The Analysis of Failure Times in the Presence of Competing Risks

Prentice et al. (1978)

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Motivations for Competing Risks

- Single cause vs multiple causes for failure process
- Competing Risks analysis on:
  (1) inference on the effects of treatment/exposure on specific types of failure
  (2) interrelations among failure types
  (3) failure rates for some causes given "removal" of some/all other causes
- Example:
  Acute Leukemia Bone marrow transplantation:(i) recurrence, (ii) GVHD, (iii) pneumonia

(1) inference on the effects of treatment/exposure on specific types of failure:

$T >= 0$, the time of failure, which may be right censored

$J \in \{1, 2, ...m\}$, the type of failure, which will be unknown if T is censored

$\mathbf{z} = (z_1, ..., z_p)$, regression vector

(1) inference on the effects of treatment/exposure on specific types of failure:

Overall hazard function (Cox 1972):

$$\lambda(t; \mathbf{z}) \tag{1}$$

Cause-specific hazard function (Prentice and Breslow 1978):

$$\lambda_j(t; \mathbf{z}) \tag{2}$$

(1) inference on the effects of treatment/exposure on specific types of failure:

Conclusion: The likelihood factor for $\lambda_j(t;\mathbf{z})$ is precisely the same as

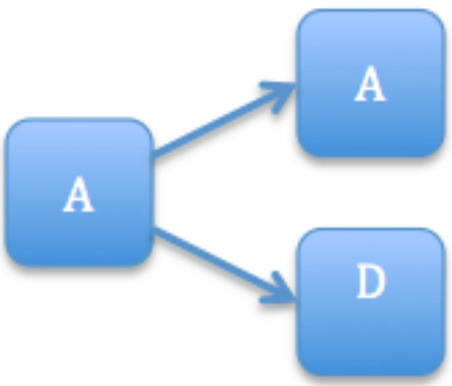
would be obtained by regarding all failure types other than j as censored at the individual's failure time. Thus, any of the standard methods for estimating $\lambda(t;\mathbf{z})$ can be applied for inference on $\lambda_j(t;\mathbf{z})$.

(1) inference on the effects of treatment/exposure on specific types of failure:

Bone marrow translantation example:
(1)recurrence : j=1;
(2)GVHD: j=2;
(3)pheumonia: j=3

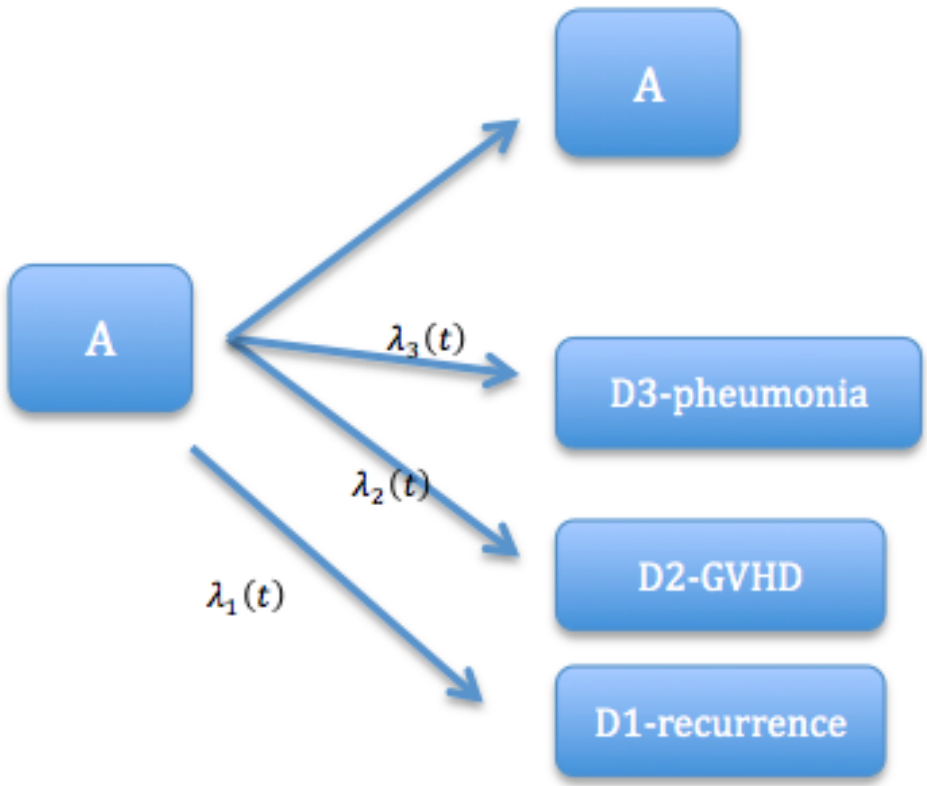
Recurrence-specific Hazard Function $\lambda_1(t; \mathbf{z})$ could be obtained by treating GVHD and pheumonia failure as consored.

(1) inference on the effects of treatment/exposure on specific types of failure:



t $t + \Delta t$

Overall $\lambda(t)$



Cause-Specific $\lambda_j(t)$

(2) Interrelations among failure types:

- With data of the type $(T, J; \mathbf{z})$, interelation among failure types is nonidentifiable. Therefore, with z time independent, we can not study the interrelation, or even test for independence among competing failure modes.

- One promising approach to study the relationship among failure types involves the definition of risk-indicator variables as time-dependent covariates.

(2) Interrelations among failure types:

Bone marrow translantation example:

Interrelations between GVHD and leukemia recurrence:

Define a GVHD risk-indicator $z(t)$, that takes value 0 between $t = 0$ and diagnosis of GVHD and value 1 after.

$\widehat{\beta} = -.792$ which suggests that the leukemia relapse rate is reduced by an estimated multiplicative factor $exp(\widehat{\beta}) = .45$

(3) Failure rate estimation following cause removal:

Estimation of failure probabilities given the removal of some or all other causes:

- Not well defined until mechanism for cause removal is clearly specified.
- Strong assumptions on study conditions.

(3) Failure rate estimation following cause removal:

Bone marrow translantation example:

Mechanism to remove GVHD: strengthening donor-recipient matching criteria

Recurrent leukemia relapse rates would increase.

Mechanism to remove GVHD: treatment to control GVH reaction.

If the treatment has antileukemia potential, recurrent leukemia relapse rates would decrease.