How to make cancer survival statistics more useful for patients and clinicians

– an application using localized prostate cancer in Sweden

Sandra Eloranta*

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* Department of Medical Epidemiology and Biostatistics
Karolinska Institutet, Stockholm

Introduction

- Every day, oncologists and their patients are confronted with difficult treatment decisions.

- Recommendations from the treating clinician vs information available from other sources (cancer reports, scientific papers etc).

- Not all reported survival statistics are useful to predict the outcome of newly diagnosed patients.

Introduction

- Tutorial paper explaining recently developed, statistical methods.

  1. Relative survival
  2. Importance of accounting for competing risks
  3. Period analysis to predict the future prognosis of recently diagnosed patients

- Discuss ways to adapt survival statistics to improve risk communication

Prostate cancer in Sweden

- About 10 000 incident cases/year.
- Increasing incidence after the introduction of PSA testing.
- Mortality relatively stable - more slow-growing cases today compared to earlier.
- Treatment with curative intent were not widely used until the late 1990s (and then mostly among younger patients).

What determines treatment for PC

1. The spread and aggressiveness of the disease
2. PSA-level
3. The patient´s age, general health and life expectancy
4. The preference of the patient

- The main types of treatment available today:

1. Active monitoring/Watchful waiting
2. Surgery (radical prostatectomy)
3. Radiation therapy
4. Hormonal therapy

Data

- Data from the National Prostate Cancer Register in Sweden

- Individual level information on TNM-stage, Gleason score and PSA-level at diagnosis was used to determine clincial risk categories.

- Intermediate and high risk PC diagnosed between 1996-2008 were selected (follow-up until the end of 2009).

Relative survival – Net survival

- Relative survival

$$R(t) = \frac{S(t)}{S^*(t)}$$

- *S(t)* - observed survival among patients
- *S*(t)* - expected survival in a cancer-free group.

- Excess mortality – mortality analogue of relative survival.

$$\lambda(t) = h(t) - h^*(t)$$

Crude survival - when there are competing risks

- Estimates of net survival do not account for competing risks.

- The theory behind competing risks is widely accepted among theoretical statisticians but applied less frequently in practice.

- From a risk communication perspective, *crude survival* provide an estimate of the actual risk that a patient has to die from their cancer.


Age 75 at diagnosis
Net probability of death
(1 – relative survival)
Dead (PC)
Alive
A
0.73
0.27
Years since diagnosis
Age 75 at diagnosis
Crude probability of death
Dead (PC)
Dead (other causes)
alive
B
0.39
0.43
0.18
Years since diagnosis


Age 60 at diagnosis
C
Dead (PC)
Alive
0.69
0.31
Net probability of death
(1 – relative survival)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
2
4
6
8
10
Years since diagnosis
Age 60 at diagnosis
D
Dead (PC)
Dead (other causes)
Alive
0.61
0.10
0.29
Crude probability of death
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
2
4
6
8
10
Years since diagnosis

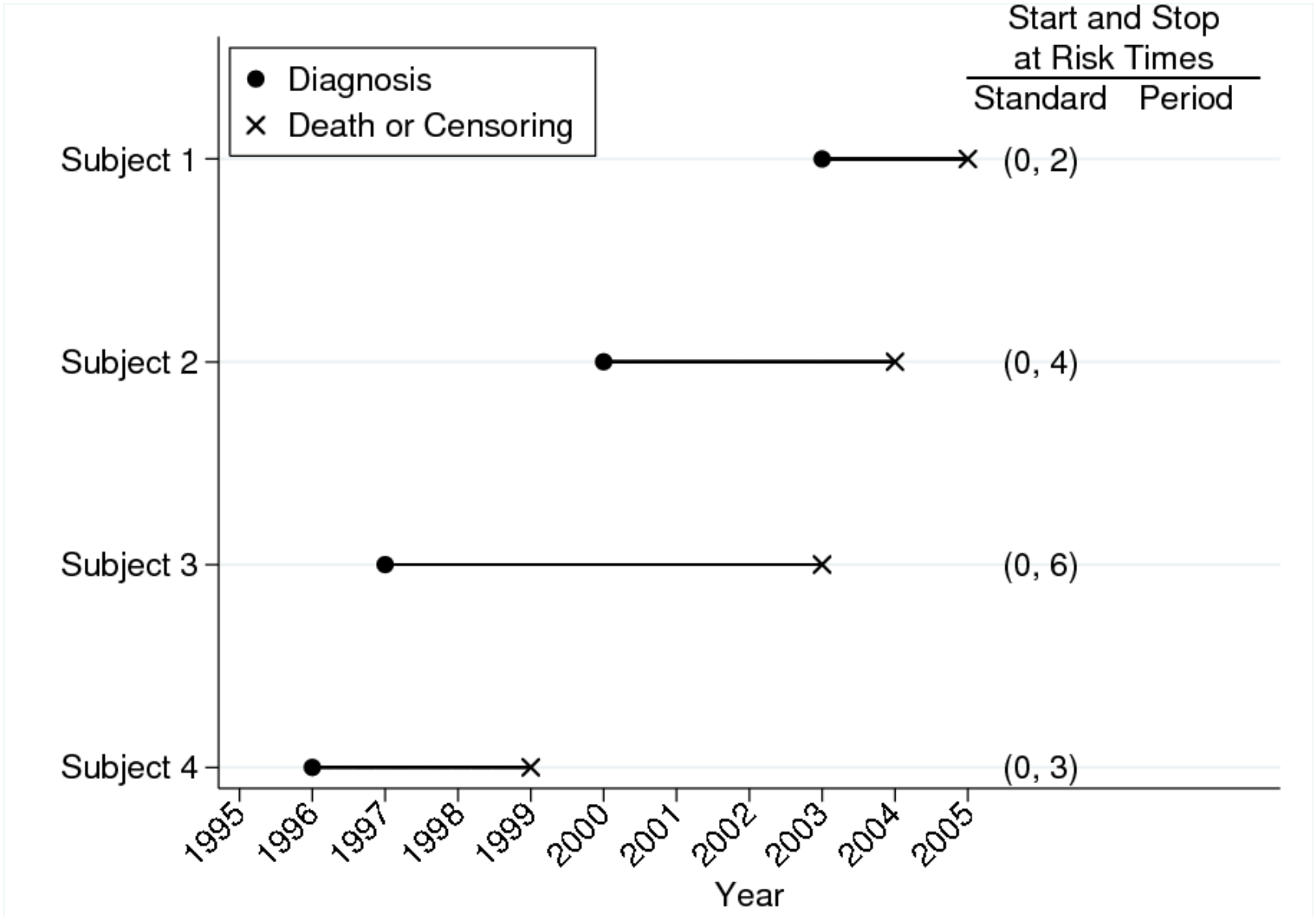
Period analysis

- Useful if the primary interest is to project survival for patients diagnosed in recent years (Brenner H).

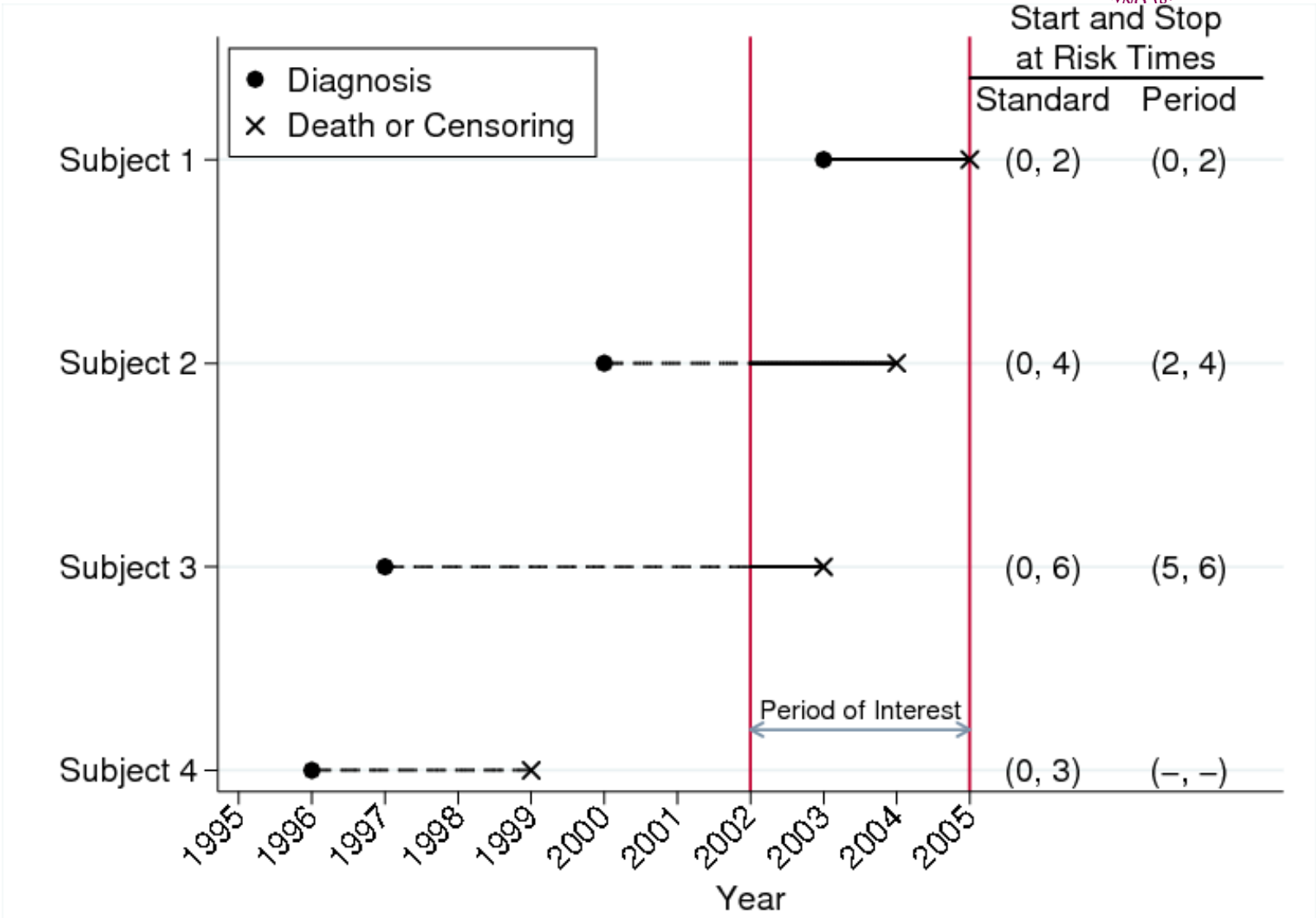
- In contrast, many cancer studies report on the survival experience of patients diagnosed many years in the past.

- Essentially a survival model with delayed entry at a pre-defined time window.

Cohort analysis



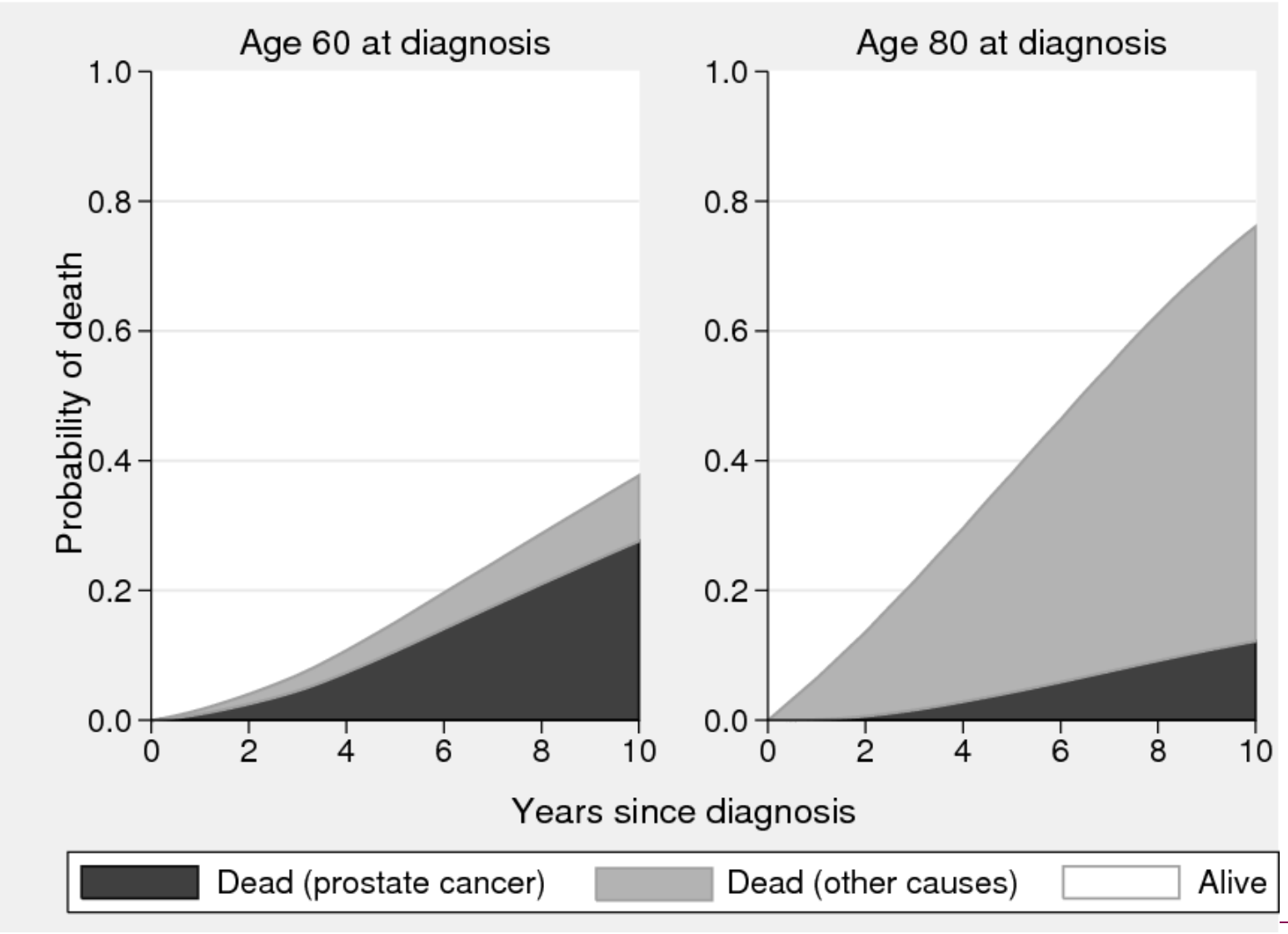
Period analysis



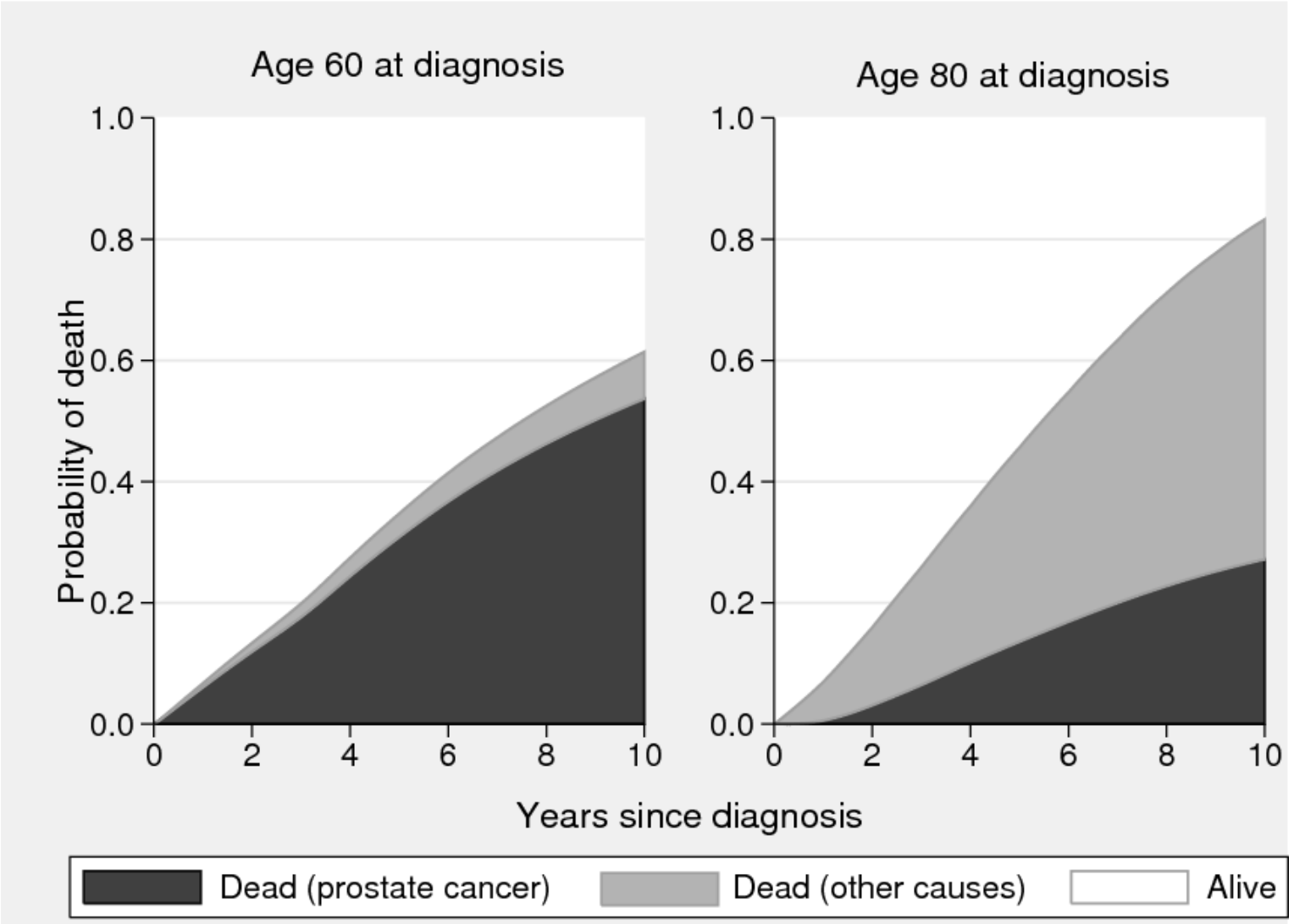
Modelling approach

- Relative survival was estimated using flexible parametric survival models.
- Period window: 2006 - 2010 by fitting a delayed entry model
- Crude probabilities of death were calculated post estimation
- All analysis were used using the stpm2 command in the Stata software.

Hormonal treatment
– Intermediate risk group



Hormonal treatment
– High risk group



Reporting of natural frequencies

”Of 100 patients similar to you, and who received hormonal treatment we would expect to see the following 10 years after diagnosis:”

	Age at diagnosis: 60		Age at diagnosis: 80	
	Intermediate risk	High risk	Intermediate risk	High risk
Dead PC	28	54	12	27
Dead other	10	8	64	56
Alive	62	38	24	17
Total	100	100	100	100

Summary/Conclusions

- Different audiences are best served by different types of statistics (and summaries/reports).

- Taking competing deaths into account was particularly important for patients aged more than 70 years at diagnosis

- We advocate the use of period estimates of crude survival also in cancer registry reports etc as they are more useful in a clinical setting.

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References

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- **Estimating the crude probability of death due to cancer and other causes using relative survival models.** Lambert PC, Dickman PW, Nelson CP and Royston P. *Statistics in Medicine 2010*

- **Period analysis for up-to-date cancer survival data: theory, empirical evaluation, computational realisation and applications.** Brenner H and Hakulinen T. *2004 European Journal of Cancer*

Definition of risk categories

(according to a modified version of the National Comprehensive Cancer Network classification)

- **Intermediate risk category:**
  I. Clinical local stage T1-2 (UICC, 2002, 6th version),
  II. N0, NX-,
  III. M0, MX and
  IV. Serum levels of PSA between 10-20 ng/ml or Gleason score 7.

- **Locally advanced high risk category:**
  I. Clinical local stage T3-4,
  II. N0, NX,
  III. M0, MX and/or
  IV. Serum levels of PSA between 20-50 ng/ml and/or Gleason score 8 or higher.

Conservative treatment