GSERM - 2018 Introduction to Survival Data

June 6, 2018 (afternoon session)

Survival Analysis

- Models for time-to-event data.
- Roots in biostats/epidemiology, plus engineering, sociology, economics.
- Examples...
 - Political careers, confirmation durations, position-taking, bill cosponsorship, campaign contributions, policy innovation/adoption, etc.
 - Cabinet/government durations, length of civil wars, coalition durability, etc.
 - War duration, peace duration, alliance longevity, length of trade agreements, etc.
 - · Strike durations, work careers (including promotions, firings, etc.), criminal careers, marriage and child-bearing behavior, etc.

Characteristics of Time-To-Event Data

- *Discrete* events (i.e., not continuous),
- Take place over time,
- May not (or never) experience the event (i.e., possibility of censoring).

Survival Data Basics: Terminology

 Y_i = the duration until the event occurs,

 Z_i = the duration until the observation is "censored"

 $T_i = \min\{Y_i, Z_i\},$

 $C_i = 0$ if observation i is censored, 1 if it is not.

Survival Data Basics: The Density

$$f(t) = \Pr(T_i = t)$$

Issues:

- $T_i = t$ iff $T_i > t 1$, t 2, etc.
- $C_i = 0$ (censoring)

Survival Data Basics: Survivor Function

$$\Pr(T_i \leq t) \equiv F(t) = \int_0^t f(t) dt$$

$$\Pr(T_i \ge t) \equiv S(t) = 1 - F(t)$$

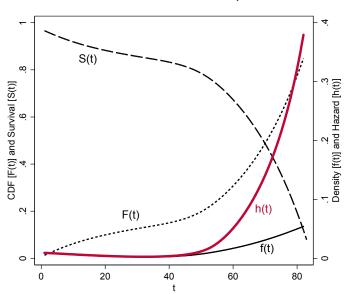
$$= 1 - \int_0^t f(t) dt$$

Survival Data Basics: The Hazard

$$Pr(T_i = t | T_i \ge t) \equiv h(t) = \frac{f(t)}{S(t)}$$

$$= \frac{f(t)}{1 - \int_0^t f(t) dt}$$

Example: Human Mortality



Some Useful Equivalencies

$$f(t) = \frac{-\partial S(t)}{\partial t}$$

Implies

$$h(t) = \frac{\frac{-\partial S(t)}{\partial t}}{S(t)}$$
$$= \frac{-\partial \ln S(t)}{\partial t}$$

More Useful Things: Integrated Hazard

Define

$$H(t) = \int_0^t h(t) dt.$$

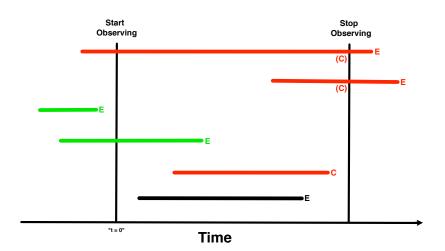
Implies

$$H(t) = \int_0^t \frac{-\partial \ln S(t)}{\partial t} dt$$
$$= -\ln[S(t)]$$

and

$$S(t) = \exp[-H(t)]$$

Censoring and Truncation



Censoring

- Defined by the researcher
- Conditionally independent of both T_i and X_i
- Doesn't mean that the observation provides no information

Estimating S(t)

Assume N observations, absorbing events, and no ties. Then define

 n_t = number of observations "at risk" for the event at t, and

 d_t = number of observations which experience the event

at time t.

Then

$$\widehat{S(t_k)} = \prod_{t \le t_k} \frac{n_t - d_t}{n_t}$$

Variance of $\widehat{S(t)}$

$$\mathsf{Var}[\widehat{S(t_k)}] = \left[\widehat{S(t_k)}\right]^2 \sum_{t \leq t_k} \frac{d_t}{n_t(n_t - d_t)}$$

Note:

- $Var[\widehat{S(t_k)}]$ is increasing in S(t),
- ullet is also increasing in d_t , but
- is decreasing in n_t .

Estimating H(t)

"Nelson-Aalen":

$$\widehat{H(t_k)} = \sum_{t < t_k} \frac{d_t}{n_t}$$

...which gives an alternative estimator for the survival function equal to:

$$\widehat{S(t_k)} = \exp[-\widehat{H(t_k)}]$$

$$= \exp\left[-\sum_{t \leq t_k} \frac{d_t}{n_t}\right]$$

Bivariate Hypothesis Testing

| | Treatment | Placebo | Total |
|----------|-----------------|-----------------|----------------|
| Event | d_{1t} | d_{0t} | d_t |
| No Event | $n_{1t}-d_{1t}$ | $n_{0t}-d_{0t}$ | $n_t - d_t$ |
| Total | n_{1t} | n _{0t} | n _t |

Log-Rank Test:

$$Q = \frac{\left[\sum (d_{1t} - \frac{n_{1t}d_t}{n_t})\right]^2}{\left[\frac{n_{1t}n_{0t}d_t(n_t - d_t)}{n_t^2(n_t - 1)}\right]}$$
$$\sim \chi_1^2$$

A Diversion: Survival Models and Counting Processes

Assume

- Event is absorbing,
- Y_i is duration to the event
- Z_i is duration to censoring
- Observe $T_i = \min(Y_i, Z_i)$, and
- C_i:
 - $C_i = 0$ if $T_i = Z_i$,
 - $C_i = 1$ if $T_i = Y_i$.
- $T_i \neq T_j \ \forall \ i \neq j \ (\text{no "ties"})$

Three Key Variables

1. Counting Process Indicator:

$$N_i(t) = I(T_i \leq t, C_i = 1)$$

2. Risk Indicator:

$$R_i(t) = I(T_i > t)$$

3. Intensity Process:

$$\lambda_i(t) dt = R_i(t)h(t)$$

Additional Things

With

$$\Lambda_i(t) = \int_0^t \lambda_i(t) dt$$

we can think of

$$N_i(t) = \Lambda_i(t) + M_i(t)$$

or

$$M_i(t) = N_i(t) - \Lambda_i(t).$$

Martingales!

$$E(X_{t+s}|X_0, X_1, ...X_i, ...X_t) = X_t \ \forall \ s > 0$$

Data Structure and Organization: Non-Time-Varying

| id | durat | censor | timein | timeout | Х |
|----|-------|--------|--------|---------|------|
| 1 | 4 | 0 | 30 | 34 | 0.12 |
| 2 | 2 | 1 | 12 | 14 | 0.19 |
| 3 | 5 | 1 | 5 | 10 | 0.09 |
| | | | | | |
| N | 10 | 1 | 21 | 31 | 0.22 |

Time-Varying Data

| id | durat | censor | timein | timeout | X | Z |
|----|-------|--------|--------|---------|------|-----|
| 1 | 1 | 0 | 30 | 31 | 0.12 | 331 |
| 1 | 2 | 0 | 31 | 32 | 0.12 | 412 |
| 1 | 3 | 0 | 32 | 33 | 0.12 | 405 |
| 1 | 4 | 0 | 33 | 34 | 0.12 | 416 |
| 2 | 1 | 0 | 12 | 13 | 0.19 | 226 |
| 2 | 2 | 1 | 13 | 14 | 0.19 | 296 |
| 3 | 1 | 0 | 5 | 6 | 0.09 | 253 |
| 3 | 2 | 0 | 6 | 7 | 0.09 | 311 |
| 3 | 3 | 0 | 7 | 8 | 0.09 | 327 |
| 3 | 4 | 0 | 8 | 9 | 0.09 | 344 |
| 3 | 5 | 1 | 9 | 10 | 0.09 | 301 |
| | | | | | | |
| | | | | | | |

Analyzing Survival Data in R

```
survival object (non-time-varying):
library(survival)
NonTV<-read.csv(NonTVdata.csv)
NonTV.S<-Surv(NonTV$duration, NonTV$censor)

survival object (time-varying):
TV<-read.csv(TVdata.csv)
TV.S<-Surv(TV$starttime, TV$endtime, TV$censor)</pre>
```

An Example

OECD Cabinet survival [Strom (1985); King et al. (1990)],

N = 314 cabinets in 15 countries

Outcome: Duration of cabinet, in months

Covariates (all non-time varying):

- · Fractionalization
- · Polarization
- · Formation Attempts
- · Investiture
- · Numerical Status
- · Post-Election
- · Caretaker

Also: Indicator for whether the cabinet ended within 12 months of the end of the "constitutional inter-election period" $(\rightarrow$ censored)

KABL Data

> head(KABL)

| | id | country | durat | ciep12 | fract | polar | format | invest | numst2 | ${\tt eltime2}$ | caretk2 |
|---|----|---------|-------|--------|-------|-------|--------|--------|--------|-----------------|---------|
| 1 | 1 | 1 | 0.5 | 1 | 656 | 11 | 3 | 1 | 0 | 1 | 0 |
| 2 | 2 | 1 | 3.0 | 1 | 656 | 11 | 2 | 1 | 1 | 0 | 0 |
| 3 | 3 | 1 | 7.0 | 1 | 656 | 11 | 5 | 1 | 1 | 0 | 0 |
| 4 | 4 | 1 | 20.0 | 1 | 656 | 11 | 2 | 1 | 1 | 0 | 0 |
| 5 | 5 | 1 | 6.0 | 1 | 656 | 11 | 3 | 1 | 1 | 0 | 0 |
| 6 | 6 | 1 | 7.0 | 1 | 634 | 6 | 4 | 1 | 1 | 1 | 0 |

> KABL.S<-Surv(KABL\$durat,KABL\$ciep12)

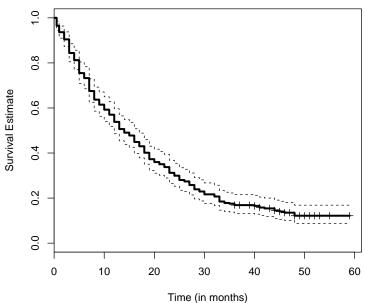
> KABL.S[1:50,]

```
[1] 0.5 3.0 7.0 20.0 6.0 7.0 2.0 17.0 27.0 49.0+
        29.0 49.0+ 6.0
[11]
    4.0
                        23.0 41.0+ 10.0
                                       12.0
                                            2.0 33.0
[21]
    1.0 16.0 2.0
                    9.0
                        3.0 5.0 5.0 6.0 45.0+ 23.0
[31] 41.0
         7.0 49.0+ 46.0
                        9.0 51.0+ 10.0
                                       32.0
                                            28.0
                                                 3.0
[41] 53.0+ 17.0 59.0+ 9.0 52.0+ 3.0 23.0
                                       33.0
                                             1.0 30.0
```

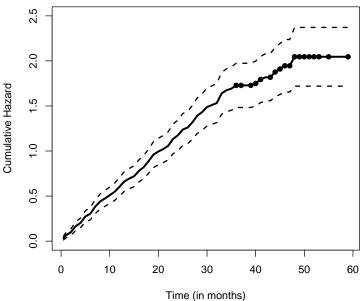
Example survfit Object

```
> KABL.fit<-survfit(KABL.S~1)
> str(KABL.fit)
List of 13
$ n : int 314
$ time : num [1:54] 0.5 1 2 3 4 5 6 7 8 9 ...
$ n.risk : num [1:54] 314 303 294 284 265 255 237 230 212 200 ...
$ n.event : num [1:54] 11 9 10 19 10 18 7 18 12 7 ...
$ n.censor : num [1:54] 0 0 0 0 0 0 0 0 0 ...
$ surv : num [1:54] 0.965 0.936 0.904 0.844 0.812 ...
$ type : chr "right"
$ std.err : num [1:54] 0.0108 0.0147 0.0183 0.0243 0.0271 ...
$ upper : num [1:54] 0.986 0.964 0.938 0.885 0.856 ...
$ lower : num [1:54] 0.945 0.91 0.873 0.805 0.77 ...
$ conf.type: chr "log"
$ conf.int : num 0.95
$ call : language survfit(formula = KABL.S ~ 1)
- attr(*, "class")= chr "survfit"
```

Plotting $\widehat{S(t)}$



Plotting $\widehat{H(t)}$



Comparing $\widehat{S(t)}$ s

```
Log-rank test:
```

> survdiff(KABL.S~invest,data=KABL,rho=0)

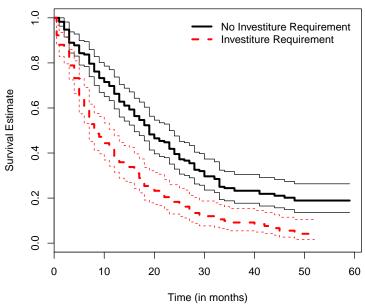
Call:

survdiff(formula = KABL.S ~ invest, data = KABL, rho = 0)

N Observed Expected (0-E)^2/E (0-E)^2/V invest=0 172 137 178.7 9.72 30.5 invest=1 142 134 92.3 18.81 30.5

Chisq= 30.5 on 1 degrees of freedom, p= 3.26e-08

Comparing $\widehat{S(t)}$ s



A General Parametric Model

$$f(t) = \lim_{\Delta t \to 0} \frac{\Pr(t \le T < t + \Delta t)}{\Delta t}$$

$$S(t) = \Pr(T \ge t)$$

$$= 1 - \int_0^t f(t) dt$$

$$= 1 - F(t)$$

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

$$= \lim_{\Delta t \to 0} \frac{\Pr(t \le T < t + \Delta t | T \ge t)}{\Delta t}$$

Likelihood

$$L = \prod_{i=1}^{N} [f(T_i)]^{C_i} [S(T_i)]^{1-C_i}$$

$$\ln L = \sum_{i=1}^{N} \left\{ C_{i} \ln \left[f(T_{i}) \right] + (1 - C_{i}) \ln \left[S(T_{i}) \right] \right\}$$

$$\ln L|\mathbf{X},\boldsymbol{\beta} = \sum_{i=1}^{N} \left\{ C_{i} \ln \left[f(T_{i}|\mathbf{X},\boldsymbol{\beta}) \right] + (1 - C_{i}) \ln \left[S(T_{i}|\mathbf{X},\boldsymbol{\beta}) \right] \right\}$$

The Exponential Model

$$h(t) = \lambda$$

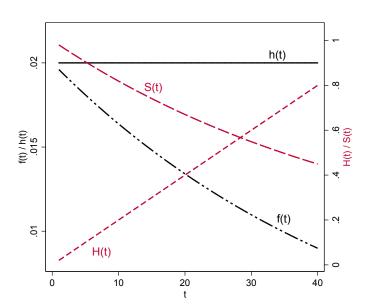
$$H(t) = \int_0^t h(t) dt$$
$$= \lambda t$$

$$S(t) = \exp[-H(t)]$$
$$= \exp(-\lambda t)$$

$$f(t) = h(t)S(t)$$

= $\lambda \exp(-\lambda t)$

The Exponential Model, Illustrated



Covariates

$$\lambda_i = \exp(\mathbf{X}_i \beta).$$

$$S_i(t) = \exp(-e^{\mathbf{X}_i\beta}t).$$

Exponential (log-)Likelihood

$$\ln L = \sum_{i=1}^{N} \left\{ C_{i} \ln \left[\exp(\mathbf{X}_{i}\beta) \exp(-e^{\mathbf{X}_{i}\beta}t) \right] + (1 - C_{i}) \ln \left[\exp(-e^{\mathbf{X}_{i}\beta}t) \right] \right\}$$

$$= \sum_{i=1}^{N} \left\{ C_{i} \left[(\mathbf{X}_{i}\beta)(-e^{\mathbf{X}_{i}\beta}t) \right] + (1 - C_{i})(-e^{\mathbf{X}_{i}\beta}t) \right\}$$

Exponential: "AFT"

$$\ln T_i = \mathbf{X}_i \gamma + \epsilon_i$$

$$T_i = \exp(\mathbf{X}_i \gamma) \times u_i$$

$$\epsilon_i = \ln T_i - \mathbf{X}_i \gamma$$

Interpretation: Hazard Ratios

$$\begin{aligned} \mathsf{HR}_k &= \frac{h(t)|\widehat{X_k} = 1}{h(t)|\widehat{X_k} = 0} \\ h_i(t) &= \exp(\beta_0) \exp(\mathbf{X}_i \beta) \end{aligned}$$

$$\mathsf{HR}_k &= \frac{h(t)|\widehat{X_k} = 1}{h(t)|\widehat{X_k} = 0} \\ &= \frac{\exp(\hat{\beta}_0 + X_1 \hat{\beta}_1 + \dots + \hat{\beta}_k (1) + \dots)}{\exp(\hat{\beta}_0 + X_1 \hat{\beta}_1 + \dots + \hat{\beta}_k (0) + \dots)} \\ &= \frac{\exp(\hat{\beta}_k \times 1)}{\exp(\hat{\beta}_k \times 0)} \\ &= \exp(\hat{\beta}_k) \end{aligned}$$

More Generally

$$HR_k = \frac{\hat{h}(t)|X_k + \delta}{\hat{h}(t)|X_k}$$
$$= \exp(\delta \, \hat{\beta}_k)$$

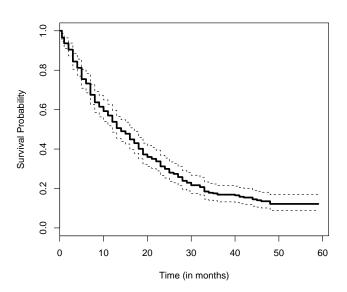
$$\mathsf{HR}_{\frac{i}{j}} = \frac{\mathsf{exp}(\mathbf{X}_i\hat{eta})}{\mathsf{exp}(\mathbf{X}_j\hat{eta})}$$

Example: King et al. (1990) Data

> summary(KABL)

```
id
                                      durat
                                                      ciep12
                    country
Min.
       : 1.00
                 Min. : 1.000
                                  Min. : 0.50
                                                 Min.
                                                         :0.0000
1st Qu.: 79.25
                 1st Qu.: 4.000
                                 1st Qu.: 6.00
                                                 1st Qu.:1.0000
Median :157.50
                 Median : 7.000
                                 Median :14.00
                                                 Median :1.0000
Mean
       :157.50
                 Mean
                        : 7.182
                                 Mean
                                         :18.44
                                                 Mean
                                                         :0.8631
3rd Qu.:235.75
                 3rd Qu.:10.000
                                  3rd Qu.:28.00
                                                 3rd Qu.:1.0000
Max.
       :314.00
                 Max.
                        :15.000
                                 Max.
                                        :59.00
                                                 Max.
                                                       :1.0000
   fract
                   polar
                                    format.
                                                    invest
Min.
       :349.0
                Min.
                       : 0.00
                               Min.
                                       :1.000
                                               Min.
                                                       :0.0000
1st Qu.:677.0
                1st Qu.: 3.00
                               1st Qu.:1.000
                                               1st Qu.:0.0000
Median :719.0
                Median :14.50
                               Median :1.000
                                               Median :0.0000
Mean
       :718.8
               Mean
                       :15.29
                               Mean
                                       :1.904
                                             Mean
                                                       :0.4522
3rd Qu.:788.0
                3rd Qu.:25.00
                               3rd Qu.:2.000
                                               3rd Qu.:1.0000
Max.
       :868.0
                Max.
                       :43.00
                               Max.
                                       :8.000
                                               Max.
                                                       :1.0000
   numst2
                    eltime2
                                    caretk2
Min.
       :0.0000
                 Min.
                        :0.0000
                                 Min.
                                         :0.00000
1st Qu.:0.0000
                 1st Qu.:0.0000
                                 1st Qu.:0.00000
                Median :0.0000
                                 Median :0.00000
Median :1.0000
       :0.6306
                       :0.4873
                                        :0.05414
Mean
                 Mean
                                 Mean
3rd Qu.:1.0000
                 3rd Qu.:1.0000
                                  3rd Qu.:0.00000
Max.
       :1.0000
                 Max.
                       :1.0000
                                  Max.
                                         :1.00000
```

Cabinet Durations: Kaplan-Meier



Exponential Model (AFT form)

```
> KABL.S<-Surv(KABL$durat.KABL$ciep12)</p>
> xvars<-c("fract","polar","format","invest","numst2","eltime2","caretk2")
> MODEL<-as.formula(paste(paste("KABL.S ~ ", paste(xvars,collapse="+"))))
> KABL.exp.AFT<-survreg(MODEL.data=KABL.dist="exponential")
> summary(KABL.exp.AFT)
Call:
survreg(formula = MODEL, data = KABL, dist = "exponential")
              Value Std. Error
                                  z
(Intercept) 3.72460 0.630834 5.90 3.54e-09
fract
          -0.00116 0.000905 -1.29 1.98e-01
polar
          -0.01610 0.006097 -2.64 8.28e-03
format.
         -0.09097 0.045544 -2.00 4.58e-02
invest -0.36937 0.139398 -2.65 8.06e-03
numst2 0.51464 0.129233 3.98 6.83e-05
eltime2 0.72316 0.134999 5.36 8.47e-08
caretk2
         -1.30035 0.259566 -5.01 5.45e-07
Scale fixed at 1
Exponential distribution
Loglik(model) = -1025.6 Loglik(intercept only) = -1100.7
Chisq= 150.21 on 7 degrees of freedom, p= 0
Number of Newton-Raphson Iterations: 4
n = 314
```

Exponential Model (hazard form)

```
> KABL.exp.PH<-(-KABL.exp.AFT$coefficients)
```

> KABL.exp.PH

(Intercept) fract polar format invest -3.724598700 0.001163784 0.016098468 0.090965318 0.369367997

numst2 eltime2 caretk2 -0.514643548 -0.723161401 1.300349770

Exponential: Hazard Ratios

- > KABL.exp.HRs<-exp(-KABL.exp.AFT\$coefficients)
- > KABL.exp.HRs

```
(Intercept) fract polar format invest numst2 0.02412278 1.00116446 1.01622875 1.09523102 1.44681993 0.59771361
```

eltime2 caretk2 0.48521587 3.67058030

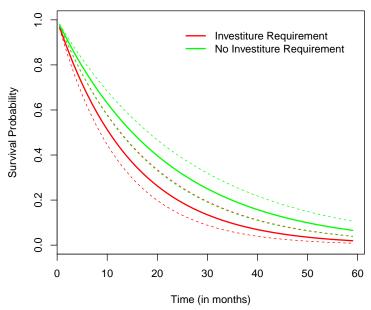
Hazard Ratios: Interpretation

- On average, an investiture requirement *increases* the *hazard* of cabinet failure by $100 \times (1.447 1) = 44.7$ percent.
- On average, an investiture requirement *decreases* the predicted *survival* time by

```
100 \times [1 - \exp(-0.369)] = 100 \times (1 - 0.691)
= 30.1 percent.
```

Comparing Predicted Survival

Comparing Predicted Survival



The Weibull Model, I

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

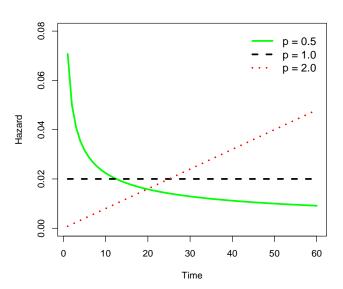
$$S(t) = \exp \left[-\int_0^t \lambda p(\lambda t)^{p-1} dt \right]$$
$$= \exp(-\lambda t)^p$$

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

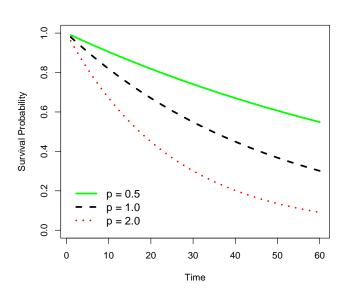
The Importance of p

- $p=1 o ext{exponential model}$
- $p > 1 \rightarrow \text{rising hazards}$
- 0 declining hazards

Weibull Hazards Illustrated



Weibull Survival



Covariates

$$\lambda_i = \exp(\mathbf{X}_i \beta)$$

Weibull: AFT

$$T_i = \exp(\mathbf{X}_i \gamma) \times \sigma u_i$$

Means:

$$p = 1/\sigma$$

$$\beta = -\gamma/\sigma$$

Weibull Example (AFT)

```
> KABL.weib.AFT<-survreg(MODEL,data=KABL,dist="weibull")
> summary(KABL.weib.AFT)
Call:
survreg(formula = MODEL, data = KABL, dist = "weibull")
              Value Std. Error
                                          р
(Intercept) 3.69641 0.491590 7.52 5.51e-14
fract.
           -0.00106 0.000705 -1.50 1.33e-01
polar
         -0.01508 0.004677 -3.22 1.26e-03
       -0.08675 0.035133 -2.47 1.35e-02
format
invest -0.33019 0.106991 -3.09 2.03e-03
numst2 0.46352 0.100367 4.62 3.87e-06
eltime2 0.66381 0.104265 6.37 1.93e-10
caretk2 -1.31758 0.201065 -6.55 5.64e-11
Log(scale) -0.26079 0.049971 -5.22 1.80e-07
Scale= 0.77
Weibull distribution
Loglik(model) = -1013.5 Loglik(intercept only) = -1100.6
Chisq= 174.23 on 7 degrees of freedom, p= 0
Number of Newton-Raphson Iterations: 5
n = 314
```

Weibull Example (hazard)

```
> KABL.weib.PH<-(-KABL.weib.AFT$coefficients)/(KABL.weib.AFT$scale)
```

> KABL.weib.PH

```
(Intercept) fract polar format invest -4.797770943 0.001374065 0.019573990 0.112598478 0.428574214
```

numst2 eltime2 caretk2 -0.601628072 -0.861597589 1.710156135

Weibull Hazard Ratios

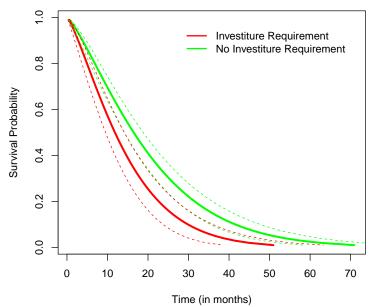
```
> KABL.weib.HRs<-exp(KABL.weib.PH)
> KABL.weib.HRs

(Intercept) fract polar format invest numst2
0.008248112 1.001375009 1.019766817 1.119182466 1.535067285 0.547918858
eltime2 caretk2
0.422486583 5.529824807
```

Interpretation:

• On average, an investiture requirement *increases* the *hazard* of cabinte failure by $100 \times (1.535 - 1) = 53.5$ percent.

Comparing Predicted Survival Curves



The Gompertz Model (hazard)

$$h(t) = \exp(\lambda) \exp(\gamma t)$$

$$S(t) = \exp\left[-rac{e^{\lambda}}{\gamma}(e^{\gamma t}-1)
ight]$$

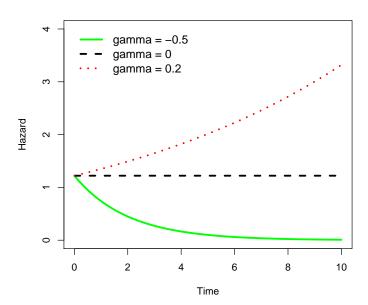
with

$$\lambda_i = \exp(\mathbf{X}_i \beta)$$

 γ is for "Gompertz"

- $\gamma = 0 o$ constant hazard
- $\gamma > 0 \rightarrow {\rm rising\ hazard}$
- $\gamma <$ 0 \rightarrow declining hazard

Gompertz Hazards



Gompertz Estimates

```
> library(flexsurv)
```

> KABL.Gomp

Call:

flexsurvreg(formula = MODEL, data = KABL, dist = "gompertz")

Estimates:

| | data mean | est | L95% | U95% | exp(est) | L95% | U95% |
|---------|-----------|----------|----------|----------|----------|---------|---------|
| shape | NA | 0.02320 | 0.01150 | 0.03490 | NA | NA | NA |
| rate | NA | 0.01520 | 0.00407 | 0.05680 | NA | NA | NA |
| fract | 719.00000 | 0.00140 | -0.00039 | 0.00319 | 1.00000 | 1.00000 | 1.00000 |
| polar | 15.30000 | 0.01890 | 0.00666 | 0.03120 | 1.02000 | 1.01000 | 1.03000 |
| format | 1.90000 | 0.10700 | 0.01590 | 0.19800 | 1.11000 | 1.02000 | 1.22000 |
| invest | 0.45200 | 0.41200 | 0.13700 | 0.68600 | 1.51000 | 1.15000 | 1.99000 |
| numst2 | 0.63100 | -0.60800 | -0.86800 | -0.34900 | 0.54400 | 0.42000 | 0.70500 |
| eltime2 | 0.48700 | -0.87300 | -1.15000 | -0.59400 | 0.41800 | 0.31600 | 0.55200 |
| caretk2 | 0.05410 | 1.46000 | 0.94500 | 1.98000 | 4.32000 | 2.57000 | 7.24000 |

N = 314, Events: 271, Censored: 43 Total time at risk: 5789.5

Log-likelihood = -1018.317, df = 9

AIC = 2054.634

> KABL.Gomp<-flexsurvreg(MODEL,data=KABL,dist="gompertz")

The Log-Logistic Model

$$In(T_i) = \mathbf{X}_i \beta + \sigma \epsilon_i$$

$$S(t) = \frac{1}{1 + (\lambda t)^p}$$

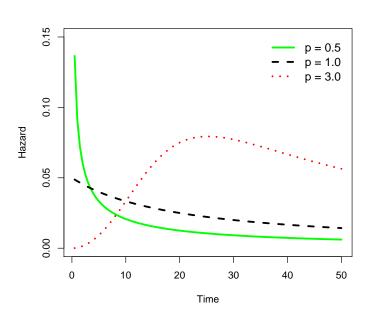
$$h(t) = \frac{\lambda p(\lambda t)^{p-1}}{1 + (\lambda t)^p}$$

$$f(t) = \frac{\lambda p(\lambda t)^{p-1}}{1 + (\lambda t)^p} \times \frac{1}{1 + (\lambda t)^p}$$

$$= \frac{\lambda p(\lambda t)^{p-1}}{[1 + (\lambda t)^p]^2}$$

$$\lambda_i = \exp(\mathbf{X}_i \beta)$$

Log-Logistics Illustrated



Example: Log-Logistic

```
> KABL.loglog<-survreg(MODEL,data=KABL,dist="loglogistic")
> summary(KABL.loglog)
Call:
survreg(formula = MODEL, data = KABL, dist = "loglogistic")
              Value Std. Error
                                   z
                                           р
(Intercept) 3.333841 0.54735 6.09 1.12e-09
fract.
          -0.000913 0.00079 -1.15 2.48e-01
polar
         -0.019092 0.00588 -3.24 1.18e-03
       -0.096975 0.04315 -2.25 2.46e-02
format
invest -0.357403 0.12876 -2.78 5.51e-03
numst2 0.479507 0.12104 3.96 7.45e-05
eltime2 0.627837 0.12405 5.06 4.16e-07
caretk2 -1.252349 0.23151 -5.41 6.32e-08
Log(scale) -0.568276
                     0.05116 -11.11 1.14e-28
Scale = 0.567
Log logistic distribution
Loglik(model) = -1024 Loglik(intercept only) = -1099
Chisq= 150.05 on 7 degrees of freedom, p= 0
Number of Newton-Raphson Iterations: 4
n = 314
```

Other Parametric Survival Models

- Log-Normal
- Rayleigh (Weibull w/p = 2)
- Logistic
- t
- Generalized Gamma

Software

R:

- survreg (in survival)
- rms package
- flexsurv package
- eha package
- SurvRegCensCov package (Weibull models)

Software

Notes on parametric models with time-varying covariate data:

- · Stata handles time-varying data with aplomb.
- · R does not.
 - survreg (in the survival package) will not estimate models with time-varying data (it will not take a survival object of the form Surv(start,stop,censor)).
 - · psm (in the rms package) will also not accept time-varying data.
 - aftreg and phreg (part of the eha package) will accept time-varying data. phreg accepts survival objects of the form Surv(start, stop, censor). aftreg does as well, and notes in its documentation that "(I)f there are [sic] more than one spell per individual, it is essential to keep spells together by the id argument. This allows for time-varying covariates." In practice, this functions somewhat inconsistently.
- Recommendations: If you want to use R to fit parametric survival models with time-varying covariate data, stick with proportional hazards formulations, and use phreg. Also, Weibull models tend to be easier to fit than exponentials in this framework.