

• Current age:  $Z(t) = \text{age} + t$ , where age is the age at the entry to the study

$$\lambda(t|Z) = \lambda_0(t) \cdot \exp\{\alpha(\text{age} + t) + \beta Z\} = \lambda_0(t) \cdot e^{\alpha t} \cdot \exp\{\alpha \text{age} + \beta Z\}$$

and now compute it with model where only age stuff is in the model:  $\tilde{\lambda}(t|Z) = \tilde{\lambda}_0(t) \cdot \exp\{\tilde{\alpha} \text{age} + \tilde{\beta} Z\}$

age=0, Z=0  $\Rightarrow \lambda_0(t) \cdot e^{\alpha t}$  vs  $\tilde{\lambda}_0(t)$ , so interpretation of baseline hazard changes

$\hookrightarrow$  interpretation of  $\lambda$  and  $\alpha$  is tied together

$$\frac{\tilde{\lambda}(t|Z_1)}{\tilde{\lambda}(t|Z_2)} \stackrel{Z_1=Z_2}{\sim} \exp\{\tilde{\alpha}(\text{age}_1 - \text{age}_2)\} \rightsquigarrow \tilde{\alpha} = \tilde{\lambda}(t|\text{age}+1, Z) / \tilde{\lambda}(t|\text{age}, Z)$$

$$\frac{\lambda(t|Z_1)}{\lambda(t|Z_2)} \stackrel{Z_1=Z_2}{\sim} \exp\{\alpha(\text{age}_1 - \text{age}_2)\} \rightsquigarrow \alpha = \lambda(t|\text{age}+1, Z) / \lambda(t|\text{age}, Z)$$

} the same interpretation and also  $\alpha = \tilde{\alpha}$  because partial likelihood has the same shape

What if in interaction?  $\lambda(t|Z) = \lambda_0(t) \cdot \exp\{\alpha(\text{age} + t) + \beta \cdot Z + \gamma(\text{age} + t) \cdot Z\}$

$$\tilde{\lambda}(t|Z) = \tilde{\lambda}_0(t) \cdot \exp\{\tilde{\alpha}(\text{age}) + \tilde{\beta} \cdot Z + \tilde{\gamma} \cdot \text{age} \cdot Z\}$$

age=0=Z  $\rightsquigarrow \lambda_0(t) \cdot e^{\alpha t}$  vs  $\tilde{\lambda}_0(t)$  and only age=0  $\rightsquigarrow \lambda_0(t) \cdot e^{\alpha t + \gamma t Z} \cdot e^{\beta Z}$  vs  $\tilde{\lambda}_0(t) \cdot e^{\tilde{\beta} Z}$

under Z=0 we are under the same conditions as above  $\rightarrow \alpha$  and  $\tilde{\alpha}$  have the same interpretation

$$\frac{\lambda(t|\text{age}=0, Z_1)}{\lambda(t|\text{age}=0, Z_2)} = \exp\{\tilde{\beta}(Z_1 - Z_2)\} \quad \text{but} \quad \frac{\lambda(t|\text{age}=0, Z_1)}{\lambda(t|\text{age}=0, Z_2)} = \frac{\lambda_0(t) \exp\{\alpha t + \beta Z_1 + \gamma t Z_1\}}{\lambda_0(t) \exp\{\alpha t + \beta Z_2 + \gamma t Z_2\}} = \exp\{\beta(Z_1 - Z_2) + \gamma t(Z_1 - Z_2)\}$$

general limit in Z:  $\frac{\tilde{\lambda}(t|\text{age}, Z+1)}{\tilde{\lambda}(t|\text{age}, Z)} = \exp\{\tilde{\beta} + \tilde{\gamma} \cdot \text{age}\}$  but:  $\frac{\lambda(t|\text{age}, Z+1)}{\lambda(t|\text{age}, Z)} = \exp\{\beta + \gamma(\text{age} + t)\}$

combined:  $\frac{\frac{\lambda(t|\text{age}+1, Z+1)}{\lambda(t|\text{age}+1, Z)}}{\frac{\lambda(t|\text{age}, Z+1)}{\lambda(t|\text{age}, Z)}} = e^{\tilde{\gamma}}$   $\frac{\frac{\lambda(t|\text{age}+1, Z+1)}{\lambda(t|\text{age}+1, Z)}}{\frac{\lambda(t|\text{age}, Z+1)}{\lambda(t|\text{age}, Z)}} = \frac{e^{\beta + \gamma(\text{age}+1+t)}}{e^{\beta + \gamma(\text{age}+t)}} = e^{\gamma}$

PL without interaction:  $\prod_{i=1}^n \frac{\exp\{\tilde{\alpha} A_i + \tilde{\beta} Z_i\}}{\sum_{j=1}^n Y_j(t_i) \exp\{\tilde{\alpha} A_j + \tilde{\beta} Z_j\}} \rightsquigarrow \alpha = \tilde{\alpha}$   
 $\beta = \tilde{\beta}$

PL with interaction:  $\prod_{i=1}^n \frac{\exp\{\tilde{\alpha} A_i + \tilde{\beta} Z_i + \tilde{\gamma} A_i Z_i\}}{\sum_{j=1}^n Y_j(t_i) \exp\{\tilde{\alpha} A_j + \tilde{\beta} Z_j + \tilde{\gamma} A_j Z_j\}} \rightsquigarrow$

$\rightsquigarrow$  in general  $(\alpha, \beta, \gamma) \neq (\tilde{\alpha}, \tilde{\beta}, \tilde{\gamma})$

in (B) using  $tt()$  function:  $\text{coxph}(\text{Surv}(\text{time}, \text{delta}) \sim \text{bili} + tt(\text{age}), \text{data} = \text{pbc})$  (time transformation)

in this example yields the same coefficients as  $\sim \text{bili} + \text{age}$

however " $\sim \text{bili} * \text{age}$ " and " $\sim \text{bili} * tt(\text{age})$ " do have similar, but not the same estimates of coefficients

Warning: time and age need to be in the same units! Ex: age [years]  $\Rightarrow$  use  $\sim \text{bili} * tt(\text{age})$ ,  $tt = \text{function}(x, t, \dots)$   
 $\{x + t / 365.25\}$   
 within coxph function