Lecture eighteen: The accelerated Failure Time (AFT) Model

The AFT model states that the survival function of an individual with covariate $\mathbf{x}$ at time t is the same as the survival function of an individual with a baseline survival function at a time t/ϕ where $\phi = exp(\alpha'\mathbf{x})$ for convenience. The covariates act multiplicatively on the time scale.

1. $S_S(t)$: survival function for standard treatment, a baseline distribution known. Unlike the baseline hazard $h_0(t)$ in the Cox model, which is arbitrary.

2. $S_N(t) = S_S(t/\phi)$: survival function for the new treatment

3. The new treatment effect is modeled by the acceleration parameter $1/\phi$.

4. Regardless of treatment assignment or individual characteristics/prognosis, the treatment group's survival follows the same family of distributions.

5. The new treatment and other factors change survival by altering the value of the acceleration parameter $1/\phi$:

$$S_N(t) = S_S(t/\phi(\mathbf{x}))$$

   A reasonable assumption or an acceptable fact?

6. Objectives of Modeling

   (a) To model $\phi(\mathbf{x})$ as a function of covariates $\mathbf{x}$.

   (b) To check the adequacy of acceleration model.

   (c) To check the adequacy of the family of distribution as a reasonable approximation.

7. Interpretation

   (a) Survival of new treatment group is $\phi(\mathbf{x})$ times as long as the reference population.

   (b) $\phi(\mathbf{x})$: acceleration rate which 'speeds up' or 'slows down' the passage of time.

(c) $\phi(\mathbf{x}) = 1$: Covariates have no impact on survival.

(d) $\phi(\mathbf{x}) > 1$: prolonged survival.

(e) $\phi(\mathbf{x}) < 1$: shortened survival.

(f) Example: $\phi(\mathbf{x}) = 2$

t	1	2	4
$S_S(t)$	0.8	0.6	0.2
$S_N(t) = S_S(0.5t)$	$S_S(0.5)$	0.8	0.6

(g) if covariate x leads to increased $\phi(x)$, it is a 'protection' factor; if x leads to decreased $\phi(x)$, it is 'risk' factor.

(h) It is convenient to set $\phi(\mathbf{x}) = exp(\alpha'\mathbf{x})$ (compare Cox model for hazard function).

8. The AFT model in terms of hazard function

The density function between two groups

$$f_N(t) = \phi^{-1} f_S(t/\phi)$$

and relation between hazard function is

$$h_N(t) = \phi^{-1} h_S(t/\phi)$$

If only consider the treatment factor($x = 0$ or 1), ignoring other covariates then

$$h_i(t) = e^{-\alpha x_i} h_0(t/e^{\alpha x_i}).$$

9. Comparison with PH model

(a) consider a piecewise exponential model

$$h_0(t) = \begin{cases} 0.5 & \text{if } t \leq 1 \\ 1 & \text{if } t > 1 \end{cases} \tag{1}$$

and survival function is

$$S_0(t) = \begin{cases} e^{-0.5t} & \text{if } t \leq 1 \\ e^{-0.5-(t-1)} & \text{if } t > 1 \end{cases} \tag{2}$$

(b) Under a PH model

$$h_P(t) = \psi h_0(t).$$

and

$$S_P(t) = [S_0(t)]^{\psi}.$$

(c) Under a AFT model

$$h_A(t) = \phi^{-1} h_0(t/\phi).$$

and

$$S_A(t) = [S_0(t/\phi)].$$

(d) let $\psi = \phi^{-1} = 2$. (the median survival times under the two models are 0.69 and 0.6 months, respectively).

Under AFT model, the increase in hazard for group II from 1.0 to 2.0 occurs sooner than under PH model. The 'kink' in the survivor function also occurs earlier under the AFT model.

10. The percentile-percentile plot

(a) Without censoring, we can get the QQ plot using the samples directly.

(b) Taking censoring into consideration, notice

$$t_0(p) = S_0^{-1}(\frac{100 - p}{100}),$$

and

$$t_1(p) = S_1^{-1}(\frac{100 - p}{100}).$$

Under AFT model, it's easy to show

$$t_0(p) = \phi^{-1} t_1(p).$$

(c) if $\hat{t}_0(p)$ and $\hat{t}_1(p)$ are estimated percentiles in the two groups, then a plot of them gives a straight line if the AFT model is appropriate. The slope, which is the acceleration factor $1/\phi$, can be roughly estimated by PROC REG in SAS.

(d) Example 5.13: Breast cancer study

percentile	g1	g2
10	47	13
20	69	26
30	148	35
40	181	48
50	.	61
60	.	113
70	.	143
80	.	.
90	.	.

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The REG Procedure
Model: MODEL1
Dependent Variable: g1

Root MSE             19.08788    R-Square     0.9823
Dependent Mean      111.25000    Adj R-Sq     0.9764
Coeff Var            17.15764

                    Parameter Estimates

                     Parameter      Standard
Variable   DF         Estimate         Error    t Value    Pr > |t|

g2          1          3.72039       0.28861      12.89      0.0010
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11. The general AFT model

12. The general form of AFT in terms of hazard

$$h_i(t) = e^{-\eta_i} h_0(t/e^{\eta_i}),$$

where $\eta_i = \alpha_1 x_{1i} + \ldots + \alpha_p x_{pi}$.

The corresponding survivor function for the ith individual is

$$S_i(t) = S_0(t/e^{\eta_i}),$$

13. Log-linear form of AFT model: Consider following transformation of r.v. T_i of survival time:

$$log\, T_i = \mu + \alpha_1 x_{i1} + \alpha_2 x_{i2} + \ldots + \alpha_p x_{ip} + \sigma\epsilon_i.$$

Then, we have (follow the steps at page 196)

$$S_i(t) = P\{exp(\mu + \sigma\epsilon_i) \geq t/exp(\alpha' x_i)\},$$

and

$$S_i(t) = S_0(t/exp(\alpha' x_i)),$$

and the acceleration factor is $exp(-\alpha' x_i)$ for the ith individual.

The survivor function for ith individual can also be expressed in terms of survivor function of ϵ_i:

$$S_i(t) = S_{\epsilon_i}\{\frac{log\, t - \mu - \alpha' x_i}{\sigma}\}.$$

14. The Weibull AFT model

(a) AFT property

if baseline hazard is from $W(\lambda, \gamma)$

$$h_0(t) = \lambda\gamma t^{\gamma-1}$$

then

$$h_i(t) = (e^{-\eta_i})^{\gamma}\lambda\gamma t^{\gamma-1}$$

which is the hazard function of $W(\lambda e^{-\gamma\eta_i}, \gamma)$. We say Weibull has AFT property (cf. PH property of Weibull distribution). Under both models, the shape parameter is unchanged

(b) The relation of parameters under two models (p179 or p199)
Two groups: The acceleration factor is $\phi^{-1} = e^{-\alpha}$ under AFT model and the hazard ratio is $\phi^{-\gamma} = e^{-\gamma\alpha}$ under PH model.

15. The log-logistic AFT model If the baseline hazard is from $log-logistic(\theta, \kappa)$

$$h_0(t) = \frac{e^{\theta}\kappa t^{\kappa-1}}{1+e^{\theta}t^{\kappa}},$$

then under AFT model, the hazard of the death at time t for the ith individual is

$$h_i(t) = e^{-\eta_i}h_0(e^{-\eta_i}t)$$
$$= \frac{e^{\theta-\kappa\eta_i}\kappa t^{\kappa-1}}{1+e^{\theta-\kappa\eta_i}t^{\kappa}},$$

which is the hazard of $log - logistic(\theta - \kappa\eta_i, \kappa)$ - AFT property.

16. The log-normal AFT model

Similarly, we can show that the survival time of ith individual has log-normal distribution parameters $\mu + \eta_i$ and σ.

$$S_0(t) = 1 - \Phi(\frac{log\, t - \mu}{\sigma}),$$

and

$$S_i(t) = 1 - \Phi(\frac{log\, t - \eta_i - \mu}{\sigma}),$$

since under AFT model

$$S_i(t) = S_0(e^{-\eta_i}t).$$

Figure 1:

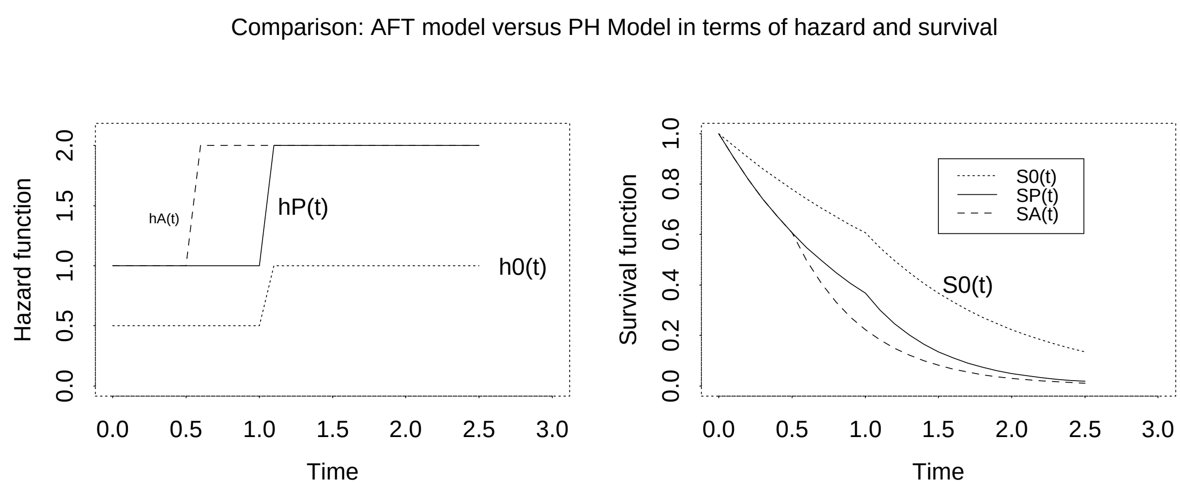
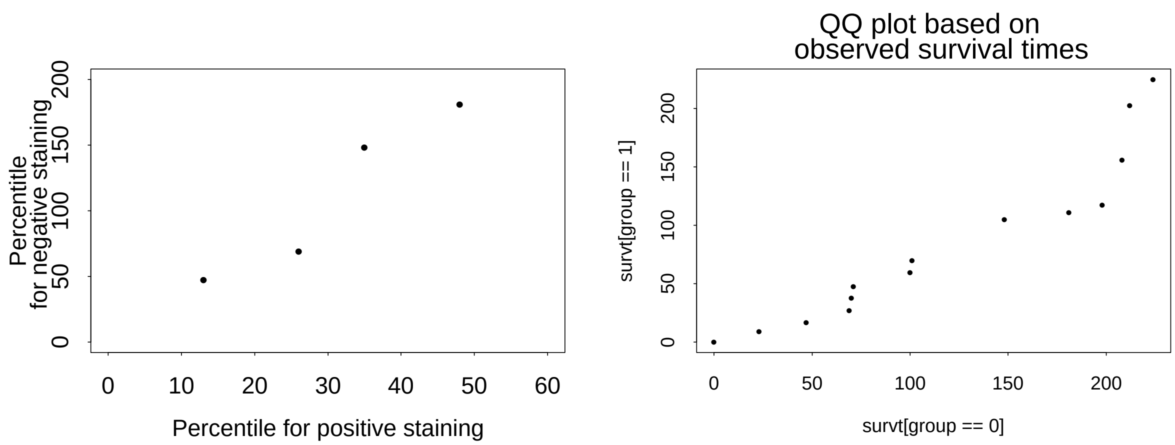

Comparison: AFT model versus PH Model in terms of hazard and survival
Hazard function
hA(t)
hP(t)
h0(t)
0.0
0.5
1.0
1.5
2.0
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Time
Survival function
S0(t)
SP(t)
SA(t)
S0(t)
0.0
0.2
0.4
0.6
0.8
1.0
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Time

Figure 2:


Percentile
for negative staining
0
50
100
150
200
0
10
20
30
40
50
60
Percentile for positive staining
QQ plot based on
observed survival times
survt[group == 1]
0
50
100
150
200
0
50
100
150
200
survt[group == 0]