Development and Validation of a Clinically Usable Prediction Model for Other-Cause Mortality in Men with Prostate Cancer using Two Prospective National Cohorts

Elizabeth C Chase[1], Alex K Bryant[2], Robert T Dess[2], William C Jackson[2], Daniel E Spratt[2], Matthew J Schipper[1,2]

[1]University of Michigan Department of Biostatistics

[2]University of Michigan Department of Radiation Oncology

ecchase@umich.edu

PURPOSE/OBJECTIVE(S)

Other-cause (OC) mortality is the primary cause of death in men with localized prostate cancer. For this reason, life expectancy is a critical component of NCCN treatment guidelines. However, **few tools exist to predict OC mortality in this setting.** Existing tools may be too complex for routine clinical use.

Aim: Develop and validate a **clinically usable model for OC mortality risk prediction in men with prostate cancer** to personalize treatment decision making.

MATERIAL & METHODS

We build our model using a sample of 2,420 men over age 40 free of non-prostate cancer who participated in the National Health and Nutrition Examination Survey (NHANES) between 1999-2010, with mortality follow-up through 2014. We consider a broad range of health predictors and three candidate models: a Cox model in men ages 40+, a Cox model in men ages 55+, and a survival random forest. Because **NHANES is not a prostate cancer patient population**, we conduct sensitivity analyses of the effect of prostate cancer.

We validate our models in a sample of 8,220 men over age 55 with prostate cancer from the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial (PLCO). After selecting the best performing model based on C-index, we assess model performance using AUC and calibration plots. We assess the impact of OC mortality predictions on treatment decisions.

RESULTS

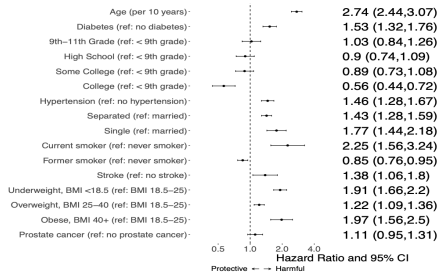

Figure 1: Forest plot of predictors for final OC mortality prediction model fit in NHANES training data. The model also includes interactions between age and diabetes, education, hypertension, and stroke.

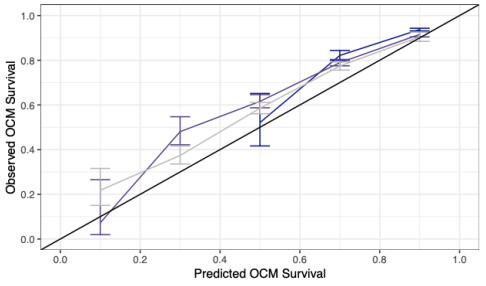

Figure 2: Calibration plot for final OC mortality model. The blue line is calibration at 5 years; purple is calibration at 10 years; gray is calibration at 14 years. Overall, calibration is good, with some evidence of pessimism at higher years.

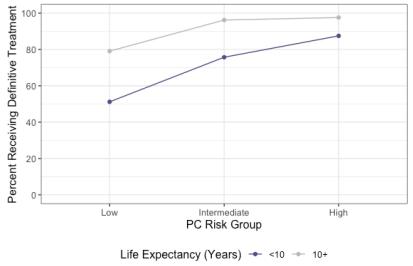

Figure 3: Proportion of patients receiving definitive treatment (prostatectomy, radiation, or radiation + hormone therapy) grouped by OC mortality prediction and prostate cancer risk group.

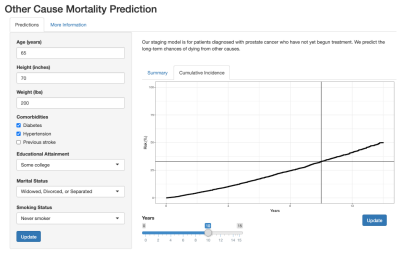

Figure 4: Sample prediction from final OC mortality prediction model. More predictions can be explored by clicking on the figure above, or by going to: https://elizabethchase.shinyapps.io/ocm_app/

The Cox model fit to men ages 40+ was the best-performing model, with a **C-index of 0.7** and an **AUC of 0.78 in the validation cohort** at 14 years. It features **only eight predictors** (age, diabetes, education, hypertension, marital status, smoking status, stroke, BMI), the effects of which are given in Figure 1. Diabetes, hypertension, smoking, previous stroke, and increased age are associated with increased risk of OC mortality, while increased education, being married, and being normal weight are protective. Calibration of the model is generally good, with some pessimism at 14 years (Figure 2). Figure 3 presents proportion of patients receiving definitive treatment across prostate cancer and OC mortality risk for PLCO patients. **We see evidence that clinicians are taking OC mortality into account when assigning treatment,** as patients with reduced life expectancy are overall less likely to receive definitive treatment. **However, patients with low to intermediate risk prostate cancer and reduced life expectancy are still often overtreated**. Half of patients with low risk prostate cancer and life expectancy <10 years received definitive treatment, which goes against NCCN guidelines, and similarly almost 80% of patients with intermediate risk prostate cancer and reduced life expectancy. Figure 4 presents an example prediction using our app; **more predictions can be explored by going to the link in the figure caption.**

SUMMARY/CONCLUSION

We present a **parsimonious and accurate** prediction model for OC mortality in US prostate cancer patients, built and tested in **two diverse, prospective national cohorts**. It requires eight easily obtained predictors and can be accessed at https://elizabethchase.shinyapps.io/ocm_app/.

We believe it will be of **particular use for patients at low to moderate risk of OC mortality with intermediate to high risk prostate cancer**, who are more likely to receive incorrect treatment because of undue optimism or pessimism about their life expectancy. We also demonstrate **the potential for using non-cancer patient data to estimate OC mortality risk** for cancer sites where OC mortality is the driver of overall mortality.

REFERENCES/ACKNOWLEDGEMENTS

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