.12
M	0	49	55	0.91617	0.88068	0.04 / 3.598
M	0	43	57	0.93771	0.90639	0.03
M	0	44	54	0.93477	0.88810	0.05
M	0	61	70	0.81873	0.66166	0.21
M	0	45	60	0.93161	0.83135	0.11
M	0	63	72	0.79052	0.61441	0.25
M	0	74	80	0.56238	0.38355	0.38
M	0	70	74	0.66166	0.50601	0.27

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$\sum d_i = 9 \rightarrow O(\tau)$, $Var(z(\tau)) = \Sigma(H_0(T_j) - H_0(L_j)) = 5.378 \rightarrow E(\tau)$

$z(\tau) = O(\tau) - E(\tau) = 9 - 5.378 = 3.622$

$$\therefore \frac{z^2(t)}{Var(z(\tau))} = 2.439 \sim \chi^2_{(1)}$$

$\therefore P(\chi^2_{(1)} > 2.439) = 0.118 > 0.05$ (α).

(Accept the null hypothesis)

Two or More Sample Test:

Test Statistic : $$Z_j(\tau) = \sum_{i=1}^{D} W_j(t_i)\left[\frac{d_{ij}}{Y_{ij}} - \frac{d_i}{Y_i}\right], \quad j = 1(1)K$$

$$W_j(t_i) = Y_{ij}\, W(t_i)$$

1.810

$$\therefore Z_j(\tau) = \sum_{i=1}^{D} W(t_i)\left[d_{ij} - Y_{ij}\frac{d_i}{Y_i}\right]$$
$$= \sum_{i=1}^{D} W(t_i)\, d_i \left[\frac{d_{ij}}{d_i} - \frac{Y_{ij}}{Y_i}\right]$$

Covariance : $$\hat{\sigma}_{jg} = -\sum_{i=1}^{D} W^2(t_i)\frac{Y_{ij}}{Y_i}\cdot\frac{Y_{ig}}{Y_i}\left(\frac{Y_i - d_i}{Y_i - 1}\right)d_i, \quad g \neq j$$

$$T = [Z_1(\tau)\, Z_2(\tau) \dots Z_{K-1}(\tau)]\, \Sigma^{-1}\, [Z_1(\tau)\, Z_2(\tau) \dots Z_{K-1}(\tau)]'$$

$$T \sim \chi^2_{K-1}$$

For $K=2$: $$T = \frac{\sum_{i=1}^{D} W^2(t_i)\left[d_{i1} - Y_{i1}\frac{d_i}{Y_i}\right]}{\sqrt{\sum_{i=1}^{D} W^2(t_i)\frac{Y_{i1}}{Y_i}\left(1 - \frac{Y_{i1}}{Y_i}\right)\left[\frac{Y_i - d_i}{Y_i - 1}\right]d_i}}$$

For log-rank, $W(t_i) = 1$

$T \sim N(0,1) \rightarrow$ sample size large

$T^2 \sim \chi^2_{(1)}$

7.4 (a)

t_i	Y_{i1}	d_{i1}	Y_{i2}	d_{i2}	Y_i	d_i	$d_{i1} - Y_{i1}\left(\frac{d_i}{Y_i}\right)$	$\frac{Y_{i1}}{Y_i}\left(1-\frac{Y_{i1}}{Y_i}\right)\left(\frac{Y_i-d_i}{Y_i-1}\right)d_i$
1	52	1	28	1	80	2	−0.3	0.45
3	51	2	27	1	78	3	0.04	0.66
4	49	1	26	1	75	2	−0.31	0.45
5	48	0	25	2	73	2	−1.32	~~[illegible]~~ 0.44
8	48	0	23	1	71	1	−0.68	~~[illegible]~~ 0.22
10	48	1	21	0	69	1	0.30	0.21
12	47	0	21	1	68	1	−0.69	0.21
13	47	2	20	1	67	3	−0.10	0.61
16	45	2	19	0	64	2	0.59	0.41
18	43	0	19	1	62	1	−0.69	0.21
23	43	0	18	1	61	1	−0.70	0.21
24	43	1	17	0	60	1	+0.28	0.20
26	42	1	17	1	59	2	−0.42	0.40
27	41	1	16	1	57	2	−0.49	0.40
28	40	1	15	0	55	1	0.27	0.20
30	39	2	15	1	54	3	−0.17	0.20
32	37	1	14	0	51	1	0.27	0.58
41	36	1	14	0	50	1	0.28	0.20
42	35	0	14	1	49	1	−0.71	0.20
51	35	1	13	0	48	1	0.27	0.20
56	34	0	13	1	47	1	−0.72	0.20
62	33	0	12	1	45	1	−0.73	0.20
65	33	1	11	0	44	1	0.25	0.20
67	32	1	11	0	43	1	0.28	0.19
69	31	0	10	1	41	1	−0.76	0.19
70	31	1	9	0	40	1	0.23	0.18
72	30	1	9	0	39	1	0.23	0.17
73	29	1	9	0	38	1	0.24	0.18
77	27	1	8	0	35	1	0.23	0.18
91	19	1	8	0	27	1	0.3	0.21
93	18	1	8	0	26	1	0.31	0.21
96	16	1	8	0	24	1	0.33	0.22
100	14	1	8	0	22	1	0.37	0.23
104	12	1	8	2	20	3	−0.8	0.24
112	8	0	5	1	13	1	−0.62	0.24
129	7	0	4	1	11	1	−0.64	0.23
157	5	1	3	0	8	1	0.58	0.23
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	1	0.43	0.24

$$\Sigma\left(d_{i1} - r_{i1}\left(\frac{d_i}{r_i}\right)\right) = -5.54$$

$$\cancel{\Sigma\left(d_{i1} - r_{i1}\left(\frac{d_i}{r_i}\right.\right.}$$

$$\Sigma \frac{r_{i1}}{r_i}\left(1 - \frac{r_{i1}}{r_i}\right)\left(\frac{r_i - d_i}{r_i - 1}\right) d_i = 10.44$$

$\therefore$ Test statistic $$T^2 = \frac{(-5.54)^2}{10.44} = 2.94 \sim \chi^2_{(1)}$$

$$P(\chi^2_{(1)} > 2.94) = 0.089 > 0.05$$

(Accept)

FOR 3 SAMPLES :-

t_i	r_{i1}	d_{i1}	r_{i2}	d_{i2}	r_{i3}	d_{i3}	r_i	d_i	$d_{i1} - r_{i1}\left(\frac{d_i}{r_i}\right)$	$d_{i2} - r_{i2}\left(\frac{d_i}{r_i}\right)$

$$\underbrace{\frac{r_{i1}}{r_i}\left(1 - \frac{r_{i1}}{r_i}\right)\left(\frac{r_i - d_i}{r_i - 1}\right) d_i}_{\sigma_{11}} \qquad \underbrace{\frac{r_{i2}}{r_i}\left(1 - \frac{r_{i2}}{r_i}\right)\left(\frac{r_i - d_i}{r_i - 1}\right) d_i}_{\sigma_{22}} \qquad \underbrace{\frac{r_{i1}}{r_i} \cdot \frac{r_{i2}}{r_i}\left(\frac{r_i - d_i}{r_i - 1}\right) d_i}_{\sigma_{12} = \sigma_{21}}$$

$$z_1 = \frac{\Sigma d_{i1} - r_{i1}\left(\frac{d_i}{r_i}\right)}{\sqrt{\sigma_{11}}}, \quad z_2 = \frac{\Sigma d_{i2} - r_{i2}\left(\frac{d_i}{r_i}\right)}{\sqrt{\sigma_{22}}}$$

$$\Sigma = \begin{bmatrix} \sigma_{11} & -\sigma_{12} \\ -\sigma_{21} & \sigma_{22} \end{bmatrix}, \quad \chi^2 = [z_1 \ z_2]\ \Sigma^{-1} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} \sim \chi^2_{(2)}$$

t_i	Y_{i1}	d_{i1}	Y_{i2}	d_{i2}	Y_{i3}	d_{i3}	Y_i	d_i	$d_{i1}-Y_{i1}\left(\frac{d_i}{Y_i}\right)$	$d_{i2}-Y_{i2}\left(\frac{d_i}{Y_i}\right)$	$\frac{Y_{i1}}{Y_i}\cdot\frac{Y_{i2}}{Y_i}\left(\frac{Y_i-d_i}{Y_i-1}\right)d_i$	$\frac{Y_{i1}}{Y_i}\left(1-\frac{Y_{i1}}{Y_i}\right)\left(\frac{Y_i-d_i}{Y_i-1}\right)d_i$
20	10	1	10	0	10	0	30	1	0.67	−0.33	0.11	0.22
21	9	1	10	0	10	0	29	1	0.69	−0.34	0.11	0.21
23	8	1	10	0	10	0	28	1	0.71	−0.36	0.10	0.20
24	7	2	10	0	10	0	27	2	0.48	−0.74	0.18	0.37
26	5	2	10	1	10	0	25	3	1.4	−0.2	0.22	0.44
27	3	1	9	0	10	0	22	1	0.86	−0.41	0.06	0.12
28	2	1	9	1	10	0	21	2	0.81	0.14	0.08	0.16
29	1	0	8	2	10	0	19	2	−0.10	1.16	0.02	0.09
30	1	1	6	2	10	0	17	3	0.52	0.94	0.02	0.15
31	0	0	4	2	10	1	14	3	0	1.14	0	0
32	0	0	2	1	9	1	11	2	0	0.84	0	0
34	0	0	1	0	8	1	9	1	0	−0.11	0	0
35	0	0	1	0	7	1	8	1	0	−0.13	0	0
36	0	0	0	0	6	1	6	1	0	0	0	0
38	0	0	0	0	5	2	5	2	0	0	0	0
39	0	0	0	0	3	1	3	1	0	0	0	0
									7.34	1.4	$\sigma_{12}=\sigma_{21}=0.9$	$\sigma_{11}=1.96$