

Survival Models for the Social and Political Sciences

Week 3: The Logic of Survival Models and Single Sample Data

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Introduction

- ▶ Survival data can be either discrete or continuous depending on how time is measured.
- ▶ Nonparametric estimators of survival are always discrete, however.
- ▶ Both books introduce the mathematical underpinnings of survival models in Chapter 2 that were previewed last week.
- ▶ The key is understanding the **hazard** and **survival** functions.
- ▶ Next we will move on to Cox regression, which removes distributional assumptions seen this week.

Review of Risk Principles

- ▶ Simple *risk* is:

$$\text{Risk} = \frac{\text{Number of events observed}}{\text{Number in the group}}.$$

- ▶ *New York Times, October 12, 2012*: 14,000 patients had a steroid drug (linked to a contaminated drug made by the New England Compounding Center in Framingham, Mass) injected into their spine that may have been contaminated with a fungus that could cause meningitis. Since 282 have contracted meningitis and 23 died:

$$\text{risk of meningitis} = \frac{282}{14000} = 0.020143 \quad \text{risk of death} = \frac{23}{14000} = 0.0016429$$

- ▶ The *rate* is equal to the risk but defined over a period of time. Example:
 - ▷ If 600,000 die in the UK in a given year out of a population of 60,000,000, then the rate is 0.01 deaths *per person year*.
 - ▷ Sometimes such numbers are multiplied by a factor to make them more intuitive, such as the above number expressed as: 10 deaths per 1000 population per year.

Review of Risk Principles

- ▶ A rate requires the following:
 - ▷ a specified time period
 - ▷ a known population size
 - ▷ the number of events of interest occurring during this period in this population.
- ▶ **Events** are divided into types:
 - ▷ **permanent**, and the case is considered “no longer at risk” (removed from the at-risk population)
 - ▷ **temporary**, and the case eventually returns to the at-risk population.
- ▶ So temporary exiting cases can return and exit again, raising the rate.

Review of Risk Principles

- ▶ A related quantity to rate that takes into account cases exiting and returning to the at-risk population is the **incidence**:

$$\text{Incidence} = \frac{\text{Number of events in a defined period}}{\text{Total person-time at risk}} \times 1000,$$

also called the *incidence density rate* and the *person-time incidence rate*.

- ▶ **Incidence is not Prevalence**:

- ▷ *prevalence* is a measure of the total number of cases of disease in a population at any point in time,

- ▷ *incidence* is the rate of occurrence of new cases over some time period,

...so incidence conveys information about the risk of getting the disease, but prevalence indicates how widespread the disease is and does not cover a time period.

Review of Risk Principles

- ▶ The **Crude Mortality Rate** (called the “crude death rate”) is:

$$\text{CMR} = \frac{\text{Number of deaths occurring in a year}}{\text{Mid-year population}} \times 1000.$$

- ▶ Sometimes “mid-year population” is substituted with “average population”
- ▶ Multiplying by 1000 is not universal, and 100,000 is also common.
- ▶ The **Case-Fatality Rate** is the proportion of persons with a particular condition (cases) who die from that condition:

$$\text{CFR} = \frac{\text{Number of cause-specific deaths among the incident cases}}{\text{Number of incident cases}} \times 10^n.$$

- ▶ Thus CFR is a measure of the **severity** of the condition.
- ▶ The time periods for the numerator and the denominator do not need to be the same: the denominator could be cases of HIV/AIDS diagnosed during the calendar year 1990, and the numerator, deaths among those diagnosed with HIV in 1990, could be from 1990 to the present.

Review of Risk Principles

- The *Age-Specific Mortality Rate* is defined as:

$$\text{ASMR} = \frac{\text{Number of deaths occurring in a specified age group}}{\text{Mid-year number in that age group}} \times 1000$$

- The CDC defines specific definitions as well:

Measure	Numerator	Denominator	10 ⁿ
Crude death rate	Total number of deaths during a given time interval	Mid-interval population	1,000 or 100,000
Cause-specific death rate	Number of deaths assigned to a specific cause during a given time interval	Mid-interval population	100,000
Proportionate mortality	Number of deaths assigned to a specific cause during a given time interval	Total number of deaths from all causes during the same time interval	100 or 1,000
Death-to-case ratio	Number of deaths assigned to a specific cause during a given time interval	Number of new cases of same disease reported during the same time interval	100
Neonatal mortality rate	Number of deaths among children < 28 days of age during a given time interval	Number of live births during the same time interval	1,000
Postneonatal mortality rate	Number of deaths among children 28–364 days of age during a given time interval	Number of live births during the same time interval	1,000
Infant mortality rate	Number of deaths among children < 1 year of age during a given time interval	Number of live births during the same time interval	1,000
Maternal mortality rate	Number of deaths assigned to pregnancy-related causes during a given time interval	Number of live births during the same time interval	100,000

Population Attributable Risk

- ▶ The overall impact of negative effects on public health is a combination of: *relative risk* and the *proportion of the population exposed*.
- ▶ Denote $I_{\text{Population}}$ as the incidence in the population, I_{Exposed} as the incidence in the exposed group, and $I_{\text{Non-Exposed}}$ as the incidence in the unexposed group.
- ▶ Then the **population attributable risk** is the excess incidence proportion due to the risk factor:

$$AR = \frac{I_{\text{Population}} - I_{\text{Non-Exposed}}}{I_{\text{Population}}} = \frac{\frac{a+b}{N}(RR - 1)}{1 + \frac{a+b}{N}(RR - 1)},$$

where $\frac{a+b}{N}$ is the proportion of the population exposed to the risk factor.

- ▶ Warning: the epidemiology literature (and others) has other definitions and specialized versions of the AR.

Population Attributable Risk

- UK workers in a slate quarry:

	Exposure or Risk Factor–Occupation	
	Slate Worker	Non-Slate Worker
Died in follow-up Period	379	230
Survived follow-up Period	347	299
Total	726	529

- So $I_{\text{Population}} = (379 + 230)/(726 + 529) = 0.48526$, and $I_{\text{Non-Exposed}} = 230/529 = 0.43478$.

- Calculating:

$$AR = \frac{I_{\text{Population}} - I_{\text{Non-Exposed}}}{I_{\text{Population}}} = \frac{0.48526 - 0.43478}{0.48526} = 0.10403.$$

Box-Steffensmeier and Jones Example

Pearson, Frederic S., and Robert A. Baumann. "International Military Intervention, 1946-1988. Inter-University Consortium for Political and Social Research, Data Collection 6035." Ann Arbor, MI (1993).

TABLE 2.1: Example of Event History Data: Military Interventions

Intervention	Intervenor	Target	Duration	Contiguity ^a	C ^b
1	U.K.	Albania	1	0	0
46	El Salvador	Honduras	657	1	0
81	U.S.	Panama	274	0	1
184	Bulgaria	Greece	12	1	0
236	Taiwan	China	7456	1	0
278	Botswana	S. Africa	1097	1	0
332	Uganda	Kenya	409	1	1
467	Israel	Egypt	357	1	0
621	Malawi	Mozambique	631	1	1
672	India	Pakistan	173	1	0

^a Intervenor and Target separated by 150 miles of water or less are coded as contiguous; ^bC denotes "censored": disputes on-going as of 31 Dec. 1988 are treated as right-censored. Data are Pearson-Baumann Militarized Intervention Data (ICPSR 6035).

Notes on Table 2.1, Right Censoring

- ▶ The duration of intervention between El Salvador and Honduras is 657 days.
- ▶ The duration of intervention between Malawi and Mozambique is 631 days.
- ▶ But these are really very different numbers: $C^b = 0$ for the first case and $C^b = 1$ for the second case.
- ▶ This means that Malawi-Mozambique is right censored in the data and we do not know when the intervention ended.
- ▶ Ignoring this right censoring in the model leads to obviously biased results.

Notes on Table 2.1, Covariate Effects

- ▶ With survival models what we are really interested in is making standard regression statements using covariates.
- ▶ In this case we might be interested in whether contiguity between the two nations affects the duration of the intervention.
- ▶ Given such a regression model (which we are on the way to developing) we will get a coefficient such that a positive sign means that contiguity elongates the event length and a negative sign means that contiguity hastens the event.
- ▶ In the language of survival models we say that contiguity increases or decreases the **risk** of an intervention ending.
- ▶ Contiguity is an example of a **time-independent** covariate since it is fixed over the length of the study.
- ▶ Conversely **time-varying** covariates (TVCs) are those that can change for cases during the time covered by the data (in this case say economic variables).

The Heterogeneity of Events

- ▶ So far we have looked single-spell, single event, or one-way transition processes.
- ▶ A nation can engage in multiple interventions at the same time.
- ▶ Events like an intervention can stop and then restart.
- ▶ An event can occur in multiple ways: an intervention in the example can end because of a treaty, armistice, third party entrance, surrender, stalemate, compromise, or escalation to a higher order of militarization.
- ▶ The Nicaragua-Costa Rica dispute example (BSJ Table 2.2 on page 11) is an example of these complexities.

The Heterogeneity of Events, Nicaragua-Costa Rica Example

- ▶ There are multiple spells/duration lengths from multiple MIDs.
- ▶ There are also multiple events: stalemate and compromise.
- ▶ Since we know the dates and durations, we also know the duration of peace in between MIDs, which can also be analyzed with survival models, going from 9 cases to 18.
- ▶ We learn more by understanding how the event type affects the duration of non-conflict between MIDs (think about how WWI ended).

Yet Another *Swedish* Dataset

- ▶ A life table is constructed for Swedish females in 2010 from Statistics Sweden (SCB) by:
 - ▷ start with a column for each age: 0-100
 - ▷ then add a column for the number of females of each age at 2010 (an average of 2010 and 2011 since SCB measures at the end of the year): *period data*
 - ▷ the third column is the number of deaths at each age
 - ▷ risk is deaths/population for each age, for example $117/55407 = 0.0021116$
 - ▷ column 5, *alive at age x*, is the size of the birth cohort year by year.

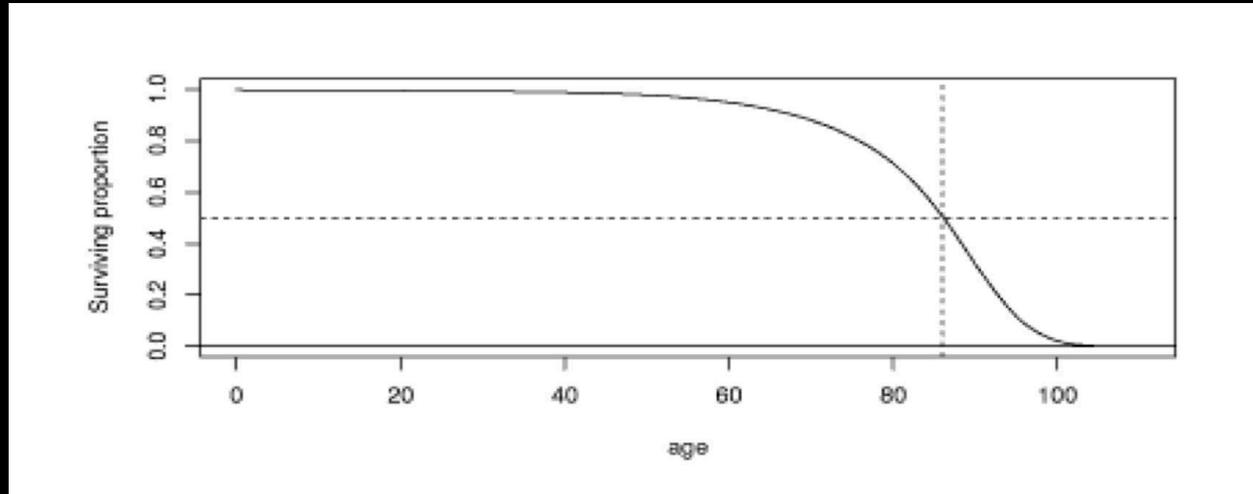
Yet Another *Swedish* Dataset

- ▶ The last column is the objective of the table:
 - ▷ it is the size of the birth cohort exposed to previous years of risk
 - ▷ start with 100,000 by convention at age 0: synthetic cohort data
 - ▷ for age 1 we expect $100,00 \times 0.0021$ girls to die, leaving 99,789 at exactly one year of age
 - ▷ those in the synthetic cohort data live their “lives” under the risk conditions of 2009, as if risk was locked-in (permanently fixed) at that time.
 - ▷ this is artificial but useful.

Yet Another *Swedish* Dataset Life Table**TABLE 2.1**Life table for Swedish females 2010

age(x)	pop	deaths	risk(%)	alive at age x
0	55 407	117	0.211	100 000
1	54 386	22	0.040	99 789
2	53 803	11	0.020	99 748
3	53 486	7	0.013	99 728
4	52 544	4	0.008	99 715
...
96	3 074	1 030	33.507	6 529
97	2 204	817	37.061	4 341
98	1 473	624	42.363	2 732
99	920	433	47.065	1 575
100+	1 400	837	59.786	834

Yet Another *Swedish* Dataset, Survival Function



Survival Function

- ▶ The last figure showed the survival function for the SCB data.
- ▶ This is the probability of surviving past t :

$$S(t) = p(T \geq t), \quad t \geq 0$$

where T is the random variable for life length, and t is a fixed point of interest.

- ▶ The Broström book alternates between t and t_0 , and uses the first when making general statements and the second when talking about a specified time.
- ▶ In the SCB data T is interpreted as the future life length of a randomly chosen female from the sample frame.
- ▶ In basic models, $S(t)$ is assumed to be smooth and uniformly differentiable at all points.

Theory: Where We Left Off

- ▶ We will use a **proportional hazards model** for the critical event.
- ▶ The **hazard function** gives the proportion of cases who fail just after time t given that they have survived until time t .
- ▶ From a PDF for the event over time, $f(t)$, define the distribution function (CDF) of time t and the **survival function**:

$$F(t) = \int_0^t p(T < t) dt \qquad S(t) = p(T \geq t) = 1 - F(t).$$

The hazard function is created by:

$$h(t) = \lim_{\delta t \rightarrow 0} \left[\frac{p(t \leq T < t + \delta t | T \geq t)}{\delta t} \right],$$

also called the **instantaneous hazard rate**, the **instantaneous death rate**, the **intensity rate**, and the **force of mortality**.

- ▶ Note that:

$$h(t) = \frac{f(t)}{S(t)} = -\frac{d}{dt}(\log S(t)), \qquad S(t) = \exp(-H(t)), \quad \text{where } H(t) = \int_0^t h(u) du$$

Density Function

- ▶ The density function is related to the survival by:

$$f(t) = -\frac{\partial}{\partial t}S(t), \quad t \geq 0.$$

- ▶ For a very small s value and arbitrary t_0 :

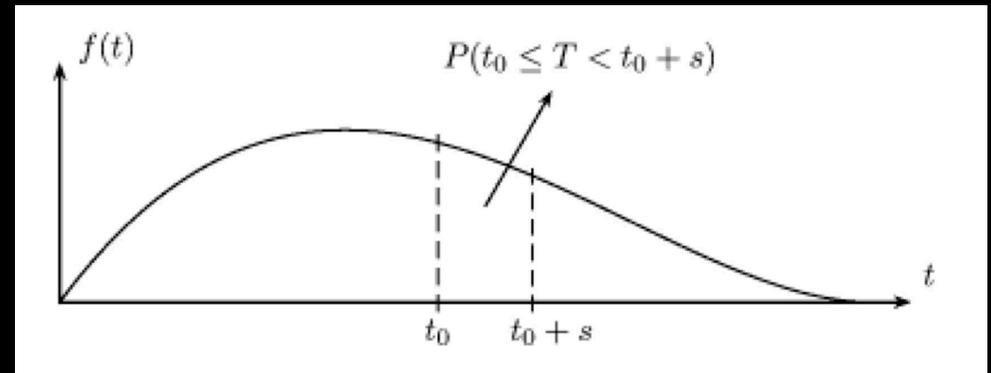
$$p(t_0 \leq T < t_0 + s) \approx sf(t_0),$$

which is illustrated by the figure at right as an approximation since this is not a right trapezoid.

- ▶ More exactly:

$$f(t) = \lim_{s \rightarrow 0} \frac{p(t \leq T < t + s)}{s}, \quad t \geq 0,$$

which is an unconditional statement.

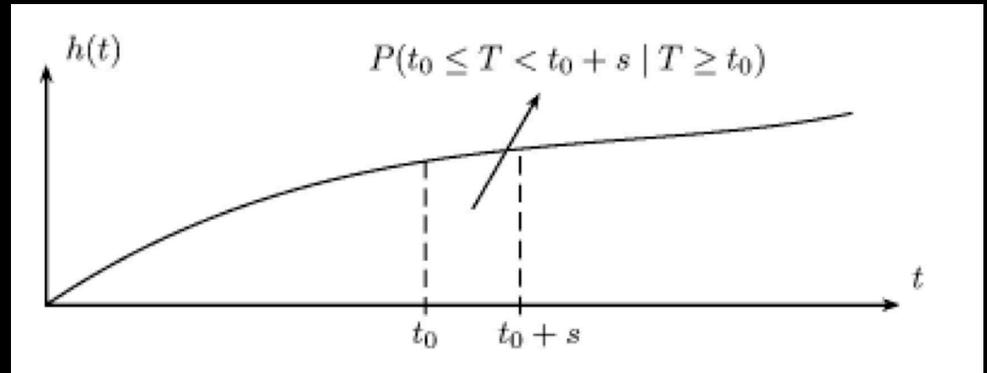


Hazard Function

- ▶ This is the instantaneous probability of the event at exactly t , given no event before then.
- ▶ Consider the s getting very small, then:

$$h(t_0) = \lim_{s \rightarrow 0} \frac{p(t_0 \leq T < t_0 + s | T \geq t_0)}{s},$$

(for $t_0 \geq 0$) which is a conditional statement.



The Cumulative Hazard Function

- ▶ The cumulative hazard function is just the integral of the hazard function (like a CDF):

$$F(t) = H(t) = \int_0^t h(x)dx, \quad t \geq 0.$$

- ▶ Here x is just an integration variable (it goes away), and the Broström book confusingly uses s .
- ▶ This form successively accumulates risk as time continues.
- ▶ The cumulative hazard function is easier to manipulate in statistical models than the hazard function, which is a property we will exploit.

Defining Proportional Hazards

- ▶ Also called “relative risk.”
- ▶ This is by far the most widely used general survival regression specification.
- ▶ It starts with a **baseline or underlying hazard function** that all units share, $h(t)$.
- ▶ Then the predictors in the form of covariates and associated coefficients act on each units hazard through $\exp(\mathbf{X}\boldsymbol{\beta})$, which is typically called the **relative hazard function**.
- ▶ The general form of the regression specification is:

$$h(t|\mathbf{X}) = h(t) \exp(\mathbf{X}\boldsymbol{\beta}),$$

- ▶ An appropriately bounded parametric hazard function can be used for the baseline hazard function.
- ▶ This week we parametrically define $h(t)$ but next week we will leave it unspecified.

Notes On Proportional Hazards

- ▶ Depending on the parametric form chosen the relative hazard component may or may not have an intercept.
- ▶ The proportional hazards model can be linearized with respect to the RHS by applying the natural logarithm:

$$\begin{aligned}\log h(t|\mathbf{X}) &= \log h(t) + \mathbf{X}\boldsymbol{\beta} \\ \log H(t|\mathbf{X}) &= \log H(t) + \mathbf{X}\boldsymbol{\beta}\end{aligned}$$

- ▶ Model specifications are exposed to all of the usual concerns about mis-specification.
- ▶ Additional assumptions Required for the proportional hazards model:
 - ▷ The true form of the underlying functions, $h(t)$, $H(t)$, and $S(t)$, are all specified correctly.
 - ▷ The relationship between the linear additive component and the log hazard is linear.
 - ▷ In the absence of interactions, the linear additive component applies additively on the log hazard.
 - ▷ The effect of the linear additive components is the same for all values of time, t .

Proportional Hazards Coefficient Interpretation

- ▶ Consider how to interpret the j th coefficient from the proportional hazards model.
- ▶ Recall the elegant interpretation of linear model regression coefficients.
- ▶ The regression coefficient for X_j (β_j) is the increase in the log hazard rate at some fixed point in t in time if X_j is increased by one unit and all other covariates are held constant:

$$\begin{aligned}\beta_j &= \log(t|X_1, X_2, \dots, [X_j + 1], X_{j+1}, \dots, X_k) - \log(t|X_1, X_2, \dots, [X_j], X_{j+1}, \dots, X_k) \\ &= \log \left[\frac{t|X_1, X_2, \dots, [X_j + 1], X_{j+1}, \dots, X_k}{t|X_1, X_2, \dots, [X_j], X_{j+1}, \dots, X_k} \right]\end{aligned}$$

- ▶ This can be re-expressed as:

$$\exp(\beta_j) = \left[\frac{t|X_1, X_2, \dots, [X_j + 1], X_{j+1}, \dots, X_k}{t|X_1, X_2, \dots, [X_j], X_{j+1}, \dots, X_k} \right]$$

Proportional Hazards Coefficient Interpretation

- ▶ Therefore the effect of increasing X_j by 1 is to increase the hazard of the event of study by $\exp(\beta_j)$ at all times (there is no conditionality on time) in:

$$\exp(\beta_j) = \left[\frac{t|X_1, X_2, \dots, [X_j + 1], X_{j+1}, \dots, X_k)}{t|X_1, X_2, \dots, [X_j], X_{j+1}, \dots, X_k)} \right]$$

- ▶ Suppose more generally that we increase X_j by some amount δ holding other covariates constant:

$$\Delta \frac{h(t|\mathbf{X})}{\log h(t)} = \frac{h(t) \exp(\mathbf{X}'\boldsymbol{\beta})}{h(t) \exp(\mathbf{X}\boldsymbol{\beta})} = \exp((\mathbf{X}' - \mathbf{X})\boldsymbol{\beta})$$

where $\mathbf{X}'\boldsymbol{\beta}$ is $\mathbf{X}\boldsymbol{\beta}$ such that X_j is changed by δ .

Proportional Hazards Coefficient Interpretation

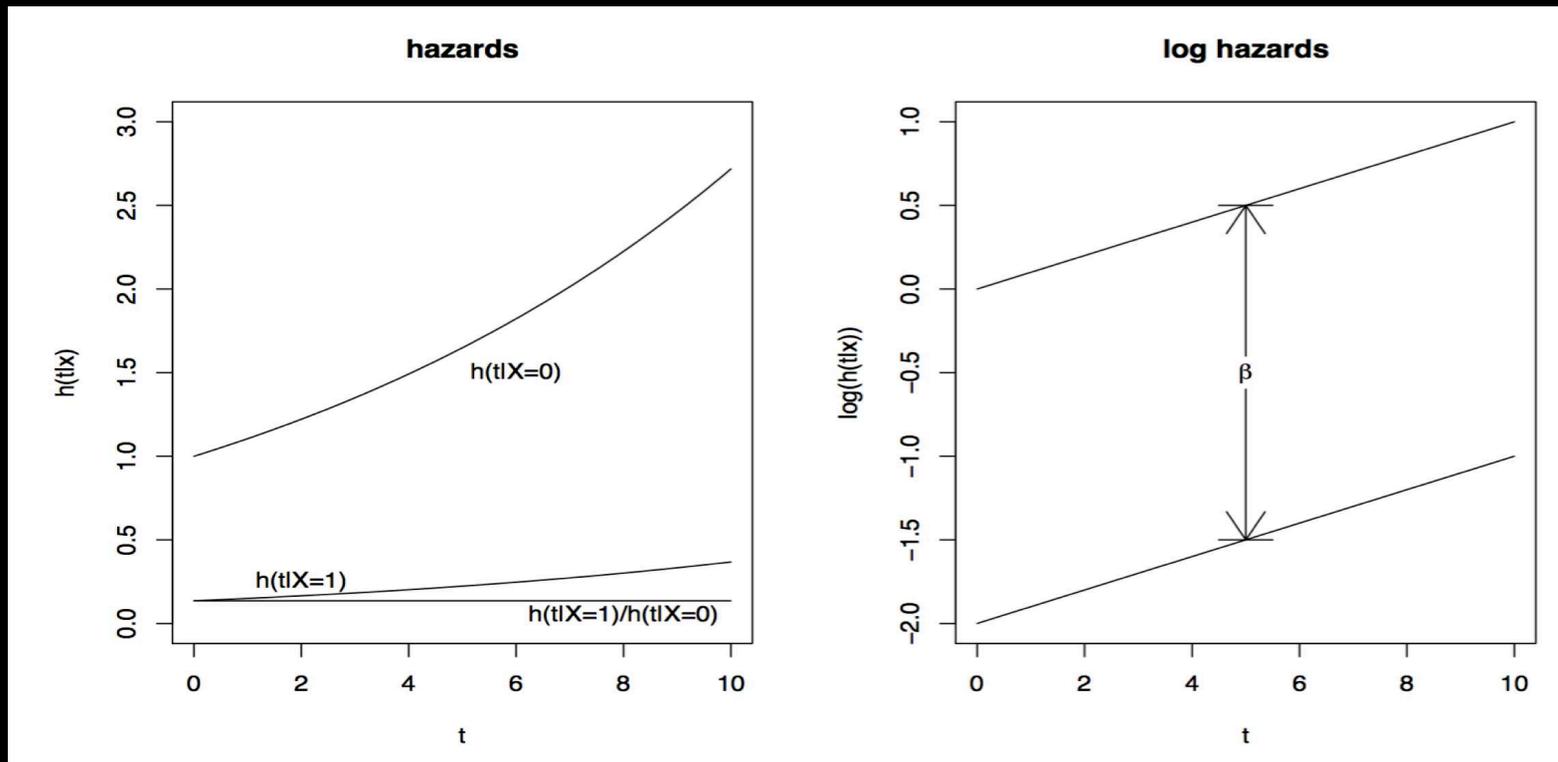
- ▶ Suppose X_1 is the treatment indicator: zero for control ($X_1 = 0$), one for treatment ($X_1 = 1$) with no other explanatory variables.
- ▶ In this case the proportional hazards model with no intercept is given for the two cases by:

$$h(t|X_1 = 0) = h(t)$$

$$h(t|X_1 = 1) = h(t) \exp(\beta_1)$$

- ▶ We can also express the same general effect holding the other explanatory variables constant.

Proportional Hazards Coefficient Interpretation



The Exponential Distribution

- ▶ The simplest model of time to event is the exponential distribution:

$$f(t) = \lambda e^{-\lambda t}, \quad \lambda > 0, t \geq 0,$$

with expected value $1/\lambda$.

- ▶ Its hazard function is constant:

$$h(t) = \lambda.$$

- ▶ The Cumulative hazard function is then:

$$H(t) = \int_0^t h(x) dx = \lambda t,$$

since:

$$\frac{d}{dt} \lambda t = \lambda.$$

- ▶ The survival function is:

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

The Exponential Distribution

- ▶ Often the exponential distribution is used to model machine survival.
- ▶ This has the property called “no aging” since the hazard function stays constant: the hazard rate plotted against time is a flat line.
- ▶ The assumption of no aging means that older units have the same hazard as younger units, which is not very realistic with animal/human survival.
- ▶ It can be realistic over a short period of time: *piece-wise constant hazard*.
- ▶ The percentiles of duration times are given by:

$$t(\text{p'tile}) = \lambda^{-1} \log \left(\frac{100}{100 - \text{p'tile}} \right)$$

where $t(\text{p'tile})$ is the percentile of interest. So the median survival time is calculated by:

$$t(50) = \lambda^{-1} \log \left(\frac{100}{100 - 50} \right) = \lambda^{-1} \log(2).$$

The Exponential Survival Model

- ▶ The parametric exponential survival model is specified by linking the single parameter to a linear additive structure.

- ▶ So for the i th case the expected duration time is $\lambda_i^{-1} = \mathbb{E}(t_i)$, leading to:

$$\lambda_i^{-1} = \exp(\mathbf{X}_i\boldsymbol{\beta})$$

where $\mathbf{X}_i\boldsymbol{\beta}$ includes an intercept.

- ▶ So that for the full sample:

$$\lambda = \exp(-\mathbf{X}\boldsymbol{\beta})$$

meaning that since the hazard rate is $h(t) = \lambda$ we get:

$$h(t) = \exp(-\mathbf{X}\boldsymbol{\beta})$$

- ▶ This can be rewritten as:

$$h(t) = \exp(-\beta_0) \exp(-\mathbf{X}\boldsymbol{\beta})$$

showing that the baseline hazard rate, $\exp(\beta_0)$, is a constant here.

- ▶ Here $\exp(-\mathbf{X}\boldsymbol{\beta})$ is called the *acceleration factor*.

The Exponential Survival Model

- ▶ So any change to the hazard rate is purely a function of the linear additive component.
- ▶ And these changes are then multiplied by the baseline hazard rate.
- ▶ Suppose we had only one dichotomous explanatory variable in the model:

$$h(t) = \exp(-\beta_0) \exp(-x_1\beta_1)$$

meaning that the baseline hazard rate is $\exp(-\beta_0)$ applied only for $x_1 = 0$, and the hazard rate for $x_1 = 1$ is $\exp(-\beta_0) \exp(-x_1\beta_1)$.

- ▶ This shows the **proportional hazards property** as simply as possible:

$$\frac{h_i(t|x_1 = 1)}{h_i(t|x_1 = 0)} = \exp(-\beta_1)$$

by notationally equating $\exp(-\beta_0) = h_i(t|x_1 = 0)$, giving the required assumption.

The Exponential Survival Model

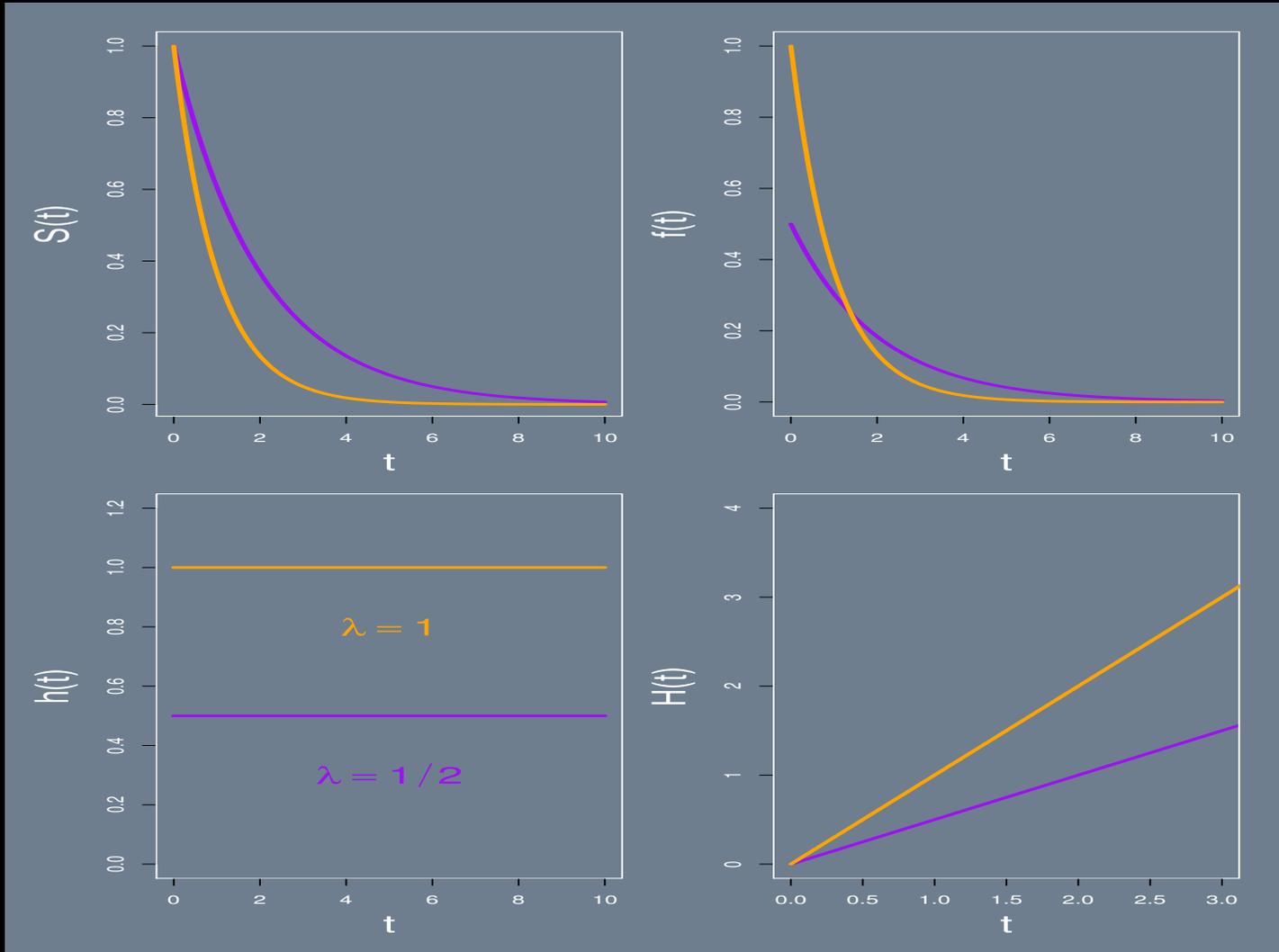
- ▶ The exponential distribution is *memoryless*, meaning that the distribution of increased survival time is not conditional on surviving up to certain time:

$$P(E > t + s | E > s) = P(E > t), \quad s, t \in [0, \infty)$$

for $t > s$.

- ▶ The mean of the exponential distribution is λ^{-1} and this also determines the variance, λ^{-2} .
- ▶ This means that the variance cannot be estimated separately and is completely determined by the estimate of the mean.
- ▶ This limitation leads to the use of other forms.

Exponential Survival Model Illustrated



Exponential Survival Model Example

► Selvin's SFMHS data:

▷ 174 white male participants in Britain

▷ $n_0 = \text{NEED}$ non-smoking with $d_0 = \text{NEED}$ deaths and $n_0 - d_0 = 9$ censored

▷ $n_1 = \text{NEED}$ smoking with $d_1 = \text{NEED}$ deaths and $n_1 - d_1 = 10$ censored

► The regression output is given by:

Variables	Symbols	Estimates	Std. errors	p-values
Baseline	b_0	-3.210	—	—
Nonsmoker/Smoker	b_1	0.135	0.161	0.404
Loglikelihood = -641.216				

Exponential Survival Model Example

- ▶ The estimated exponential hazards model is then:

$$\hat{h}(t|X) = \exp(\hat{b}_0 + \hat{b}_1 X) = \exp(-3.210 + 0.135X).$$

- ▶ For the nonsmokers:

$$\hat{h}(t|X = 0) = \exp(-3.210) = 0.040.$$

- ▶ For the smokers:

$$\hat{h}(t|X = 1) = \exp(-3.210 + 0.135) = 0.046.$$

- ▶ The hazard ratio is calculated by:

$$HR = \frac{0.046}{0.040} = 1.144 = \exp(0.135).$$

Gamma Distribution

- ▶ If the exponential distribution is too restrictive, a more flexible form is the gamma distribution.
- ▶ PDF rate version: $\mathcal{G}(x|\alpha, \beta) = \frac{\beta^\alpha}{\Gamma(\alpha)} x^{\alpha-1} \exp[-x\beta]$, $0 \leq x < \infty$, $0 \leq \alpha, \beta$.
- ▶ PDF scale version: $\mathcal{G}(x|\alpha, \beta) = \frac{\beta^{-\alpha}}{\Gamma(\alpha)} x^{\alpha-1} \exp[-x/\beta]$, $0 \leq x < \infty$, $0 < \alpha, \beta$.
- ▶ $E[X] = \frac{\alpha}{\beta}$, rate version.
- ▶ $\text{Var}[X] = \frac{\alpha}{\beta^2}$, rate version.
- ▶ $E[X] = \alpha\beta$, scale version.
- ▶ $\text{Var}[X] = \alpha\beta^2$, scale version.
- ▶ Note: the χ^2 distribution is $\mathcal{G}(\frac{\nu}{2}, \frac{1}{2})$ (ν is the degrees of freedom parameter), and the exponential distribution ($\mathcal{EX}(\beta)$) is $\mathcal{G}(1, \beta)$ (rate version).

Gamma Survival Model

- ▶ Express the gamma survival model PDF in the rate version with survival notation:

$$f(t) = \frac{\lambda^\rho}{\Gamma(\rho)} t^{\rho-1} \exp[-t\lambda]$$

where $0 \leq t < \infty$, $\lambda, \rho > 0$.

- ▶ The survival function can only be expressed with an integral:

$$S(t) = 1 - \frac{1}{\Gamma(\rho)} \int_0^{\lambda t} x^{\rho-1} \exp(-x) dx.$$

- ▶ We then have the hazard function by:

$$h(t) = \frac{f(t)}{S(t)}$$

which increases monotonically if $\rho > 1$, decreases monotonically if $\rho < 1$, and tends to λ as t goes to infinity.

- ▶ When $\rho = 1$, the gamma model simplifies to the exponential model.

Gamma Survival Model Example

- ▶ This dataset comprises measurements of fatigue life (thousands of cycles until rupture) of rectangular strips of 6061-T6 aluminum sheeting, subjected to periodic loading with maximum stress of 21,000 psi (pounds per square inch), as reported by Birnbaum and Saunders (1958).
- ▶ 102 strips were run until all of them failed (1 was spoiled).
- ▶ The data:

```
time <- c(370,1016,1235,1419,1567,1820,706,1018,1238,1420,1578,1868,  
          716,1020,1252,1420,1594,1881,746,1055,1258,1450,1602,1890,  
          785,1085,1262,1452,1604,1893,797,1102,1269,1475,1608,1895,  
          844,1102,1270,1478,1630,1910,855,1108,1290,1481,1642,1923,  
          858,1115,1293,1485,1674,1940,886,1120,1300,1502,1730,1945,  
          886,1134,1310,1505,1750,2023,930,1140,1313,1513,1750,2100,  
          960,1199,1315,1522,1763,2130,988,1200,1330,1522,1768,2215,  
          990,1200,1355,1530,1781,2268,1000,1203,1390,1540,1782,2440,  
          1010,1222,1416,1560,1792)  
ID <- 1:length(aluminum)  
event <- rep(1,length=length(ID))  
aluminum.df <- data.frame("ID"=ID, "time"=time, "event"=event)
```

Gamma Survival Model Example

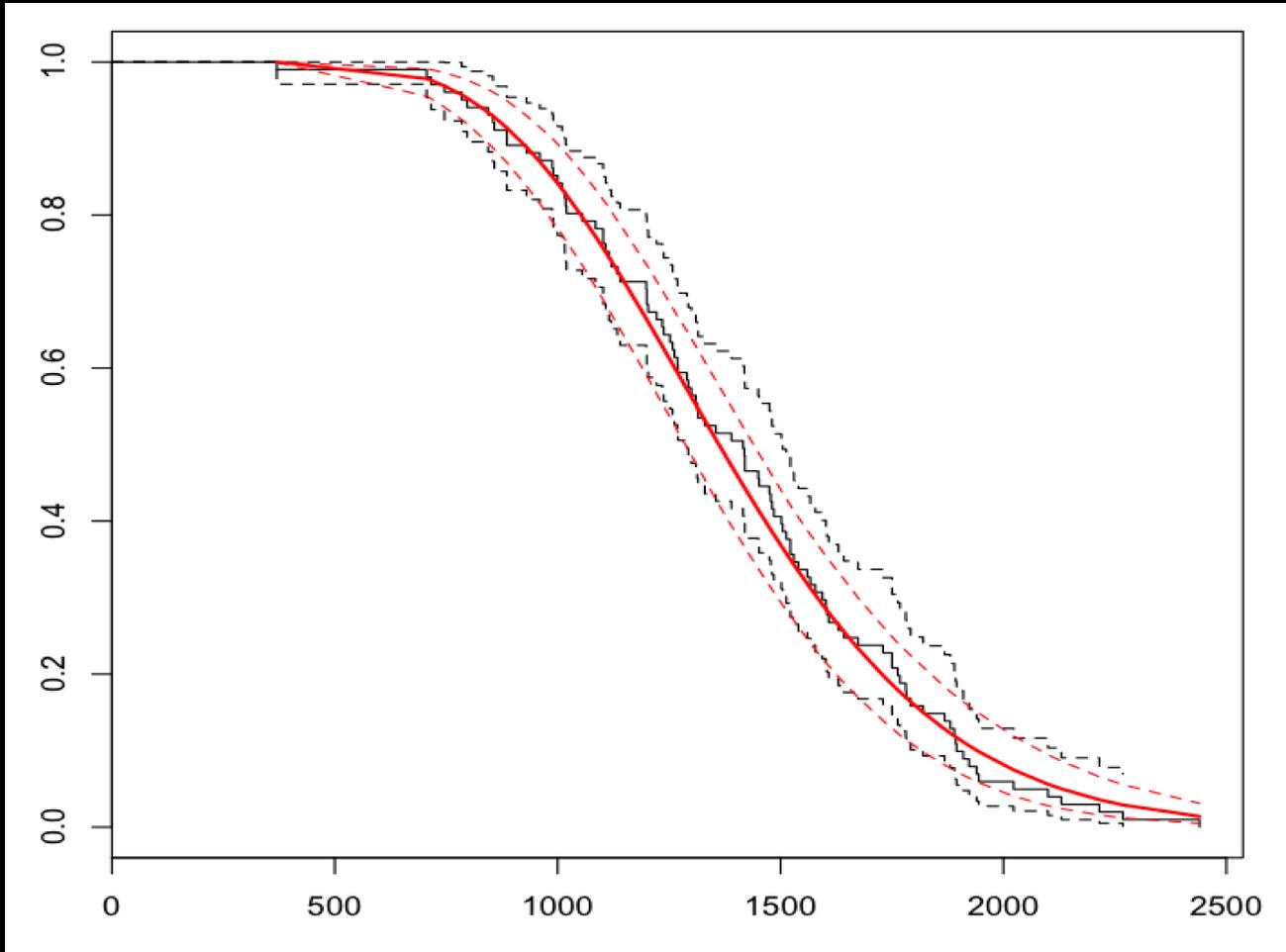
- ▶ The library `flexsurv` allows several different distributions to be specified, even custom distributions.
- ▶ Specify the model with a gamma distribution and get the parameters, plus a plot:

```
library(flexsurv)
aluminum.fit <- flexsurvreg(Surv(ID,time,event) ~ 1, dist="gamma",
                           data=aluminum.df)
```

```
aluminum.fit$coefficients
  shape    rate
2.47275 -4.77213
```

```
plot(aluminum.fit)
```

Gamma Survival Model Example



Discrete Time Models

- ▶ Motivation: even though time is continuous, nonparametric estimation methods impose discreteness.
- ▶ Any measure of time has to be discrete.
- ▶ Also, collectors of data often do not make time measurements highly granular, like measuring life in years (generating ties).
- ▶ For the support:

$$r_1, r_2, r_3, \dots, r_k$$

the random variable R has the PMF:

$$p_i = p(R = r_i), \quad i = 1, \dots, k$$

with $p_i > 0$, $\forall i$, and $\sum_{i=1}^k p_i = 1$.

Discrete Time Models

- ▶ The cumulative hazard function is:

$$F(t) = \sum_{i:r_i \leq t} p_i$$

(notice the “less than or equal.” $i : r_i \leq t$).

- ▶ The survival function is:

$$S(t) = \sum_{i:r_i \geq t} p_i$$

(notice the “greater than or equal.” $i : r_i \geq t$).

Discrete Time Models

- The hazard function is given by:

$$h_i = p(R = r_i | R \geq r_i) = \frac{p_i}{\sum_{j=1}^k p_j}, \quad i = 1, \dots, k$$

which only gives values bounded by $[0 : 1]$.

- We can relate these functions, from recursion:

$$p_i = h_i \prod_{j=1}^{i-1} (1 - h_j), \quad i = 1, \dots, k$$

and substitute this into $S(t)$ to get the discrete time survival function:

$$S(r_i) = \sum_{j=1}^k p_j = \prod_{j=1}^{i-1} (1 - h_j)$$

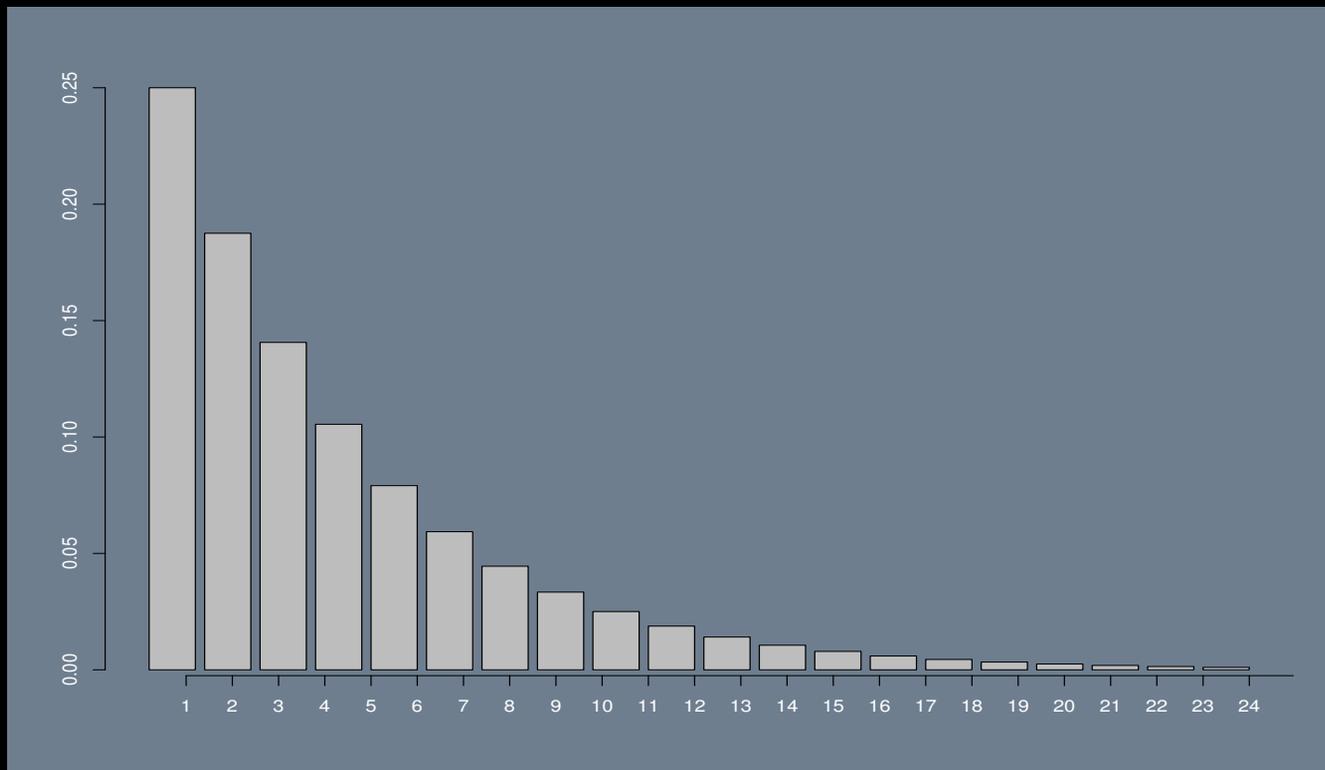
with the general form:

$$S(t) = \prod_{j:r_j < t} (1 - h_j), \quad t \geq 0,$$

which is clearly decreasing in t .

Definition of the Geometric Distribution

- ▶ PMF: $\mathcal{GEO}(x|p) = p(1-p)^{x-1}$, $x = 1, 2, \dots$, $0 \leq p \leq 1$.
- ▶ $E[X] = \frac{1}{p}$.
- ▶ $\text{Var}[X] = \frac{1-p}{p^2}$.



The Geometric Distribution

- ▶ The geometric distribution can be thought of as the discrete version of the exponential distribution.
- ▶ It has support on $1, 2, \dots$ (sometimes defined to include zero) rather than > 0 .
- ▶ Like the exponential distribution, the geometric also has a constant hazard function:

$$h_i = h, \quad 0 < h < 1, \quad i = 1, 2, \dots$$

(no aging).

- ▶ The PMF is:

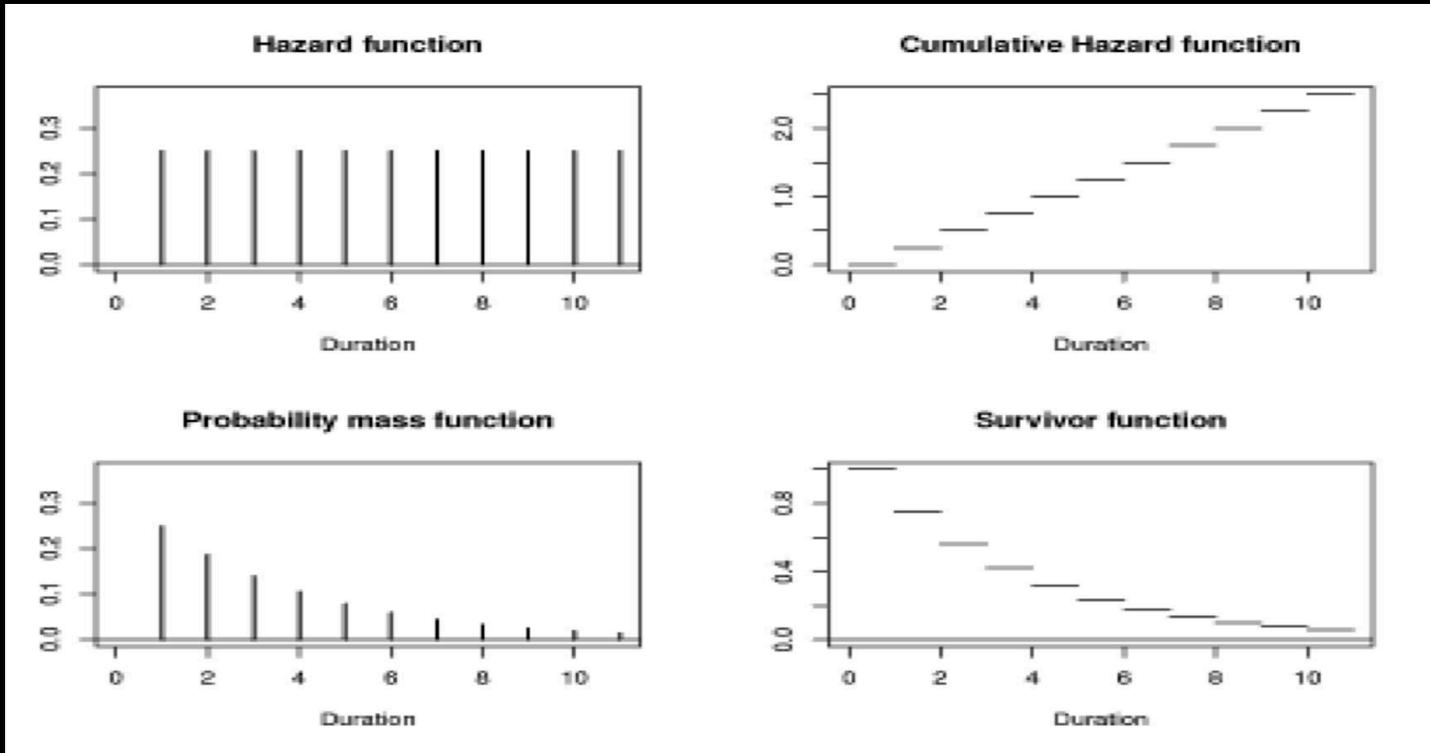
$$p_i = h(1 - h)^{i-1}$$

- ▶ The survival function is then:

$$S(t) = (1 - h)^{\lfloor t \rfloor}, \quad t \geq 0$$

Note that $\lfloor t \rfloor$ is more appropriate than the Broström book's version.

Geometric Distribution with $h = 0.25$



Hazard Atoms

- ▶ First define the **risk set** at duration t as $R(t) =$ the set of all cases still alive just prior to time t .
- ▶ This definition accounts for cases that have an event at t or are right censored at exactly time t .
- ▶ The Broström book's example is:

$$R(1) = \{1, 2, 3, 4, 5\}$$

$$R(4) = \{1, 3\}$$

$$R(6) = \{3\}$$

- ▶ Assuming the probability of an event when none happened is zero, count events and divide by the size of the risk set gives the hazard atoms: NEED TO CHECK THESE

$$\hat{h}(1) = \frac{1}{5} = 0.2$$

$$\hat{h}(4) = \frac{1}{2} = 0.5$$

$$\hat{h}(6) = \frac{1}{1} = 1.0$$

Cumulative Estimators

- ▶ Hazard items are not very revealing without some form of smoothing (kernel smoothers, etc).
- ▶ Denote $h(s)$ as the hazard atom at time s , with estimate $\hat{h}(s)$.
- ▶ The Nelson-Aalen estimator is:

$$\hat{H}(t) = \sum_{s \leq t} \hat{h}(s), \quad t \geq 0$$

which gives a upward staircase diagram (Broström Figure 2.8).

- ▶ The Kaplan-Meier estimator is:

$$\hat{S}(t) = \prod_{s < t} (1 - \hat{h}(s)), \quad t \geq 0$$

which gives a downward staircase diagram (Broström Figure 2.9).

Application

- ▶ Back to the `mort` dataset:

```
lapply(c("eha", "survival"), library, character.only=TRUE)
```

```
data(mort)
```

```
mort[1:10,]
```

	id	enter	exit	event	birthdate	ses
1	1	0.000	20.000	0	1800.010	upper
2	2	3.478	17.562	1	1800.015	lower
3	3	0.000	13.463	0	1800.031	upper
4	3	13.463	20.000	0	1800.031	lower
5	4	0.000	20.000	0	1800.064	lower
6	5	0.000	0.089	0	1800.084	lower
7	5	0.089	20.000	0	1800.084	upper
8	6	0.000	20.000	0	1800.094	upper
9	7	0.000	3.388	0	1800.105	upper
10	7	3.388	14.063	1	1800.105	lower

- ▶ Here `event` means: 1 for died during the period of study, and 0 means right censored.

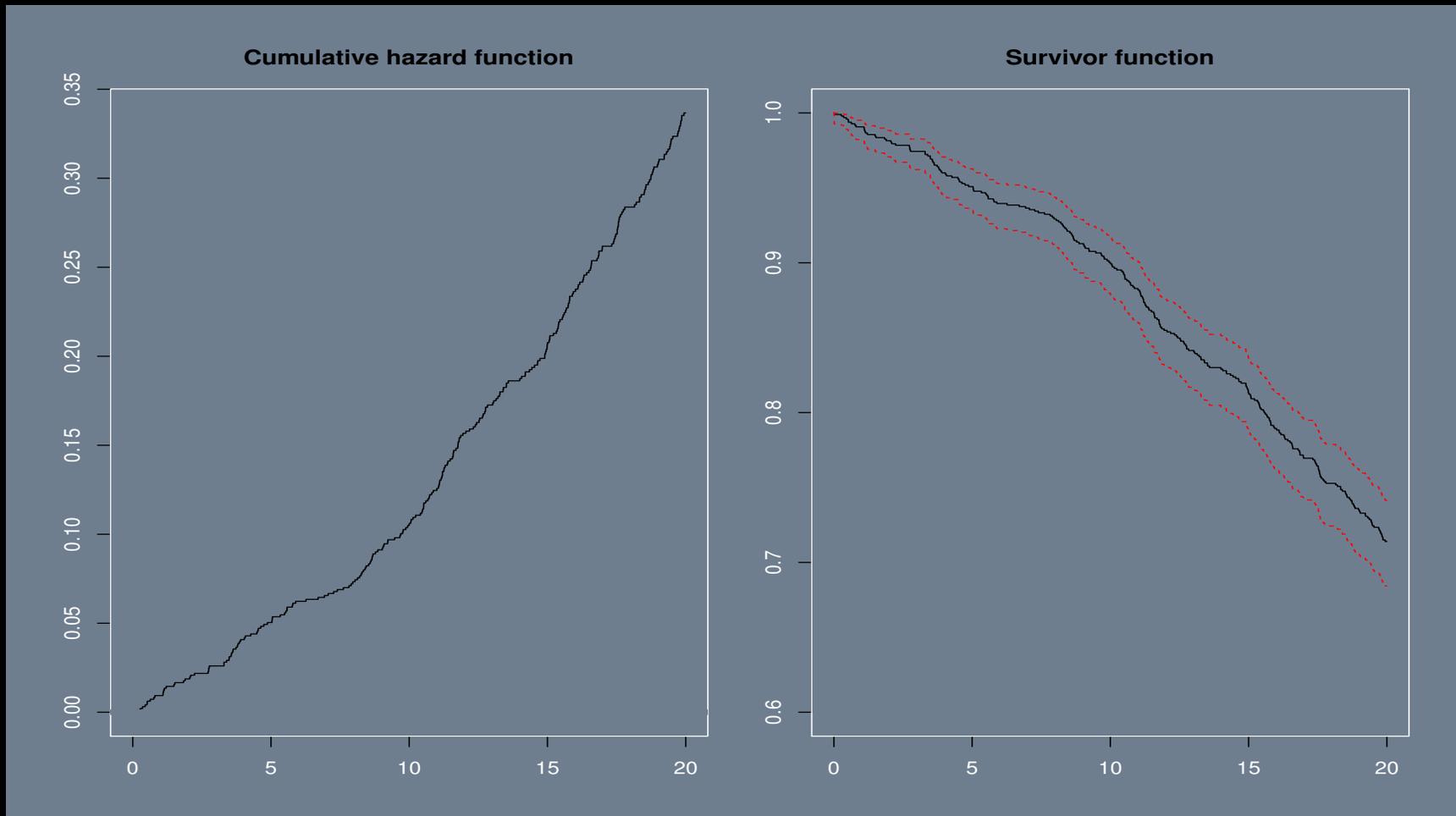
Application: Nonparametric Estimation

- ▶ Create both the Nelson-Aalen and the Kaplan-Meier plots:

```
par(mfrow=c(1,2),mar=c(3,3,3,1),oma=c(1,1,1,1),col.axis="white",  
    col.lab="white", col.sub="white",col="white",bg="slategray")  
with(mort, plot(Surv(enter, exit, event), fn = "cum"))  
abline(h=0,col="slategray",lwd=5)  
with(mort, plot(Surv(enter, exit, event), fn = "surv",ylim=c(0.6,1.0)))
```

- ▶ The definition of duration here starts at the age each man turns 20, until age 40 or death (about 22%).

Application: Graph of Nonparametric Estimation



Looking At the Kaplan-Meier Baseline Hazard Values

```
fit <- coxph(Surv(enter, exit, event) ~ 1,data=mort)
```

```
summary(survfit(fit))
```

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
0.012	969	1	0.999	0.00103	0.997	1.000
0.269	966	1	0.998	0.00146	0.995	1.000
0.354	965	1	0.997	0.00179	0.993	1.000
0.450	962	1	0.996	0.00206	0.992	1.000
:						
19.823	684	1	0.717	0.01450	0.689	0.746
19.851	683	1	0.716	0.01452	0.688	0.745
19.856	683	1	0.715	0.01454	0.687	0.744
19.936	682	1	0.714	0.01455	0.686	0.743

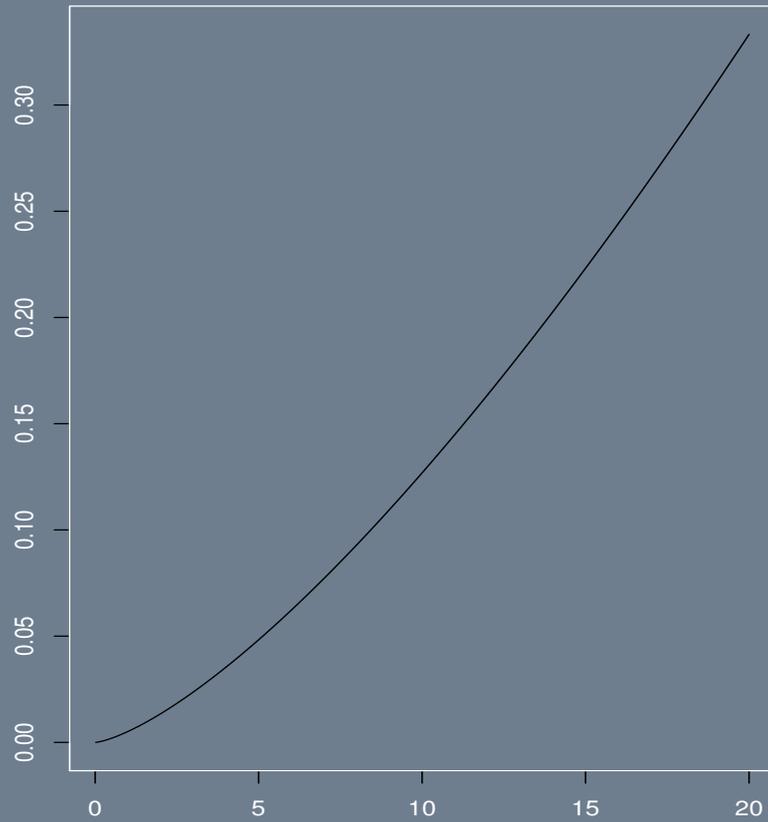
Parametric Estimation

- ▶ A “parametric proportional hazards model with no covariates.”
- ▶ Use `phreg` which uses the Weibull distribution as a default:

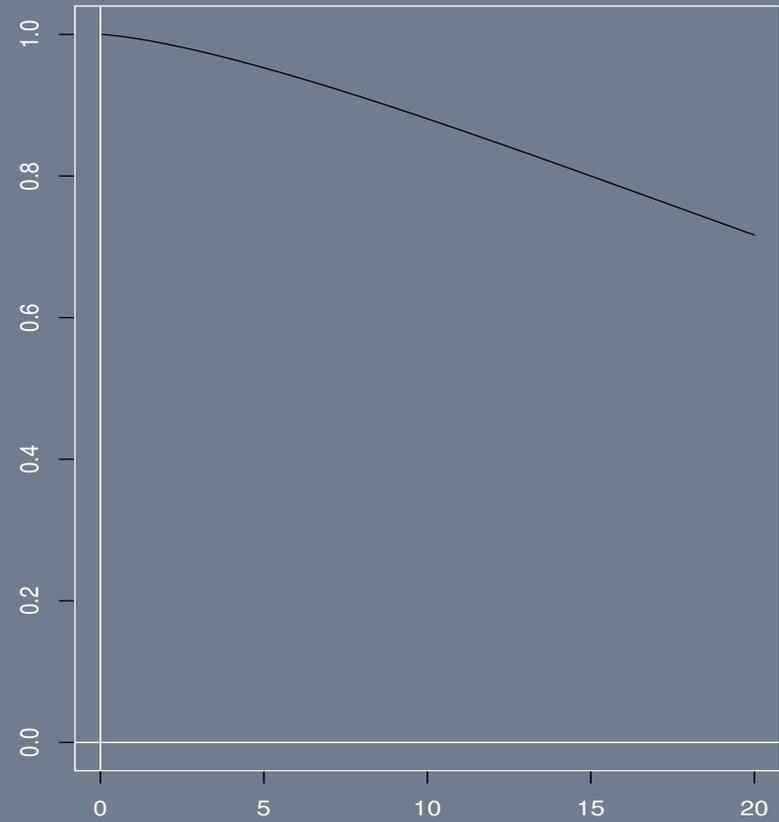
```
fit.w <- phreg(Surv(enter, exit, event) ~ 1, data=mort)
par(mfrow=c(1,2),mar=c(3,3,3,1),oma=c(1,1,1,1),col.axis="white",
    col.lab="white", col.sub="white",col="white",bg="slategray")
plot(fit.w, fn = "cum")
plot(fit.w, fn = "sur",ylim=c(0.6,1.0)) # NOTE: "sur" NOT "surv"
```

Application: Graph of Weibull Estimation

Weibull cumulative hazard function

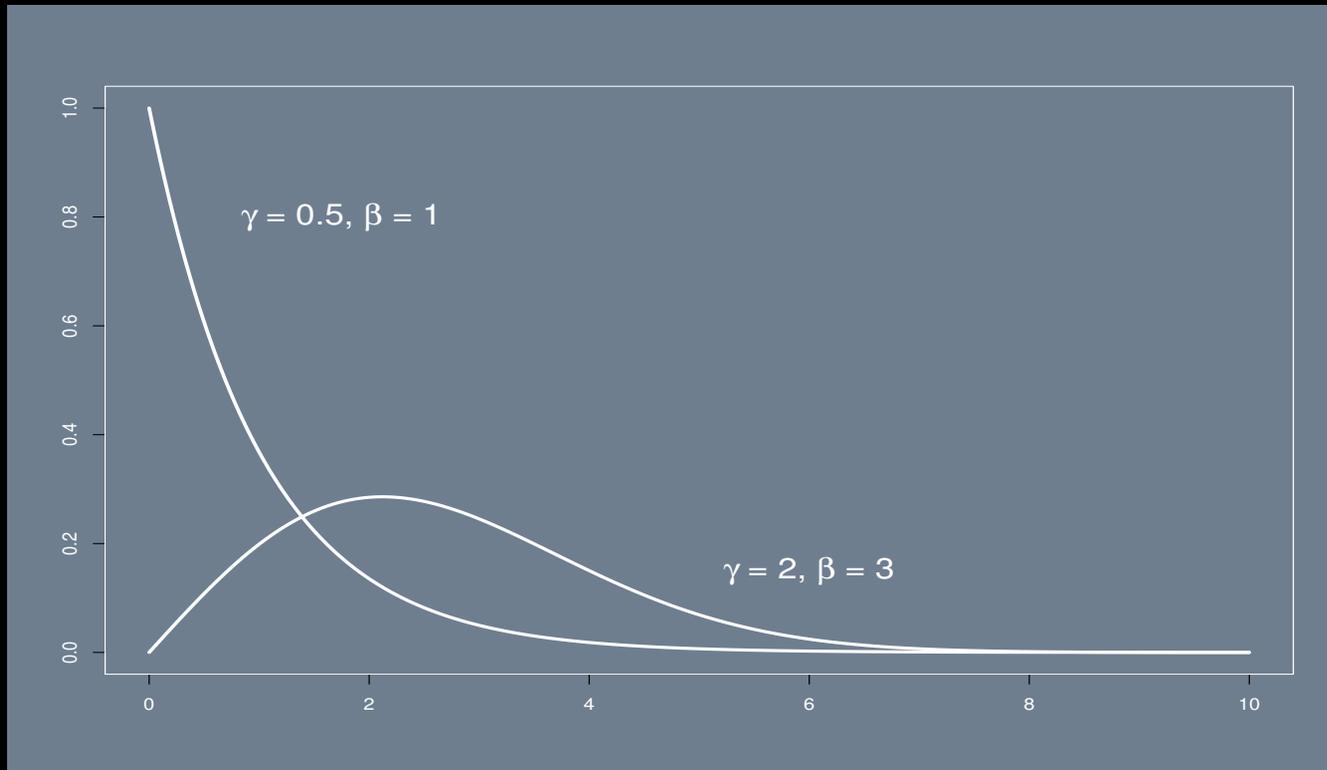


Weibull survivor function



Weibull PDF

- ▶ PDF: $w(x|\gamma, \beta) = \frac{\gamma}{\beta} x^{\gamma-1} \exp\left(-\left(\frac{x}{\beta}\right)^\gamma\right)$ if $x \geq 0$ and 0 otherwise, where: $\gamma, \beta > 0$.
- ▶ $E[\mathbf{X}_{ij}] = \beta \Gamma\left[1 + \frac{1}{\gamma}\right]$.
- ▶ $\text{Var}[X_{ij}] = \beta^2 \left(\Gamma\left[1 + \frac{2}{\gamma}\right] - \gamma \left[1 + \frac{1}{\gamma}\right]^2 \right)$



Weibull Survival

- ▶ The Weibull distribution is more flexible than the exponential or gamma, and therefore more useful for modeling survival data.
- ▶ This extra flexibility is achieved with an additional parameter, λ , which serves as a positive scale parameter.

- ▶ The hazard function is given by:

$$h(t) = \lambda p (\lambda t)^{p-1}$$

where $t, \lambda, p > 0$.

- ▶ The baseline hazard for the Weibull can be monotonically increasing ($p > 1$), monotonically decreasing ($p < 1$), or flat ($p = 1$, like the exponential) with respect to time.

- ▶ The density function is given by:

$$f(t) = \lambda p (\lambda t)^{p-1} \exp(-(\lambda t)^p).$$

- ▶ The survivor function is simply:

$$S(t) = \exp(-(\lambda t)^p).$$

Weibull Survival

- ▶ The mean survival time (expected life) is:

$$\mathbb{E}(t) = \frac{\Gamma(1 + \frac{1}{p})}{\lambda}.$$

- ▶ The percentiles of duration times are given by:

$$t(\text{p'tile}) = \lambda^{-1} \log \left(\frac{100}{100 - \text{p'tile}} \right)^{\frac{1}{p}}$$

where $t(\text{p'tile})$ is the percentile of interest. So the median survival time is calculated by:

$$t(50) = \lambda^{-1} \log \left(\frac{100}{100 - 50} \right)^{\frac{1}{p}} = \lambda^{-1} \log(2)^{\frac{1}{p}}.$$

The Weibull Survival Model

- ▶ The parametric Weibull model is specified by linking the single parameter to a linear additive structure.
- ▶ For the full sample:

$$\log(T) = \mathbf{X}\boldsymbol{\beta} + \sigma\epsilon$$

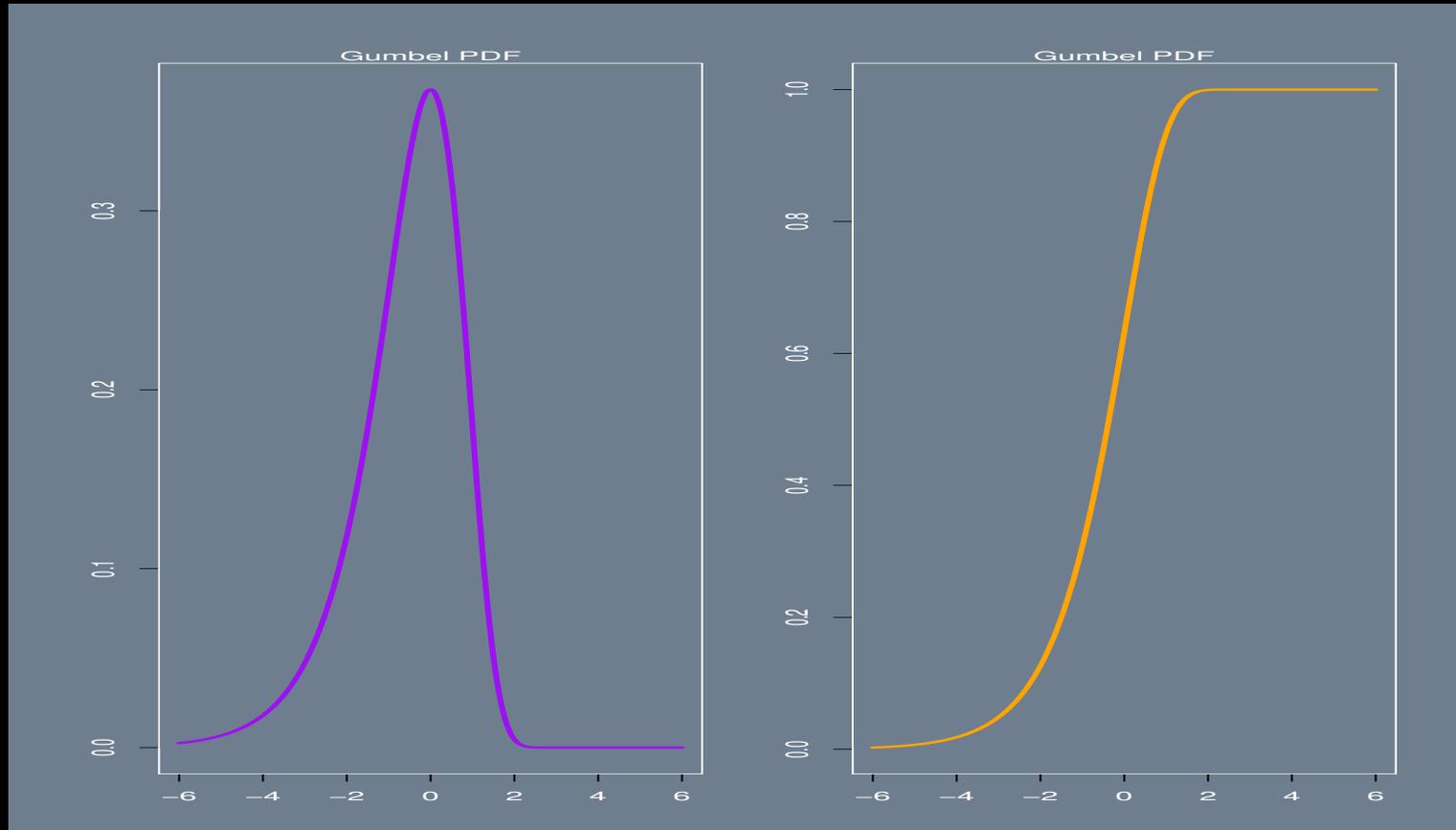
where σ is a scale parameter applied to ϵ which is a residual vector whose components are distributed Type-I extreme value (Gumbel):

$$f(\epsilon|\mu, \beta) = \frac{1}{\beta} \exp((\epsilon - \mu)/\beta) \exp[-\exp((\epsilon - \mu)/\beta)]$$

where μ is the location parameter and β is the scale parameter. The standard form of the PDF with $\mu = 0$ and $\beta = 1$ is $f(\epsilon) = \exp(\epsilon) \exp(-\exp(\epsilon))$, and the corresponding CDF is $F(\epsilon) = \exp(-\exp(\epsilon))$.

- ▶ This model is sometimes called an **accelerated failure time** (AFT) model because the log function on the LHS means that there is an exponential on the RHS around the linear additive component.

The Weibull Survival Model



The Weibull Survival Model

- ▶ The Weibull regression model can also be expressed differently as a proportional hazards model:

$$h(t|\mathbf{x}) = h_{0t} \exp(\mathbf{x}_1\beta_1 + \cdots + \mathbf{x}_k\beta_k)$$

where the baseline hazard is $h_{0t} = \exp(\beta_0)pt^{p-1}$.

- ▶ More compactly, this is:

$$h(t|\mathbf{x}) = pt^{p-1} \exp(\mathbf{x}\boldsymbol{\beta})$$

where p is the Weibull shape parameter, and $\lambda = \exp(\mathbf{x}\boldsymbol{\beta})$ is the Weibull scale parameter.

Weibull Model of UN Peacekeeping Missions

- ▶ The data durations of United Nations peacekeeping missions from 1948 to 2001 (BSJ pages 27-31, originally from Green, Kahl, and Diehl [1998]).
- ▶ There is one explanatory variable with three categories: civil war, interstate conflict, and internationalized civil war (the baseline category).
- ▶ The estimates in BSJ are MLEs from **Stata** where they run the exponential model, the Weibull AFT model, and the Weibull proportional hazards model.
- ▶ Since the exponential model is the Weibull model with $p = 1$ we can test the nested model difference.

Weibull Model of UN Peacekeeping Missions

TABLE 3.1: Weibull Model of U.N. Peacekeeping Missions

Variable	Model Parameterized As:		
	Exponential Model	Weibull A.F.T.	Weibull Prop. Hazards
Constant	Estimate (s.e.) 4.35 (.21)	Estimate (s.e.) 4.29 (.27)	Estimate (s.e.) -3.46 (.50)
Civil War	-1.16 (.36)	-1.10 (.45)	.89 (.38)
Interstate Conflict	1.64 (.50)	1.74 (.62)	-1.40 (.51)
Shape Parameter		$\sigma = 1.24 (.15)$	$p = .81 (.10)$
N	54	54	54
Log-Likelihood	-86.35	-84.66	-84.66

The baseline category denoted by the constant term represents the category of "internationalized civil wars." The column labeled "Accelerated Failure Time" presents the Weibull model estimates parameterized in terms of the model in Equation (3.21). The column labeled "Proportional Hazards" presents the Weibull model estimates parameterized in terms of the model in Equation (3.18).

Weibull Model of UN Peacekeeping Missions

▶ Since the Weibull reduces to the exponential when $p = 1$ (equivalently $\sigma = 1$), then we can test for time dependency: the exponential assumes flat/constant hazard and the Weibull does not.

▶ This test is given by:

$$z = \frac{p - 1}{SE(p)} = \frac{0.807 - 1}{1.774} = -1.93,$$

where $\hat{p} = 0.807$ (rounded in the table) with $SE(\hat{p}) = 1.774$ (not reported in the book).

▶ Therefore there is evidence that $p < 1$ (so $\sigma > 1$), meaning that the hazard rate is decreasing over time.

▶ The interpretation is that the longer UN peacekeeping lasts, the lower the risk of it terminating.

Weibull Model of UN Peacekeeping Missions

- ▶ The biggest contrast in Table 3.1 is between the two Weibull specifications where:
 - ▷ The AFT model is linear for $\log(T)$ so a positive coefficient is indicative of longer durations for increasing values of the explanatory variable.
 - ▷ Conversely, the proportional hazards model explains the hazard rate, so positive coefficients imply greater hazard with increasing values of the explanatory variable.
- ▶ For example the Civil coefficient in the AFT model is -1.10 , which can be transformed to the PH version by:

$$-(-1.10)/\sigma = 0.89.$$

Back To Censoring in BSJ Terminology

- ▶ We saw that the hazard rate, $h(t)$, can be expressed as the ratio of the PDF to the survival function, and this can be expressed in the form of definite integrals:

$$h(t) = \frac{f(t)}{S(t)} = \frac{\int_t^{t+\Delta t} f(u)du}{\int_t^{\infty} f(u)du}$$

which is the ratio of unconditional failure to survival.

- ▶ In practical situations the upper limit of the integral in the survival function is not ∞ , but is some time point set by the study, which forms the **known right censoring point**:

$$S(t) = \int_t^{t=C_i} f(u)du$$

for the i^{th} case.

- ▶ For the left censoring case, we don't have a survivor function in this context since $S(t) = 1 - H(t)$ is undefined (BSJ are wrong here and also confuse censoring versus truncation).

Censored Data Likelihood Function

- ▶ Suppose we have n cases all with observed events t_i (no censoring), then the likelihood function is imply the product of the relevant PDF:

$$\mathcal{L} = \prod_{i=1}^n f(t_i).$$

- ▶ Now there are some cases that that live past the time the study ends, t^* , so the likelihood function is now:

$$\mathcal{L} = \prod_{t_i \leq t^*} f(t_i) \prod_{t_i > t^*} S(t_i),$$

so that the uncensored cases contribute information to the likelihood function through event times, and the censored cases contribute information only through the survival function at the end-point.

- ▶ Note: on page 18 BSJ confusingly switch between t^* and t_i^* . Indexing by cases implies a more complex research design, which have not yet encountered.

Censored Data Likelihood Function

- ▶ This can be further clarified through a standard re-expression of the likelihood function.
- ▶ Start with defining a **non-censoring indicator function**:

$$\delta_i = \begin{cases} 1 & \text{if } t_i \leq t^* \\ 0 & \text{if } t_i > t^* \end{cases}$$

- ▶ Now the likelihood function for data with censoring can be expressed with a single product as:

$$\mathcal{L} = \prod_{i=1}^n \{f(t_i)\}^{\delta_i} \{S(t_i)\}^{1-\delta_i}$$

which shows the bias imposed by omitting right censored cases.

Assignment for Week 3

1. Reproduce Figure 3.1 in Box-Steffensmeier and Jones. Note that this requires rerunning the models.
2. Run a Kaplan-Meier analysis with your data.
3. Submit the data for your empirical paper.