Modeling the cumulative incidence function of clustered competing risk data

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Clustered competing risk data

Key terms:

- Clustered: groups with a dependence structure (e.g. families);
- Causes competing by *something*.

Something?

- **Failure** of an industrial or electronic component;
- **Occurence** or **cure** of a disease or some biological process;
- **Progress** of a patient clinic state.

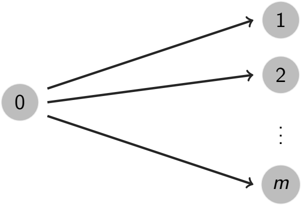
Independent of the application, always the same framework

Group	ID	Cause 1	Cause 2	Censorship	Time	Feature
1	1	Yes	No	No	10	A
1	2	No	No	Yes	8	A
2	1	No	No	Yes	7	B
2	2	No	Yes	No	5	A

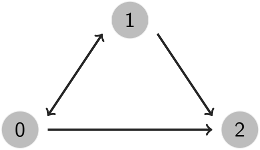
Data designs

Failure time process

Competing risk process



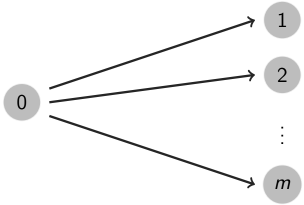
Multistate process



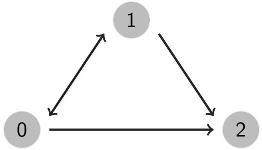
Data designs

Failure time process

Competing risk process



Multistate process



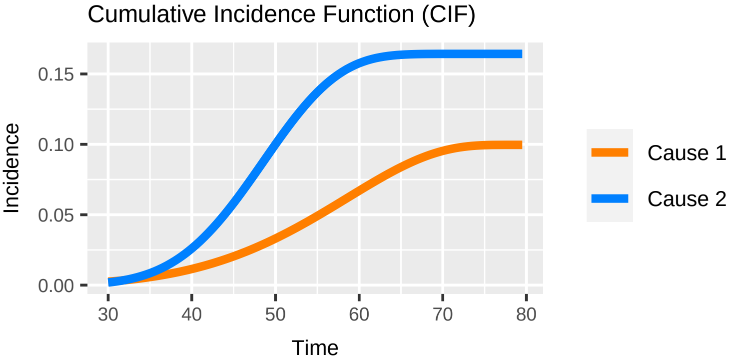
Modeling framework

We have to choose which scale we model the **survival experience**.
Usually, is the

hazard (failure rate) scale : $\quad \lambda(t \mid \text{features}) = \lambda_0(t) \times c(\text{features}).$

In the competing risk setting ...

a more attractive possibility is to work on the probability scale, focusing on the cause-specific



i.e.

$$\text{CIF} = \mathbb{P}[\text{ failure time} \leq t,\ \text{ a given cause} \mid \text{features }]$$

Main focus application: cancer incidence in twins

Clustered competing risks data
↳ Clusters? Families
↳Family studies
↳ Twins data

Family studies $\Rightarrow$ within-family dependence

That may reflect

- Disease **heritability**;
- The impact of shared **environmental effects**;
    - **Parental effects**:
      continuity of the phenotype across generations.

Our contribution: a hierarchical approach

Thinking on two competing causes

... for the outcome y_{ijt} of a subject i, family j, in the time t, we have

$$y_{ijt} \mid \underbrace{\{u_{1j}, u_{2j}, \eta_{1j}, \eta_{2j}\}}_{\text{latent effects}} \sim \text{Multinomial}(p_{1ijt}, p_{2ijt}, p_{3ijt})$$

$$\begin{bmatrix} u_{1j} \\ u_{2j} \\ \eta_{1j} \\ \eta_{2j} \end{bmatrix} \sim \begin{matrix}\text{Multivariate} \\ \text{Normal}\end{matrix} \left(\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma^2_{u_1} & \sigma_{u_1,u_2} & \sigma_{u_1,\eta_1} & \sigma_{u_1,\eta_2} \\ & \sigma^2_{u_2} & \sigma_{u_2,\eta_1} & \sigma_{u_2,\eta_2} \\ & & \sigma^2_{\eta_1} & \sigma_{\eta_1,\eta_2} \\ & & & \sigma^2_{\eta_2} \end{bmatrix} \right)$$

$$\begin{aligned} p_{kijt} &= \frac{\partial \text{CIF}}{\partial t} \\ &= \frac{\partial}{\partial t} \underbrace{\pi_k(X, u_1, u_2 \mid \beta)}_{\substack{\text{cluster-specific} \\ \text{risk level}}} \underbrace{\Phi[w_k g(t) - X^\top \gamma_k - \eta_k]}_{\substack{\text{cluster-specific} \\ \text{failure time trajectory}}}, \end{aligned}$$

$k = 1, 2.$

Contributions & challenges

- A clear and simpler modeling structure;
- **There is no free lunch**
  Computational challenges overcame via an
  efficient implementation and estimation routines;
- The data is very simple,
  we just know the outcome (**yes** or **no**);
- We have to be able to build the CIF curves;
- And accommodate the within-family dependence properly,
  that can happen in different manners;
- ...

Joint work with

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Thank you

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