GSERM – **2023** Introduction to Survival Analysis

June 23, 2023

Survival Analysis

"Survival" / "Duration" / "Event History" Models

- Models for time-to-event data.
- Roots in biostats/epidemiology, plus engineering, sociology, economics.

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

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

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

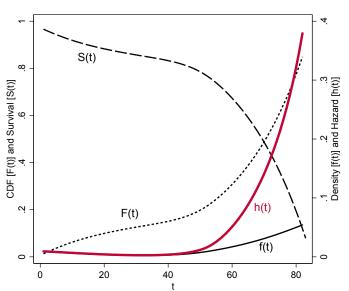
$$= 1 - \int_0^t f(t) dt$$

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

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

More Useful Things: Integrated Hazard

Define

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

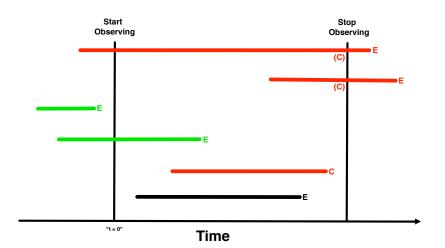
Implies

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

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

 $d_t = \operatorname{\mathsf{number}}$ of observations which experience the event

at time t.

Then

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

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

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

Note:

- $Var[\hat{S}(t_k)]$ is increasing in S(t),
- 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:

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

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

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:

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

Data Structure and Organization: Non-Time-Varying

| id | durat | censor | timein | timeout | X |
|----|-------|--------|--------|---------|------|
| 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 | Х | 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)</pre>
```

TV.S<-Surv(TV\$starttime, TV\$endtime, TV\$censor)

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+

[11] 4.0 29.0 49.0+ 6.0 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

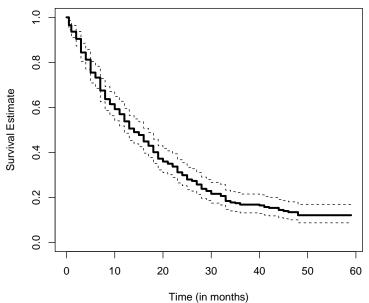
[31] 41.0 7.0 49.0+ 46.0 9.0 51.0+ 10.0 32.0 28.0 3.0

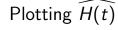
[41] 53.0+ 17.0 59.0+ 9.0 52.0+ 3.0 23.0 33.0 1.0 30.0
```

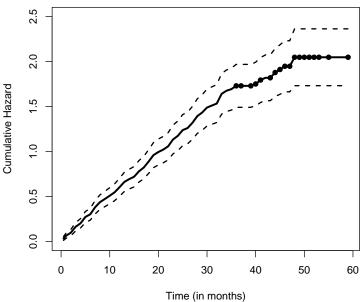
Example survfit Object

```
> KABL.fit<-survfit(KABL.S~1)</pre>
> 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 $\widehat{S(t)}$







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

```
Log-rank test:
```

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

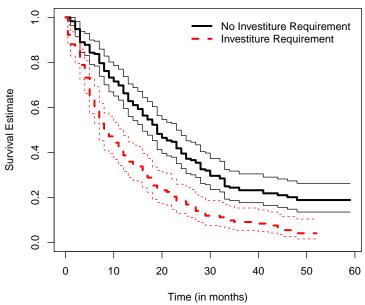
Call:

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

| | N | Observed | Expected | $(0-E)^2/E$ | $(0-E)^2/V$ |
|------------------|-----|----------|----------|-------------|-------------|
| ${\tt invest=0}$ | 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



Parametric Survival Regression

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

$$h(t) = \lambda$$

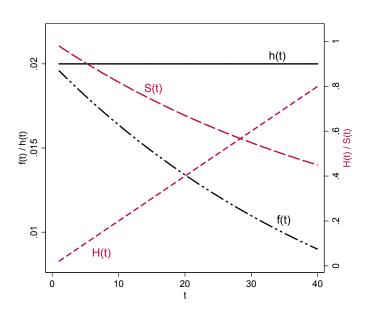
$$H(t) = \int_0^t h(t) dt$$
$$= \lambda t$$

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

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

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

The Exponential Model, Illustrated



Exponential Model (continued)

Covariates:

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

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

Log-likelihood:

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

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

Interpretation: Hazard Ratios

$$\mathsf{HR}_k = \frac{h(t)|\widehat{X_k} = 1}{h(t)|\widehat{X_k} = 0}$$
 $h_i(t) = \exp(eta_0)\exp(\mathbf{X}_ieta)$

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

More Generally

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

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

Interpretation: Survival Rates

Predicted survival is:

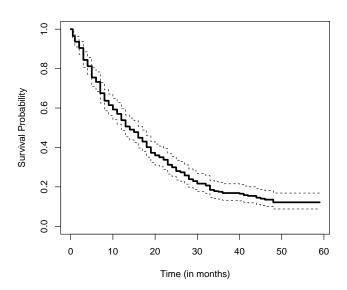
$$\widehat{S(t)} = \exp(-e^{\mathbf{X}_i\hat{\beta}}t).$$

So:

- Increases in hazards \rightarrow decreases in survival times.
- Proportional increases in hazards rightarrow proportional decreases in survival times.
- Specifically, a one-unit increase in *X* implies a proportional change in the predicted survival time of:

$$1 - \exp(-\hat{eta})$$

Cabinet Durations: Kaplan-Meier



Exponential Model

```
> KABL.S<-Surv(KABL$durat,KABL$ciep12)
> xvars<-c("fract", "polar", "format", "invest", "numst2", "eltime2", "caretk2")
> MODEL<-as.formula(paste(paste("KABL.S ~ ", paste(xvars,collapse="+"))))
> KABL.exp<-phreg(MODEL,data=KABL,dist="weibull",shape=1)
> KABL.exp
Call:
phreg(formula = MODEL, data = KABL, dist = "weibull", shape = 1)
Covariate
                  W mean
                             Coef Exp(Coef)
                                             se(Coef)
                                                        Wald p
fract
                 692.734
                            0.001
                                      1.001
                                                0.001
                                                         0 198
polar
                            0.016
                                     1.016
                                               0.006
                                                         0.008
                  10.521
format
                   1.690
                           0.091
                                    1.095
                                              0.046
                                                         0.046
invest
                  0.332
                           0.369 1.447 0.139
                                                         0.008
numst2
                  0.713
                           -0.515 0.598 0.129
                                                         0.000
eltime2
                   0 665
                           -0.723
                                      0.485
                                               0 135
                                                         0.000
caretk2
                   0.009
                            1.300
                                      3.671
                                               0.260
                                                         0.000
log(scale)
                             3.725
                                                0.631
                                                         0.000
Shape is fixed at 1
Events
                         271
Total time at risk
                         5789.5
Max. log. likelihood
                        -1025.6
LR test statistic
                        150.21
Degrees of freedom
Overall p-value
                         Ω
```

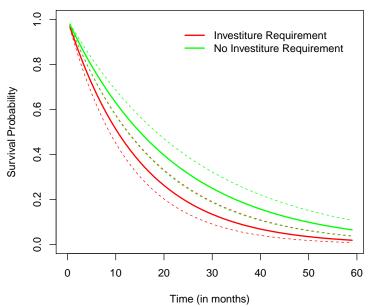
Hazard Ratios: Interpretation

- 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



Hazard is:

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

Survival function:

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

Density:

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

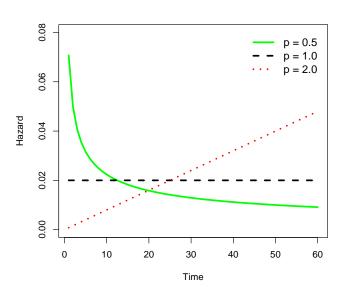
Covariates:

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

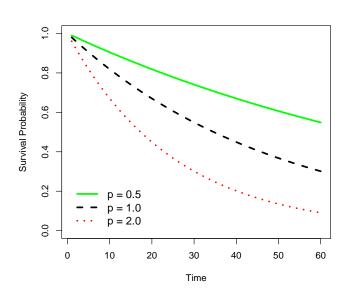
The Importance of p

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

Weibull Hazards Illustrated



Weibull Survival



Weibull Example

- > KABL.weib<-phreg(MODEL,data=KABL,dist="weibull")
- > KABL.weib

Call:
phreg(formula = MODEL, data = KABL, dist = "weibull")

| Covariate | W.mean | Coef | <pre>Exp(Coef)</pre> | se(Coef) | Wald p |
|------------|---------|--------|----------------------|----------|--------|
| fract | 692.734 | 0.001 | 1.001 | 0.001 | 0.133 |
| polar | 10.521 | 0.020 | 1.020 | 0.006 | 0.001 |
| format | 1.690 | 0.113 | 1.119 | 0.046 | 0.014 |
| invest | 0.332 | 0.429 | 1.535 | 0.139 | 0.002 |
| numst2 | 0.713 | -0.602 | 0.548 | 0.131 | 0.000 |
| eltime2 | 0.665 | -0.862 | 0.422 | 0.138 | 0.000 |
| caretk2 | 0.009 | 1.710 | 5.530 | 0.276 | 0.000 |
| log(scale) | | 3.696 | | 0.492 | 0.000 |
| log(shape) | | 0.261 | | 0.050 | 0.000 |

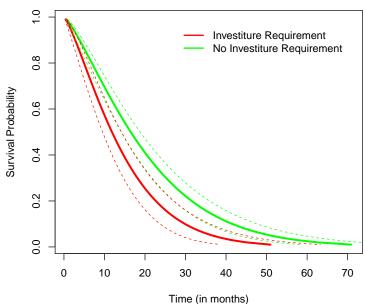
| Events | 271 |
|----------------------|---------|
| Total time at risk | 5789.5 |
| Max. log. likelihood | -1013.5 |
| LR test statistic | 174.23 |
| Degrees of freedom | 7 |
| Overall n-value | 0 |

Weibull Example (continued)

Interpretation:

- Hazard ratios are interpreted as in the exponential model, i.e., $100 \times \exp(\hat{\beta})$ is the percentage change in the hazard associated with a one-unit change in X
- So (e.g.) on average, an investiture requirement *increases* the hazard of cabinet failure by $100 \times (1.535 1) = 53.5$ percent
- $\log(\hat{p}) = 0.261$, so $\hat{p} = \exp(0.261) = 1.30$, which implies that the estimated hazard of cabinet failure is *increasing* over time

Comparing Predicted Survival Curves



Other Parametric Survival Models

- Gompertz
- Lognormal / log-Logistic
- Rayleigh (Weibull w/p = 2)
- Logistic
- t
- Gamma + Generalized Gamma

R Packages: Parametric Survival Models

A (probably partial) list:

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

Software

Notes on parametric models with time-varying covariate data:

- · Stata handles time-varying data with aplomb.
- · R (generally) 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.

Cox's Proportional Hazards Model

Basic idea:

$$h_i(t) = h_0(t) \exp(\mathbf{X}_i \beta)$$

Note:

- $h_0(t) \equiv h(t|X=0)$
- Changes in **X** shift h(t) proportionally

Cox (1972) (continued)

HR =
$$\frac{h_0(t)\exp(X_1\hat{\beta})}{h_0(t)\exp(X_0\hat{\beta})}$$
$$= \exp[(1-0)\hat{\beta}]$$
$$= \exp(\hat{\beta})$$

Cox (1972) (continued)

Also, because

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

then

$$S(t) = \exp\left[-\int_0^t h(t) dt\right]$$

$$= \exp\left[-\exp(\mathbf{X}_i\beta) \int_0^t h_0(t) dt\right]$$

$$= \left[\exp\left(-\int_0^t h_0(t) dt\right)\right]^{\exp(\mathbf{X}_i\beta)}$$

$$= \left[S_0(t)\right]^{\exp(\mathbf{X}_i\beta)}$$

Partial Likelihood

Assume N_C distinct event times t_i , with no "ties."

Then:

```
Pr(Individual k experienced the event at t_j \mid One observation experienced the event at t_j)
= \frac{\Pr(\mathsf{At}\text{-risk observation } k \text{ experiences the event of interest at } t_j)}{\Pr(\mathsf{One at}\text{-risk observation experiences the event of interest at } t_j)}
= \frac{h_k(t_j)}{\sum_{\ell \in R_j} h_\ell(t_j)}
```

Partial Likelihood (continued)

$$L_{i} = \frac{h_{0}(t_{j}) \exp(\mathbf{X}_{i}\beta)}{\sum_{\ell \in R_{j}} h_{0}(t_{j}) \exp(\mathbf{X}_{\ell}\beta)}$$

$$= \frac{h_{0}(t_{j}) \exp(\mathbf{X}_{i}\beta)}{h_{0}(t_{j}) \sum_{\ell \in R_{j}} \exp(\mathbf{X}_{\ell}\beta)}$$

$$= \frac{\exp(\mathbf{X}_{i}\beta)}{\sum_{\ell \in R_{j}} \exp(\mathbf{X}_{\ell}\beta)}$$

$$L = \prod_{i=1}^{N} \left[\frac{\exp(\mathbf{X}_{i}\beta)}{\sum_{\ell \in R_{j}} \exp(\mathbf{X}_{\ell}\beta)} \right]^{C_{i}}$$

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

Notes on Partial Likelihood

- PL is
 - Consistent
 - Asymptotically normal
 - Slightly inefficient (but asymptotically efficient)
- Considers order of events, but not actual duration
- Censored events: Modify R_j
- No ties

Example: Interstate War, 1950-1985

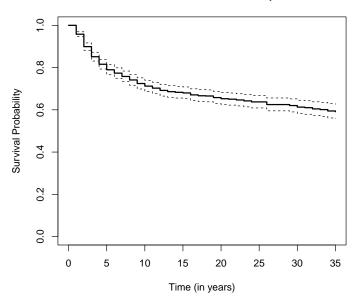
- Dyad-years for "politically-relevant" dyads
- *N* = 827. *NT* = 20448.
- Covariates:
 - Whether (=1) or not the two countries are allies,
 - Whether (=1) or not the two countries are *contiguous*,
 - The capability ratio of the two countries,
 - The lower of the two countries' (GDP) growth (rescaled),
 - The lower of the two countries' democracy (POLITY IV) scores (rescaled to [-1,1]), and
 - The amount of *trade* between the two countries, as a fraction of joint GDP.

The Data

> summary(OR)

```
dyadid
                  year
                              start
                                             stop
                                                         futime
Min. : 2020
              Min.
                    :1951
                         Min. : 0.00
                                        Min.
                                               : 1.00
                                                      Min.
                                                            : 5.00
              1st Qu.:1965 1st Qu.: 5.00
                                                      1st Qu.:23.00
1st Qu.:100365
                                        1st Qu.: 6.00
Median :220235 Median :1972 Median :11.00
                                        Median :12.00
                                                      Median :31.00
Mean :253305 Mean :1971 Mean :12.32 Mean :13.32 Mean
                                                            :28.97
              3rd Qu.:1979 3rd Qu.:19.00 3rd Qu.:20.00
3rd Qu.:365600
                                                      3rd Qu.:35.00
              Max. :1985 Max. :34.00
                                        Max. :35.00
Max. :900920
                                                      Max.
                                                            :35.00
  dispute
                 allies
                               contig
                                           trade
Min. :0.00000 Min.
                     :0.0000 Min. :0.0000 Min. :0.00000
1st Qu.:0.00000 1st Qu.:0.0000 1st Qu.:0.0000
                                            1st Qu.:0.00000
Median :0.00000 Median :0.0000
                             Median :0.0000
                                            Median :0.00020
Mean :0.01981 Mean :0.3563 Mean :0.3099
                                            Mean :0.00231
3rd Qu.:0.00000 3rd Qu.:1.0000 3rd Qu.:1.0000
                                            3rd Qu.:0.00120
Max. :1.00000 Max.
                     :1.0000
                             Max. :1.0000 Max. :0.17680
   growth
                  democracy capratio
                       :-1.0000
                                Min. : 0.0100
Min.
      :-0.264900 Min.
1st Qu.:-0.004800 1st Qu.:-0.8000
                               1st Qu.: 0.0462
Median: 0.014700 Median: -0.7000
                                Median: 0.2220
Mean : 0.007823 Mean :-0.3438
                                Mean : 1.6677
3rd Qu.: 0.027800 3rd Qu.: 0.2000
                                3rd Qu.: 1.1560
Max. : 0.164700 Max. : 1.0000
                                Max.
                                      :78.9296
```

The Data (Kaplan-Meier plot)



Software

R:

- coxph in survival (preferred)
- cph in design
- Plots: plot(survfit(PHobject))

Stata:

- Basic command = stcox
- stset first
- Options: robust, various methods for ties, postestimation commands

Model Fitting

```
> ORCox.br<-coxph(OR.S~allies+contig+capratio+growth+democracy+trade,
               data=OR, na.action=na.exclude, method="breslow")
> summary(ORCox.br)
 n= 20448, number of events= 405
            coef exp(coef) se(coef) z Pr(>|z|)
allies -0.34849
                 0.70576 0.11096 -3.141 0.001686 **
contig 0.94861 2.58213 0.12173 7.793 6.55e-15 ***
growth -3.69487 0.02485 1.19950 -3.080 0.002068 **
democracy -0.38194   0.68254   0.09915 -3.852   0.000117 ***
trade -3.22857 0.03961 9.45588 -0.341 0.732776
Signif. codes: 0 *** 0.001 ** 0.01 * 0.05 . 0.1 1
```

Model Fitting (continued)

```
exp(coef) exp(-coef) lower .95 upper .95
allies
           0.70576
                      1.4169 5.678e-01 8.772e-01
contig
           2.58213 0.3873 2.034e+00 3.278e+00
           0.80009 1.2499 7.231e-01 8.853e-01
capratio
growth
           0.02485 40.2402 2.368e-03 2.608e-01
           0.68254
                      1.4651 5.620e-01 8.289e-01
democracy
trade
           0.03961
                     25.2436 3.540e-10 4.433e+06
Concordance= 0.714 (se = 0.015)
Rsquare= 0.01 (max possible= 0.234)
Likelihood ratio test= 210.3 on 6 df.
                                      p=0
Wald test
                    = 159.8 on 6 df.
                                      0=q
Score (logrank) test = 185.8 on 6 df,
                                      p=0
```

Interpretation: Hazard Ratios

$$HR = \exp[(\mathbf{X}_j - \mathbf{X}_k)\hat{\beta}]$$

Means:

- $HR = 1 \leftrightarrow \hat{\beta} = 0$
- $HR > 1 \leftrightarrow \hat{\beta} > 0$
- $HR < 1 \leftrightarrow \hat{\beta} < 0$

Percentage difference = $100 \times \{\exp[(\mathbf{X}_j - \mathbf{X}_k)\hat{\beta}] - 1\}$.

Example: Hazard Ratios

From above:

```
exp(coef) exp(-coef) lower .95 upper .95 allies 0.70576 1.4169 5.678e-01 8.772e-01 contig 2.58213 0.3873 2.034e+00 3.278e+00 capratio 0.80009 1.2499 7.231e-01 8.853e-01 growth 0.02485 40.2402 2.368e-03 2.608e-01 democracy 0.68254 1.4651 5.620e-01 8.289e-01 trade 0.03961 25.2436 3.540e-10 4.433e+06
```

Interpretation:

- · Countries which are *allies* have an expected $(0.706 1) \times 100) = 29.4$ percent lower hazard of conflict than those that are not.
- · Contiguous countries have $(2.582 1) \times 100 = 158$ percent higher hazards of conflict than non-contiguous ones.
- · A one-unit increase in *democracy* corresponds to a $(0.683 1) \times 100 = 31.7$ percent decrease in the expected hazard of conflict.

Hazard Ratios: Scaling Covariates

```
It is good for one-unit changes to be meaningful / realistic...
> OR$growthPct<-OR$growth*100
> summary(coxph(OR.S~allies+contig+capratio+growthPct+democracy+trade,
               data=OR,na.action=na.exclude, method="breslow"))
         exp(coef) exp(-coef) lower .95 upper .95
allies
           0.70576
                       1.4169 5.678e-01 8.772e-01
contig
           2.58213 0.3873 2.034e+00 3.278e+00
capratio 0.80009 1.2499 7.231e-01 8.853e-01
growthPct
           0.96373 1.0376 9.413e-01 9.867e-01
democracy
           0.68254 1.4651 5.620e-01 8.289e-01
trade
                      25.2436 3.540e-10 4.433e+06
           0.03961
```

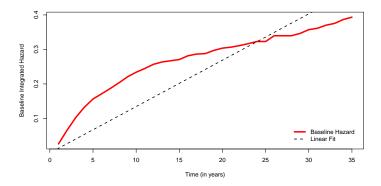
Note:

- · Previous HR for growth = $0.02485 \rightarrow 97.5$ percent decrease in $\hat{h}(t)$
- · HR for growthPct is now 0.964; 1 unit increase ightarrow 4% decrease in $\hat{h}(t)$
- Same result, proportionally: $0.96373^{100} = 0.02485$

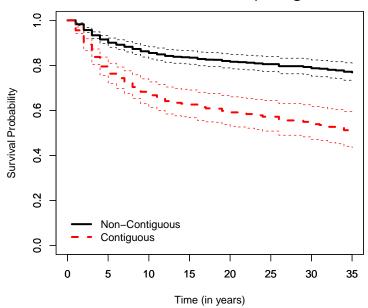
Baseline Hazards

Because the Cox model is semiparametric, it uses a conventional / univariate (Nelson-Aalen) estimate of the "baseline" hazard:

OR.BH<-basehaz(ORCox.br,centered=FALSE)</pre>



Comparing Survival Curves



Cox vs. Parametric Models

Conceptual considerations:

- Theory
- Nature of h(t)
- Relative importance: Bias vs. efficiency
- Need / willingness for out-of-sample predictions / forecasting

Cox, On His Model

Reid: "What do you think of the cottage industry that's grown up around [the Cox model]?"

Cox: "In the light of further results one knows since, I think I would normally want to tackle the problem parametrically... I'm not keen on non-parametric formulations normally."

Reid: "So if you had a set of censored survival data today, you might rather fit a parametric model, even though there was a feeling among the medical statisticians that that wasn't quite right."

Cox: "That's right, but since then various people have shown that the answers are very insensitive to the parametric formulation of the underlying distribution. And if you want to do things like predict the outcome for a particular patient, it's much more convenient to do that parametrically."

- From Reid (1994).

Survival Model Variants and Extensions...

- Discrete-Time Models
- Stratification
- Cox Models for repeated events
- Models with "frailties"
- Competing risks
- Models for "cured" subpopulations
- Joint Models for Survival and Longitudinal Outcomes
- Complex sampling schemes
- Multilevel / spatial / etc. models for survival outcomes