△Accelerated Failure Time model

survival time : X , covariate Z

$$Y = \ell nX$$

$$Y = \mu + \gamma Z + \varepsilon \qquad (\varepsilon = \sigma W)$$

△ ε : unspecified (nonparametric)

$$\begin{cases} \text{1. An attractive alternative model to cox model} \\ \text{2. Direct physical interpretation} \end{cases}$$

Estimation : By ① rank estimate

② Generalized Estimating equation

Note that : γ : + then Z ↑ Y ↑ (help survival)

− then Z ↑ Y ↓ (hurt survival)

various forms of AFT and Cox models

(1) AFT : $S(x|z) = S_0(x \exp -\gamma^T z)$

Cox : $S(x|z) = \left[S_0(x)\right]^{\exp \beta^T z}$

(2) ☆ AFT : $Y = \mu + \gamma^T Z + \sigma W$

Cox : $\ell n\left[-\ell n\, S(x|z)\right] = \beta^T z + \ell n\left[-\ell n\, S_0(x)\right]$

(3) AFT : $h(x|z) = h_0(xe^{-\gamma^T z}) \exp(-\gamma^T z)$

☆ Cox : $h(x|z) = h_0(x) \exp(\beta^T z)$

Cox model : easy to do inference but hard to interpret

△Clustered survival time

Breast cancer v.s. mutation of BRCA gene (Ashkenazi Jewish population)

risk

① Cluster

② Frailty

③ Mixed effect Cox model

$$h_{ij}(t_{ij}) = h_0(t_{ij}) \cdot w_i \cdot e^{z_{ij}\beta}$$

$$w \sim \frac{w^{\frac{1}{\theta}-1} e^{-\frac{w}{\theta}}}{\Gamma\left(\frac{1}{\theta}\right)\theta^{\frac{1}{\theta}}}$$

gamma distribution

Competing risk

Multiple events

① Simplistic method

treat other event time as censor

△ However this method is questionable !

This censor is not independent !!

△ Cause-specific hazards and cumulative incidence functions

K distinct causes of death

one can experience at most one of K causes of death

Cause-specific CDF $\Rightarrow F_j(t) = P(T \le t, C = j) = \int_0^t h_j(u)\, S(u)du$

$$F_j(\infty) = P(C = j)$$

- The cause-specific hazard of jth cause

$$h_j(t) = \lim_{\Delta t \to 0} \frac{P(t<T<t+\Delta_t, C=j \mid T>t)}{\Delta t}$$

$$\Rightarrow h(t) = \sum_{j=1}^{k} h_j(t)$$

- D ordered event times $\Rightarrow t_1 < t_2 < \cdots < t_D$

$$\hat{h}(t_i) = \frac{d_i}{n_i}$$

$$\widehat{h_k}(t_i) = \frac{d_{ik}}{n_i}$$

$$\Leftrightarrow \hat{h}(t_i) = \frac{\sum_{k=1}^{\bar{k}} d_{ik}}{n_i}$$

$$\hat{F}_k(t) = \sum_{t_i \le t} \hat{S}(t_{i-1}) \hat{h}_k(t_i) \Leftarrow$$ Cumulative incidence function

Common way to display: stacked plot

Ex: Prostate cancer data

n = 14294 $\begin{cases} 0 \ censored \\ 1 \ death \ from \ prostate \ cancer \\ 2 \ death \ from \ other \ cancer \end{cases}$

Need install mstate package and use "Cuminc" command

Consider Age 80+ population

- Regression methods for cause-specific hazards

special challenges ⇒ It's difficult to define precisely the hazard function on which the covariate should operate.

simple method (Putter et.al.(2007)) treat other events as censored

vice versa!!

$\boxed{\text{Fine and Gray}}$

$$\overline{h_k}(t) = -\frac{d \log\left(1-F_k(t)\right)}{dt} \rightarrow \overline{h_k}(t|z) = \overline{h}_{0k}(t)e^{z\beta}$$

Use Fine and Gray method $\Rightarrow$ package "cmprsk" command "crr".

Consider T_2 stage patients in prostate cancer data.

- Run R codes to see the example.

Other causes:

- gradepoor risk ratio 0.126 (Fine and gray) vs. 0.281 (Putter et al.)

Prostate cancer :

- gradepoor risk ratio 1.132 vs. 1.22

Recurrent event (ordered event)

① AG (Andersen-Gill)

$$Y_i(t)\lambda_0(t)\exp(X_i(t)\beta)$$

$\boxed{\text{Poisson process}}$

② WLW (Wei , Lin and Weissfeld)

$$Y_{ij}(t)\lambda_{0j}(t)exp(X_i(t)\beta_j)$$

jth event

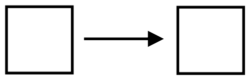
③ Conditional model (PWP , Prentice , William & Peterson)

similar to AG but effect for events may be difficult.

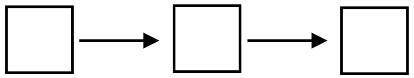
Ex : One has event on 10,30,42

	Interval	Stratum
AG	(0,10]	1
	(10,30]	1
	(30,42]	1
WLW	(0,10]	1
	(0,30]	2
	(0,42]	3
PWP	(0,10]	1
	(10,30]	2
	(30,42]	3

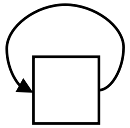
Time to first event



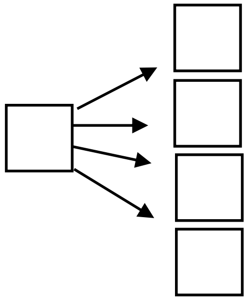
Conditional(PWP)



AG



WLW



Ex : Smith has experienced his second event on day 32.

Who are the subjects at risk when Smith has his second event ?

AG : All subjects who were under observation on day 32.

WLW : All subjects who were under observation on day 32 , and have not yet had a second event.

PWP : All subjects who were under observation on day 32,have not yet had a second event , and have experienced a first event.

PWP

t	coef	exp(coef)	se(coef)	robustse	z	Pr(>|z|)
tx	-0.41836	0.658129	0.304194	0.293599	-1.425	0.154
num	0.11421	1.120987	0.053999	0.051294	2.227	0.026
size	-0.00745	0.992576	0.073207	0.063265	-0.118	0.906
tx:strata(interval)interval=2	-0.03349	0.967067	0.500317	0.552349	-0.061	0.952
tx:strata(interval)interval=3	0.350949	1.420415	0.667693	0.501027	0.7	0.484
tx:strata(interval)interval=4	0.622714	1.86398	0.749012	0.591132	1.053	0.292
tx:strata(interval)interval=5	NA	NA	0	0	NA	NA

Event 1	-0.41836
Recurrent Event 2	-0.4519
Recurrent Event 2	-0.0674
Recurrent Event 2	0.2044

WLW

	coef	exp(coef)	se(coef)	robustse	z	Pr(>lzl)	
tx	-0.44654	0.63984	0.30522	0.29072	-1.536	0.12454	
num	0.15686	1.16983	0.05244	0.05089	3.082	0.00205	**
size	0.01421	1.01431	0.07029	0.0654	0.217	0.82801	
tx:strata(interval)interval=2	0.13506	1.14461	0.49823	0.4969	0.272	0.78577	
tx:strata(interval)interval=3	0.44582	1.56177	0.56088	0.60339	0.739	0.45999	
tx:strata(interval)interval=4	0.50452	1.65619	0.65574	0.649	0.777	0.43693	
tx:strata(interval)interval=5	NA	NA	0	0	NA	NA	

Event 1	-0.4465
Recurrent Event 2	-0.3115
Recurrent Event 2	-0.0001
Recurrent Event 2	0.0987