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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 lead to the detection of more indolent prostate cancer (CaP) in healthy men. Prostate cancer treatment and screening must therefore balance the potential for life gained vs. the potential for harm. Fundamental to this balance is physician awareness of a patient's estimated life expectancy.

Objective—To review the evidence on life expectancy (LE) differences between men diagnosed with CaP and the general population. To examine clinician and model predicted LE and examine 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) statement guidelines. Free text protocols of the following search terms were used “life expectancy prostate cancer”, “life expectancy non-cancer”, “non-cancer mortality prostate”, “comorbidity-adjusted life expectancy”. Two internet search engines were queried daily, for one month, for the search term “life expectancy calculator”, and the top 20 results were examined.

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Evidence Synthesis—Of 992 articles and 32 websites screened, 17 articles and 9 websites were selected for inclusion. Men with non-screening detected CaP, as well as distant disease at diagnosis, were found to have a shorter LE than age-matched peers, whereas men with localized CaP had a 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 vary in ease of use, but government life tables provide LE estimates near the mean of all examined calculators.

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

Patient Summary—In this report we examine the differences in life expectancy for men diagnosed with prostate cancer compared to the general population and ways of predicting life expectancy to help guide treatment decisions. We found that current models of predicting life expectancy, specific to prostate cancer, might not be any better than government life tables or simple rules-of-thumb.

Keywords

Prostate cancer; Life Expectancy; Survival; Prediction

Introduction

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

In 2012, only 40% of the U.S. male population over 50 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 (figure 1a). On one hand, those who consider themselves at higher risk (AAM, positive family history) may elect to undergo screening, however 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 increased healthcare utilization[5].

While selection bias impacts the population diagnosed with CaP, lead-time bias and length bias have profound effects on the characteristics of the cancer that is detected. Lead-time bias (Figure 1b) is demonstrated when a man undergoes PSA screening and has his prostate

cancer detected n -years earlier than it otherwise would have been, he will live n -years longer **with** CaP. Because prostate cancer is an indolent disease with a protracted preclinical state, the magnitude of this effect can be quite large; estimated to be as high as 12.3 years[6]. Length bias (Figure 1c) also occurs when cancers become detectable in their preclinical state. Rapidly fatal cancers remain in a pre-clinical state for a shorter period of time, limiting the utility of screening, whereas indolent cancers are detectable in the pre-clinical (asymptomatic) state for a prolonged period.

The net effect of these important biases has been 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 estimation to help balance the potential for life gained vs. potential for harm caused by diagnosis and/or treatment of CaP. [3] The purpose of this review is two-fold. We first review studies examining the difference in life expectancy between men diagnosed with CaP and the general population. We then review methods of predicting LE. We review studies of healthcare provider LE estimation, studies of model-predicted life expectancy, and finally publicly available, life expectancy calculators.

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 statement 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” was used to find 986 articles, which were screened for inclusion. A further 6 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, 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 Figure 2.

Predefined criteria for exclusion included: Non-English Language, assessment of treatment effect, articles that did not pertain to cancer, for studies reporting from the same dataset the most recent report was used. Two authors (J.S. and F.A.) separately reviewed the records to select the studies, with any discrepancy resolved the senior author's (Q-D.T.) determination of adherence to the pre-specified inclusion/exclusion criteria. Study type was ascertained and quality of evidence described. There was no examination of an intervention in any of the examined studies, therefore the pooling of outcome measures and meta-analysis were not undertaken.

The assessment of freely available LE calculators was made through 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 one month (July 15th-Aug 15th 2014). Websites that were

duplicates of common actuarial data (ie. SSA life tables) or those lacking clear identifying of source data were excluded. Nine readily accessible online LE calculators were identified.

Evidence Synthesis

Life Expectancy in men diagnosed with CaP (Table 1)

Studies examining the effect of cancer on patient mortality have largely focused on the excess mortality attributable to cancer[9] and there is limited data on the non-cancer mortality of cancer patients. As the population of patients surviving cancer expands due to 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), the ascertainment of which has historically been 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 used this methodology to examine 180,605 men diagnosed with CaP in the U.S. between 1990 and 2000. In their study, 5- and 10-yr estimates of relative survival were 98.9% and 94.8%, which indicates that excess mortality due to prostate cancer was as low as 1% and 5% within 5 and 10 years following diagnosis, respectively.[13] Interestingly, they noted an absence of excess mortality in men with well- or moderately-differentiated locoregional CaP across all age groups. For grades 1 and 2, the 5-yr relative survival was 5-6% higher in the CaP population than in the general population, while the 10-yr relative survival was 3-6% higher. Cho et al confirmed these findings in a study of 2000-2006 U.S. registry data, using a left-truncated survival method with the hazard of death due to other causes 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] Looking directly at other cause survival, and comparing it to U.S. life tables, they found that patients with loco-regional CaP have a survival benefit over the baseline population ranging from 4 years in 70-year-olds to 6 years in 50-year-olds. This is in contrast to men diagnosed with distant disease, whose other-cause survival was lower than in the general population. [15] (Figure 3)

These studies present evidence of the effect of healthy screener bias in the context of PSA screening. Patients diagnosed at an early stage through PSA screening may have better access to healthcare, 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 CaP 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 CaP diagnosed between 1982-2002, Baade et al found a mortality ratio of 32.6% higher than the general population, with increased mortality rates for poisoning, respiratory disease, digestive disease and cardiovascular disease.[16]

Clinician Predicted Life Expectancy Estimation (Table 2)

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

The first group to examine the “10-yr rule”, Koch et al., examined the actuarial predicted life expectancy of 261 consecutive men undergoing RRP, based on the assumption that men undergoing active treatment were considered by the treating provider to have a LE greater than 10 years. In this retrospective review, they found that 20% of men undergoing RRP had a predicted LE less than 10 years.[22] While these estimates suggest that clinicians can correctly predict LE at 10 years 80% of the time, the effect of case mix plays a significant role. If the preponderance of patients were young and healthy, LE beyond 10 years is not in question. Similar findings were observed by Krahn et al., who examined the predictions of 191 urologists, 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 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”[24]. They came to this conclusion after comparing physician (n=18) reviews to actuarial assessments of survival. Interestingly, they described an inclination toward the underestimation of LE, with a mean underestimation of 10.8%. In a hypothetical situation where guidelines suggest treatment if the estimated 10-yr survival is >50%, the authors determined physicians would on average recommend treatment 66% of the time in patients with >10-yr estimated LE, denying 36% of men appropriate treatment. Inappropriate treatment for men with LE< 10 years 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 their own limitations), thus limiting the utility of the study findings. Two groups overcame this limitation by comparing clinician-predicted survival (CPS) to actual survival (AS). Walz et al. examined the accuracy of 19 clinicians in predicting 10-yr survival of 50 patients undergoing EBRT or RP (40% had other cause mortality). Examination of the area under the curve (AUC) for receiver operating characteristic curves found that attending urologists had a discrimination of 0.67 (0.60–0.72), residents 0.69 (0.64–0.74) and medical students 0.67 (0.58–0.76). The absence of meaningful difference between 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 found 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 yrs (SD: 6.1 yr). When the authors dichotomized estimates in terms of correctly identifying which patients would live more than or less than 10 years, physicians were correct 68% of the time. They found that residents were more accurate than students or attending urologists, and found internal medicine clinicians more accurate than either Urologists or primary care providers.

A common theme amongst articles comparing the ability of healthcare providers to predict LE is that inaccuracies in prediction tend to be unrelated to 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 healthcare provider LE estimates tend to be overly optimistic when considering patients with short LE, as in patients with metastatic disease presenting for palliative treatment[27, 28]; whereas estimates of 10-yr LE are largely pessimistic. [23-25, 29]

Model-Predicted LE (Table 3)

The prediction of LE is challenging and empiric predictions of LE are subject to an individual clinician's experience, judgment, underlying personal beliefs and prejudices. Furthermore, the accurate prediction of LE of patients with prostate cancer is particularly challenging as patients with prostate cancer in the post-PSA era are largely diagnosed through screening and this population tends to live longer than their non-cancer peers (healthy screener bias, Figure 1). As a consequence of the inherent limitations in clinician-predicted survival, several investigators have sought to model overall survival in men undergoing treatment for CaP.

Albertsen et al examined a cohort of men diagnosed with CaP between 1971-1976 from the Connecticut cancer registry (n= 451). The goal of their study was to examine the effect of comorbidity on LE. As such, they examined the effect of three comorbidity indexes on survival (Kaplan-Feinstein index, Charlson Comorbidity Index, Index of Coexisting Disease). This study was novel in that it clearly demonstrated the importance of comorbidity in LE predictions; in a external validation of the model, it was found to have a c-index of 0.71.[30, 31] Tewari et al developed a series of lookup tables incorporating several clinical and demographic characteristics: age, race, comorbidity, prostate specific antigen, cancer grade, and treatment type.[32] The discrimination of this model was 0.69 for overall survival and 0.63 for cancer specific survival. In external validation, discrimination was found to be 0.70.[30]

Cowen et al performed the aforementioned external validations on a retrospective cohort of men receiving treatment for CaP and followed for 13 years (1989-2002). They also created a nomogram incorporating numerous predictors including age, CCI, performance status, angina history, blood pressure, body mass index, tobacco use, marital status, PSA, Gleason sum, clinical stage, treatment type and treatment year. The discrimination of their 10-yr survival model predictions was 0.73, a modest improvement over the Albertsen and Tewari models.

The model with the highest c-index published to date is by Walz et al. examining the risk of non-cancer mortality within 10 years of receiving definitive therapy.[33] The population used to design and test their model included 9131 Canadian men treated with either radical prostatectomy (n=5955) or EBRT (n=3176) between 1989 and 2000 and excluding all men who died from CaP. Incorporating age, treatment type and CCI, the model discrimination was 0.84. While the approach of including treatment selection into the model is appealing, as it incorporates any presumed survival advantage associated with RP, its inclusion also incorporates the biases associated with treatment selection directly into the model. In general RP is offered to healthier men than RT, so it is unsurprising that they live longer, and incorporation of this variable improves model discrimination.

Finally, Marriotta et al have recently developed a novel approach to race- and gender-specific life tables.[34] Using SEER-Medicare patients between 1992-2005 (n=1,108,085), the effect of individual comorbidities on survival was estimated with 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, an individual health- and age-adjusted LE were calculated. There are limitations to this approach, as the life tables were created for all cancers and are not specific for CaP. Furthermore, the discrimination of the models is modest for younger patients soon after diagnosis (66 yr-old women = 0.73, 66 yr-old man = 0.68), but is poor in older patients 10 years after diagnosis (80 yr-old women = 0.58, 80 yr-old man = 0.57). Nonetheless their approach has the advantage of being able to be incorporated into the analysis of observational data.[35]

Actuarial Predicted Survival (Table 4)

Given that actuarial predicted survival is considered as the standard for LE prediction by several of the 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”, 9 unique LE prediction tools were found (see Table 4).[36-44] The number of data points to calculate LE ranged from 2 (Social Security Administration) to 40 (Livingto100.com).[37, 44] The most common questions asked (in over 75% of calculators) were gender, age, weight, height, smoking, alcohol intake, driving habits, blood pressure. Only a single calculator (Wharton/UPENN) asked about prostate cancer history. [39]

To estimate the variance in calculator-predicted LE, we calculated the LE in each of the 9 calculators for a series of hypothetical patient. For example: a 65yo, white male, 68 inches tall, 185 lbs, hypercholesterolemia on statins, no family history, 45 pack-yr smoking history, married, non-manual labor, \$50,000 annual income, normal sleep patterns. SSA life table predictions demonstrated a LE of 83.9 yrs for all white men aged 65, the range of actuarial predictions for the hypothetical patient was from 77.5 (Bankrate) to 84.88 (Wharton).[39, 43]

The fact that SSA life tables provide estimates of LE near the mean for the freely available calculators (82.66yrs(SD +/- 3.44)) is of clinical importance as LE estimates from SSA life tables can be easily ascertained and incorporated into patient counseling. While the

methodology of online calculators is proprietary and not published alongside the calculators, they appear to provide fairly consistent estimates of LE. This is unsurprising given that most ask similar questions about the major risk factors for cardiovascular disease, the leading cause of death in the US. Given that many men undergoing treatment for CaP receive androgen deprivation therapy (which is associated with both fatal and non-fatal CV and metabolic events[45]) as a component of their treatment, LE estimates incorporating CV risk factors may require further adjustment.

Discussion

To summarize, the population of men diagnosed with CaP is different from similarly aged men without CaP diagnosis, in large part due to selection bias and the “healthy screener” effect. Two important biases associated with screening diagnosed cancers, lead-time and length bias, suggest that contemporary patients diagnosed with CaP will live for a significant period of time with the diagnosis. This is supported by data showing that the LE for most CaP patients is in fact higher than what would be expected in age- and race-matched peers[15] and that diagnosis with loco-regional CaP is not associated with excess mortality. [13]

Consequently, the accurate estimation of LE in CaP patients is of paramount importance to avoid unnecessary treatment in men unlikely to benefit, but also to afford men with a protracted LE the opportunity for cure. While on average, avoiding surgery in men over 70 and radiotherapy in men over 75 unless cancer is very aggressive and patient is above average health may be prudent, personalizing this decision based on an individuals LE using age and comorbidity would be ideal.

The ability of the currently available prediction models to discriminate 10-yr LE ranged from 0.65-0.84, however discrimination (C-index, AUC), as a measure of a predictive model's performance, has significant limitations. Discrimination measures how well a model can discriminate between two hypothetical patients (ie. which patient has a higher vs. lower LE or higher vs. lower probability of 10-yr LE). It is critically dependent on the variation of predictors in the modeled cohort as well as the prevalence of the predictor in the cohort. Calibration is the characteristic of a model that 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 dataset and poorly calibrated on another. For a predictive model to be of clinical use its performance on a population of interest must first be ascertained[46].

Conclusion

The accuracy of clinician-predicted survival is limited and it is unclear that the 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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Figure 1.

Three biases associated with screening detected cancers that necessitate the assessment of competing mortality when treating men with prostate cancer (CaP). **Selection bias** or the “healthy screener effect” (Figure 1a): Men undergoing prostate specific antigen (PSA) screening may have better diets, healthier lifestyles, and improved access to care relative to unscreened men. **Lead-time bias** (Figure 1b): the detection of prostate cancer with PSA can lead to improved perceived survival in absence of any modification of the disease course. **Length bias** (Figure 1c): PSA screening detects CaP in the asymptomatic phase; because fast-growing tumors have a shorter asymptomatic phase than slower-growing tumors, PSA screening will preferentially detect indolent cancer.

Figure 2.
Flow chart of the systematic review.

Figure 3.

The “healthy screener” effect in CaP: Compared to U.S. life tables, patients with loco-regional prostate cancer have an other-cause survival benefit over the baseline population ranging from 4 years in 70-year-olds to 6 years in 50-year-olds. This is in contrast to men diagnosed with distant disease, whose other-cause survival was lower than in the general population. Estimated non-cancer survival probability for male cancer patients conditional on surviving to 50 years of age, Surveillance, Epidemiology, and End Results, 2000–2006. Reproduced with permission, from Cho et al American Journal of Epidemiology, Oxford University Press.

Table 1
Studies demonstrating life expectancy differences between men diagnosed with CaP and the general population

Reference	Study type	Data Source	Year	Study population	Analysis	Findings	Limitations
Brenner and Arndt	Retrospective Cohort	SEER	2005	U.S. men (n=180,605) diagnosed with prostate cancer between 1990-2000	Period analysis of 5 & 10 year survival. Relative survival estimates derived by Hakulinen's method using sex, age, race specific life tables.	5 & 10 yr relative survival estimates (SE): Overall: 98.9% (0.4) & 94.8% (0.7) Grade 1: 106.1 (1.4) & 106.0 (2.0) Grade 2: 105.1 (0.4) & 103.4 (0.9) Grade 3-4: 92.3 (1.1) & 82.4 (1.8) Distant Stage: 31.3 (2.0) & 19.9 (1.9)	Missing stage at diagnosis in 8.2% of patients
Baade et al	Retrospective Cohort	Queensland Cancer Registry	2006	People 20-79 y/o diagnosed with cancer in Queensland Australia 1982-2002, matched to the total Queensland population	Indirectly age standardized mortality ratios for non-cancer mortality in cancer patients	Diagnoses- 13,010 SMR (a)= 132.6 (126-140) Increased mortality rates for poisoning, respiratory disease, digestive disease, cardiovascular disease	Largely unscreened population, population censored at 80, focus on premature mortality
Cho et al.	Retrospective Cohort	SEER-Medicare	2012	U.S. patients (50/older) diagnosed with cancer between 2000-2006 (315,155 with prostate cancer)	Other cause survival analyzed by a left-truncated survival method, relative to U.S. life tables	Median non-cancer conditional survival benefit(b,c): at 50 yrs old: +6yrs(loco-regional), -6yrs (distant) at 60 yrs old: +6yrs(loco-regional), -3yrs (distant) at 70 yrs old: +4yrs (loco-regional), -1yrs (distant)	all cancer patients included

^a SMR = Indirectly age-standardised mortality ratio. A value of 100 suggests that the mortality among the cancer cohort is the same as the mortality in the Queensland population over the same period, matched by age group and sex. 95% confidence intervals in brackets SE- standard error.

^b Results are conditional on surviving at 50, 60, and 70 years of age.

^c Negative values represent median survival ages lower than those of the general US population.

Table 2
Studies examining health care provider life expectancy prediction

Reference	Study Type	Disease Entity	Year	Study population	Analysis	Results	Limitations
Muer et al	Prospective cohort	NSCLC(non small cell lung Ca)	1996	196 patients diagnosed with NSCLC, treated conservatively	Comparison of clinician predicted survival (CPS) to actual survival (AS)	Physician LE Predictions: Within 1 month- 10% (19/156) Within 3 months- 59% (115/196) Within 4 months- 71% (139/196) Specificity for predicting survival <3mo : 93% Sensitivity for predicting survival <3mo : 52%	Highly selective: only examined patients not seeking curative intent
Koch et al	Retrospective Review	Prostate Cancer	1997	261 men who had undergone RRP. Single institution. Physician estimated LE > 10yrs	Comparison of physician estimated LE with Actuarial Life tables	20% (51/261) undergoing RRP had LE predicted to be <10yr. 10% (26/261) physician estimated LE was <10yr and RRP was carried out at patient insistence	retrospective review, single institution
Krahn et al	Survey	Prostate Cancer	2002	191 Urologists reviewing 18 patient scenarios	Comparison to physician LE estimates to a Markov model including age and comorbidity	Physician LE Predictions: within 1 year: 31% within 3 years: 67% LE<10yr: predicted 82% avg prediction error +/- 2.4-5.2 years	Scenario based format limits incorporation of subtle clinical patient characteristics Use of Markov model as referent standard limits accuracy
Wilson et al	Survey	No presenting condition	2005	18 Physicians reviewing 70 patient scenarios: 4 Urologists 2 Oncologists 12 Trainee Physicians	Comparison to physician estimated 10-yr survival probability to actuarial estimates, ANOVA and Bland-Altman Analysis	Physician 10yr survival estimate: mean: -10.8% underestimation (95%CI: -10.1 to -11.5) range: -33.2% to +3.9%	Relatively few physicians sampled UK physicians only Scenario based format limits incorporation of subtle clinical patient characteristics
Chow et al	Prospective cohort	Metastatic Cancer	2005	6 radiation oncologists providing survival estimates on 739 consecutive palliative therapy patients	Comparison of clinician predicted survival (CPS) to actual survival (AS)	AS - CPS: mean weeks (95%CI) overall: -12.3 (-15.0, -9.5) @ AS < 12 wk: -21.9 (-24.6, -19.2) @ AS 13-26 wk: -19.7 (-24.2, -15.2) @ AS 27-52 wk: -9.7 (-15.4, -4.0) @ AS >52 wk: 23.0 (12.3, 33.8)	Few physicians sampled Single institution Highly selected patient population presenting for palliation
Walz et al.	Survey/Retrospective Review	Prostate Cancer	2007	19 clinicians Estimating survival > 10yr for 50 patients undergoing RP or EBRT (40% had other cause mortality)	Comparison of CPS (based on clinical vignette) to AS at ten years. Area under the curve calculated for	AUC for predicting the 10-year LE: All 19 participants: (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)	Retrospective review, Single institution, Use of case vignettes

Reference	Study Type	Disease Entity	Year	Study population	Analysis	Results	Limitations
					three clinical groups defined as staff, residents and medical students. three clinical groups defined as staff, residents and medical students. three clinical groups defined as staff, residents and medical students.		
Clarke et al	Survey	No presenting condition	2009	20 Physicians 20 Nurses 20 Medical students reviewing 70 cases	Comparison of CPS to actuarial life tables	Actuarial predicted survival - CPS: mean years (95%CI) Overall: - 1.83 (-2.47, -1.19) Physicians: - 1.46 (-2.61, -0.31) Nurses: -1.79 (-3.06 to -0.53) Medical students: - 2.24 (-3.32 to -1.16) yrs p-value between groups: 0.61	Use of case vignettes
Leung et al	Survey/Retrospective Review	No presenting condition	2012	58 Physicians 25 Residents 17 Medical students Reviewing 7 charts of deceased patients	Comparison of clinician predicted survival (CPS) to actual survival (AS)	AS - CPS: mean years (95%CI) Staff: -2.11(-2.71, -1.5) Residents: -1.51(-2.39, -0.62) Medical Students: -2.11(-2.71, -1.5) Urology: -1.88(-2.52, -1.25) Family Med: -2.48(-3.79, -1.17) Internal Med: -1.05(-2.23, 0.14) Dichotomous 10-yr prediction: 67.4%	Retrospective review Single institution

Table 3

Model predicted LE calculations

Reference	Study Type	Disease Entity	Year	Study population/Data source	Analysis	Results	Limitations
Alnbjerg et al	retrospective cohort	Prostate Cancer	1996	451 men 65-75 dx'd with localized CaP 1971-76. Conservative Tx Connecticut Tumor Registry	Proportional hazards modeling of 3 comorbidity indexes compared to baseline hazard adjusted for age and Gleason score: Kaplan-Feinstein index Charleson Comorbidity Index Index of Coexisting Disease	Comorbidity score from all models was a significant predictor of mortality after adjustment for age and Gleason score	Lack of PSA data or contemporary diagnosis/treatment paradigms
Tewari et al	retrospective cohort	Prostate Cancer	2004	1611 men with CaP 4,538 age matched controls	Propensity Score Matched comparison, Model Variables: age, race, comorbidity, prostate specific antigen, cancer grade, and treatment type	10-year overall survival: 67% 10-yr Cancer specific survival: 93% C-index values Overall survival: 0.69 Cancer specific survival: 0.63	Retrospective study design Non-randomized treatment assignment Modeling assumptions
Cowen et al	retrospective cohort	Prostate Cancer	2005	506 men receiving Tx for localized CaP > 13 yrs F/U	Nomogram created using proportional hazards regression to derive 10 yr survival estimates. Discrimination assessed by c-statistic. Model variables: age, CCI, general performance, angina history, blood pressure, body mass index, tobacco use, marital status, PSA value, Gleason sum, clinical stage, and treatment type	Discrimination of Cowen model: 0.73 Discrimination of Alnbjerg model * : 0.71 Discrimination of Tewari model * : 0.70	Retrospective study design Non-randomized treatment assignment Homogenous population Modeling assumptions
Walz et al	Registry Cohort	Prostate Cancer	2007	9,131 men treated with either RP or RT between 1989-2000 (receiving no secondary therapy	All mortality considered no CaP mortality. Nomogram created using Cox proportional hazards regression to derive 10 yr survival estimates. Model Variables: Age, CCI, treatment type	The nomogram predicting 10 year LE after either RP or EBRT was 84.3% accurate in split sample validation A cutoff of 70% or less was 84% accurate in identifying men who did not survive beyond 10 years.	Retrospective study design Non-randomized treatment assignment No external validation Modeling assumptions
Mariotto et al	Registry Cohort	Newly Diagnosed Cancer	2013	1,108,085 patients who were diagnosed with cancer between 1992 and 2005	Calculation of health adjusted age: Cox proportional hazards estimate the effects of comorbid conditions on	Discrimination of LE Model: Men: 1 yr / 10 yr after diagnosis Age 66: 0.73 / 0.65	Retrospective study design Non-randomized treatment assignment

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Reference	Study Type	Disease Entity	Year	Study population/Data source	Analysis	Results	Limitations
					noncancer death Comparison noncancer death Comparison noncancer death Comparison	Age 50: 0.64 / 0.58 Age 60: 0.64 / 0.58 Age 70: 0.64 / 0.58 Age 80: 0.64 / 0.57	Modeling assumptions No dichotomous 10-yr assessment

* -tested on the population from the Cowen study