

LOG LOGISTIC SURVIVAL MODEL - AFT

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2025-08-25

The log-logistic survival model is a parametric survival model where survival times are assumed to follow a log-logistic distribution. It is commonly used in survival analysis when the hazard rate is non-monotonic (it first increases, reaches a peak, and then decreases).

Load required packages

```
library(tidyverse)
library(flexsurv)
library(survival)
```

Load the data

```
d <- read_csv("C:/Users/ADMIN/Desktop/Data
Science/Datasets/survival/loglogistic_simulated_survival.csv")
```

Recode categorical variables

```
d$sex <- ifelse(d$sex == 1, "Male", "Female")
d$sex <- factor(d$sex)
d$treatment <- ifelse(d$treatment == 1, "drug", "placebo")
d$treatment <- factor(d$treatment)
```

Quick check

```
glimpse(d)

## Rows: 600
## Columns: 6
## $ time      <dbl> 4.5587, 1.5165, 1.7022, 6.7065, 27.3270, 20.3171,
6.6724, 0....
## $ event      <dbl> 1, 0, 1, 1, 0, 1, 1, 0, 1, 1, 0, 0, 1, 1, 0, 0, 0, 1, 1,
1, ...
## $ age        <dbl> 65.0, 58.6, 66.5, 75.2, 57.7, 57.7, 75.8, 67.7, 55.3,
65.4, ...
## $ sex        <fct> Female, Male, Male, Male, Male, Male, Female, Female,
Female...
## $ treatment <fct> placebo, drug, placebo, drug, placebo, placebo, drug,
placeb...
## $ biomarker <dbl> 0.756, 0.384, 1.361, 0.726, 0.496, 0.178, 0.984, 2.896,
2.70...

with(d, table(event))
```

```
## event
##    0    1
## 332 268
```

----- AFT MODELS -----

AFT via flexsurv (log-logistic)

```
aft_llogis <- flexsurvreg(Surv(time, event) ~ age + sex + treatment +
  biomarker,
                        data = d, dist = "llogis")
print(aft_llogis)
```

Call:

```
## flexsurvreg(formula = Surv(time, event) ~ age + sex + treatment +
##   biomarker, data = d, dist = "llogis")
##
```

Estimates:

	data	mean	est	L95%	U95%	se
exp(est)						
## shape	NA	1.52611	1.38555	1.68092	0.07523	
NA						
## scale	NA	25.65934	12.47679	52.77013	9.43964	
NA						
## age	59.86467	-0.01563	-0.02678	-0.00448	0.00569	
0.98450						
## sexMale	0.50667	0.15691	-0.06173	0.37556	0.11156	
1.16989						
## treatmentplacebo	0.48833	0.32868	0.10956	0.54780	0.11180	
1.38913						
## biomarker	1.19133	0.22254	0.07882	0.36626	0.07333	
1.24924						
##	L95%	U95%				
## shape	NA	NA				
## scale	NA	NA				
## age	0.97358	0.99553				
## sexMale	0.94014	1.45580				
## treatmentplacebo	1.11579	1.72944				
## biomarker	1.08201	1.44233				
##						
## N = 600, Events: 268, Censored: 332						
## Total time at risk: 6998.104						
## Log-likelihood = -1119.203, df = 6						
## AIC = 2250.406						

Model Setup

Model: Log-logistic Accelerated Failure Time (AFT) model

Outcome: Survival time (Surv(time, event))

Predictors: age, sex, treatment, biomarker

Distribution Parameters

Shape = 1.526 (95% CI: 1.39 – 1.68)

Controls how “peaked” or “spread out” the survival curve is.

1 means the hazard initially increases with time, peaks, then decreases.

Scale = 25.66 (95% CI: 12.48 – 52.77)

This is a baseline time parameter. Higher scale shifts survival curve to longer survival times.

Covariates (AFT interpretation)

In AFT models, coefficients represent the log acceleration factor.

$\exp(\text{est})$ = acceleration factor (time ratio).

1: longer survival (protective).

<1: shorter survival (risk factor).

Age: The estimated coefficient for age is -0.0156, with $\exp(\beta) = 0.985$.

This means that for each 1-year increase in age, survival time is expected to be about 1.5% shorter. The effect is small but statistically significant.

Sex (Male vs Female): The coefficient for males is 0.157, with $\exp(\beta) = 1.17$. This suggests that males have about 17% longer survival compared to females. However, since the 95% confidence interval (0.94–1.46) includes 1, this effect is not statistically significant.

Treatment (Placebo vs Drug): The treatment coefficient is 0.329, with $\exp(\beta) = 1.389$. Patients receiving placebo appear to have about 39% longer survival compared to those receiving the drug. The confidence interval (1.12–1.73) indicates that this effect is statistically significant.

Biomarker: The coefficient for the biomarker is 0.223, with $\exp(\beta) = 1.249$. Each unit increase in the biomarker is associated with about 25% longer survival. The confidence interval (1.08–1.44) shows this is a statistically significant effect.

Model Fit

N = 600 (268 deaths, 332 censored).

Log-likelihood = -1119.2.

AIC = 2250.4 → useful for comparing with other models (e.g., Weibull, log-normal).

Key Takeaways

Older age → shorter survival.

Treatment effect is surprising: placebo patients lived longer than treated ones (maybe treatment is harmful, or sicker patients got treated).

Biomarker → strong positive predictor of survival.

Sex → not statistically significant.

Log-logistic fit: hazard is non-monotonic (rises, then falls), so it fits diseases/events where risk peaks then declines.

AFT via survreg (parametric AFT; different parameterization)

```
aft_llogis_sr <- survreg(Surv(time, event) ~ age + sex + treatment +  
  biomarker,  
                        data = d, dist = "loglogistic")  
summary(aft_llogis_sr)  
##  
## Call:  
## survreg(formula = Surv(time, event) ~ age + sex + treatment +  
##      biomarker, data = d, dist = "loglogistic")
```

```
##               Value Std. Error      z      p
## (Intercept)    3.24491    0.36771  8.82 <2e-16
## age           -0.01563    0.00569 -2.75 0.0060
## sexMale        0.15691    0.11156  1.41 0.1595
## treatmentplacebo 0.32868    0.11180  2.94 0.0033
## biomarker      0.22254    0.07333  3.03 0.0024
## Log(scale)    -0.42272    0.04929 -8.58 <2e-16
##
## Scale= 0.655
##
## Log logistic distribution
## Loglik(model)= -1119.2   Loglik(intercept only)= -1132.5
##  Chisq= 26.5 on 4 degrees of freedom, p= 2.5e-05
## Number of Newton-Raphson Iterations: 4
## n= 600
```

Age ($\beta = -0.0156$, $p = 0.006$)

For every 1-year increase in age, survival time is multiplied by $\exp(-0.0156) \approx 0.985$.

This means older patients have ~1.5% shorter survival time per year of age. Effect is statistically significant.

Sex (Male vs Female; $\beta = 0.157$, $p = 0.16$)

Males have a time ratio of $\exp(0.157) \approx 1.17$.

This suggests that males live ~17% longer than females, but the result is not statistically significant ($p > 0.05$).

Treatment (Placebo vs Drug; $\beta = 0.329$, $p = 0.0033$)

Patients on placebo have a time ratio of $\exp(0.329) \approx 1.39$.

This means placebo patients survive ~39% longer than those on the drug, and this effect is statistically significant.

Biomarker ($\beta = 0.223$, $p = 0.0024$)

Each unit increase in biomarker is associated with a time ratio of $\exp(0.223) \approx 1.25$.

So, higher biomarker levels correspond to ~25% longer survival time, and the effect is significant.

Scale parameter (Scale = 0.655, $\log(\text{scale}) = -0.423$, $p < 2e-16$)

This describes variability in survival times. A scale < 1 suggests that the hazard function rises quickly and then falls off (common with log-logistic).

Overall model fit

Likelihood ratio test: $\chi^2(4) = 26.5$, $p < 0.0001 \rightarrow$ The covariates collectively improve model fit compared to intercept-only.

Sample size: $n = 600$, so findings are reasonably powered.

In short:

Older age shortens survival.

Males tend to live longer, but not significantly.

Placebo group survives longer than drug group (significant).

Higher biomarker values predict longer survival (significant).

————— Prediction —————

Create a representative dataset for predictions

```
newdat_aft <- d %>%
  group_by(treatment) %>%
  summarize(
    age = mean(age),
    biomarker = median(biomarker),
    sex = names(sort(table(sex), decreasing = TRUE))[1],
    .groups = "drop"
  ) %>%
  mutate(sex = factor(sex, levels = levels(d$sex)))

print(newdat_aft)

## # A tibble: 2 × 4
##   treatment    age biomarker sex
##   <fct>      <dbl>    <dbl> <fct>
## 1 drug        59.7      0.994 Male
## 2 placebo    60.0      0.989 Female
```

Predict with flexsurv: survival estimates over a grid of times

```
tgrid <- seq(0, quantile(d$time, 0.99), length.out = 200)

aft_surv_list <- lapply(split(newdat_aft, newdat_aft$treatment), function(nd)
{
  s <- summary(aft_llogis, newdata = nd, type = "survival", t = tgrid)
  data.frame(time = tgrid, surv = s[[1]]$est, treatment = nd$treatment)
})

aft_surv_df <- do.call(rbind, aft_surv_list)
```

————— Plot survival curves —————

```
ggplot(aft_surv_df, aes(x = time, y = surv, linetype = treatment)) +
  geom_step(size = 1.2) +
  labs(title = "AFT (Log-logistic) – Predicted Survival by Treatment",
       x = "Time", y = "Survival Probability") +
```

```
theme_minimal(base_size = 14) +  
theme(legend.title = element_blank())
```

