SCHROLL PRIZE FOR EXCELLENCE

Dansk Epidemiologisk Selskab – Annual meeting 2021

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NATIONAL CENTRE FOR REGISTER-BASED RESEARCH
DEPARTMENT OF ECONOMICS
AND BUSINESS ECONOMICS
AARHUS UNIVERSITY

NIELS BOHR PROFESSORSHIP PSYCHIATRIC EPIDEMIOLOGY
Danmarks Grundforskningsfond Danish National Research Foundation

OUTLINE

- Mortality associated with mental disorders
  - Methods to estimate life expectancy (Life Years Lost)
  - Results based on Danish registers
- Questions / Discussion

~~- Machine Learning~~
~~- Causal Inference~~

INTRODUCTION

- **Lifetime prevalence of mental disorders is high (1 in 3 persons)** (Pedersen *et al*. 2014)

- **Mental disorders are associated with premature mortality** (Chesney *et al*. 2014)
  - **Excess mortality usually estimated by Mortality Rate Ratios (MRR): instantaneous risk of dying**
  - **Cause-specific MRRs (*e.g.* suicide, cancer, accidents, diabetes)**

- **Reduced life expectancy widely understood by the general community**
  - **Mental disorders in Australia: 12-16 years shorter life expectancy** (Lawrence *et al*. 2013)
    (Schizophrenia: 12-16 years shorter – Depression: 12-15 years shorter)
  - **Mental disorders in Denmark: 15-20 years shorter** (Nordentoft *et al*. 2013)
    (Schizophrenia: 16-20 years shorter (Laursen *et al*. 2014)**)**

INTRODUCTION

- **Previous methods to estimate life expectancy in those with mental disorders**
  - **Assumption: all disorders diagnosed at one specific age (*e.g.* at age 15 years)**
  - **Differences in life expectancy (12-20 years) likely to be overestimated**

- **Recent development of new methods: the Life Years Lost method**
  - **Summarize over real age-of-onset distribution** (Andersen 2017)
  - **Decompose difference in life expectancy into specific causes of death** (Andersen 2013)

- **Reduction in life expectancy for those with mental disorders in Denmark**
  - **7-10 years shorter for any mental disorders [vs. 15-20 years]** (Erlangsen *et al.* 2017)
  - **11-13 years shorter for those with schizophrenia [vs. 16-20 years]** (Laursen *et al*. 2018)

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Life expectancy and Life Years Lost

WHAT IS LIFE EXPECTANCY?

Life expectancy is the average period a person live.

- **For an extinct cohort (e.g. those born in 1750):**

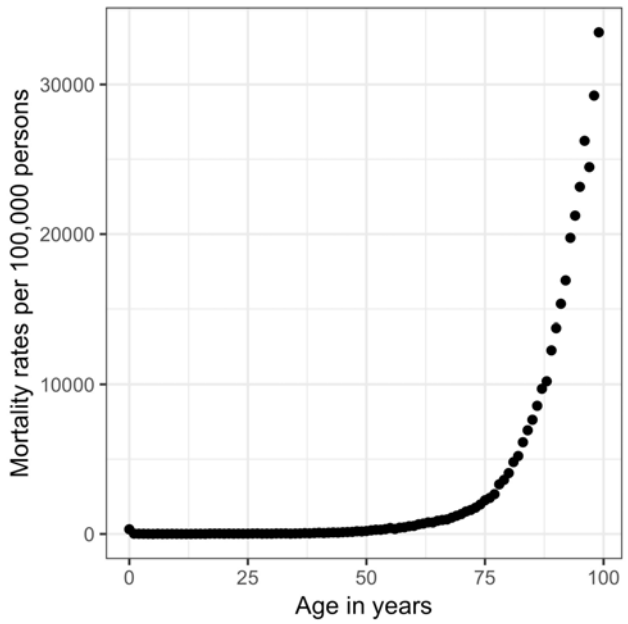
  Consider the average of ages at time of death for all individuals.

WHAT IS LIFE EXPECTANCY?

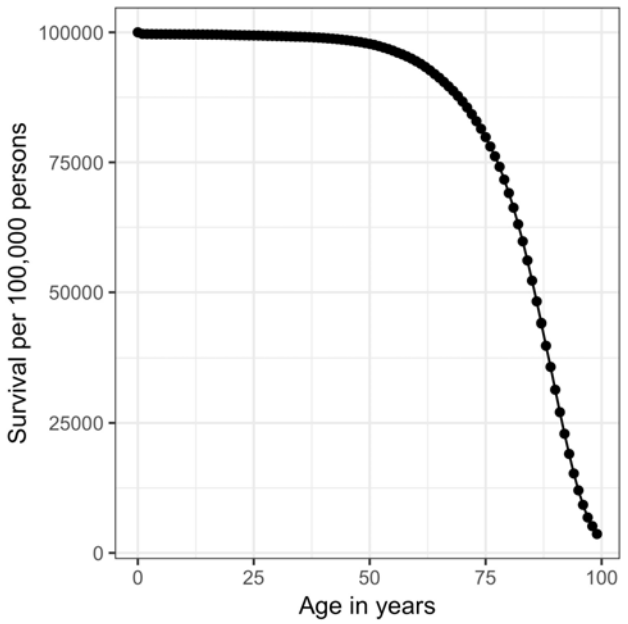
- **For a cohort that is not extinct (e.g. life expectancy for newborns in 2021):**

  We build a survival curve considering age-specific mortality rates in 2021 and we estimate the area under the survival curve.

Mortality rates



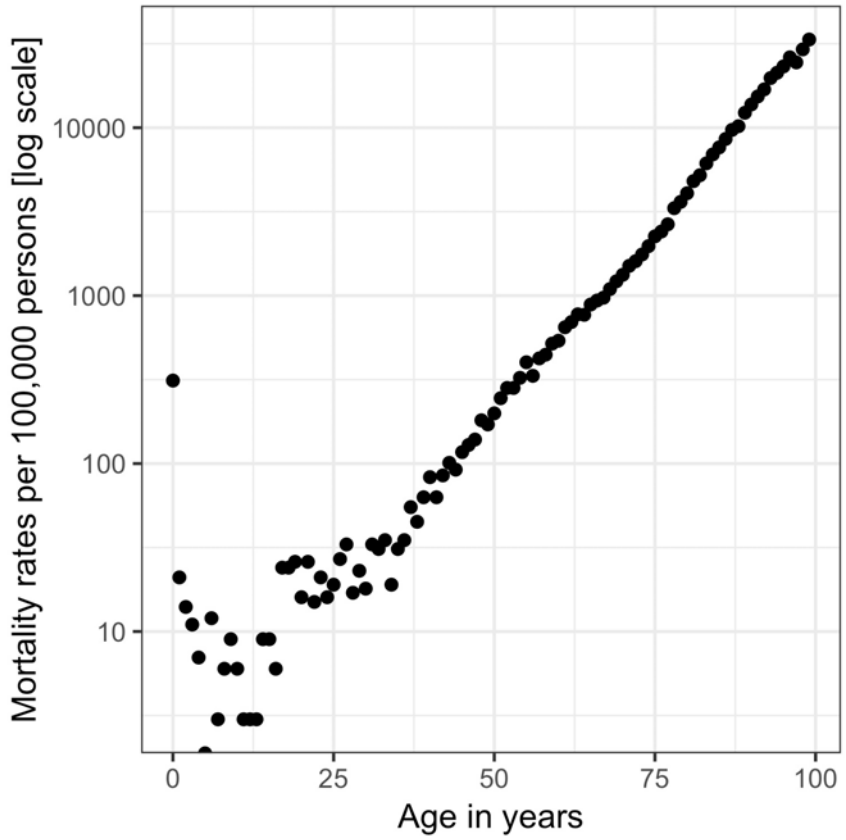
Survival curve

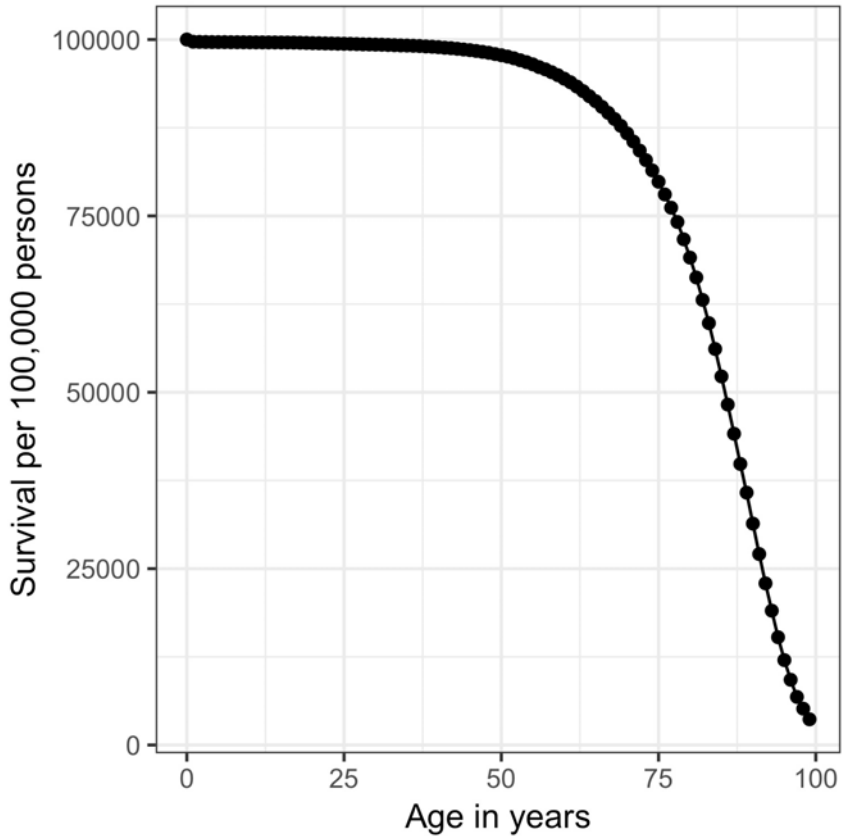


Assumption: mortality rates in 2021 remain constant in the future i.e. **a newborn baby in 2021 will always experience mortality rates from year 2021**

ESTIMATION OF THE SURVIVAL CURVE

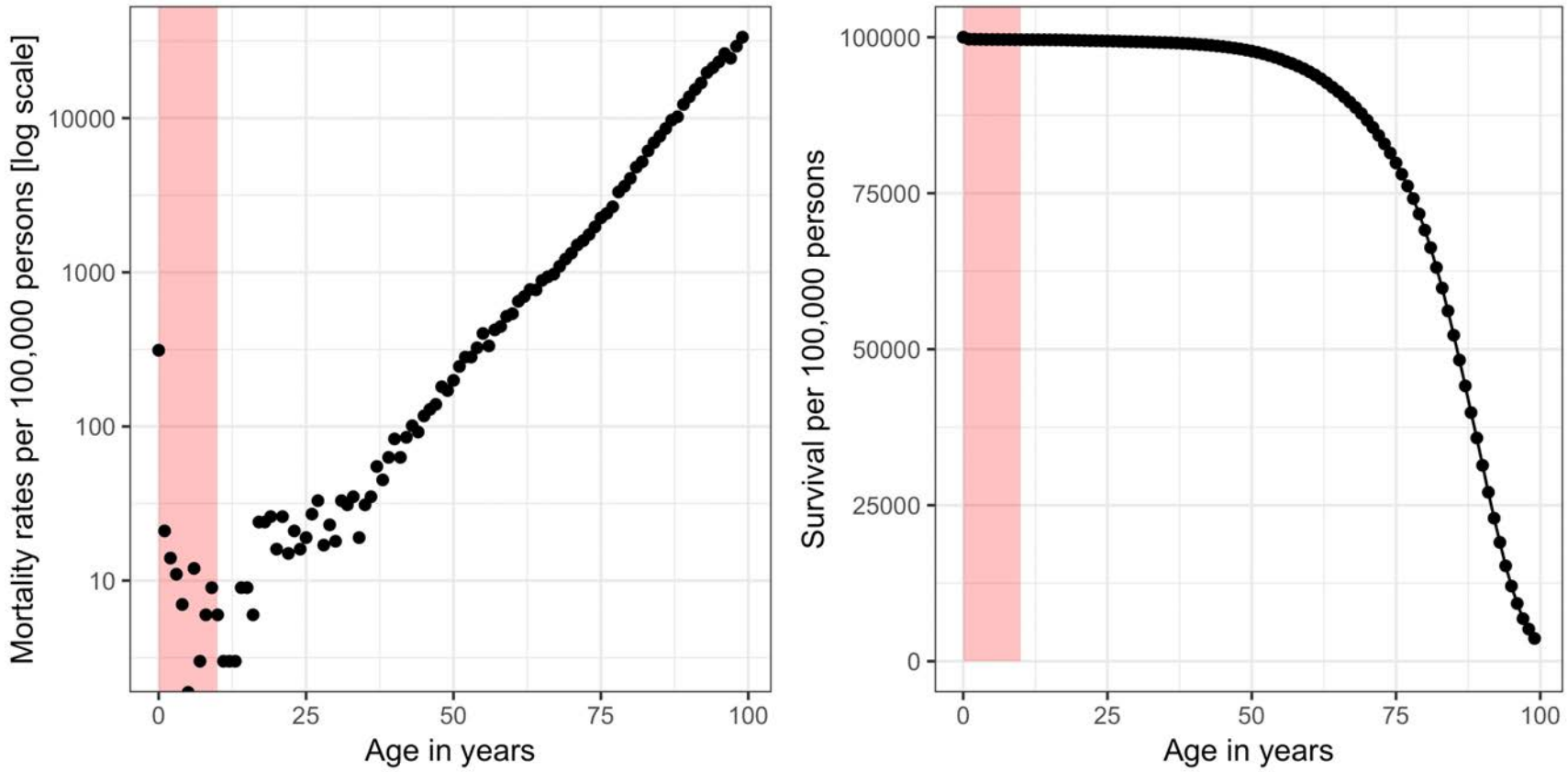
Mortality rates in log scale to see in more detail.





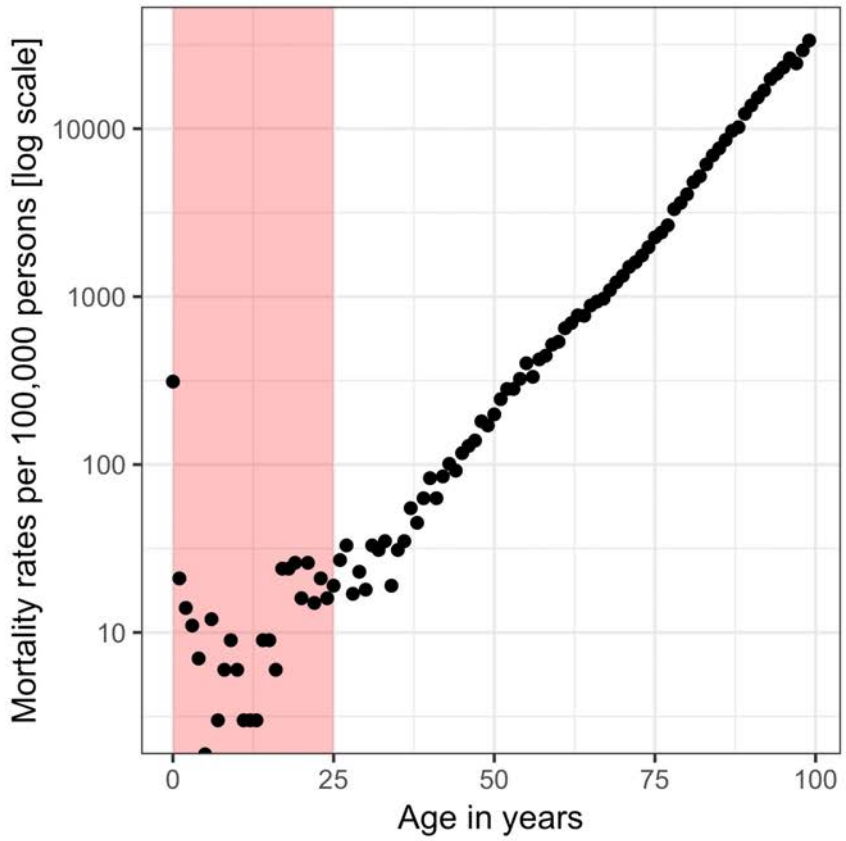
ESTIMATION OF THE SURVIVAL CURVE

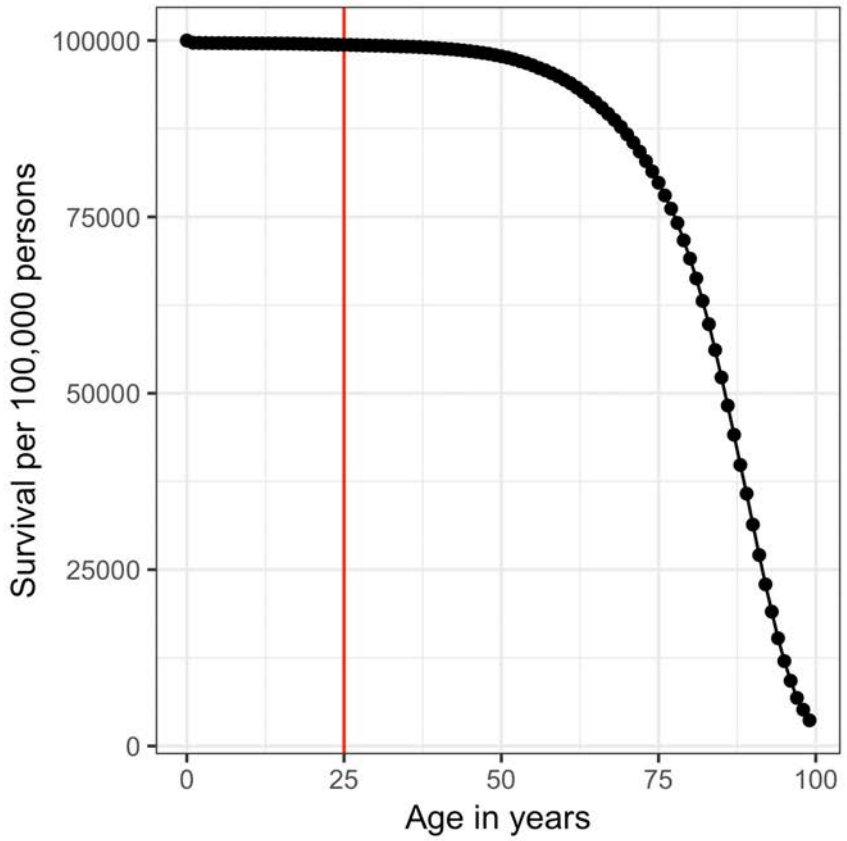
Estimated drop in survival for newborns at ages 0-10 years is based on those aged 0-10 years in 2016.



ESTIMATION OF THE SURVIVAL CURVE

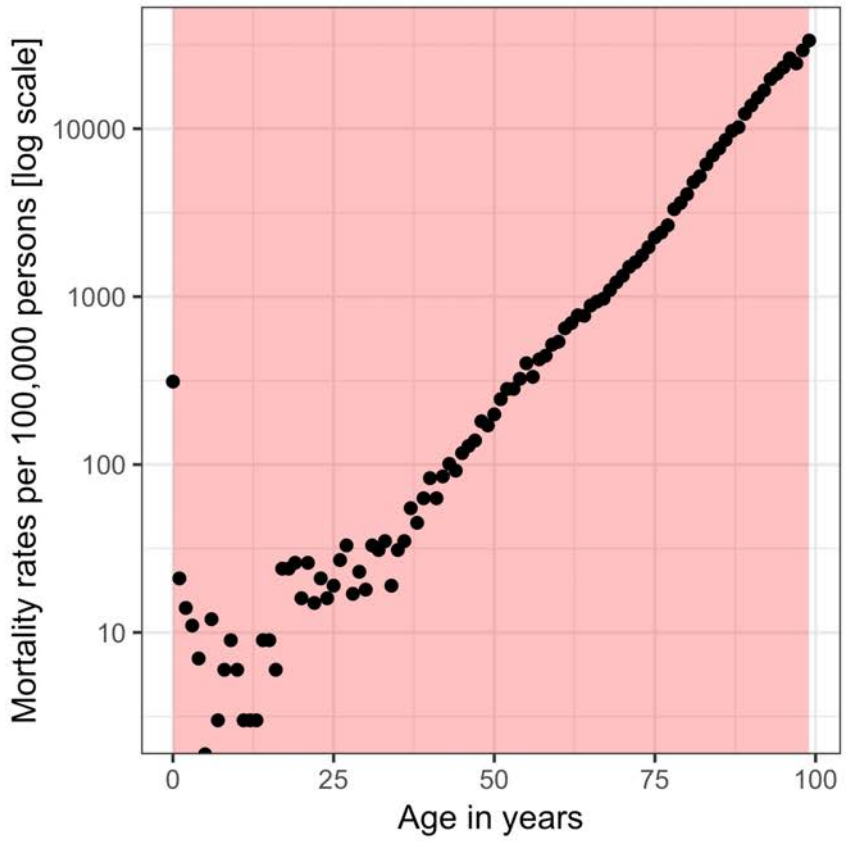
Specific survival estimate for newborns at age 25 years is based on those aged 0-25 years in 2016.

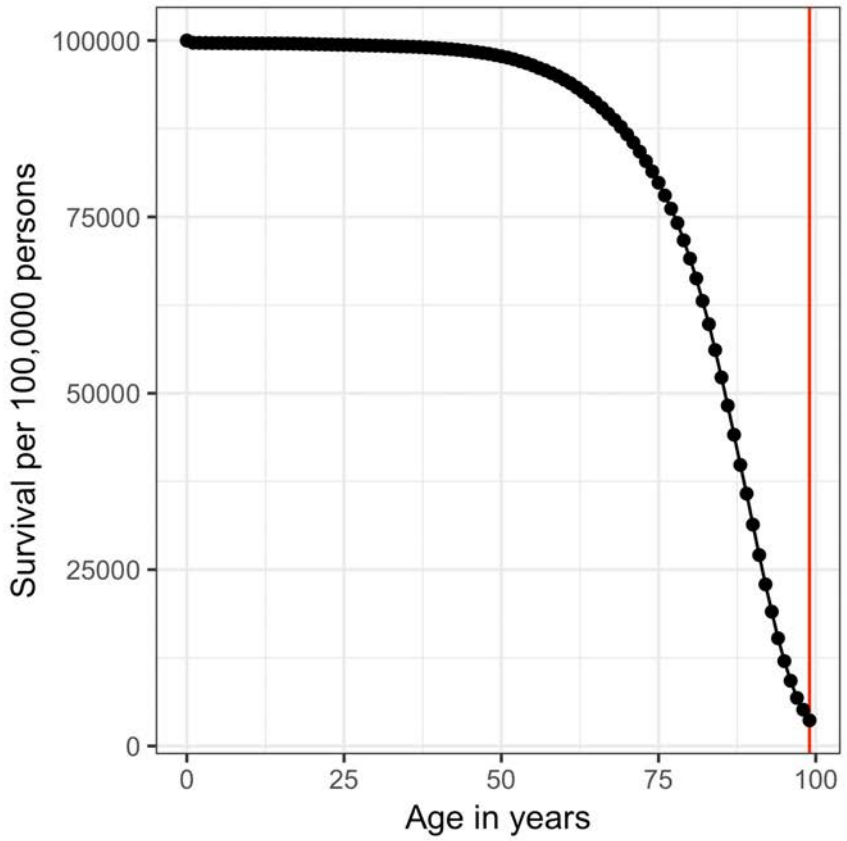




ESTIMATION OF THE SURVIVAL CURVE

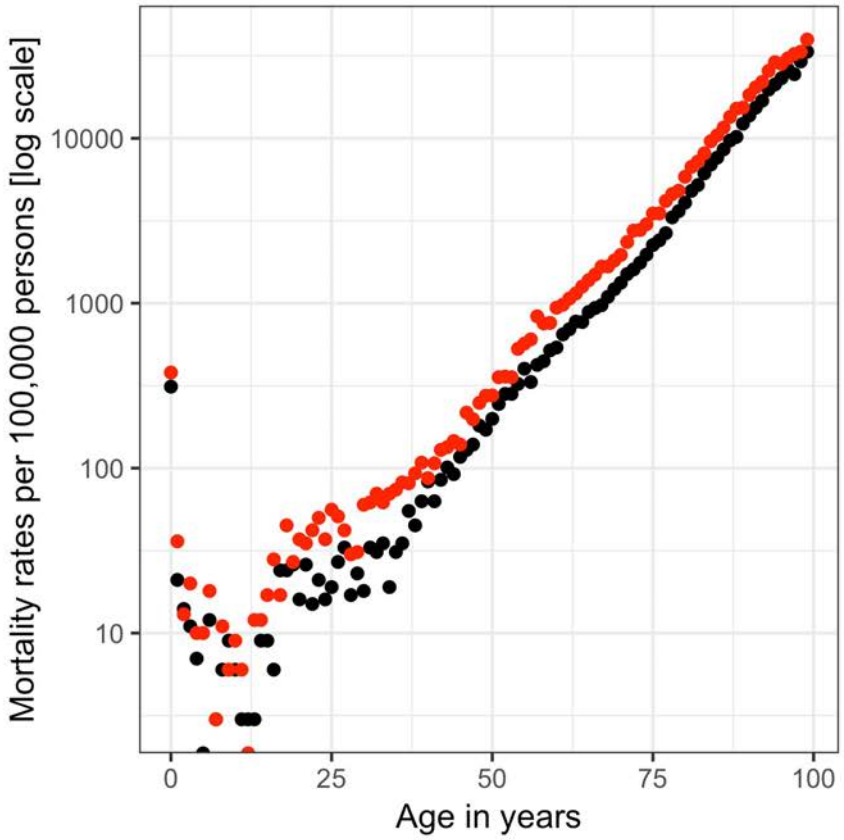
Specific survival estimate for newborns at age 99 years is based on those aged 0-99 years in 2016.

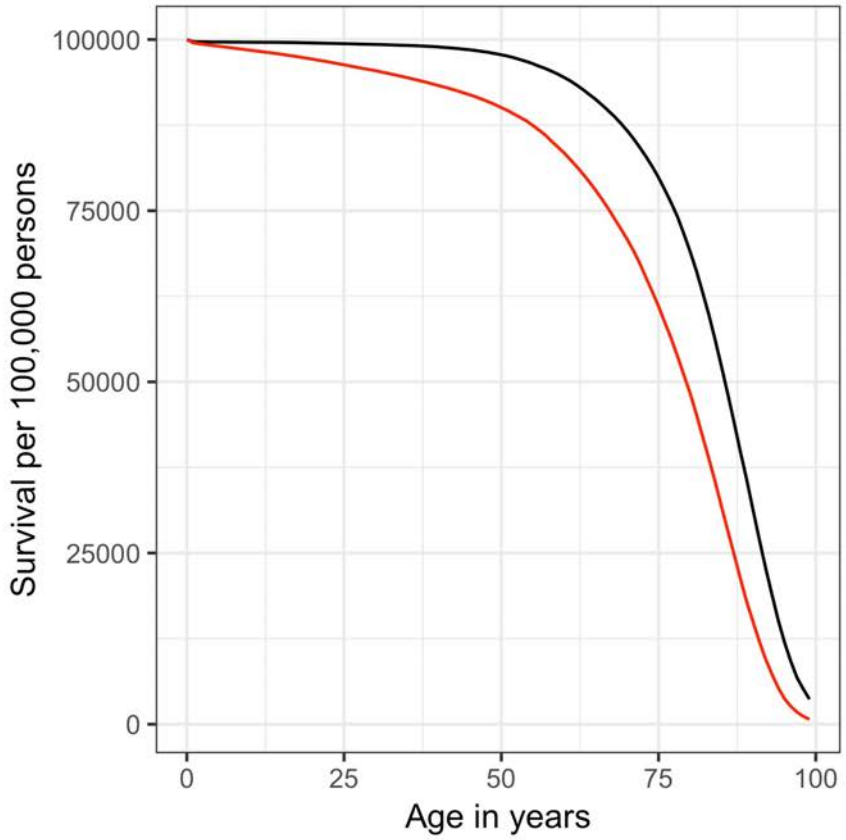




LIFE EXPECTANCY IN TWO GROUPS

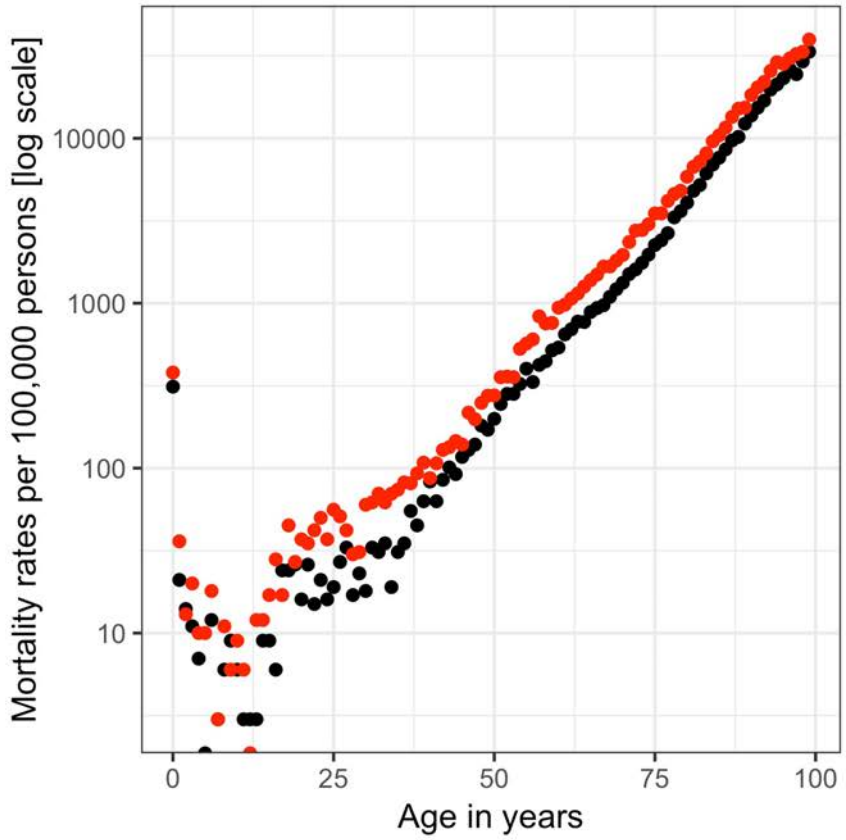
We can estimate survival curves separately for the two groups using group-specific mortality rates.

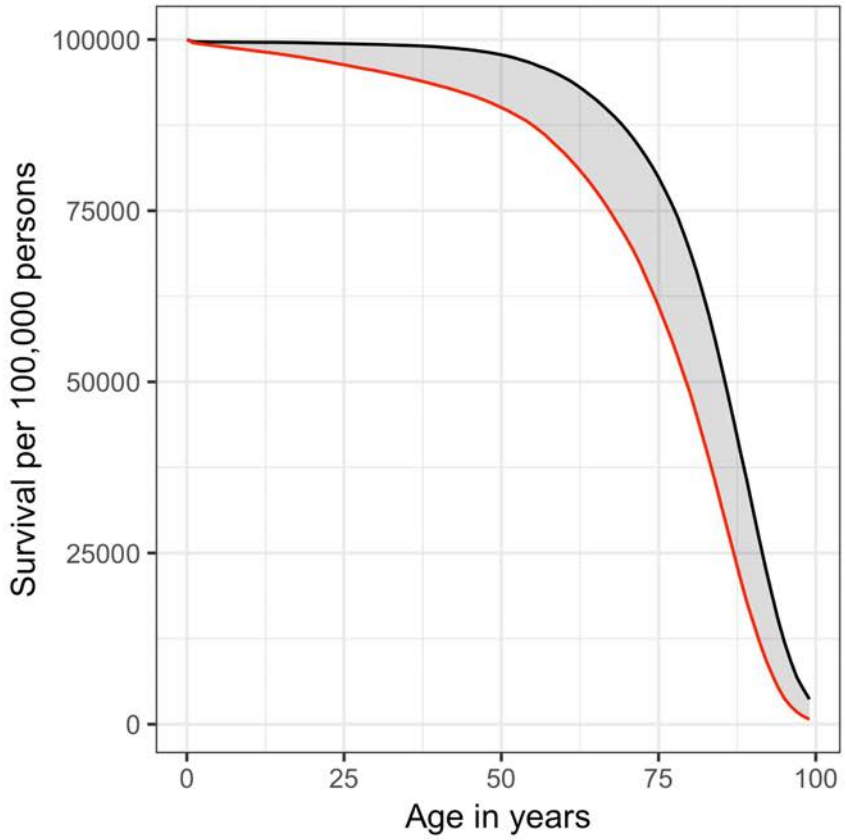




LIFE EXPECTANCY IN TWO GROUPS

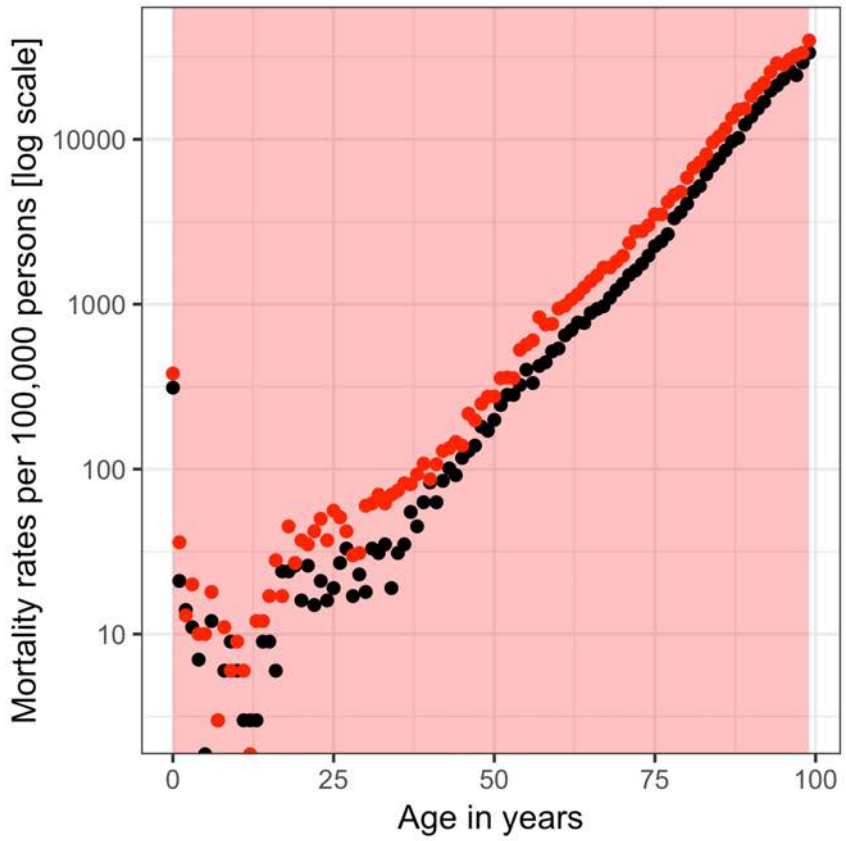
The difference in life expectancy (or life years lost) is the area between the two curves.

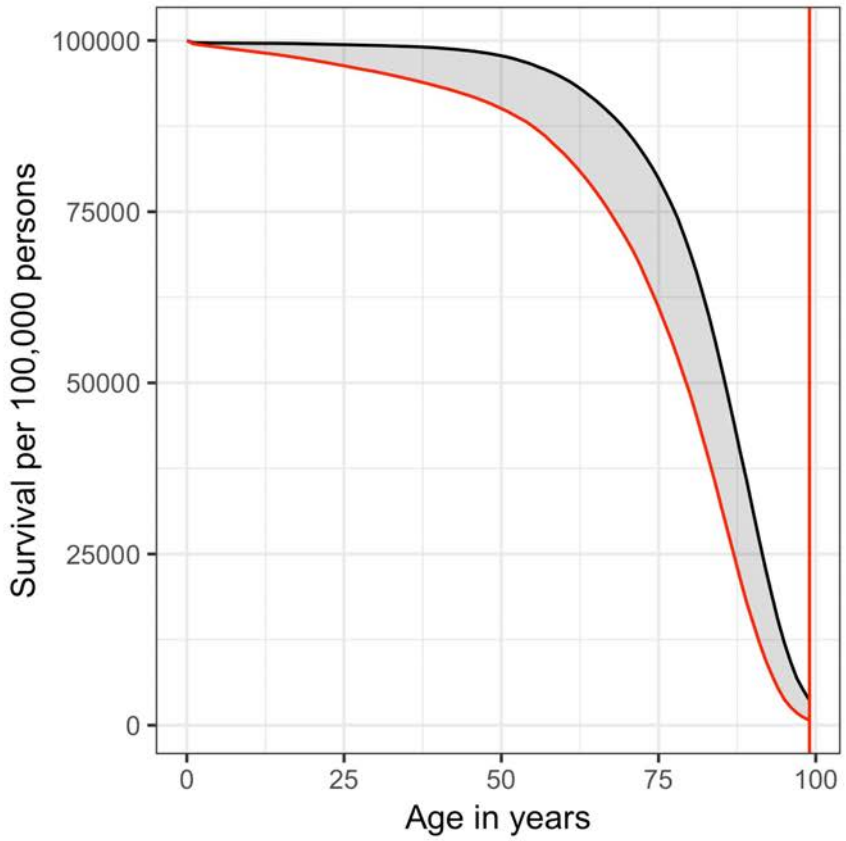




LIFE EXPECTANCY IN TWO GROUPS

Assumption: someone in “red/black group” experiences **always** (from birth) the mortality rates in that group.





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LIFE EXPECTANCY FOR DISORDERS

If we use group-specific mortality rates (e.g. smokers and non-smokers)

- Assume that a smoker smokes throughout the entire life (analogous for non-smokers)

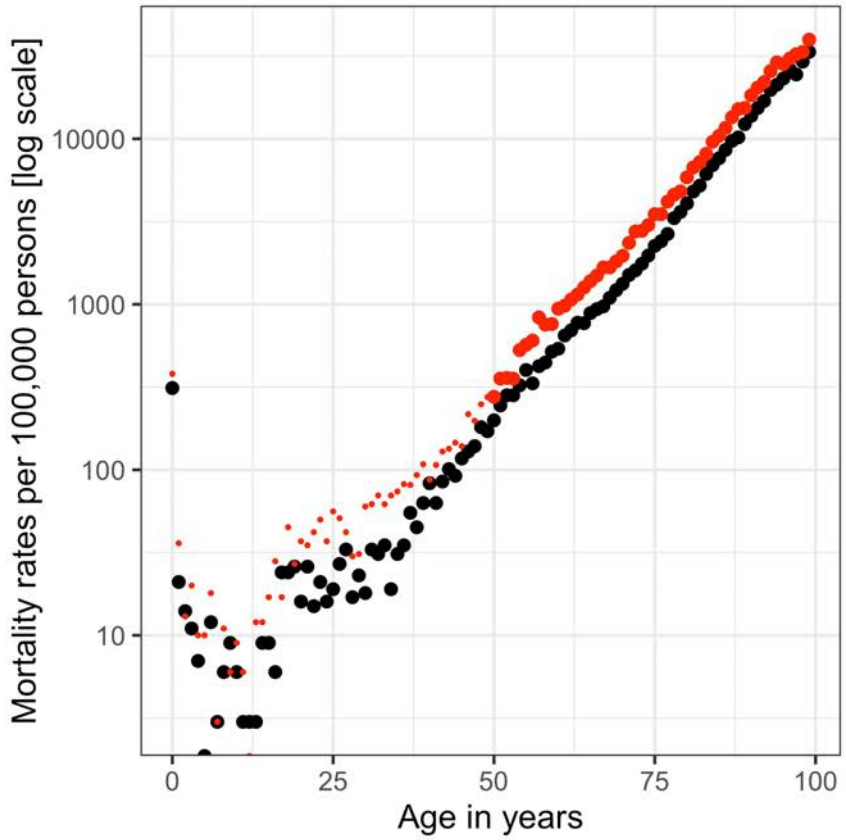
Not reasonable to assume that some disorders or conditions are present at birth

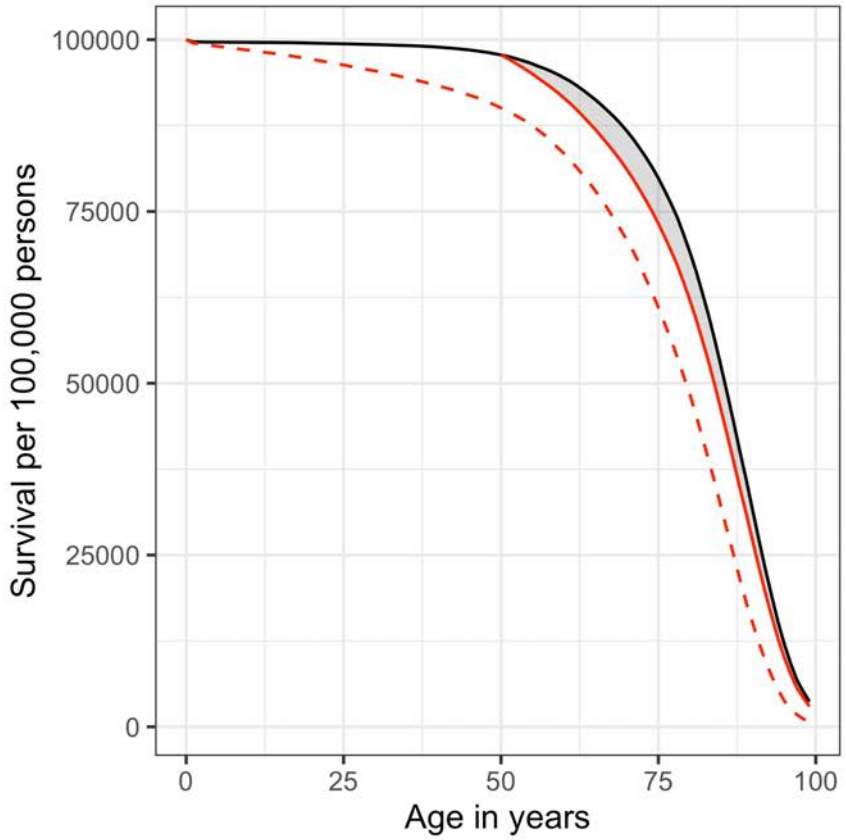
Instead, researchers assumed all were diagnosed at one specific age:

- Mental disorders: age 15 years *(Lawrence et al. 2013; Nordentoft et al. 2013)*
- Type I diabetes: age 20 years *(Livingstone et al. 2015)*
- Colon cancer: age 55 years *(Andersson et al. 2015)*

LIFE EXPECTANCY FOR DISORDERS

Life Years Lost among those with a disease: imagine fixed onset at age 50 years





LIFE EXPECTANCY FOR DISORDERS

It is reasonable to assume not everyone has a disease/condition since birth.

But we still have one important limitation: choosing the cut-off point (e.g. 15 years)

- Is it reasonable to assume a fixed age at onset?

The Life Years Lost method overcomes this limitation. In addition, it allows to decompose total differences in life expectancy (LYL) into specific causes of death.

- *Andersen, PK. (2017). Life years lost among patients with a given disease. Stat Med, 36(22), 3573–3582.*
- *Andersen, PK. (2013). Decomposition of number of life years lost according to causes of death. Stat Med, 32(30), 5278–5285.*
- *Plana-Ripoll O, …, Andersen PK. (2020). lillies: an R package for the estimation of excess Life Years Lost among patients with a given disease or condition. PLoS One,15(3): e0228073.*
  - ✓ *Package **lillies** available in CRAN*

New method to estimate Life Years Lost in persons with a specific disease or condition

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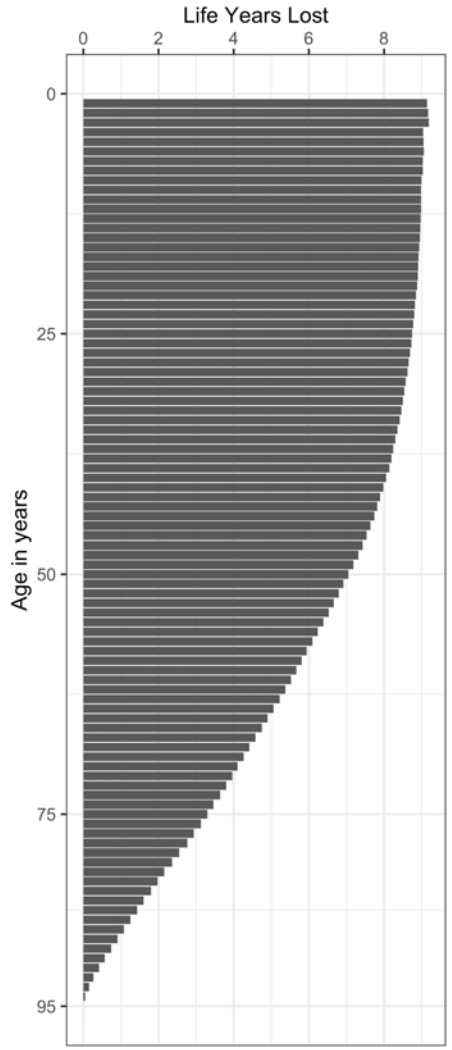
ESTIMATION OF LIFE YEARS LOST

The Life Years Lost method suggests:

1. To calculate **differences in remaining life expectancy** (or Life Years Lost) at each specific age at diagnosis:

$$LYL_x = LYL_x^1 - LYL_x^0 \quad \text{for each} \quad x \in ages$$

[Interpretation for those alive and diagnosed on that specific age]



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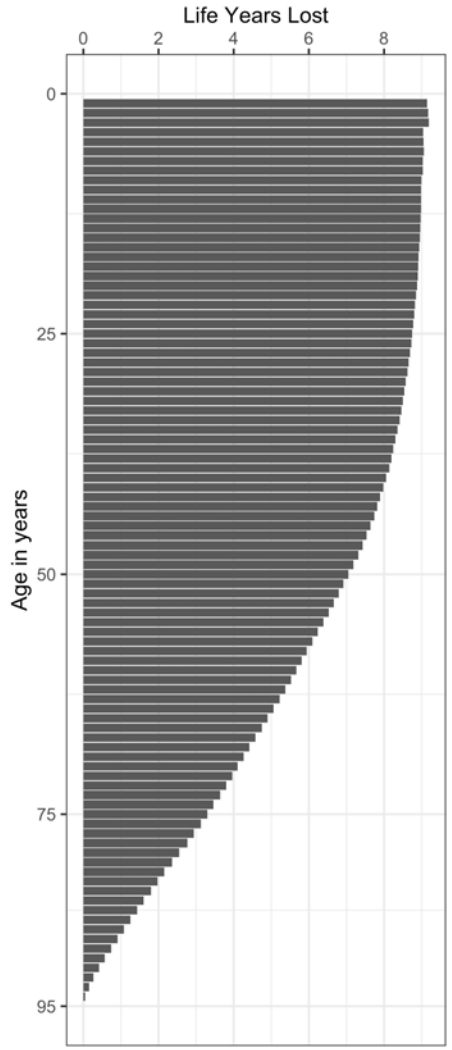
2. Average the previous estimates into one single estimate in order to **take into consideration the real age-of-onset distribution**.

$$LYL = \sum_{x \in ages} LYL_x = \sum_{i=0}^{95} n_i \cdot LYL_i$$



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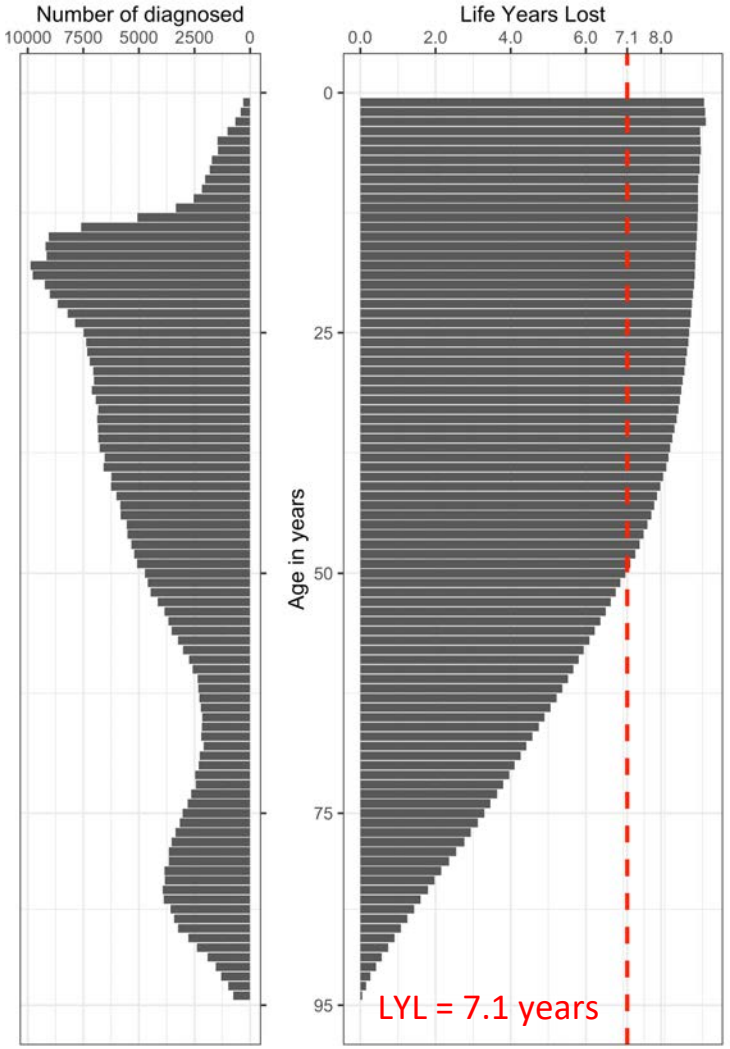
- **Interpretation**: average reduction in remaining life expectancy (or Life Years Lost) after disease diagnosis.



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21 MAY 2021

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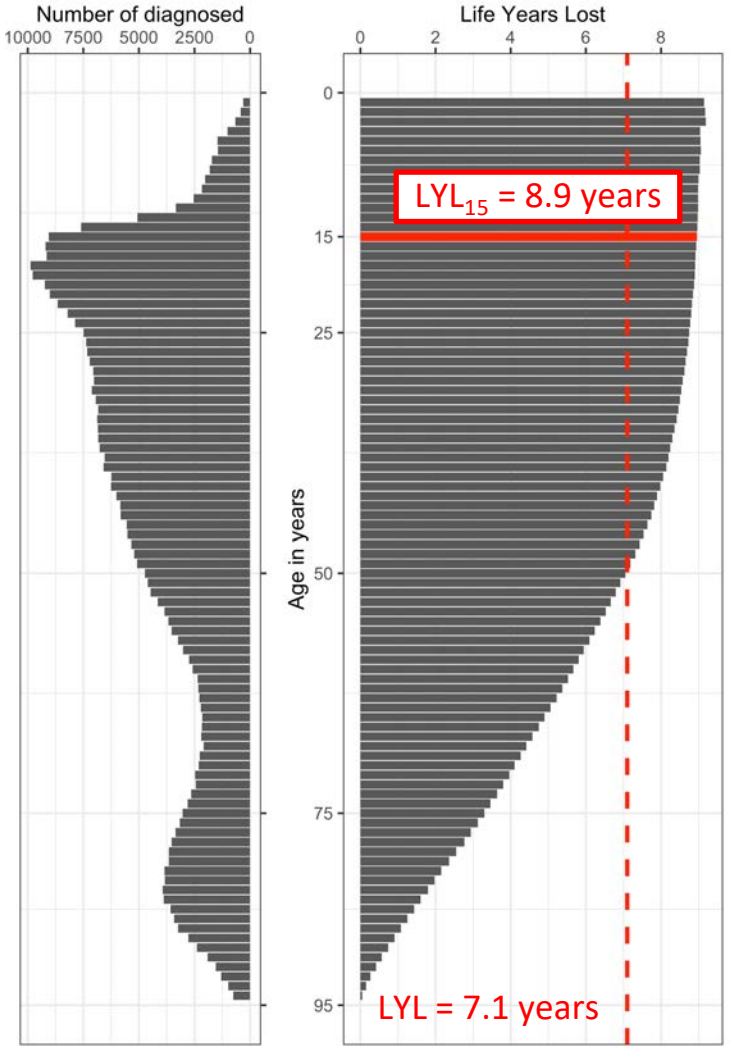

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Excess mortality associated with mental disorders in Denmark

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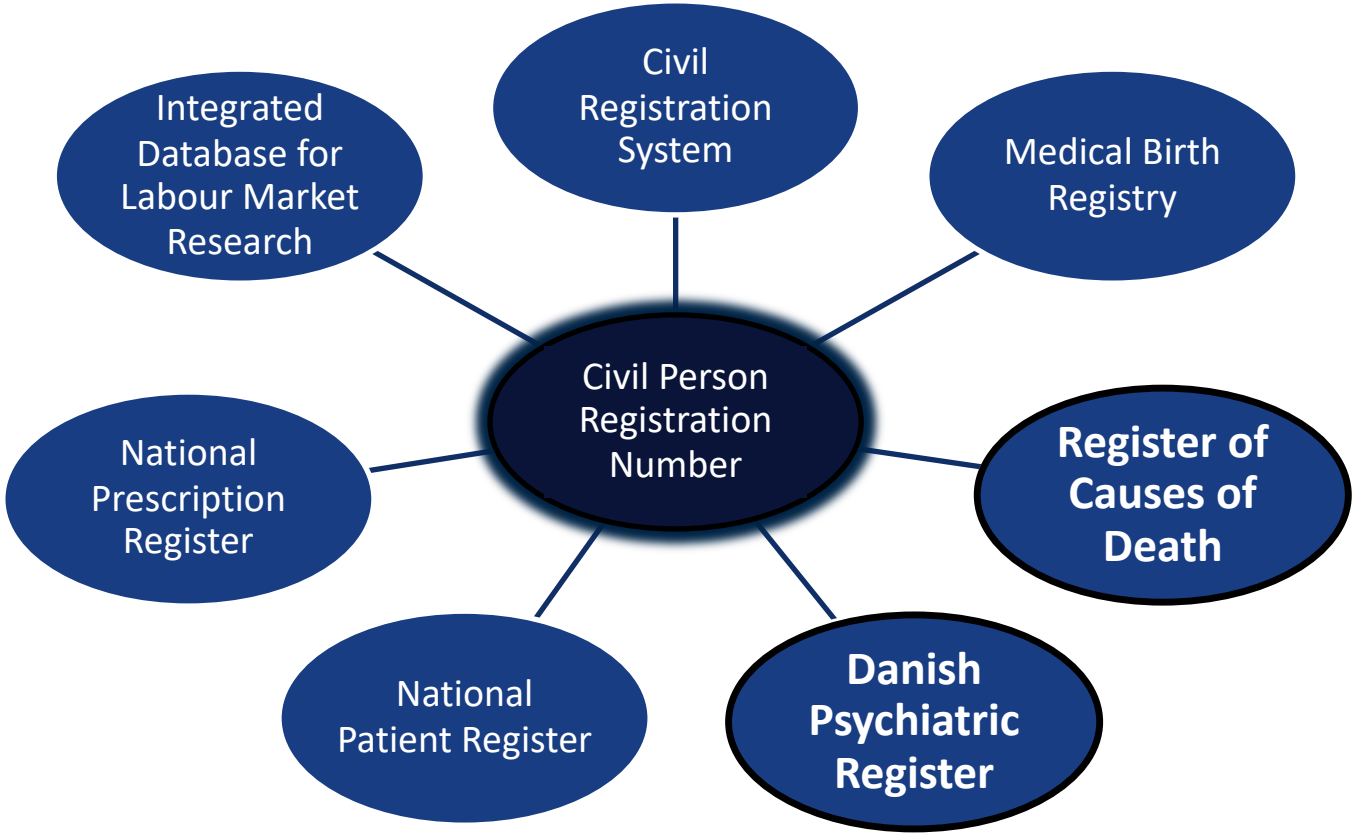
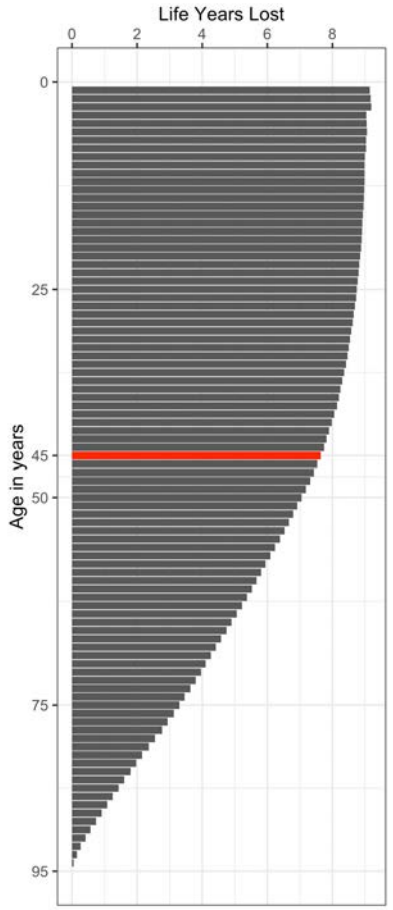


Identification of all individuals living in Denmark in 1995-2015

N = 7.4 million

LIFE YEARS LOST AT AGE 45 YEARS



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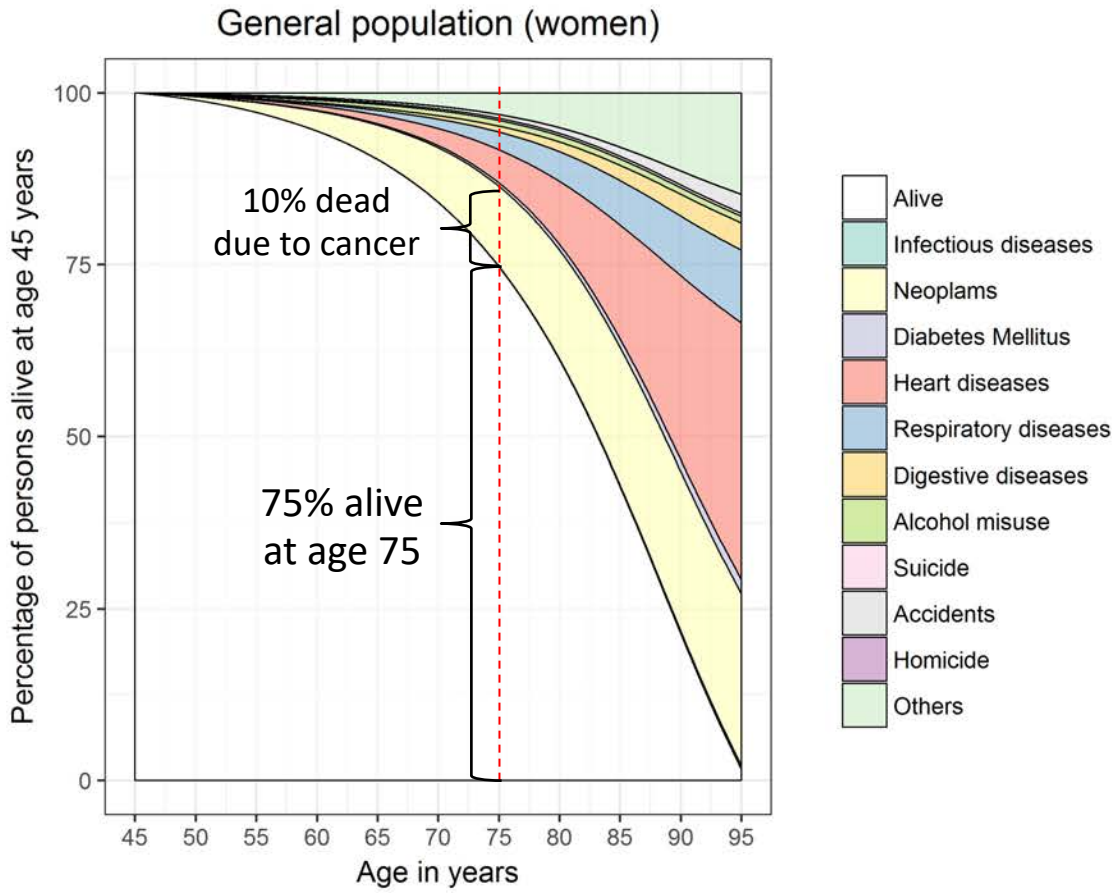

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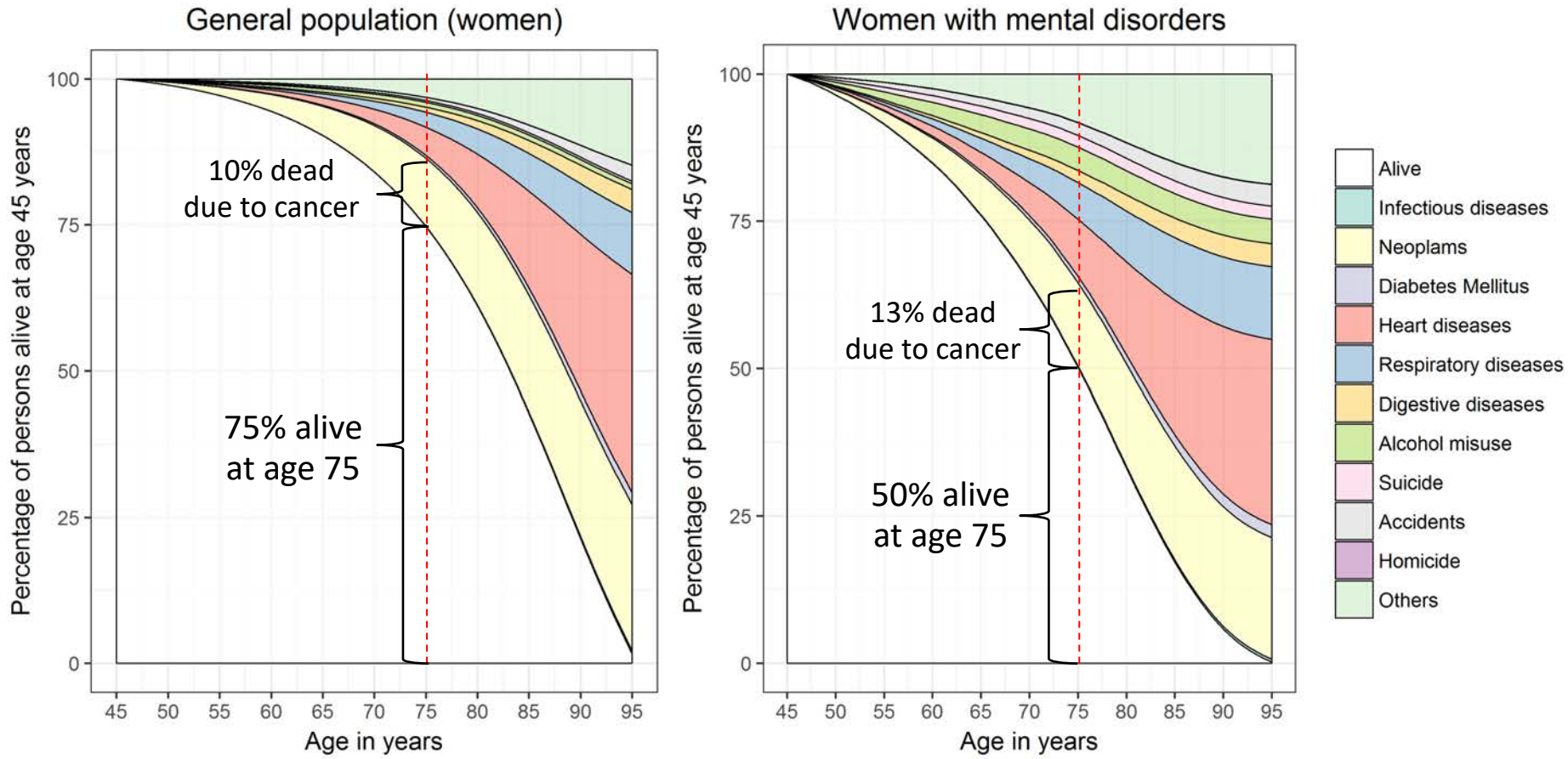
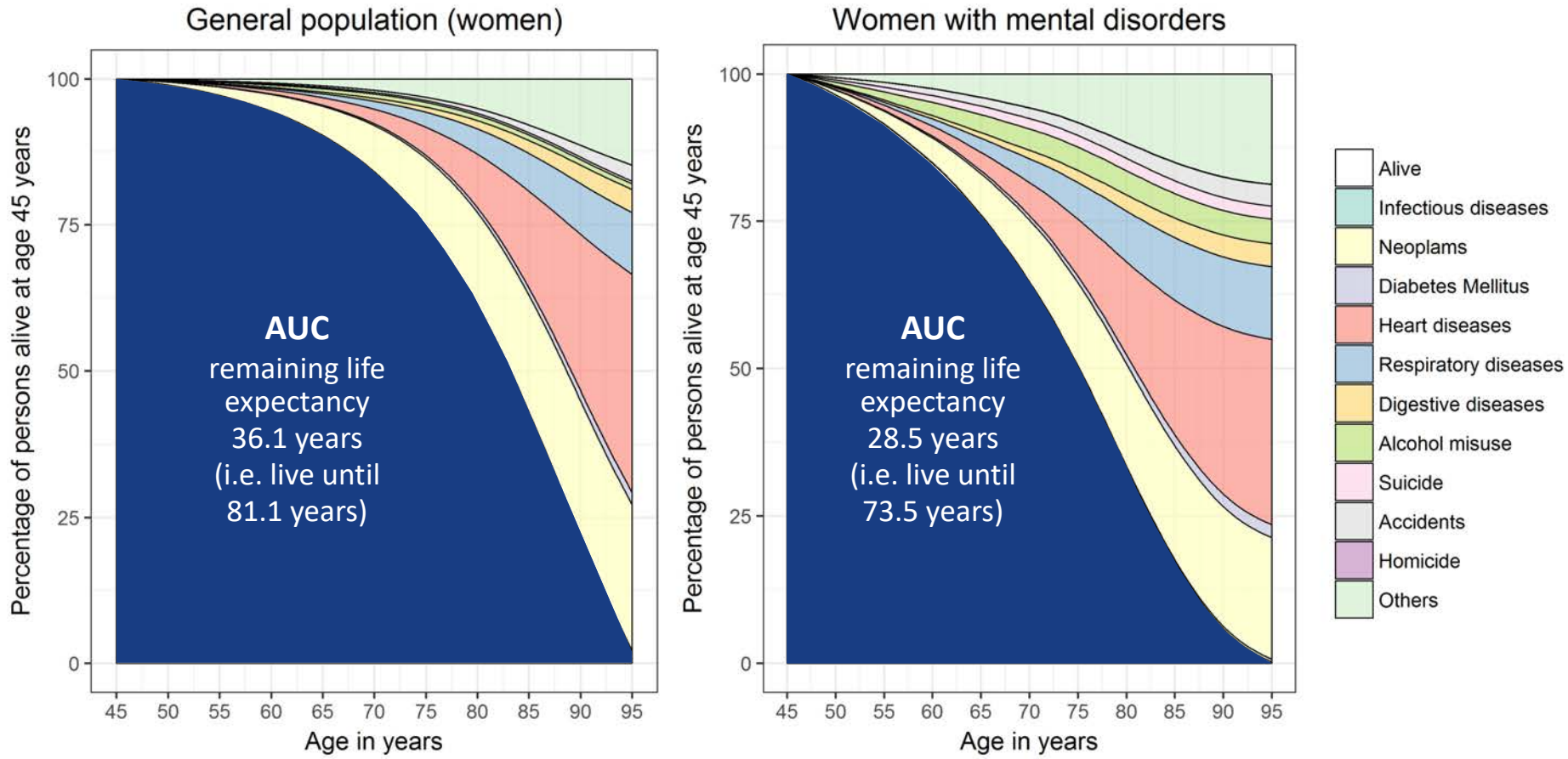


LIFE YEARS LOST AT AGE 45 YEARS



LIFE YEARS LOST AT AGE 45 YEARS

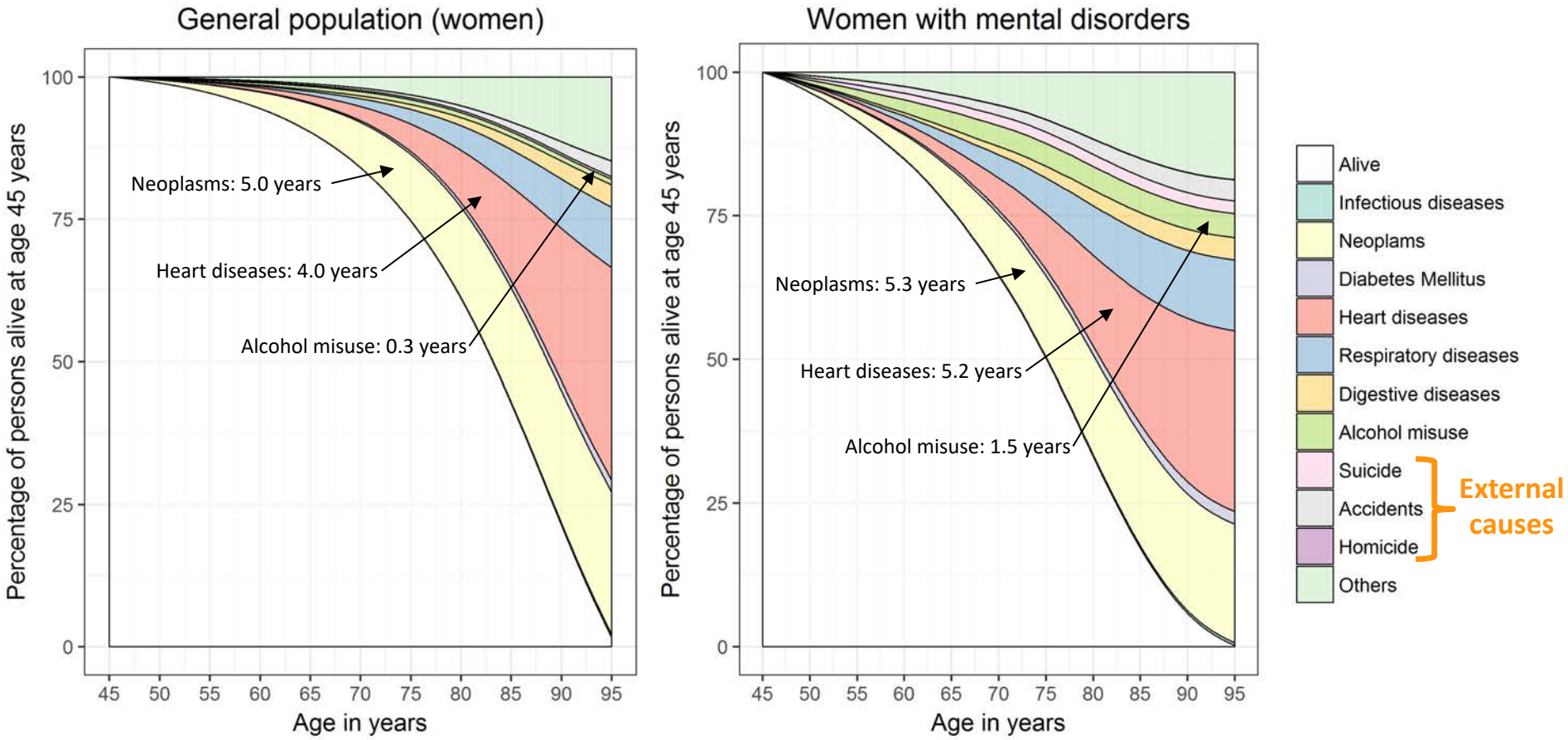
Total LYL: 36.1 – 28.5 = 7.6 years

- Neoplasms: 0.3 years
- Heart dis.: 1.2 years
- Alcohol: 1.2 years
- etc.

Total LYL: 7.6 years

Natural causes: 6.4 years

External causes: 1.2 years



R PACKAGE 'LILLIES'

R functions:

```
LYL45 <- lyl(data = population, t = age_death, status = cause_death,
             age_specific = 45, tau = 95)
plot(LYL45)
summary(LYL45)
```

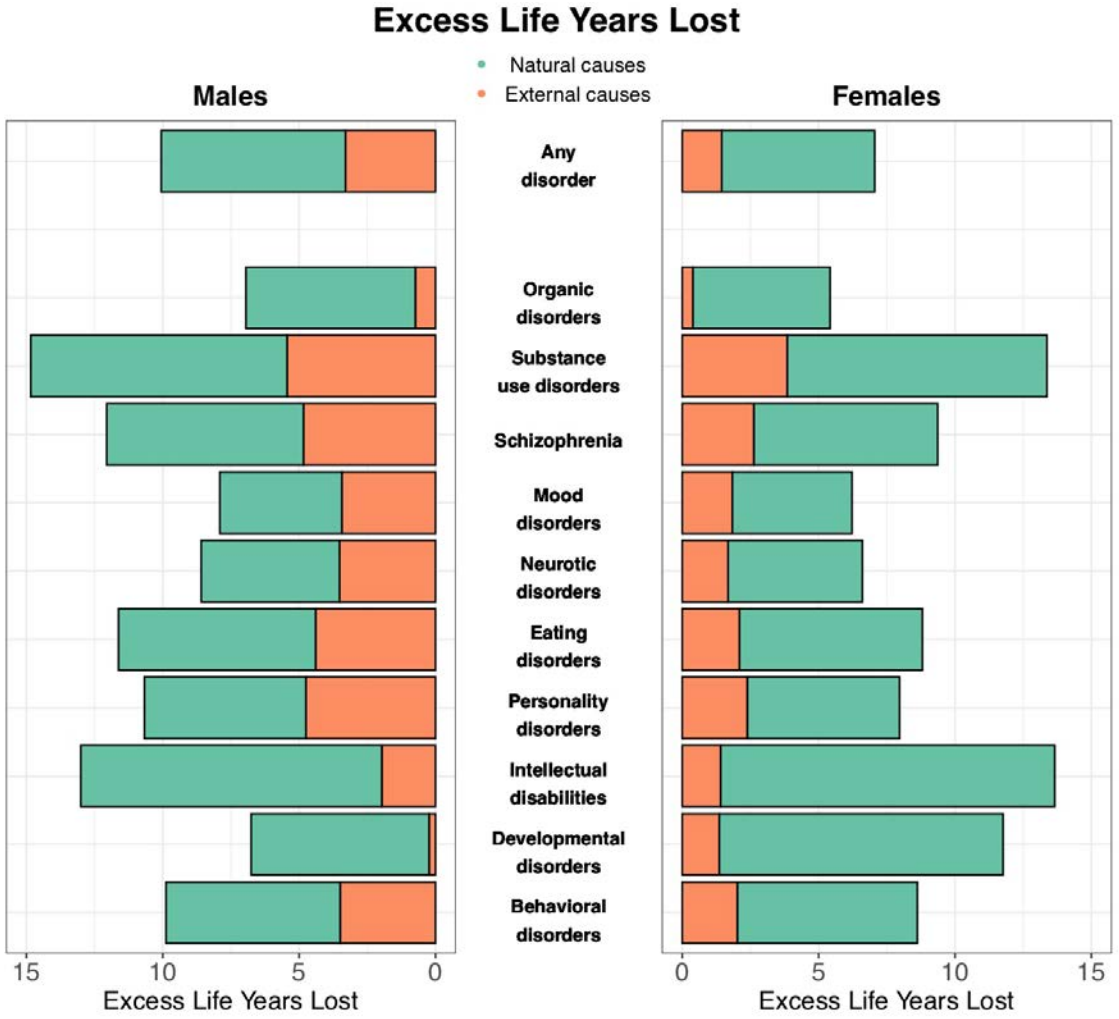
Only for persons aged 45 years: need to replicate for all ages at onset and take the average

```
LYL_avg <- lyl_range(data = population, t = age_death, status = cause_death,
                     age_begin = 0, age_end = 94, tau = 95)
plot(LYL_avg)
summary(LYL_avg, weights = population$age_dx)
```

RESULTS: LIFE YEARS LOST

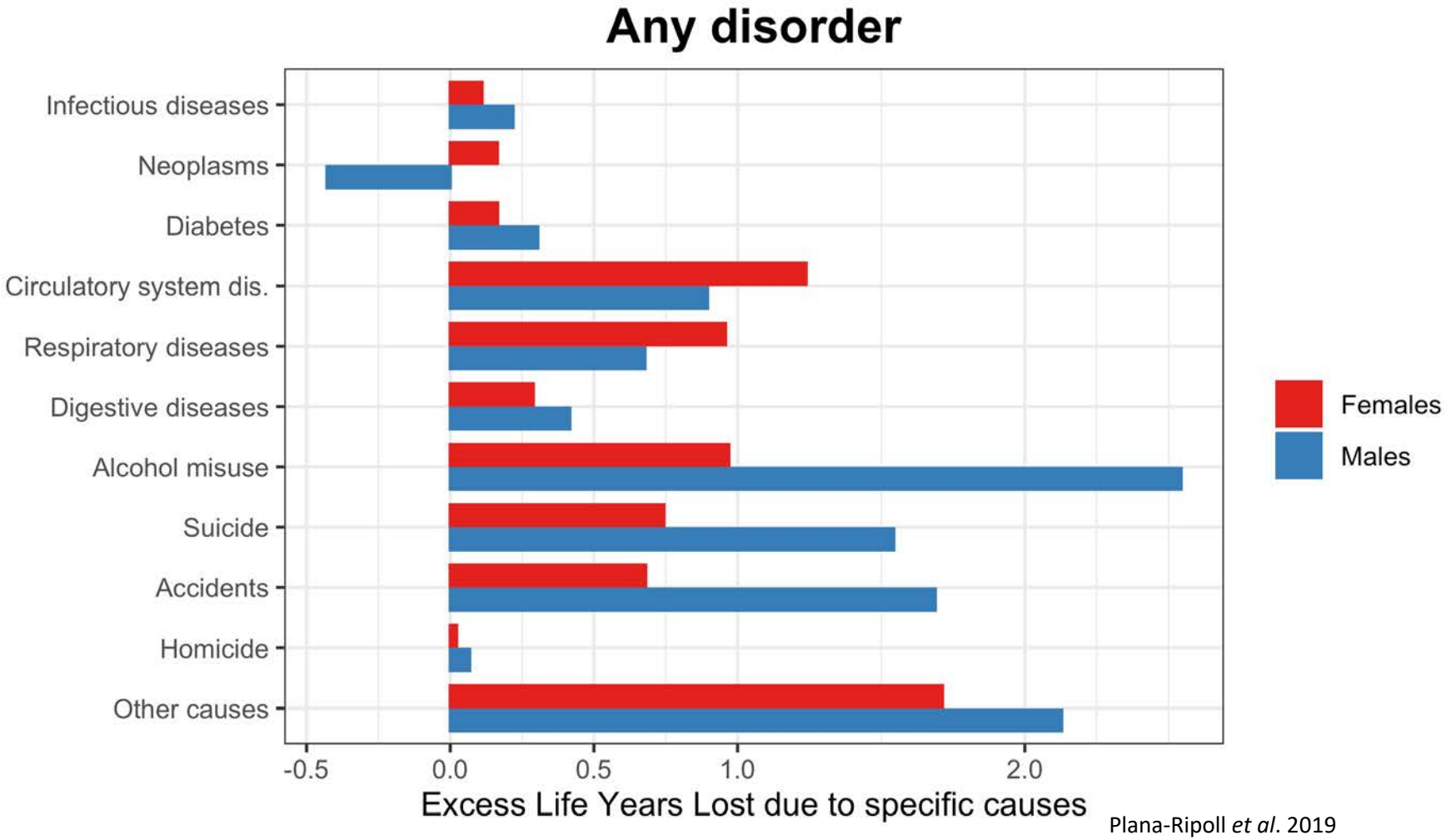
Plana-Ripoll *et al*. 2019

RESULTS: LIFE YEARS LOST



Plana-Ripoll *et al*. 2019

RESULTS: LIFE YEARS LOST



Plana-Ripoll *et al*. 2019

RESULTS: LYL - MRR

Plana-Ripoll *et al*. 2019

RESULTS: LIFE YEARS LOST

Plana-Ripoll *et al*. 2019

WWW.NBEPI.COM/MORTALITY

CONCLUSIONS

- Life expectancy (Life Years Lost) difficult to estimate in those with time-varying conditions
  - Necessary to choose a cut-off point

- The Life Years Lost method overcomes past limitations
  - Average over real age-at-onset distribution
  - An R package and tutorial are available

- Life expectancy for those with mental disorders is 7-10 years shorter
  - All types of mental disorders associated with shorter life expectancy
    - ✓ All-cause mortality
    - ✓ Cause-specific mortality (except neoplasms in men)
  - Mental disorders diagnosed in hospital settings

FUTURE RESEARCH

- Use surveys to complement data from registers (e.g. identify mild cases of mental disorders)
- Measuring variability in life years lost for those with mental disorders
- Identify factors associated with variability (e.g. comorbidity, socio-economic characteristics)
- Understand the role of socio-economic factors in the excess comorbidity and mortality

WE ARE LOOKING FOR POSTDOCS AND PhD STUDENTS

ACKNOWLEDGEMENTS


John McGrath


Preben B Mortensen


Per K Andersen


Natalie Momen


Nanna Weye

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THANK YOU

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REFERENCES

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