# Survival Data Analysis Parametric Models

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# Agenda

- Basic Parametric Models
  - Review: hazard & cumulative hazard functions; likelihood function
  - Proportional hazards versus accelerated failure
  - Exponential model
  - Weibull model
  - Log-Normal model
  - Log-Logistic model
  - Checking assumptions
  - Gamma model
  - Goodness of fit and residuals
- Other Models
  - Changepoint model (piecewise exponential model )
    - Reference: Matthews & Farewell 1982
  - Gamel-Boag (cure fraction) model
    - Reference: Frankel & Longmate 2002
  - Weibull model with random effects
  - Bayesian analysis of Weibull model

# Probability density function

$$Random survival time\, T > 0$$

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

# Hazard function

- Specifies the instantaneous rate of failure at T=t

$$h(t) = \lim_{\Delta t \to 0^+} \frac{P(t \le T < t + \Delta t \,|\, T \ge t)}{\Delta t}$$

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

See K&M Section 2.3

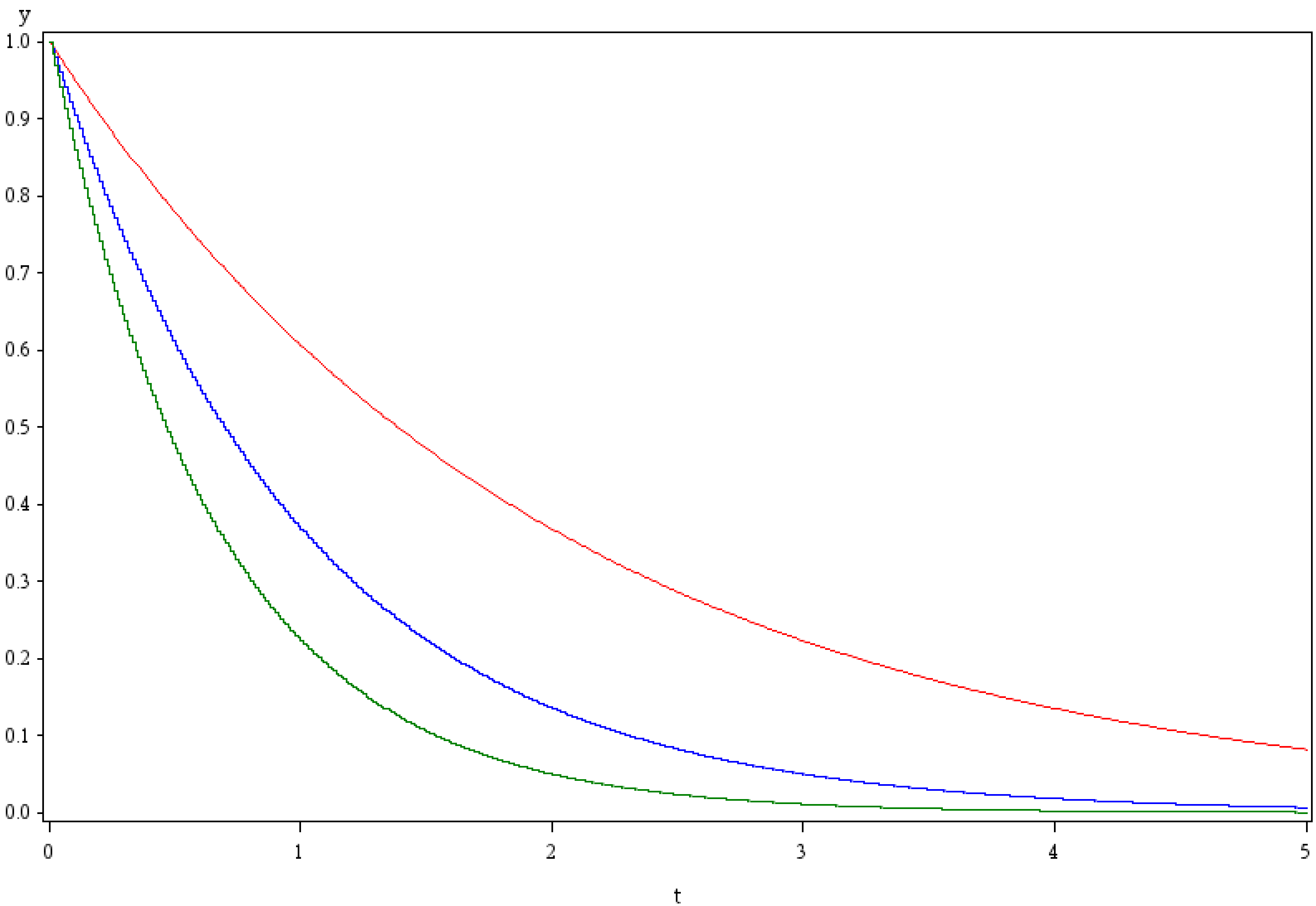
# Cumulative hazard function

$$S(t) = P[T > t] = e^{-H(t)},$$

$$\text{where } H(t) = \int_{u=0}^{t} h(u)\,du\,.$$

$$\text{Note } H(t) = -\log S(t)$$

Function y=exp(-at), a,t>0 (Red: a=0.5 Blue: a=1 Green: a=1.5)



# Likelihood

- Full likelihood for parametric models
- Assuming censoring is independent of failure and non-informative:

$$L \propto \prod_{i \in D}^{n} f(x_i) \prod_{i \in R} S(C_r)$$

K&M 3.5.1

$$L = \prod_{i=1}^{n} \Pr(t_i, \delta_i)$$

$$where\ T = \min(X, C_r)$$

$$and\ \Pr(t, \delta) = \left[f(t)\right]^{\delta} \left[S(t)\right]^{1-\delta}$$

# Likelihood

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

K&M 3.5.3

$$= \prod_{i=1}^{n} \left[ h(t_i) \exp[-\int_0^{t_i} h(s)ds \right]^{\delta_i} \left[ \exp[-\int_0^{t_i} h(s)ds \right]^{1-\delta_i}$$

$$= \prod_{i=1}^{n} [h(t_i)]^{\delta_i} \exp\left[-\int_0^{t_i} h(s)ds\right]$$

$$= \prod_{i=1}^{n} [h(t_i)]^{\delta_i} \exp\left[-H(t_i)\right]$$

# Parametric Survival models

- Fully specified model with hazard rate a function of covariates (including intercept)
- Proportional Hazards (PH)
  - constant **hazard ratios** across time
  - Exponential, Weibull
- Accelerated Failure Models (AFT)
  - constant **time ratios** across survival percentiles
  - Exponential, Weibull, Log Normal, Log Logistic

# PH versus AFT

$$e.g. \quad X \text{ is binary}$$

PH

$$HR = \frac{h_1(x=1,t)}{h_0(x=0,t)} = e^{-\beta}$$

AFT

$$TR = \frac{t_{50}(x=1,\beta)}{t_{50}(x=0,\beta)} = e^{\beta}$$

Exponential Model

# PH versus AFT

PH

$$h(t \mid X) = h_0(t) e^{-\beta' X}$$

$$S(t \mid X) = S_0(t)^{e^{-\beta' X}}$$

AFT

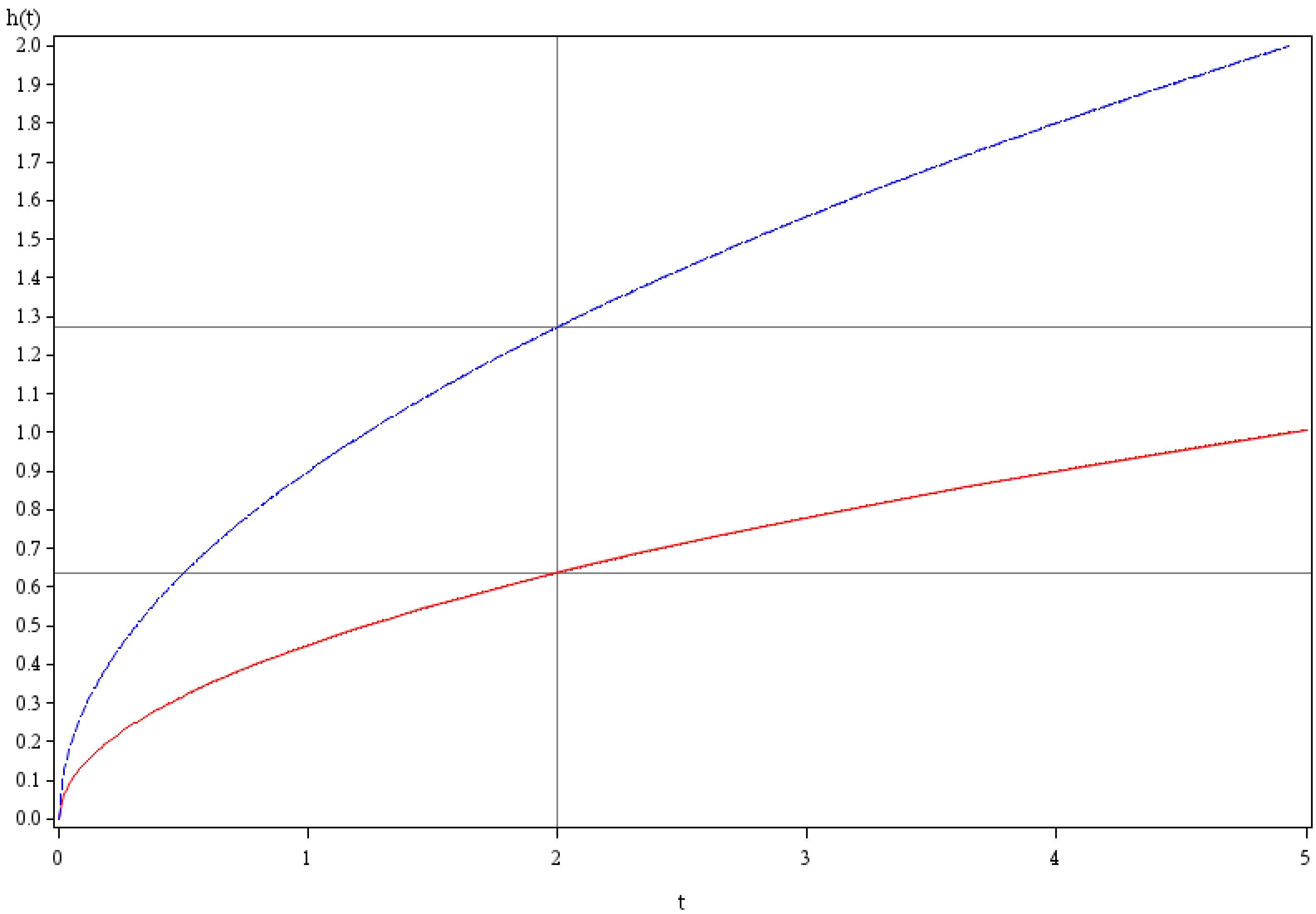
$$h(t \mid X) = h_0(e^{-\beta' X} t) e^{-\beta' X}$$

$$S(t \mid X) = S_0(e^{-\beta' X} t)$$

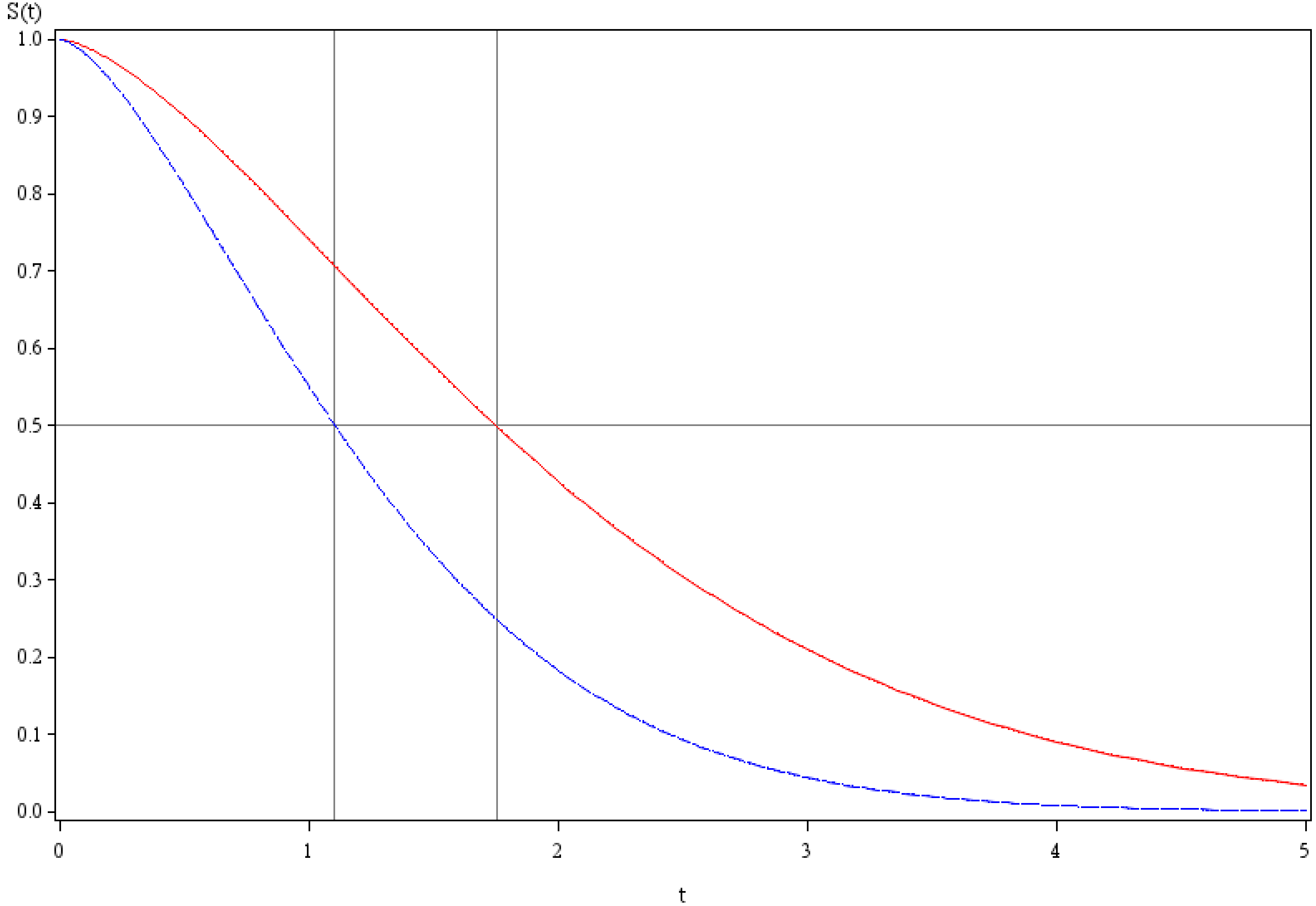
Acceleration factor: $e^{-\beta' X}$

Be careful of parameterization of models in texts and software.

## Sample Weibull hazard plots - HR=2.0 (Red: lambda=0.3  Blue lambda=0.6)



# Sample Weibull survival plots - TR=0.63 (or AF=2, Red: lambda=0.3 Blue lambda=0.6)



# Error distributions

$$f(\varepsilon) = \exp(\varepsilon - \exp(\varepsilon))$$

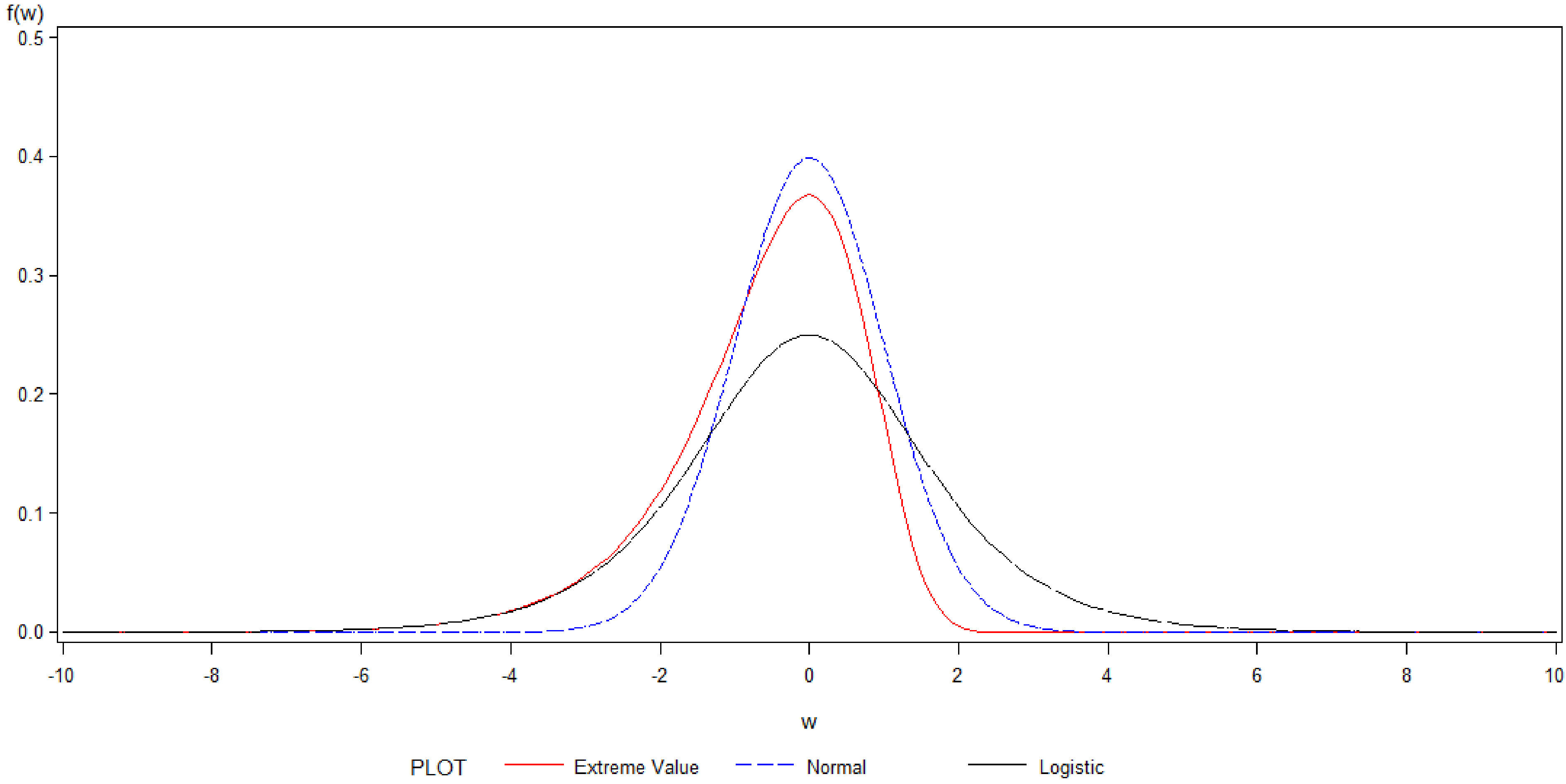
$$f(\varepsilon) = \frac{\exp(-\frac{\varepsilon^2}{2})}{\sqrt{2\pi}}$$

$$Y = \log T = X\beta + \sigma\varepsilon$$

$$f(\varepsilon) = \frac{e^{\varepsilon}}{\left(1 + e^{\varepsilon}\right)^2}$$

Be careful of parameterization of models in texts and software.

# Error distributions



# Exponential Model

- constant hazard functions
- both PH and AFT model
- underlying error function has an extreme value function with σ=1

$$w = \ln(t)$$
$$\lambda = \exp(-u)$$
$$S(w) = \exp(-\exp(w-u))$$

$$S(t) = e^{-\lambda t}$$
$$h(t) = \lambda$$
$$Median = \frac{-\ln(.5)}{\lambda} = \frac{.69}{\lambda}$$
$$Mean = \frac{1}{\lambda}$$

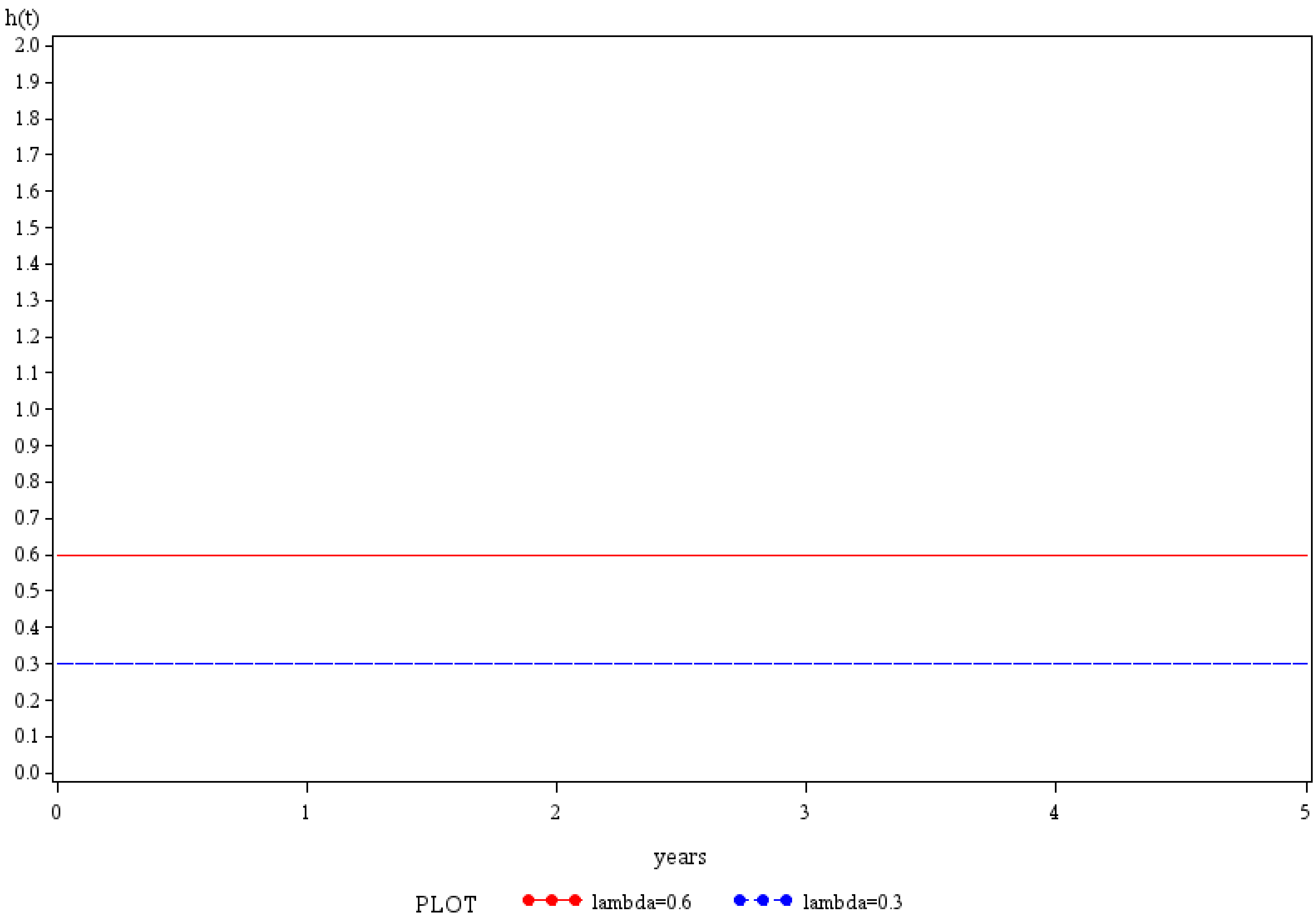
# Exponential Model

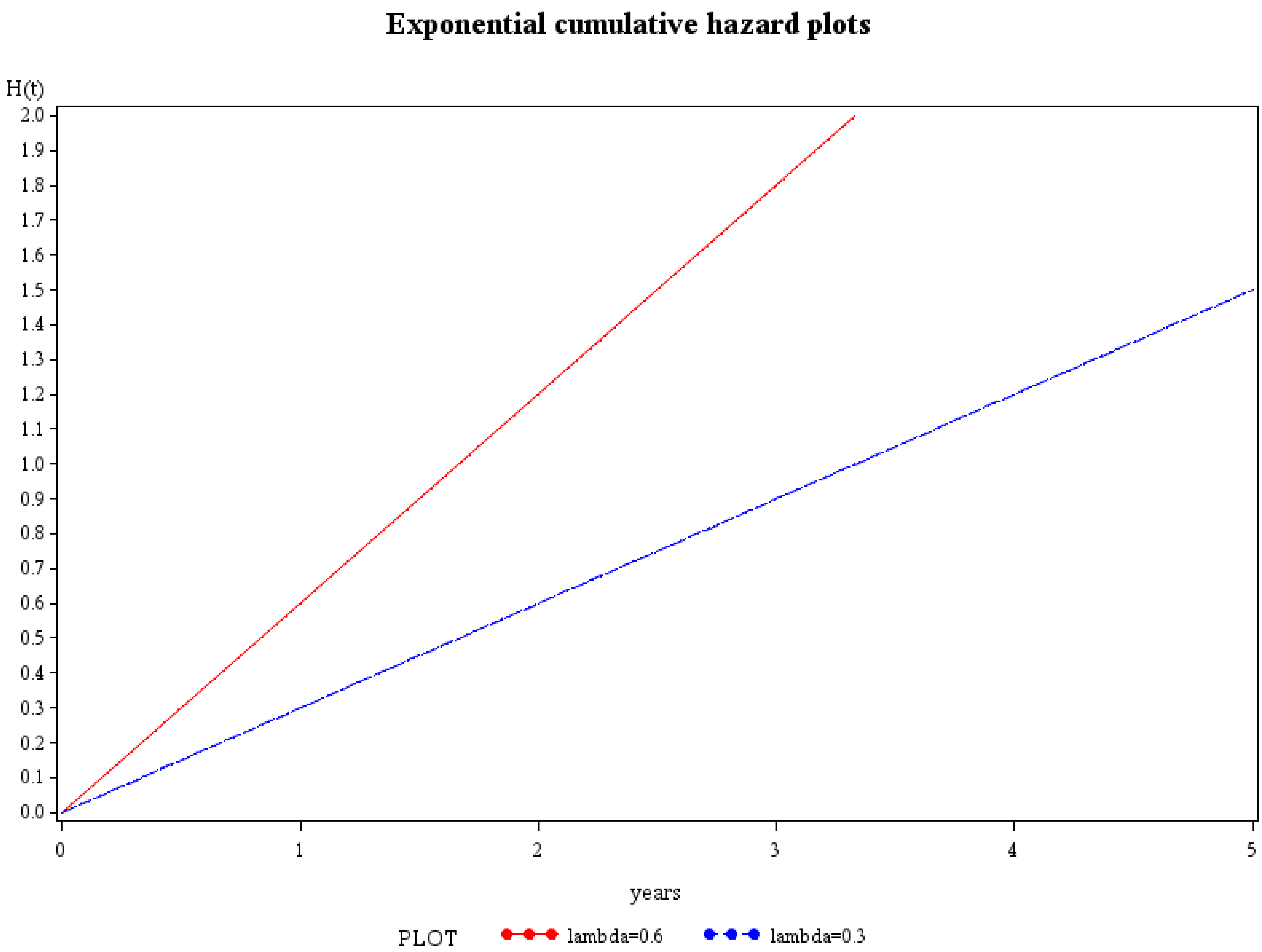
$$L(\lambda) = \prod_{i=1}^{n} [\lambda]^{\delta_i} \exp\left[-\lambda t_i\right]$$

$$l(\lambda) = \sum_{i=1}^{n} (\delta_i \log[\lambda] - \lambda t_i)$$

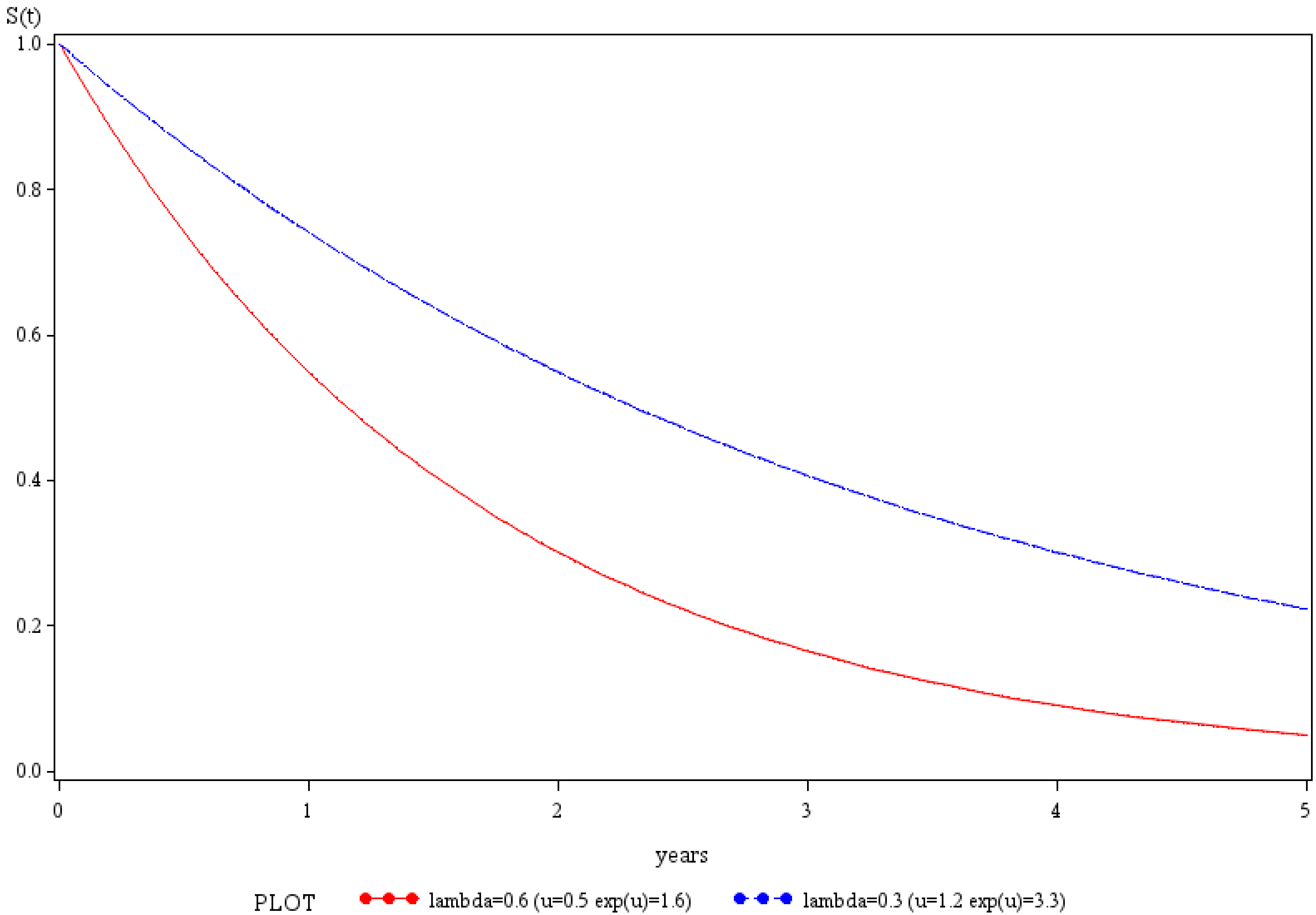
$$mle \quad \hat{\lambda} = \frac{\sum_{i=1}^{n} \delta_i}{\sum_{i=1}^{n} t_i}$$

# Exponential hazard plots




Exponential cumulative hazard plots
H(t)
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
1
2
3
4
5
years
PLOT
lambda=0.6
lambda=0.3

# Exponential survival plots



# Weibull

- monotone increasing or decreasing hazard functions
- both PH and AFT model
- Exponential model is special case (γ=1)

$$w = \ln(t),\ \sigma = \frac{1}{\lambda}$$

$$\lambda = \exp(-u/\sigma)$$

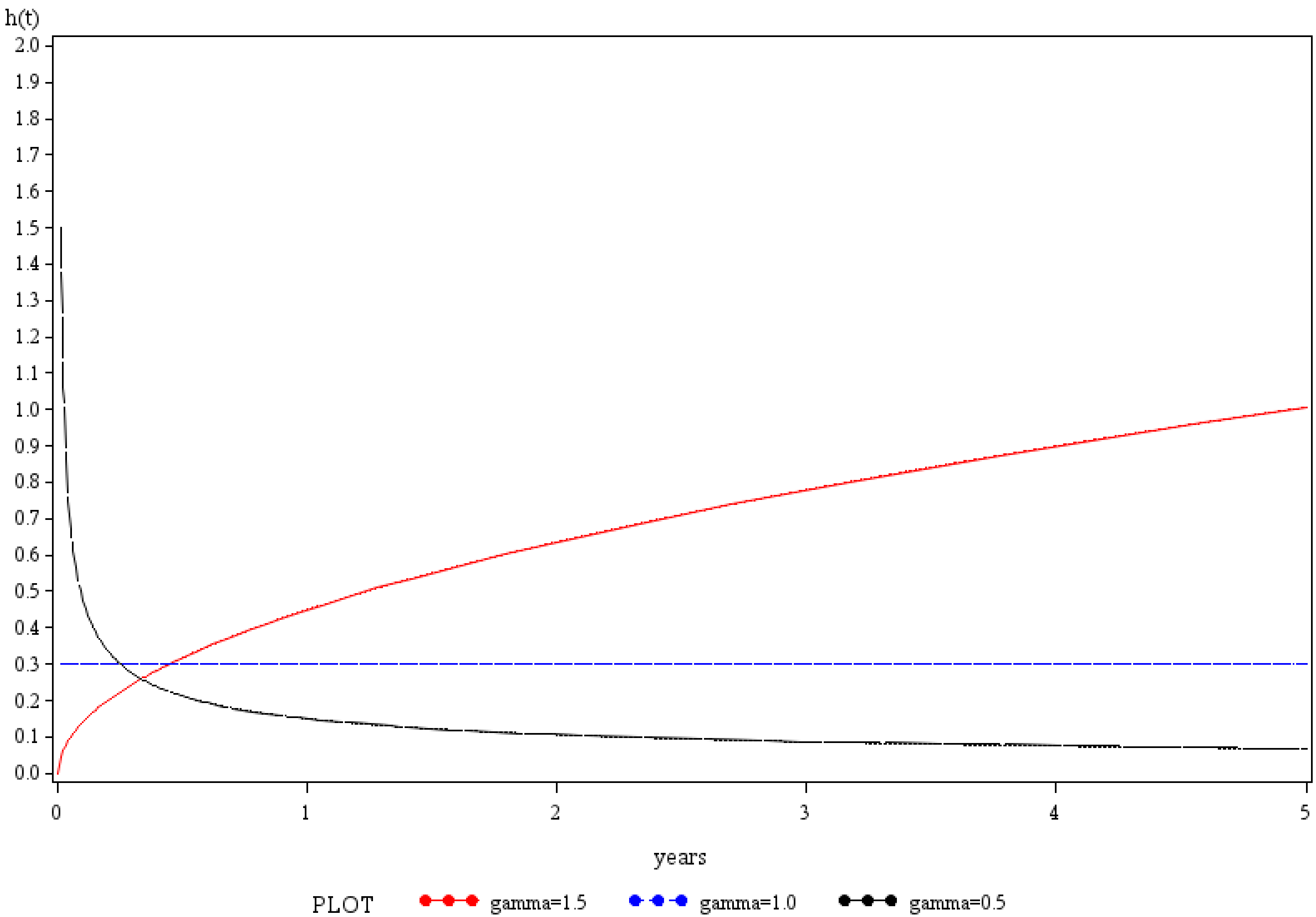
$$S(w) = \exp(-\exp(\frac{w-u}{\sigma}))$$

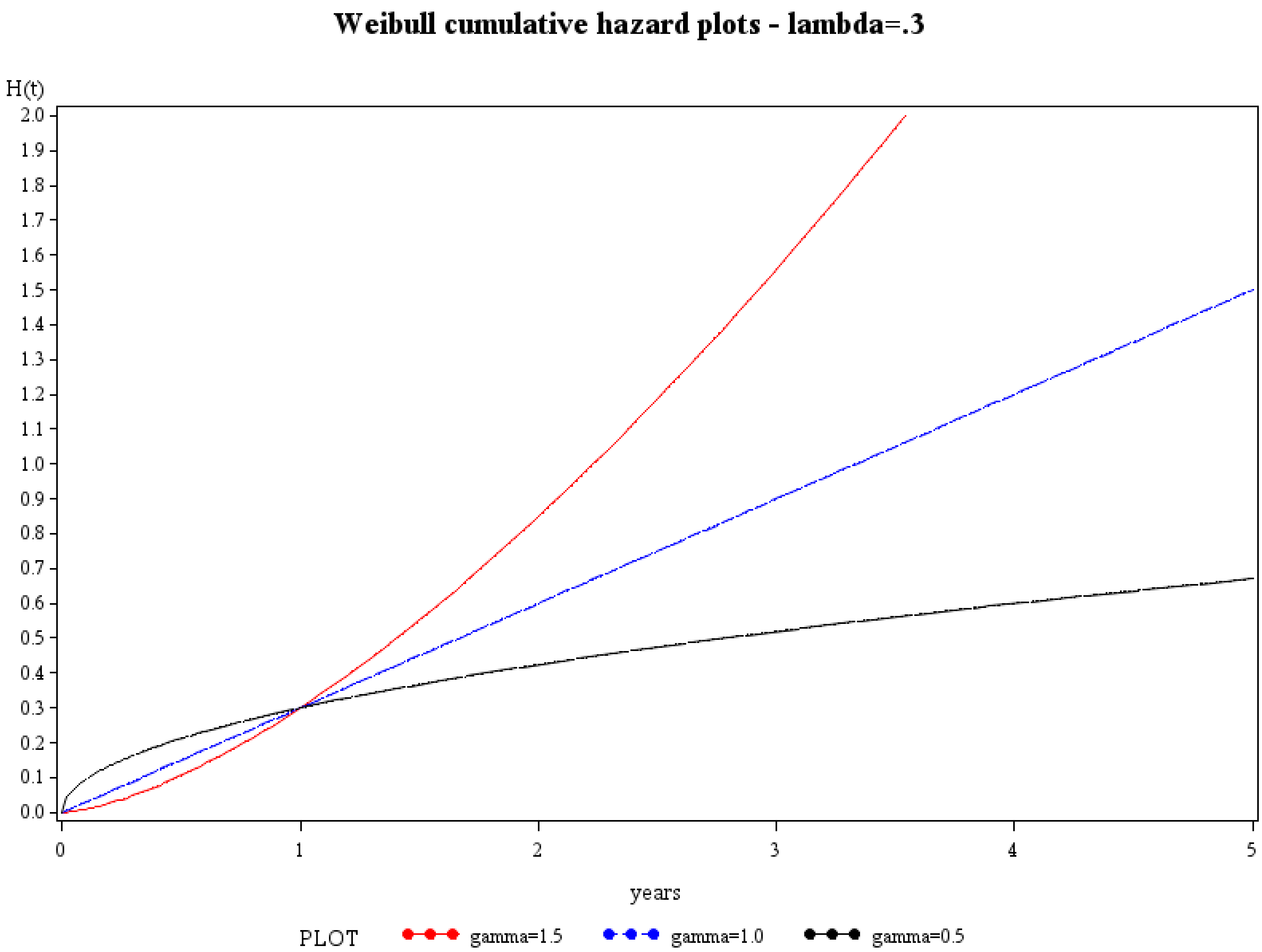
$$S(t) = e^{-\lambda t^{\gamma}}$$

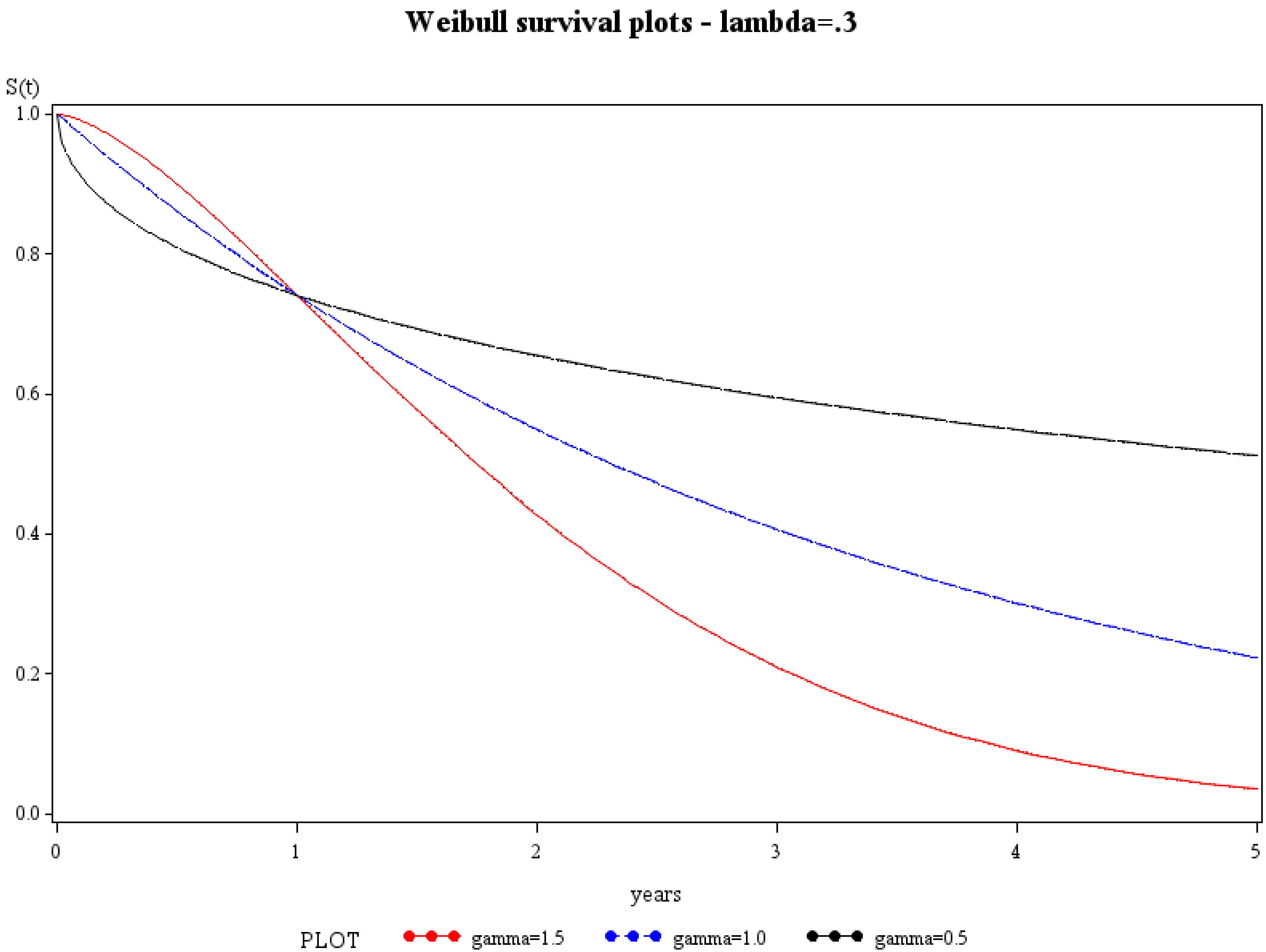
$$h(t) = \gamma \lambda t^{\gamma - 1}$$

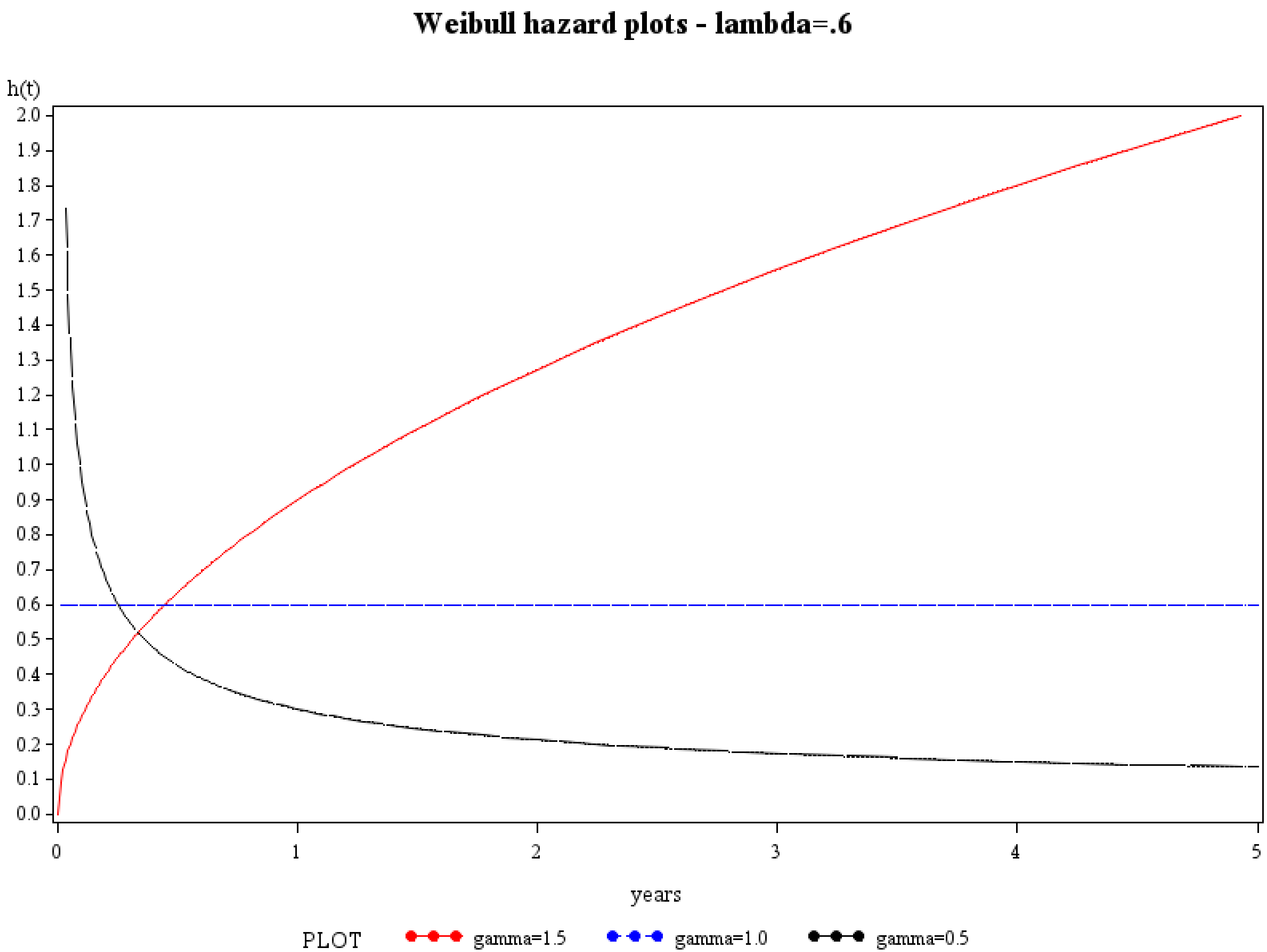
$$Median = \left( \frac{-\ln(.5)}{\lambda} \right)^{\frac{1}{\gamma}}$$

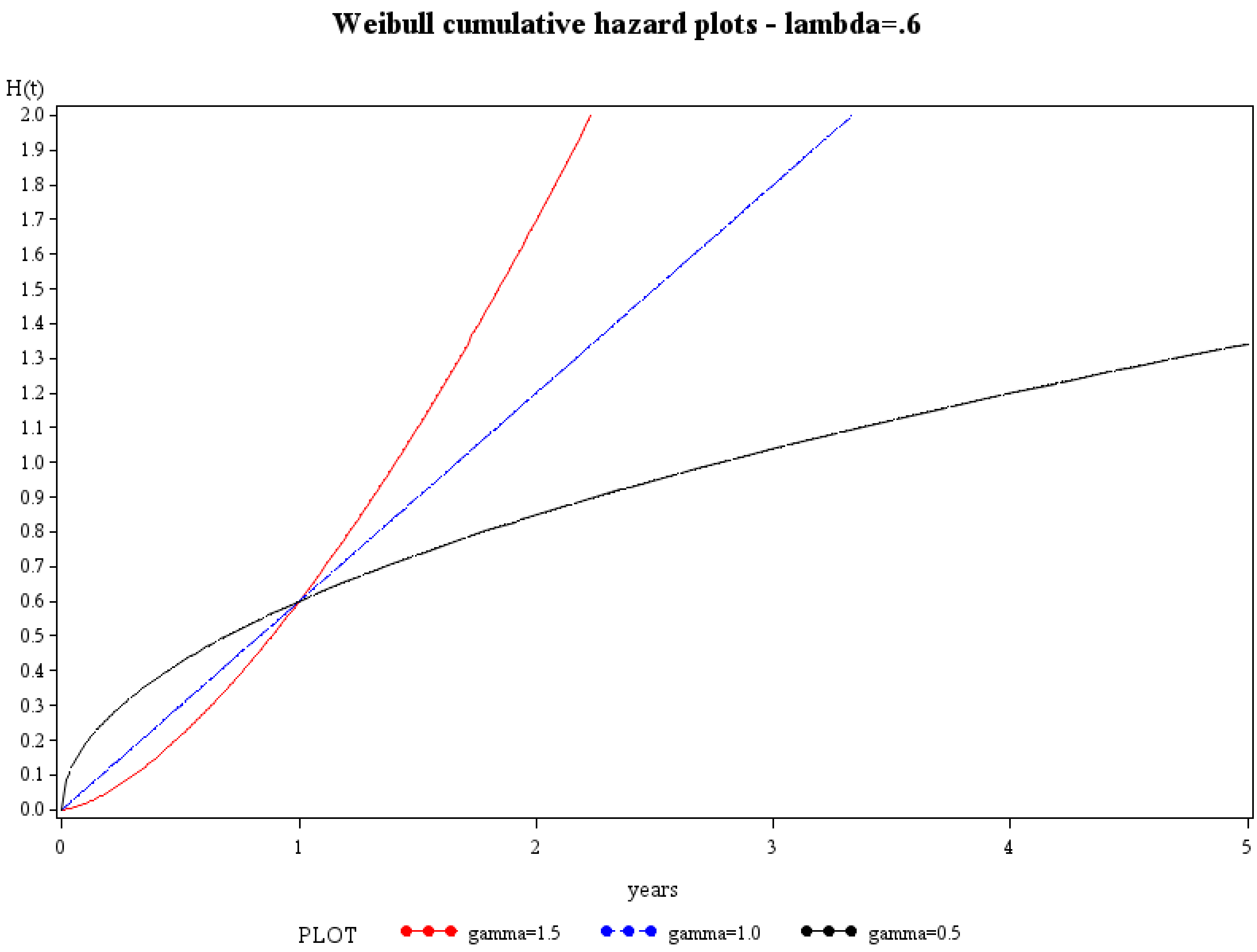
# Weibull hazard plots - lambda=.3

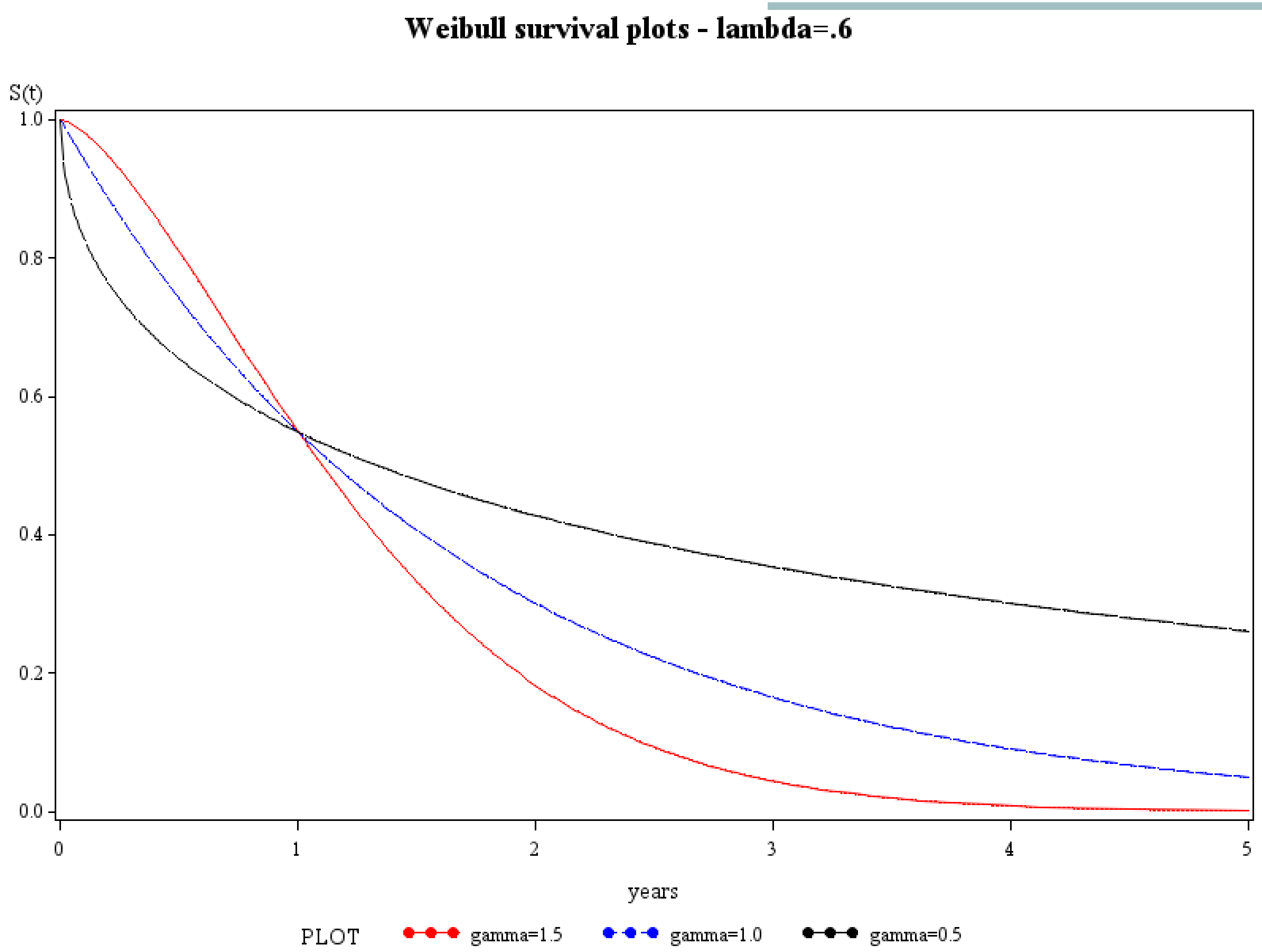



Weibull cumulative hazard plots - lambda=.3
H(t)
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
1
2
3
4
5
years
PLOT
gamma=1.5
gamma=1.0
gamma=0.5


Weibull survival plots - lambda=.3
S(t)
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
years
PLOT
gamma=1.5
gamma=1.0
gamma=0.5


Weibull hazard plots - lambda=.6
h(t)
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
1
2
3
4
5
years
PLOT
gamma=1.5
gamma=1.0
gamma=0.5


Weibull cumulative hazard plots - lambda=.6
H(t)
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
1
2
3
4
5
years
PLOT
gamma=1.5
gamma=1.0
gamma=0.5


Weibull survival plots - lambda=.6
S(t)
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
years
PLOT
gamma=1.5
gamma=1.0
gamma=0.5

# Weibull models:

| lambda | gamma | sigma | u | median |
|---|---|---|---|---|
| 0.3 | 0.5 | 2 | 2.4 | 5.3 |
| 0.3 | 1 | 1 | 1.2 | 2.3 |
| 0.3 | 1.5 | 0.7 | 0.8 | 1.7 |
| 0.6 | 0.5 | 2 | 1 | 1.3 |
| 0.6 | 1 | 1 | 0.5 | 1.2 |
| 0.6 | 1.5 | 0.7 | 0.3 | 1.1 |

# Log Normal

- hazard functions rise to a maximum then slowly decline, AFT model only

$$S(t) = 1 - \Phi\left(\frac{\ln(t) - \mu}{\sigma}\right)$$

$$f(t) = \frac{1}{t\sigma\sqrt{2\pi}} e^{\left(-\frac{1}{2}\left(\frac{\ln(t)-\mu}{\sigma}\right)^2\right)}$$

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

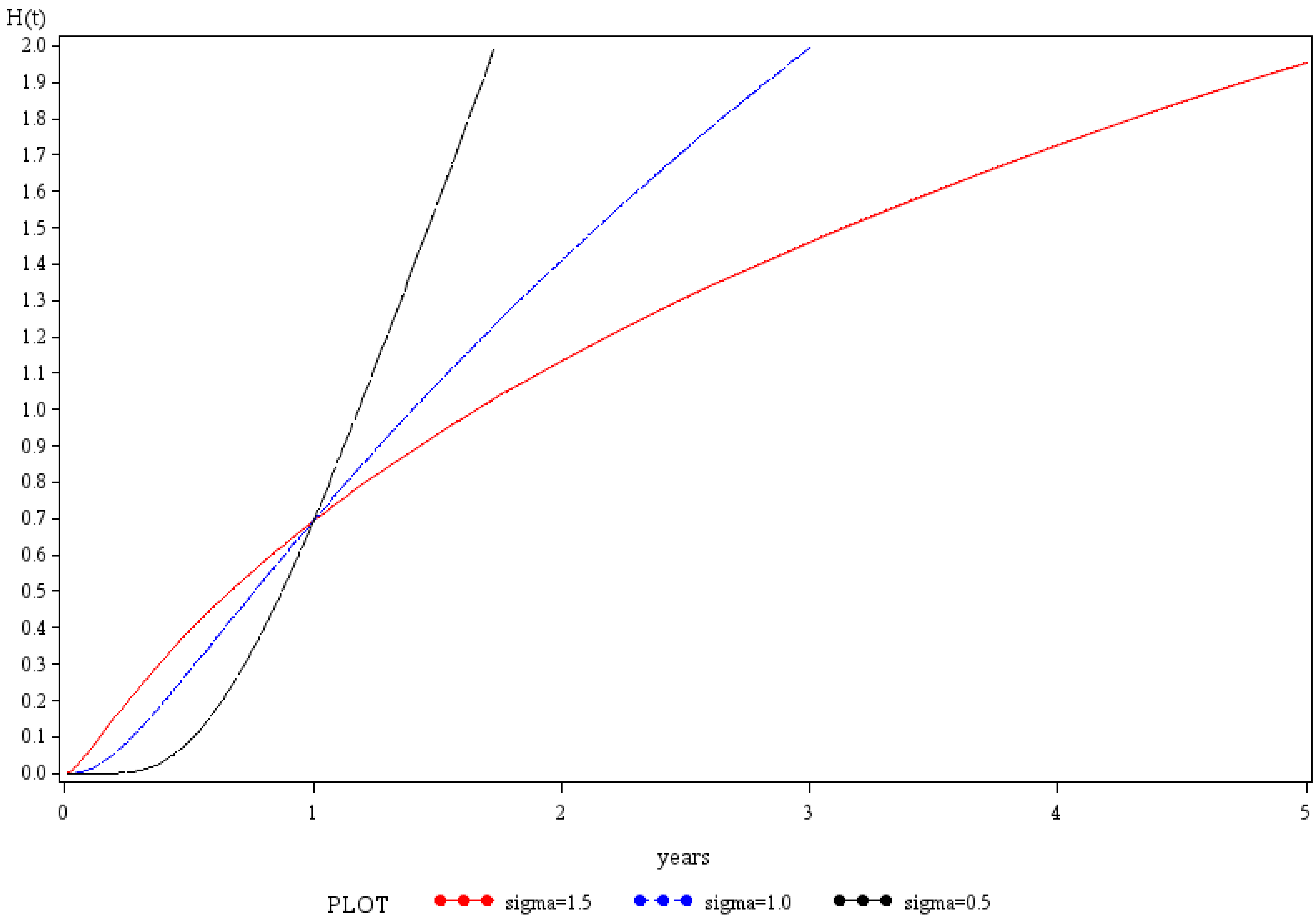
$$Median = e^{\left(\sigma\Phi^{-1}(.5)+\mu\right)} = e^{\mu}$$

$$Mean = e^{\left(\mu+0.5\sigma^2\right)}$$

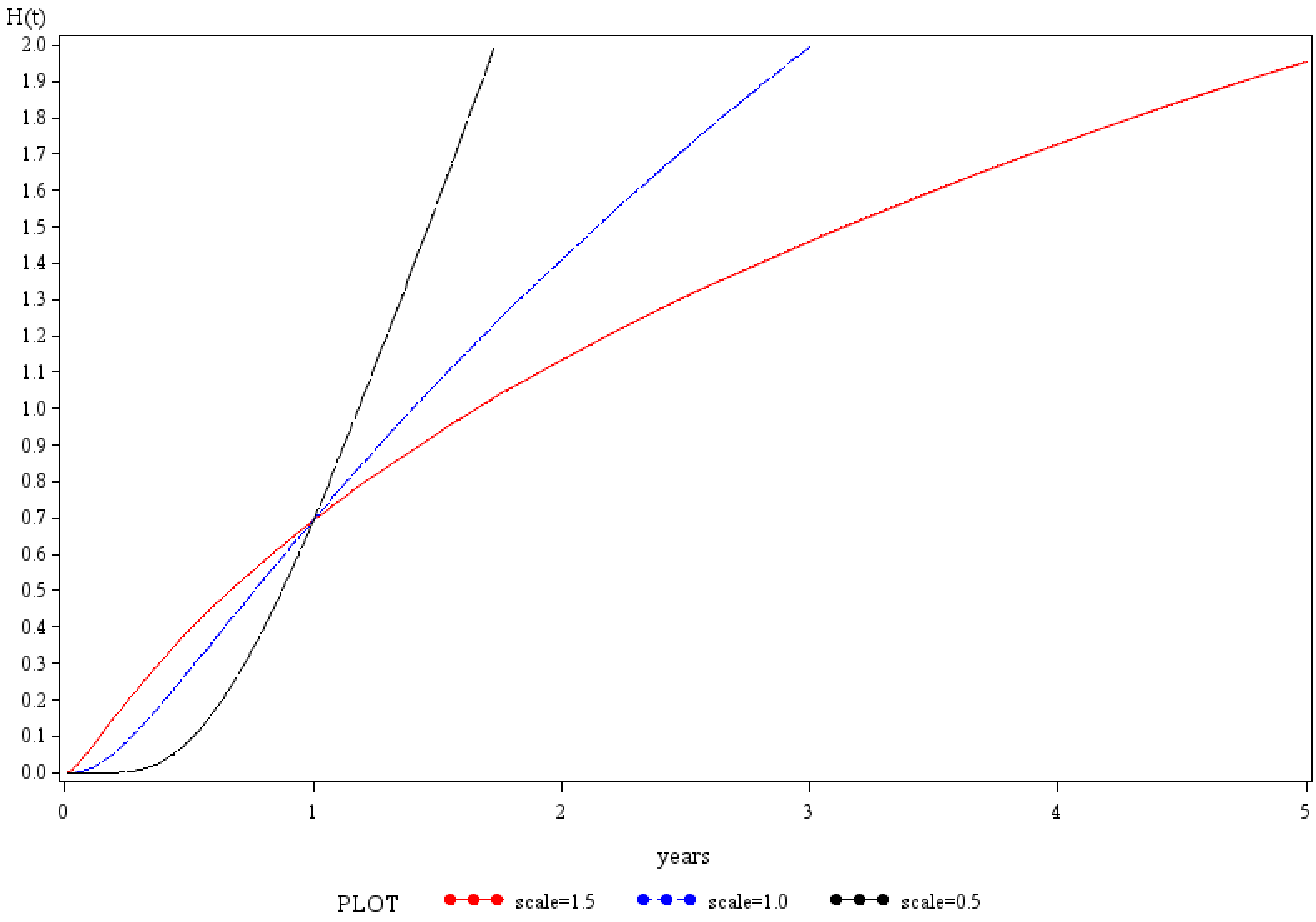
$$w = \ln(t)$$

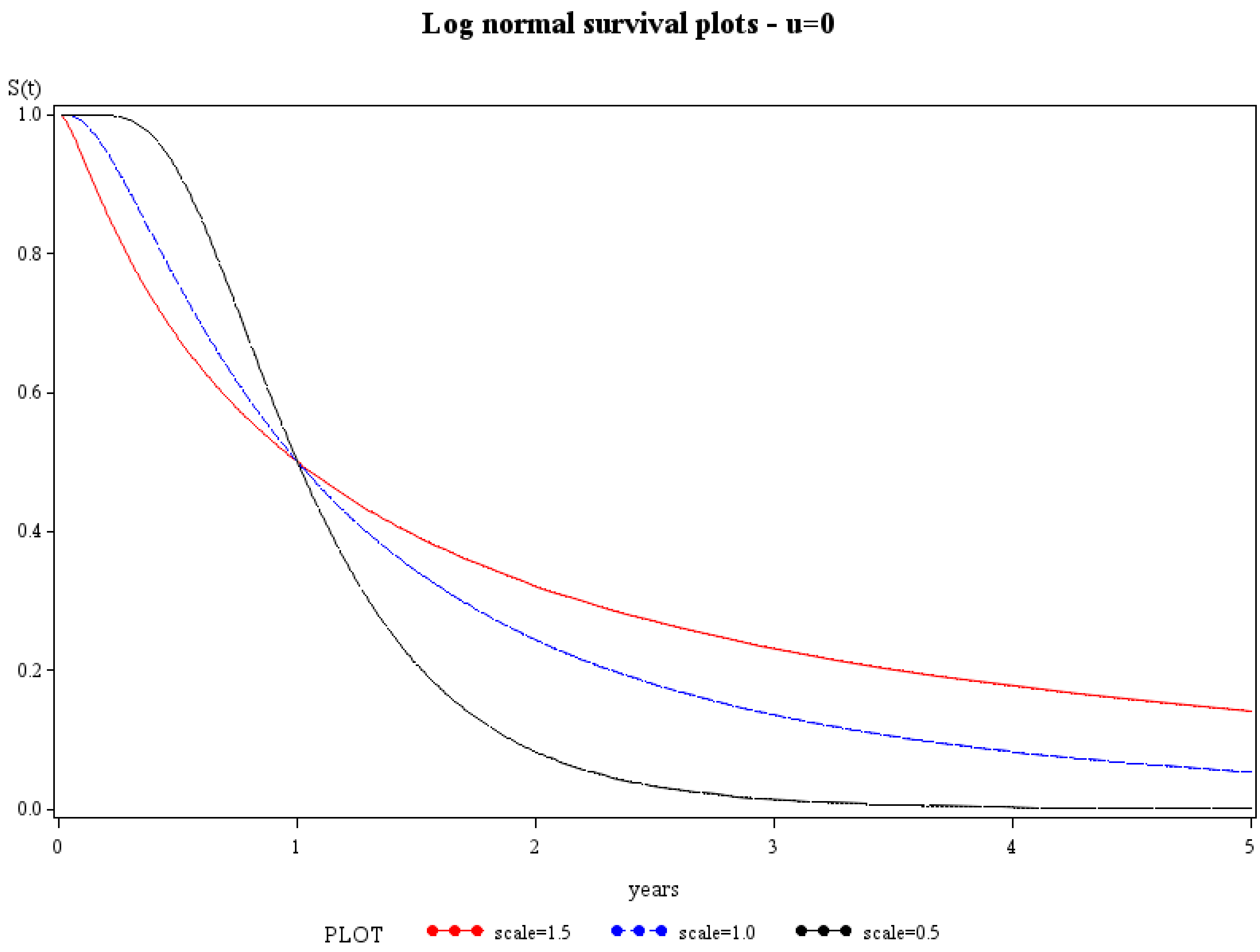
$$S(w) = 1 - \Phi(\frac{w-u}{\sigma})$$

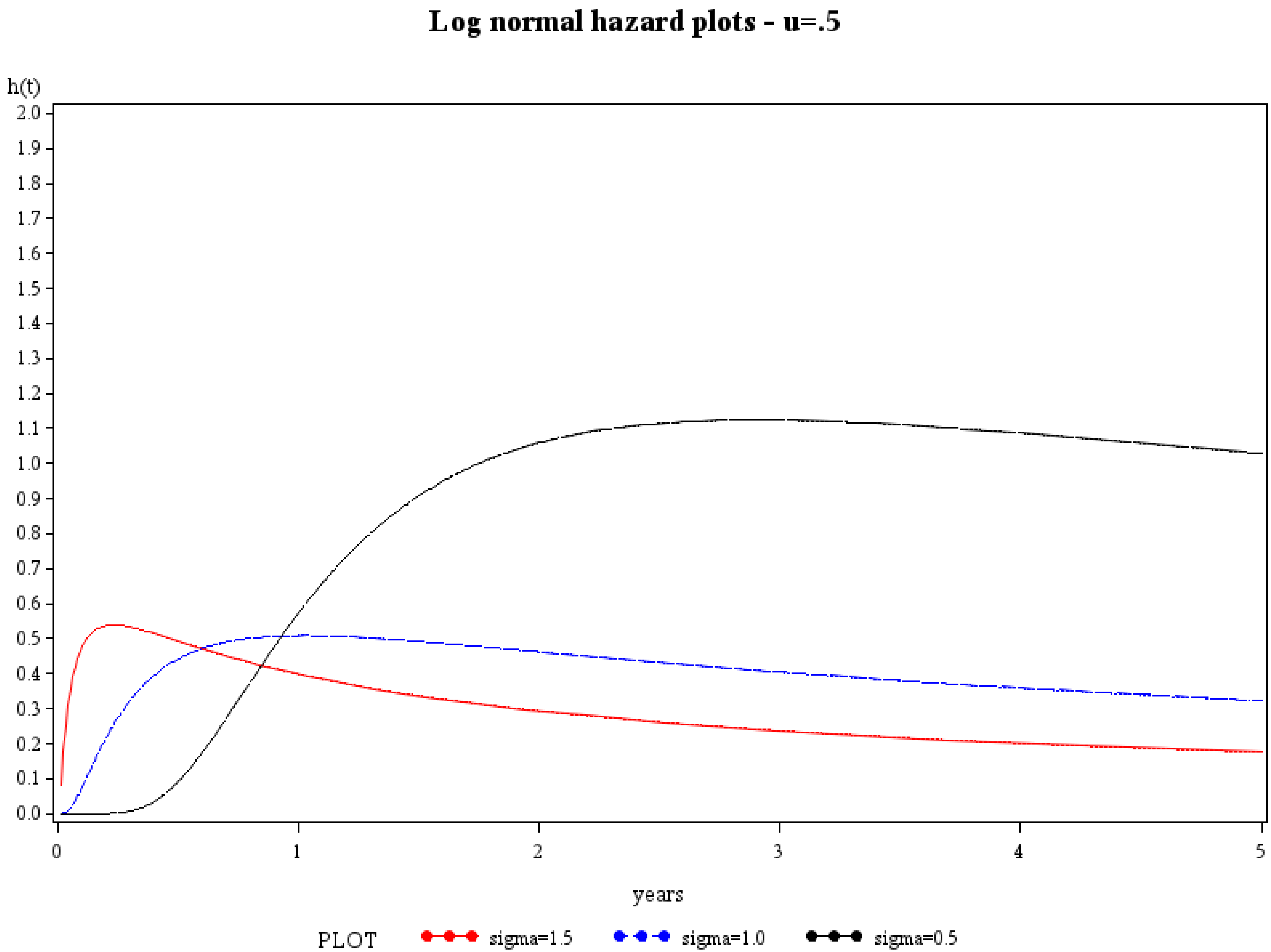
# Log normal cumulative hazard plots - u=0



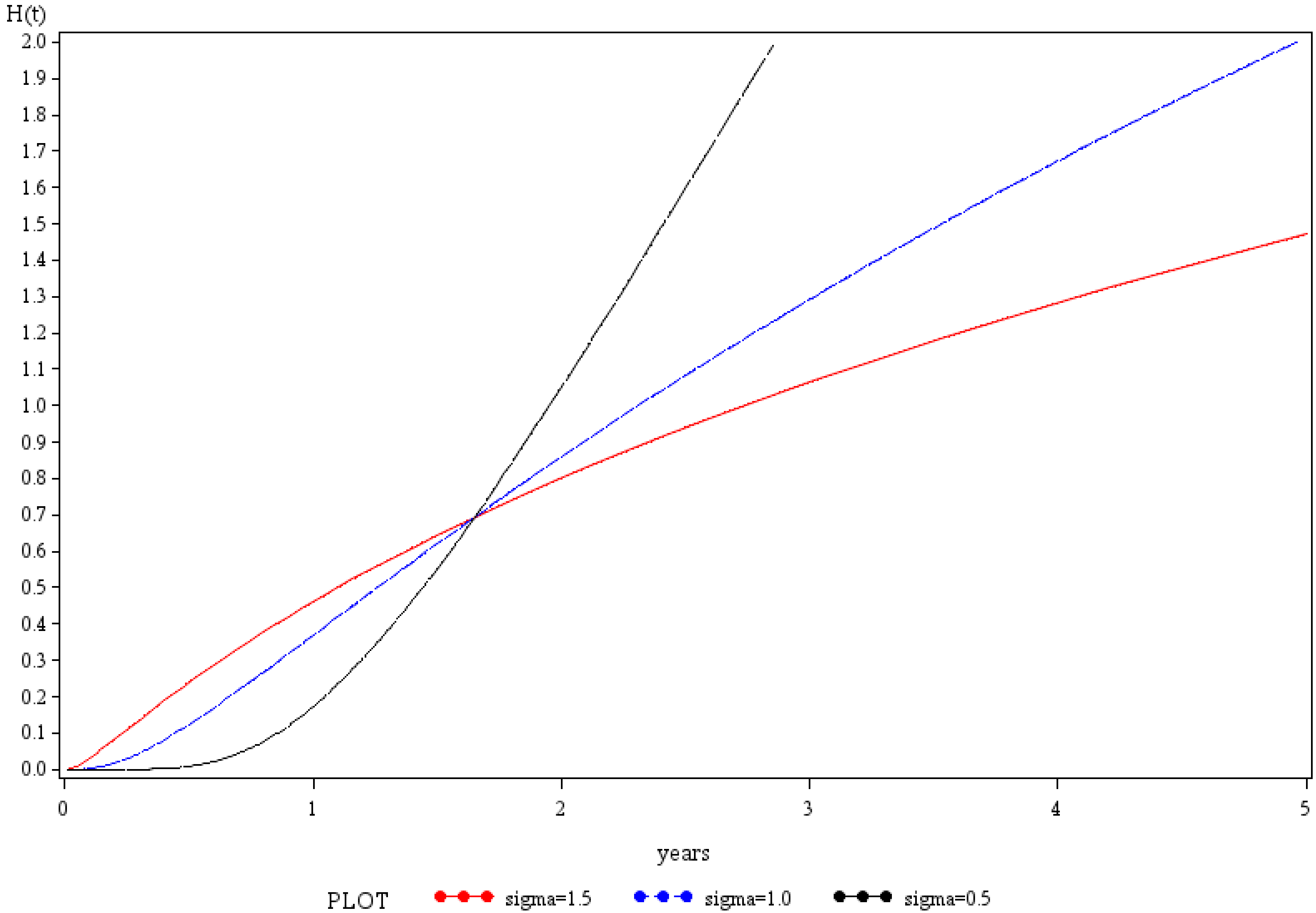
# Log normal cumulative hazard plots - u=0



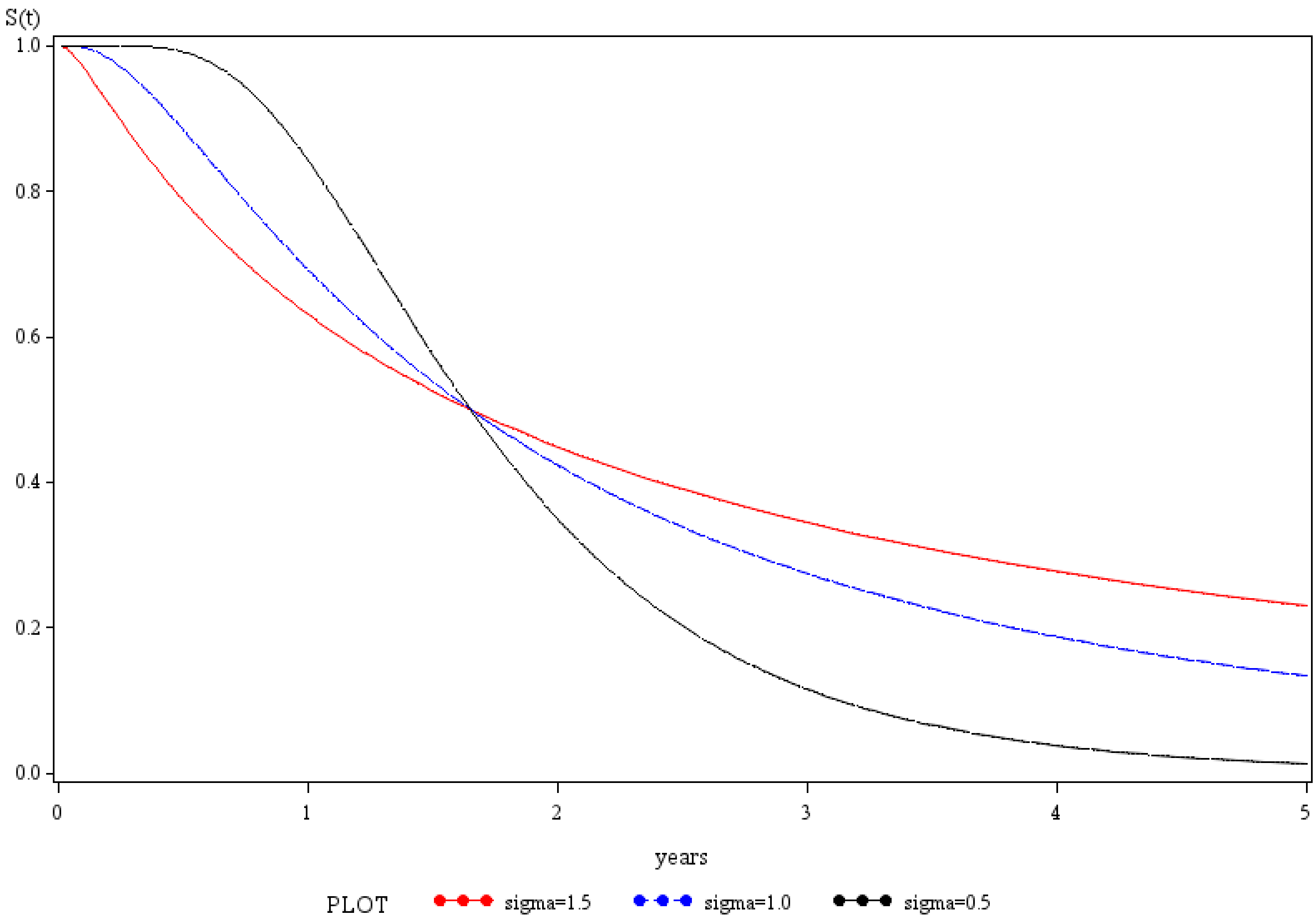

Log normal survival plots - u=0
S(t)
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
years
PLOT
scale=1.5
scale=1.0
scale=0.5


Log normal hazard plots - u=.5
h(t)
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
1
2
3
4
5
years
PLOT
sigma=1.5
sigma=1.0
sigma=0.5

# Log normal cumulative hazard plots - u=.5



## Log normal survival plots - u=.5



# Log-normal models:

| u | sigma | mean | median |
|---|---|---|---|
| 0 | 1.5 | 1 | 3.1 |
| 0 | 1 | 1 | 1.6 |
| 0 | 0.5 | 1 | 1.1 |
| 0.5 | 1.5 | 1.6 | 5.1 |
| 0.5 | 1 | 1.6 | 2.7 |
| 0.5 | 0.5 | 1.6 | 1.9 |

# Log Logistic

- hazard functions rise to a maximum then slowly decline or are monotone decreasing , AFT model only

$$S(t) = \frac{1}{1+\alpha t^{\gamma}}$$

$$f(t) = \frac{\alpha\gamma t^{(\gamma-1)}}{(1+\alpha t^{\gamma})^2}$$

$$h(t) = \frac{f(t)}{S(t)} = \frac{\alpha\gamma t^{(\gamma-1)}}{1+\alpha t^{\gamma}}$$

$$Median = \left(\frac{1}{\alpha}\right)^{\frac{1}{\gamma}}$$

$$w = \ln(t)\,,\ \gamma = \frac{1}{\sigma}$$

$$\alpha = \exp(-\frac{u}{\sigma})$$

$$S(w) = (1+\exp\left(\frac{w-u}{\sigma}\right))^{-1}$$

# Log Logistic

- also models constant odds ratio of survival

$$S(t) = \frac{1}{1+\alpha t^{\gamma}}$$

$$f(t) = \frac{\alpha\gamma t^{(\gamma-1)}}{(1+\alpha t^{\gamma})^2}$$

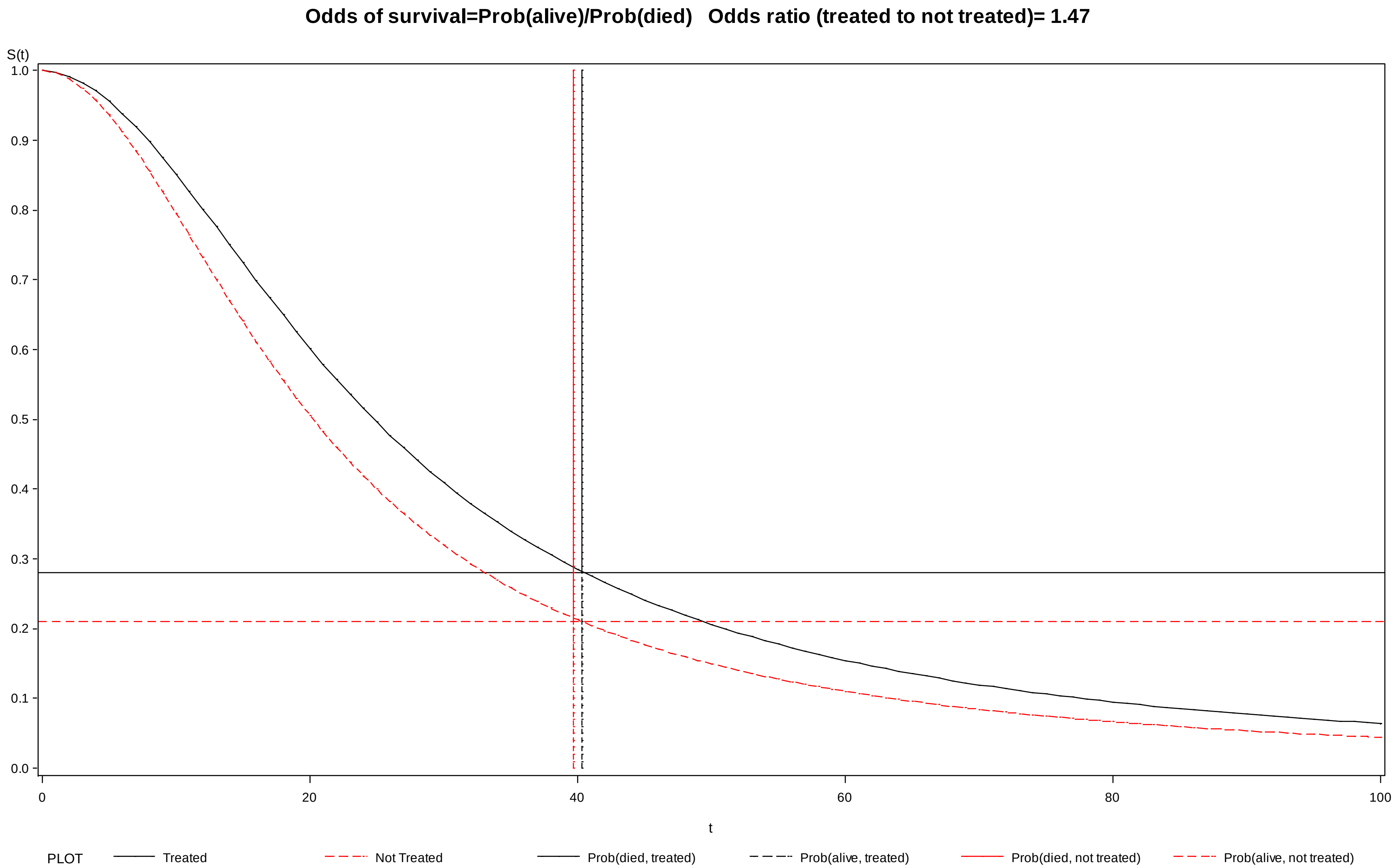
$$h(t) = \frac{f(t)}{S(t)} = \frac{\alpha\gamma t^{(\gamma-1)}}{1+\alpha t^{\gamma}}$$

$$Median = \left(\frac{1}{\alpha}\right)^{\frac{1}{\gamma}}$$

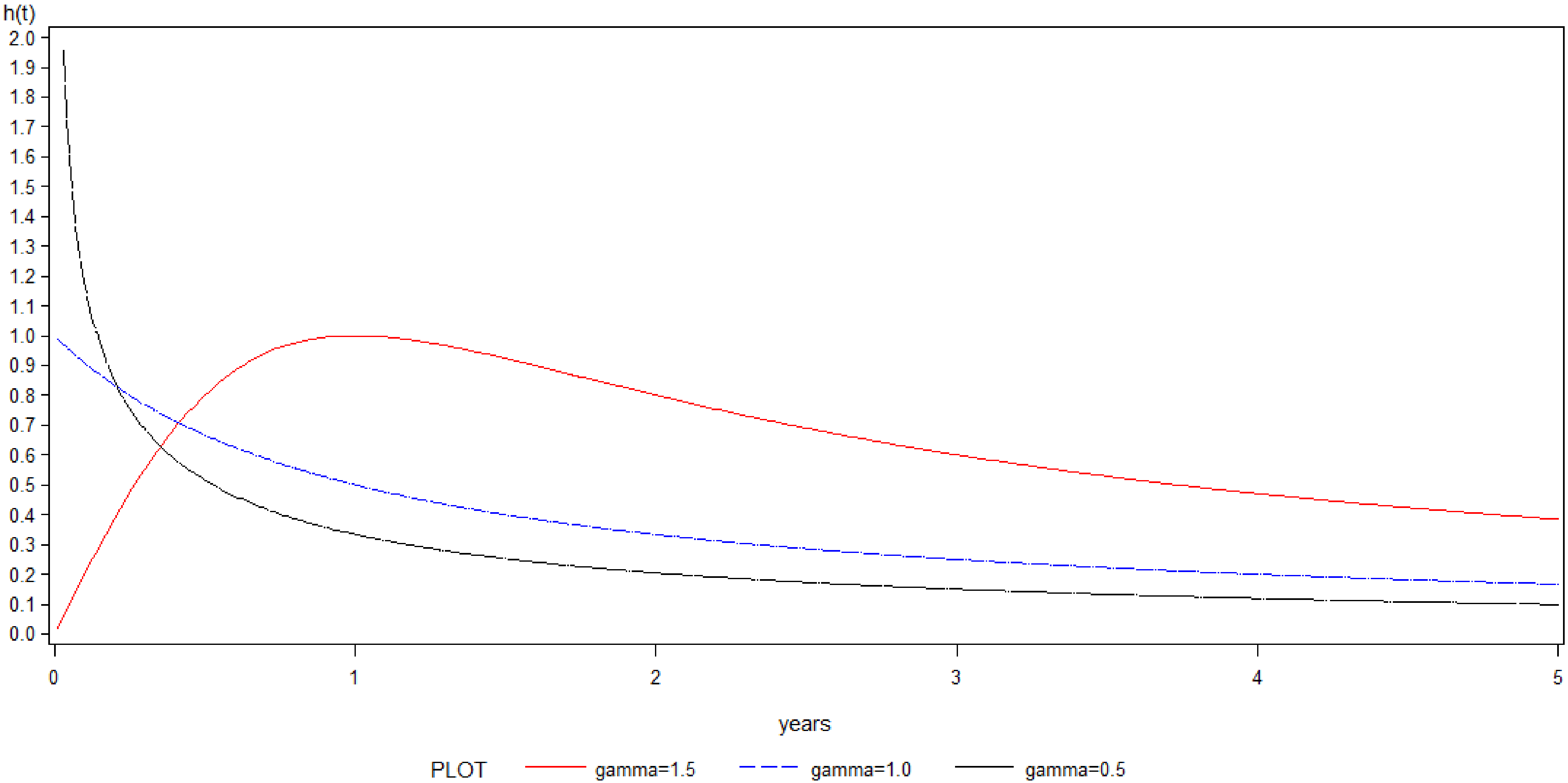
$$Odds = \frac{S(t)}{1-S(t)}$$

$$= \frac{1}{\alpha t^{\gamma}}$$

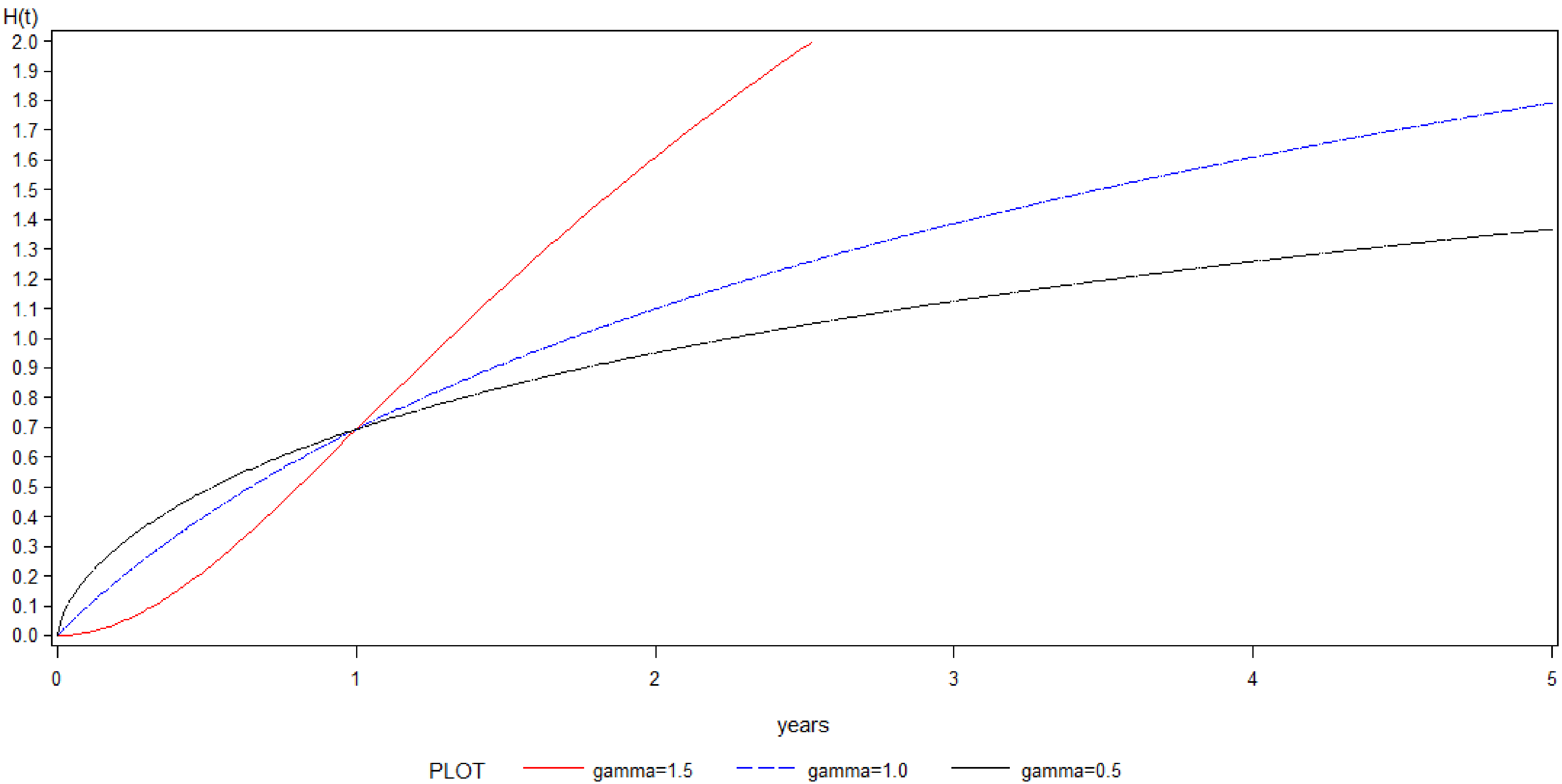
$$Odds\ ratio(2\ vs\ 1) = \frac{\alpha_1}{\alpha_2}$$


Odds of survival=Prob(alive)/Prob(died) Odds ratio (treated to not treated)= 1.47
S(t)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
20
40
60
80
100
t
PLOT
Treated
Not Treated
Prob(died, treated)
Prob(alive, treated)
Prob(died, not treated)
Prob(alive, not treated)

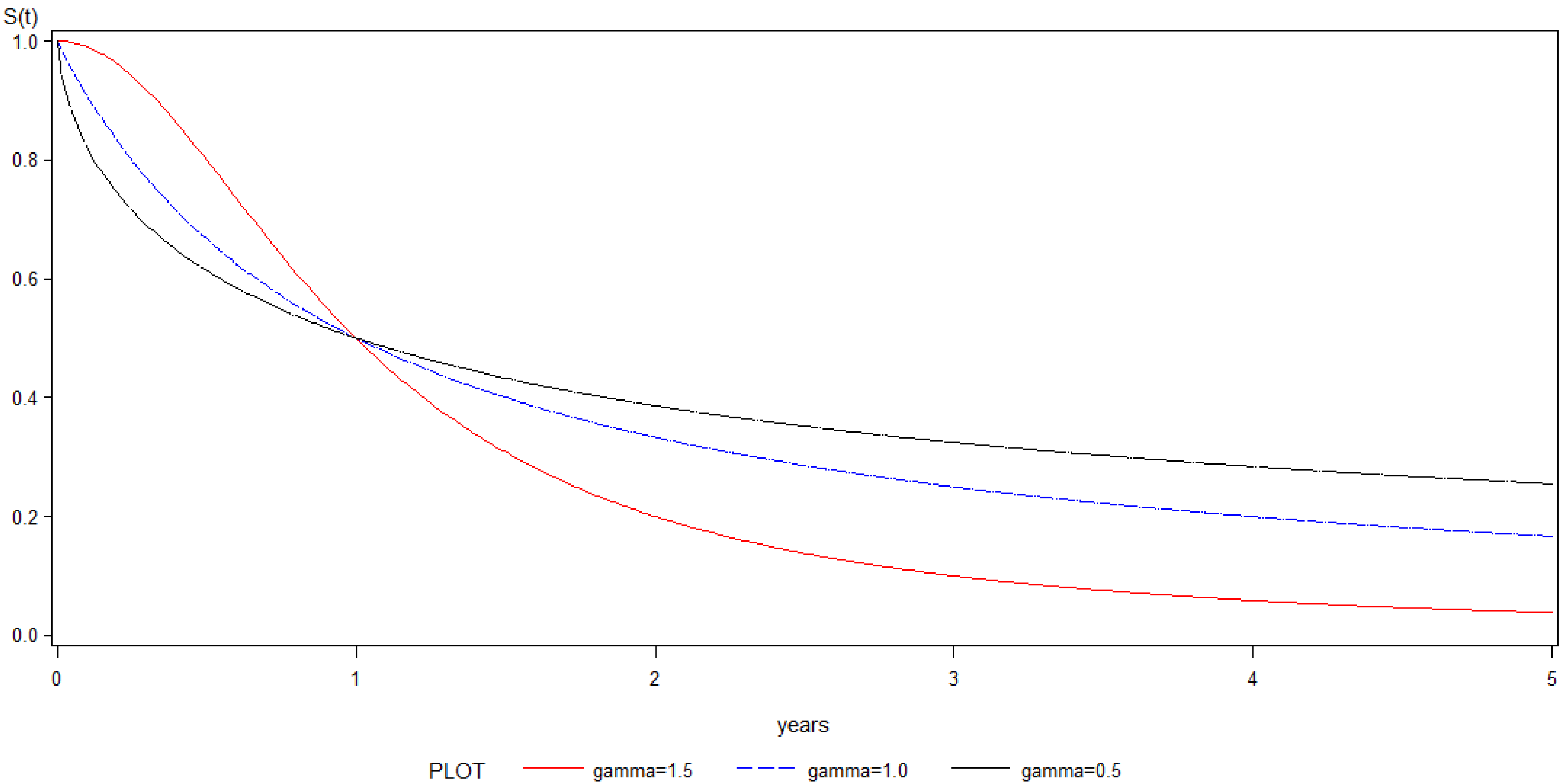
# Log logistic hazard plots - alpha=1



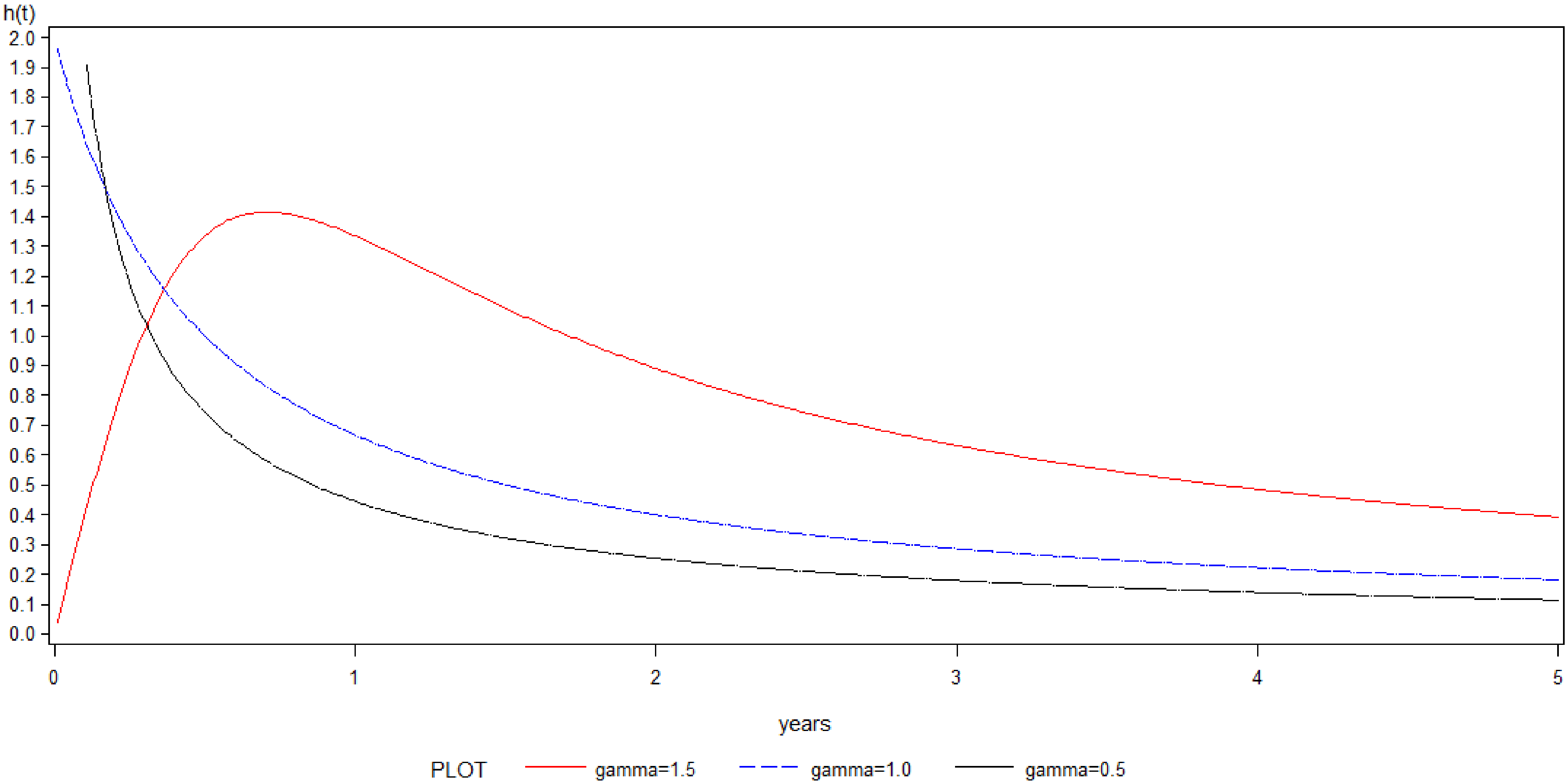
# Log logistic cumulative hazard plots - alpha=1



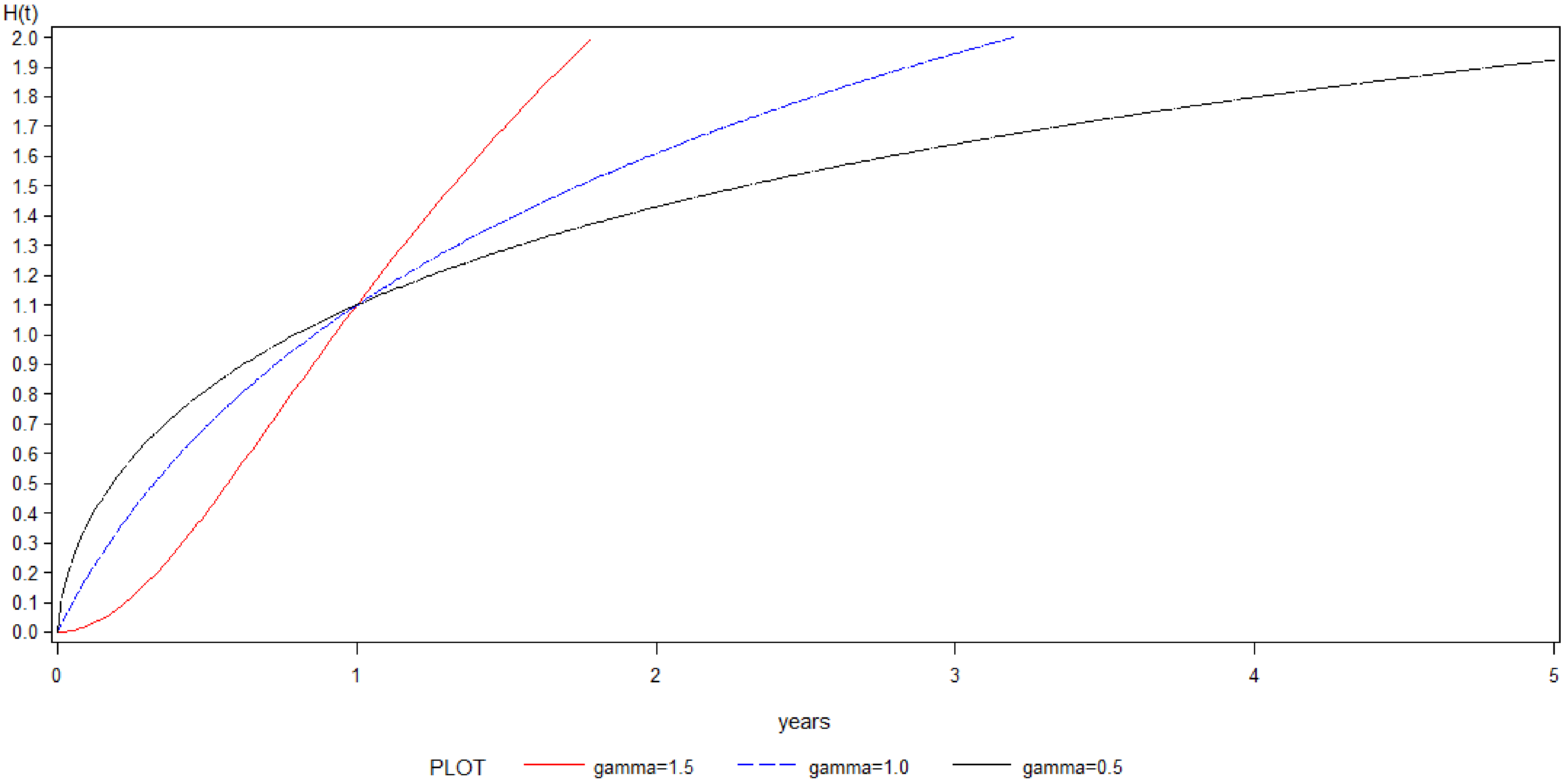
# Log logistic survival plots - alpha=1



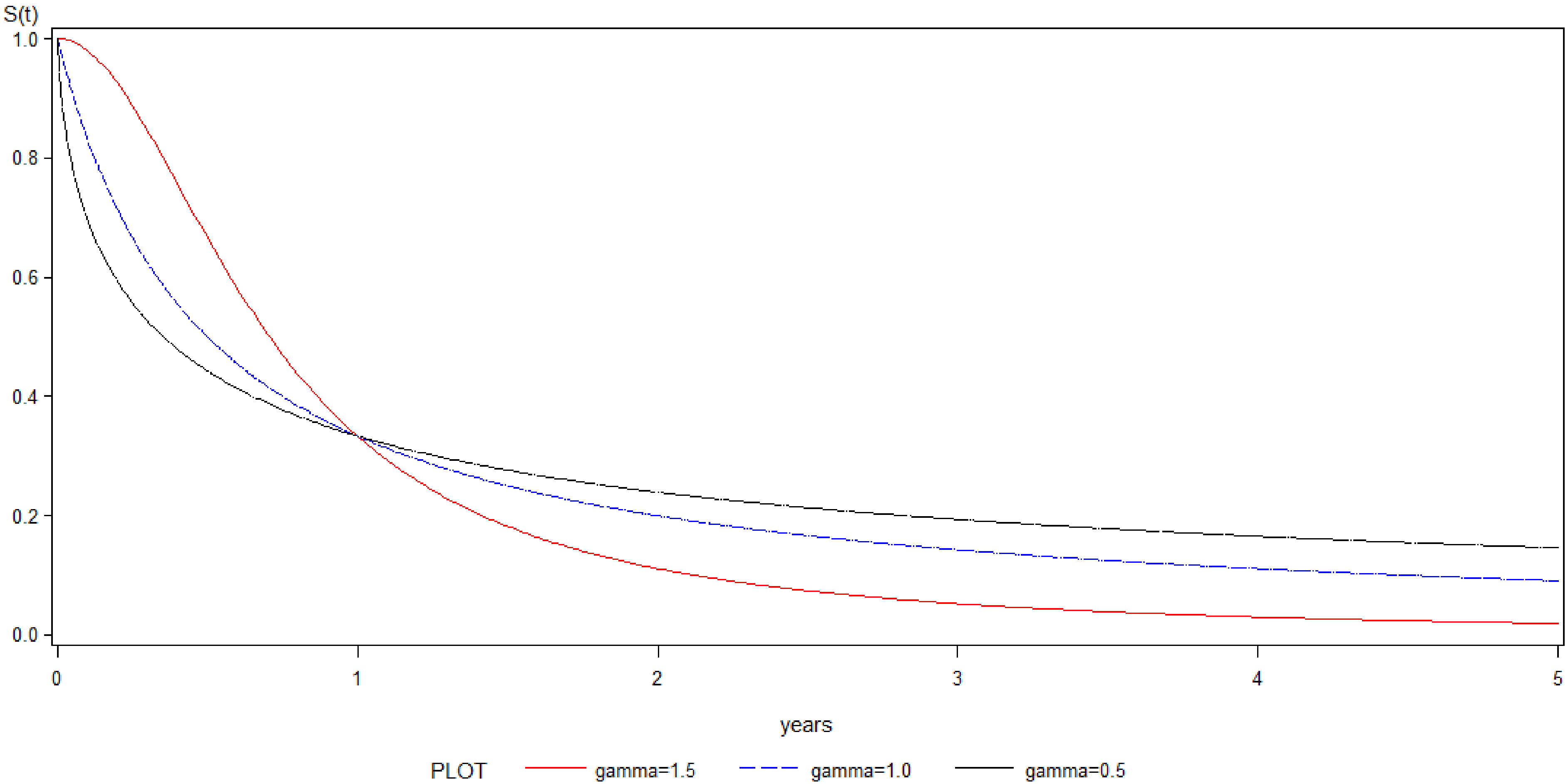
# Log logistic hazard plots - alpha=2



# Log logistic cumulative hazard plots - alpha=2



# Log logistic survival plots - alpha=2



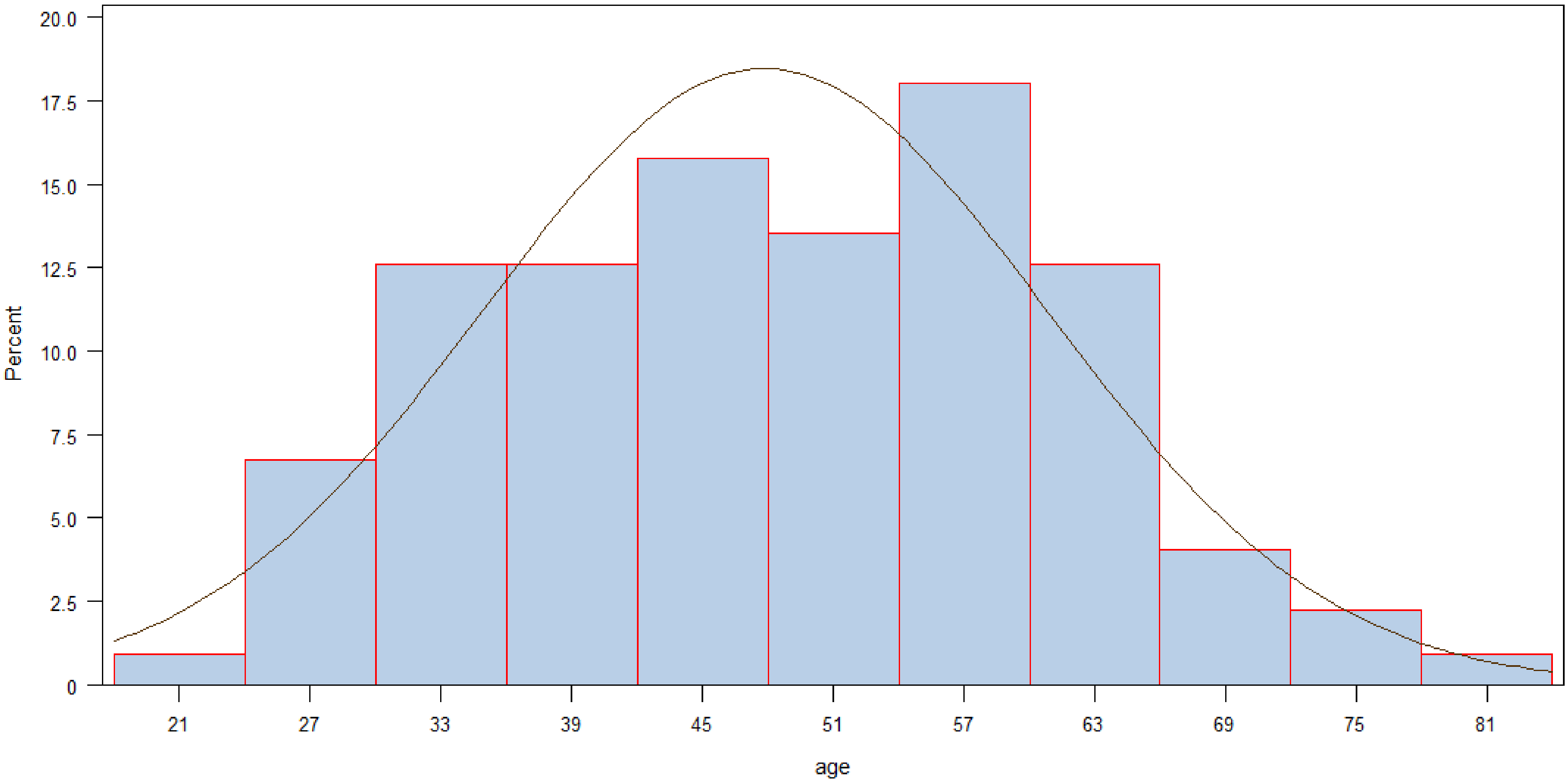
# Log-logistic models:

| alpha | gamma | sigma | u | median |
|---|---|---|---|---|
| 1 | 2 | 0.5 | 0 | 1 |
| 1 | 1 | 1 | 0 | 1 |
| 1 | 0.67 | 1.5 | 0 | 1 |
| 2 | 2 | 0.5 | -0.3 | 0.7 |
| 2 | 1 | 1 | -0.7 | 0.5 |
| 2 | 0.67 | 1.5 | -1 | 0.4 |

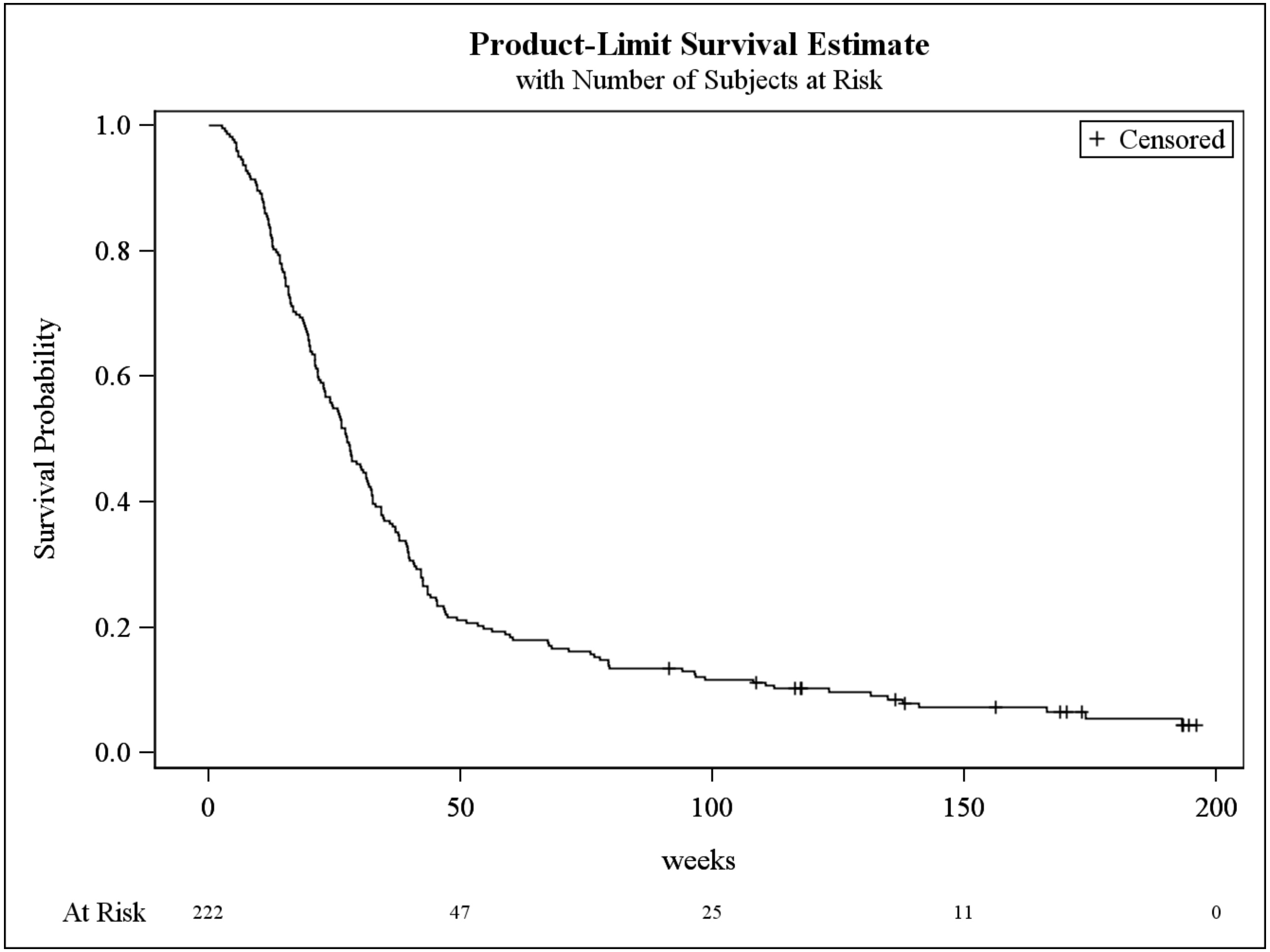
# Example Data Set

- Patients diagnosed with brain cancer are randomized to a treatment group versus placebo.
- N=222, with only 15 censored cases
- Mean age around 48 years and 64% male.
- Other covariates are available in data set.

# Distribution age



# Overall Survival

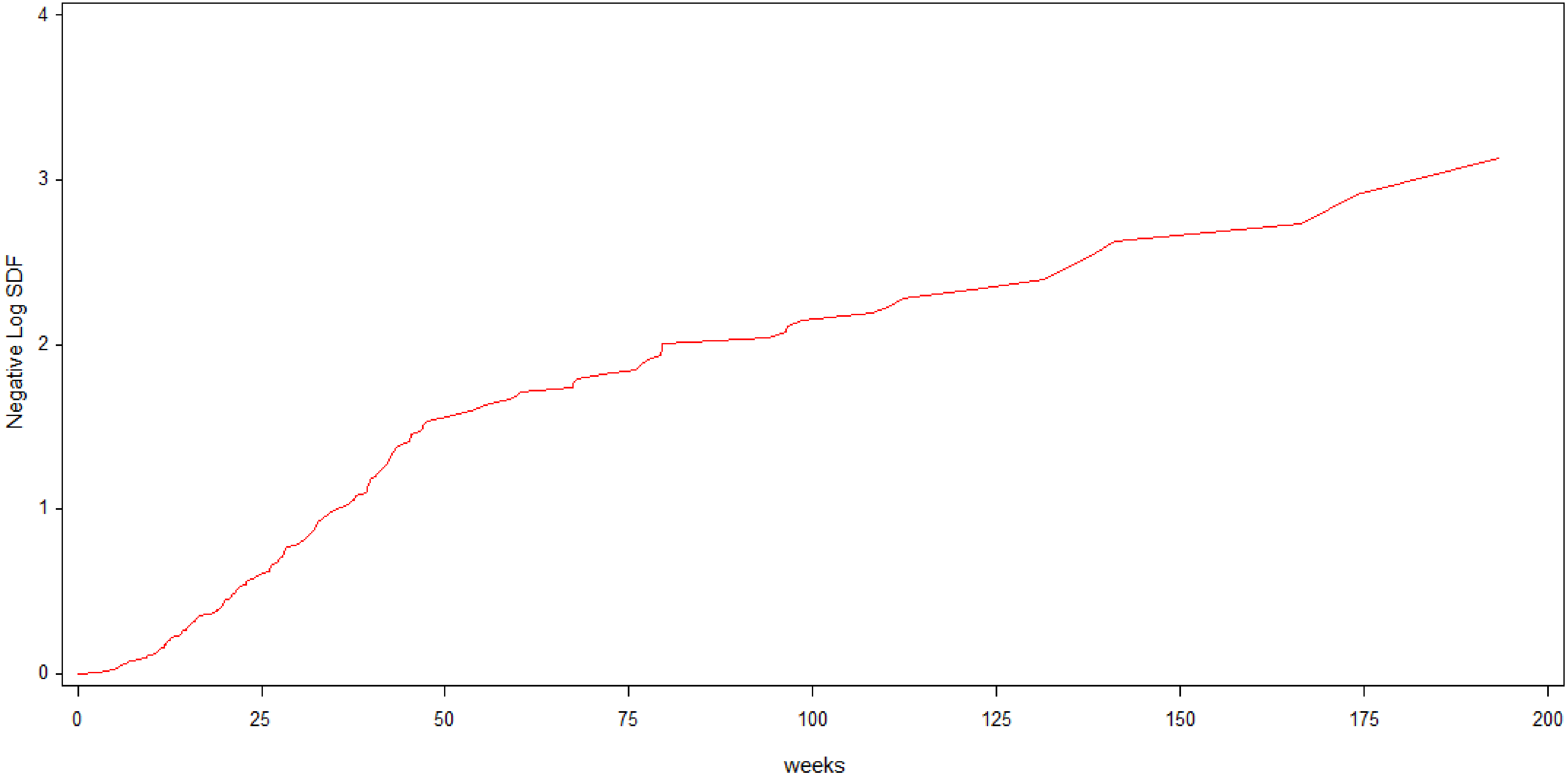



Estimated median=27.4 and mean=44.5

# -logS(t) Plot

- Plot versus t
- If a straight line then exponential model ($H(t)=\lambda t$)

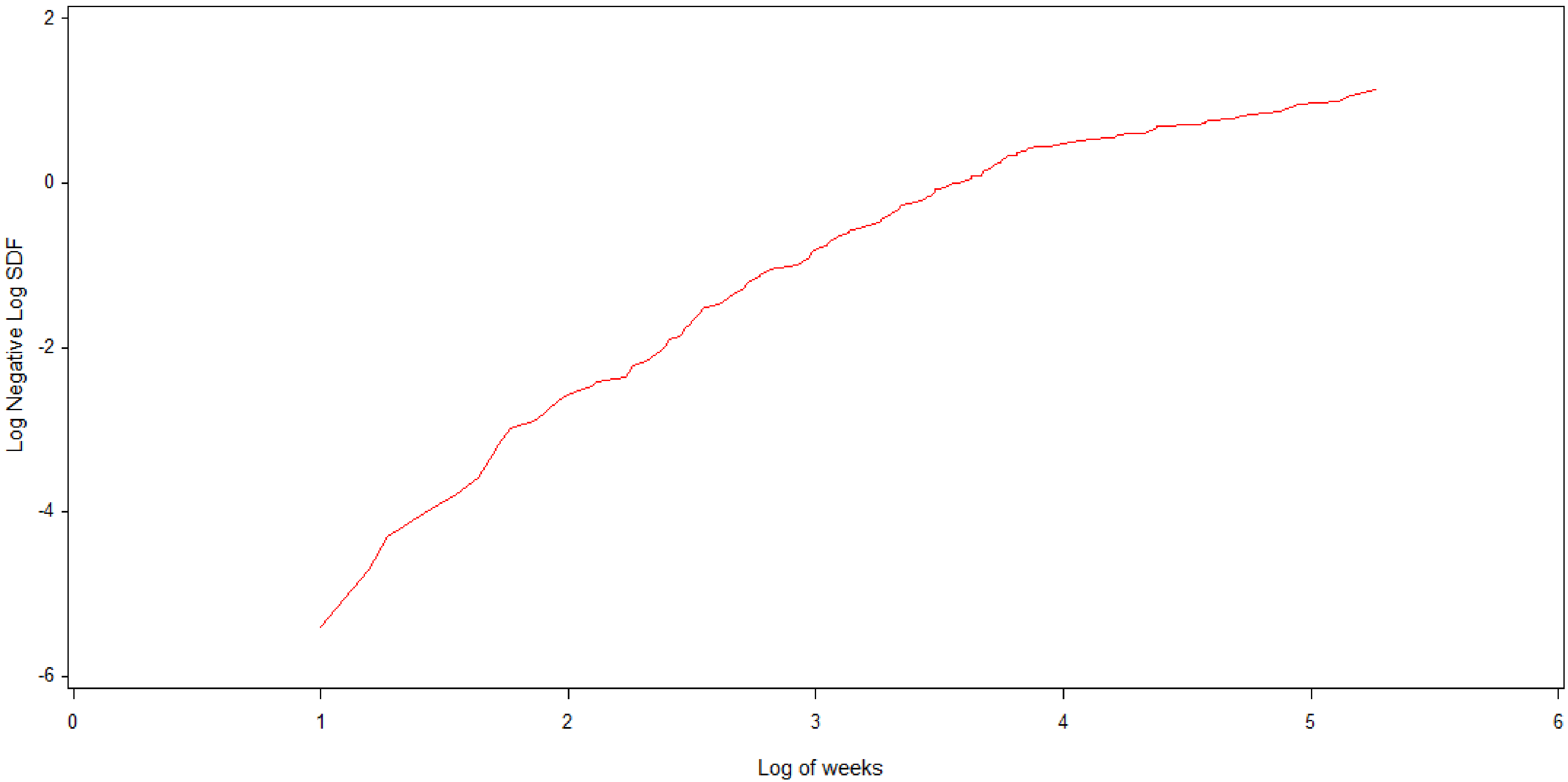
# LifeTest: Overall Survival



# log-logS(t) Plot

- Plot versus log(t)
- If a straight line then Weibull model
  - $H(t)=\lambda t^{\gamma}$
  - $\log H(t)=\log(\lambda)+\gamma\log(t)$

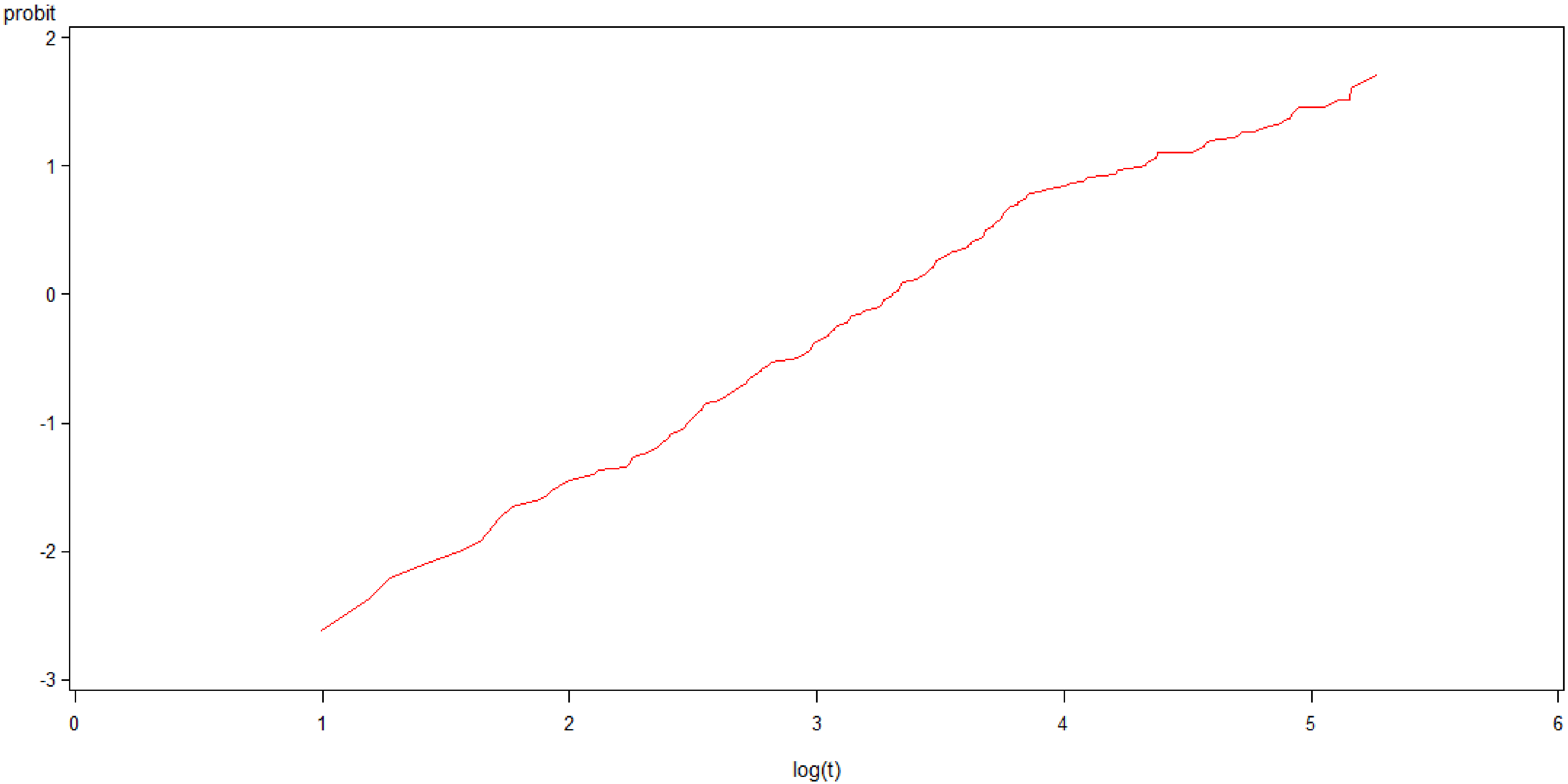
# LifeTest: Overall Survival



# Probit Plot

- Plot $\Phi^{-1}(1-S(t))$ versus $\log(t)$
- If a straight line then Log Normal model
  - $S(t)=1-\Phi((\log(t)-u)/\sigma)$

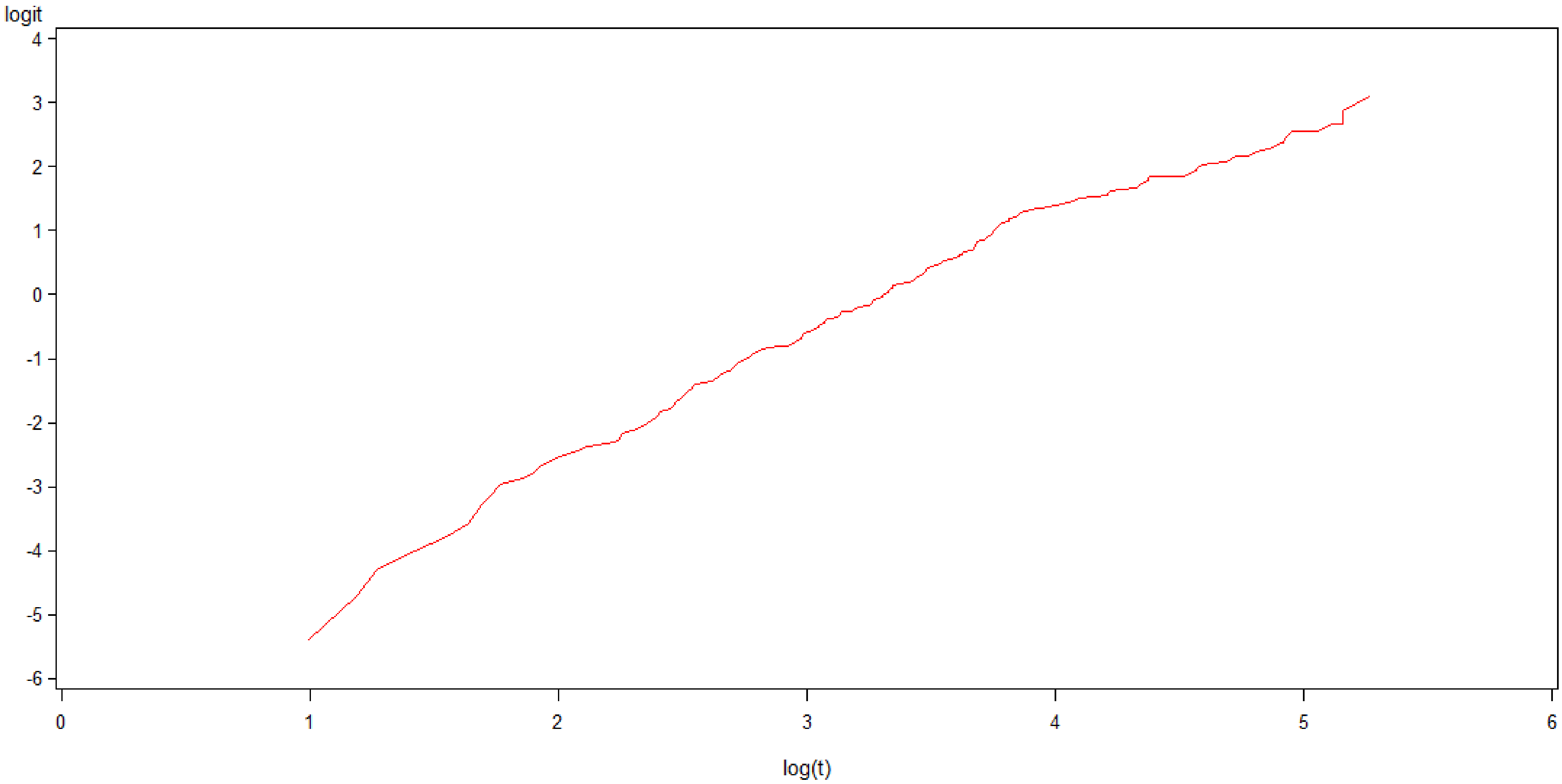
# Probit(CDF) Plot



# Logit Plot

- Plot log((1-S(t)) /S(t)) versus log(t)
- Plot of odds of having the event by time t
- If a straight line then Log Logistic model
  - $S(t)=1/(1+\alpha t^{\gamma})$

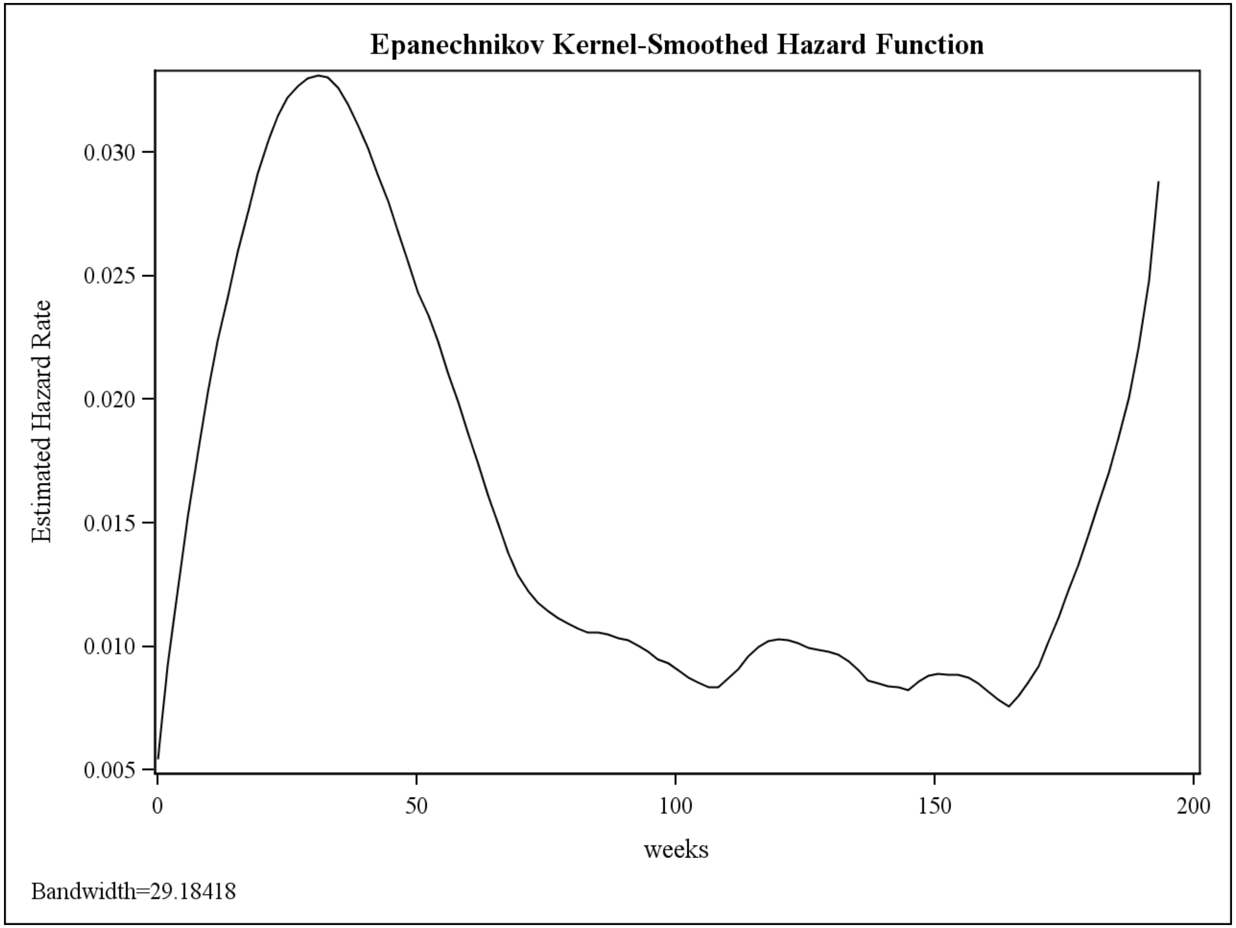
# Logit(CDF) Plot



# Other options

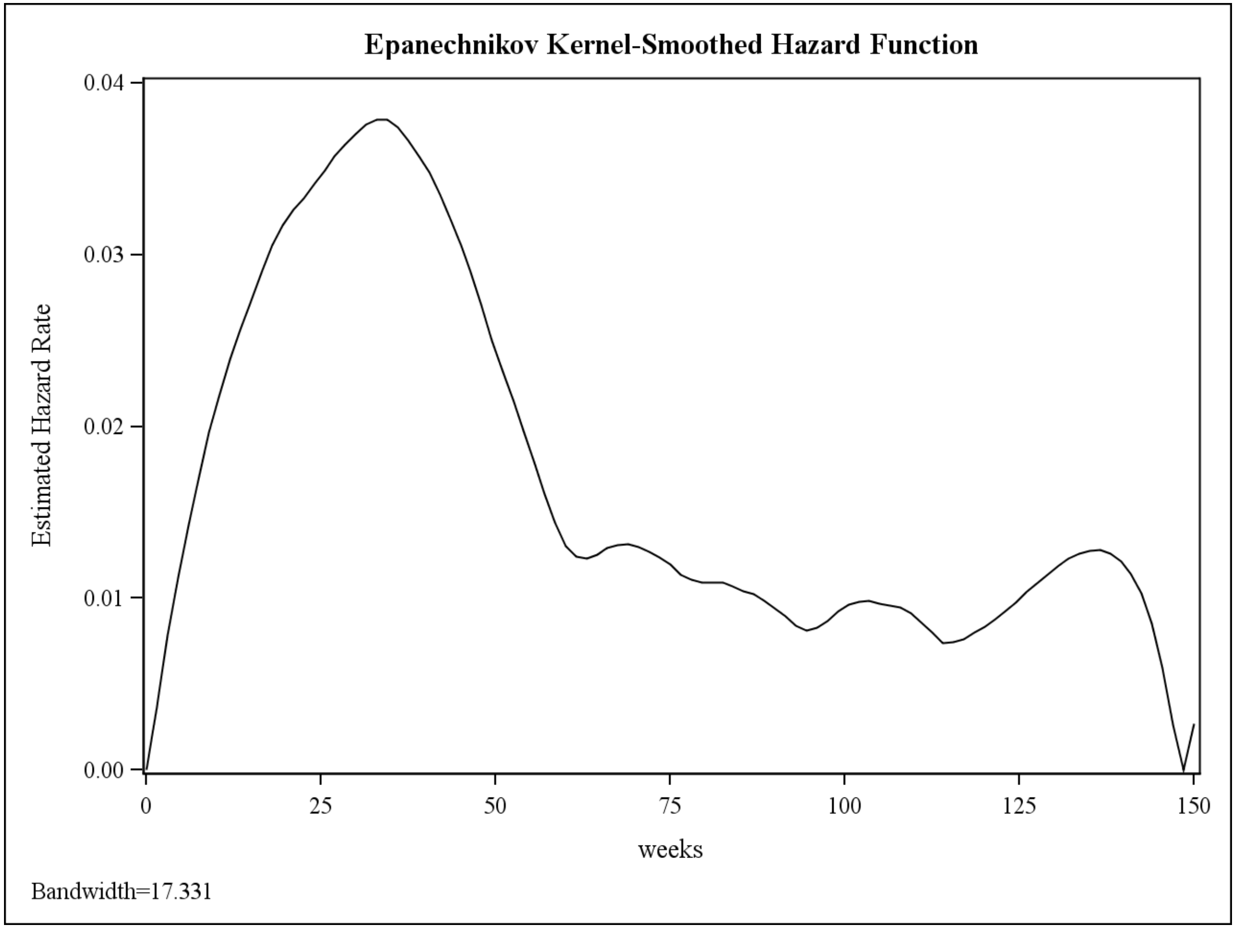
- Non-parametric smoothing of hazard function
- Probability plots
- Likelihood ratio tests of nested models (Gamma)
- Check distribution of t or log(t) for the non-censored cases

# Smoothed Hazard Function



# Smoothed Hazard Function

(reduced range)

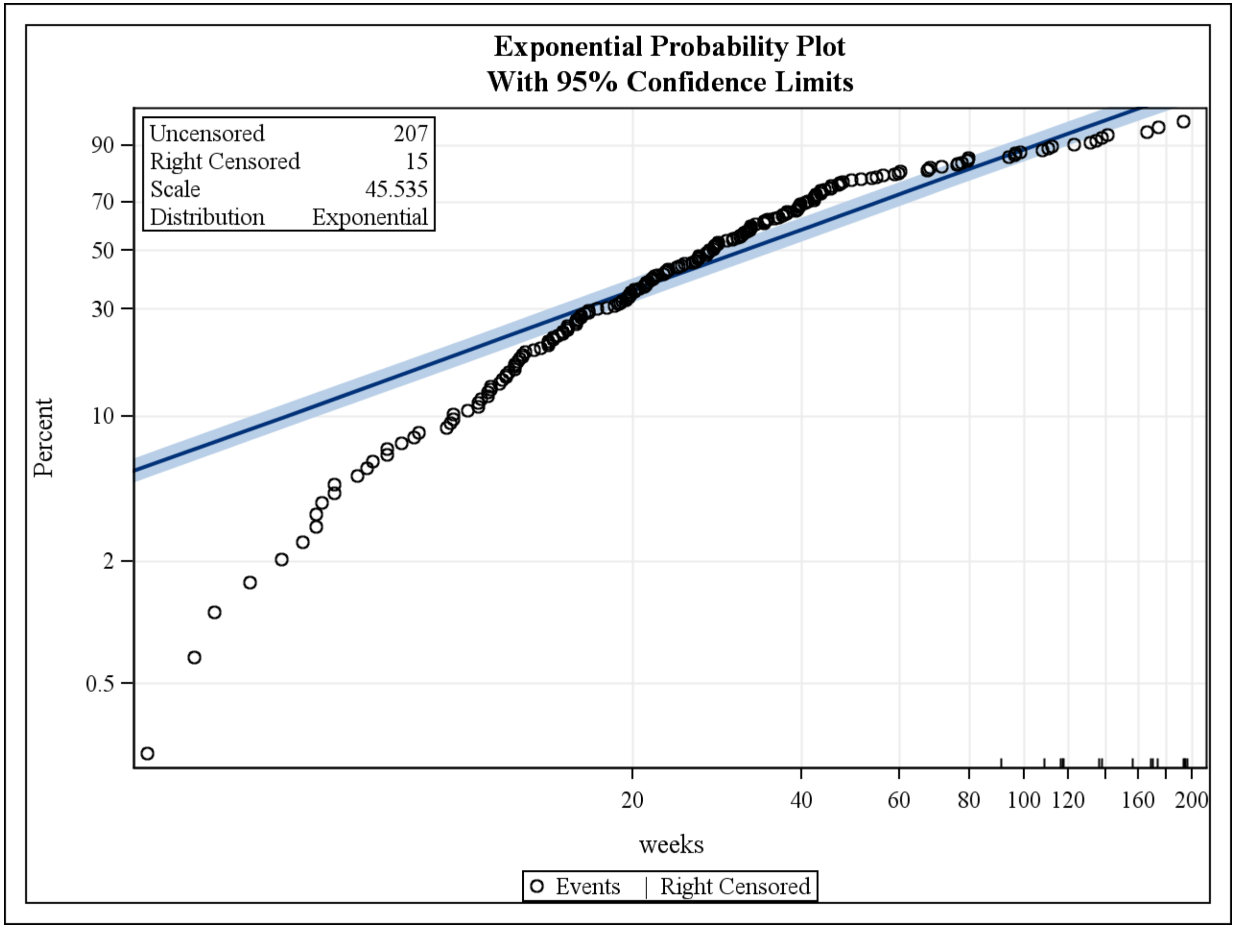


# SAS Code (SAS 9.4 using ODS graphics)

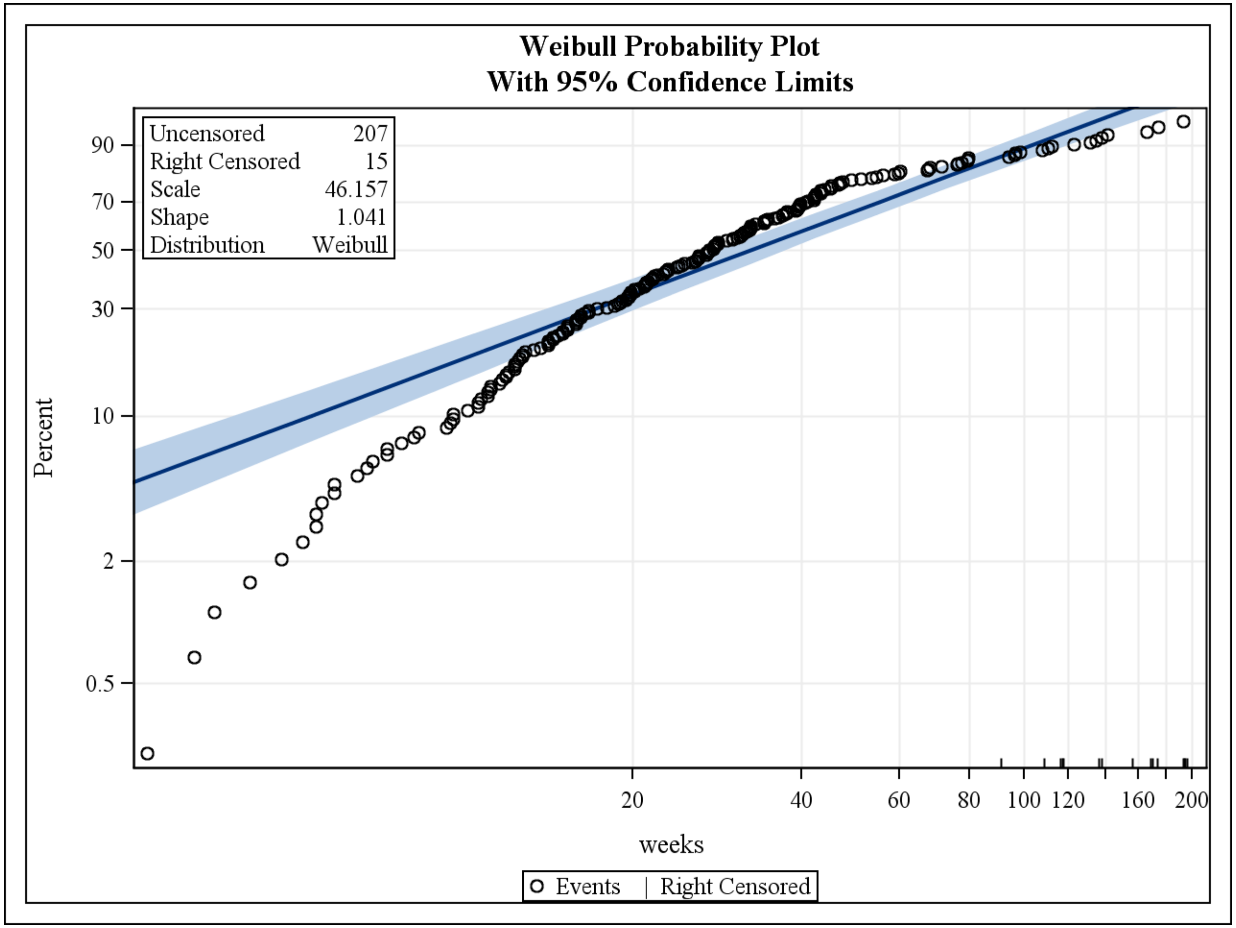
```
proc lifereg data=sda.brain;
  model weeks*event(0)=/d=exponential;
  probplot;
  inset;
  title 'LifeReg: Overall Survival - Probability Plot (Exponential)';
run;
```

```
proc lifetest data=sda.brain
              plot=(survival(atrisk outside) hazard logsurv loglogs)
              notable;
  time weeks*event(0);
  title 'LifeTest: Overall Survival: hazard';
run;
```

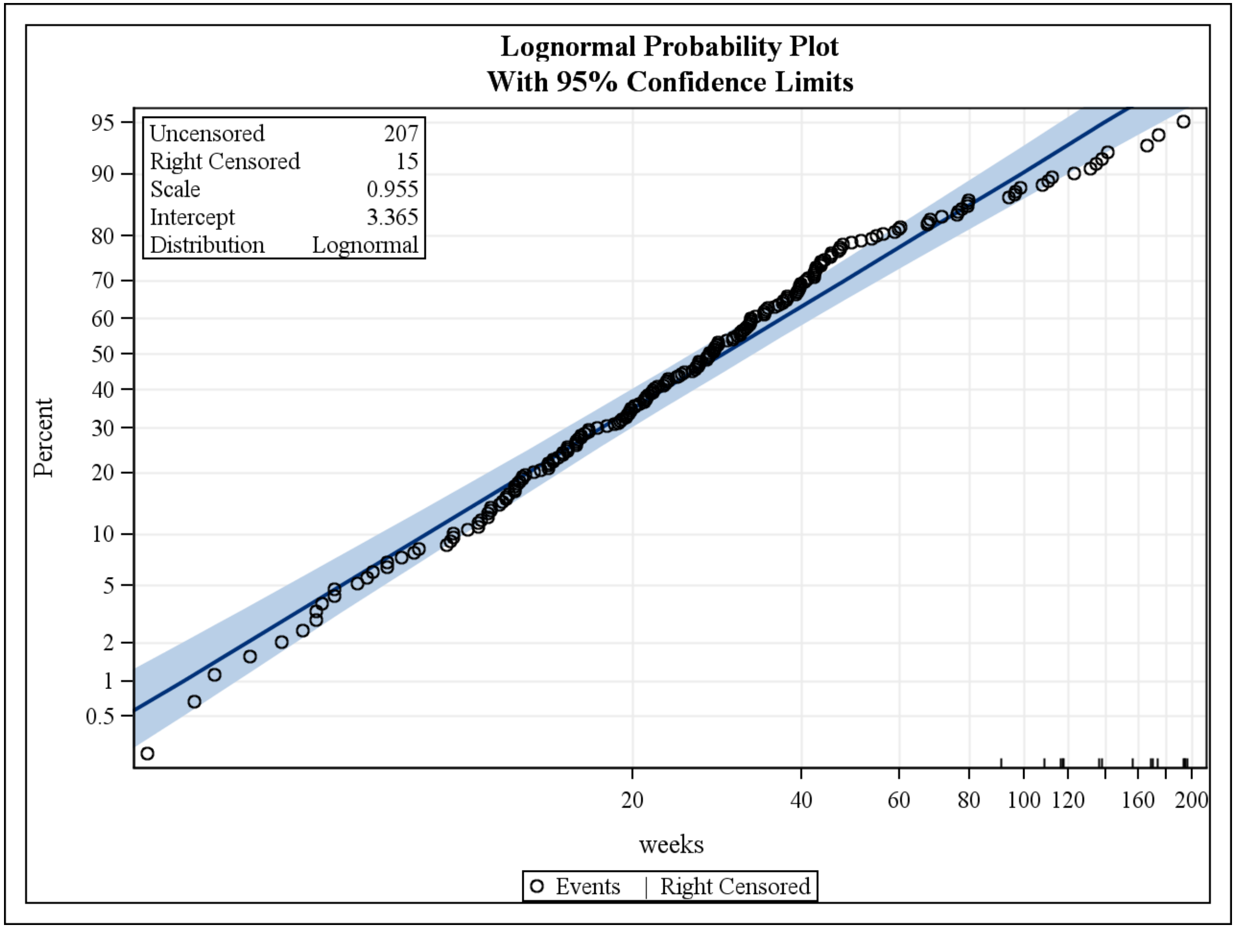
# Exponential Probability Plot



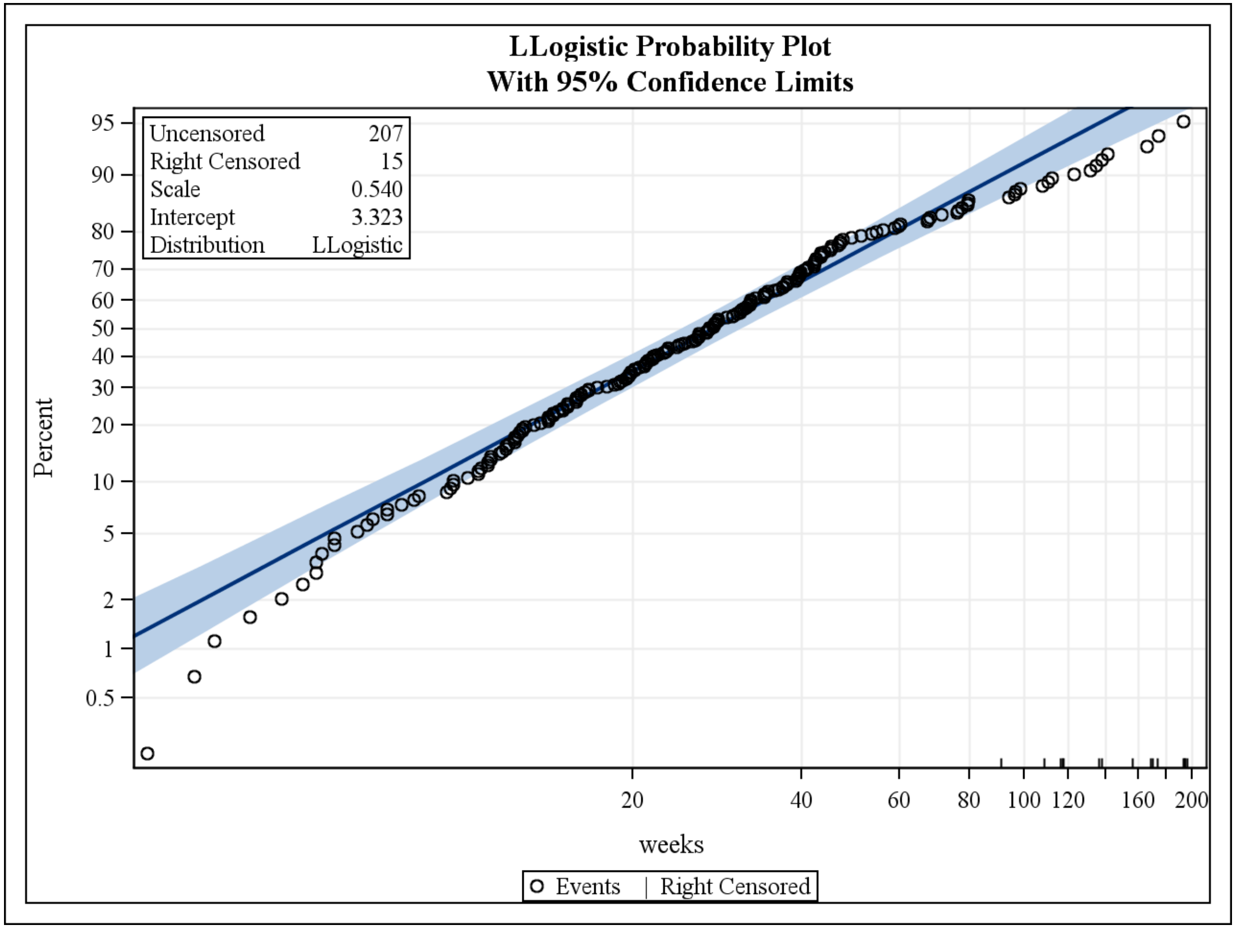
# Weibull Probability Plot



# Log Normal Probability Plot

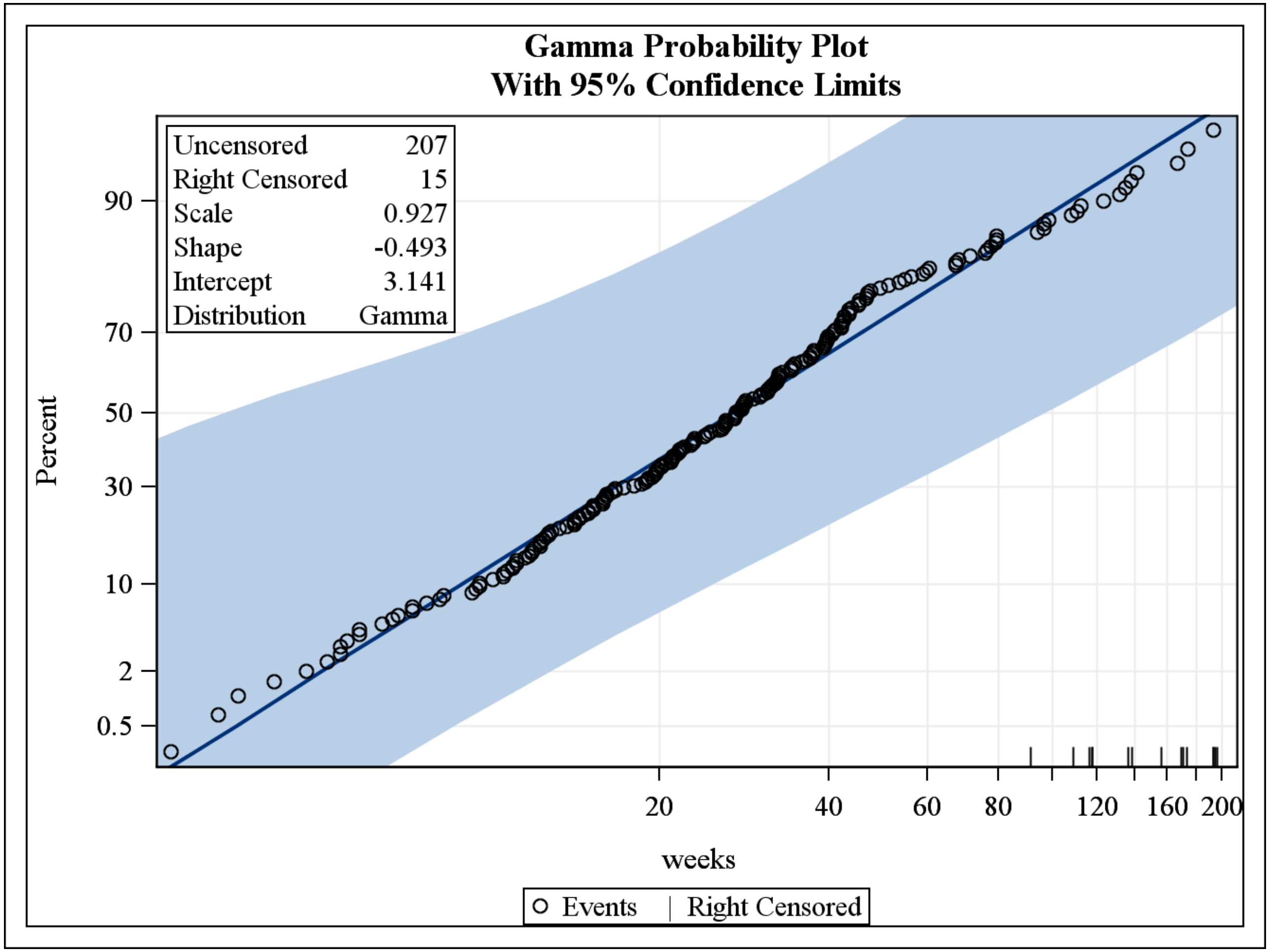


# Log Logistic Probability Plot



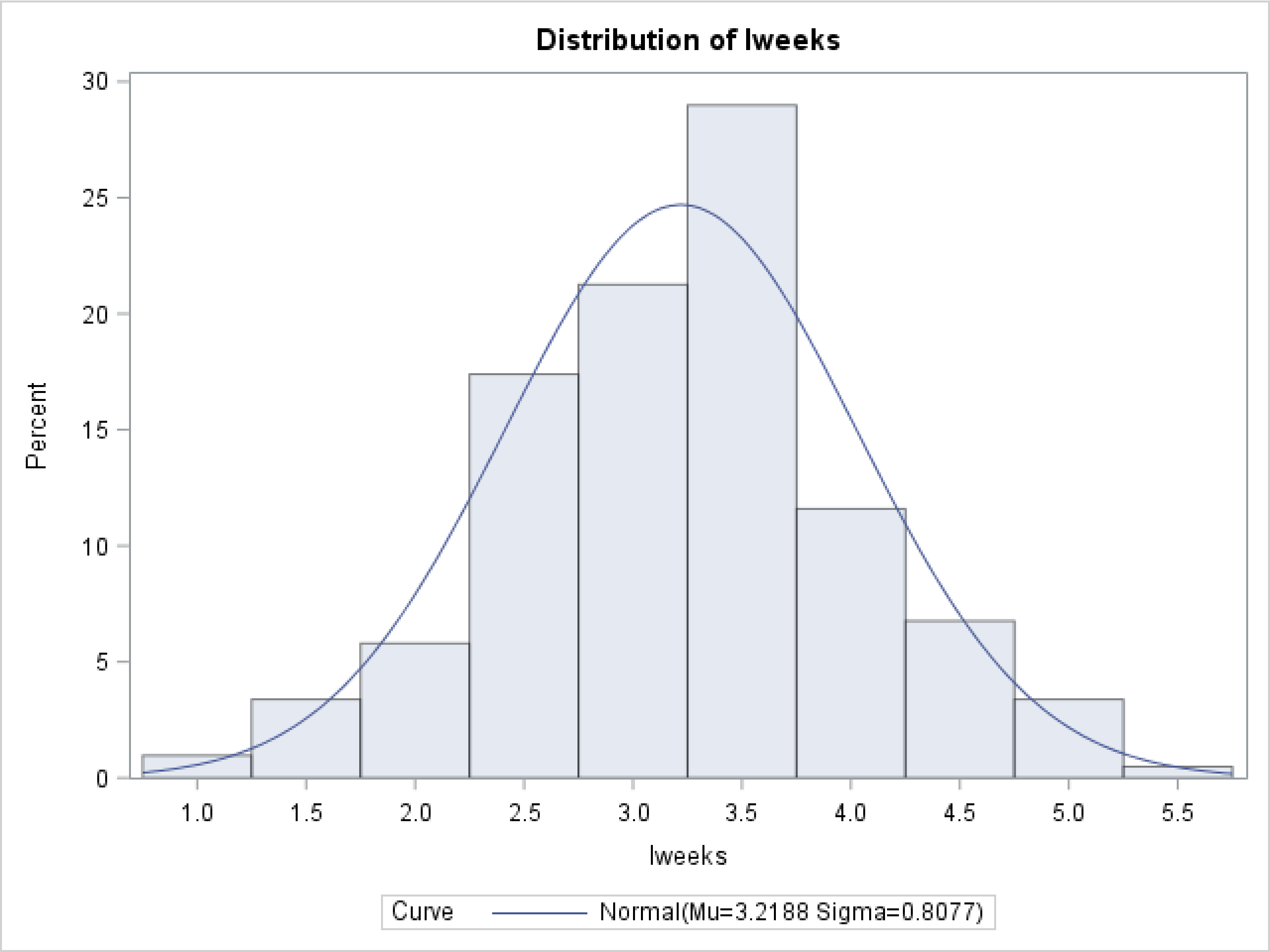
# Gamma Model

- SAS fits the generalized 3-parameter model
- it can fit a Weibull (exponential) and log-normal model (test using likelihood ratio test)
- it can also fit a model with a U-shaped hazard function
- Survivor and hazard functions involve incomplete gamma functions

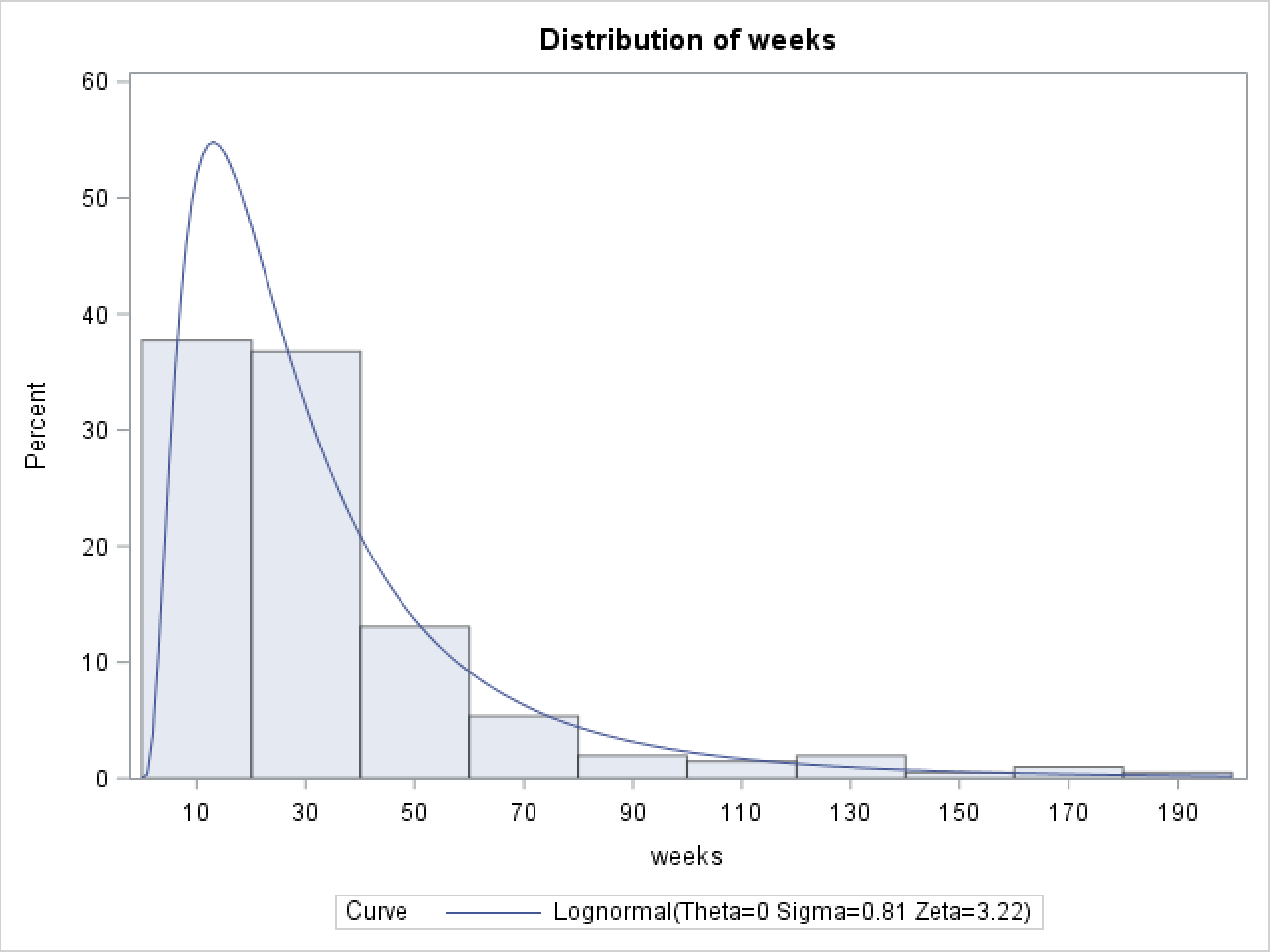


Gamma Probability Plot
With 95% Confidence Limits
Uncensored 207
Right Censored 15
Scale 0.927
Shape -0.493
Intercept 3.141
Distribution Gamma
Percent
90
70
50
30
10
2
0.5
20
40
60
80
120
160
200
weeks
Events
Right Censored

# Events only (Proc Univariate):

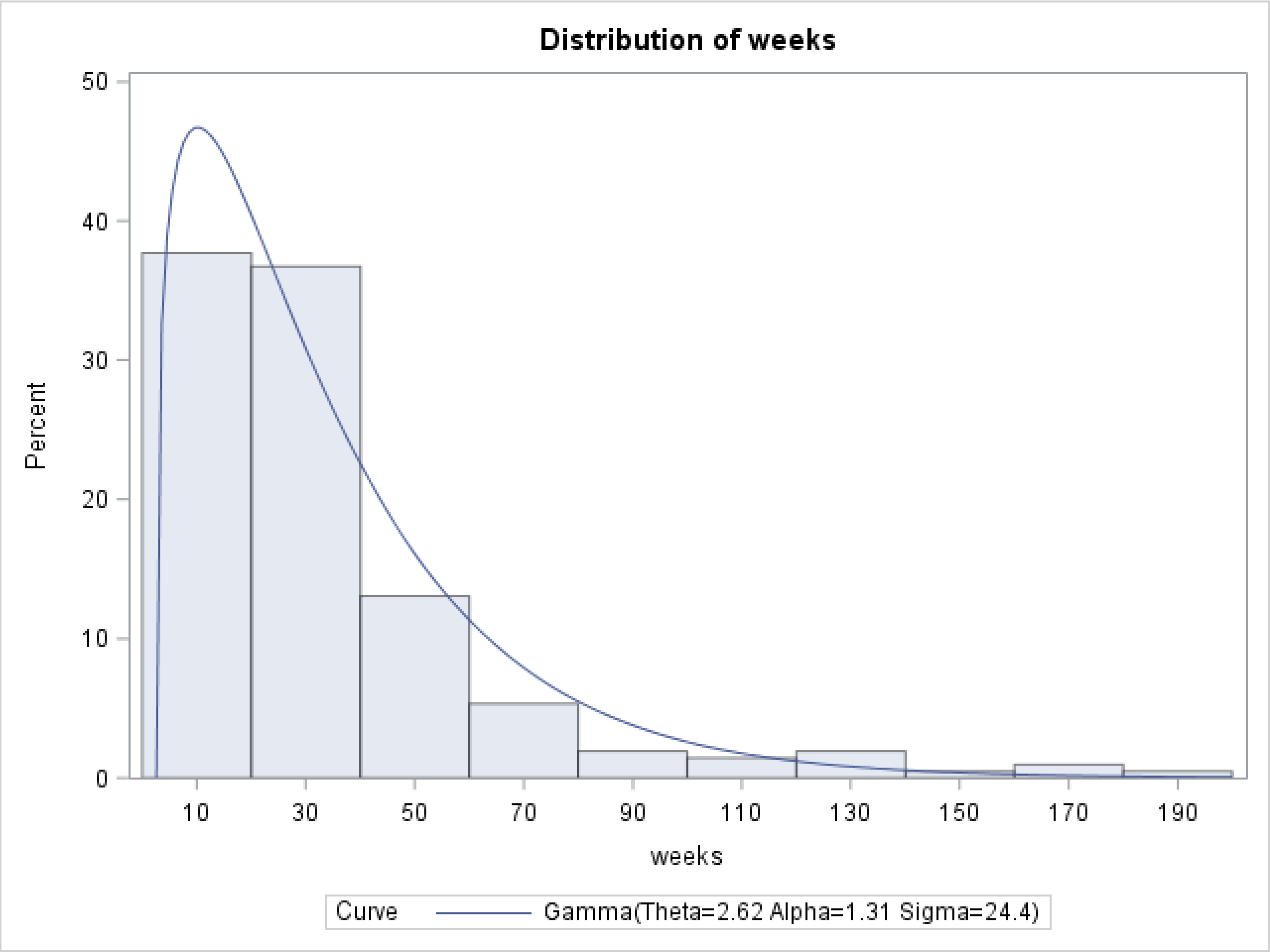


Events only (Proc Univariate):




Note: CDF plots also available in Proc Univariate

Events only (Proc Univariate):




Note: different parameterization than Proc Lifetest.

# Unadjusted model

# Basic data summary

| Variable | Sum |
|---|---|
| event | 207 |
| weeks | 9426 |

```
Estimated rate: 207/9426=0.02196
                ln(0.02196)=-3.8185
```

```
overall median      27.430      95% CI (23.14,  31.43)
mean                44.528      SE= 3.285
```

# Exponential (Intercept only)

-2 Log Likelihood=662.275, AIC=664.275

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.8185 | 0.0695 | 3.6823 | 3.9547 | 3018.22 | <.0001 |
| Scale | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |
| Weibull Scale | 1 | 45.5348 | 3.1649 | 39.7357 | 52.1803 | | |
| Weibull Shape | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |

Lagrange Multiplier Statistics

| Parameter | Chi-Square | Pr > ChiSq |
|---|---|---|
| Scale | 0.6216 | 0.4304 |

$\lambda = \exp(-\ 3.8185) = 0.02196$

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

$h(t) = \lambda$

$\text{Median} = -\ln(.5)/\lambda = 31.4$

$\text{Mean} = 1/\lambda = 45.5$

# Weibull(Intercept only)

-2 Log Likelihood=661.693 AIC=665.693

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.8321 | 0.0692 | 3.6965 | 3.9676 | 3069.48 | <.0001 |
| Scale | 1 | 0.9608 | 0.0498 | 0.8679 | 1.0636 | * 1/shape | |
| Weibull Scale | 1 | 46.1571 | 3.1925 | 40.3054 | 52.8583 | | |
| Weibull Shape | 1 | 1.0408 | 0.0540 | 0.9402 | 1.1522 | * gamma | |

```
λ = exp(- 1.0408 * 3.8321) = 0.0185
γ = 1.0408
S(t) = exp(-λ*t**γ)
h(t) = γ*λ*(t**(γ-1))
Median = (-ln(.5)/λ)**(1/γ) = 32.3
```

# Weibull(Intercept only) Alternate parameterizations

```
Using extreme value distribution:
μ=3.8321
σ=0.9608
S(t) = exp(-exp(( log(t)-μ) / σ ))

Another common parameterization:
b=exp(u)=exp(3.8321)
γ = 1.0408
S(t) = exp(-(t/b)**γ)
```

# Log Normal(Intercept only)

-2 Log Likelihood=608.002, AIC=612.002

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.3653 | 0.0644 | 3.2389 | 3.4916 | 2726.77 | <.0001 |
| Scale | 1 | 0.9553 | 0.0479 | 0.8659 | 1.0540 | | |

```
u = 3.3653
σ = 0.9553
S(t) = 1-Φ((ln(t)-u)/σ)
f(t) = 1/(sqrt(2*π)*t*σ)*exp(-1/2*((ln(t)-u)/σ)**2)
h(t) = f(t)/S(t)
Median = exp(u) = 28.9
Mean = exp(u+0.5σ**2) = 45.7
```

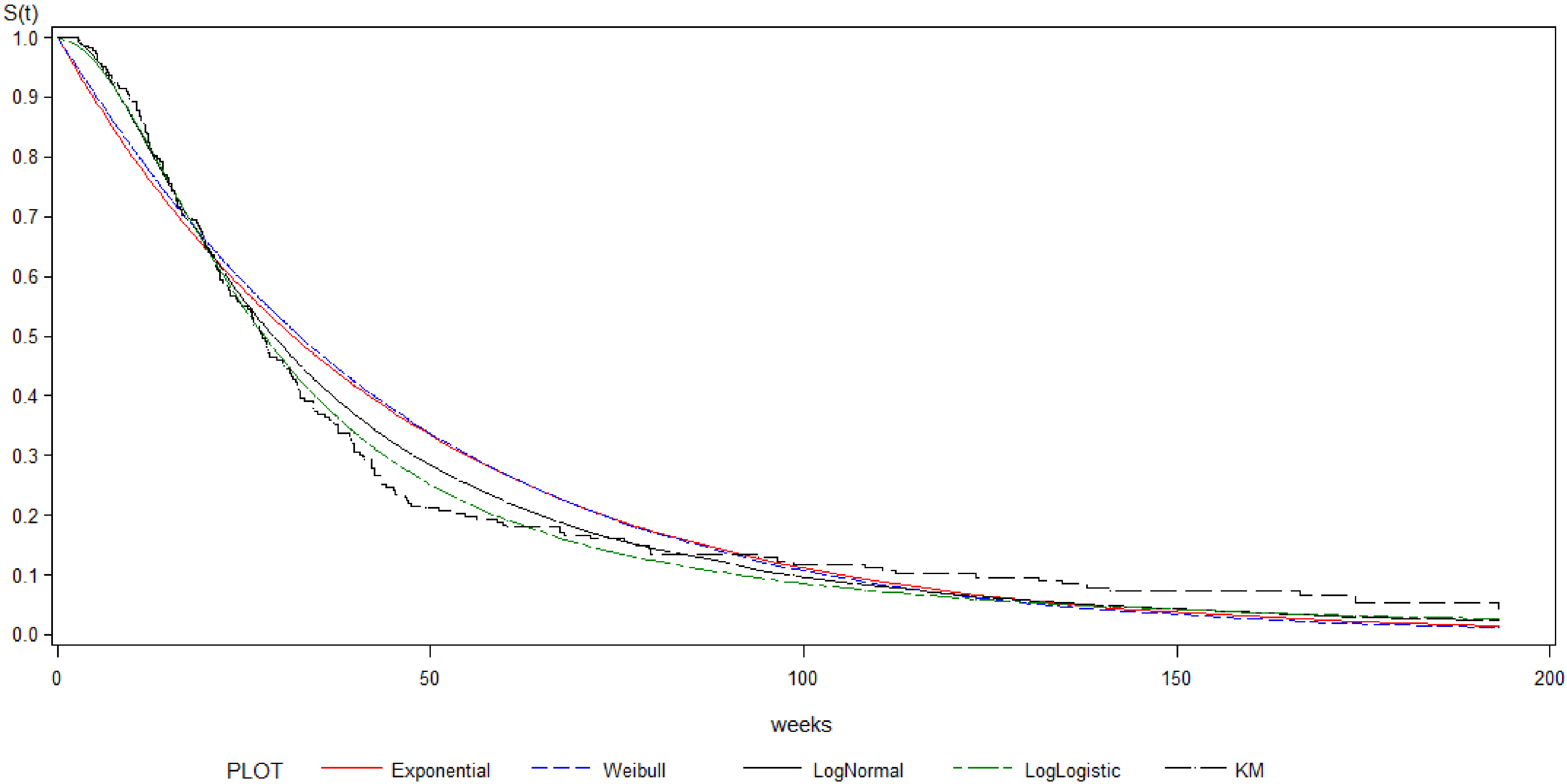
# Log Logistic (Intercept only)

-2 Log Likelihood=604.338, AIC=608.338

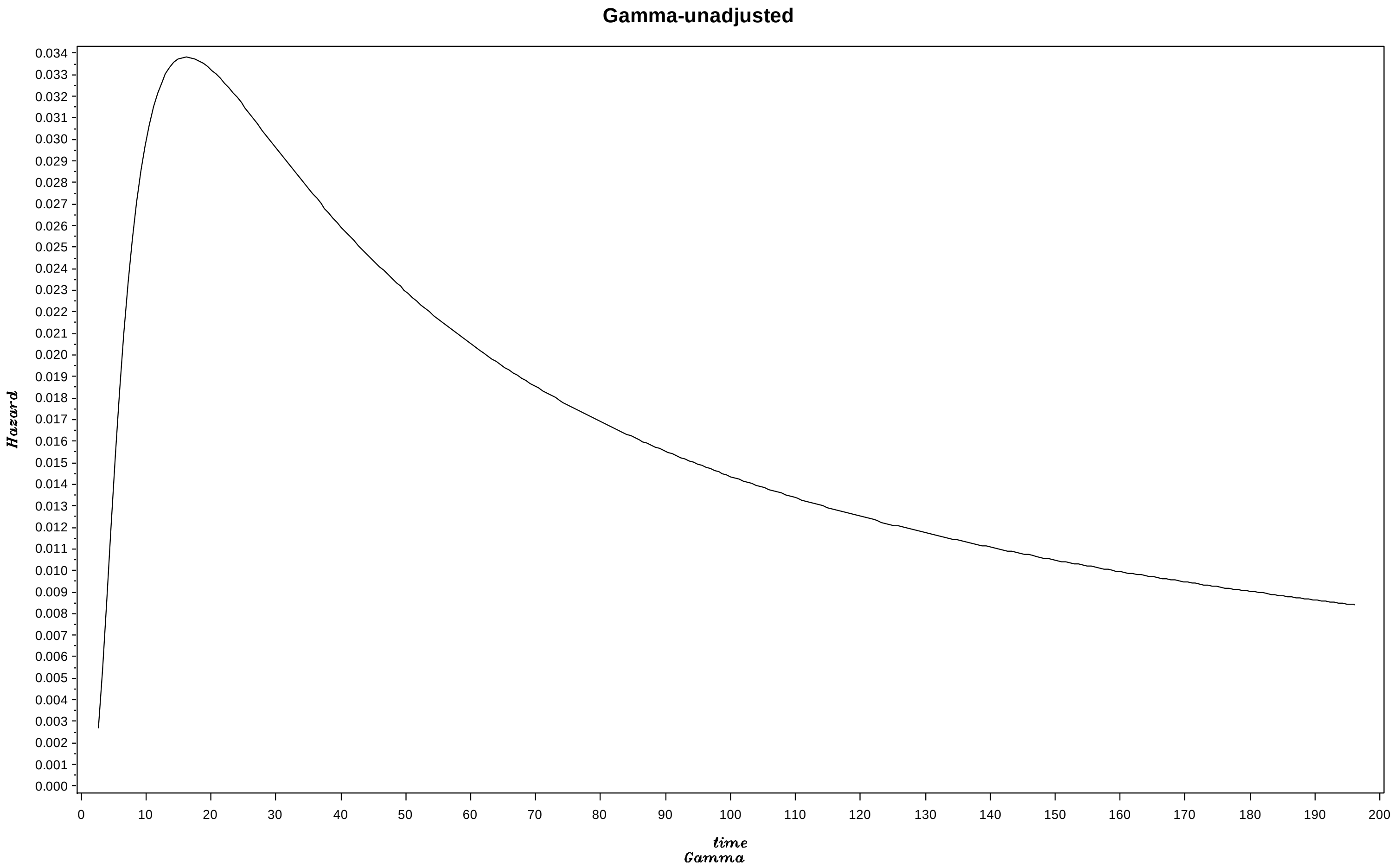
| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.3233 | 0.0625 | 3.2008 | 3.4458 | 2828.98 | <.0001 |
| Scale | 1 | 0.5398 | 0.0315 | 0.4815 | 0.6052 | | |

```
α = exp(- 3.3233 / 0.5398) = 0.0021
γ = 1/ 0.5398 = 1.8525
S(t) = 1/(1+α*t**γ)
f(t) = (α*γ*t**(γ-1))/(1+α*t**γ)**2
h(t) = f(t)/S(t)
Median = (1/α)**(1/γ) = 27.8
```

# Comparison of Survival Models



# Gamma hazard (Allison LIFEHAZ macro)



# Gamma model (Intercept only)

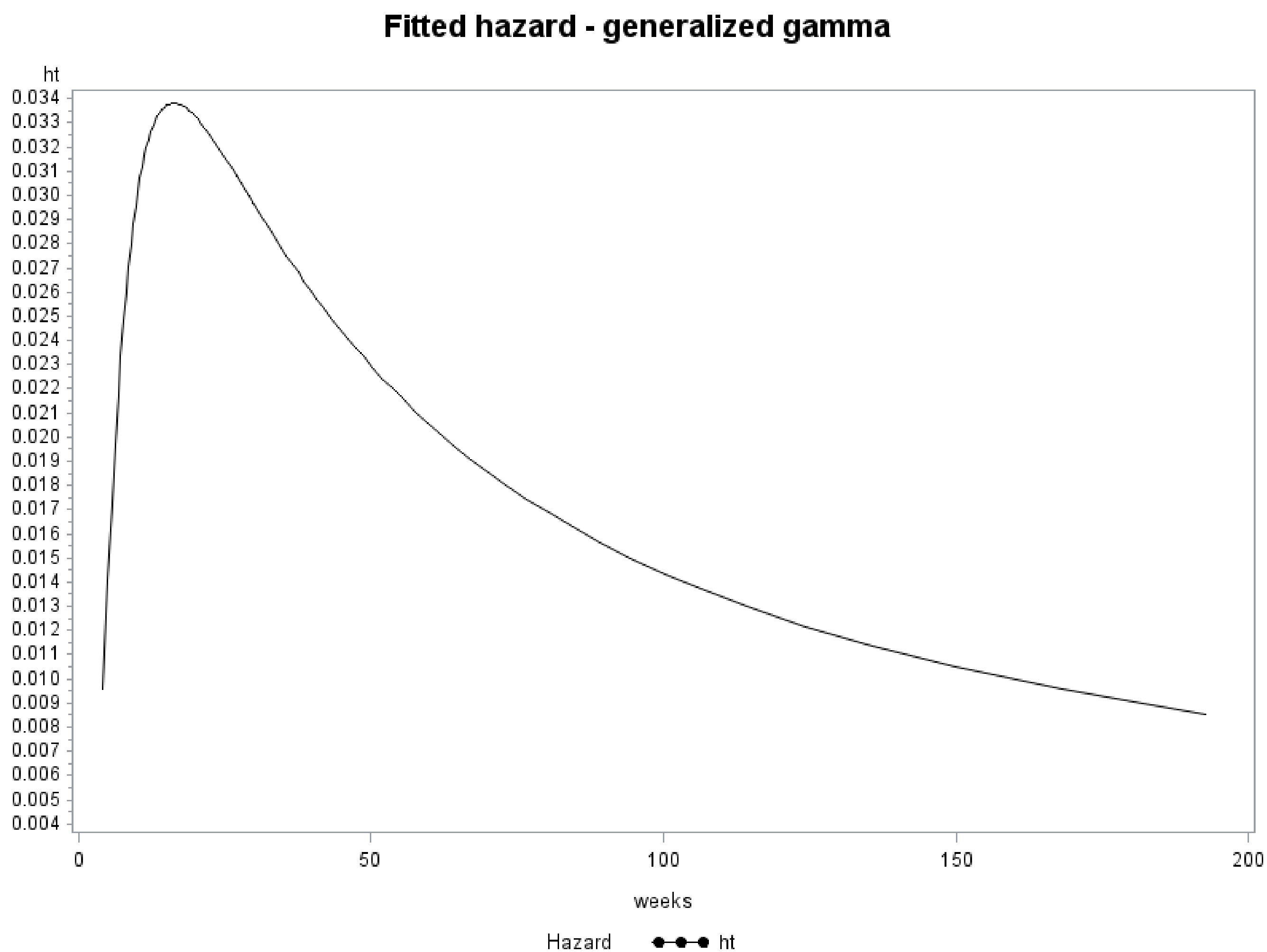
-2 Log Likelihood=600.334, AIC=606.334

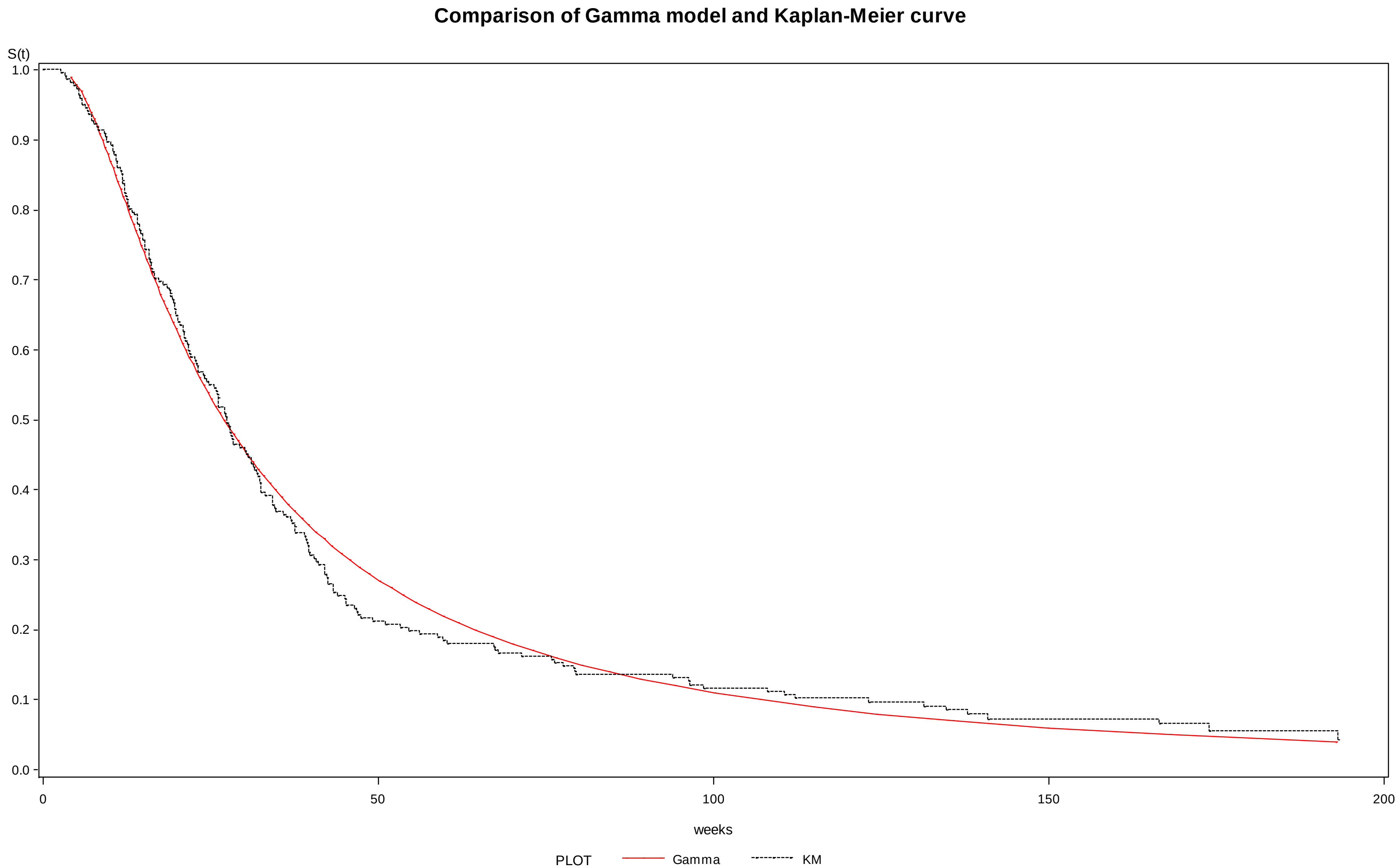
| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.1407 | 0.1006 | 2.9434 | 3.3380 | 973.70 | <.0001 |
| Scale | 1 | 0.9272 | 0.0479 | 0.8379 | 1.0259 | | |
| Shape | 1 | -0.4929 | 0.1733 | -0.8326 | -0.1533 | | |

If shape parameter is 0 then log-normal model
If shape parameter is 1 then Weibull model
If shape =1 and scale=1 then exponential model
If shape and scale are equal, then standard gamma distribution

Likelihood ratio test: Gamma vs log normal
chi-square = 608.001-600.334 = 7.667 , p=0.006

# Unadjusted model fit




Comparison of Gamma model and Kaplan-Meier curve
S(t)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
50
100
150
200
weeks
PLOT
Gamma
KM

# Model Comparison

| Model | -2logL | AIC | AICC | BIC |
|---|---:|---:|---:|---:|
| Exponential | 662.3 | 664.3 | 664.3 | 667.7 |
| Weibull | 661.7 | 665.7 | 665.7 | 672.5 |
| LogNormal | 608.0 | 612.0 | 612.1 | 618.8 |
| LogLogistic | 604.3 | 608.3 | 608.4 | 615.1 |
| Gamma | 600.3 | 606.3 | 606.4 | 616.5 |

# Akaike Information Criteria

- AIC=-2log(Likelihood)+2(p+k)
- k=1 (exponential)
- k=2 for Weibull, log logistic and log normal
- k=3 for generalized gamma
- In our example, AIC for gamma (606.3) is close to AIC for log-logistic (608.3).

K&M 12.4.3

$$AICC = AIC + \frac{2p(p+1)}{n-p-1} \qquad BIC = -2\log L + p\log(n)$$

# Adjusted model

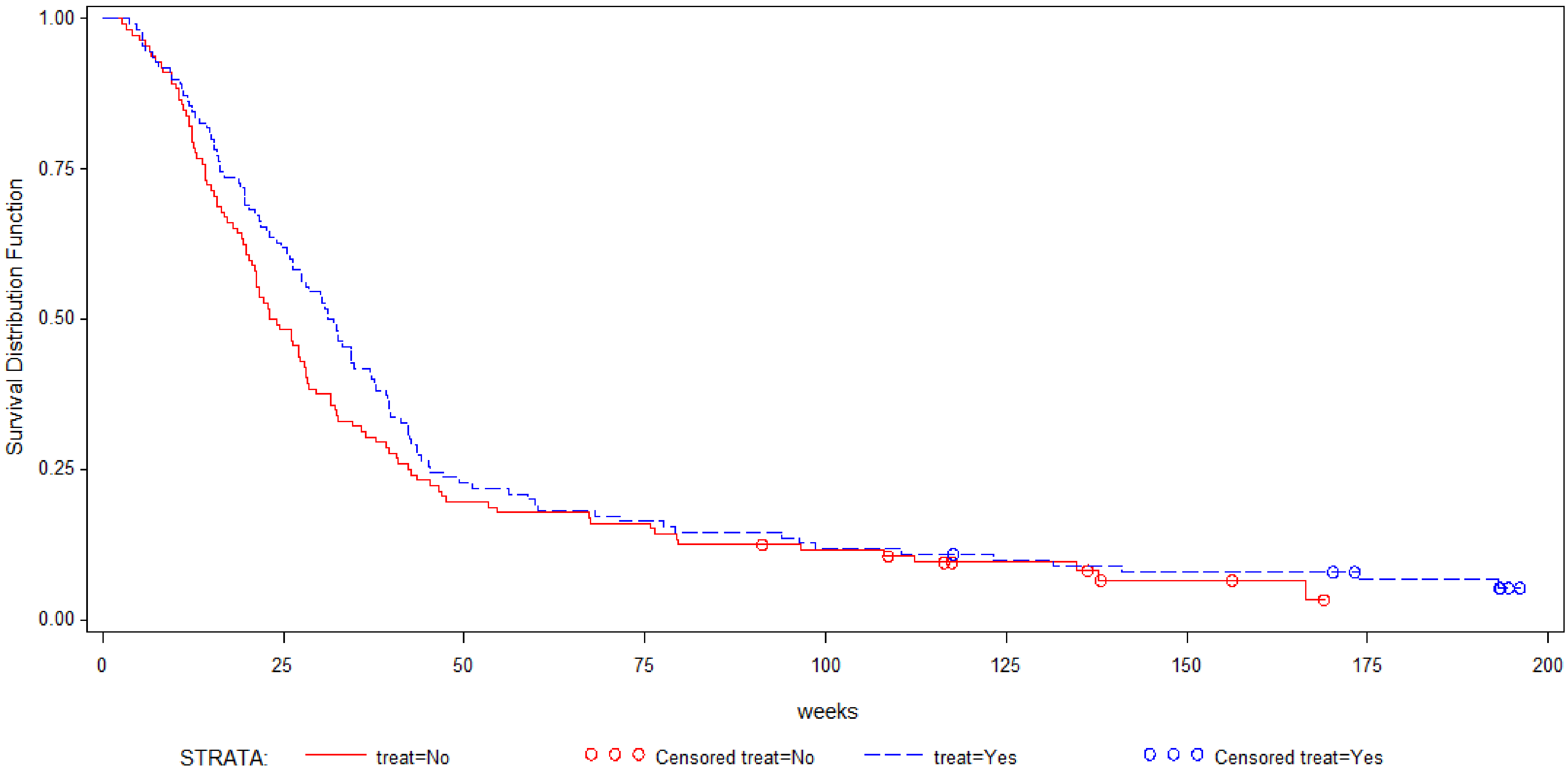
- Use preferred model building strategy to add covariates into the model (to be discussed further next month)
- Choosing two binary covariates for illustration
  - Treated (treat=1); not treated (treat=0)
  - Age <50 (age50=0) and age≥50 (age50=1)

# Covariates: median survival

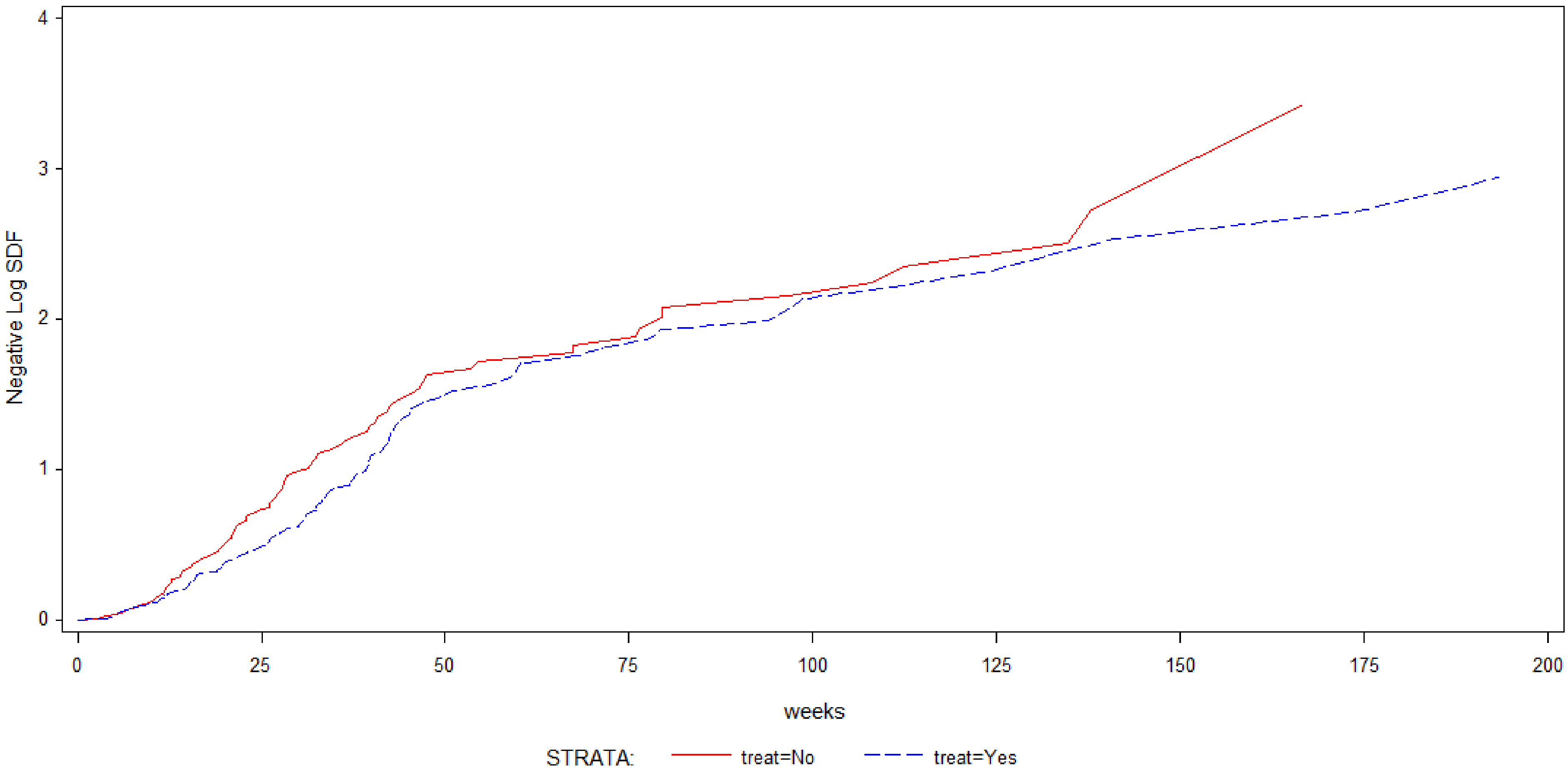
```
median treat=No :   23.57  (20.57, 28.00)

median treat=Yes :  31.50  (26.29, 37.00)
```

```
median age<50 :   32.43  (27.14, 39.71)

median age>=50 :  21.50  (19.00, 27.29)
```

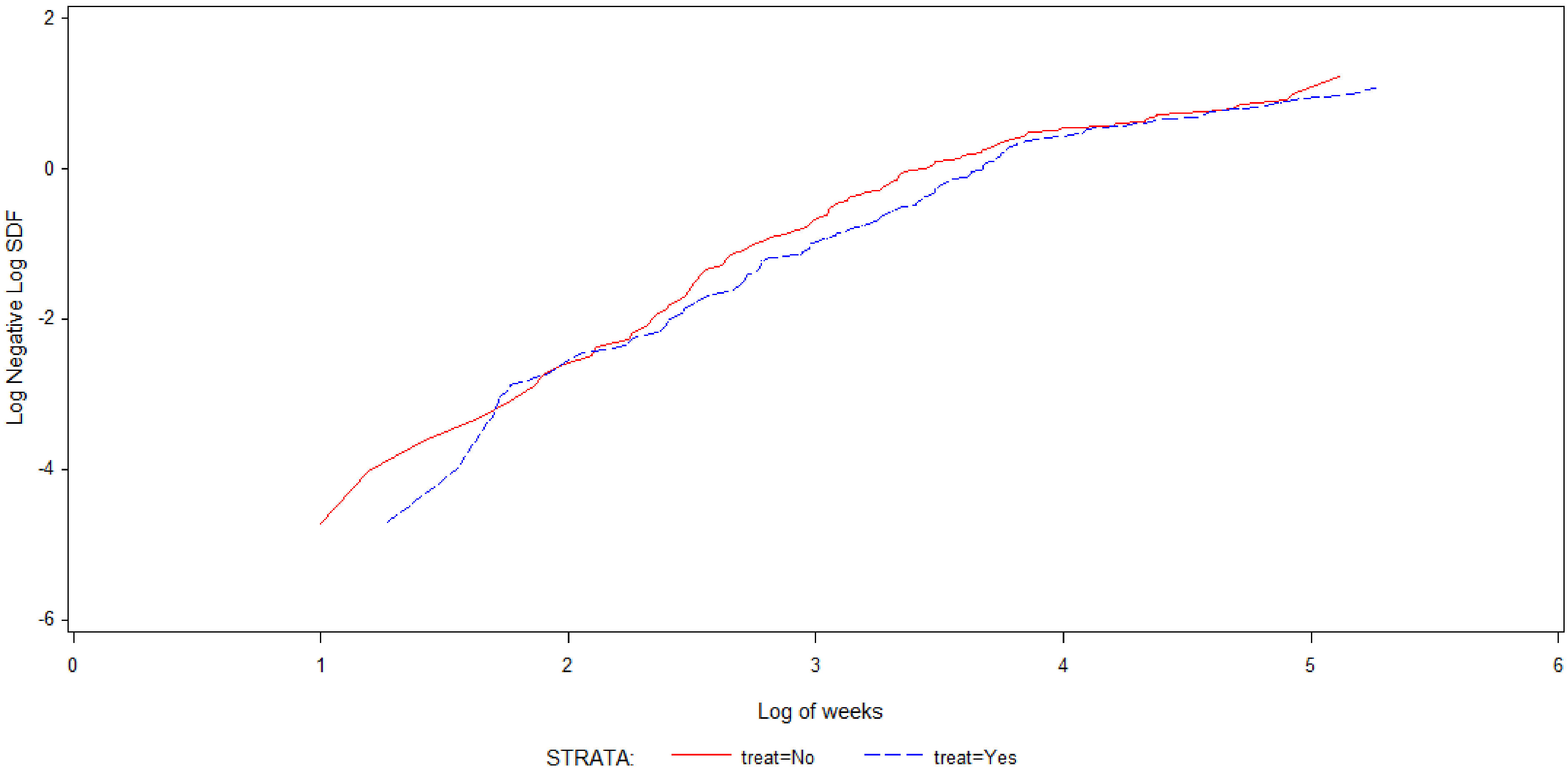
# LifeTest: Treatment group



# LifeTest: Treatment group



# LifeTest: Treatment group



# Exponential (treatment)

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.7220 | 0.0981 | 3.5298 | 3.9142 | 1440.73 | <.0001 |
| treat | 1 | 0.1853 | 0.1390 | -0.0871 | 0.4578 | 1.78 | 0.1825 |
| Scale | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |
| Weibull Shape | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |

HR=exp(-beta)=exp(-0.1853)=0.83

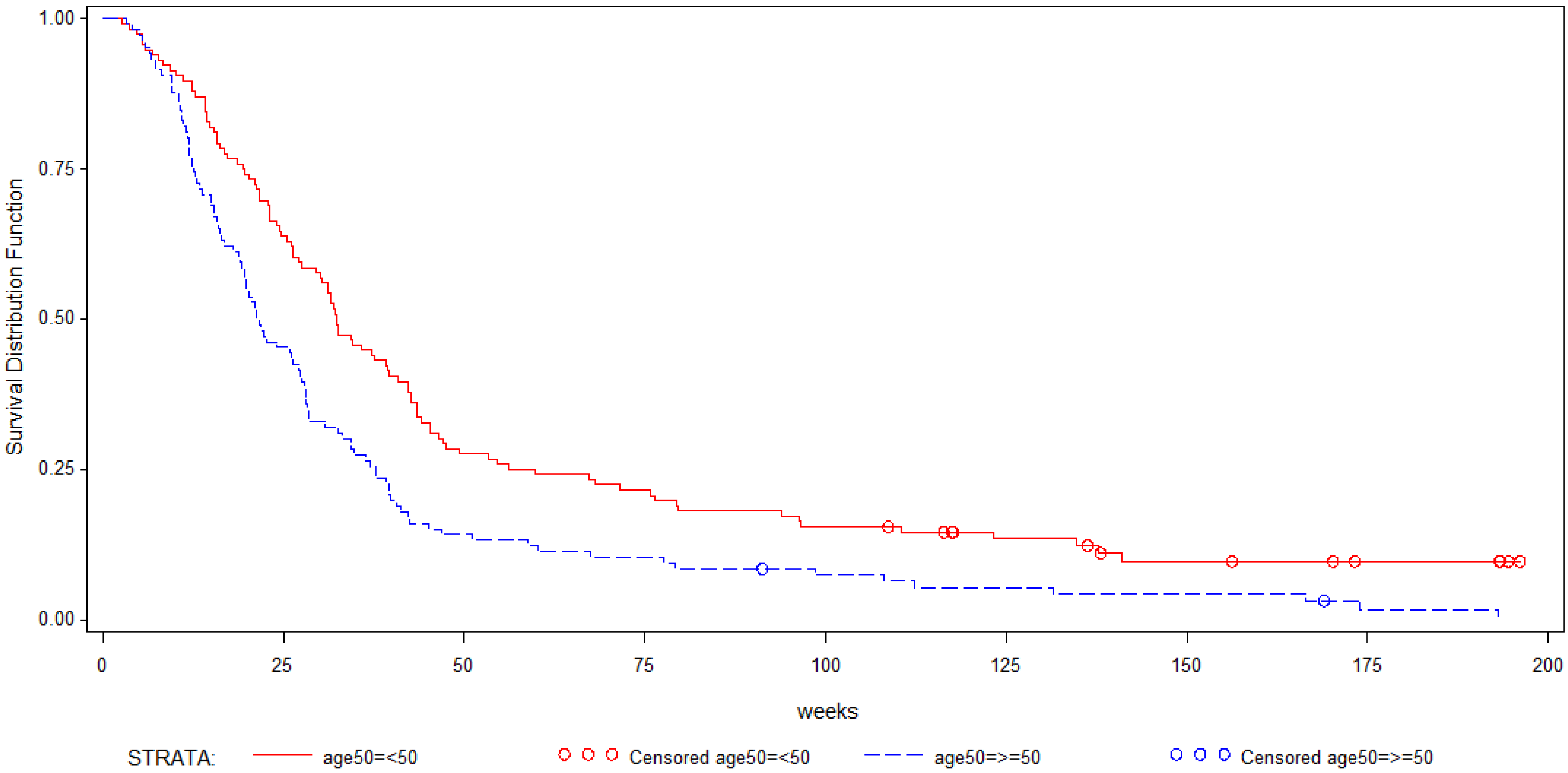
TR=exp(beta)=exp(0.1853)=1.20

# Exponential (Hazard Ratio)

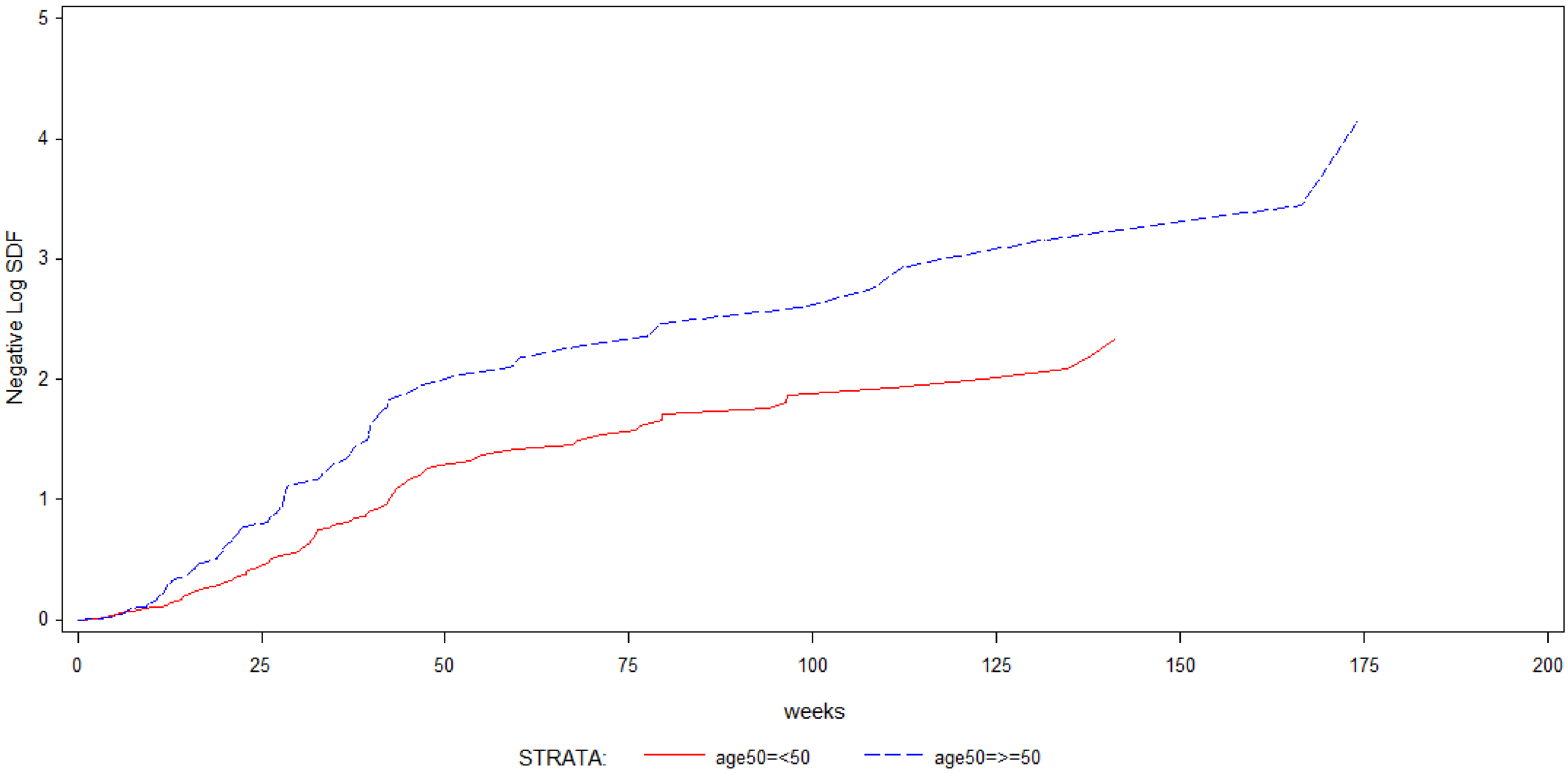
```
Note closed form solution for hazard ratio can be calculated
from the summary data below (unadjusted for other covariates):

No treatment: 104/4300=0.0242 (note log(0.0242)=-3.722) and
Yes, treated: 103/5126=0.0201

HR:  0.0201/0.0242 = 0.8306
Log(HR): log(0.0201/0.0242)=-0.1856
TR: exp(0.1856)=1.204
```

```
(output from proc means)

treat     Obs     Variable            Sum

No        112     event               104
                  weeks              4300

Yes       110     event               103
                  weeks              5126
```

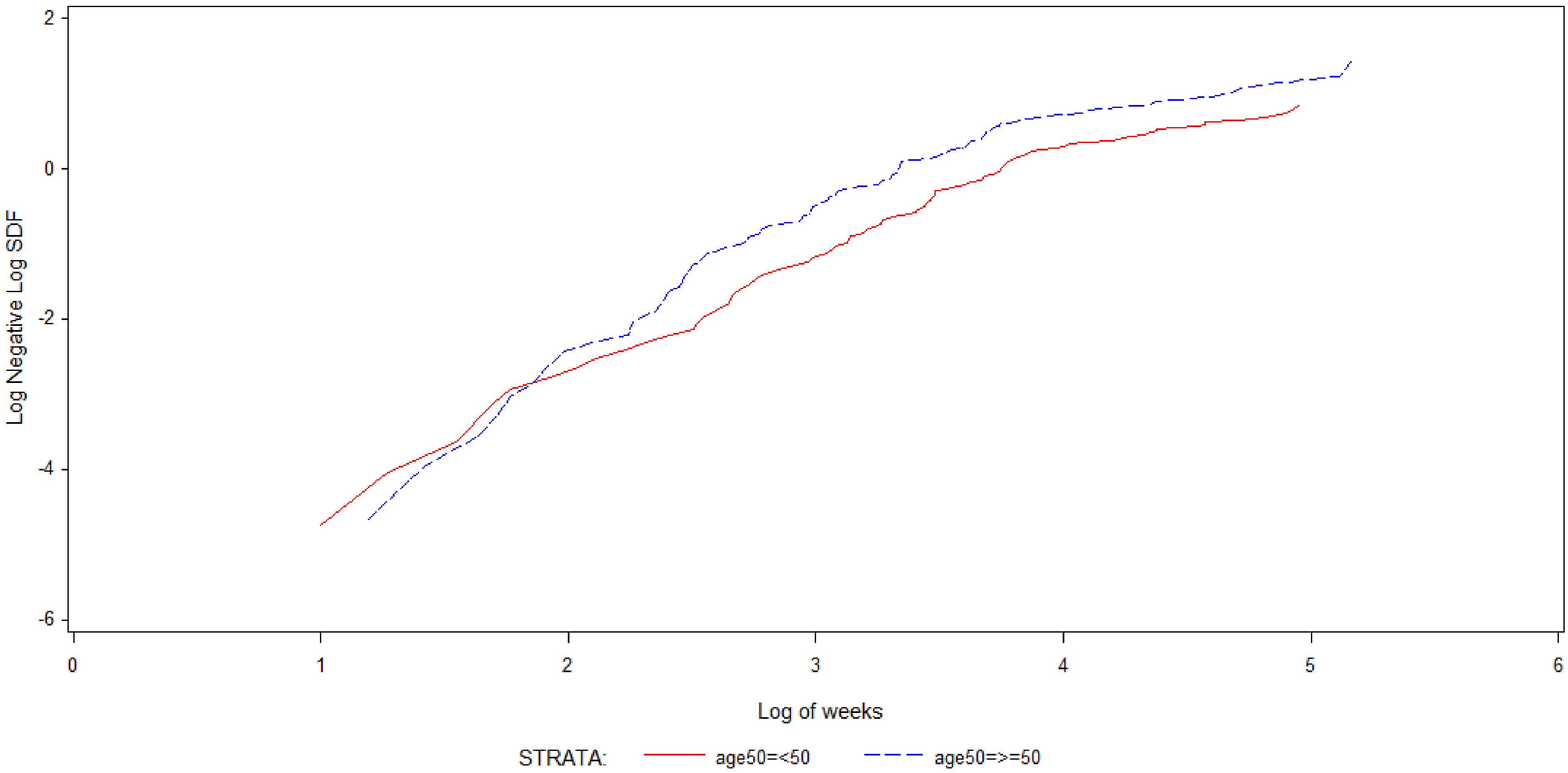
# LifeTest: Age group



# LifeTest: Age group



# LifeTest: Age group



# Exponential/Weibull (age grouped)

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 4.0394 | 0.0985 | 3.8463 | 4.2325 | 1680.64 | <.0001 |
| age50 | 1 | -0.5018 | 0.1390 | -0.7743 | -0.2293 | 13.03 | 0.0003 |

λ = exp(-(4.0394 - 0.5018*age50))

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 4.0569 | 0.0933 | 3.8740 | 4.2397 | 1891.78 | <.0001 |
| age50 | 1 | -0.4927 | 0.1303 | -0.7480 | -0.2374 | 14.31 | 0.0002 |
| Scale | 1 | 0.9356 | 0.0481 | 0.8459 | 1.0349 | | |
| Weibull Shape | 1 | 1.0688 | 0.0550 | 0.9663 | 1.1822 | | |

λ = exp(- 1.0688 *(4.0569 - 0.4927*age50))
HR = exp(-beta*1.0688) = 1.69
TR = exp(beta) = 0.61  AF = 1.64

# Goodness of fit

- Sample plots
  - How well does model match Kaplan-Meier curves?
- Cox-Snell residuals
  - Log-log(SDF) or cumulative hazard of residuals is a straight line?

$$r_j = \hat{H}(T_j \mid Z_j)$$

$$\textit{where } \hat{H} \textit{ is estimated from data}$$

$$\textit{and } r_j \textit{ distributed } \exp(1)$$

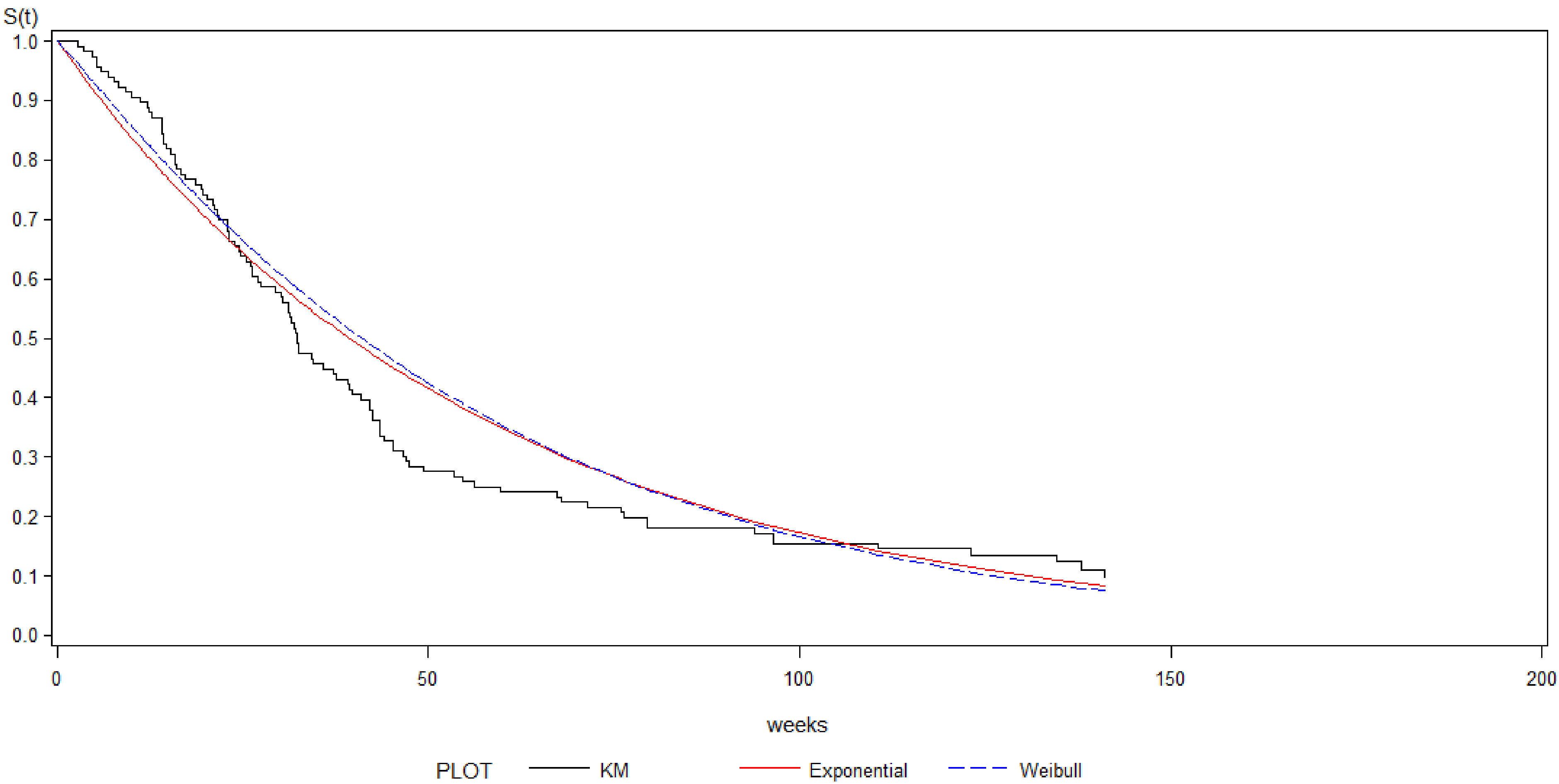
$$\textit{SAS output}: -\log(S(\frac{\log t_i - x_i' b}{\sigma}))$$

Other residuals: e.g. normal deviate residuals, see Nardi & Schemper

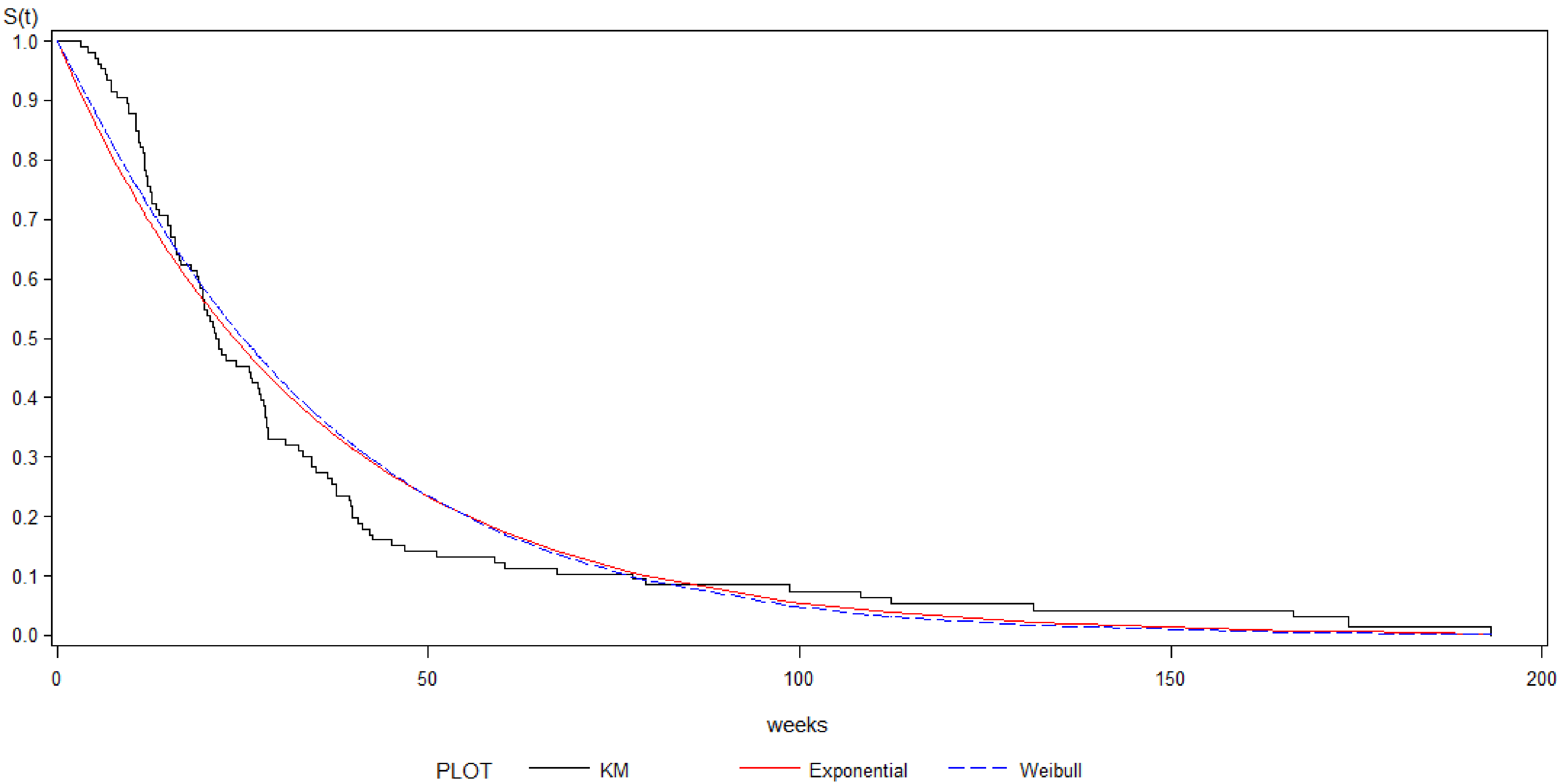
# Goodness of fit

- Martingale residuals
  - Klein & Moeschberger: "estimate of the excess number of deaths seen in the data, but not predicted by model"
  - $\delta_j - H(T_j|Z_j)$ i.e. $\delta_j - r_j$
- Deviance residuals
  - Klein & Moeschberger: "more symmetric about 0"
  - Transformed martingale residuals

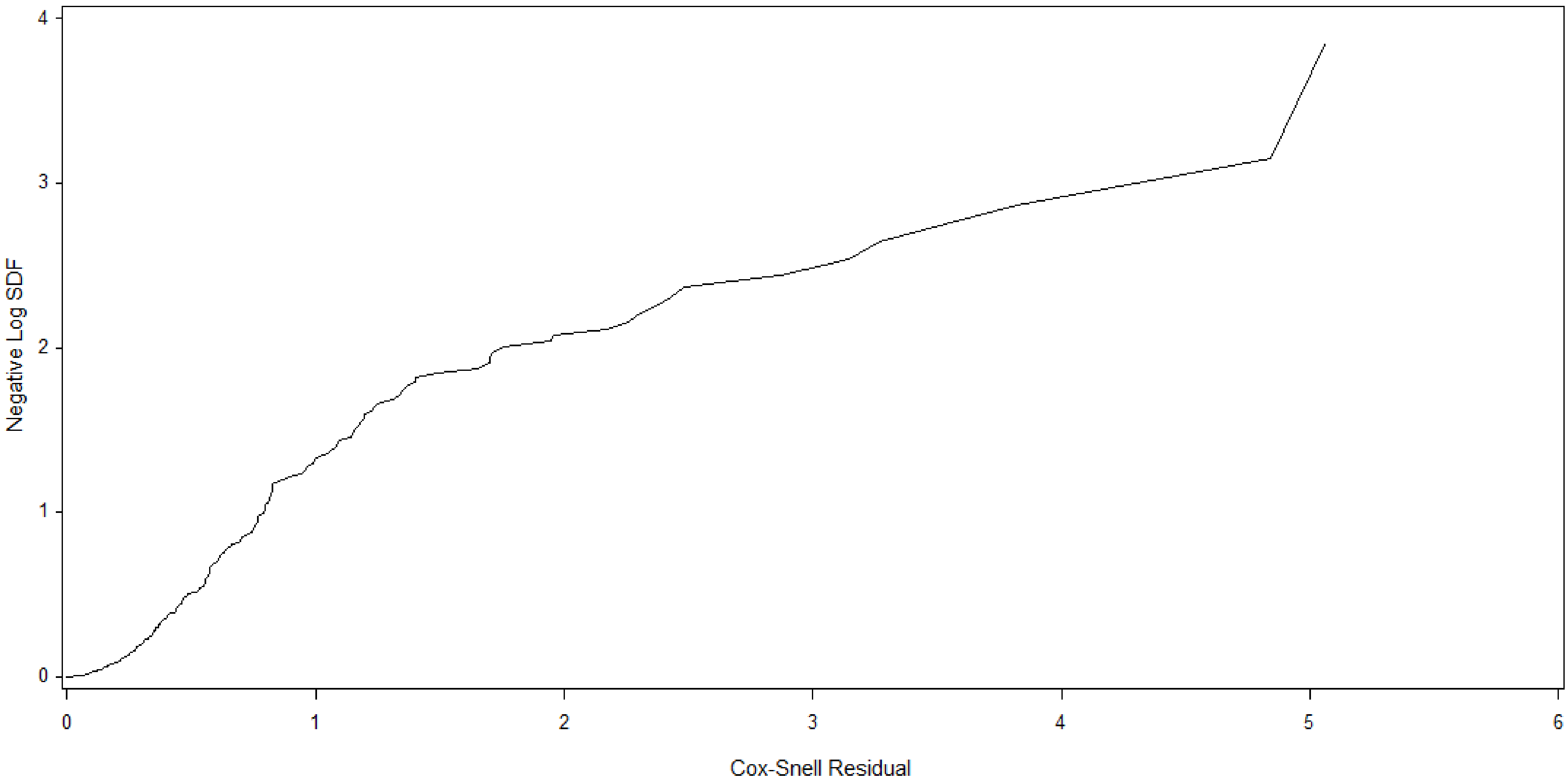
# Comparison of Exponential and Weibull Models-Age<50



# Comparison of Exponential and Weibull Models-Age>=50



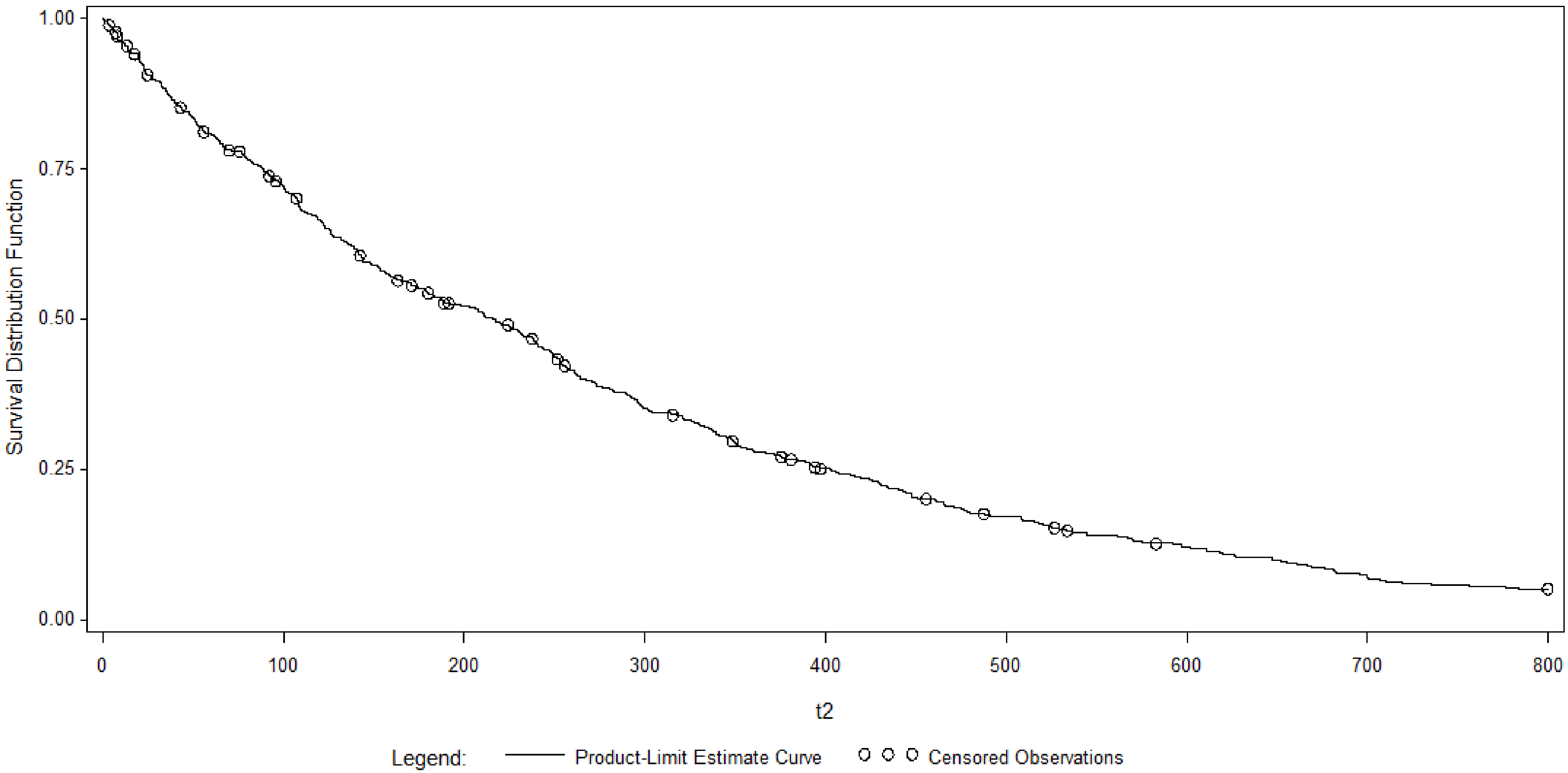
# Cox-Snell Residuals-Exponential



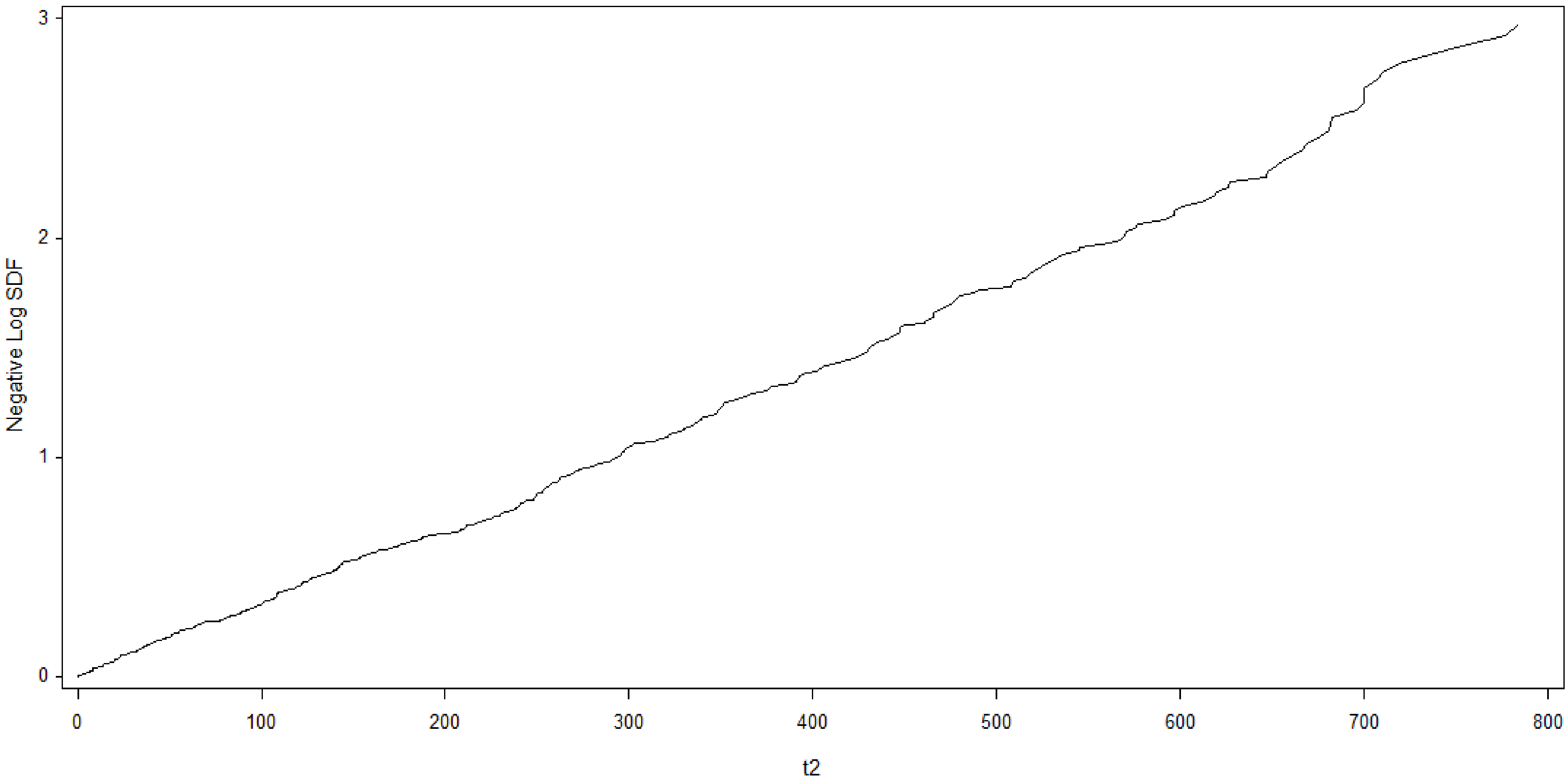
# Simulated Exponential Data

- To show what plots look like using randomly generated data from an exponential distribution

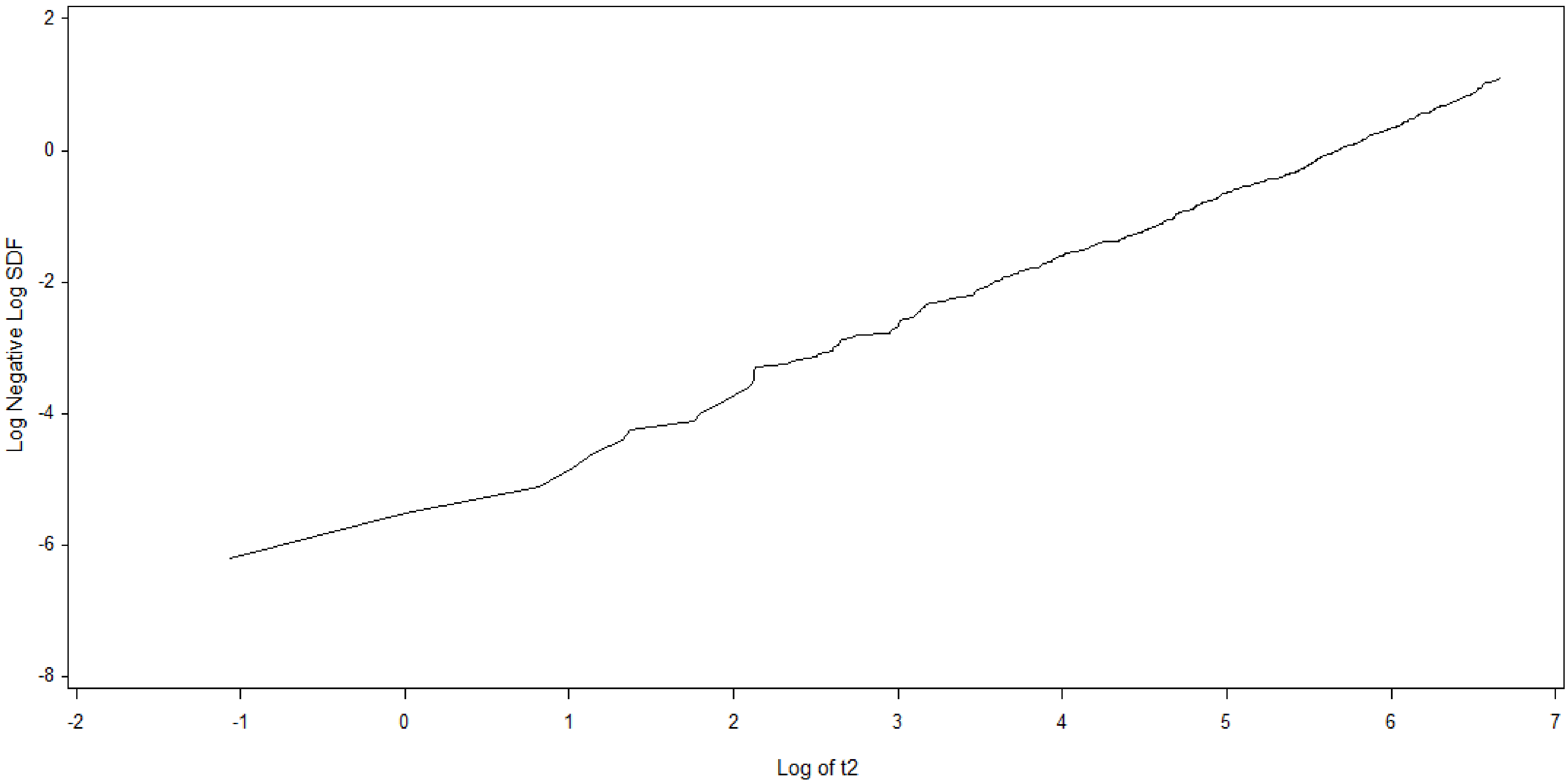
# Simulated Exponential Data



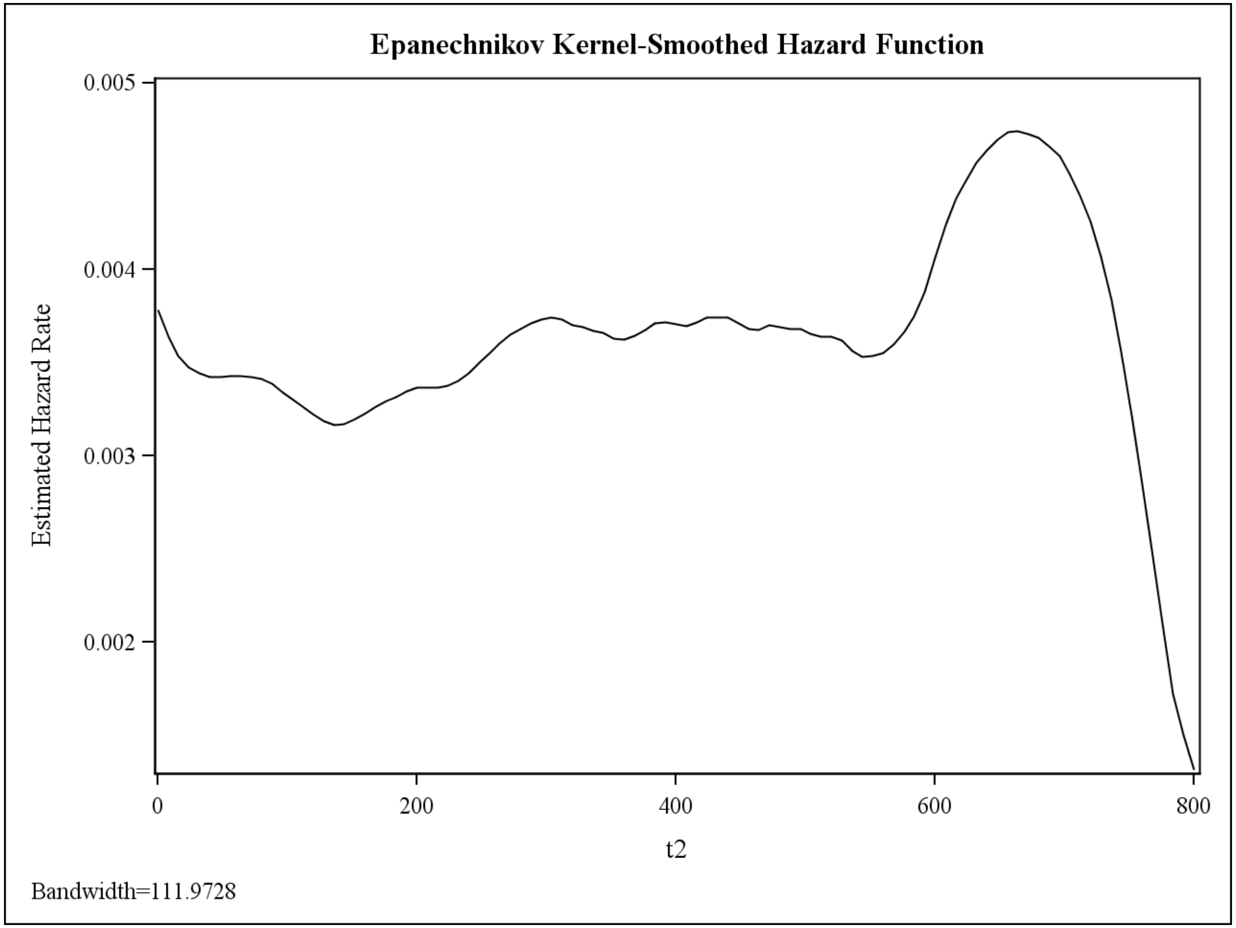
# Simulated Exponential Data



# Simulated Exponential Data



# Simulated Exponential Data



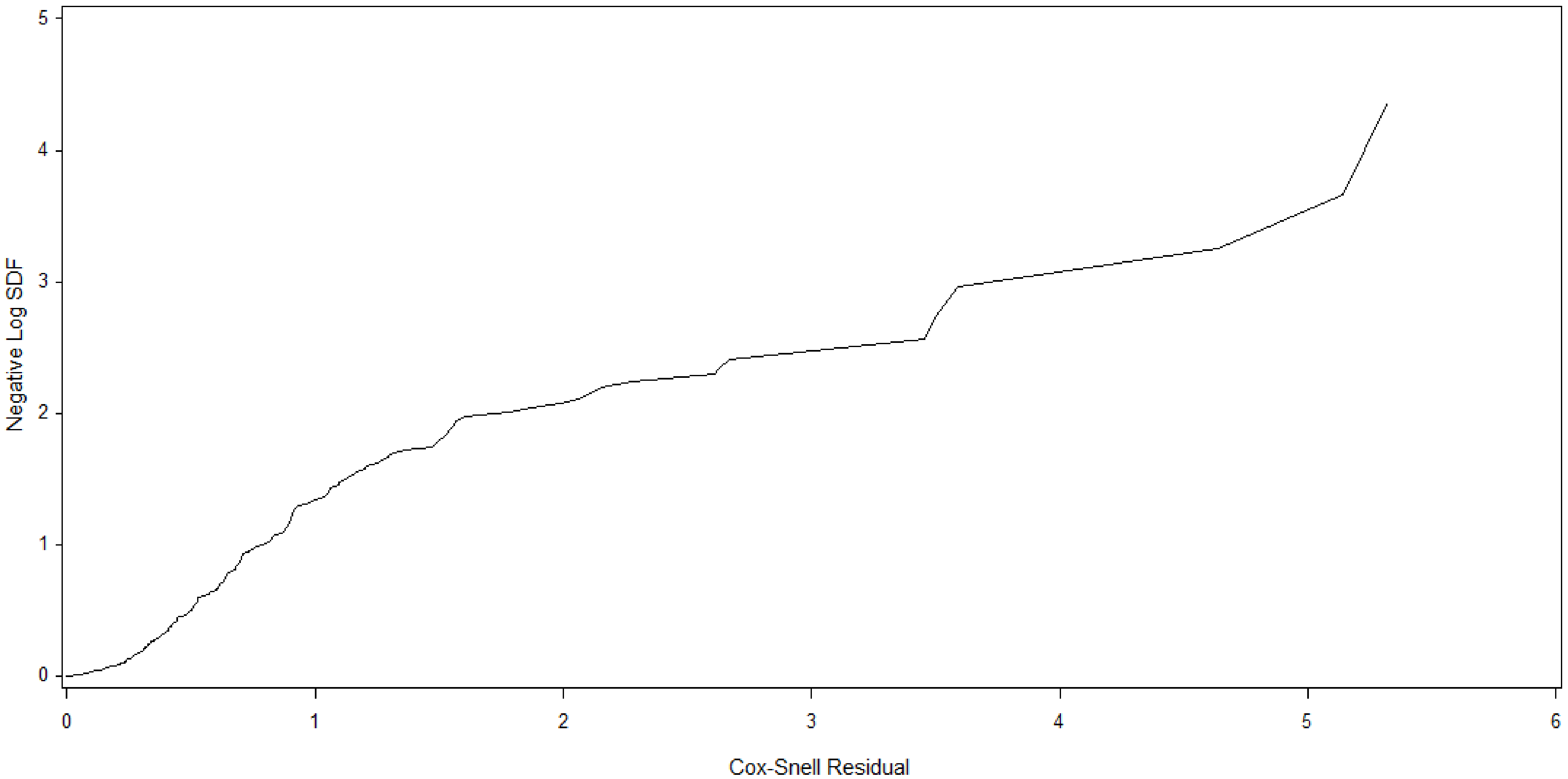
# Exponential (treatment and age)

-2 Log Likelihood = 647.648

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.9439 | 0.1206 | 3.7075 | 4.1804 | 1069.08 | <.0001 |
| treat | 1 | 0.1825 | 0.1390 | -0.0900 | 0.4549 | 1.72 | 0.1893 |
| age50 | 1 | -0.5007 | 0.1390 | -0.7732 | -0.2283 | 12.98 | 0.0003 |
| Scale | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |
| Weibull Shape | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |

HR(treat)=exp(-beta)=exp(-0.1825)=0.83
TR(treat)=exp(beta)=exp(0.1825)=1.20

# Cox-Snell Residuals - Exponential



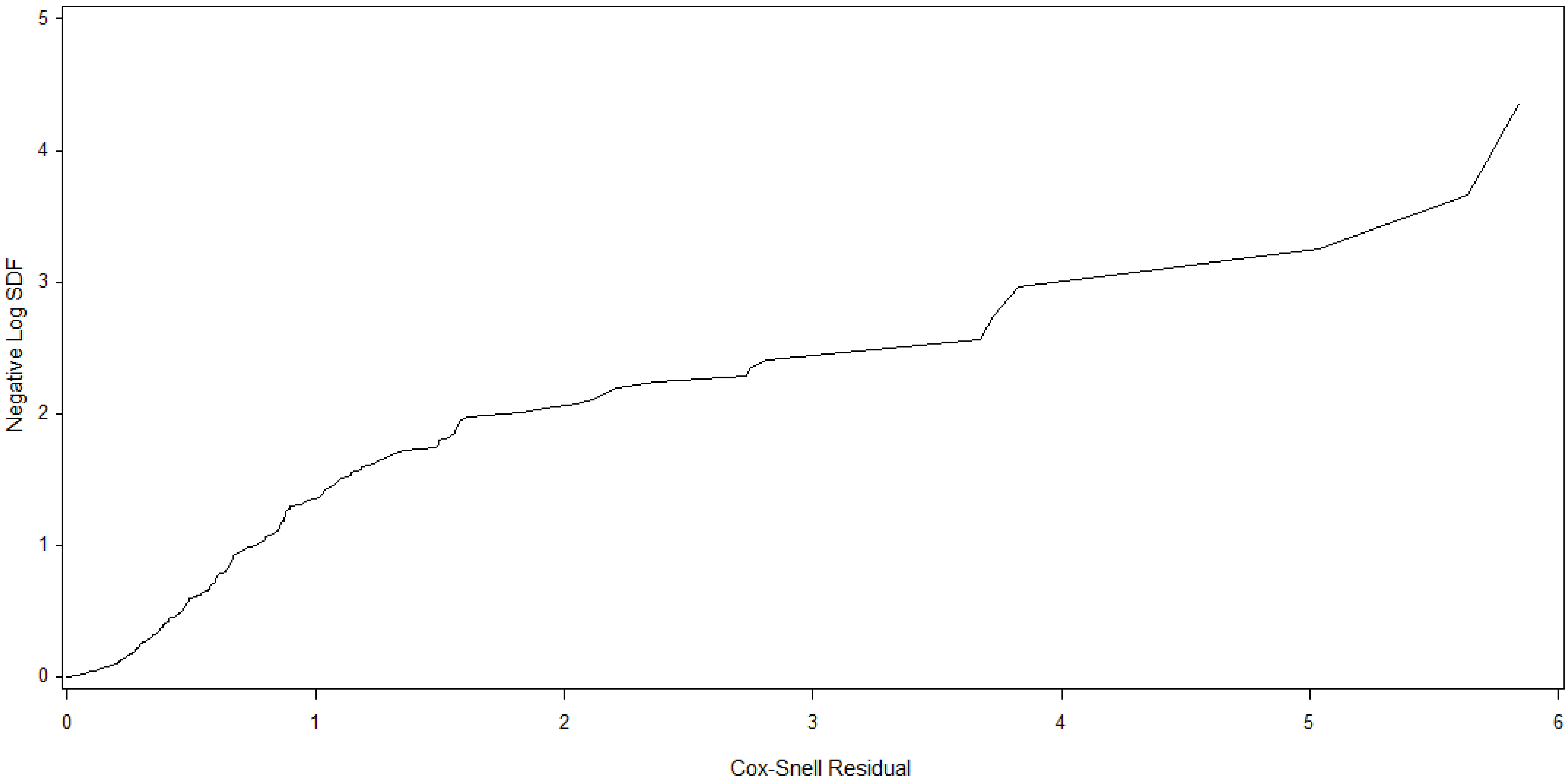
# Weibull(treatment and age)

-2 Log Likelihood = 645.784

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.9622 | 0.1132 | 3.7403 | 4.1842 | 1224.33 | <.0001 |
| treat | 1 | 0.1825 | 0.1294 | -0.0711 | 0.4361 | 1.99 | 0.1585 |
| age50 | 1 | -0.4904 | 0.1296 | -0.7444 | -0.2363 | 14.31 | 0.0002 |
| Scale | 1 | 0.9308 | 0.0479 | 0.8415 | 1.0296 | | |
| Weibull Shape | 1 | 1.0744 | 0.0553 | 0.9713 | 1.1884 | | |

HR(treat)=exp(-beta*gamma)=exp(-0.1825*1.0744)=0.82
TR(treat)=exp(beta*gamma)**sigma
=exp(0.1825*1.0744)**0.9308=1.20

# Cox-Snell Residuals - Weibull



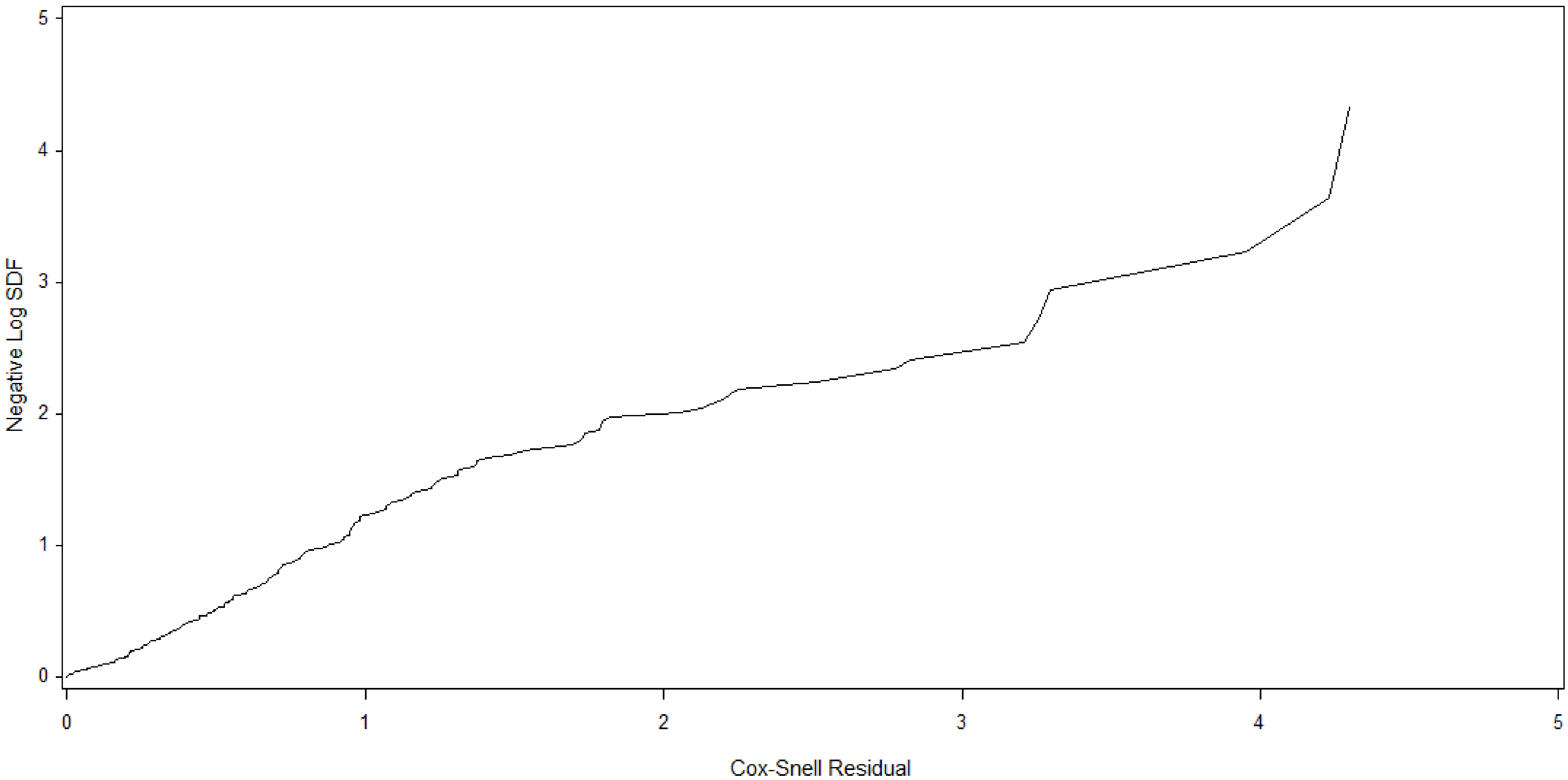
# Log Normal(treatment and age)

-2 Log Likelihood = 595.383

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.4768 | 0.1072 | 3.2667 | 3.6869 | 1051.87 | <.0001 |
| treat | 1 | 0.1744 | 0.1253 | -0.0711 | 0.4200 | 1.94 | 0.1639 |
| age50 | 1 | -0.4144 | 0.1254 | -0.6602 | -0.1686 | 10.92 | 0.0010 |
| Scale | 1 | 0.9288 | 0.0466 | 0.8418 | 1.0247 | | |

TR(treat)=exp(beta)=exp(0.1744)=1.19

# Cox-Snell Residuals - LogNormal



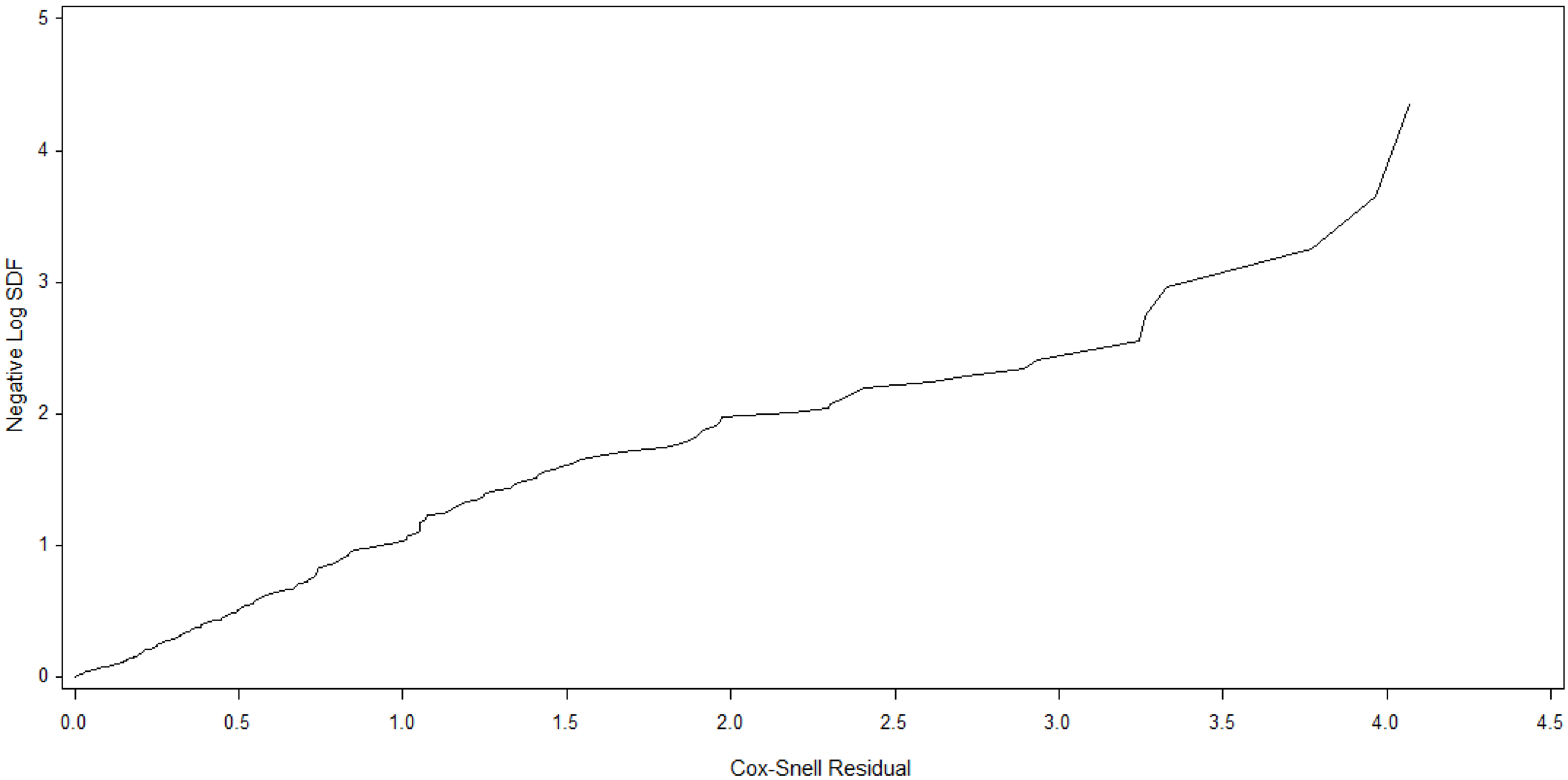
# Log Logistic(treatment and age)

```
-2 Log Likelihood = 589.891
```

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 3.4289 | 0.1031 | 3.2268 | 3.6309 | 1105.96 | <.0001 |
| treat | 1 | 0.2029 | 0.1200 | -0.0323 | 0.4380 | 2.86 | 0.0909 |
| age50 | 1 | -0.4204 | 0.1200 | -0.6555 | -0.1852 | 12.28 | 0.0005 |
| Scale | 1 | 0.5198 | 0.0304 | 0.4635 | 0.5830 | | |

```
TR(treat)=exp(beta/sigma)**sigma
         =exp(0.2029/0.5198)**0.5198=1.23
OR(treat)=exp(beta/sigma)=exp(0.2029/0.5198)=1.48
```

# Cox-Snell Residuals - LogLogistic

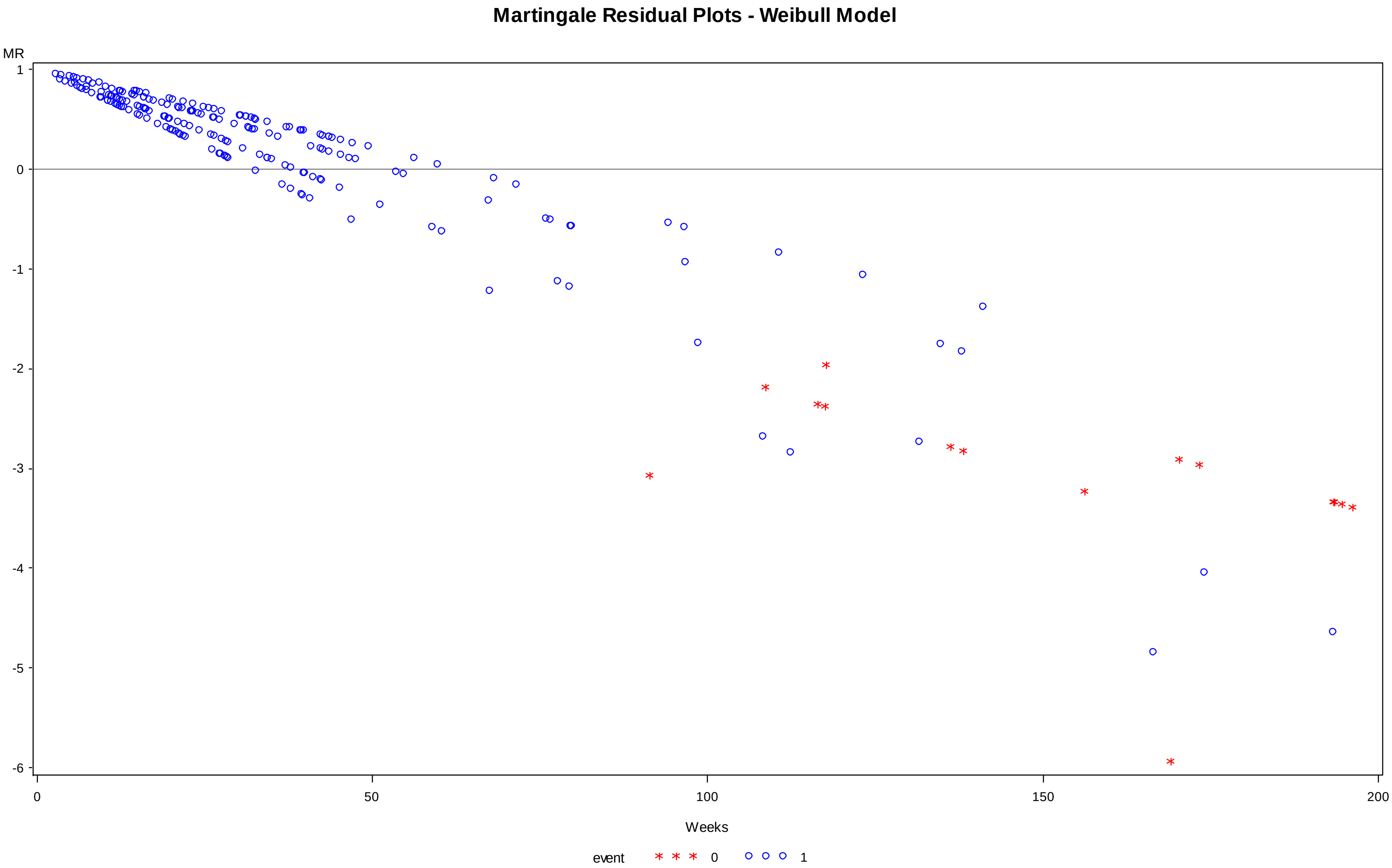


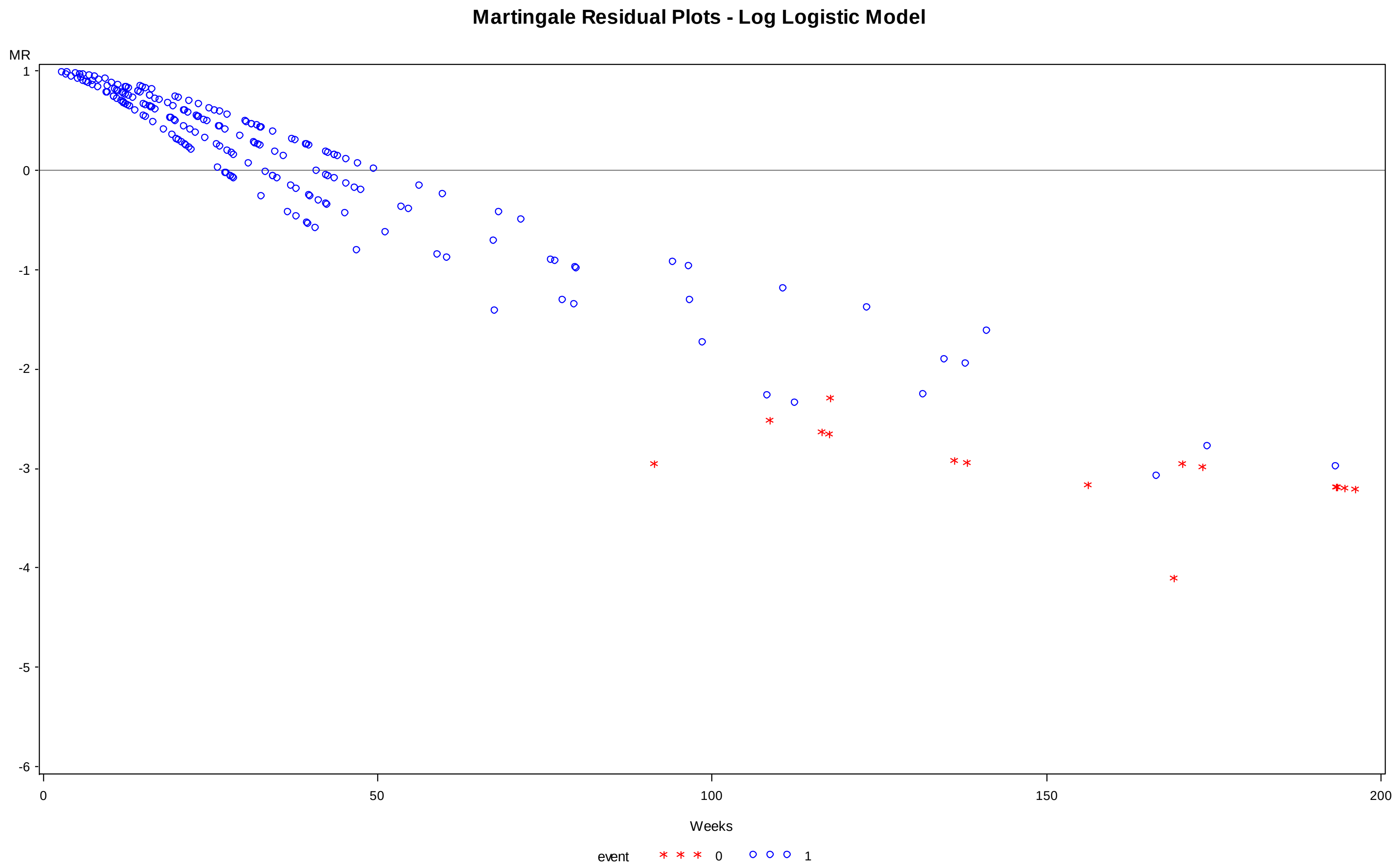
# Residuals (SAS Code)

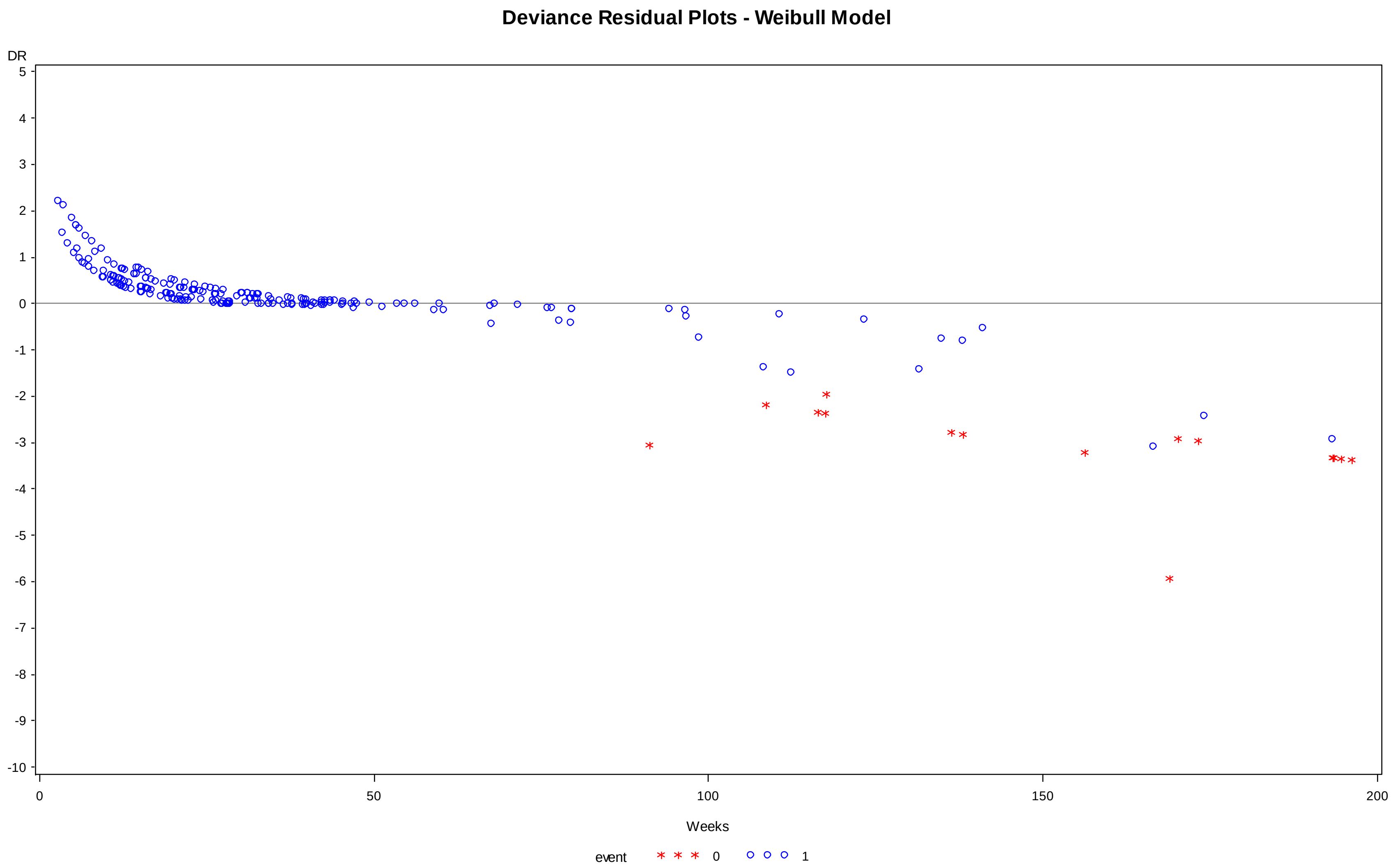
```
/* Cox-Snell */
proc lifereg data=sda.brain;
  model weeks*event(0)=treat age50/d=weibull;
  output out=wout cres=cres sres=sres p=predm  std=stdm;
  title 'LifeReg: Treatment & Age groups - Weibull';
run;

proc lifetest data=wout plots=(ls) notable;
  * looking for evidence that cres is exponential using the -log(S(t)) plot;
  * note that censoring value is maintained from original data set;
  time cres*event(0);
  title1 'Cox-Snell Residuals - Weibull';
run;
```

```
 /* martingale and deviance*/
  lambda=exp(-(3.9439+0.1825*treat-0.5007*age50));
  sexp=exp(-lambda*weeks);
  xbexp=3.9439+0.1825*treat-0.5007*age50;
  chexp=-log(sexp);
  martexp=event-chexp;
  devexp=sign(martexp)*(-2*(martexp+event*log(event-martexp)))**1/2;
```

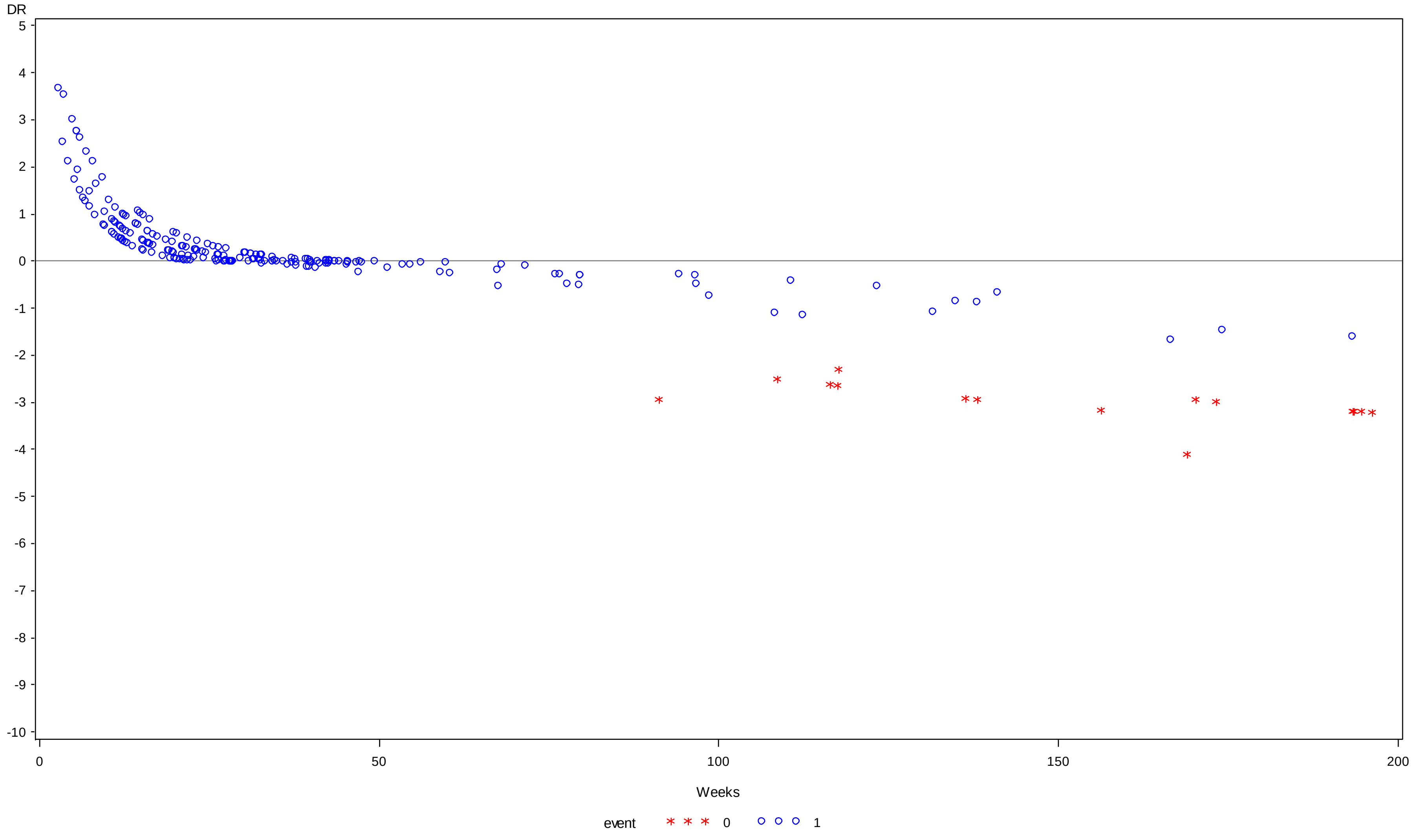
January 30, 2019
CHL5209H




Martingale Residual Plots - Log Logistic Model
MR
1
0
-1
-2
-3
-4
-5
-6
0
50
100
150
200
Weeks
event
0
1

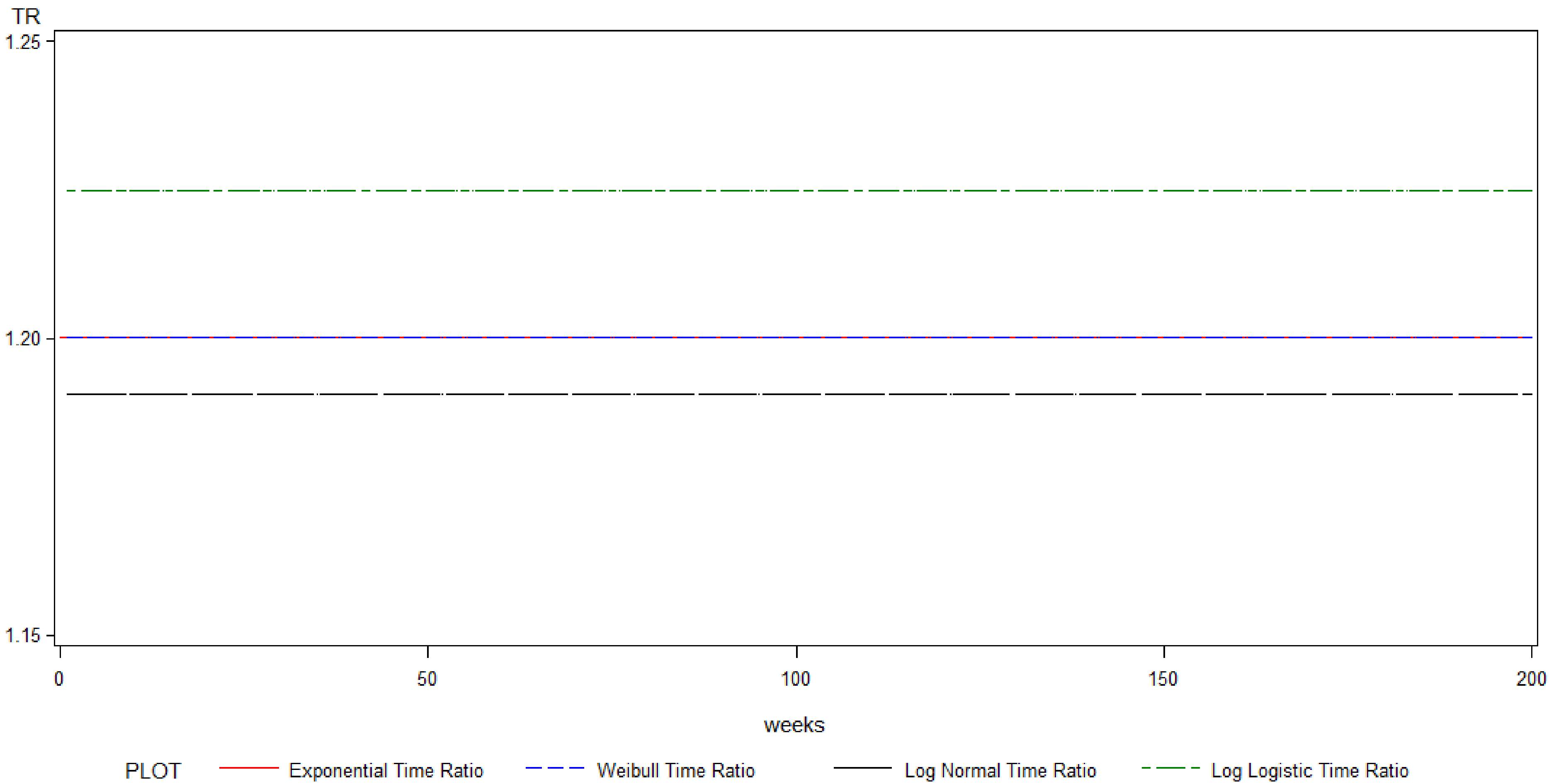

Deviance Residual Plots - Weibull Model
DR
5
4
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
0
50
100
150
200
Weeks
event
0
1

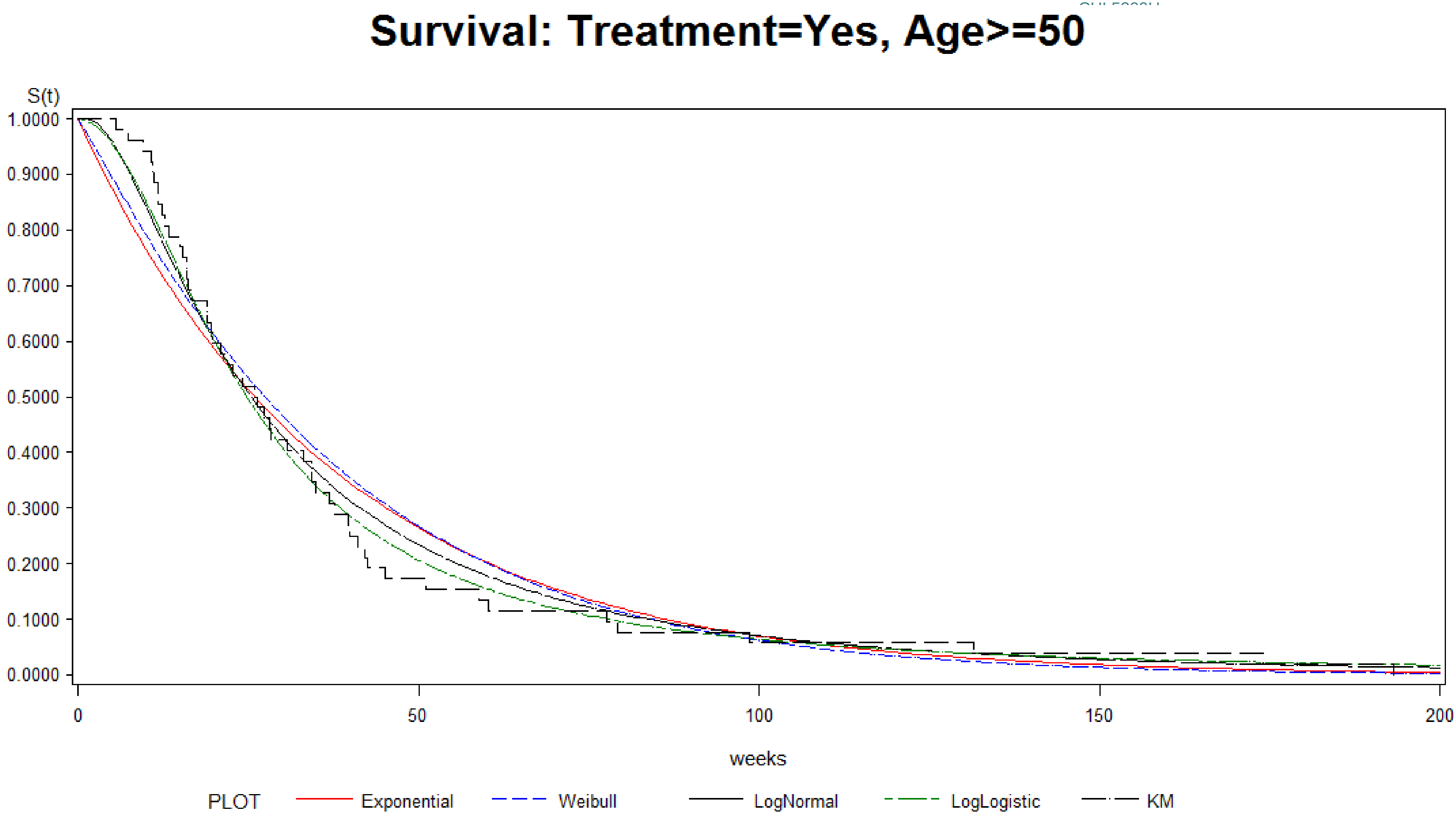
# Deviance Residual Plots - Log Logistic Model



# Model summaries

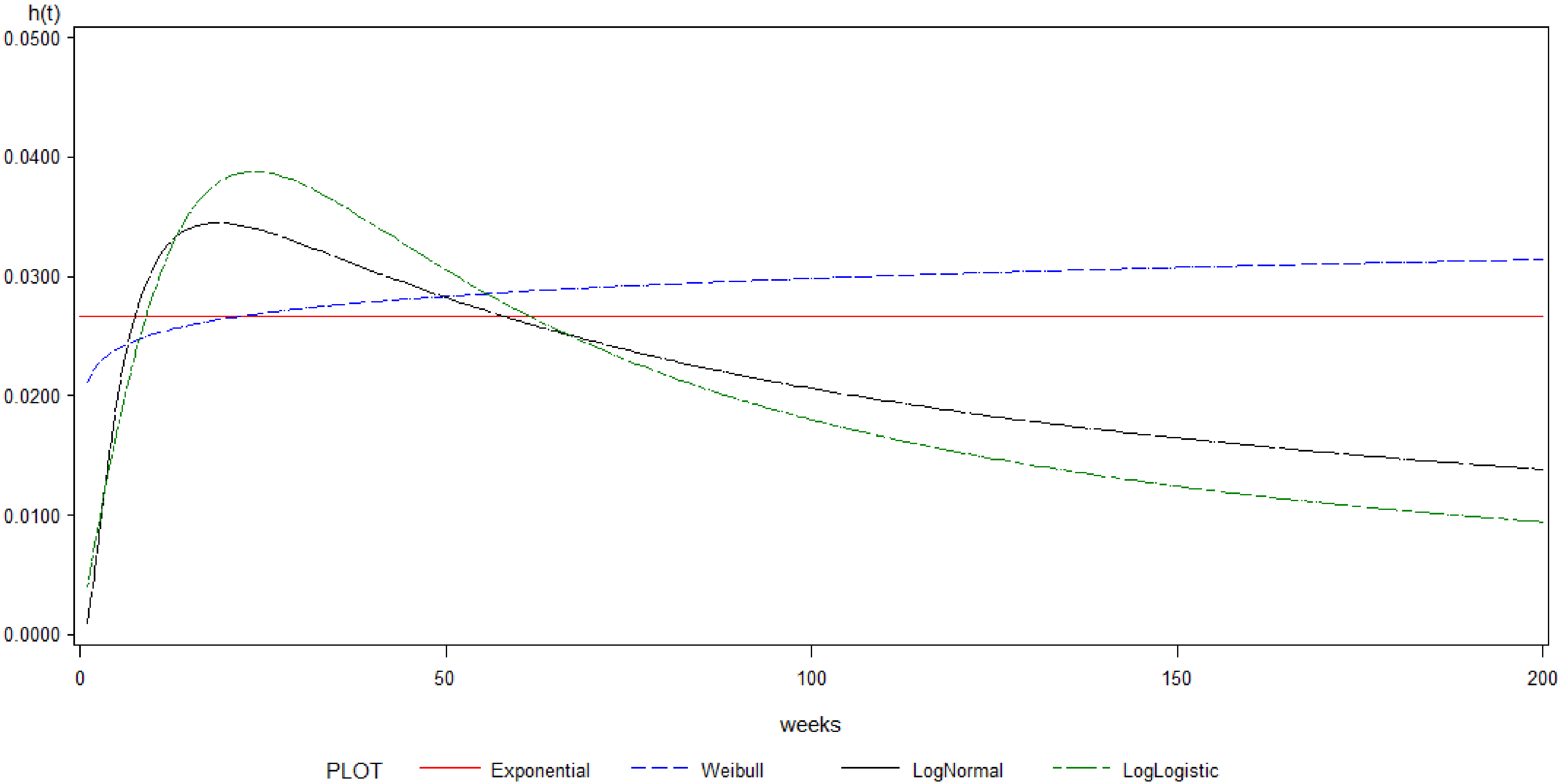
# Time Ratios for Treatment - All Models



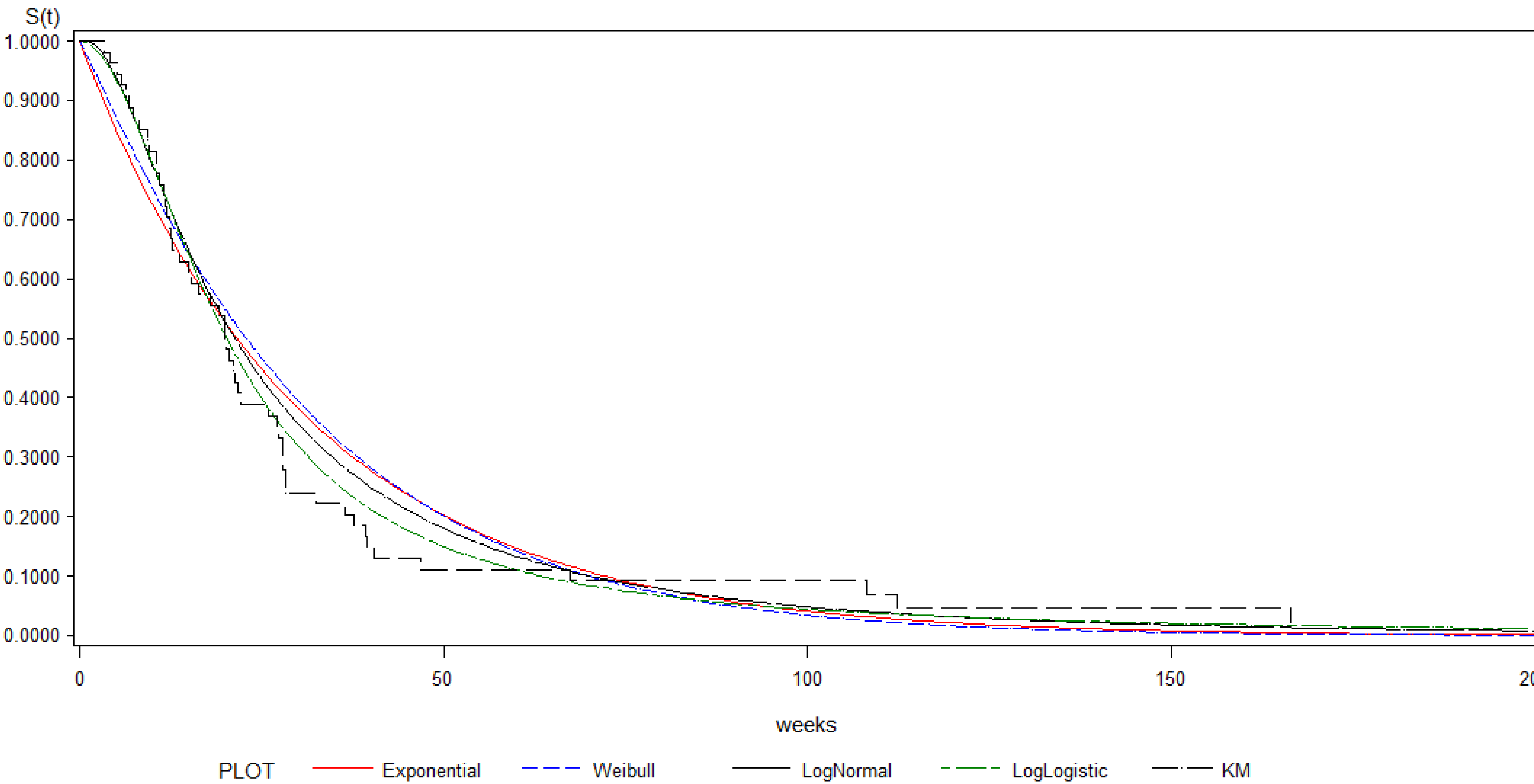


Survival: Treatment=Yes, Age>=50
S(t)
1.0000
0.9000
0.8000
0.7000
0.6000
0.5000
0.4000
0.3000
0.2000
0.1000
0.0000
0
50
100
150
200
weeks
PLOT
Exponential
Weibull
LogNormal
LogLogistic
KM

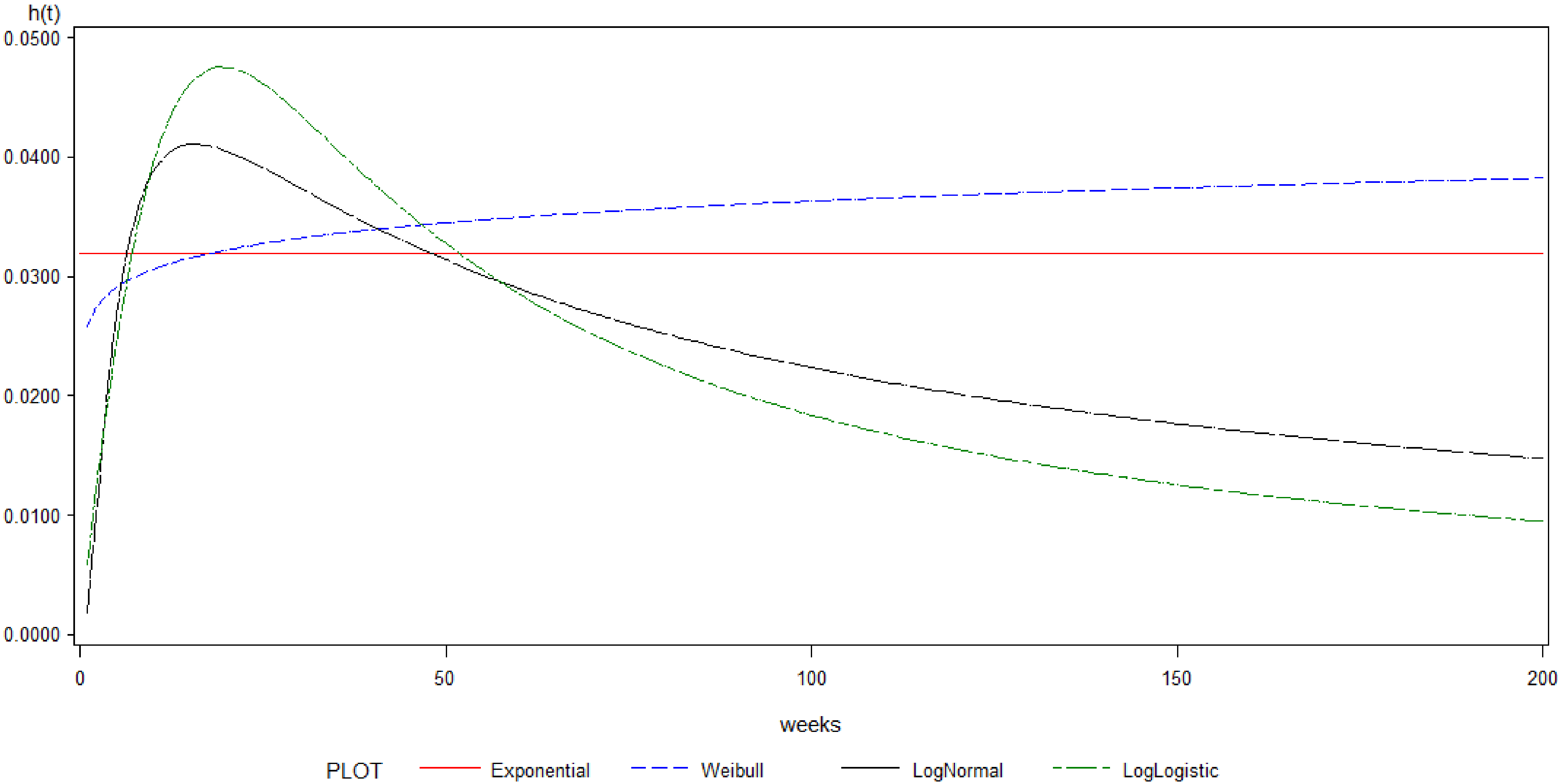
# Hazard: Treatment=Yes, Age>=50



# Survival: Treatment=No, Age>=50



# Hazard: Treatment=No, Age>=50



# Exponential Summary

| t (weeks) | Age>=50 | Exponential S(t), Treatment=1 | Exponential h(t), Treatment=1 | Exponential Median, Treatment=1 | Exponential S(t), Treatment=0 | Exponential h(t), Treatment=0 |
|---|---|---|---|---|---|---|
| 26 | Yes | 0.5004 | 0.0266 | 26.0284 | 0.4356 | 0.0320 |
| 52 | Yes | 0.2504 | 0.0266 | 26.0284 | 0.1898 | 0.0320 |
| 104 | Yes | 0.0627 | 0.0266 | 26.0284 | 0.0360 | 0.0320 |

| t (weeks) | Exponential Median, Treatment=0 | Exponential Hazard Ratio(t) | Exponential beta(Treatment); | Exponential Time Ratio | Exponential Median Ratio |
|---|---|---|---|---|---|
| 26 | 21.6864 | 0.8332 | 0.1825 | 1.2002 | 1.2002 |
| 52 | 21.6864 | 0.8332 | 0.1825 | 1.2002 | 1.2002 |
| 104 | 21.6864 | 0.8332 | 0.1825 | 1.2002 | 1.2002 |

# Weibull Summary

| t (weeks) | Age>=50 | Weibull S(t), Treatment=1 | Weibull h(t), Treatment=1 | Weibull Median, Treatment=1 | Weibull S(t), Treatment=0 | Weibull h(t), Treatment=0 |
|---|---|---|---|---|---|---|
| 26 | Yes | 0.5203 | 0.0270 | 27.4720 | 0.4516 | 0.0328 |
| 52 | Yes | 0.2526 | 0.0284 | 27.4720 | 0.1875 | 0.0346 |
| 104 | Yes | 0.0552 | 0.0299 | 27.4720 | 0.0295 | 0.0364 |

| t (weeks) | Weibull Median, Treatment=0 | Weibull Hazard Ratio(t) | Weibull beta(Treatment); | Weibull Time Ratio | Weibull Median Ratio |
|---|---|---|---|---|---|
| 26 | 22.8892 | 0.8219 | 0.1825 | 1.2002 | 1.2002 |
| 52 | 22.8892 | 0.8219 | 0.1825 | 1.2002 | 1.2002 |
| 104 | 22.8892 | 0.8219 | 0.1825 | 1.2002 | 1.2002 |

# Log Normal Summary

| t (weeks) | Age>=50 | Log Normal S(t), Treatment=1 | Log Normal h(t), Treatment=1 | Log Normal Median, Treatment=1 | Log Normal S(t), Treatment=0 | Log Normal h(t), Treatment=0 |
|---|---|---|---|---|---|---|
| 26 | Yes | 0.4909 | 0.0336 | 25.4521 | 0.4166 | 0.0388 |
| 52 | Yes | 0.2209 | 0.0278 | 25.4521 | 0.1693 | 0.0309 |
| 104 | Yes | 0.0648 | 0.0202 | 25.4521 | 0.0443 | 0.0219 |

| t (weeks) | Log Normal Median, Treatment=0 | Log Normal Hazard Ratio(t) | Log Normal beta(Treatment); | Log Normal Time Ratio | Log Normal Median Ratio |
|---|---|---|---|---|---|
| 26 | 21.3788 | 0.8675 | 0.1744 | 1.1905 | 1.1905 |
| 52 | 21.3788 | 0.9013 | 0.1744 | 1.1905 | 1.1905 |
| 104 | 21.3788 | 0.9237 | 0.1744 | 1.1905 | 1.1905 |

```
beta=σ*(probit(1-slnorm0) - probit(1-slnorm1));
   /* log normal scale and S(t) for each group */
TR=exp(beta)
```

# Log Logistic Summary

| t (weeks) | Age>=50 | Log Logistic S(t), Treatment=1 | Log Logistic h(t), Treatment=1 | Log Logistic Median, Treatment=1 | Log Logistic S(t), Treatment=0 | Log Logistic h(t), Treatment=0 |
|---|---|---|---|---|---|---|
| 26 | Yes | 0.4776 | 0.0387 | 24.8138 | 0.3822 | 0.0457 |
| 52 | Yes | 0.1941 | 0.0298 | 24.8138 | 0.1402 | 0.0318 |
| 104 | Yes | 0.0597 | 0.0174 | 24.8138 | 0.0412 | 0.0177 |

| t (weeks) | Log Logistic Median, Treatment=0 | Log Logistic Hazard Ratio(t) | Log Logistic beta(Treatment); | Log Logistic Time Ratio | Log Logistic Median Ratio | Log Logistic Odds S(t)/(1-S(t), Treatment=1 |
|---|---|---|---|---|---|---|
| 26 | 20.2570 | 0.8457 | 0.2029 | 1.2249 | 1.2249 | 0.9141 |
| 52 | 20.2570 | 0.9373 | 0.2029 | 1.2249 | 1.2249 | 0.2409 |
| 104 | 20.2570 | 0.9807 | 0.2029 | 1.2249 | 1.2249 | 0.0635 |

| t (weeks) | Log Logistic Odds S(t)/(1-S(t), Treatment=0 | Log Logisitic Odds Ratio | Log Logistic Alpha, Treatment=1 | Log Logistic Alpha, Treatment=0 | Log Logisitic Alpha Ratio |
|---|---|---|---|---|---|
| 26 | 0.6187 | 1.4775 | 0.0021 | 0.0031 | 1.4775 |
| 52 | 0.1631 | 1.4775 | 0.0021 | 0.0031 | 1.4775 |
| 104 | 0.0430 | 1.4775 | 0.0021 | 0.0031 | 1.4775 |

# Discussion

- Not limited to parametric models discussed today. For example:
  - Changepoint model (piecewise exponential model)
  - Gamel-Boag model (allows for a proportion of subjects to be long term survivors)
  - Weibull with random effects
- Bayesian analysis, Weibull model

# Changepoint model

- When the hazard rate is constant within in time periods and changes at known timepoint
- For example, brain cancer hazard rate is constant for the first year of follow up but hazard rate is reduced if patient survives at least one year.

$$\boxed{\begin{aligned} S(t) &= e^{-\lambda_1 t} && t \le \tau \\ &= e^{-\lambda_1 \tau} e^{-\lambda_2 (t-\tau)} && t > \tau \end{aligned}}$$

# SAS code to restructure data

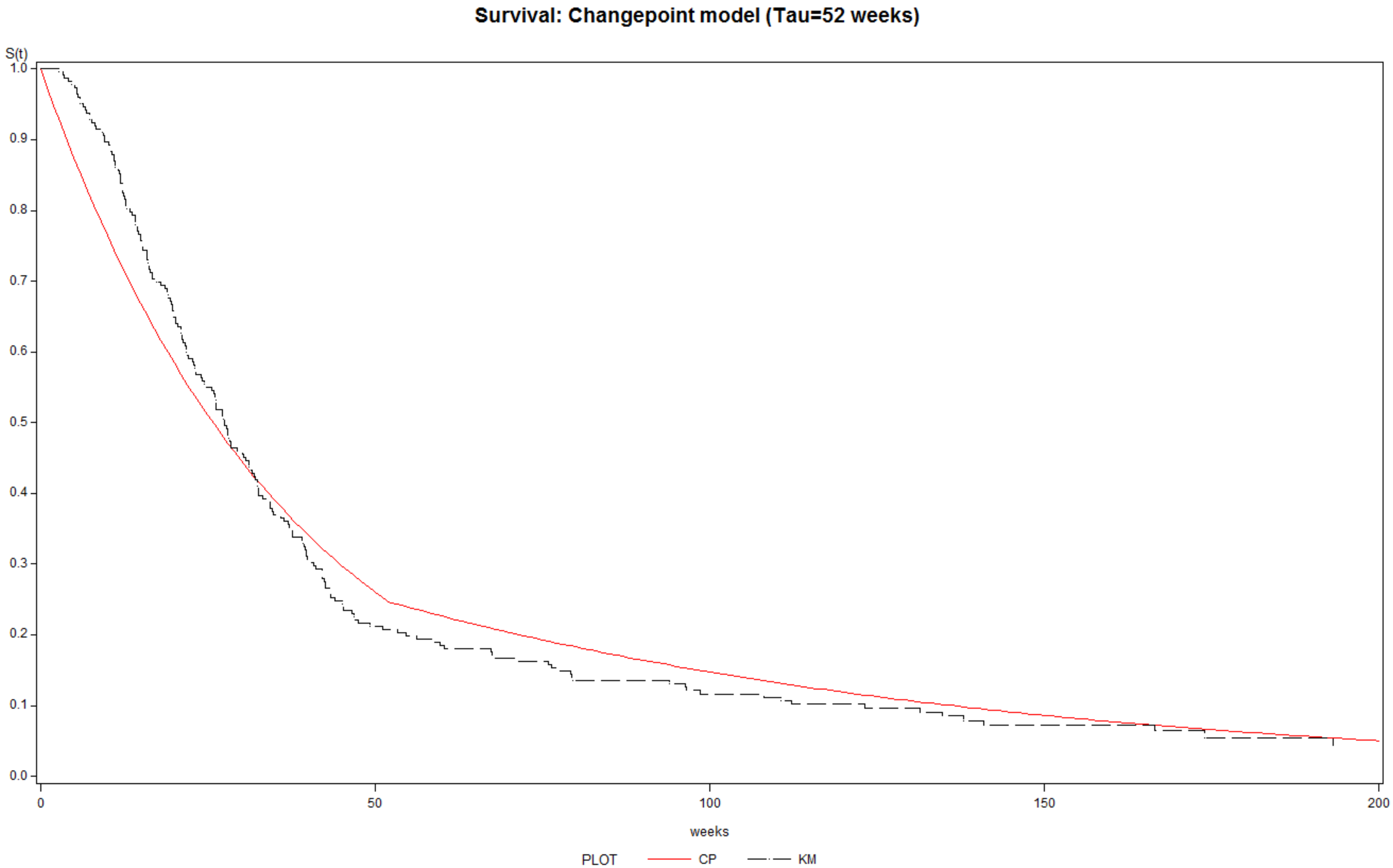
```
data brain2(keep=id weeks event weeks2 event2 year1);
  set sda.brain;
  id=_n_;
  if weeks<=52
     then do;
              event2=event;
               weeks2=weeks;
               year1=1;
               output;
         end;
     else do;
             event2=0;
               weeks2=52;
               year1=1;
               output;
               event2=event;
               weeks2=weeks-52;
               year1=0;
               output;
         end;
run;
```

# SAS code to fit the model

```
proc lifereg data=brain2;
  model weeks2*event2(0)=year1/d=exponential;
  title 'Piecewise Exponential';
run;

data brain3;
  do weeks=0 to 200 by 1;  /* time frame */
  lambda1=exp(-(4.533-.9175));  * = 0.0269;
  lambda2=exp(-(4.533));        * = 0.0107;
  if weeks<=52
     then sexp=exp(-lambda1*weeks);
     else sexp=exp(-lambda1*52)*exp(-lambda2*(weeks-52));
  output;
  end;
run;
```

# Changepoint model

| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 4.5330 | 0.1796 | 4.1809 | 4.8850 | 636.98 | <.0001 |
| year1 | 1 | -0.9175 | 0.1948 | -1.2993 | -0.5357 | 22.19 | <.0001 |
| Scale | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |
| Weibull Shape | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |


Survival: Changepoint model (Tau=52 weeks)
S(t)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
50
100
150
200
weeks
PLOT
CP
KM

# Gamel-Boag Model

- Allows for a proportion of subjects to be long term survivors.
- Events are modeled using log-normal model.

$$S(t \mid x) = p(x) + (1 - p(x))S_f(t \mid x)$$

$$p(x) = \frac{e^{x'\beta}}{1 + e^{x'\beta}}$$

$$\ln(t_i) = x_i'\gamma + e_i \qquad e_i \sim N(0, \sigma)$$

# SAS code to fit log-normal model

```
/* log normal model using proc lifereg */
proc lifereg data=sda.brain;
  model weeks*event(0)=age50/d=lnormal;
  title 'LifeReg: Survival by age group (Log normal)';
run;

/* log normal model using proc nlmixed - maximize loglikelihood */
proc nlmixed data=sda.brain;
  bounds sig > 0;
  parms bint=0 bage50=0 sig=1;
  pi=3.14159;
  u = bint+bage50*age50;
  S_t   = 1-probnorm((lweeks-u)/sig);
  f_t   = 1/(sqrt(2*pi)*weeks*sig)*exp(-1/2*((lweeks-u)/sig)**2);
  ll    = (event=1)*log(f_t) + (event=0)*log(S_t);
  model weeks ~ general(ll);
  title 'Log-normal model, adjusted for age';
run;
```

# SAS code to fit Gamel-Boag model

```
/* Gamel-Boag cure model using proc nlp (SAS/OR), maximize modified
loglikelihood, reference Frankel & Longmate */

proc nlmixed data=sda.brain;
  bounds sig > 0;
  parms bint=0 bage50=0 bint2=0 bage502=0 sig=1 ;
  pi=3.14159;
  u = bint+bage50*age50;
  p=exp(bint2+bage502*age50)/(1+exp(bint2+bage502*age50));
      /* model proportion cured by age group */
  S_t   = p+(1-p)*(1-probnorm((lweeks-u)/sig));
  f_t   = (1-p)*(1/(sqrt(2*pi)*weeks*sig)*exp(-1/2*((lweeks-u)/sig)**2));
  ll    = (event=1)*log(f_t) + (event=0)*log(S_t);
  model weeks ~ general(ll);
  title 'Gamel-Boag model, proportion cured adjusted for age';
run;
```

# SAS code to fit Weibull with random effects

```
proc nlmixed data=brain;
  bounds gamma > 0;
  parms bint=0 bage50=0 gamma=1 logsig=-1;
  linp = bint+bage50*age50+z;
  lambda = exp(-linp);
  S_t    = exp(-(lambda*weeks)**gamma);
  f_t    = gamma*lambda*((lambda*weeks)**(gamma-1))*S_t;
  ll     = (event=1)*log(f_t) + (event=0)*log(S_t);
  model weeks ~ general(ll);
  random z ~ normal(0,exp(2*logsig)) subject=id out=reweibull;
  title 'Weibull model with random effects, adjusted for age';
run;
```

# SAS output from Proc Lifereg

| | | | Standard | | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | **DF** | **Estimate** | **Error** | **95% Confidence Limits** | | **Chi-Square** | **Pr > ChiSq** |
| Intercept | 1 | 3.56 | 0.09 | 3.39 | 3.74 | 1660.94 | <.0001 |
| age50 | 1 | -0.42 | 0.13 | -0.66 | -0.17 | 10.90 | 0.001 |
| Scale | 1 | 0.93 | 0.05 | 0.85 | 1.03 | | |

# SAS output from Proc NLMIXED (1)

| | | Standard | | | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | **Estimate** | **Error** | **DF** | **t Value** | **Pr > \|t\|** | **95% Confidence Limits** | |
| bint | 3.56 | 0.09 | 222 | 40.75 | <.0001 | 3.39 | 3.74 |
| bage50 | -0.42 | 0.13 | 222 | -3.3 | 0.0011 | -0.66 | -0.17 |
| sig | 0.93 | 0.05 | 222 | 19.95 | <.0001 | 0.84 | 1.03 |

AIC 1935.9

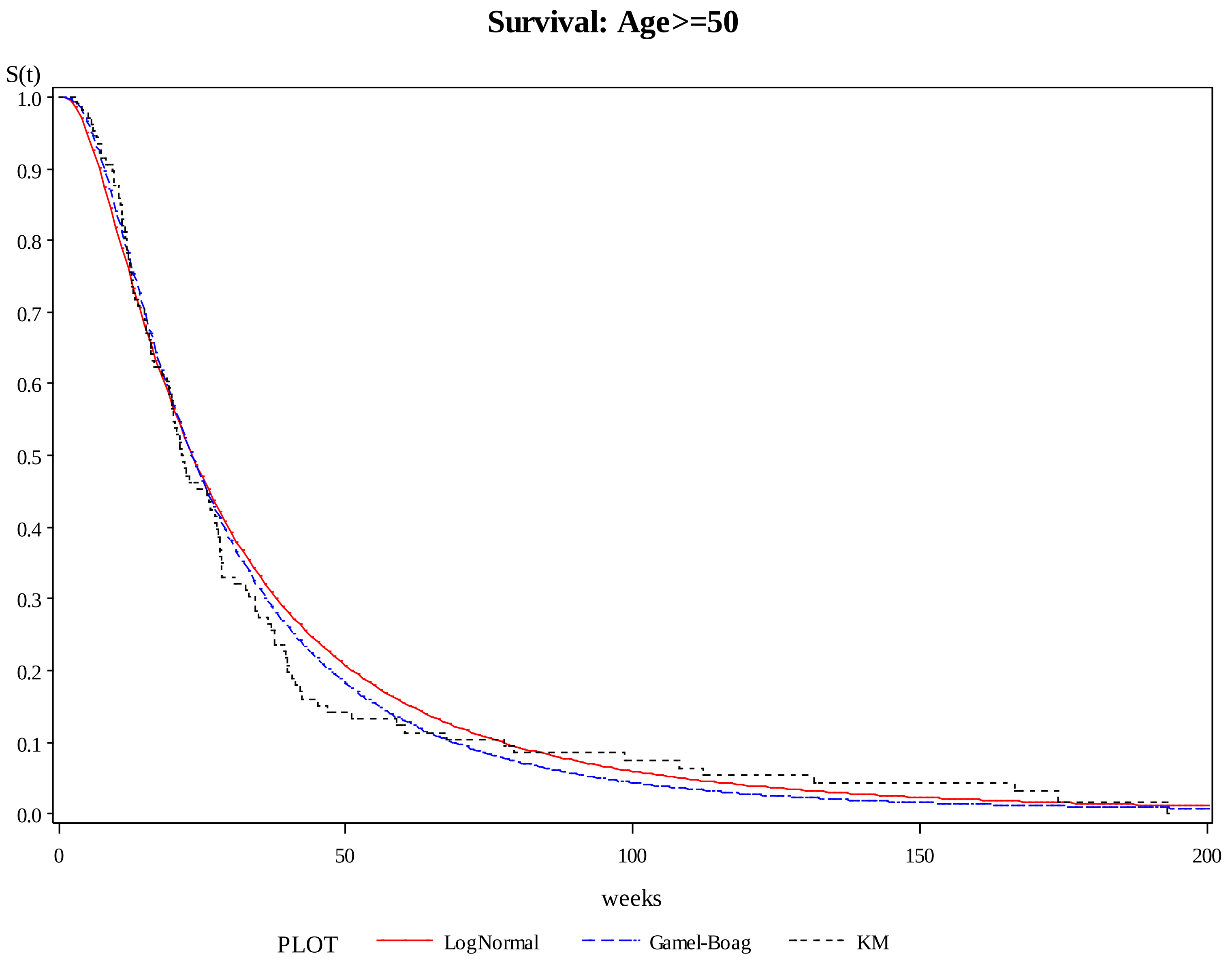
# SAS output from Proc NLMIXED (2)

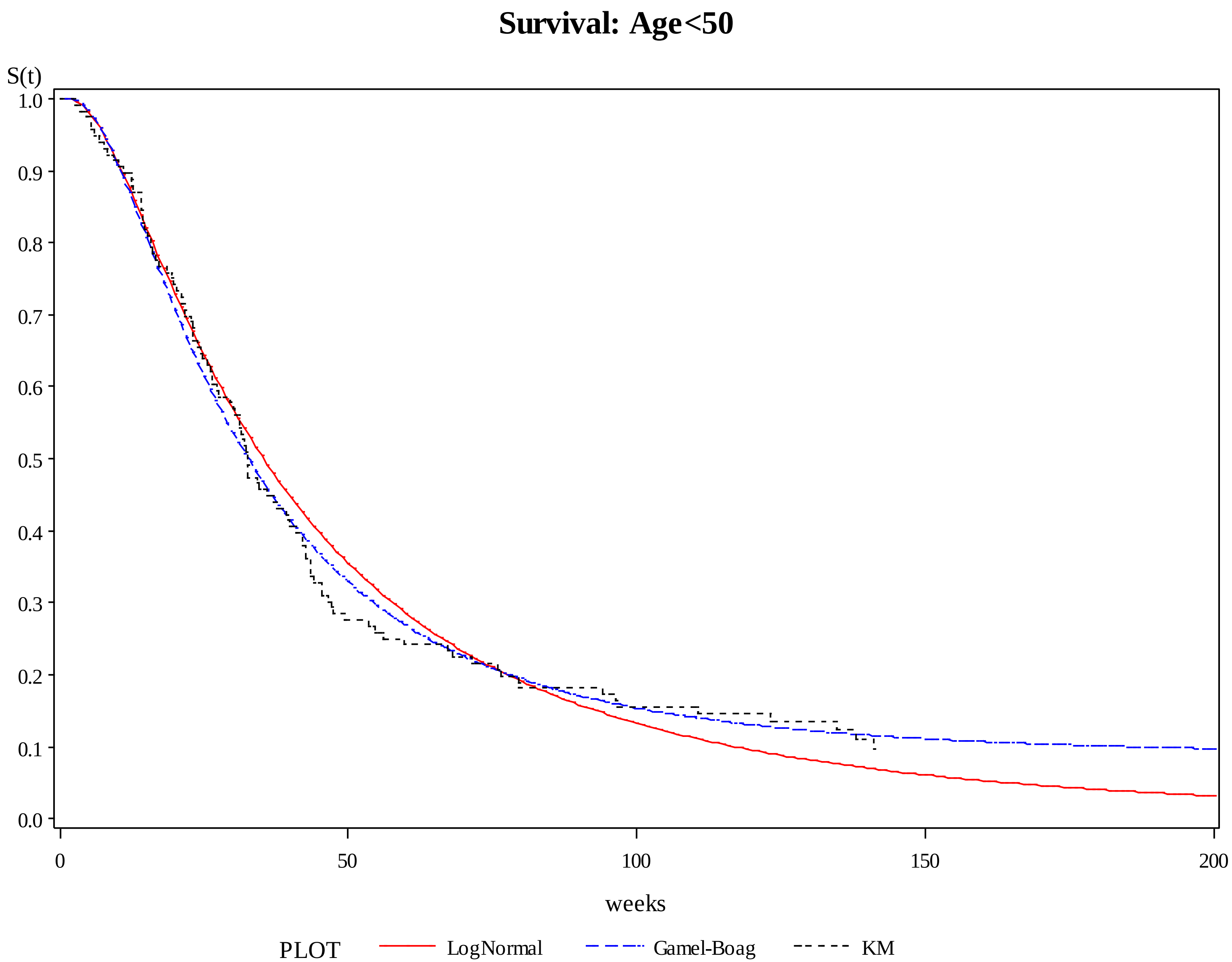
| | | Standard | | | | | |
|---|---|---|---|---|---|---|---|
| Parameter | Estimate | Error | DF | t Value | Pr > \|t\| | 95% Confidence Limits | |
| bint | 3.38 | 0.09 | 222 | 37.82 | <.0001 | 3.21 | 3.56 |
| bage50 | -0.24 | 0.12 | 222 | -1.97 | 0.0505 | -0.48 | 0.00 |
| bint2 | -2.35 | 0.39 | 222 | -5.98 | <.0001 | -3.13 | -1.58 |
| bage502 | -3.70 | 5.21 | 222 | -0.71 | 0.4786 | -13.95 | 6.56 |
| sig | 0.84 | 0.05 | 222 | 17.44 | <.0001 | 0.75 | 0.94 |

AIC 1929.0

Proportion cured each age group and OR:

| p1 | p0 | or | lor |
|---|---|---|---|
| 0.002 | 0.087 | 0.025 | -3.695 |


Survival: Age>=50
S(t)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
50
100
150
200
weeks
PLOT
LogNormal
Gamel-Boag
KM


Survival: Age<50
S(t)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
50
100
150
200
weeks
PLOT
LogNormal
Gamel-Boag
KM

# Bayesian analysis

- Gibbs sampling used for the location-scale models
- Can add priors for model parameters
- Can output posterior samples

```
proc lifereg data=sda.brain;
  model weeks*event(0)=age50/d=weibull;
  bayes WeibullShapePrior=gamma seed=1254 outpost=postweibull;
run;
```

Analysis of Maximum Likelihood Parameter Estimates

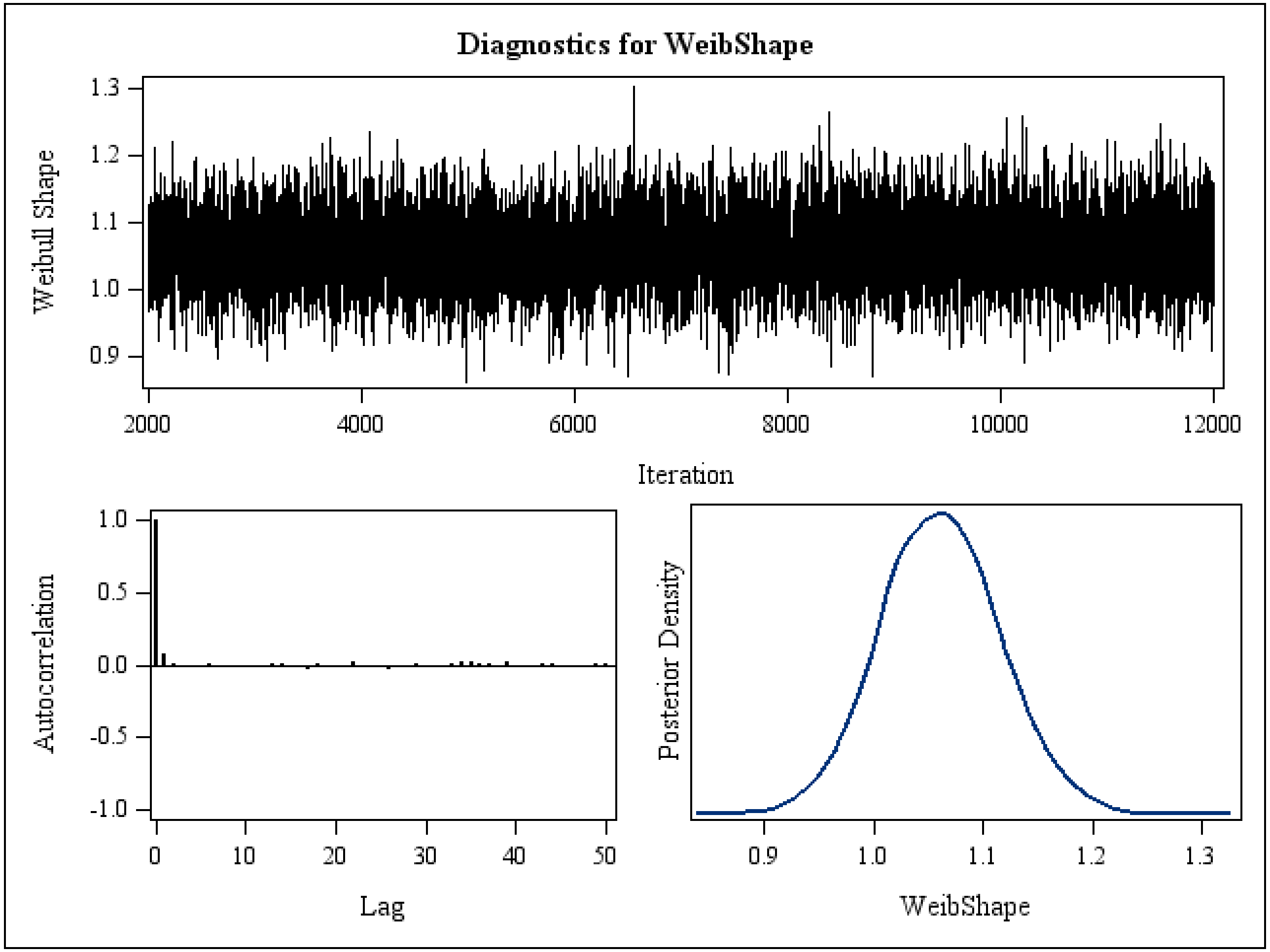
| Parameter | DF | Estimate | Standard Error | 95% Confidence Limits | |
|---|---|---|---|---|---|
| Intercept | 1 | 4.0569 | 0.0933 | 3.8740 | 4.2397 |
| age50 | 1 | -0.4927 | 0.1303 | -0.7480 | -0.2374 |
| Scale | 1 | 0.9356 | 0.0481 | 0.8459 | 1.0349 |
| Weibull Shape | 1 | 1.0688 | 0.0550 | 0.9663 | 1.1822 |

Posterior Summaries

| Parameter | N | Mean | Standard Deviation | Percentiles 25% | 50% | 75% |
|---|---|---|---|---|---|---|
| Intercept | 10000 | 4.0594 | 0.0942 | 3.9950 | 4.0584 | 4.1222 |
| age50 | 10000 | -0.4922 | 0.1325 | -0.5815 | -0.4922 | -0.4039 |
| WeibShape | 10000 | 1.0613 | 0.0545 | 1.0241 | 1.0605 | 1.0977 |

Posterior Intervals

| Parameter | Alpha | Equal-Tail Interval | | HPD Interval | |
|---|---|---|---|---|---|
| Intercept | 0.050 | 3.8787 | 4.2463 | 3.8755 | 4.2407 |
| age50 | 0.050 | -0.7532 | -0.2307 | -0.7571 | -0.2368 |
| WeibShape | 0.050 | 0.9555 | 1.1703 | 0.9551 | 1.1695 |


Diagnostics for WeibShape
Weibull Shape
1.3
1.2
1.1
1.0
0.9
2000
4000
6000
8000
10000
12000
Iteration
Autocorrelation
1.0
0.5
0.0
-0.5
-1.0
0
10
20
30
40
50
Lag
Posterior Density
0.9
1.0
1.1
1.2
1.3
WeibShape

# Discussion: Why fit parametric models?

- Able to describe the hazard rate
- AF model alternative when hazard rates are non-proportional
- Easier and more convenient to predict outcome for a particular outcome (see Reid (1994) conversation with D.R. Cox)
- If underlying hazard function is correctly specified, then parametric models 'give more precise estimates' (K & M, p.373).
- Applications where parametric models are compared to Cox proportional hazard models:
  - Chapman et al (2006). Application of log-normal model which authors conclude has a 'major advantage over the Cox model'
  - Nardi and Schemper (2003). Authors 'compare Cox and parametric models in clinical settings'.
  - Carroll (2003). Author 'illustrates the practical benefits of a Weibull-based analysis'.

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