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A systematic literature review of life expectancy prediction tools for localized prostate cancer patients

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Abstract

Purpose—We aimed to develop a clinical decision support tool for clinicians counseling patients with localized prostate cancer. The tool would provide estimates of patient life expectancy from age, comorbidities, and tumor characteristics. We reviewed the literature to find suitable prediction models.

Materials and Methods—We searched the literature for prediction models for life expectancy. Models were evaluated in terms of whether they provided an estimate of risk, incorporated comorbidities, were clinically feasible and gave plausible estimates. Clinical feasibility was defined in terms of whether the model provided coefficients, could be used in the initial consultation for men across a wide range of ages without an undue burden of data gathering.

Results—Models in the literature were characterized by the use of life years rather than a risk of death, questionable approaches to comorbidities, implausible estimates, questionable recommendations, and poor clinical feasibility. We found tools based on applying an unvalidated approach to assessing comorbidities to a clearly erroneous life expectancy table, or required a treatment decision be made before life expectancy could be calculated or gave highly implausible estimates, such as a substantial risk of prostate cancer specific mortality even for a highly comorbid 80 year old with Gleason 6 disease.

Conclusions—We found gross deficiencies in current tools that predict risk of death from other causes. No existing model was suitable for implementation in our clinical decision support system.

Keywords

life expectancy; radical prostatectomy

Introduction

Assessment of life expectancy is a critical element in treatment decision-making for localized prostate cancer, with only those men expected to live for many years being considered for immediate curative treatment. Assessment of life expectancy is now incorporated into many treatment guidelines, with those of the National Comprehensive

Cancer Network (NCCN) being a typical example (“Life expectancy estimation is critical to informed decision-making in prostate cancer early detection and treatment.”)[1] These guidelines also present algorithms for making treatment decisions based on cancer risk and life expectancy.

We sought to develop a clinical decision support tool that could be used during initial consultations for prostate cancer treatment. We wanted to consider whether life expectancy and cancer risk could be integrated in more complex ways than the NCCN’s approach of a given life expectancy for a given risk category (e.g. 10 years for low risk disease). We hoped to develop a tool that gave the probability of death from untreated prostate cancer at specific time points based on cancer risk, and the probability of death from other causes, based on age and health status. The tool would then combine these numbers to calculate a risk of death from prostate cancer taking into account the risk of death from other causes. Our aims were consistent with decision tools widely used in other cancers, such as the Adjuvant online model for predicting benefit of adjuvant chemotherapy for women with breast cancer. [2]

Given that evaluation of life expectancy and prostate cancer risk is recommended as a key part of decision making for most of the 250,000 US men diagnosed annually with prostate cancer, we expected that we would be able to use an existing, validated “off the shelf” prediction model and that our main work would involve programming the interface to be used in clinic. We performed a literature search in order to find suitable tools. What we found surprised us: models recommended in the literature were either inappropriate for routine clinical use or gave grossly inadequate estimates. We therefore repeated our initial search and evaluation more systematically, in order to give a more formal review of life expectancy estimation in prostate cancer. Here we report our findings.

Materials and Methods

A PubMed search was performed from 1985 through June of 2014, using the following key words, including both medical subject heading (MeSH) terms and free language words/phrases: “prostate cancer life expectancy”, “prostate cancer mortality”, and “comorbidity adjusted life expectancy”. We also considered the reference lists for all studies selected by the search. Articles were manually screened to determine whether they met the criteria for this review. We were only interested in articles that provided life expectancy estimates for males based on age and health status.

For each of the final articles we performed a thorough analysis to determine if the tool could be utilized in the clinical setting and produce accurate predictions. Each of the final articles selected were evaluated on the basis of four criteria: 1) provided risk estimates and not remaining number of life years, 2) used a valid approach to defining comorbidities, 3) the tool could be implemented in the clinical setting, and 4) the estimates were plausible. These criteria were seen as central to our goal of developing a life expectancy tool that could be used at the point of care.

First, risk estimates were preferred over remaining number of life years because not only do clinicians generally have a better understanding of risk than life expectancy, but it is difficult to combine remaining number of life years with the probability of cancer-specific mortality based on tumor characteristics in order to provide adjusted estimates of prostate risk.

Additionally, the cut-point of life expectancy sufficient to warrant treatment can be lower for high risk cancers, but it can be difficult to justify a specific cut-point for a particular level of cancer risk. For instance, the NCCN's use of 10 years as the minimum life expectancy for low risk disease is not explicitly justified and certainly seems low, given the indolent course of such tumors. It would suggest, for example, that it would be justified to treat a 76 year-old man with average health who had Gleason 6, T1C disease. Moreover, the life-expectancy cut-points for men with intermediate risk disease were not addressed, even though life-expectancy might influence treatment decisions in this group.

Second, our primary goal was to create a tool for individualized patient care and so the model must use a valid approach for including comorbidities. Since there are important differences in risk between comorbidities, we sought a model that incorporated such differences by weighting comorbidities appropriately in the risk model. A man with congestive heart failure as a sole comorbidity would have the same total number of comorbidities as a man with asthma, but would likely have a lower life expectancy. Additionally, the comorbidities and their associated risks must be pertinent to a contemporary prostate cancer patient. Typically, risks of other-cause mortality from specific comorbidities will vary over time (e.g. HIV in 1980 vs. 2014). Therefore, the comorbidities for any model must provide risks that are appropriate for a contemporary patient.

Third, the tool must be feasible for clinical practice. For that reason, the model must provide the necessary coefficients so software could be developed for a clinical decision support tool. Since our goal was to create a the tool that would aid in the process of treatment selection, we required that the model should not require a treatment to be prespecified before use, should be applicable to men across a wide range of ages, defined as 45–90, and should not involve any other restrictions on the population such as being limited to only clinical stage T2 patients. Additionally, we specified that the tool should not require more than 20 data points as a routine part of clinical work up since we did not want life expectancy estimation to add undue burden.

Finally, we checked that the model provided plausible estimates that were approximately consistent with our expectations. A tool that will be utilized at the point of care to assist with decision-making must consider accuracy its top priority. Therefore, each tool must produce reasonable estimates for a wide range of test cases.

Results

The search returned a large number of results for each phrase: 874 for “prostate cancer life expectancy”, 583 for “prostate cancer mortality”, and 96 “comorbidity adjusted life expectancy”. After screening the retrieved articles and scanning the reference lists of those meeting our inclusion criteria, we identified a total of 14 articles. Three used life tables to assist predicting life expectancy [3–5], ten presented prediction models [4–13], and three

presented risk scores [14–16]. Of the three papers that used life tables, two used the United States life tables [3, 5] while the other used the United Kingdom life tables [4]. The remaining studies used SEER or Medicare data [5–8], came from US institutions [9, 11–16] or a Canadian Health insurance database [10].

We evaluated each of these articles against the 4 previously mentioned criteria and no tool met all 4 criteria for clinical use. (Appendix 1)

Use of life years remaining rather than risk of death

The life expectancy tool recommended by the NCCN[1] and in official course materials of the American Urological Association, is the Social Security Administration tables.[17] These present the number of expected years left at a given age, such as 17.5 for a 65 year old and 9.7 for a 77 year old. As pointed out above, estimates in this form cannot easily be integrated with cancer risk.

Invalid approach to comorbidities

Life expectancy depends on both age and health status. Yet many of the tools we found either ignored comorbidities or used them in questionable ways. The NCCN recommends adjusting life expectancy by adding 50% for patients in the best quartile of health and subtracting 50% for patients in the worst quartile of health.

There are several problems with this approach. First, what defines “best” and “worst” is based on the clinician’s subjective and unguided assessment. This is unsubstantiated and indeed, the literature suggests that clinicians are poor judges of prognosis on the basis of patient health.[18, 19] Second, the assumption of similar life expectancy within quartiles is highly problematic. Life expectancy at age 60 is 21 years, which is adjusted to 10.5 years for those in the lowest quartile of health. Under the NCCN guidelines, this would suggest that all 60 year-olds should be treated, even those in hospice care or with multiple, serious illnesses.

A more formal comorbidity assessment is the Charlson comorbidity index.[14] This is based on a sample of 559 New Yorkers admitted as in-patients in 1987. The applicability and accuracy of this model to contemporary out-patients remains extremely unclear, for instance, HIV infection is given a risk score 6 times that of heart disease.

Two other comorbidity indices, the Kaplan-Feinstein index [15] and the index of coexistent disease (ICED)[16], raised similar concerns as the Charlson comorbidity index. Both evaluated a limited number of comorbidities and were developed on small cohorts that were not initially treated for prostate cancer.

Furthermore, Albertsen et al. [20] evaluated all three comorbidity indices on a small cohort of men with clinically localized prostate cancer(n=451) and demonstrated only a modest ability of these indices to stratify patient’s all and other cause mortality. For example, the Charlson comorbidity index and ICED had a 15-year cumulative mortality of about 30% for a patient without comorbidities and 50% for all other patients while the Kaplan-Feinstein

index had 15-year cumulative mortality estimates of about 60% for the highest group, 50% for the middle groups, and 40% for the lowest group.

Implausible estimates and questionable recommendations

Some of the models we investigated provided estimates or recommendations that were highly questionable at face value. The Social Security Administration tables include all men at a given age, including those who are morbidly ill and would therefore be unlikely to present for treatment of localized prostate cancer. There is also direct empirical evidence that men presenting with prostate cancer are typically healthier than the general population. [21] As a result, these tables underestimate life expectancy for a typical prostate cancer patient. Conversely, as pointed out above, the NCCN guidelines suggest that radical prostatectomy be considered for 25% of 80 year-olds, and for a 60-year old with multiple, serious comorbidities.

Another model we evaluated was presented as an online tool (http://www.roswellpark.org/apps/prostate_cancer_estimator) based on the findings from Kim et al.[3]. This tool provides a life expectancy in terms number of remaining years and a risk of death from prostate cancer based on the inputs of age, health status, and Gleason score. Many of the estimates for the risk of death from prostate cancer are obviously implausible. For example, the tool gave a healthy 50 year-old male with a Gleason 6 disease a 50% lifetime risk of death from prostate cancer. For the model to give a risk of prostate cancer death below 2%, a patient had to be aged at least 100, be in the bottom quartile of health and have Gleason 6 disease.

The measure of actuarial life expectancy (MALE) model [4], based on UK data, gave life expectancies that differed importantly from US Social Security Administration data. For instance, the MALE model gives an estimated probability of 15-year survival for a healthy 65 year-old that is lower than the average for the US population (55% vs. 59%), even though the latter includes men who are seriously ill.

Lack of clinical feasibility

Several models we considered would be difficult or impossible to implement in clinical practice (Appendix 2). One model did not provide the necessary coefficients for clinical application and was developed on SEER data, which are limited to patients 66 and older.[6] Three other models developed on Medicare or SEER data were also limited men over the age of 65 and would not be applicable to younger patients presenting with prostate cancer. [5, 7, 8] Four models presented risks of other cause mortality only after a treatment was already selected. [9–12] These estimates are clearly influenced by treatment selection. For instance, in the Walz et al. model, a 65-year-old patient with 3 comorbidities would have a 10-year probability of death from other causes of 80% if treated by radiotherapy but 40% by surgery. Radiotherapy is clearly not associated with an $80\% - 40\% = 40\%$ death rate from toxicity, so this difference must reflect selective referral to radiotherapy for less healthy patients. A model that estimates other-cause life expectancy or survival after treatment is selected is inappropriate because the aim of our decision tool was to help determine treatment decision-making, for instance, selecting a less morbid treatment for a patient with shorter expected survival.

Tewari et al. [13] presented tables of 10-year overall survival for both white and black males but these were limited to clinically localized T1–T2 prostate cancer, utilized the Charlson comorbidity index, and also required a treatment to be selected.

The MALE model [4] required an abundance of specific comorbidity details such as angina classification or the level of aortic stenosis. In our view, obtaining such extensive information would not be feasible during an initial consultation for prostate cancer treatment. It is also questionable whether a substantial proportion of patients would know correct responses to questions such as the type of atrial fibrillation.

Discussion

We found gross deficiencies in current tools that predicted risk of death from other causes. Tools were either inappropriate for use in the clinic or provided highly questionable estimates or recommendations, such as surgery for low risk cancer in a substantial proportion of 80 year olds. Although treatment guidelines consider life expectancy as a criterion for determining treatment options, we were unable to identify any tools that could be appropriately used into a point-of-care decision aid.

Jeldres et al. [22] encountered similar problems when evaluating tools that could aid clinicians in predicting life expectancy for prostate cancer patients. Although they report concordance indices ranging from 0.60 – 0.84, the tools with higher discrimination, those of Walz et al. [10] and Cowen et al. [12], both required a treatment to be selected to obtain predictions

Kim et al. [23] also report on the lack of life expectancy tools being utilized by clinicians. They found that only one in four radiation oncologists or urologists used a formal method for evaluating life expectancy. This finding might best be interpreted as rational behavior, given the lack of appropriate tools.

Providing support for the completeness of our literature search, Shariat et al. [24, 25] presented catalogs of currently available prostate cancer prediction tools. Of the 111 models in total, only 5 pertained to life expectancy. All of these were included in our review.

In conclusion, we were unable to identify a life expectancy tool that could be integrated into a point-of-care decision aid to inform initial treatment decision-making in prostate cancer. We are therefore currently developing and evaluating a new tool and plan to report on our findings in the future.

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Appendix 1

Evaluation of selected life expectancy publications

Reference	Model type	Data source	Provided risk estimates	Appropriate comorbidity use	Clinically feasible	Plausible estimates
Charlson et al.[14]	Risk Score	New York Hospital-Cornell Medical Center	Yes	No	Yes	No
Kaplan et al.[15]	Risk Score	West Haven Veterans Administration Hospital	No	No	No	N/A
Greenfield et al.[16]	Risk Score	Four California and Massachusetts teaching hospitals	No	No	No	N/A
Kim et al.[3]	Life tables	Social Security Administration Tables	Yes	No	No	No
Feuer et al.[6]	Prediction Model	SEER	Yes	No	No	Yes
Clarke et al.[4]	Life tables/Prediction Model	Government Actuary Department UK life tables	Yes	Yes	No	No
Tan et al.[7]	Prediction Model	Medicare claims data	No	Yes	No	N/A
Cho et al.[8]	Prediction Model	SEER	No	Yes	No	N/A
Mariotto et al. [5]	Prediction Model/Life tables	SEER	Yes	Yes	No	Yes
Kutikov et al.[9]	Prediction Model	CaPSURE	Yes	No	No	Yes
Walz et al.[10]	Prediction Model	Quebec Health Plan database	Yes	No	No	Yes
Tewari et al.[11]	Prediction Model	Henry Ford Health System	No	No	No	N/A
Cowen et al.[12]	Prediction Model	Community based, tertiary care health center	Yes	No	No	Yes
Tewari et al.[13]	Prediction Model	Henry Ford Health System	Yes	No	No	Yes

Appendix 2

Clinical feasibility of life expectancy publications

Reference	Provided Coefficients	No treatment prespecified	Appropriate age requirements	Data are part of routine clinical practice
Charlson et al.[14]	Yes	Yes	Yes	Yes
Kaplan et al.[15]	No	Yes	Possibly	Yes
Greenfield et al.[16]	Yes	Yes	Yes	No
Kim et al.[3]	Yes	Yes	No	Yes
Feuer et al.[6]	Yes	Yes	No	Yes
Clarke et al.[4]	Yes	Yes	Yes	No
Tan et al.[7]	Yes	Yes	No	No
Cho et al.[8]	Yes	Yes	No	Yes
Mariotto et al. [5]	Yes	Yes	No	Yes
Kutikov et al.[9]	Yes	No	No	Yes
Walz et al.[10]	Yes	No	No	Yes
Tewari et al.[11]	No	No	No	Yes
Cowen et al.[12]	Yes	No	Possibly	Yes
Tewari et al.[13]	No	No	Possibly	Yes