

... some glimpses, at least

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Hazard, “mathematical version” of incidence:

$$\alpha(t) = \frac{1}{dt} P(t \leq T < t + dt | T \geq t)$$

Integrated (aka cumulative) hazard:

$$A(t) = \int_0^t \alpha(s) ds$$

Survival function:

$$S(t) = \exp\{-A(t)\} = \exp\left\{-\int_0^t \alpha(s) ds\right\}$$

A bit more correct: $S(t) = \prod_{0 \leq s \leq t} (1 - dA(s))$ (product integral)

Usual stuff:

- Kaplan-Meier estimator $\hat{S}(t)$ for $S(t)$
- Ignore the actual $\alpha(t)$

However, difficult to extend, e.g. to competing risks
($S(t)$ does not always make sense)

More direct:

- Kaplan-Meier follows: $\hat{S}(t) \approx \exp \left\{ -\hat{A}(t) \right\}$
- Nelson-Aalen estimator $\hat{A}(t)$ for $A(t) = \int_0^t \alpha(s) ds$



IMPORTANT:

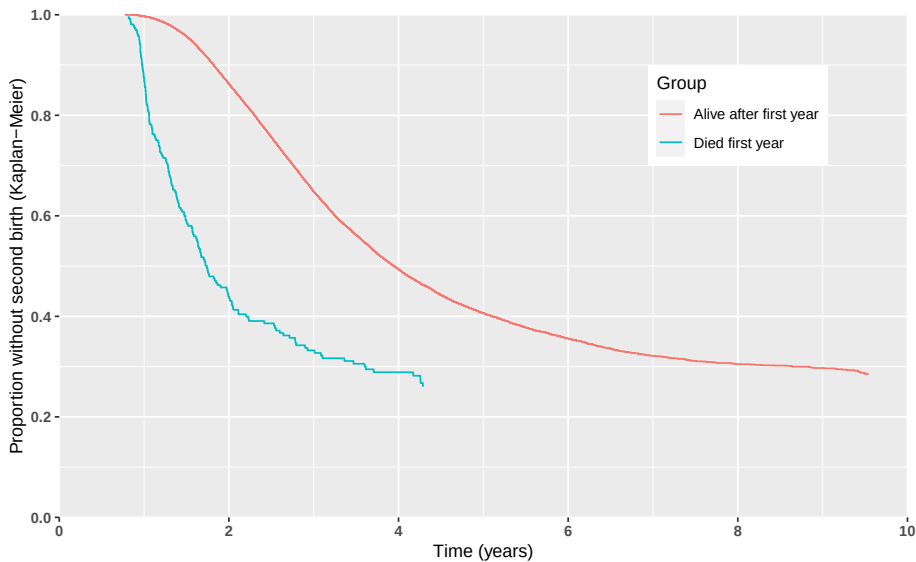
- The derivative, i.e. *the slope* of $A(t)$ is the hazard $\alpha(t)$

EXAMPLE: TIME FROM FIRST TO SECOND BIRTH

- Medical Birth Registry
- Time from first to second birth
- About 53,000 mothers with first birth in 1983-1997
- 262 of these lost the first child within one year

(Just an example, not a complete analysis...!)

KAPLAN-MEIER CURVES COMPARING GROUPS

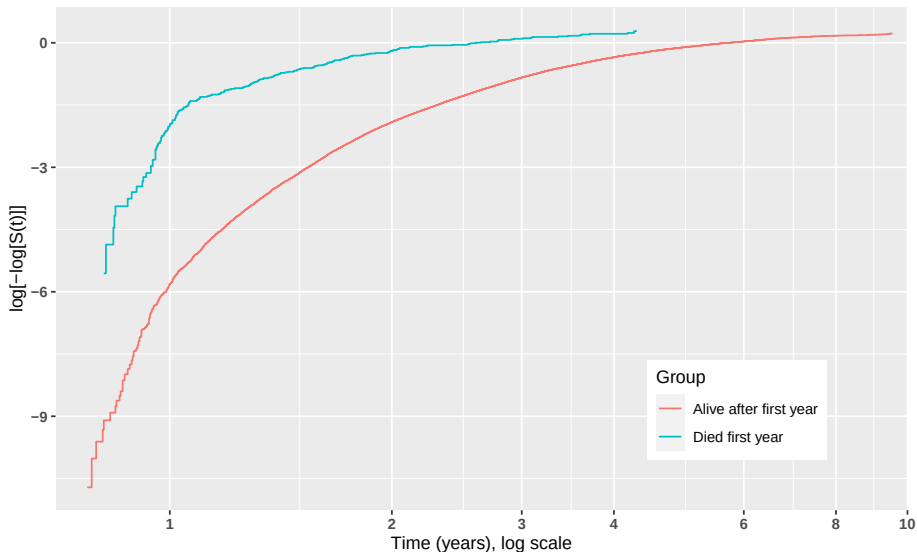


Hazard rate ratio (overall):

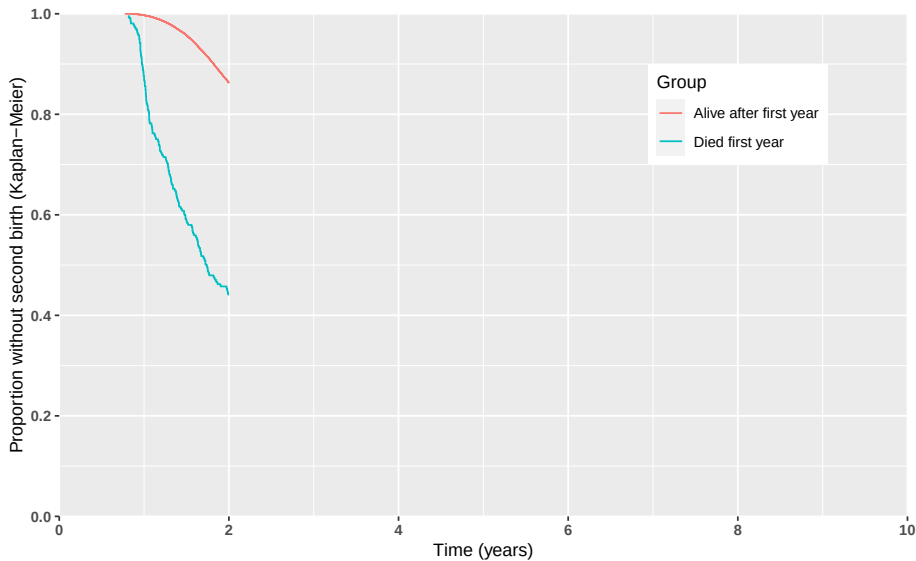
2.6 (95%CI: 2.3–3.0)

LOG-MINUS-LOG CURVES OF KAPLAN-MEIER

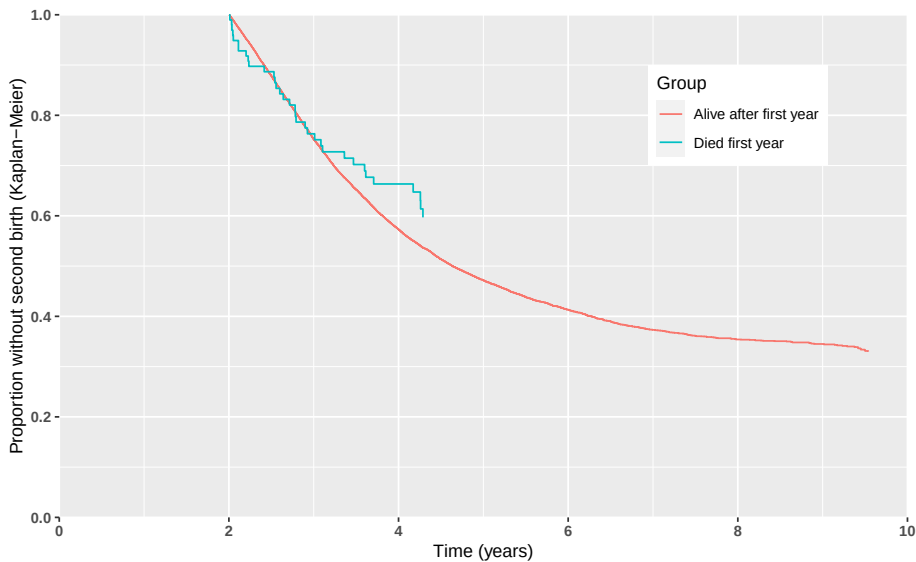
CHECK FOR NON-PROPORTIONAL HAZARDS



KAPLAN-MEIER CURVES, PART I



KAPLAN-MEIER CURVES, PART II (RESET TO 1)



Hazard rate ratio (overall):

2.6 (95%CI: 2.3–3.0)

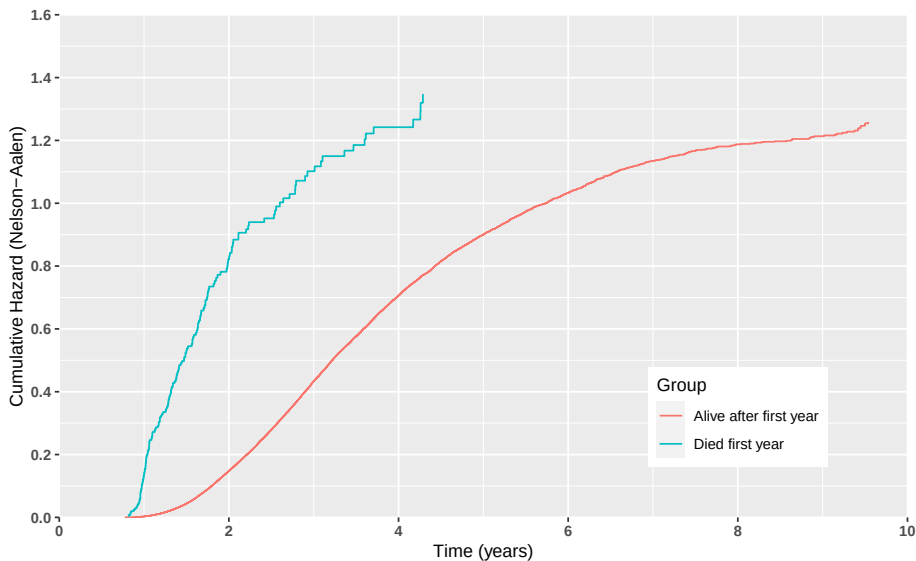
Hazard rate ratio (up until year 2):

4.8 (95%CI: 4.1–5.7)

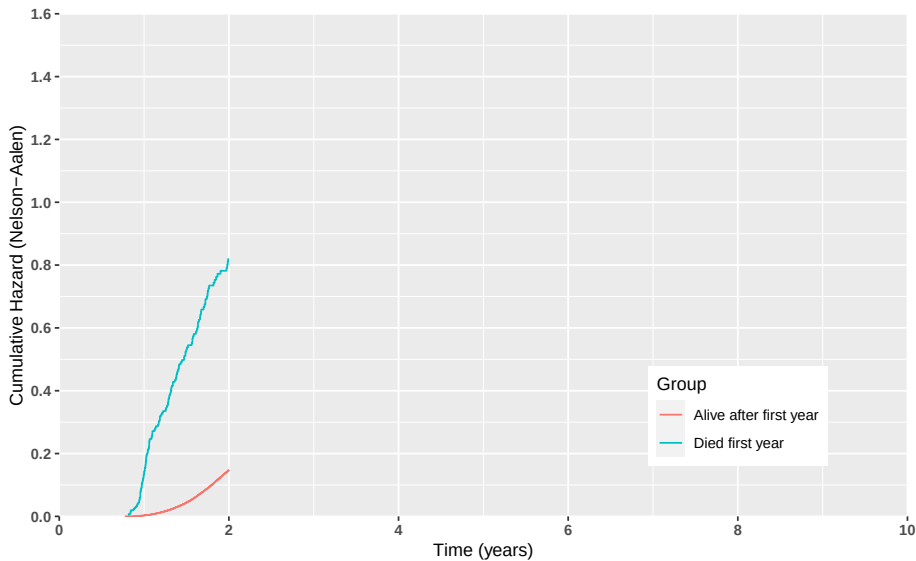
Hazard rate ratio (after year 2):

0.79 (95%CI: 0.58–1.1)

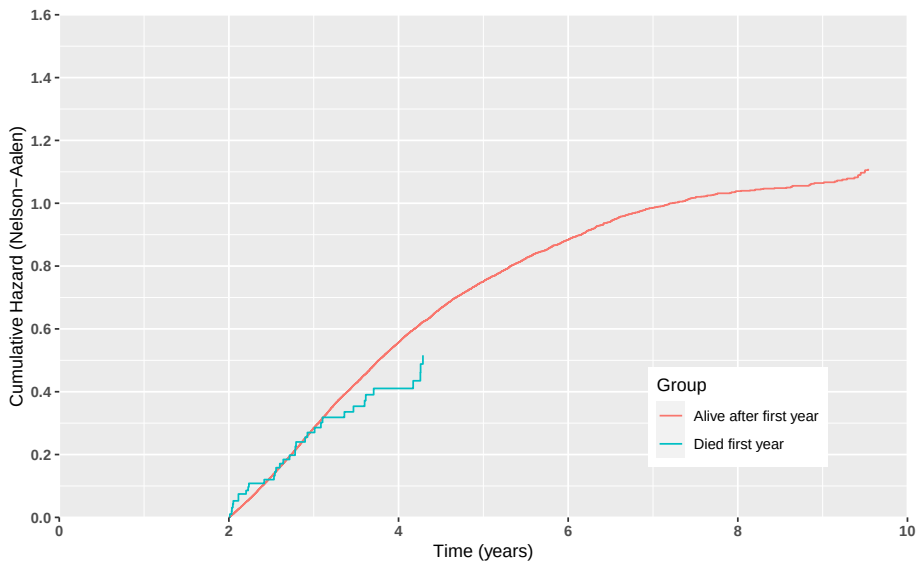
NELSON-AALEN CUMULATIVE HAZARD CURVES



NELSON-AALEN CUMULATIVE HAZARD, PART I



NELSON-AALEN CUMULATIVE HAZARD, PART II (RESET TO 0)



COX (PROPORTIONAL HAZARDS) REGRESSION

TIME-DEPENDENT COVARIATES

HAZARD:

$$\alpha(t) = \alpha_0(t) \exp(\beta_1 \cdot x_1(t) + \dots)$$

- $\alpha_0(t)$ is the *baseline hazard*
- $x_1(t), x_2(t), \dots$ are *time-dependent* covariates
- $\beta_1, \beta_2, \dots$ are the corresponding parameters

Effect:

$\exp(\beta_1)$ is the **multiplicative** effect on the hazard, associated with an unit increase in $x_1(t)$ *at any time* t .

AALEN ADDITIVE HAZARDS REGRESSION

TIME-DEPENDENT COVARIATES AND TIME-DEPENDENT PARAMETERS

HAZARD:

$$\alpha(t) = \beta_0(t) + \beta_1(t) \cdot x_1(t) + \dots$$

- $\beta_0(t) = \alpha_0(t)$ is the *baseline hazard*
- $x_1(t), x_2(t), \dots$ are *time-dependent* covariates
- $\beta_1(t), \beta_2(t), \dots$ are the corresponding *time-dependent* parameters
- Note the improvement: $\beta_i(t)$ are *allowed to depend on time!*

Effect:

$\beta_1(t)$ is the **additive** effect on the hazard, associated with an unit increase in $x_1(t)$ *specifically at time t*.

INTERPRETATION

COX MULTIPLICATIVE MODEL, HAZARD RATE RATIO

$$\alpha_{\text{alive}}(t) = \alpha_0(t)$$

$$\alpha_{\text{died}}(t) = \alpha_0(t) \exp(\beta_1)$$

$$\text{HRR} = \frac{\alpha_{\text{died}}(t)}{\alpha_{\text{alive}}(t)} = \exp(\beta_1)$$

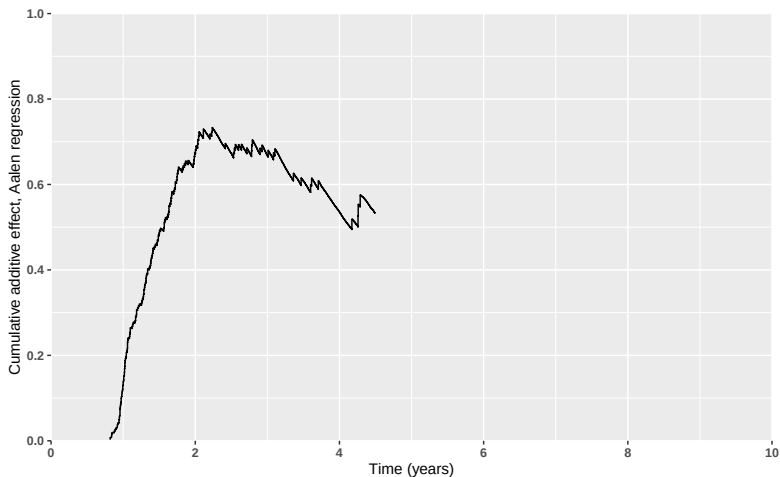
AALLEN ADDITIVE MODEL, HAZARD RATE DIFFERENCE

$$\alpha_{\text{alive}}(t) = \beta_0(t)$$

$$\alpha_{\text{died}}(t) = \beta_0(t) + \beta_1(t)$$

$$\text{HRD} = \alpha_{\text{died}}(t) - \alpha_{\text{alive}}(t) = \beta_1(t)$$

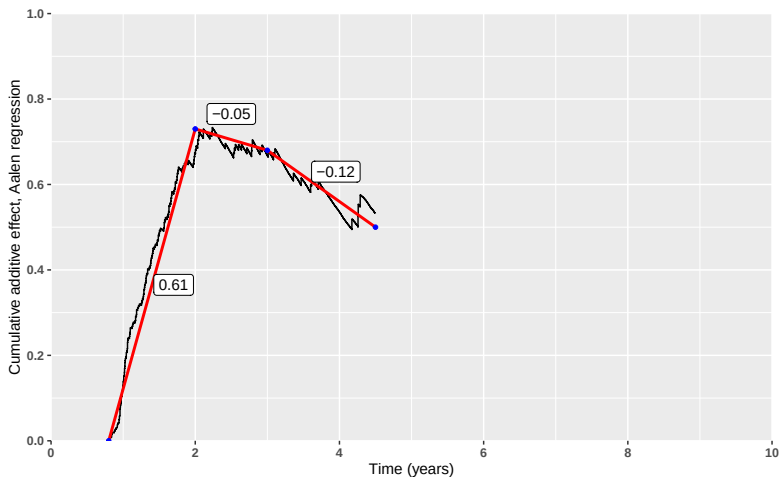
Aalen ESTIMATE OF CUMULATIVE DIFFERENCE



The estimated curve is $B_1(t) = \int_0^t \beta_1(s) ds$

So the slope is $\beta_1(t)$

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Time-dependent covariates:

- Covariates can change over time
- But effect of covariates assumed constant over time
- Available in both Cox and Aalen

Time-dependent effects:

- The *effect* of covariates can change over time
- This can be combined with time-dependent covariates
- Available only in Aalen
- (...although various types of Cox-adaptations do exist)

Thank you!