How to estimate cancer survival

(an overview)

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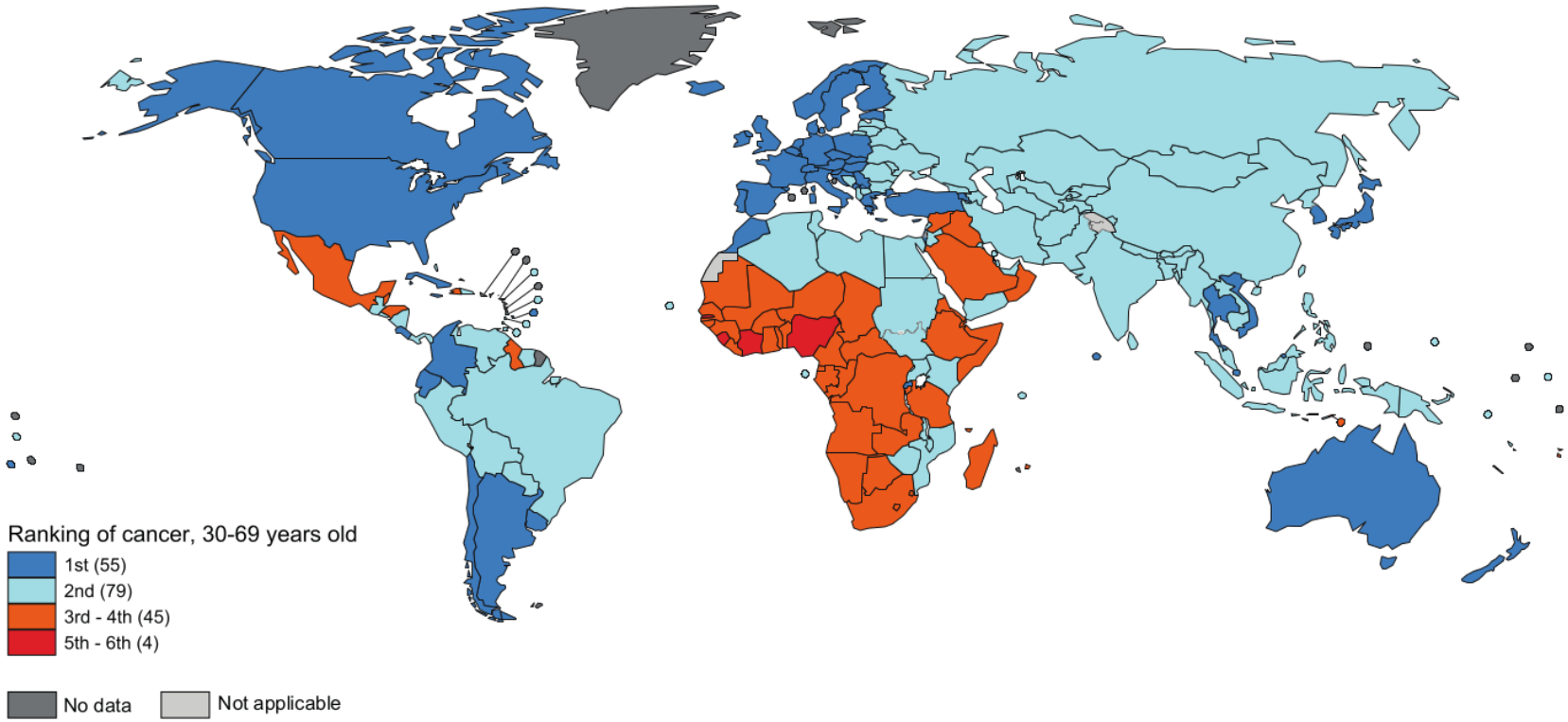
The global cancer burden



Global map of cancer as a leading cause of premature death (i.e. at ages 30-69 years)

Figure: Wild C.P., Weiderpass E., Stewart B.W., editors (2020). *World Cancer Report: Cancer Research for Cancer Prevention.* Lyon, France: International Agency for Research on Cancer.

The *unequal* cancer burden

Inequalities in cancer

"The **systematic** differences in cancer occurence (incidence, mortality and survival) that exist between and within countries."[1]

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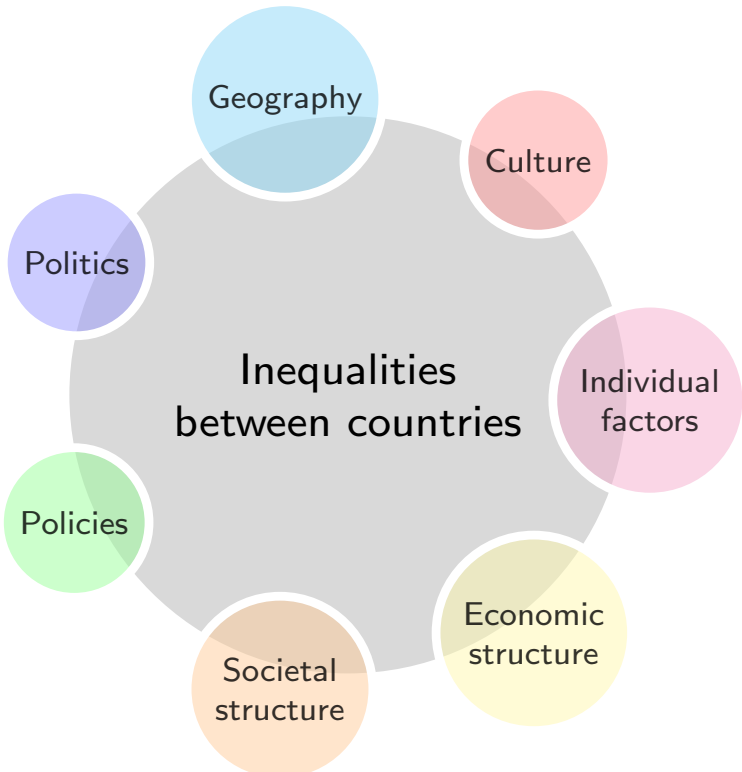

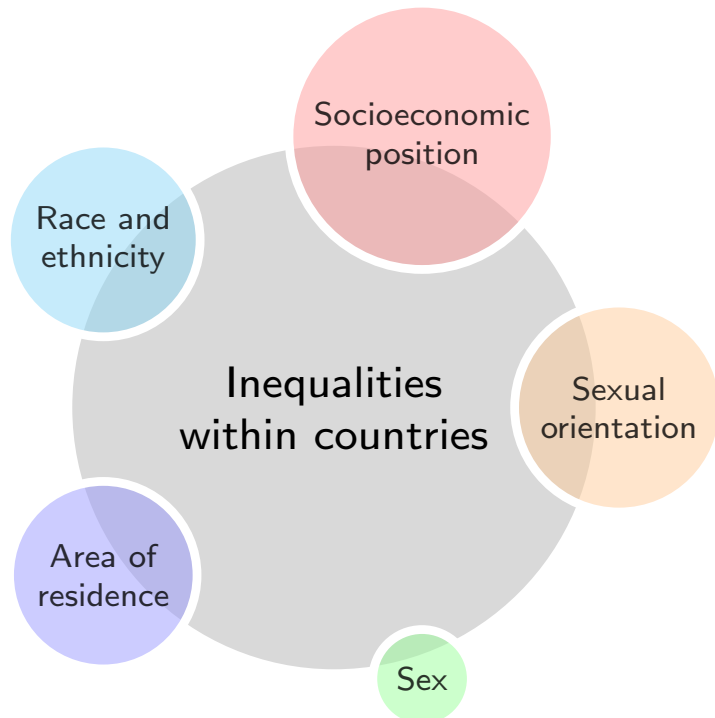

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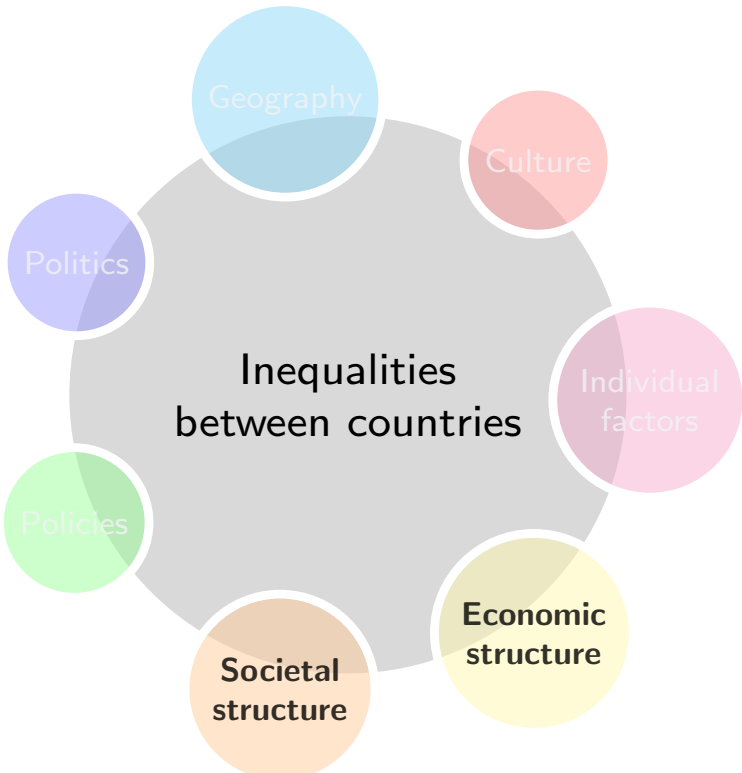

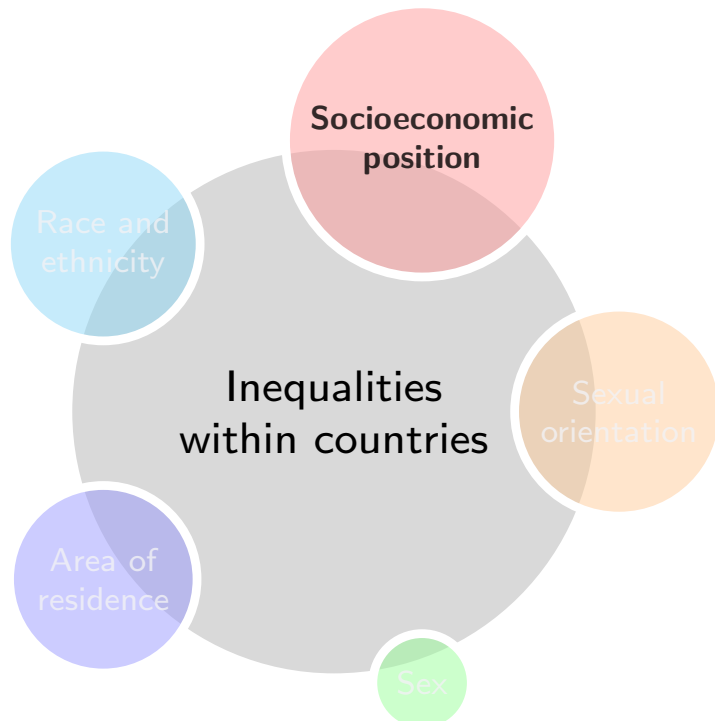

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Evidence of cancer inequalities between countries

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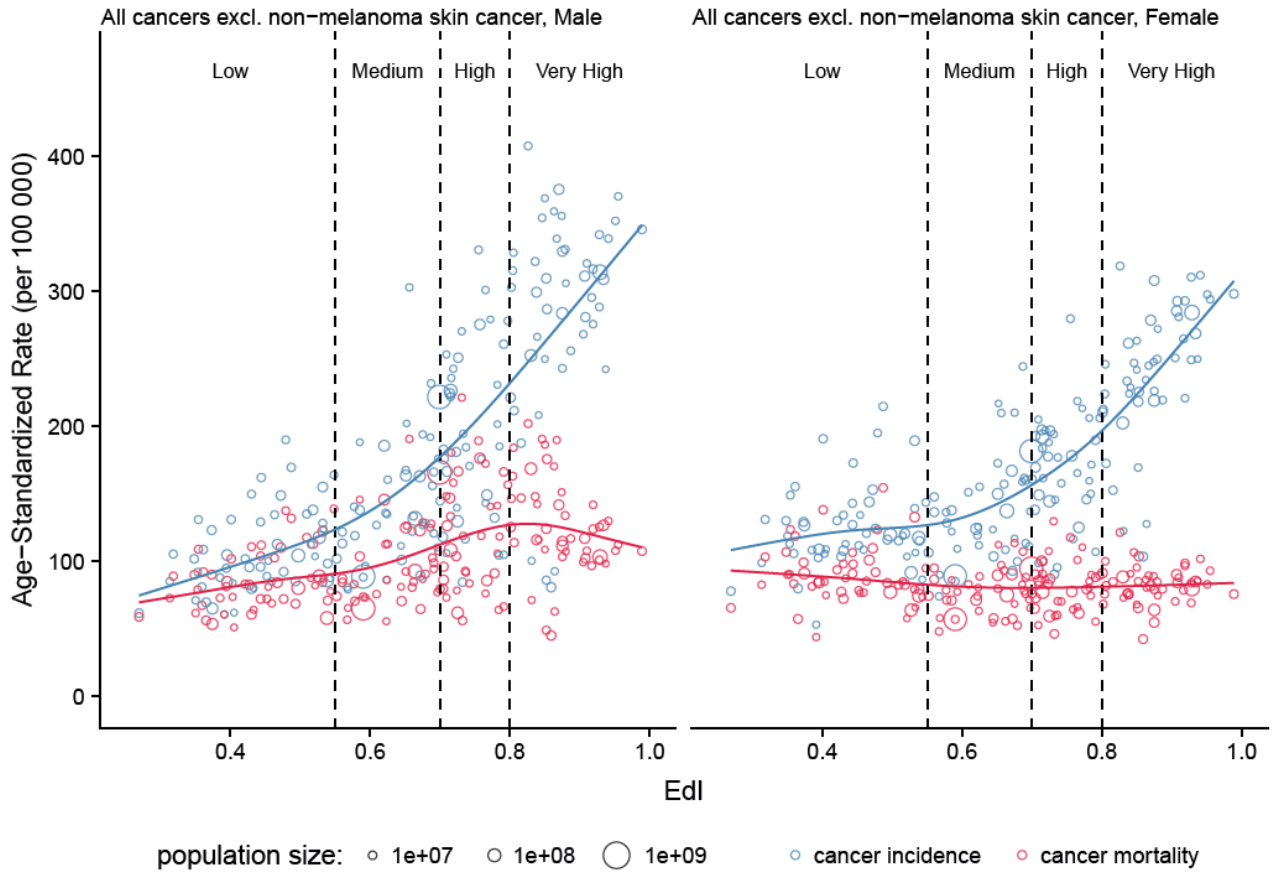

Age-standardize (world population) incidence and mortality rates of all cancer types, by average of socioeconomic development in 2012.

Figure: Wild C.P., Weiderpass E., Stewart B.W., editors (2020). *World Cancer Report: Cancer Research for Cancer Prevention.* Lyon, France: International Agency for Research on Cancer.

Evidence of cancer inequalities within countries

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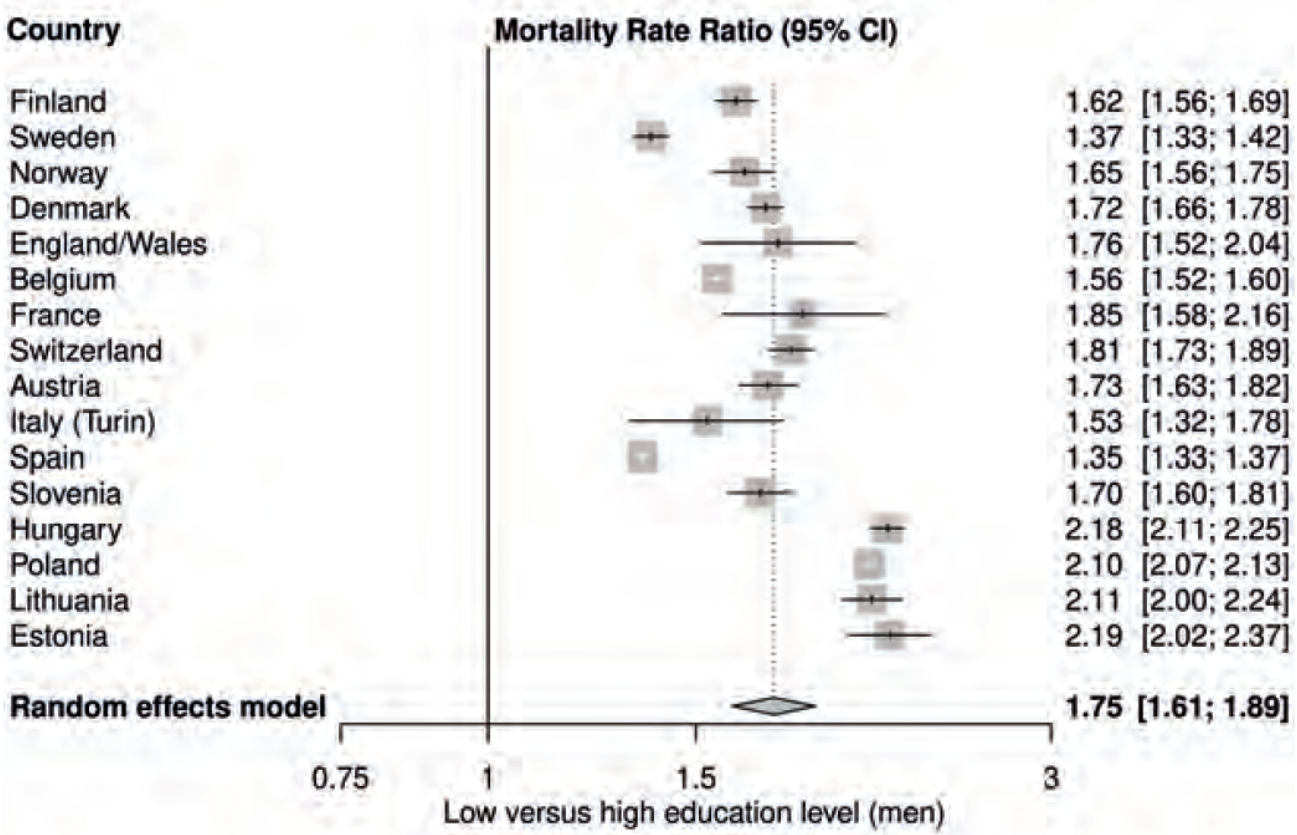

Rate ratios and the corresponding 95% CI of mortality from all cancer combined for men with a low versus high education level

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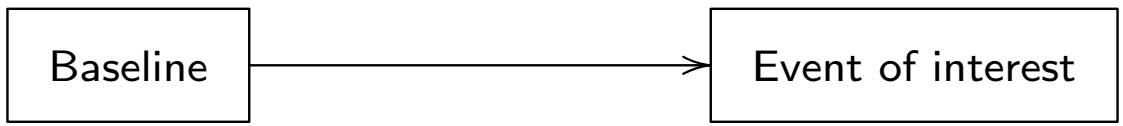
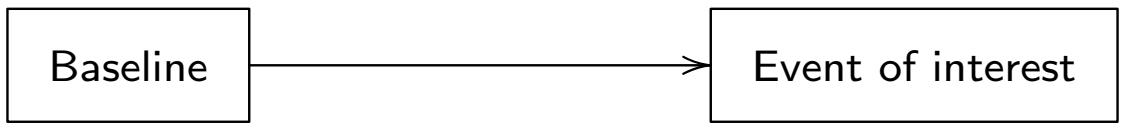
Figure: Wild C.P., Weiderpass E., Stewart B.W., editors (2020). *World Cancer Report: Cancer Research for Cancer Prevention.* Lyon, France: International Agency for Research on Cancer.

Survival analysis



- $T =$ "Time of the event"

Survival analysis



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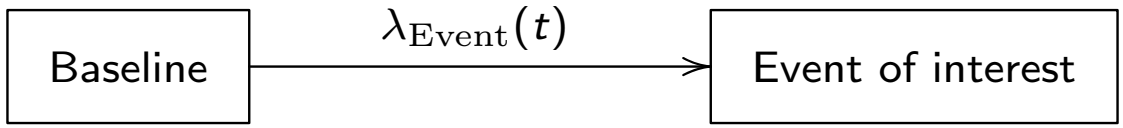

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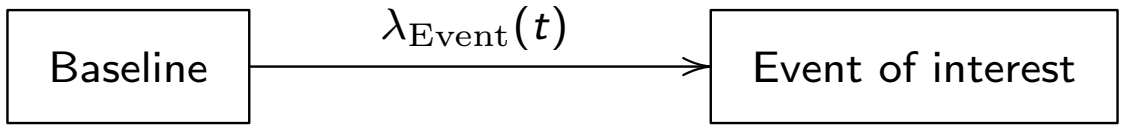

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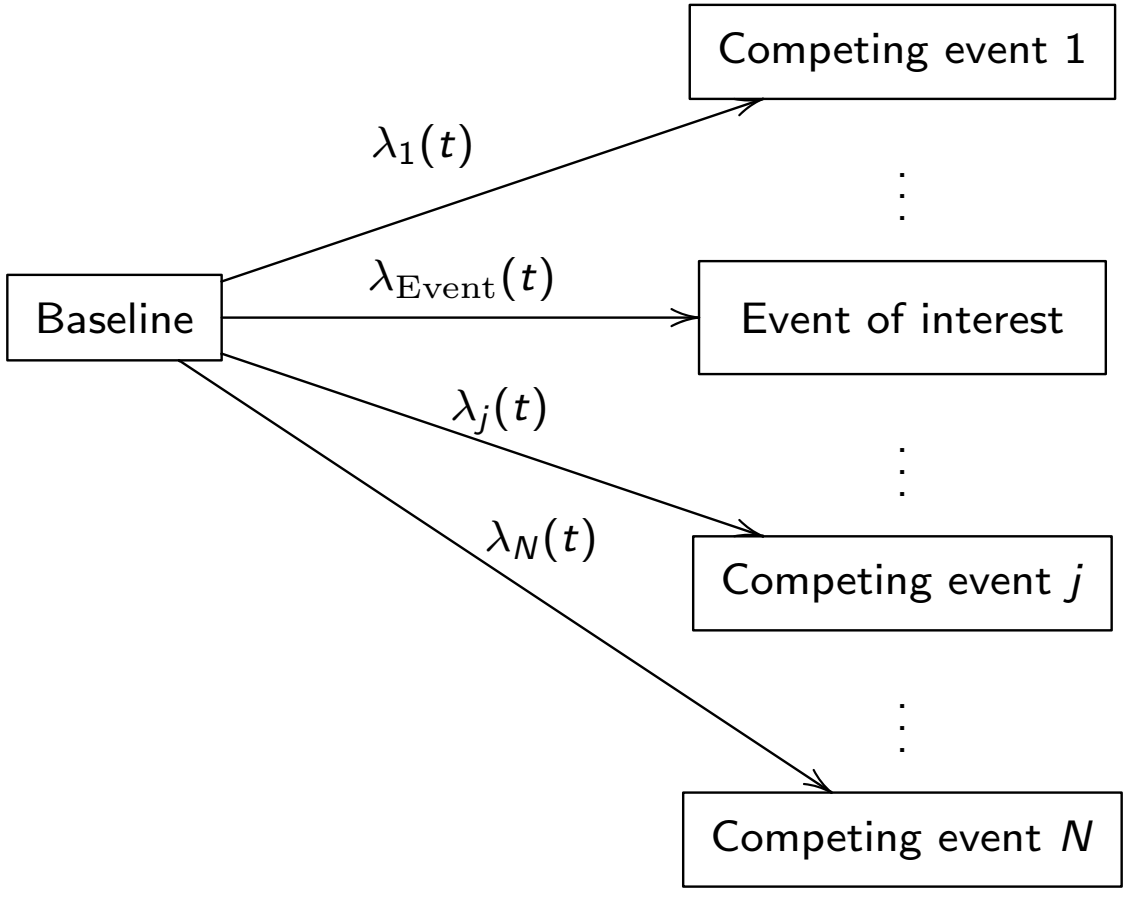
Main objective of survival analysis: estimation of $S(t)$ or $\lambda(t)$.

Survival analysis

Life is not easy



Survival analysis

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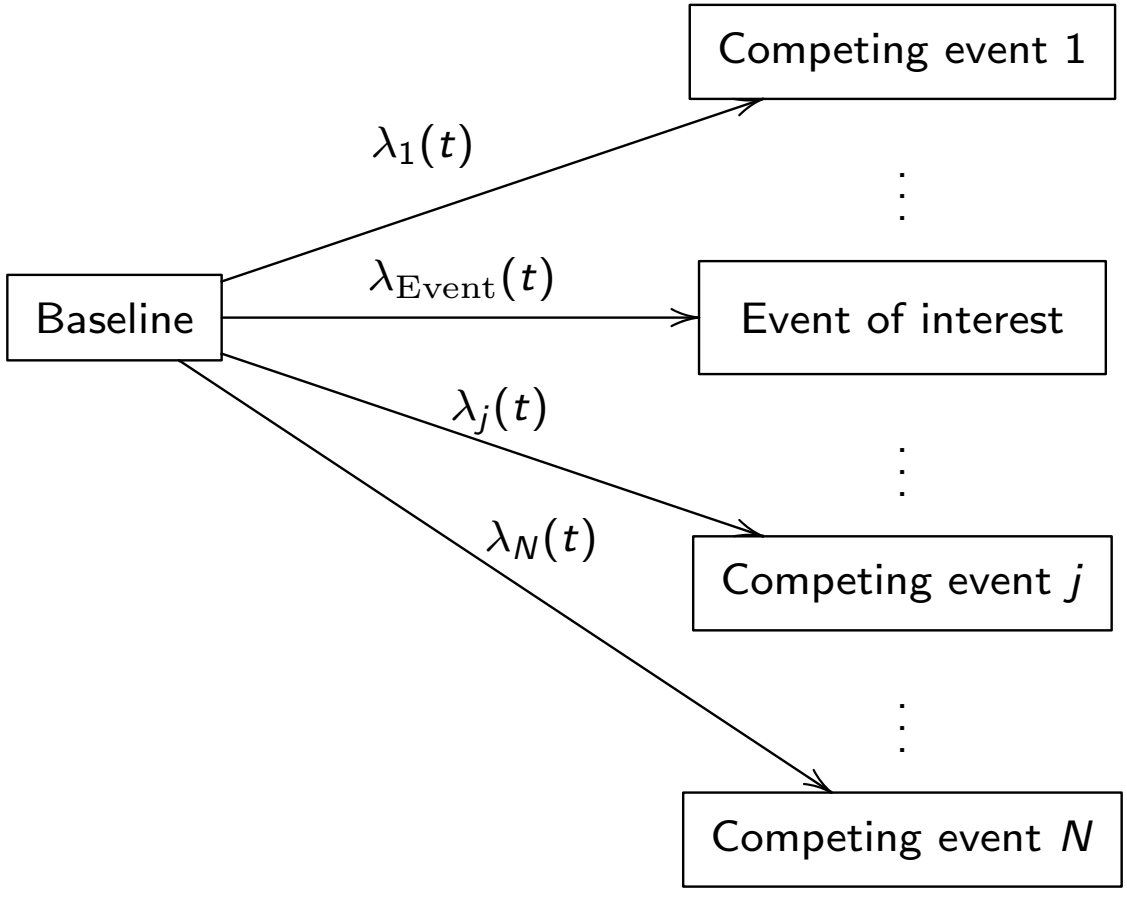


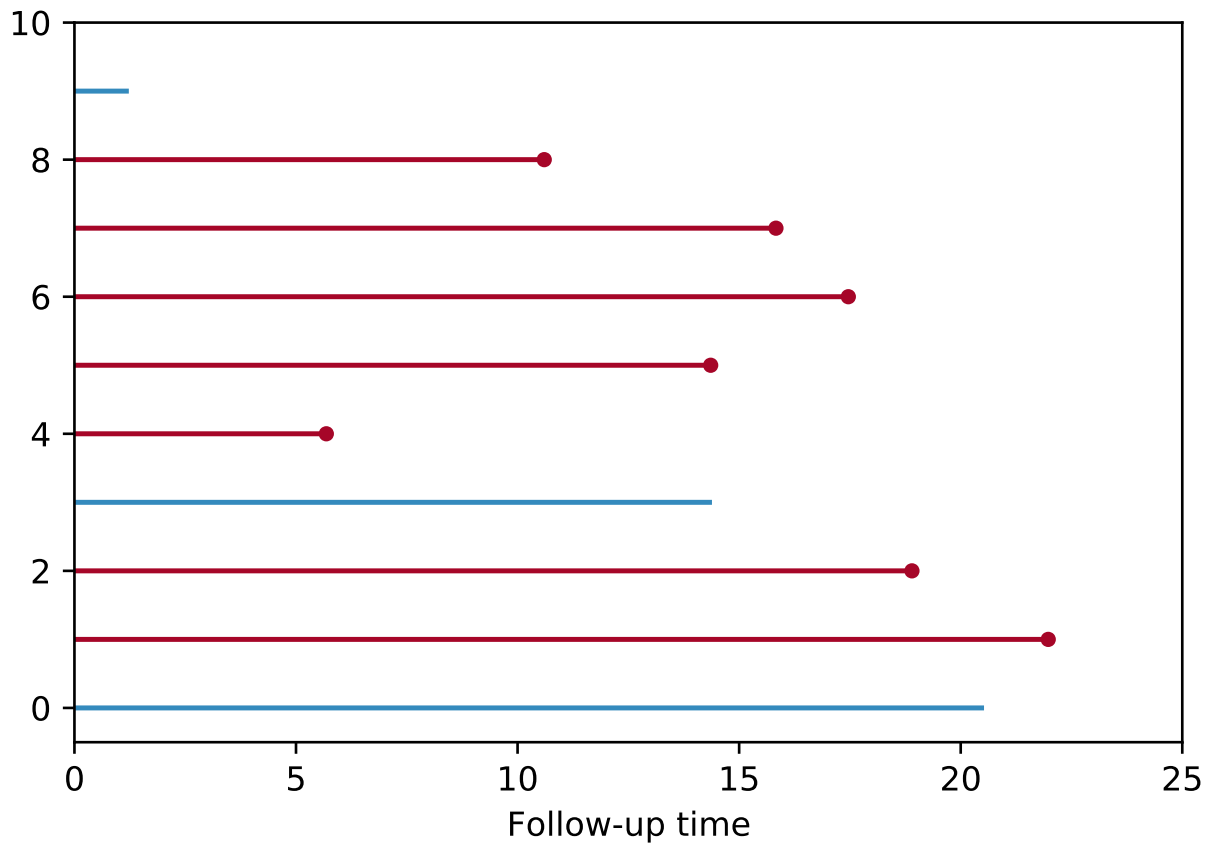
Individuals transitioning to a competing event are informative while they are at risk!

Survival analysis

Censoring

Survival analysis

Censoring



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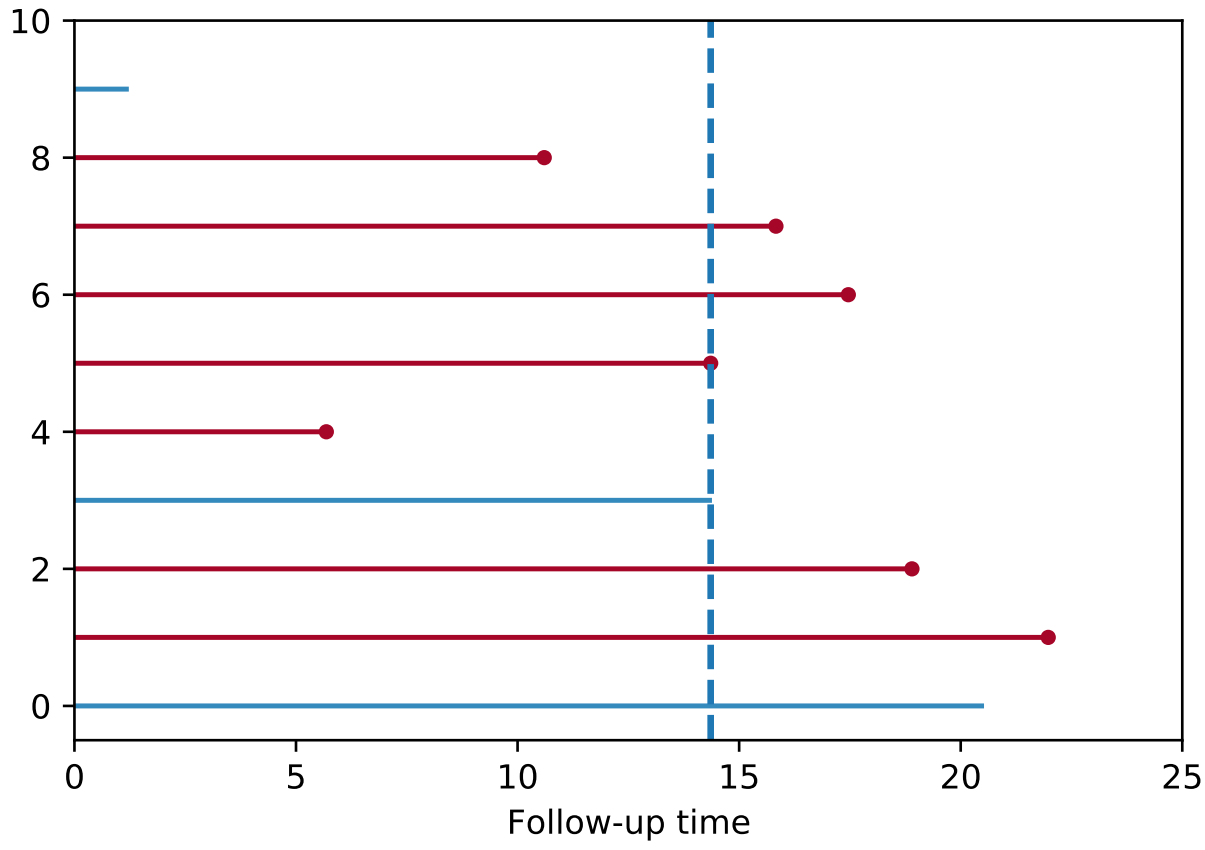
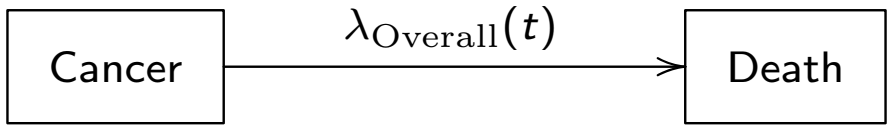


Censored individuals contribute to hazard estimation when they are still at risk

The observed cancer survival



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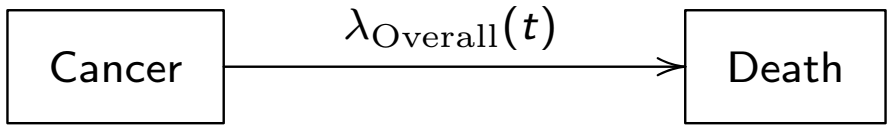

- Not all cancer patients die because of their cancer

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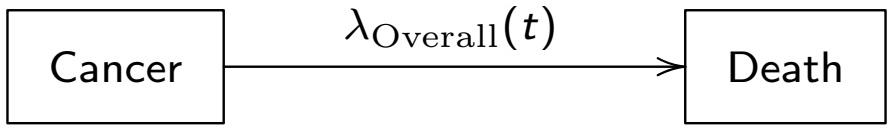

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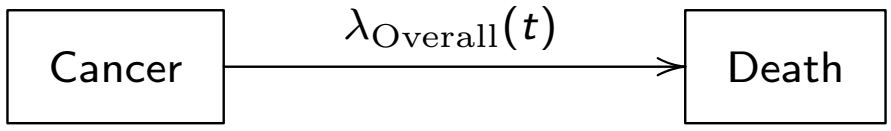

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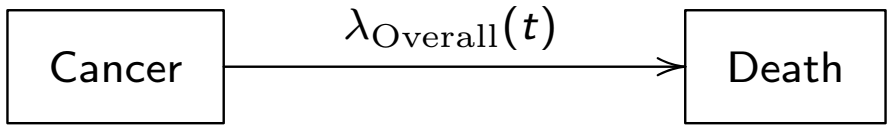

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- Test the efficiency of health-care systems

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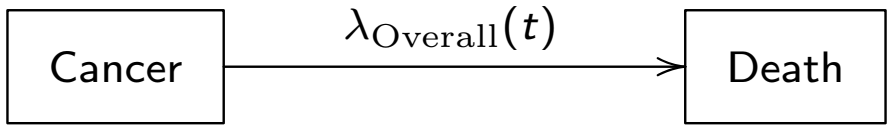

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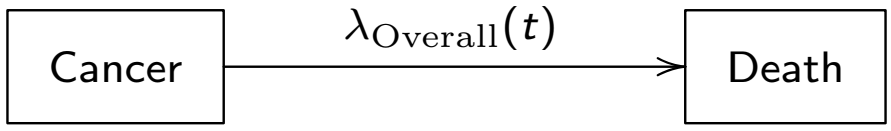

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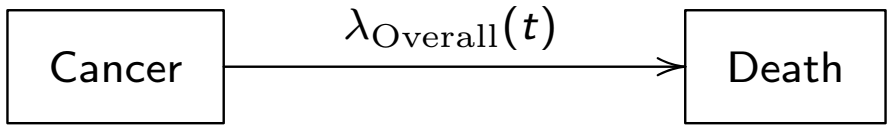

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When we want to

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- Compare cancer survival among different countries or periods
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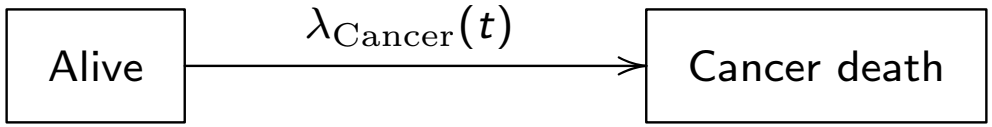
we need a mortality indicator which is independent of the general population mortality

The concept of net survival

Net survival is the survival that would be observed in a **hypothetical world** where cancer would be the only cause of death



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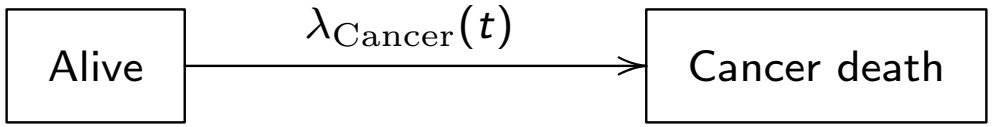

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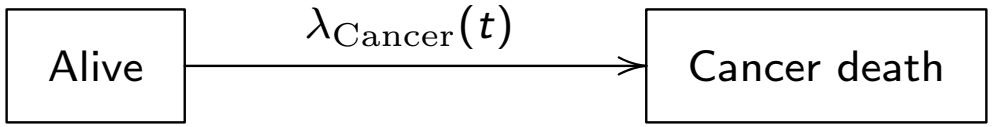

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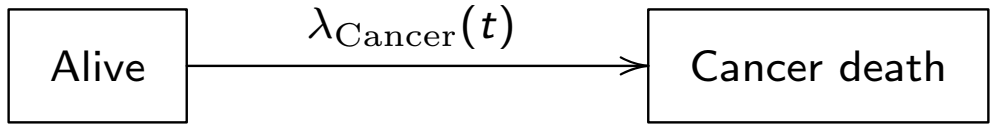

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How to estimate survival in a **hypothetical** world?

Cause-specific survival

If causes of death are available:

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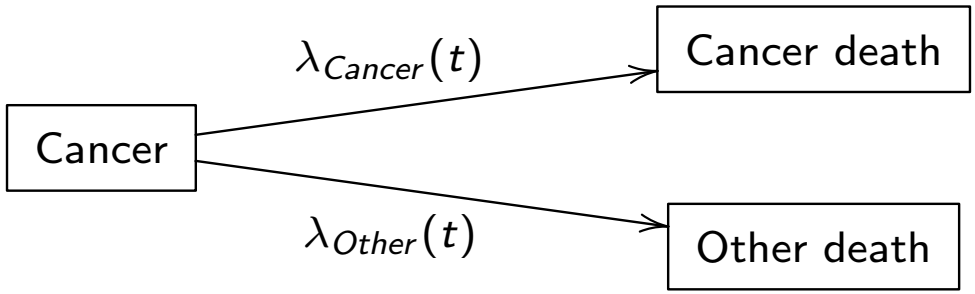

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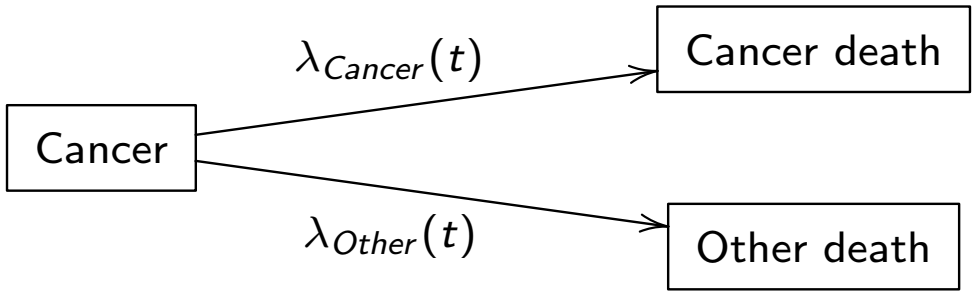

Main sources of bias

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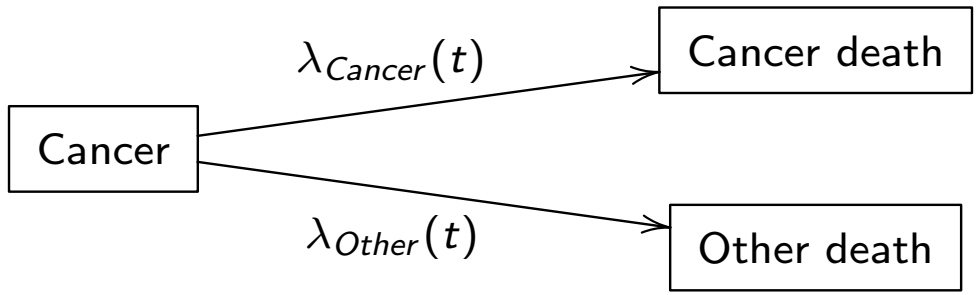

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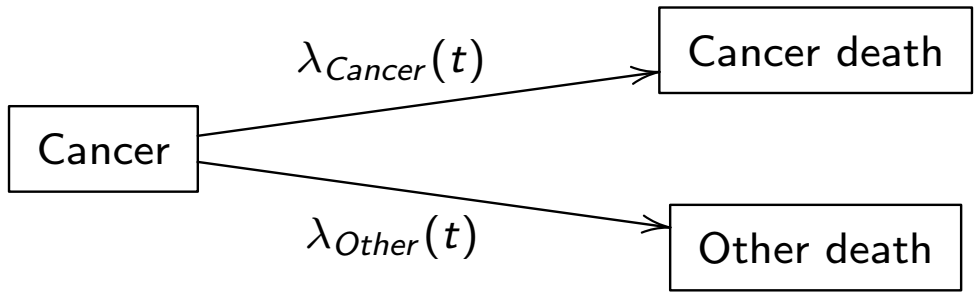

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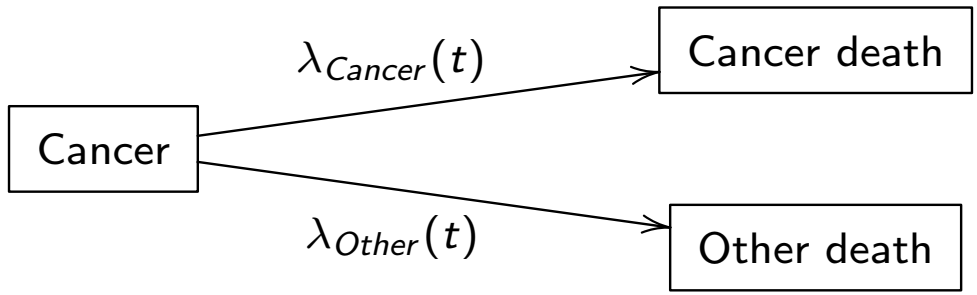

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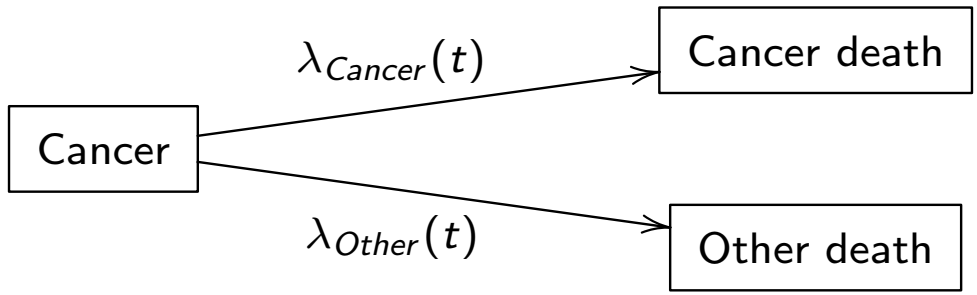
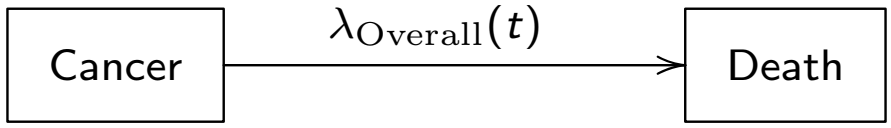


Main sources of bias

- Causes of death **misclassification**
  - Lack of sensitivity/specificity
  - Identification of the **underlying cause of death**
- Causes of death are not always available and/or reliable

Relative survival



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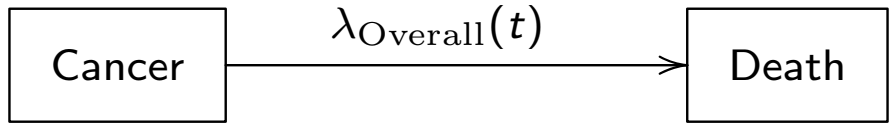
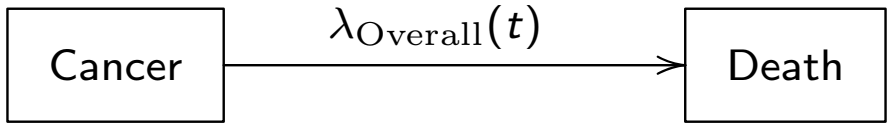


$$\lambda_{\mathrm{Overall}}(t; x, z, a) = \lambda_{\mathrm{Cancer}}(t; x, a) + \lambda_{\mathrm{Other}}(a + t; z)$$

a: age at diagnosis, x, z: set of covariates

Relative survival



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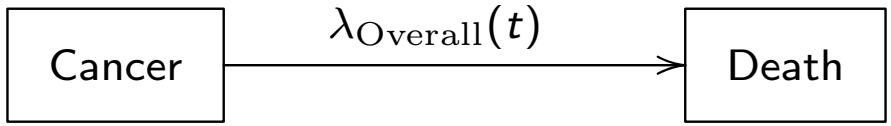

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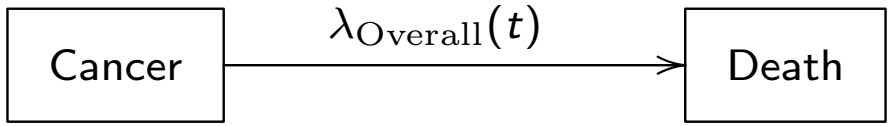

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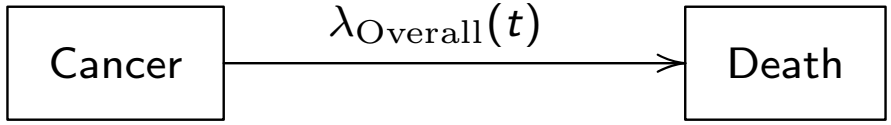
- **Lack of comparability** between cancer cohort and general population

Relative survival



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Main source of bias

- **Lack of comparability** between cancer cohort and general population

False in general!

$$\lambda_{\text{Other}}^{\text{Cancer}} \neq \lambda_{\text{Other}}^{\text{General population}}$$

Relative survival

When it is possible to estimate λ_{Other}

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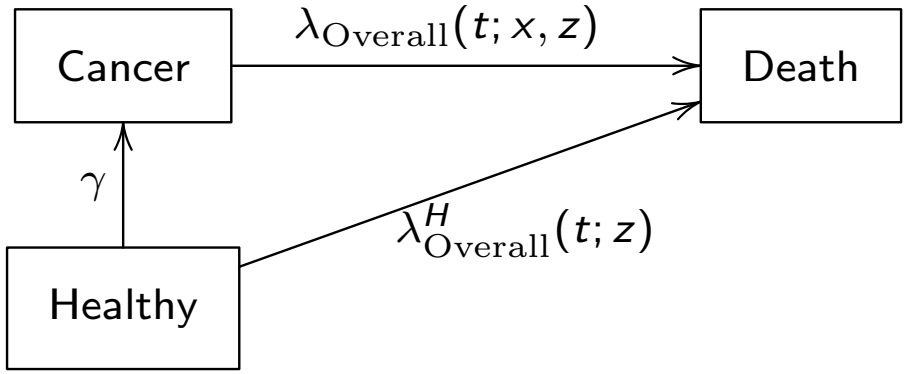

Relative survival

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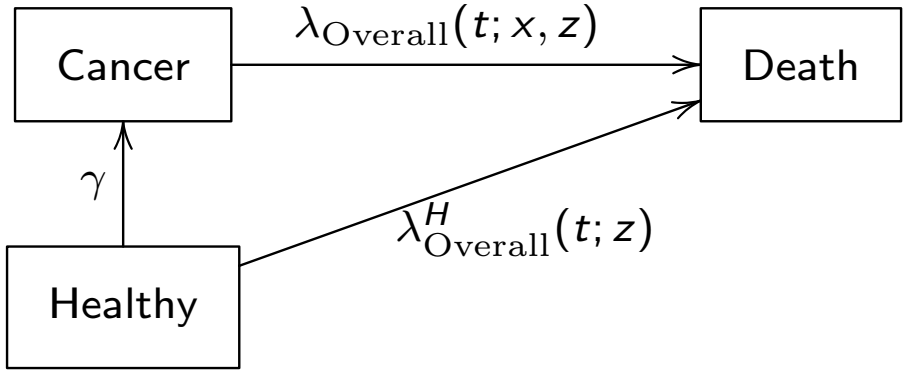

Comparability hypothesis: $\lambda^{H}_{\mathrm{Overall}}(t; z) \approx \lambda_{\mathrm{Other}}(t; z)$ for all $t \geq 0$.

Relative survival

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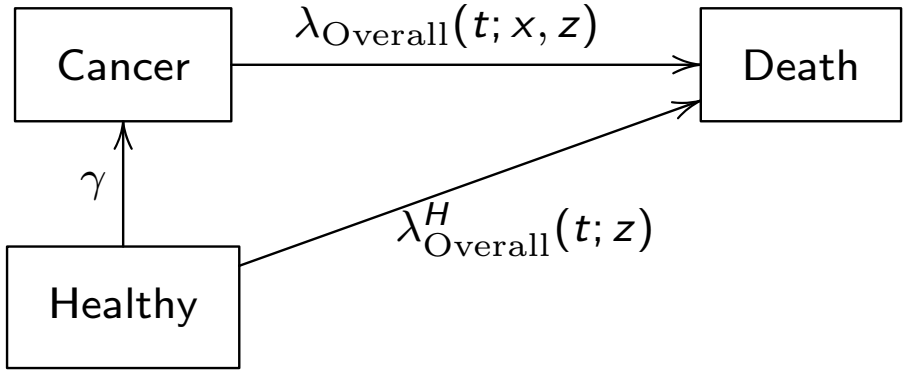

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Relative survival estimation: $\lambda_{\mathrm{Overall}}(t; x, z) = \lambda_{\mathrm{Cancer}}(t; x) + \lambda^{H}_{\mathrm{Overall}}(t; z)$

Relative survival

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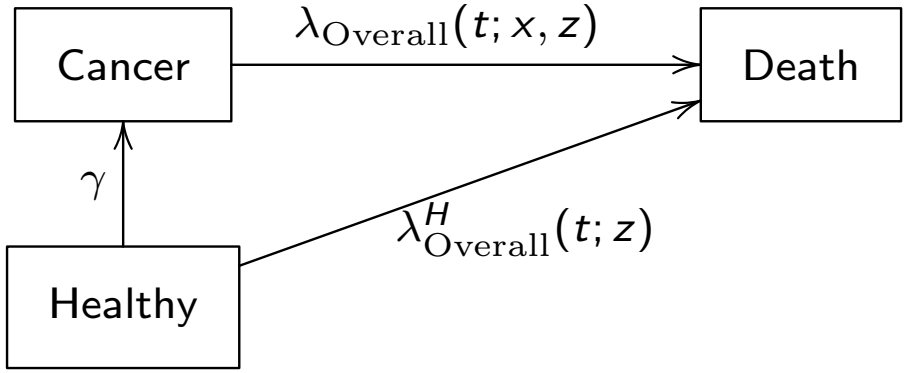

Comparability hypothesis: $\lambda^{H}_{\mathrm{Overall}}(t; z) \approx \lambda_{\mathrm{Other}}(t; z)$ for all $t \geq 0$.

Relative survival estimation: $\lambda_{\mathrm{Overall}}(t; x, z) = \lambda_{\mathrm{Cancer}}(t; x) + \lambda^{H}_{\mathrm{Overall}}(t; z)$

Acess to two comparable populations is unsual/difficult

Net survival estimation on EPIC cohort

Javier González-Delgado, Vivian Viallon[3], Grégoire Rey[4] and Hadrien Charvat[5]

3. Nutritional Methodology and Biostatistics Branch, International Agency for Research on Cancer, Lyon, France.
4 Inserm, Centre d'épidémiologie sur les causes médicales de décès (CépiDc), Le Kremlin-Bicêtre.
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European Prospective Investigation into Cancer and Nutrition (EPIC)[2]

- ∼521.000 participants recruited across 23 European centers
- Followed for almost 15 years
- More than 58.000 reported deaths
- 75 covariates describing dietary exposure, lifestyle factors, anthropometry and biological parameters
- Acess to high quality cause of death information
- 67.000 participants diagnosed with cancer

[2]International Agency for Research on Cancer. EPIC study. 2020. Retrieved from https://epic.iarc.fr

Net survival estimation on EPIC cohort

General population and EPIC cohort are not comparable

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EPIC relative survival estimate using general population mortality to estimate λ_{Other}.

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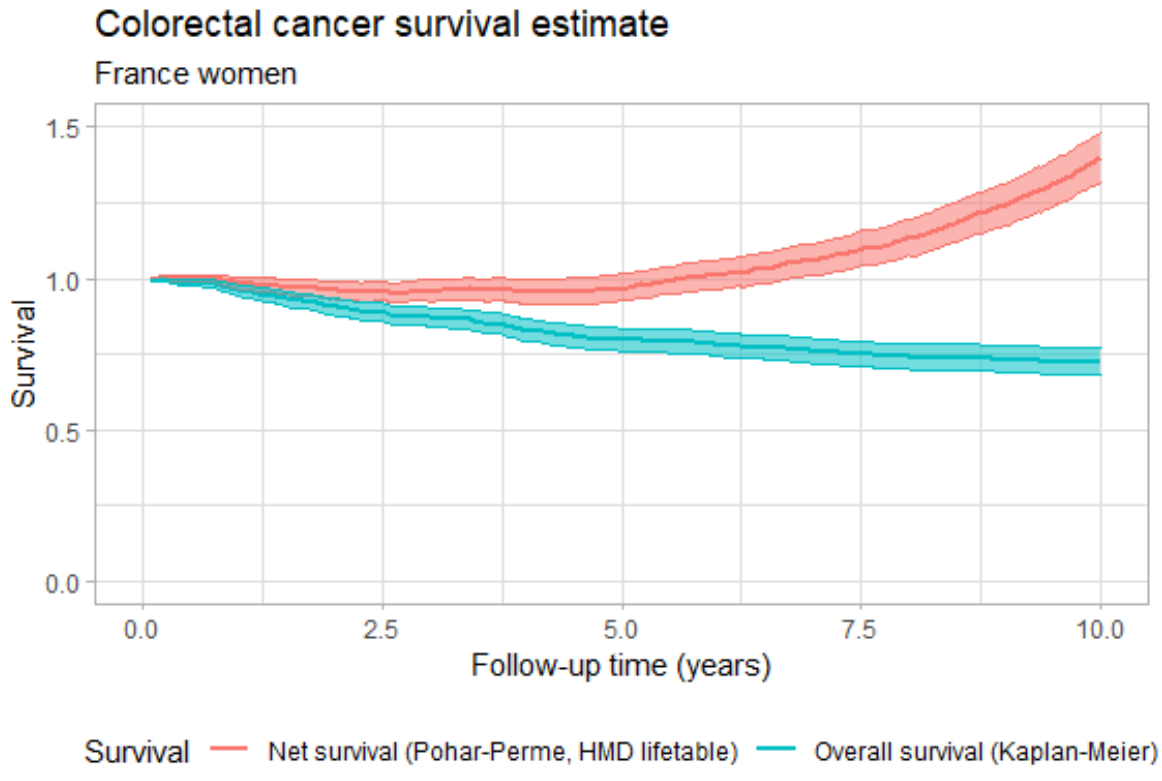

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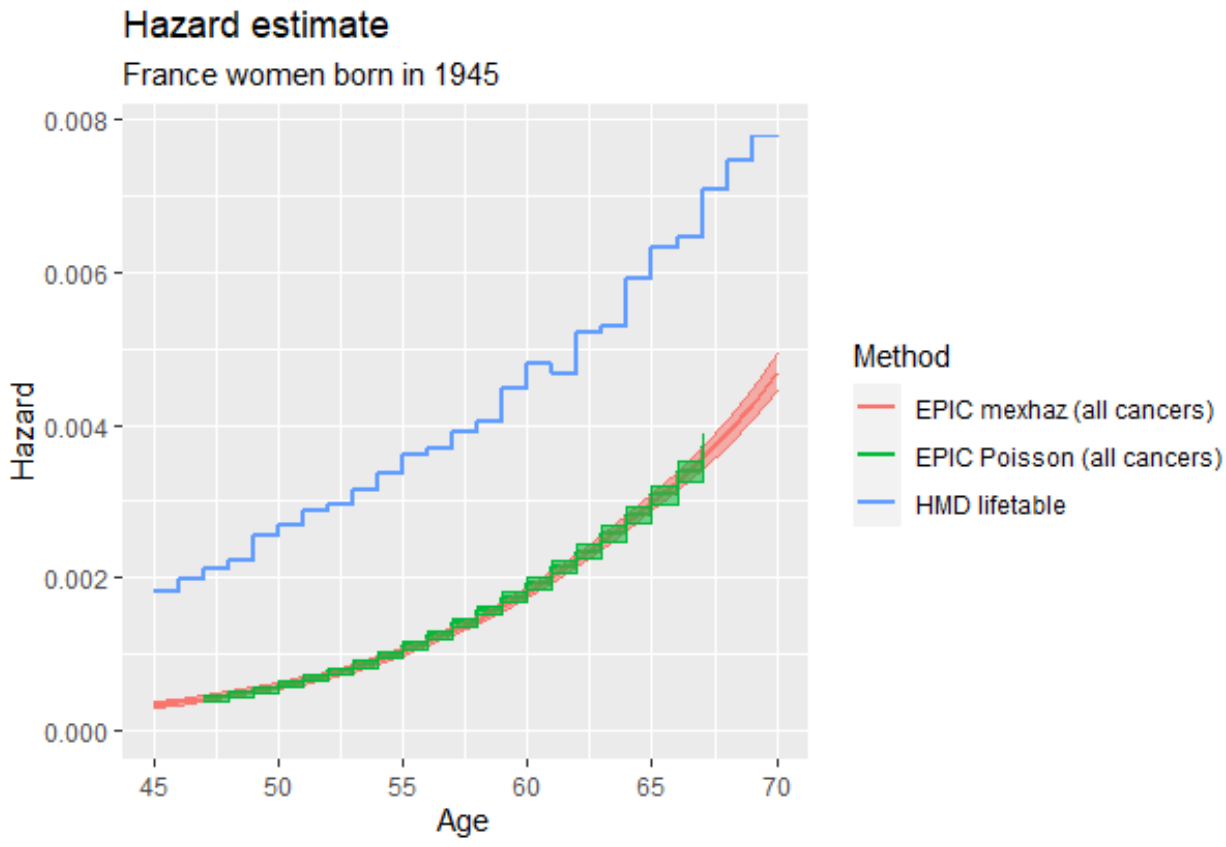
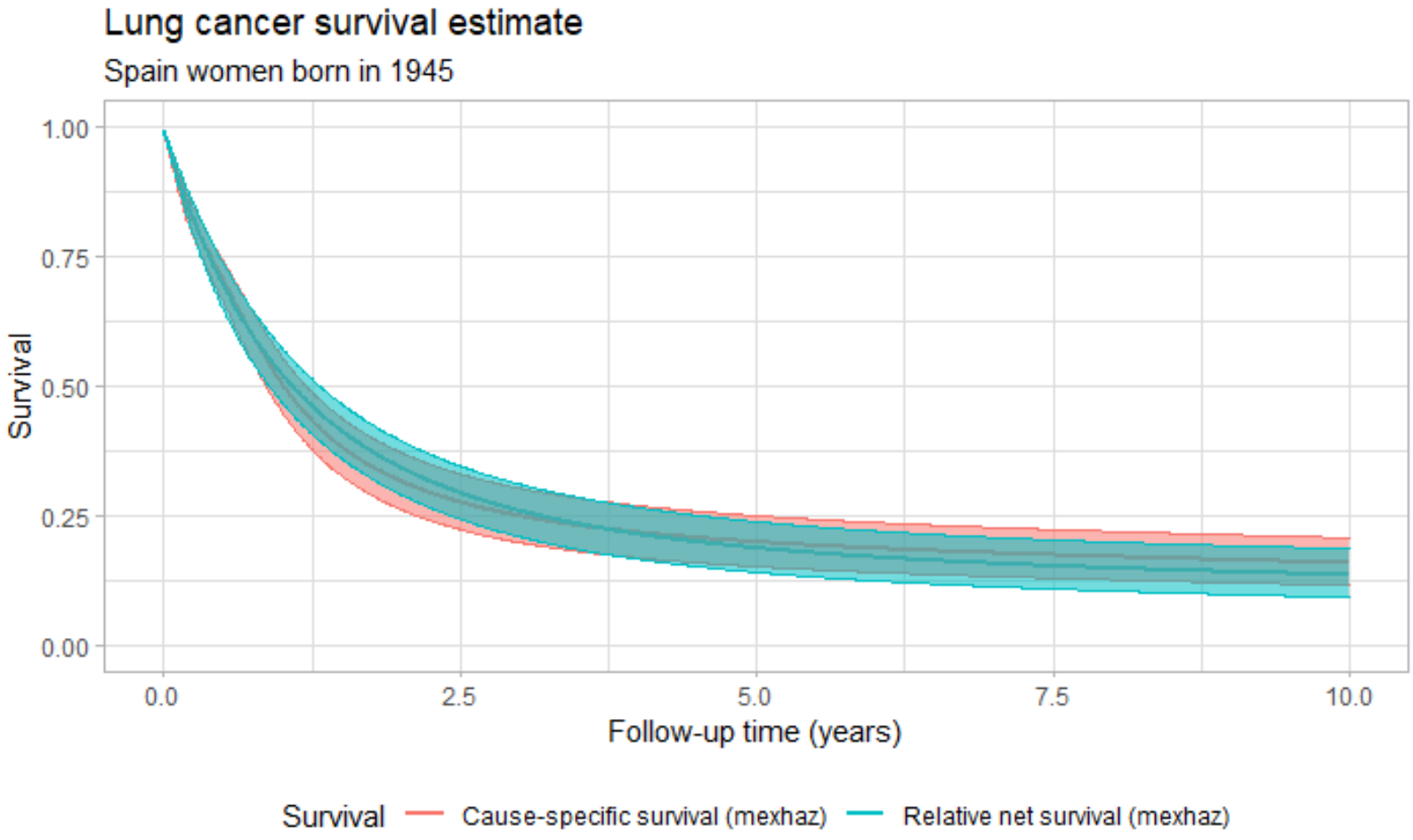


Net survival estimation on EPIC cohort

Relative and cause-specific survival

Net survival estimation on EPIC cohort

Relative and cause-specific survival



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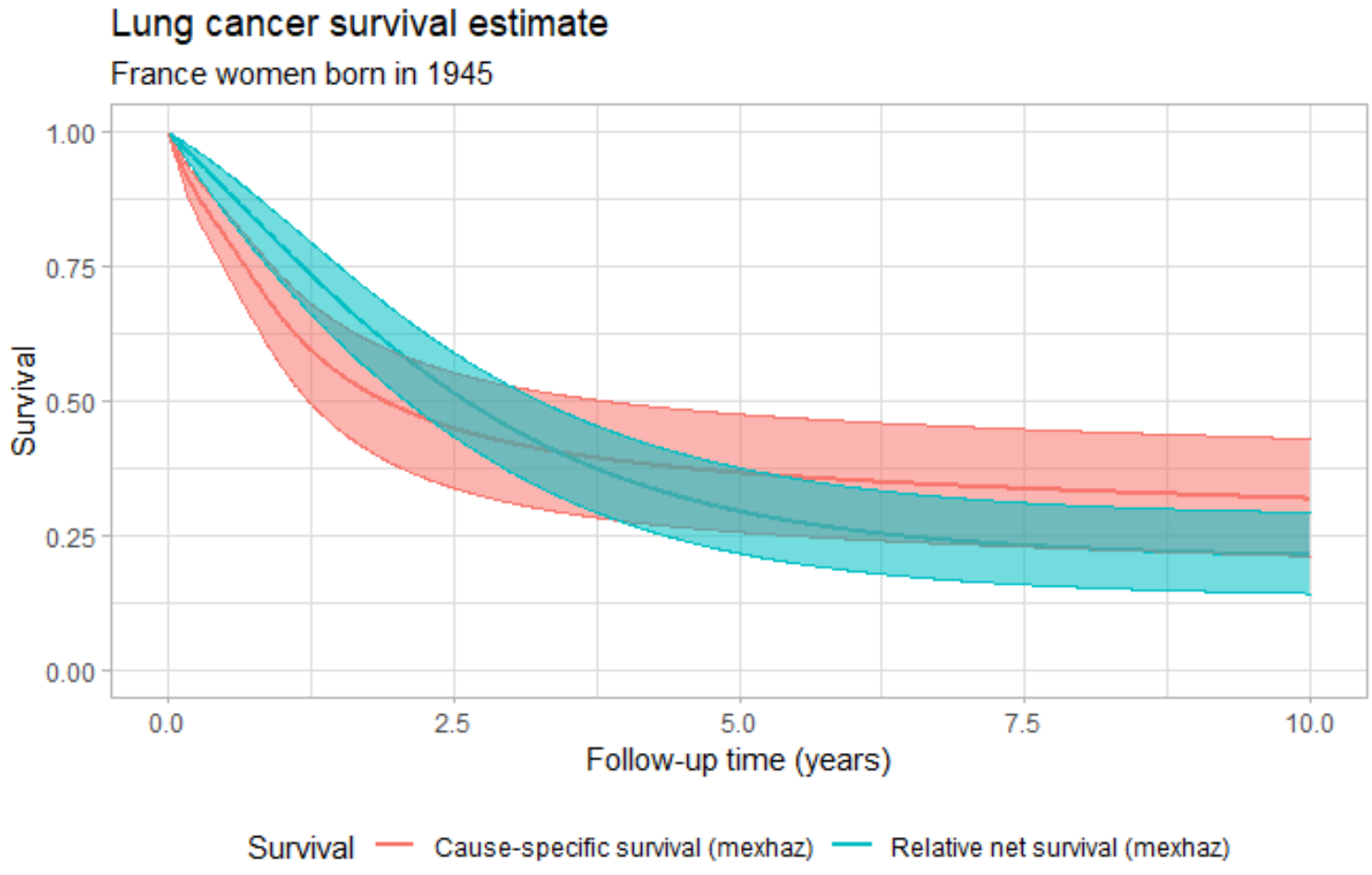

Net survival estimation on EPIC cohort

Relative and cause-specific survival: taking covariates into account

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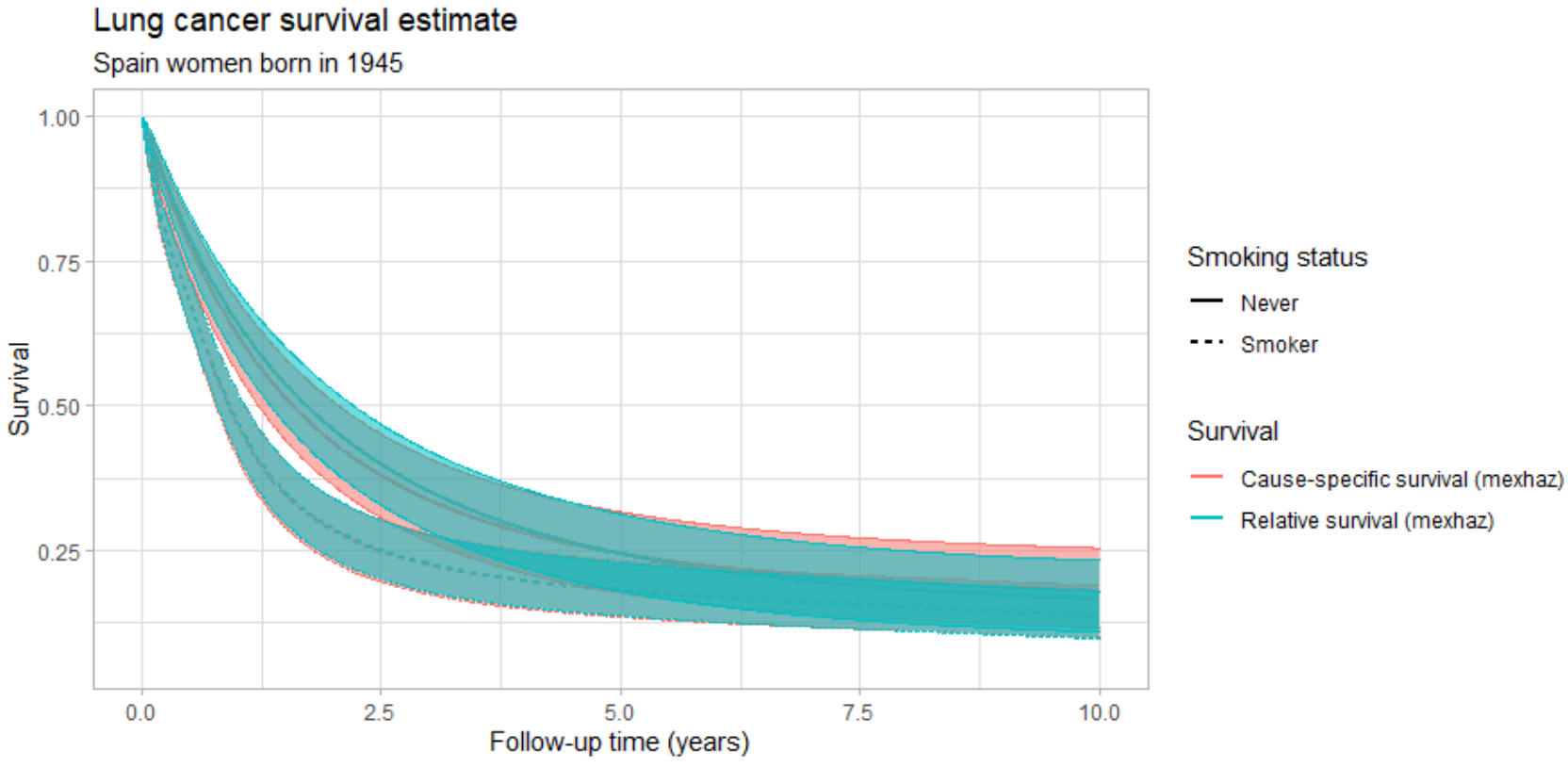
Relative and cause-specific survival: taking covariates into account



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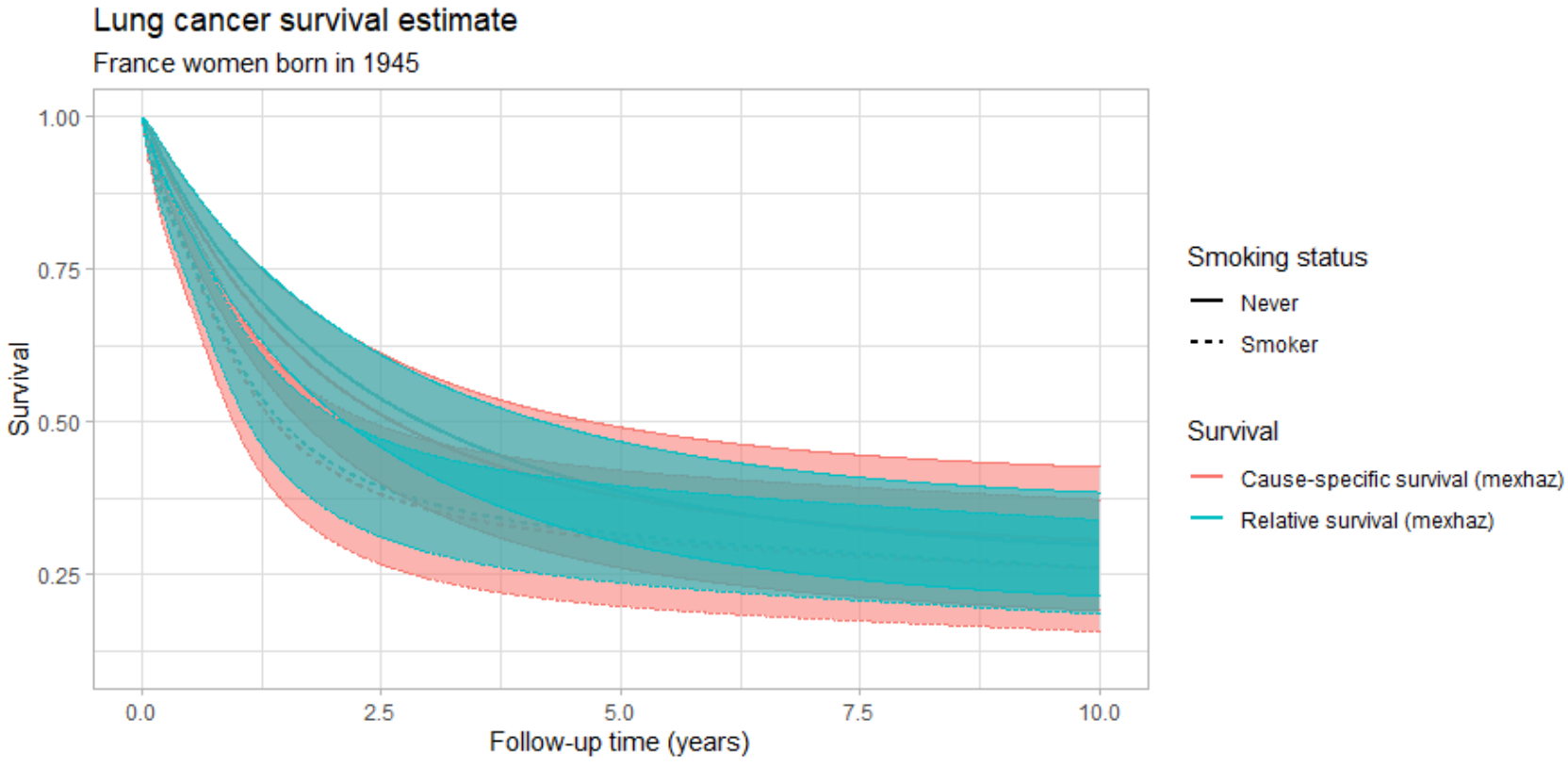

Some conclusions

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Thank you for your attention!