3. Alternative regression models

- Two major classes:
  - hazard models based on rates: proportional hazards model
  - failure time models based on actual failure times: accelerated failure time model

- General relative risk model (Prentice & Self, 1983, Ann. Stat.)

$$\lambda(t \mid Z) = \lambda_0(t) r(\beta Z)$$

  - exponential form: $r(\beta Z) = \exp(\beta Z)$
  - linear form: $r(\beta Z) = 1 + \beta Z$

- Additive hazards model (Lin & Ying, 1994, Bmka):

$$\lambda(t \mid Z) = \lambda_0(t) + \beta Z$$

  - interpretation: additive covariate effect
  - embedded constraint: $\lambda_0(t) + \beta Z > 0$
  - QPS model estimation

$$E[dN_i(t) - Y_i(t)\beta Z_i dt \mid \mathscr{F}_{t-}] = Y_i(t)\lambda_0(t)dt$$

  - invariant in marginalization
  - extension: additive-multiplicative hazards model (Lin & Ying, 1994, Ann. Stat.)

$$\lambda(t \mid Z_1, Z_2) = \lambda_0(t)\exp(\beta Z_1) + \gamma Z_2$$

- Accelerated hazards model:

$$\lambda(t \mid Z) = \lambda_0\{t \exp(\beta Z)\}$$

  - parameter interpretation: accelerated/decelerated risk progression
  - parameter estimation: QPS approach

$$E[dN_i(te^{-\beta_0 Z_i}) \mid \mathscr{F}_{t-}; \beta_0] = Y_i(te^{-\beta_0 Z_i})e^{-\beta_0 Z_i}\lambda_0(t)dt$$

- alternative approach:
  - for any γ, transform $T_i^* = T_i e^{\gamma Z_i}$. The hazard function for transformed time becomes:

$$\lambda_i^*(t \mid Z_i) = \lambda_i(te^{-\gamma Z_i})e^{-\gamma Z_i} = \lambda_0(te^{(\beta-\gamma)Z_i})e^{-\gamma Z_i}$$

  - when $\gamma = \beta$, then we obtain the proportional hazards model

$$\lambda_i^*(t \mid Z_i) = \lambda_0(t)e^{-\beta Z_i}$$

  - algorithm motivated to find an estimate
- Chen & Wang (2000, JASA)

- General class of hazards model:

$$\lambda(t \mid Z) = \lambda_0\{t \exp(\beta Z)\} \exp(\gamma Z)$$

  - a general class to include PHM, AFTM and AHM as sub classes
  - identifiability: exponential distribution
  - model estimation: QPS approach
  - semiparametric efficiency
  - Chen & Jewell (2001, Bmka)

- Proportional odds model

$$\log \frac{S(t \mid Z)}{1 - S(t \mid Z)} = \log \frac{S_0(t)}{1 - S_0(t)} + \beta Z$$

  - Bennett (1983, Stat. Med.)
  - Murphy (1997, JASA)
  - Yang & Prentice (1999, JASA)
  - Open questions: does QPS work? how does it compare with other approaches? what's the optimal weight function for log-rank statistic when alternative is the proportional odds model?

- Generalized model

$$g\{S(t \mid Z)\} = g_0(t) + \beta Z$$

  - $g(\cdot)$ known decreasing function
  - log-log link: proportional hazards model
  - logit link: proportional odds model
  - generalized odds-rate model

$$g(s) = \log\left(\frac{1}{\lambda}\frac{1 - s^{\lambda}}{s^{\lambda}}\right) I(\lambda > 0) + \log(-\log s) I(\lambda = 0)$$

- Linear transformation model

$$h(T) = -\beta Z + \epsilon$$

  - $h(\cdot)$ is unknown
  - ϵ's distribution is known
    * extreme value distribution: proportional hazards model
    * standard logistic distribution: proportional odds model
  - Cheng & Wei (1995, Bmka)

- Proportional mean residual life model

$$m(t \mid Z) = m_0(t) \exp(\beta Z)$$

  - model interpretation
  - model constraint: $m_0(t) \exp(\beta Z) + t$ shall be monotonically non-decreasing
  - connection with hazard functions under renewal processes
  - model estimation: QPS approach
  - Oakes (1990, Bmka)
  - Chen & Cheng (2005, Bmka)

- Additive mean residual life model

$$m(t \mid Z) = m_0(t) + \beta Z$$

  - model interpretation: additional life expectancy
  - model constraint: $m_0(t) + \beta Z \geq 0$
  - model estimation: QPS and Buckley-James
  - semiparametric efficiency
  - Chen & Cheng (2006, Bmka)

- Summary
  - alternative regression models developed to address various limitations of the proportional hazards model
  - no perfect model
  - software yet to be developed
  - still an active research area