HW 01 - Colin Busby BSTA 662

Monday, January 30, 2023 12:14 PM

Ex 2.2, 2.6, 2.9, 3.2, 3.4, 3.6 Klein 2nd ed

Distribution	Hazard Rate $h(x)$	Survival Function $S(x)$	Probability Density Function $f(x)$	Mean $E(X)$
Exponential $\lambda > 0, x \ge 0$, $\alpha = 1$	λ	$\exp[-\lambda x]$	$\lambda \exp(-\lambda x)$	$\frac{1}{\lambda}$
Weibull $\alpha, \lambda > 0, x \ge 0$	$\alpha\lambda x^{\alpha-1}$	$\exp[-\lambda x^{\alpha}]$	$\alpha\lambda x^{\alpha-1}\exp(-\lambda x^{\alpha})$	$\frac{\Gamma(1+1/\alpha)}{\lambda^{1/\alpha}}$

2.2 The time in days to development of a tumor for rats exposed to a carcinogen follows a Weibull distribution with $\alpha = 2$ and $\lambda = 0.001$.

(a) What is the probability a rat will be tumor free at 30 days? 45 days? 60 days?

(b) What is the mean time to tumor? (Hint $\Gamma(0.5) = \sqrt{\pi}$.)

(c) Find the hazard rate of the time to tumor appearance at 30 days, 45 days, and 60 days.

(d) Find the median time to tumor.

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

$$S(x) = \mathbb{P}(X > x) = \int_x^\infty f(t)\,dt$$

$$\mathbb{P}(X > t) = \int_t^\infty \alpha\lambda x^{\alpha-1} e^{(-\lambda x^{\alpha})}\,dx$$

$u = -\lambda x^{\alpha}$ $\qquad dx = -\frac{x^{1-\alpha}}{\alpha\lambda}\,du$

$\frac{du}{dx} = -\alpha\lambda x^{\alpha-1}$

$$= -\int e^{u}\,du$$

$$= -e^{u}$$

$$= -e^{-\lambda x^{\alpha}}\Big|_t^\infty \qquad \lambda = 0.001 \quad \alpha = 2$$

$$= \exp(-0.001t^2)$$

$$\mathbb{P}(X > 30) = \exp(-0.001(30)^2)$$

$$= \boxed{0.4066}$$

$$\mathbb{P}(X > 45) = \exp(-0.001(45)^2)$$

$$= \boxed{0.13199}$$

$= \boxed{0.13199}$

$$P(X > 60) = \exp(-0.001(60)^2)$$
$$= \boxed{0.0273}$$

b) $\Gamma(0.5) = \sqrt{\pi}$

$$E(X) = \frac{\Gamma(1+\frac{1}{\alpha})}{\lambda^{1/\alpha}} = \frac{\Gamma(1+\frac{1}{2})}{0.001^{\frac{1}{2}}}$$

fraction

$$\Gamma(n+1) = n\Gamma(n)$$
$$\Gamma(\tfrac{1}{2}+1) = \tfrac{1}{2}\Gamma(\tfrac{1}{2})$$

integer

$$\Gamma(n+1) = n!$$

$$= \frac{\frac{1}{2}\Gamma(\frac{1}{2})}{0.001^{\frac{1}{2}}} = \frac{\sqrt{\pi}}{2} \cdot (0.001)^{-\frac{1}{2}}$$

$= \boxed{28.0249 \text{ days: mean time to tumor}}$

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

$$P(X > x) = \exp(-0.001\, x^2)$$

$$h(x) = \frac{-d}{dx} \ln(e^{-0.001 x^2}) = 0.001 \cdot 2x$$

$$h(x) = \frac{x}{500}$$

$h(30) = \frac{30}{500} = \boxed{0.06 \text{ hazard rate at 30 days}}$

$h(45) = \frac{45}{500} = \boxed{0.09 \text{ hazard rate at 45 days}}$

$h(60) = \frac{60}{500} = \boxed{0.12 \text{ hazard rate at 60 days}}$

d) $S(x_{0.5}) = e^{(-0.001(x_{0.5})^2)} = 0.5$

$$\ln(e^{-0.001\, x_{0.5}^2}) = \ln 0.5$$

$$\ln\left(e^{-0.001 x_{0.5}^2}\right) = \ln 0.5$$

$$-0.001\, x_{0.5}^2 = \ln 0.5$$

$$\sqrt{x_{0.5}^2} = \sqrt{-1000 \ln(0.5)}$$

$$x_{0.5} = \sqrt{-1000 \ln(0.5)}$$

$$\boxed{x_{0.5} = 26.327 \text{ days is median time to tumor}}$$

2.6 The Gompertz distribution is commonly used by biologists who believe that an exponential hazard rate should occur in nature. Suppose that the time to death in months for a mouse exposed to a high dose of radiation follows a Gompertz distribution with $\theta = 0.01$ and $\alpha = 0.25$. Find

(a) the probability that a randomly chosen mouse will live at least one year,

(b) the probability that a randomly chosen mouse will die within the first six months, and

(c) the median time to death.

	$h(x)$	$S(x)$	$f(x)$	$E(x)$
Gompertz $\theta, \alpha > 0, x \geq 0$	$\theta e^{\alpha x}$	$\exp\left[\frac{\theta}{\alpha}(1 - e^{\alpha x})\right]$	$\theta e^{\alpha x} \exp\left[\frac{\theta}{\alpha}(1 - e^{\alpha x})\right]$	$\int_0^\infty S(x)dx$

a) $\mathbb{P}(X > 12) = \int_{12}^{\infty} f(x)\, dx$ Using $t = 12$ months

$$= \int_t^\infty \theta e^{\alpha x} \exp\left\{\frac{\theta}{\alpha}(1 - e^{\alpha x})\right\} dx$$

$$\exp(\alpha x) \exp\left(\frac{\theta}{\alpha}(1 - e^{\alpha x})\right)$$

$$\exp\left\{\frac{\theta}{\alpha}(1 - e^{\alpha x}) + \alpha x\right\}$$

$$= \theta e^{\frac{\theta}{\alpha}} \int_t^\infty \exp\left\{\alpha x - \frac{\theta e^{\alpha x}}{\alpha}\right\} dx$$

$u = -\alpha x$

$du = -\alpha\, dx$

$$= \theta e^{\theta/\alpha}\left[-\frac{1}{\alpha} \int \exp\left\{-\frac{\theta e^{-u} + \alpha u}{\alpha}\right\} du\right]$$

$$= \theta e^{\theta/\alpha}\left[-\frac{1}{\alpha}\int \exp\left\{-\frac{\theta e^{-u}+\alpha u}{\alpha}\right\} du\right]$$

$$= \theta e^{\theta/\alpha}\left[-\frac{1}{\alpha}\int \exp\left\{\frac{\theta e^{-u}}{\alpha} - \frac{\cancel{\alpha} u}{\cancel{\alpha}}\right\} du\right]$$

$$v = e^{u} \qquad u = \ln(v)$$

$$dv = e^{u}\,du \qquad e^{-u} = \frac{1}{v}$$

$$= \theta e^{\theta/\alpha}\left[-\frac{1}{\alpha}\int \frac{e^{-\theta/\alpha v}}{v^2}\, dv\right]$$

$$z = -\frac{\theta}{\alpha v}$$

$$dz = \frac{\theta}{\alpha v^2}\, dv$$

$$= -\frac{\theta e^{\theta/\alpha}}{\alpha}\left[\frac{\alpha}{\theta}\int e^{z}\, dz\right]$$

$$= -\frac{\theta e^{\theta/\alpha}}{\alpha}\left[\frac{\alpha e^{z}}{\theta}\right]$$

$$= -\frac{\theta e^{\theta/\alpha}}{\alpha}\left[\frac{\alpha e^{-\theta/\alpha v}}{\theta}\right]$$

$$= -\frac{\theta e^{\theta/\alpha}}{\alpha}\left[\frac{\alpha e^{-\frac{\theta e^{-u}}{\alpha}}}{\theta}\right]$$

$$= \theta e^{\theta/\alpha}\left[-\frac{1}{\alpha}\int e^{\frac{-\theta e^{-u}+\alpha u}{\alpha}}\, du\right]$$

$$= \theta e^{\theta/\alpha}\left[\frac{-e^{-\theta e^{-u}/\alpha}}{\theta}\right]$$

$$= \theta e^{\theta/\alpha}\left[\frac{-\exp\left\{-\frac{\theta e^{\alpha x}}{\alpha}\right\}}{\theta}\right]$$

$$= \theta e^{\theta/\alpha}\int_t^{\infty} e^{\alpha x - \frac{\theta e^{\alpha x}}{\alpha}}\, dx$$

$$= -\exp\left\{\frac{\theta}{\alpha} - \frac{\theta e^{\alpha x}}{\alpha}\right\}\Big|^{\infty}$$

$$= -\exp\left\{\frac{\theta}{\alpha} - \frac{\theta e^{\alpha x}}{\alpha}\right\}\Bigg|_t^\infty$$

$$= -\exp\left\{\frac{\theta}{\alpha} - \frac{\theta e^{\alpha \cdot \infty}}{\alpha}\right\} - \left[-\exp\left\{\frac{\theta}{\alpha} - \frac{\theta e^{\alpha t}}{\alpha}\right\}\right]$$

$$= \exp\left\{\frac{\theta}{\alpha} - \frac{\theta e^{\alpha t}}{\alpha}\right\}$$

$$\mathbb{P}(X > 12) = \exp\left(\frac{0.01}{0.25} - \frac{0.01 e^{0.25(12)}}{0.25}\right)$$

$$= \exp\{0.04 - 0.8034$$

Is it $= 0.4661$ probability that a randomly chosen mouse will live at least 1 year

$1 - \mathbb{P}()$? or this

5) $\mathbb{P}(X < 7) = 1 - \mathbb{P}(X > 6)$

$$= 1 - \exp\left(\frac{0.01}{0.25} - \frac{0.01 e^{0.25(6)}}{0.25}\right)$$

$= 1 - 0.8699$ is it $1 - \mathbb{P}()$ or just $\mathbb{P}()$

$= 0.13$ probability that a mouse will die within the first 6 months

4 $S(x_{0.5}) = \exp\left\{\frac{\theta}{\alpha}(1 - e^{\alpha x})\right\} = 0.5$

$$\exp\left\{\frac{0.01}{0.25}(1 - e^{0.25x})\right\} = 0.5$$

$$0.04(1 - e^{0.25x}) = \ln 0.5$$

$$1 - e^{0.25x} = 25 \ln(0.5)$$

$$e^{0.25x} = 1 - 25 \ln(0.5)$$

$$e^{0.25x} = 1 - 25\ln(0.5)$$

$$0.25x = \ln(1 - 25\ln(0.5))$$

$$x_{0.5} = 4\ln[1 - 25\ln(0.5)]$$

$$\boxed{x_{0.5} = 11.634 \quad \text{median time to death}}$$

UNITS?

2.9 The time to relapse, in months, for patients on two treatments for lung cancer is compared using the following log normal regression model:

$$Y = \mathrm{Ln}(X) = 2 + 0.5Z + 2W,$$

where W has a standard normal distribution and $Z = 1$ if treatment A and 0 if treatment B.

(a) Compare the survival probabilities of the two treatments at 1, 2, and 5 years.

(b) Repeat the calculations if W has a standard logistic distribution. Compare your results with part (a).

	$h(x)$	$S(x)$	$f(x)$	$E(X)$
Log normal $\sigma > 0, x \geq 0$	$\frac{f(x)}{S(x)}$	$1 - \Phi\left[\frac{\ln x - \mu}{\sigma}\right]$	$\frac{\exp\left[-\frac{1}{2}\left(\frac{\ln x - \mu}{\sigma}\right)^2\right]}{x(2\pi)^{1/2}\sigma}$	$\exp(\mu + 0.5\sigma^2)$

a) $S(x) = \mathbb{P}(X > x)$ $\qquad Y = \ln(X) = 2 + 0.5Z + 2W$

$$= \mathbb{P}(\ln(X) > \ln(x))$$

$$= \mathbb{P}(2 + 0.5Z + 2W > \ln x)$$

$$= \mathbb{P}(2W > \ln x - 0.5Z - 2)$$

$$= \mathbb{P}\left(W > \tfrac{1}{2}(\ln x - 0.5Z - 2)\right)$$

$$= 1 - \Phi\left(\tfrac{1}{2}(\ln(x - 0.5Z - 2))\right)$$

Treatment A

$$\mathbb{P}(X > 12 \text{ months}) = 1 - \Phi\left(\tfrac{1}{2}(\ln 12 - 0.5(1) - 2)\right)$$

$$= 1 - \Phi(-0.0075)$$

$$= 1 - 0.49601$$

$$= 0.50399$$

$$\mathbb{P}(X > 24 \text{ months}) = 1 - \Phi\left(\tfrac{1}{2}(\ln 24 - 0.5 - 2)\right)$$

$$= 1 - \Phi(0.339027)$$

$$= 1 - \Phi(0.339027)$$
$$= 1 - 0.6327$$
$$= 0.3673$$

$$\mathbb{P}(X > 60 \text{ months}) = 1 - \Phi\left(\tfrac{1}{2}(\ln 60 - 2 - 0.5)\right)$$
$$= 1 - \Phi(0.79717)$$
$$= 1 - 0.78524$$
$$= 0.21476$$

<u>Treatment B</u>

$$\mathbb{P}(X > 12) = 1 - \Phi\left(\tfrac{1}{2}(\ln 12 - 2 - 0.5(0))\right)$$
$$= 1 - \Phi(0.24245)$$
$$= 1 - 0.59578$$
$$= 0.40422$$

$$\mathbb{P}(X > 24) = 1 - \Phi\left(\tfrac{1}{2}(\ln 24 - 2)\right)$$
$$= 1 - \Phi(0.589)$$
$$= 1 - 0.7221$$
$$= 0.2779$$

$$\mathbb{P}(X > 60) = 1 - \Phi\left(\tfrac{1}{2}(\ln 60 - 2)\right)$$
$$= 1 - \Phi(1.04717)$$
$$= 1 - 0.8525$$
$$= 0.1475$$

Years	Trt A	Trt B
1	0.5039	0.4042
2	0.3673	0.2779
5	0.21476	0.1475

Survival probabilities for each treatment

b) Standard Logistic

$$S(x) = \frac{1}{1+e^{\left(\frac{x-\mu}{\sigma}\right)}} = \frac{1}{1+e^{x}} \qquad y = \ln x = 2 + 0.5z + 2w$$

$$w = \frac{1}{2}(\ln x - 2 - 0.5z)$$

Trt A (z=1)

$$S(12) = \frac{1}{1+e^{\left(\frac{1}{2}(\ln(12)-2-0.5\right)}}$$

$$= 0.5019$$

$$S(24) = \left(1+e^{\left(\frac{1}{2}(\ln 24 - 2 - 0.5)\right)}\right)^{-1}$$

$$= 0.416$$

$$S(60) = \left[1 + \exp\left\{\frac{1}{2}(\ln 60 - 2 - 0.5)\right\}\right]^{-1}$$

$$= 0.3106$$

Trt B (z=0)

$$S(12) = \left[1 + \exp\left\{\frac{1}{2}(\ln 12 - 2 - 0.5(0))\right\}\right]^{-1}$$

$$= 0.4397$$

$$S(24) = \left[1 + \exp\left\{\frac{1}{2}(\ln 24 - 2)\right\}\right]^{-1}$$

$$= 0.3568$$

$$S(60) = \left[1 + \exp\left\{\frac{1}{2}(\ln 60 - 2)\right\}\right]^{-1}$$

$$= 0.2597$$

Years	Trt A	Trt B
1	0.5019	0.4397
2	0.416	0.3568
5	0.3106	0.2597

3.2 3.4 3.6

3.2 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.

(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 started sometime between 12 and 15 years after enrollment).

(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.

(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 observation.

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

a) 60^+, Type I right censored as they never developed breast cancer during the study.
Truncation: none

b) $(52, 55]$ Interval censored since the breast cancer developed during a known interval of time, but we don't know the exact time

c) Random censoring, since the participant died of unrelated causes & wasn't diagnosed with breast cancer at time of death. Participant died before the completion of the 30 yr study period.

d) Random censoring, since the participant moved away before completion of the study & was not diagnosed with breast cancer during the period of observation.

e) 1 Right censored, 1 Interval censored, 2 Random censored
↳ right censored

$$L = S(C_i) * [S(C_{L,i}) - S(C_{R,i})] * S(C_i) * S(C_i)$$

3.4 In section 1.2, a clinical trial for acute leukemia is discussed. In this trial, the event of interest is the time from treatment to leukemia relapse. Using the data for the 6-MP group and assuming that the time to relapse distribution is exponential with hazard rate λ, construct the likelihood function. Using this likelihood function, find the maximum likelihood estimator of λ by finding the value of λ which maximizes this likelihood.

$X \sim Exp(\lambda)$

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

$f(x) = \lambda exp(-\lambda x)$

$S(x) = \mathbb{P}(X > x)$

TABLE 1.1

Remission duration of 6-MP versus placebo in children with acute leukemia

Pair	*Remission Status at Randomization*	*Time to Relapse for Placebo Patients*	*Time to Relapse for 6-MP Patients*
1	Partial Remission	1	10
2	Complete Remission	22	7
3	Complete Remission	3	32+
4	Complete Remission	12	23
5	Complete Remission	8	22
6	Partial Remission	17	6
7	Complete Remission	2	16
8	Complete Remission	11	34+
9	Complete Remission	8	32+
10	Complete Remission	12	25+
11	Complete Remission	2	11+
12	Partial Remission	5	20+
13	Complete Remission	4	19+
14	Complete Remission	15	6
15	Complete Remission	8	17+
16	Partial Remission	23	35+
17	Partial Remission	5	6
18	Complete Remission	11	13
19	Complete Remission	4	9+
20	Complete Remission	1	6+
21	Complete Remission	8	10+

+ Censored observation

$$L_1 = \prod_{i=1}^{n} (\lambda e^{-\lambda t_i})^{\delta_t} exp[-\lambda t_i(1-\delta_i)]$$
$$= \lambda^r exp[-\lambda S_T] \quad , r = \Sigma \delta_i$$

Ex 3.9
pg 76
Textbook

X = time to relapse

$$L(\lambda) = [f(10) f(7) f(23) f(22) f(6) f(16) f(6) f(6) f(13)] *$$
$$S(32) S(34) S(32) S(25) S(11) S(20) S(19) *$$
$$S(17) S(35) S(9) S(6) S(10)$$

$$= \lambda^9 exp[-109\lambda] * exp[-250\lambda]$$

$$L(\lambda) = \lambda^9 exp[-359\lambda]$$

$$\frac{\partial L}{\partial \lambda} = 9\lambda^8 e^{-359\lambda} - 359\lambda^9 e^{-359\lambda} = 0$$

$$9\lambda^8 e^{-359\lambda} = 359\lambda^9 e^{-359\lambda}$$

$$e^{-359\lambda} = \frac{359}{9}\lambda e^{-359\lambda}$$

$$1 = \frac{359}{9}\lambda$$

$$\boxed{MLE \ \hat{\lambda} = \frac{9}{359}}$$

3.6 The following data consists of the times to relapse and the times to

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 λ and the time to death in relapse had a Weibull distribution with parameters θ and α.

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

+ Censored observation

(a) Construct the likelihood for the relapse rate λ.

(b) Construct a likelihood for the parameters θ and α.

(c) Suppose we were only allowed to observe a patients death time if the patient relapsed. Construct the likelihood for θ and α based on this truncated sample, and compare it to the results in (b).

a) $L(\lambda) = \lambda^{\sum S_i} \exp[-\lambda S_T]$

$= [f(5)\, f(8)\, f(12)\, f(24)\, f(32)\, f(17)] *$

$S(16)\, S(17)\, S(19)\, S(30)$

$\boxed{L(\lambda) = \lambda^6 \exp[-180\lambda]}$

b) $L(\alpha,\theta) = [f(11)\, f(12)\, f(15)\, f(45)] * S(33)\, S(28)\, S(16)\, S(17)\, S(19)\, S(30)$

$S(x) = \exp[-\theta x^{\alpha}]$

$f(x) = \alpha\theta x^{\alpha-1} \exp[-\theta x^{\alpha}]$

$\boxed{L(\alpha,\theta) = 89100^{\alpha-1}\alpha^4\theta^4 \exp[-(11^\alpha+12^\alpha+15^\alpha+45^\alpha+33^\alpha+28^\alpha+16^\alpha+17^\alpha+19^\alpha+30^\alpha)\lambda]}$

c) Left truncation, only individuals who have relapsed are observed? How do I put in terms of Survival Analysis?

$L(\alpha,\theta) = 89100^{\alpha-1}\alpha^4\theta^4 \exp[-(11^\alpha+12^\alpha+15^\alpha+28^\alpha+33^\alpha+45^\alpha)\lambda]$

It looks almost the same as part (b)