Modelling multiple time-scales with flexible parametric models

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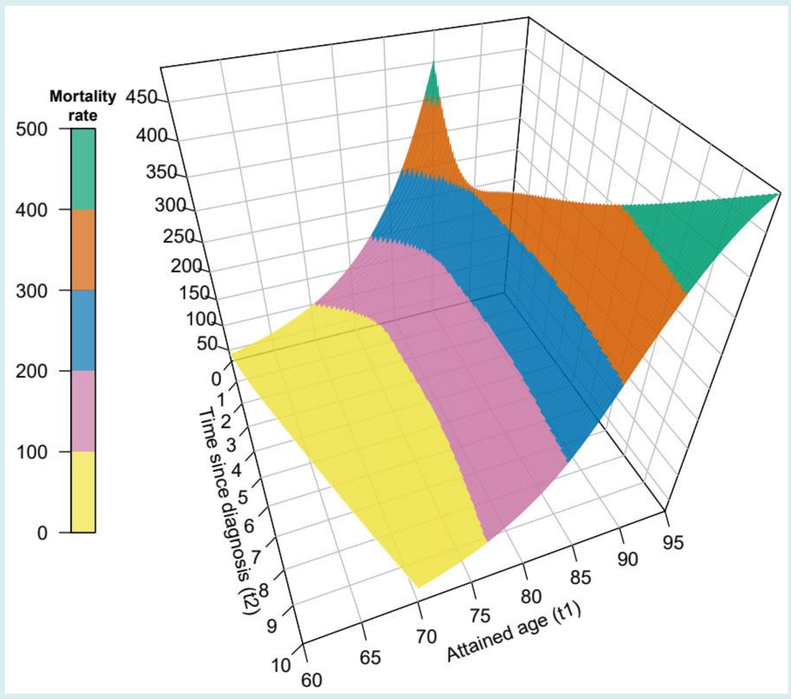


Estimated mortality rates surface per 1000 person-years over two time-scales for male MPN patients.

Conclusions

- There are situations when it is useful to include multiple time-scales in survival models
- The flexible parametric model approach enables us to model multiple time-scales as continuous functions
- Graphical representations along different time-scales improve understanding of the study outcomes

Introduction

- Multiple time-scales are often present in time-to-event data but most often not modelled simultaneously
- Examples:
  - Breast cancer incidence: age, time from childbirth
  - Chronic disease mortality: age, time since onset
- Usual approach is to split the time-scale into intervals and fit Poisson models which is not always optimal
- Another approach is to use FPMs, which are models that use restricted cubic splines in modelling the baseline hazard function

FPM with multiple time-scales

- By expressing 1 time-scale in terms of another time-scale and an offset term, then both time-scales can be incorporated into hazard model
- Log-hazard model with 2 time-scales:

$$\ln h(t_1, t_2|\boldsymbol{x}) = s_1(f(t_1); \gamma_1) + s_2(\psi(t_2); \gamma_2) + \boldsymbol{x\beta}$$
$$= s_1(f(t_1); \gamma_1) + s_2(\psi(t_1 + a_0); \gamma_2)$$

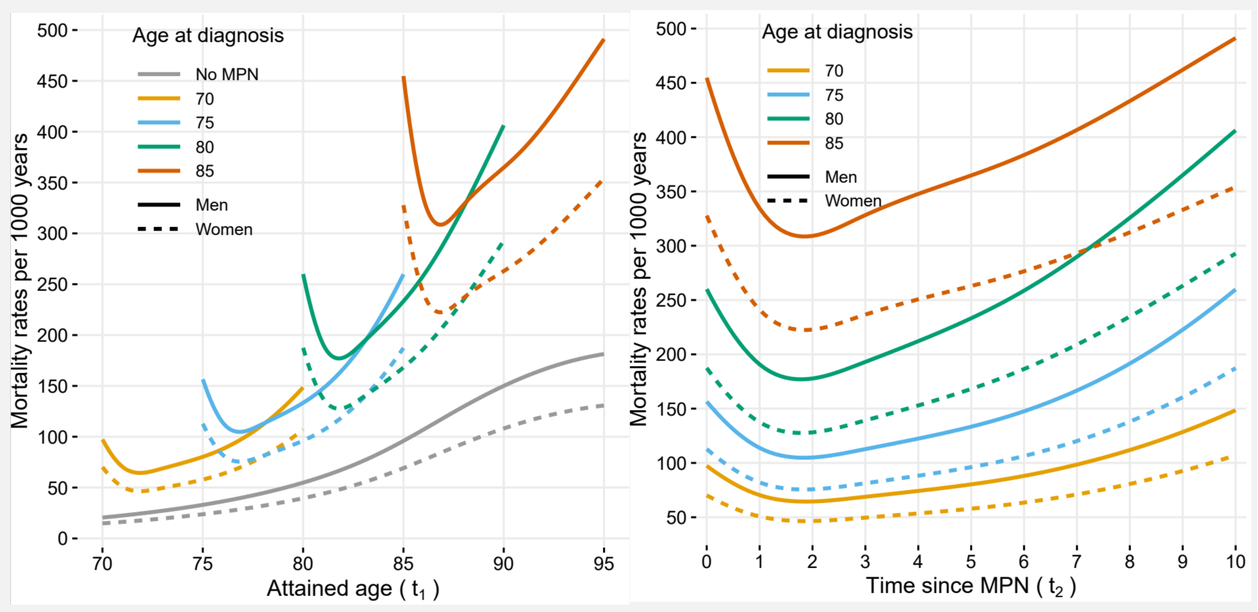
- In STATA

```
stmt x, time1(df(5)) time2(start(age0) df(3))
```

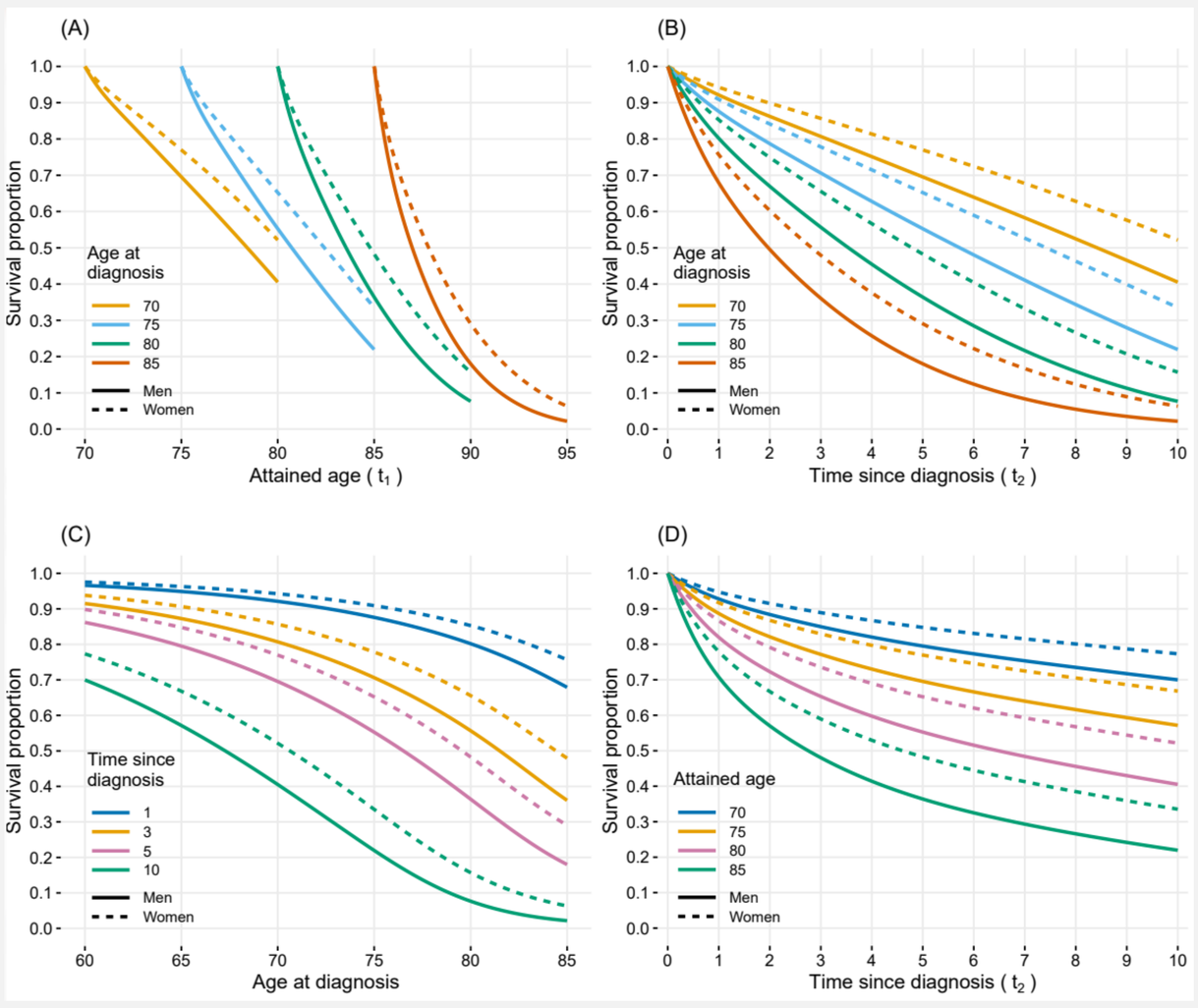
Example: MPN patients and matched controls

- MPN is a chronic bone marrow cancer with yearly incidence of approx. 400 patients
- Interested in modelling mortality in comparison to population
- Long follow-up due to indolent nature of disease
- Time-scales in example:

  t_1 = attained age for all
  t_2 = time since diagnosis for MPN subjects



Estimated mortality rates per 1000 person-years for MPN patients and matched controls: (Left panel) over attained age (t_1) for different ages at diagnosis; (Right panel) for MPN patients along time since diagnosis (t_2).



Predicted survival proportions for MPN patients: **(A)** for different ages at diagnosis over attained age (t_1); **(B)** over time since diagnosis (t_2); **(C)** with respect to age at diagnosis for patients with 1, 3, 5, 10 years since diagnosis, respectively; **(D)** over time since diagnosis for attained ages 70, 75, 80, 85 years

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