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RESEARCH LETTER

Assessment of variability in life expectancy in older men by use of new comorbidity indices. A nationwide population-based study

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Background

Accurate assessment of life expectancy is a key component in treatment decisions for men with prostate cancer (PCa). Considering the commonly high age at diagnosis, a long disease trajectory, and high risk of treatment-related adverse effects, decisions on the management for PCa should include assessment of life expectancy. Developing methods that can accurately estimate life expectancy in clinical epidemiological studies is therefore important.

Standard life table methods for life expectancy are based on age without taking comorbidity into account [1]. This is sometime sufficient, but for men with PCa, comorbidity is expected to have a strong impact on life expectancy and therefore also on the management of the PCa. A more precise estimation of life expectancy, incorporating comorbidity, is therefore warranted and enables a more accurate assessment of potential treatment benefits.

Estimation of how comorbidity influences life expectancy should ideally be based on large cohorts followed over a long period of time. If life expectancy is defined as the expected remaining years alive in absence of the cohort-defining disease at baseline, then the development of comorbidity measures and estimation of their impact on life expectancy should be restricted to a population without that disease at baseline.

Following these principles, we recently developed two new comorbidity indices based on an individual's history of diagnoses and prescribed medications: a multidimensional diagnosis-based comorbidity index (MDCI) and a drug comorbidity index (DCI) [2, 3]. Both indices discriminate risk of death better than the commonly used Charlson Comorbidity Index (CCI). We have also developed a method to estimate life expectancy for men with PCa that is based on age, CCI and DCI [4].

The aim of this study was to demonstrate the variability in life expectancy related to comorbidity in a cohort of men diagnosed with PCa, by applying our MDCI and DCI combined with a revised version of our method to a cohort of men diagnosed with PCa to estimate life expectancy.

Material and methods

The National Prostate Cancer Register (NPCR) of Sweden captures 98% of all incident cases of PCa compared to the Cancer Register to which reporting is mandated by law. The aim of NPCR is to ensure optimal care for all men with PCa. To reach this aim, NPCR registers and reports data on diagnostics, work-up and primary treatment and adherence to national guidelines [5, 6]. In Prostate Cancer data Base Sweden (PCBaSe) 5.0, NPCR has been linked to other national healthcare registers and demographic databases. We extracted data from PCBaSe 5.0 on men with PCa diagnosed between 2012 and 2020. The index date was set to the date of the PCa diagnosis. Comorbidity was measured using CCI and MDCI, and DCI. The CCI and MDCI were computed based on ICD-10 codes registered for the individual in the Swedish National Patient Register during a 10-year look-back period preceding the index date [2, 7]. The MDCI captures occurrence, recency and frequency of included ICD-10 codes, as well as total duration of hospital stays with each code. The DCI was calculated based on Anatomical Therapeutic Chemical (ATC) codes (five digits) identified in the Prescribed Drug Register during the 365-day period preceding the index date [3].

Life expectancy based on age and calendar year alone was extracted from life tables published by Statistics Sweden [8]. Life expectancy based on age, MDCI and DCI was estimated using an updated version of the previously described model [4] where the CCI was replaced by the MDCI. The reason for the modification is that MDCI discriminates risk of death better than the CCI [2], and it is, therefore, hypothesised that this could also improve prediction of life expectancy when combined with age and the DCI. The revised model was estimated using data from 645,328

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Table 1. Baseline characteristics of men diagnosed with prostate cancer between 2012 and 2020 at age 50–90 years and registered in Prostate Cancer data Base Sweden (PCBaSe) 5.0.

	N	(%)
	90,319	(100)
Age at diagnosis (years)		
Median (IQR)	69 (64–75)	
<60	8,689	(10)
60–69	32,325	(36)
70–79	35,795	(40)
80+	13,510	(15)
Life expectancy estimated based on age and comorbidities (years)		
Median (IQR)	15.8 (11.0–20.3)	
<5 years	3,856	(4)
5–10 years	14,857	(16)
10–15 years	22,641	(25)
15+ years	48,965	(54)
Charlson Comorbidity Index		
0	57,030	(63)
1	12,694	(14)
2	12,226	(14)
3+	8,369	(9)

IQR: interquartile range.

comparison men without PCa (detailed description in the online-only Supplementary Materials). The Swedish Research Ethics Authority approved the study.

Results

The revised model for life expectancy showed at least as good agreement between observed and simulated survival curves as the previous version (Supplementary Figure S2). Life expectancy was estimated in 90,319 men with PCa with a median age of 69 years (Table 1). The median life expectancy was 15.8 years (interquartile range [IQR], 11.0–20.3).

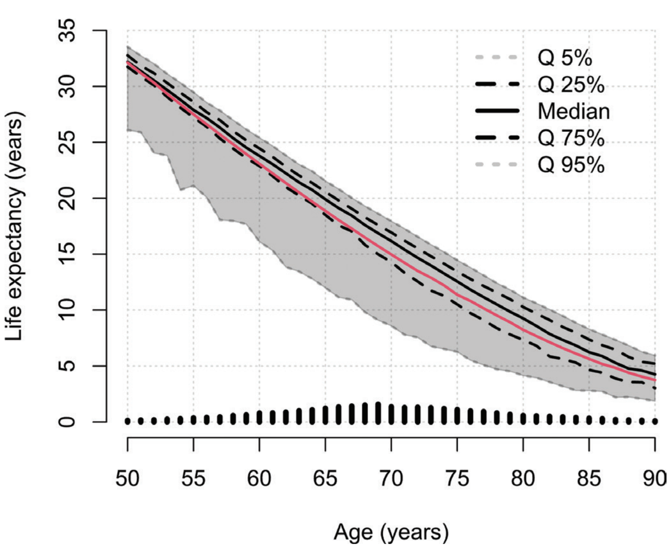

Figure 1. Life expectancy according to life tables (red) and according to age and comorbidities (black) by age at date of diagnosis. Grey-shaded region indicates the 5% and 95% quantiles (Qs) of life expectancy based on age and comorbidity, and dashed lines indicate the 25% and 75% Qs. The rug above the x-axis indicates the age distribution of the study population.

The life expectancy derived from age alone was comparable to the median life expectancy from our model that accounted for comorbidity across all ages (Figure 1). However, the model showed substantial variability related to comorbidity. For example, 4,107 men who were 70 years old had a model-based median life expectancy of 16.2 years, but depending on the burden of comorbidity, life expectancy varied from 8.6 years at the 5th percentile to 18.0 years at the 95th percentile. For 1,758 men who were 80 years old, the model-based median life expectancy was 9.3 years and varied from 4.1 at the 5th percentile to 11.1 at the 95th percentile due to differences in comorbidity.

Discussion

Our model indicates that life expectancy in men with PCa varies considerably depending on comorbidity. For a given age, life expectancy based on comorbidity could differ by as much as 10 years when comparing those with the lowest 5% and highest 5% of life expectancy estimates.

The strengths of our study include access to comprehensive high-quality data on comorbidity through linkage with population-based healthcare registries, as well as access to data on men without PCa. This study was restricted to men, which limits applicability of our model to women. However, the DCI has been validated in women with and without breast cancer and performed equally well in both sexes [3]. The MDCI requires further validation in women and in relation to other diseases. The associations between ATC/ICD-codes and mortality, which form the basis of our model, may be sensitive to variations in coding practices, disease patterns and lifestyle factors, which may differ across countries and change over time. The aim of this study was not to develop an application for individuals in clinical practice, and we caution against such implementation. In the assessment of an individual in the clinical setting, also other potential determinants of life expectancy, such as a general assessment of functional level and frailty, life style and social context, may be of relevance. Whilst our model can provide a very specific numeric prediction, it fails to incorporate such factors. Another limitation for application of the model to the individual patient is the difficulty to quantify and communicate the uncertainty of this estimate for an individual. We therefore argue that main application of this model should be on the group level in a study setting.

There are multiple potential applications for optimised comorbidity measures and estimates of life expectancy. Baseline comorbidity can be more accurately described, which facilitates subgroup comparisons. When this information is combined with model-based estimation of life expectancy, it provides an intuitive way to describe the baseline risk of death in the absence of the specific disease in question (e.g. PCa).

The decision to recommend radical treatment to men with intermediate or high risk PCa is largely dependent on life expectancy [5, 6]. Accurate measures of baseline life expectancy are therefore needed in treatment effectiveness studies. Accurate comorbidity indices can provide greater assurance that confounding by comorbidity has been accounted for when comparing study groups. The combination of MDCI and DCI has demonstrated effective control of confounding from comorbidity in comparison of outcomes in men treated with radical prostatectomy or radiotherapy [9]. Time-updated comorbidity measures to study treatment changes during long-term follow-up of men on watchful waiting according to life expectancy are another application of this method [10].

Optimised measures of comorbidity that summarises comprehensive information in healthcare registries can be used to estimate life expectancy with greater granularity than estimates based on age alone and publicly available population-based life tables. Accurate estimates of comorbidity and life expectancy are essential for effective cohort selection and comparison in register-based studies.

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Conflicts of interest

The authors report no conflicts of interest.

Disclaimer

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