Development of a Clinically Usable Prediction Model for Other-Cause Mortality in Men with Prostate Cancer

U-M Radiation Oncology, Biostatistics Division Meeting

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Cancer Data Access System

Motivation

Few good tools for estimating comorbidity-adjusted life expectancy in prostate cancer patients exist.

- Life tables probably not appropriate for patients receiving radiation therapy or prostatectomy.
- 70-year-old man’s life expectancy could range by 11.3 years with comorbidities included.
- One study found that, when asked whether a prostate cancer patient would be alive in 10 years, clinicians were correct on average 68% of the time (52%-78%).

Motivation

Recent models (Kent et al. 2016, Riviere et al. 2019) created comorbidity-adjusted life expectancy models in men with prostate cancer with C-indices of **~0.73** at 10 and 15 years, but with burdensome number of covariates and/or questionable modeling choices and data sources.

Goal

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- Clinically usable
- Statistically usable
- Validated
- Good
- For U.S. patients with prostate cancer

Training Data

- National Health and Nutrition Examination Survey (NHANES) 1999-2010
- Mortality follow-up through Dec. 31, 2014
- **NOT** a prostate cancer patient population
- Restrict to men older than 40, free of non-prostate cancer, with complete data for training predictors
- Final sample consisted of 2,420 men with 459 deaths over a mean follow-up of 103.7 months (8.6 years)
- For more information: https://www.cdc.gov/nchs/nhanes/index.htm

Training Data

- Mean age: 59.4 years
- 17.0% non-Hispanic Black; 26.7% other race; 56.3% non-Hispanic White
- 24.8% of respondents had not completed high school
- 78.2% of respondents had a BMI over 25
- 22.2% were current smokers; 18.7% had diabetes; 48.3% had hypertension
- 127 patients (5.2%) had a previous prostate cancer diagnosis

Model Building

- Considered the covariates:
    - Demographics: age, race, educational attainment, marital status
    - Comorbidities: arthritis, chronic bronchitis, diabetes, emphysema, hypertension, previous heart attack, liver disease, previous stroke, prostate cancer
    - Other risk factors: smoking status, overweight/obese

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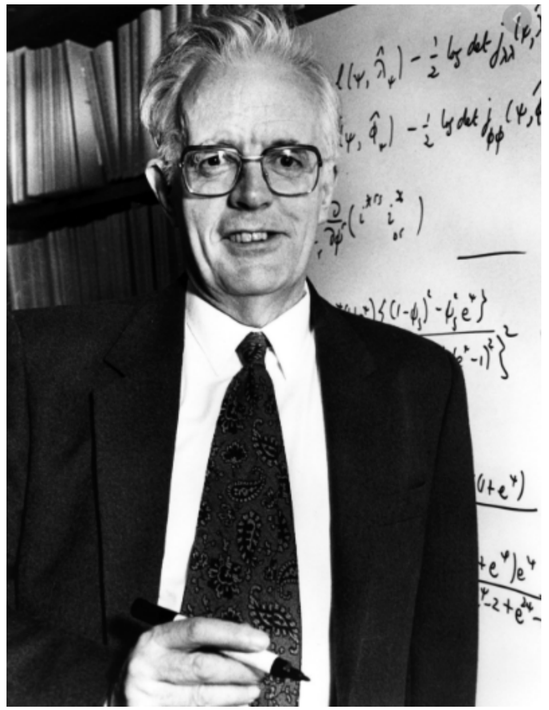
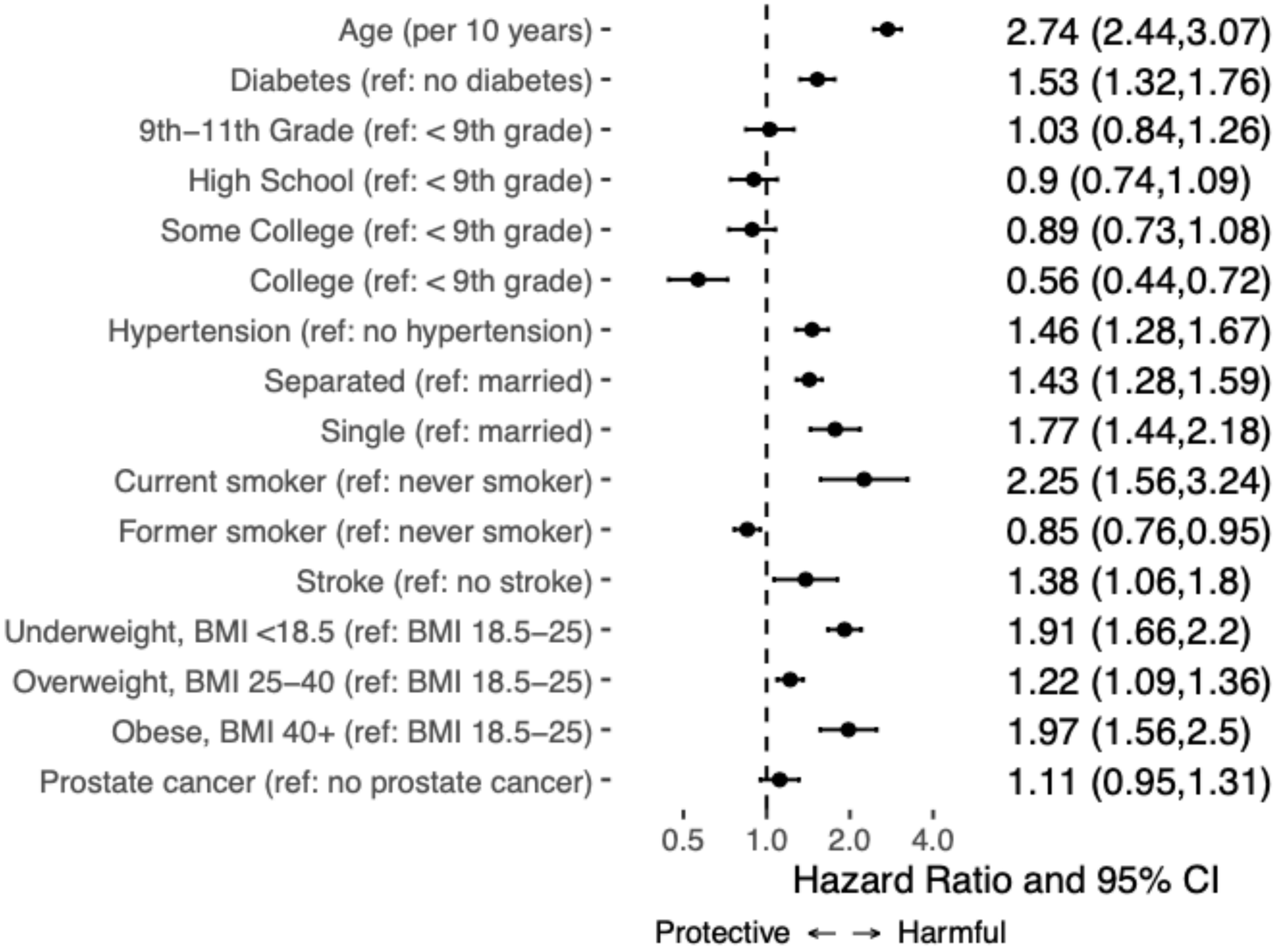
Model Building

- Considered three modeling strategies:
  - Cox proportional hazards modeling
  - Survival random forest modeling
  - Parametric spline survival modeling

- Settled on three candidate models:
  - Cox model in ages > 40
  - Survival random forest in ages > 40
  - Cox model in ages 55+



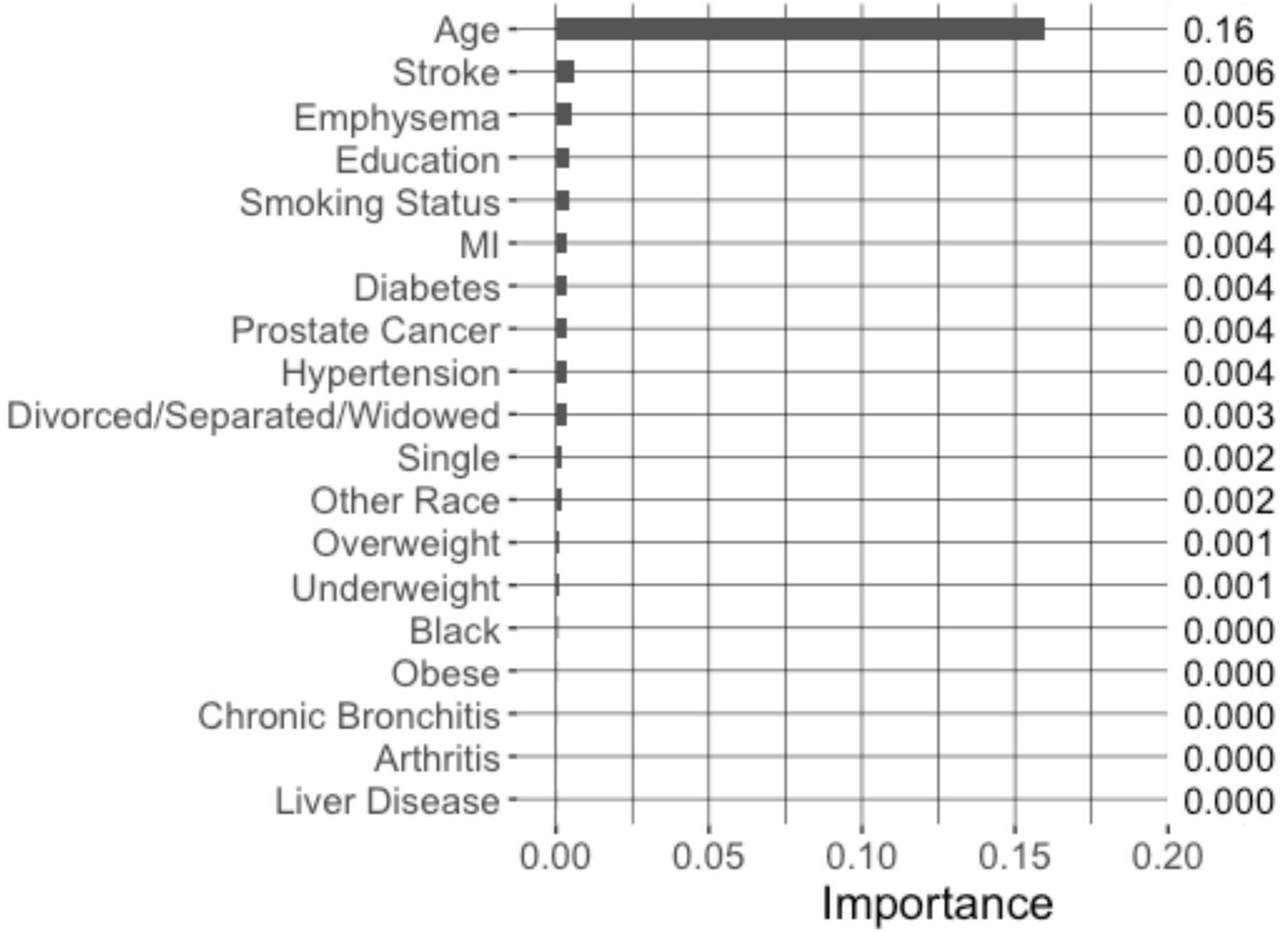
Candidate 1: Cox ages >40



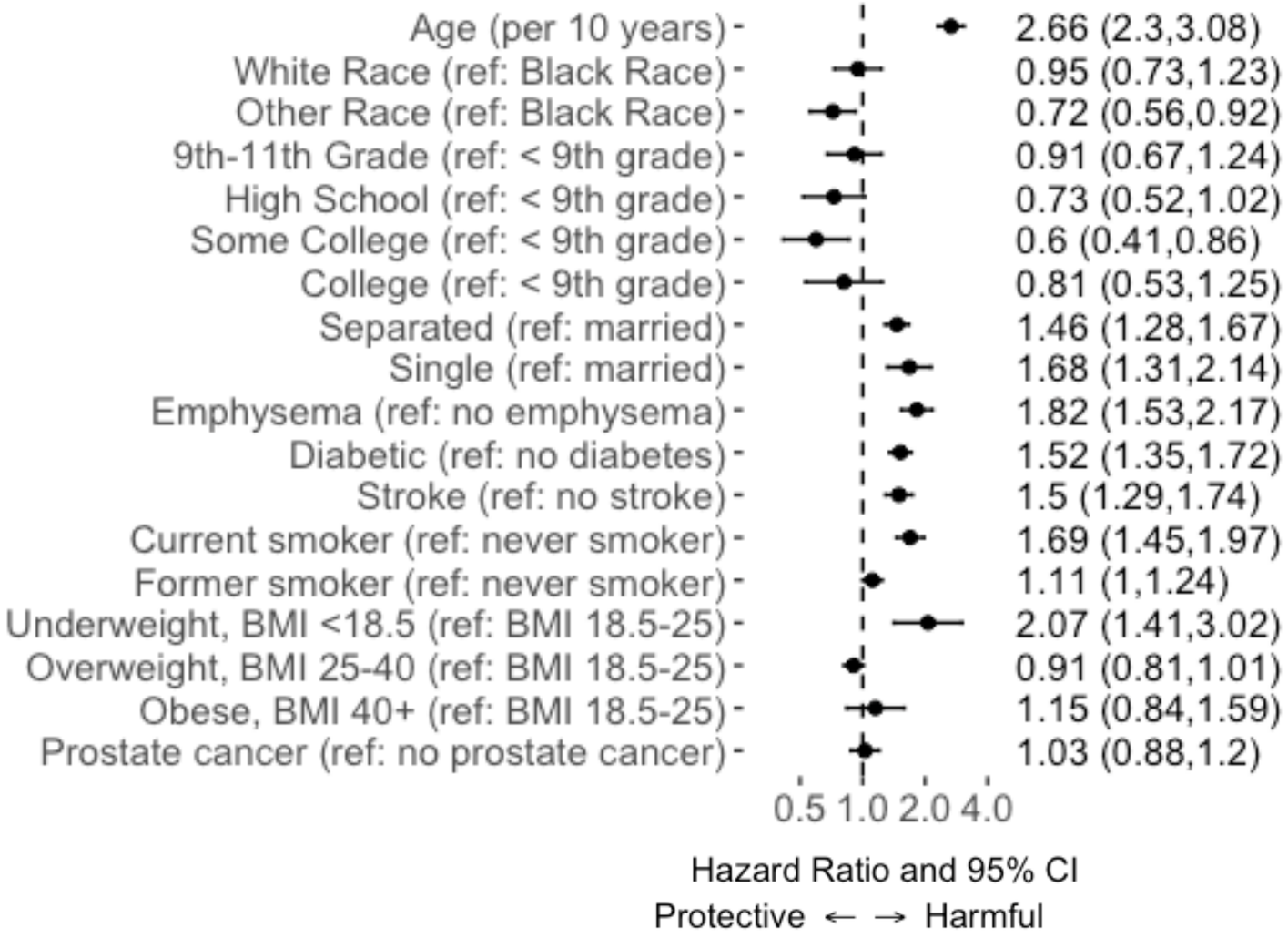
Candidate 1: Cox ages >40

Predictors in order of importance: age, smoking status, marital status, stroke, education, diabetes, hypertension, BMI, prostate cancer

Candidate 2: Random forest ages >40



Candidate 3: Cox ages 55+



Sensitivity Analyses

- Recall that NHANES is not a prostate cancer population—is this model remotely correct?
- Looked at interactions between having prostate cancer and all other predictors
- Looked at length of time from diagnosis as a predictor, and interactions
- Outputted linear predictors from our final model and used that as a predictor along with prostate cancer, length of time from diagnosis, and interactions
- Still included prostate cancer as a predictor in all candidate models

Validation Data

NATIONAL CANCER INSTITUTE
Division of Cancer Prevention

- Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO)
- Enrolled 155,000 participants from Nov. 1993-July 2001, with follow-up through Dec. 31, 2009
- Used sample of men who developed prostate cancer with complete data for model predictors
- Final sample: 8,220 men of whom 2,415 died of other causes over a mean follow-up of 127.8 months (10.7 years)
- For more information: https://prevention.cancer.gov/major-programs/prostate-lung-colorectal-and-ovarian-cancer-screening-trial

Validation Data

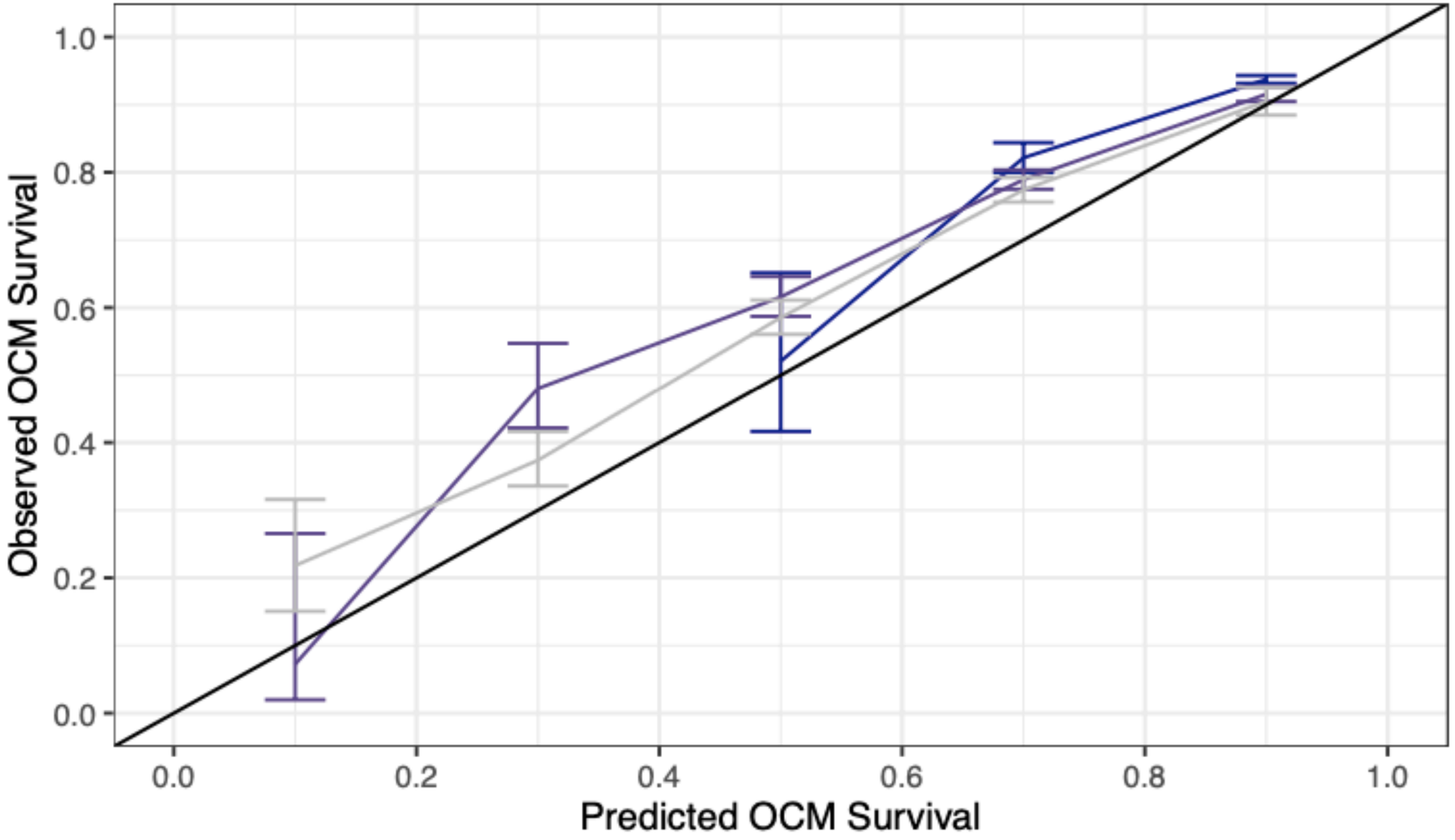
NATIONAL CANCER INSTITUTE
Division of Cancer Prevention

- Extremely different from NHANES training sample
- Mean age: 69.5 years
- 5.8% non-Hispanic Black, 5.3% other race, 89.0% non-Hispanic White
- 7.4% of the sample had not completed a high school degree
- 71.5% of respondents had a BMI over 25
- 9.0% were current smokers; 6.4% had diabetes; 33.4% had hypertension
- Only characteristic on which they weren't significantly different was having a previous heart attack; about ~12% in both samples

Model Validation

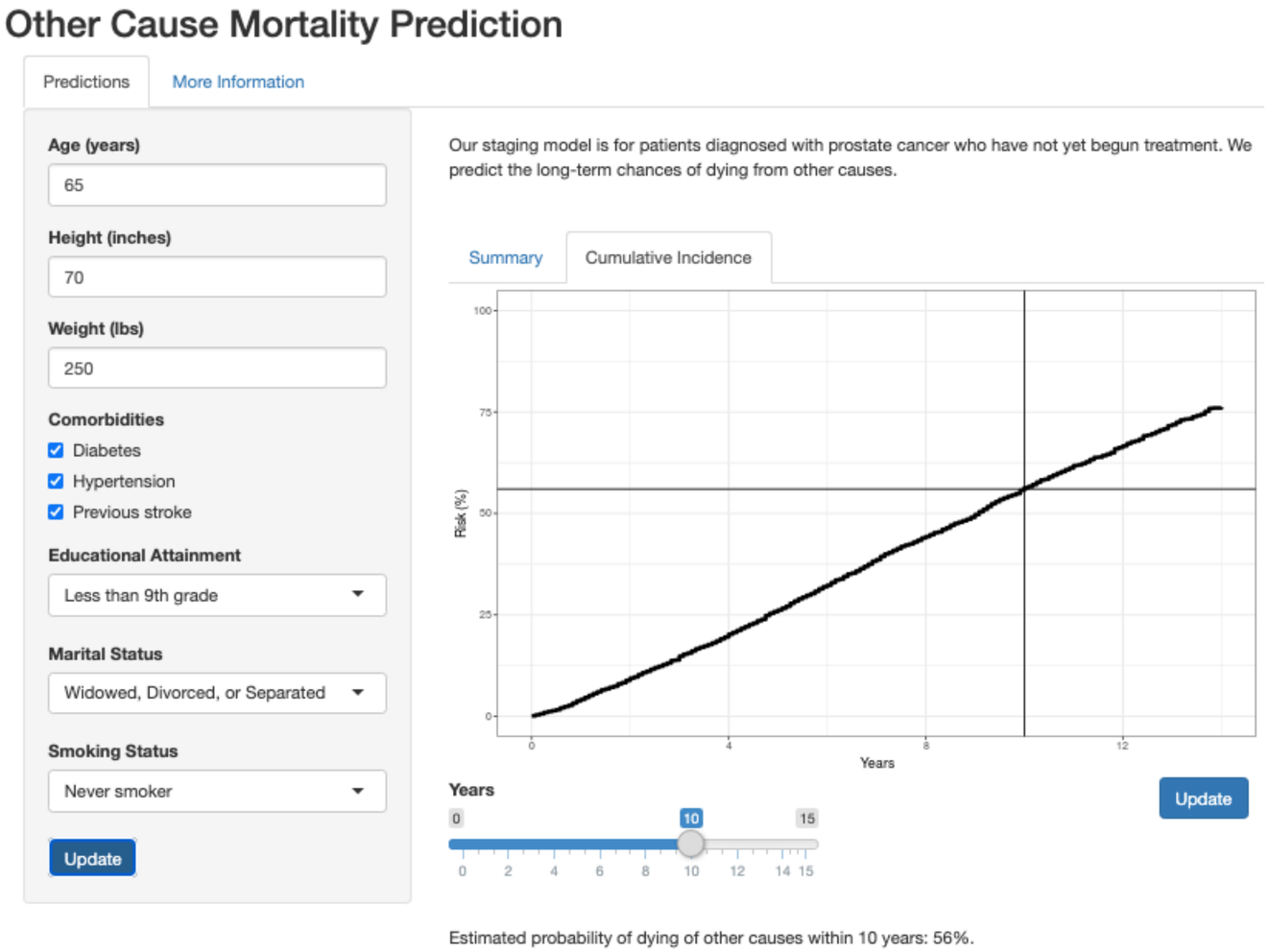
Model	AUC		
	5 Years	10 Years	14 Years
Cox Ages 55+	0.70	0.75	0.77
Cox Ages >40	0.70	0.75	0.78
Random Forest >40	0.70	0.73	0.74
SSA	0.65	0.71	0.75
NVSS	0.65	0.71	0.75

Model Calibration

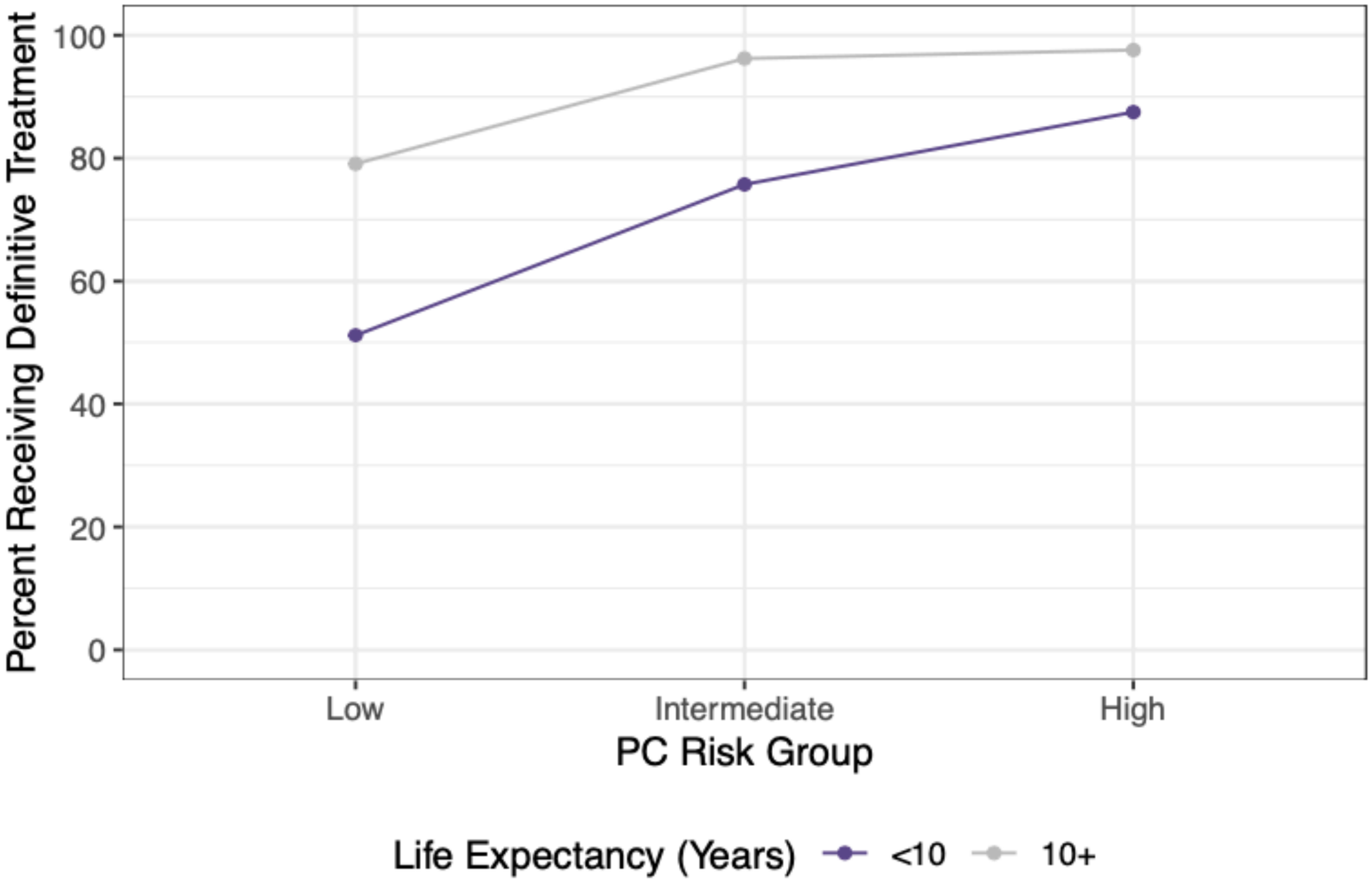


Black line: perfect calibration. Blue line: calibration at 5 years. Purple line: calibration at 10 years. Gray line: calibration at 14 years.

Characterization of OC Mortality Risk



OC Mortality and Treatment Decision-Making



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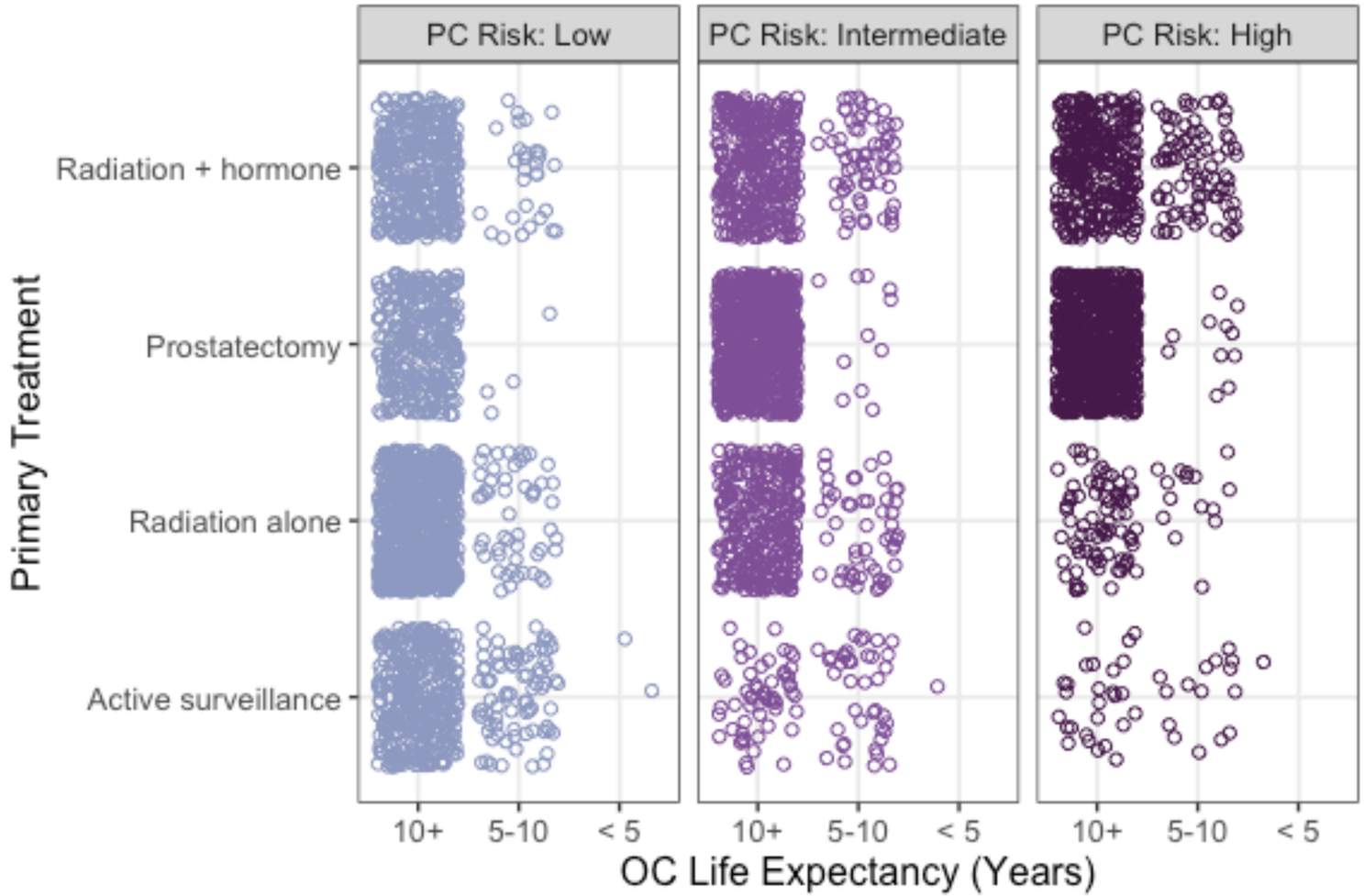

Limitations

- Model is built in a non-cancer patient population
- Unable to consider OC mortality specific endpoint in model building
- Did not use NHANES survey weights

Future Work

- Potentially combine this model with prostate cancer-specific mortality models to obtain combined decisions
- Look more at the effect of treatment on OC mortality
- Create treatment decision aids incorporating both OC mortality and PCSM

Extensions

- This approach may be generalizable to other cancer sites in which OC mortality is a driver of mortality.

- May be able to use this OC mortality model to quantify the difference in comorbidity burden between radiation patients and surgery patients.

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Thank you—questions?

S1: Comparison to SSA Predictions