Predicting Life Expectancy in Men Diagnosed with Prostate Cancer

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Abstract

Context: The widespread use of prostate-specific antigen (PSA) screening has led to the detection of more indolent prostate cancer (PCa) in healthy men. PCa treatment and screening must therefore balance the potential for life gained against the potential for harm. Fundamental to this balance is physician awareness of a patient’s estimated life expectancy (LE).

Objective: To review the evidence on LE differences between men diagnosed with PCa and the general population. To examine clinician- and model-predicted LE and publicly available LE calculators.

Evidence acquisition: A comprehensive search of the PubMed database between 1990 and September 2014 was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. Free text protocols of the following search terms were used “life expectancy prostate cancer”, “life expectancy non-cancer”, “non-cancer mortality prostate”, and “comorbidity-adjusted life expectancy”. Two internet search engines were queried daily for 1 mo for the search term “life expectancy calculator”, and the top 20 results were examined.

Evidence synthesis: Of 992 articles and 32 websites screened, 17 articles and nine websites were selected for inclusion. Men with non-screening-detected PCa and distant disease at diagnosis were found to have shorter LE than age-matched peers, whereas men with localized PCa had prolonged LE. In general, clinician-predicted 10-yr LE was pessimistic and of limited accuracy; however, model-predicted LE provided only modest improvements in accuracy (c-index of models 0.65–0.84). Online LE calculators provide consistent LE estimates, but government life tables provide LE estimates near the mean for all calculators examined.

Conclusions: The accuracy of clinician-predicted survival is limited, and while available statistical models offer improvement in discrimination, it is unclear whether they provide advantages over freely available government life tables.

Patient summary: We examined differences in life expectancy between men diagnosed with prostate cancer and the general population, and ways of predicting life expectancy to help guide treatment decisions. We found that current models for predicting life expectancy specific to prostate cancer might not be any better than government life tables or simple rules of thumb.

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1. **Introduction**

Following the adoption of widespread prostate-specific antigen (PSA) screening, cases of prostate cancer (PCa) are largely screening-detected. This has had profound effects on both the incidence and prevalence of PCa [1,2] and has introduced biases associated with screening-detected cancer that have made assessment of competing mortality risks central to the care of patients with PCa [3]. These include selection bias, lead-time bias, and length bias.

In 2012, only 40% of the US male population older than 50 yr indicated having undergone PSA testing in the previous year [4]. Not all men offered screening will undertake it, and the population that does may differ significantly from the broader at-risk population (Fig. 1A). On one hand, those who consider themselves at higher risk (African American men, positive family history) may elect to undergo screening; on the other hand, individuals who undergo screening have better overall health behaviors than those who do not. Patients electing to undergo screening may have better diets and healthier lifestyles and may more often choose definitive treatment when diagnosed with cancer [2]. The healthy screener effect was demonstrated in a study of women self-referred for ovarian cancer screening; the rate of mortality from ovarian cancer in the screened cohort was similar to the expected rate of mortality in the unscreened population. Nonetheless, the screened population had lower than expected rates of mortality from colorectal and lung cancer, suggesting healthier life choices and diet, as well as higher health care utilization [5].

While selection bias impacts the population diagnosed with PCa, lead-time bias and length bias have profound effects on the characteristics of the cancer that is detected. Lead-time bias (Fig. 1B) occurs when a man undergoes PSA screening and has his prostate cancer detected n years earlier than it otherwise would have been, so he will live for n years longer with PCa. Because prostate cancer is an indolent disease with a protracted preclinical state, the magnitude of this effect can be quite large; it has been estimated that it is as high as 12.3 yr [6]. Length bias (Fig. 1C) occurs when cancers become detectable (through screening) in their preclinical state. Rapidly fatal cancers remain in a preclinical state for a shorter period of time, limiting the utility of screening, whereas indolent cancers are detectable in the preclinical (asymptomatic) state for a prolonged period.

The net effect of these important biases is increased detection of cancers that are more indolent in healthier people. On this basis and the associated risk of overtreatment [6,7], current guidelines recommend the use of life expectancy (LE) estimation to help balance the potential for life gained against the potential for harm caused by diagnosis and/or treatment of PCa.[3] The purpose of this review is twofold. We first reviewed studies examining the difference in LE between men diagnosed with PCa and the general population. We then reviewed methods of predicting LE. We reviewed studies of LE estimation by health care providers, studies of model-predicted LE, and publicly available LE calculators.

2. **Evidence acquisition**

We conducted a systematic review of the PubMed database between 1990 and September 2014 according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines [8].

The predefined search terms “((life expectancy prostate cancer) OR life expectancy non-cancer) OR non-cancer mortality prostate) OR comorbidity adjusted life expectancy” were used to find 986 articles that were then screened for inclusion. A further six significant studies were
identified by bibliography review. All experimental and observational study designs were eligible for inclusion in this review, including but not limited to controlled clinical trials, statistical modeling, case series, and case-control and cohort studies. Comments, editorials, and review articles were not considered eligible for inclusion. Seventeen studies were included in the review. The flow chart of the systematic literature review is presented in Figure 2.

Predefined criteria for exclusion included: non-English language; assessment of treatment effect; and articles that did not pertain to cancer. For studies reporting from the same data set, the most recent report was used. Two authors (J.S. and F.A.) separately reviewed the records to select the studies; any discrepancy was resolved by the senior author (Q-D.T.) in determining adherence to the prespecified inclusion/exclusion criteria. The study type and the quality of the evidence described were ascertained. There was no examination of an intervention in any of the studies examined, so pooling of outcome measures and meta-analysis were not undertaken.

Assessment of freely available LE calculators was performed via an Internet search. Two widely used search engines (Google.com, Bing.com) were queried for the keywords “life expectancy calculator”. To account for variability in results among searches, the top 20 results were assessed daily for 1 mo (July 15–August 15 2014). Websites that were duplicates of common actuarial data (US Social Security Administration [SSA] life tables) or those lacking clear identification of source data were excluded. Nine readily accessible online LE calculators were identified.

3. Evidence synthesis

3.1. LE in men diagnosed with PCa

Studies examining the effect of cancer on patient mortality have largely focused on the excess mortality attributable to cancer [9], and there are limited data on the non-cancer mortality of cancer patients. As the population of patients surviving cancer expands because of improved detection and treatment, the impact of other-cause mortality will become an increasingly pressing health policy concern. Understanding other-cause mortality requires knowledge of the specific cause of death (COD), which is very challenging to ascertain with a degree of accuracy sufficient for analysis [10,11].

The most common approach to estimating the excess mortality associated with cancer has been relative survival, a method that does not rely on COD information [12]. Relative survival is the ratio of observed survival in a population of cancer patients relative to the background survival rate. Brenner and Arndt [13] used this methodology to examine...
Surviving to 50 yr of age, Surveillance, Epidemiology, and End Results, 2000–2006. Reproduced with permission from Cho et al [13]. Interestingly, they noted an absence of excess mortality in men with well- or moderately differentiated locoregional PCa across all age groups. For grades 1 and 2, the 5-yr relative survival was 5–6% higher among PCa patients than in the general population, while the 10-yr relative survival was 3–6% higher. Cho et al [15] confirmed these findings in a study of 2000–2006 US registry data using a left-truncated survival method in which the hazard of death due to other causes was characterized as a function of age. This study took advantage of a newly created algorithm to accurately ascribe COD in the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute [14]. Comparison of other-cause survival to US life tables revealed a survival benefit for patients with locoregional PCa over the baseline population; this benefit ranges from 4 yr in 70-yr-old men to 6 yr in 50-yr-old individuals. This is in contrast to men diagnosed with distant disease, whose other-cause survival was lower than in the general population (Fig. 3) [15].

![Fig. 3 – The healthy screener effect in prostate cancer. (A) Compared to the US male population, men with PCa have an improved non-cancer survival probability, conditional on surviving to 50 years of age. (B) Men with locoregional prostate cancer have an other-cause survival benefit over the baseline population that ranges from 4 yr in 70-yr-old to 6 yr in 50-yr-old individuals. This is in contrast to men diagnosed with distant disease, whose other-cause survival is lower than in the general population. Estimated non-cancer survival probability for male cancer patients conditional on surviving to 50 yr of age. Surveillance, Epidemiology, and End Results, 2000–2006. Reproduced with permission from Cho et al [15], American Journal of Epidemiology, Oxford University Press.](image-url)
These studies present evidence of the effect of healthy screener bias in the context of PSA screening. Patients diagnosed at an early stage via PSA screening may have better access to health care, higher socioeconomic status, and healthier behaviors, leading to a lower risk of other-cause mortality relative to the general population. Conversely, patients diagnosed with advanced cancer who did not undergo routine PSA screening may also ignore early PCa symptoms and have poor access to health care [15]. Data from the Queensland Cancer Registry support this premise. Examining other-cause mortality in a largely unscreened population of men with PCa diagnosed between 1982 and 2002, Baade et al [16] found a mortality ratio 32.6% higher than for the general population, with higher mortality rates for poisoning and respiratory, digestive, and cardiovascular (CV) diseases.

3.2. Clinician-predicted LE estimation

PSA screening for early detection of prostate cancer is a hotly contested and widely scrutinized practice. The US Preventative Services Task Force currently recommends against PSA screening in any age group [17]. Prior statements and guidelines from other national and international panels recommended screening only in men with LE of >10 yr [18–20]. Nonetheless, as recently as 2012, the prevalence of screening remained higher among men aged >80 yr (35.3%) than among those aged 55–69 yr (32.3%) [4]. Such data suggest that selective screening based on LE is not routinely practiced. In addition to screening recommendations, guidelines for PCa treatment have also used a 10-yr threshold for recommending definitive treatment with radical prostatectomy (RP) or radiotherapy (RT) [21]. However, the premise underlying these recommendations is that health care providers have the ability to predict 10-yr LE. There is limited evidence to support this conjecture.

Koch et al [22] were the first group to examine this 10-yr threshold (Table 2). They examined the actuary-predicted LE of 261 consecutive men undergoing RP with the assumption that men undergoing active treatment were considered by the treating provider to have LE of >10 yr. Their retrospective review revealed that 20% of men undergoing RP had a predicted LE of <10 yr [22]. While these estimates suggest that clinicians can correctly predict 10-yr LE approximately 80% of the time, the effect of case mix plays a significant role. If most of the patients were young and healthy, LE >10 yr is not in question. Similar findings were observed by Krahn et al [23], who examined the predictions of 191 urologists when reviewing 18 patient scenarios and compared them to a Markov model predicting LE based on age and comorbidity. They found that urologists were able to accurately estimate 10-yr LE in 82% of the scenarios examined [23].

Wilson et al [24] found that “even with detailed data on comorbidity, the clinicians in [their] study were generally inaccurate, imprecise and inconsistent in their predictions of patient 10-year survival”. They came to this conclusion after comparing physician (n = 18) reviews to actuarial assessments of survival. Interestingly, they described an inclination toward LE underestimation by a mean of 10.8%. In a hypothetical situation in which guidelines suggest treatment if the estimated 10-yr survival is >50%, the authors determined that physicians would on average recommend treatment 66% of the time for patients with an estimated LE of >10 yr, denying 36% of men appropriate treatment. Inappropriate treatment for men with LE of <10 yr was only 24%.

A limitation of the above studies was the absence of real patient survival data and the comparison to modeled survival estimates (both the Markov model and actuarial estimates have limitations), so the utility of the study findings is limited. Two groups overcame this limitation by comparing clinician-predicted survival (CPS) to actual survival (AS). Walz et al [25] examined the accuracy of 19 clinicians in predicting the 10-yr survival of 50 patients undergoing external-beam radiation therapy (EBRT) or RP (40% had other cause mortality). Examination of the area under the curve (AUC) for receiver operating characteristic curves revealed discrimination of 0.67 (0.60–0.72) for attending urologists, 0.69 (0.64–0.74) for residents, and 0.67 (0.58–0.76) for medical students. The absence of meaningful differences among these groups suggests “that neither expertise nor exposure time are important in predicting LE” [25]; both the best and worst predictions were made by urology staff. Leung et al [29] observed nearly identical findings in an analysis of 100 clinicians reviewing seven clinical scenarios summarized from the charts of deceased patients. They found that the mean estimated LE was -2 yr (standard deviation [SD] 6.1 yr). When the authors dichotomized estimates in terms of correct identification of which patients would live for more than or less than 10 yr, physicians were correct 68% of the time. They found that residents were more accurate than students or attending urologists, and internal medicine clinicians were more accurate than urologists and primary care providers.

A common theme in articles comparing the ability of health care providers to predict LE is that inaccuracies in prediction tend to be unrelated to the level of training or experience. The problem lies in the fact that “inconsistent predictions of LE may lead to patients being managed differently by the same or different doctors despite identical comorbidity” [26]. A second common theme is that the LE estimates of health care providers tend to be overly optimistic when considering patients with short LE, such as patients with metastatic disease presenting for palliative treatment [27,28], whereas estimates of 10-yr LE are largely pessimistic [23–25,29].

3.3. Model-predicted LE

Prediction of LE is challenging and empiric predictions of LE are subject to the experience, judgment, underlying personal beliefs, and prejudices of each individual clinician. Accurate LE prediction for patients with prostate cancer is particularly challenging because such patients in the post-PSA era are largely diagnosed via screening and tend to live longer than their noncancer peers (healthy screener bias, Fig. 1). As a consequence of the limitations inherent to CPS,
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>LoE</th>
<th>Disease entity</th>
<th>Year</th>
<th>Study population</th>
<th>Analysis</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>[27]</td>
<td>Case series</td>
<td>4</td>
<td>Non–small-cell lung cancer</td>
<td>1996</td>
<td>196 patients diagnosed with NSCLC, treated conservatively</td>
<td>Comparison of CPS to AS</td>
<td>Physician LE predictions: Within 1 mo: 10% (19/195) Within 3 mo: 59% (115/196) Within 4 mo: 71% (139/196) Prediction specificity: Survival &lt; 3 mo: 93% Survival &gt; 3 mo: 52%</td>
<td>Highly selective; only examined patients not seeking curative intent</td>
</tr>
<tr>
<td>[22]</td>
<td>Case series</td>
<td>4</td>
<td>PCa</td>
<td>1997</td>
<td>261 men who underwent RP at a single institution</td>
<td>Comparison of physician-estimated LE to actuarial life tables</td>
<td>20% (51/261) undergoing RP had LE predicted to be &lt; 10 yr 10% (26/261) physician-estimated LE was &lt; 10 yr and RP performed at patient insistence</td>
<td>Retrospective review, single institution</td>
</tr>
<tr>
<td>[23]</td>
<td>Survey</td>
<td>4</td>
<td>PCa</td>
<td>2002</td>
<td>191 urologists reviewing 18 patient scenarios</td>
<td>Comparison of physician LE estimates and a Markov model including age and comorbidity</td>
<td>Physician LE predictions: within 1 yr: 31% within 3 yr: 67% LE &lt; 10 yr predicted by 82% Mean prediction error ±2.4–5.2 yr</td>
<td>Scenario format limits incorporation of subtle clinical patient characteristics Use of Markov model as referent limits accuracy</td>
</tr>
<tr>
<td>[24]</td>
<td>Survey</td>
<td>4</td>
<td>No presenting condition</td>
<td>2005</td>
<td>4 urologists, 2 oncologists, and 2 trainee physicians reviewing 70 patient scenarios</td>
<td>Comparison of physician 10-yr survival estimates to actuarial estimates</td>
<td>ANOVA and Bland-Altman analysis</td>
<td>Physicia 10-yr survival estimate: mean: –10.8% underestimation (95% CI –10.1 to –11.5) range –31.2% to +9.9%</td>
</tr>
<tr>
<td>[28]</td>
<td>Case series</td>
<td>4</td>
<td>Metastatic cancer</td>
<td>2005</td>
<td>6 radiation oncologists estimating survival for 739 consecutive palliative therapy patients</td>
<td>Comparison of CPS and AS</td>
<td>Mean AS – CPS, wk (95% CI) Overall: –12.3 (–15.0 to –9.5) At AS &lt; 12 wk: –21.9 (–24.6 to –19.2) At AS 13–26 wk: –19.7 (–24.2 to –15.2) At AS 27–52 wk: –9.7 (–15.4 to –4.0) At AS &gt; 52 wk: 23.0 (12.3–33.8)</td>
<td>Few physicians sampled, single institution, highly selected patient population presenting for palliation</td>
</tr>
<tr>
<td>[25]</td>
<td>Survey/retrospective review</td>
<td>4</td>
<td>PCa</td>
<td>2007</td>
<td>19 clinicians estimated survival &gt; 10 yr for 50 patients undergoing RP or RT (40% had other-cause mortality)</td>
<td>Comparison of CPS (based on clinical vignette) to AS at 10 yr AUC calculated for three groups</td>
<td>AUC (95% CI) for predicting 10-yr LE: All 19 participants: 0.68 (0.64–0.71) Staff: 0.67 (0.60–0.72) Residents: 0.69 (0.64–0.74) Medical students: 0.67 (0.58–0.76)</td>
<td>Retrospective review, single institution, use of case vignettes</td>
</tr>
<tr>
<td>[26]</td>
<td>Survey</td>
<td>4</td>
<td>No presenting condition</td>
<td>2009</td>
<td>20 physicians, 20 nurses, and 20 medical students reviewing 70 cases</td>
<td>Comparison of CPS to actuarial life tables</td>
<td>Mean actuarial survival – CPS, yr (95% CI) Overall: –1.83 (–2.47 to –1.19) Physicians: –1.46 (–2.61 to –0.31) Nurses: –1.79 (–3.06 to –0.53) Medical students: –2.24 (–3.32 to –1.16)</td>
<td>Use of case vignettes</td>
</tr>
<tr>
<td>[29]</td>
<td>Survey/retrospective review</td>
<td>4</td>
<td>No presenting condition</td>
<td>2012</td>
<td>58 physicians, 25 residents, and 17 medical students reviewing 7 charts for deceased patients</td>
<td>Comparison of CPS to AS</td>
<td>Mean AS – CPS, yr (95% CI): Staff: –2.11 (–2.71 to –1.5) Residents: –1.51 (–2.39 to –0.62) Medical students: –2.11 (–2.71 to –1.5) Urology: –1.88 (–2.52 to –1.25) Family medicine: –2.48 (–3.79 to –1.17) Internal medicine: –1.05 (–2.23 to 0.14) Dichotomous 10-yr prediction: 67.4%</td>
<td>Retrospective review, single institution</td>
</tr>
</tbody>
</table>

LoE = level of evidence; NSCLC = non–small-cell lung carcinoma; PCa = prostate cancer; CPS = clinician-predicted survival; AS = actual survival; AUC = area under the curve; CI = confidence interval.
several investigators have sought to model overall survival in men undergoing treatment for PCa.

Albertsen et al. [31] examined a cohort of men diagnosed with PCa between 1971 and 1976 from the Connecticut cancer registry \( (n = 451) \) to determine the effect of comorbidity on LE \( (\text{Table 3}) \). They examined the effect of three comorbidity indexes on survival: the Kaplan-Feinstein index, the Charlson comorbidity index \( (\text{CCI}) \), and the index of coexisting disease. This study was novel in that it clearly demonstrated the importance of comorbidity in LE predictions; external validation of the model revealed a c index of \( 0.71 \) [30,31]. Tewari et al. [32] developed a series of lookup tables incorporating several clinical and demographic characteristics: age, race, comorbidity, prostate specific antigen, cancer grade, and treatment type. The discrimination of this model was \( 0.69 \) for overall survival and \( 0.63 \) for cancer-specific survival. In external validation, the discrimination was \( 0.70 \) [30].

Cowen et al. [30] performed the aforementioned external validation for a retrospective cohort of men who received treatment for PCa with follow-up for \( 13 \) yr \( (1989–2002) \). They created a nomogram that incorporates numerous predictors, including age, CCI, performance status, angina history, blood pressure, body mass index, tobacco use, marital status, PSA, Gleason score, clinical stage, treatment type, and treatment year. The discrimination of their \( 10 \)-yr survival model predictions was \( 0.73 \), a modest improvement over the models of Albertsen et al. [31] and Tewari et al. [32].

The model with the highest c index published to date is by Walz et al. [33], who examined the risk of noncancer mortality within \( 10 \) yr of receiving definitive therapy. The population used to design and test their model included 9131 Canadian men treated with either RP \( (n = 5955) \) or RT \( (n = 3176) \) between 1989 and 2000, and excluded all men who died from PCa. The discrimination of the model, which includes age, treatment type, and CCI, was \( 0.84 \). Although inclusion of treatment selection in the model is appealing, because it incorporates any presumed survival advantage associated with RP, the biases associated with treatment selection are also directly included in the model. In general, RP rather than RT is offered to healthier men, so it is unsurprising that such men live longer, and incorporation of this variable improves model discrimination.

Finally, Mariotta et al. [34] developed a novel approach to race- and gender-specific life tables. Using SEER-Medicare data for patients between 1992 and 2005 \( (n = 1 \ 108 \ 085) \), they estimated the effect of individual comorbidities on survival via Cox proportional hazards modeling; the coefficient estimates of the condition indicators then comprised the weights for each comorbid condition. For each patient, an individual comorbidity score was calculated as a sum of these weights. From these weights, a health- and age-adjusted LE was calculated. There are limitations to this approach, as the life tables were created for all cancers and are not specific for PCa. Furthermore, the discrimination of the model is modest for younger patients soon after diagnosis \( (0.73 \text{ for } 66 \text{-yr-old women, } 0.68 \text{ for } 66 \text{-yr-old men}) \), but is poor in older patients \( 10 \) yr after diagnosis \( (0.58 \text{ for } 80 \text{-yr-old women, } 0.57 \text{ for } 80 \text{-yr-old men}) \). Nonetheless, an advantage of the approach is that it can be incorporated into analyses of observational data [35].

### 3.4. Actuary-predicted survival

Given that actuary-predicted survival was considered the standard for LE prediction in several previous studies, we assessed the calculators freely available to the public and ascertained their usability in clinical practice. Within the top 20 web hits for the search term “life expectancy calculator”, nine unique LE prediction tools were found [36–44]. The number of data points for calculating LE ranges from two (SSA) [44] to 40 (Livingto100.com) [37]. The most common parameters required \( (\geq 75\% \text{ of calculators}) \) are gender, age, weight, height, smoking, alcohol intake, driving habits, and blood pressure. Only one calculator \( (\text{Wharton/UPENN}) \) includes PCa history [39].

To estimate the variance in calculator-predicted LE, we used the nine calculators to determine LE for a series of hypothetical patients, such as a 65-yr-old white male \( (68 \text{ inches tall, } 185 \text{ lbs}) \) with hypercholesterolemia on statins, no family history, 45-pack-yr smoking history, married, nonmanual labor, \$50,000 annual income, and normal sleep patterns. SSA life table predictions yielded LE of \( 83.9 \) yr for all white men aged 65 yr, while actuarial predictions for the hypothetical patient ranged from \( 77.5 \) yr \( (\text{Bankrate}) \) [43] to \( 84.88 \) yr \( (\text{Wharton}) \) [39].

The fact that SSA life tables provide LE estimates close to the mean for the freely available calculators \( (82.66 \pm 3.44 \text{ yr, } \text{mean } \pm \text{SD}) \) is of clinical importance, as LE estimates from SSA life tables are easy to ascertain for inclusion in patient counseling. While the methodology of online calculators is proprietary and not published, the calculators appear to provide fairly consistent LE estimates. This is unsurprising given that most ask similar questions about the major risk factors for CV disease, the leading cause of death in the USA. Given that many men undergoing treatment for PCa receive androgen deprivation therapy \( (\text{which is associated with both fatal and nonfatal CV and metabolic events}) \) as a component of their treatment, LE estimates incorporating CV risk factors may require further adjustment.

### 4. Discussion

The population of men diagnosed with PCa differs from similarly aged men without a PCa diagnosis, largely because of selection bias and the healthy screener effect. Two important biases associated with screening-diagnosed cancers, lead-time bias and length bias, suggest that contemporary patients diagnosed with PCa will live with their disease for a significant period of time. This is supported by data showing that the LE for most PCa patients is higher than what would be expected in age- and race-matched peers [15] and that a diagnosis of locoregional PCa is not associated with excess mortality [13].

Consequently, accurate estimation of LE in PCa patients is of paramount importance to avoid unnecessary treatment in men unlikely to benefit and to afford men with long LE
### Table 3 – Model-predicted life expectancy calculations

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>LoE</th>
<th>Disease entity</th>
<th>Year</th>
<th>Study population or data source</th>
<th>Analysis</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>[31]</td>
<td>Cohort</td>
<td>2c</td>
<td>PCa</td>
<td>1996</td>
<td>451 men 65–75 yr with localized PCa (1971–1976) Conservative treatment, Connecticut tumor registry</td>
<td>CPH modeling of three comorbidity indexes compared to baseline hazard adjusted for age and Gleason score: Kaplan-Feinstein index, CCI, and index of coexisting disease</td>
<td>Comorbidity score from all models was a significant predictor of mortality after adjusting for age and Gleason score</td>
<td>Lack of PSA data or contemporary diagnosis or treatment paradigms</td>
</tr>
<tr>
<td>[32]</td>
<td>Cohort</td>
<td>2c</td>
<td>PCa</td>
<td>2004</td>
<td>1611 men with PCa, 4538 age-matched controls</td>
<td>Propensity score-matched comparison Model variables: age, race, comorbidity, PSA, cancer grade, and treatment type</td>
<td>10-yr overall survival: 67% 10-yr cancer-specific survival: 93% c-index values: Overall survival: 0.69 Cancer-specific survival: 0.63</td>
<td>Retrospective design Nonrandomized treatment assignment Modeling assumptions</td>
</tr>
<tr>
<td>[30]</td>
<td>Cohort</td>
<td>2c</td>
<td>PCa</td>
<td>2005</td>
<td>506 men receiving treatment for localized PCa with &gt;13 yr follow-up</td>
<td>Nomogram created using CPH regression to derive 10-yr survival estimates Model variables: age, CCI, general performance, angina history, BP, BMI, tobacco use, marital status, PSA, Gleason, clinical stage, treatment type</td>
<td>Model discrimination by c statistic: Cowen model [30]: 0.73 Albertsen model [31]: 0.71 Tewari model [32]: 0.70</td>
<td>Retrospective design Nonrandomized treatment assignment Homogeneous population Modeling assumptions</td>
</tr>
<tr>
<td>[33]</td>
<td>Cohort</td>
<td>2c</td>
<td>PCa</td>
<td>2007</td>
<td>9131 men treated with either RP or RT between 1989-2000 (receiving no secondary therapy)</td>
<td>Nomogram predicting 10-yr LE after RP or RT was 84.3% accurate in split sample validation A cutoff of ≤70% was 84% accurate in identifying men who did not survive beyond 10 yr</td>
<td></td>
<td>Retrospective design Nonrandomized treatment assignment No external validation Modeling assumptions</td>
</tr>
<tr>
<td>[34]</td>
<td>Registry/ cohort</td>
<td>2c</td>
<td>Newly diagnosed cancer</td>
<td>2013</td>
<td>1 108 085 patients diagnosed with cancer between 1992 and 2005</td>
<td>Calculation of health-adjusted age: CPH estimate of the effect of comorbidity on noncancer death Comparison to US life tables</td>
<td>Discrimination of LE model 1 and 10 yr after diagnosis: Women aged 66 yr: 0.73 and 0.65 Women aged 80 yr: 0.64 and 0.58 Men aged 66 yr: 0.68 and 0.64 Men aged 80 yr: 0.60 and 0.57</td>
<td>Retrospective design Nonrandomized treatment assignment Modeling assumptions No dichotomous 10-yr assessment</td>
</tr>
</tbody>
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LoE = level of evidence; PCa = prostate cancer; RP = radical prostatectomy; RT = radiation therapy; CPH = Cox proportional hazards; CCI = Charlson comorbidity index; BP = blood pressure; BMI = body mass index; PSA = prostate-specific antigen; LE = life expectancy.

* Tested on the population from the study by Cowen et al [30].
...the opportunity for cure. While avoiding surgery in men aged >70 yr and RT in men aged >75 yr may be prudent unless the cancer is very aggressive and the patient has above-average health, personalizing this decision based on an individual's LE using age and comorbidity would be ideal.

The ability of currently available prediction models to discriminate 10-yr LE ranged from 0.65 to 0.84; however, discrimination (c index, AUC) as a measure of the performance of a predictive model has significant limitations. Discrimination measures how well a model can discriminate between two hypothetical patients (i.e., which patient has higher or lower LE or a higher or lower probability of 10-yr LE). It critically depends on the variation of predictors in the modeled cohort and on the prevalence of the predictor in the cohort. Model calibration describes how close a prediction is to an actual event. Studies of the available models emphasize discrimination, but model calibration is not discussed in depth. Furthermore, a model may be well calibrated on one data set and poorly calibrated on another. For a predictive model to be of clinical use, its performance in a population of interest must first be ascertained [46].

5. Conclusions
The accuracy of CPS is limited and it is unclear whether available statistical models provide any advantages over freely available government life tables. The question of how life expectancy should be estimated remains unanswered.

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