Supplementary Materials: Development and Validation of the Other-Cause Comorbidity-Adjusted Mortality (OCCAM) Model for Clinical Use in Men with Prostate Cancer

Variable Definitions

We constructed some of our variables from other NHANES variables. In particular:

- 1. We defined a patient as having hypertension if they reported a previous diagnosis of hypertension or if their blood pressure reading was hypertensive (we followed standard NHANES guidelines on constructing the blood pressure reading).
- 2. We defined a patient as having diabetes if they reported a previous diagnosis of diabetes or if their blood glucose met clinical criteria for diabetes.
- 3. We defined a patient as having high cholesterol if they reported high cholesterol, or if their blood work met clinical criteria for high cholesterol.
- 4. We defined patients as current smokers if they had smoked 100 cigarettes in their lifetime and reported smoking cigarettes every day or some days at present; we defined patients as former smokers if they had smoked 100 cigarettes in their lifetime and reported smoking not at all at present; we defined patients as never smokers if they had not smoked 100 cigarettes in their lifetime.
- 5. We defined being overweight as having BMI greater than or equal to 25 and less than 40 and being obese as having BMI greater than or equal to 40.
- 6. We collapsed marital status into three categories: married if the patient was currently married or living with a partner, separated if the patient was widowed, divorced, or separated from their partner, and single if the patient had never married.
- 7. We collapsed race into non-Hispanic white, non-Hispanic black, and all other races.

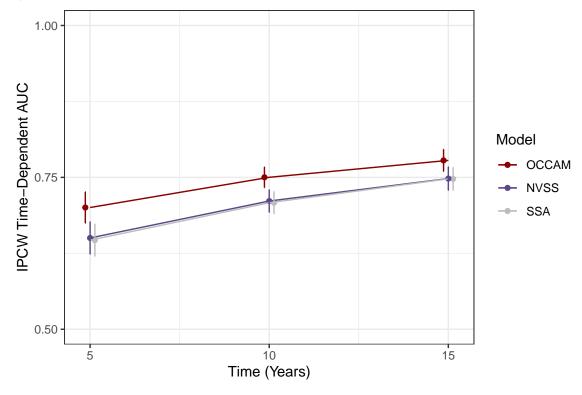
For all other variables, we used unmodified results from the NHANES questionnaires about demographics, health insurance, health care access, mental health, and medical history. For more information on variable definition and construction, please see the repository posted at: https://github.com/blindedforreview/PCOtherCause.

Supplementary Findings

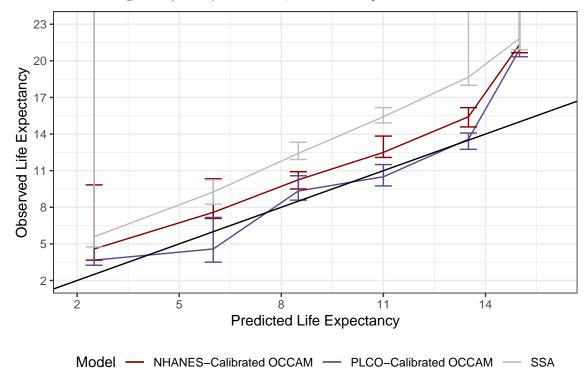
eFigure 1: Forest plot comparing the effect sizes of predictors from the unweighted and survey weighted versions of OCCAM fit in the NHANES training cohort of 7,369 men. The model also includes interactions between age and diabetes, education, hypertension, and stroke.

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## Stratified 1 - level Cluster Sampling design (with replacement)
## With (180) clusters.
## subset(nhanes_svy, inmodel4 == 1)
                                Age (per 10 years) -
                         Diabetes (ref: no diabetes) -
                  9th-11th Grade (ref: < 9th grade) -
                     High School (ref: < 9th grade) -
                    Some College (ref: < 9th grade) -
                          College (ref: < 9th grade) -
                Hypertension (ref: no hypertension) -
                           Separated (ref: married) -
                               Single (ref: married) -
                Current smoker (ref: never smoker) -
                Former smoker (ref: never smoker) -
                             Stroke (ref: no stroke) -
        Underweight, BMI <18.5 (ref: BMI 18.5-25) -
         Overweight, BMI 25-40 (ref: BMI 18.5-25) -
                Obese, BMI 40+ (ref: BMI 18.5-25) -
           Prostate cancer (ref: no prostate cancer) -
                                                           0.5
                                                                                         2.0
                                                                                                        4.0
                                                                          1.0
                                                                 Hazard Ratio and 95% CI
                                                            Model — Unweighted
                                                                                             Weighted
                                                              \text{Protective} \, \leftarrow \, \rightarrow \, \text{Harmful}
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eFigure 2: Externally validated time-dependent area-under-the-curves (AUCs) at 5, 10, and 15 years of our other-cause comorbidity-adjusted mortality (OCCAM) model, the Social Security Administration 2001 actuarial life table predictions (SSA), and the National Vital Statistics System's 2001 life expectancy predictions (NVSS). Models were validated in the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial (PLCO) cohort of 8,220 men with prostate cancer.



eFigure 3: Calibration performance of other-cause comorbidity-adjusted mortality (OCCAM) model and the Social Security Administration's 2001 actuarial life table predictions (SSA) in the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial (PLCO) cohort of 8,220 men with prostate cancer.



eTable 1: Cause-specific and competing-risks time-dependent AUCs of OCCAM in the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial (PLCO) validation cohort of 8,220 men.

Metric	5 Years	10 Years	15 Years
Cause-Specific	0.7	0.75	0.78
AUC			
Competing-Risks	0.7	0.74	0.73
AUC			

eTable 2: Time-dependent AUC of OCCAM in the three main treatment groups in the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial (PLCO) validation cohort of 8,220 men.

	Cause-Specific AUC			Competing-Risks AUC			
Treatment	5 Years	10 Years	15 Years	5 Years	10 Years	15 Years	
Prostatectomy	0.68	0.69	0.72	0.68	0.69	0.71	
Radiation alone	0.65	0.71	0.75	0.65	0.70	0.72	
Radiation +	0.63	0.71	0.73	0.63	0.70	0.67	
hormone							

eTable 3: Characteristics of a cohort of 7,596 men from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, grouped by OCCAM-predicted median survival time.

	15+	10-15	5-10	< 5	р	test
n Age (years) (mean (SD)) Race (%)	3458 65.1 (4.0)	2799 71.4 (3.9)	1307 76.4 (4.3)	32 80.8 (3.8)	<0.001 <0.001	
NHB NHW	165 (4.8) 3143 (90.9)	175 (6.3) 2468 (88.2)	97 (7.4) 1114 (85.2)	3 (9.4) 26 (81.2)		
Other Education (%) Less than 9th grade 9th-11th grade HS graduate	150 (4.3) 31 (0.9) 127 (3.7) 849 (24.6)	156 (5.6) 38 (1.4) 248 (8.9) 426 (15.2)	96 (7.3) 13 (1.0) 106 (8.1) 115 (8.8)	3 (9.4) 3 (9.4) 2 (6.2) 2 (6.2)	<0.001	
Some college College graduate Marital status (%) Married Separated	675 (19.5) 1776 (51.4) 3173 (91.8) 234 (6.8)	1041 (37.2) 1046 (37.4) 2379 (85.0) 350 (12.5)	666 (51.0) 407 (31.1) 947 (72.5) 273 (20.9)	15 (46.9) 10 (31.2) 11 (34.4) 17 (53.1)	< 0.001	
Single Smoking status (%) Current Former Never	51 (1.5) 175 (5.1) 1565 (45.3) 1718 (49.7)	70 (2.5) 262 (9.4) 1510 (53.9) 1027 (36.7)	87 (6.7) 226 (17.3) 736 (56.3) 345 (26.4)	4 (12.5) 16 (50.0) 12 (37.5) 4 (12.5)	< 0.001	
Diabetes = Yes (%) Hypertension = Yes (%) Previous stroke = Yes (%) BMI category (%) Underweight (BMI < 18.5)	101 (2.9) 846 (24.5) 8 (0.2) 2 (0.1)	224 (8.0) 1112 (39.7) 58 (2.1) 8 (0.3)	149 (11.4) 571 (43.7) 101 (7.7) 6 (0.5)	3 (9.4) 11 (34.4) 5 (15.6) 4 (12.5)	<0.001 <0.001 <0.001 <0.001	
Normal weight (BMI 18.5-25) Overweight (BMI 25-40) Obese (BMI 40+) N Stage (%) N0	802 (23.2) 2636 (76.2) 18 (0.5) 3067 (88.7)	811 (29.0) 1963 (70.1) 17 (0.6) 2389 (85.4)	517 (39.6) 761 (58.2) 23 (1.8) 1099 (84.1)	17 (53.1) 9 (28.1) 2 (6.2) 23 (71.9)	< 0.001	
N1 N2 NX	47 (1.4) 9 (0.3) 335 (9.7)	32 (1.1) 2 (0.1) 376 (13.4)	15 (1.1) 0 (0.0) 193 (14.8)	1 (3.1) 0 (0.0) 8 (25.0)		

eTable 3, cont.: Characteristics of a cohort of 7,596 men from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, grouped by OCCAM-predicted median survival time.

	15+	10-15	5-10	< 5	p	test
n	3458	2799	1307	32		
T Stage (%) T0 T1-T2a T2b-T2c	1 (0.0) 1619 (46.8) 1390 (40.2)	0 (0.0) 1813 (64.8) 727 (26.0)	0 (0.0) 963 (73.7) 270 (20.7)	0 (0.0) 25 (78.1) 7 (21.9)	<0.001	
T3a-T4 TX Gleason (%)	446 (12.9) 2 (0.1)	258 (9.2) 1 (0.0)	73 (5.6) 1 (0.1)	0 (0.0) 0 (0.0)	< 0.001	
<= 6 7	2028 (58.6) 1134 (32.8)	1524 (54.4) 893 (31.9)	604 (46.2) 451 (34.5)	12 (37.5) 9 (28.1)	V0.001	
8 9 10 PSA at diagnosis (mean (SD)) Prostate cancer risk group (%)	166 (4.8) 116 (3.4) 14 (0.4) 10.7 (88.7)	223 (8.0) 147 (5.3) 12 (0.4) 11.6 (42.5)	141 (10.8) 90 (6.9) 21 (1.6) 17.0 (64.8)	6 (18.8) 4 (12.5) 1 (3.1) 48.2 (133.6)	0.015 <0.001	
Low Intermediate High Regional NA	906 (26.2) 794 (23.0) 613 (17.7) 56 (1.6) 1089 (31.5)	809 (28.9) 622 (22.2) 550 (19.6) 34 (1.2) 784 (28.0)	326 (24.9) 327 (25.0) 296 (22.6) 15 (1.1) 343 (26.2)	3 (9.4) 5 (15.6) 12 (37.5) 1 (3.1) 11 (34.4)		
Treatment (%) Active surveillance Other ablative treatment Hormone alone Radiation alone	219 (6.3) 41 (1.2) 99 (2.9) 627 (18.1)	352 (12.6) 73 (2.6) 215 (7.7) 690 (24.7)	279 (21.3) 52 (4.0) 224 (17.1) 297 (22.7)	15 (46.9) 1 (3.1) 10 (31.2) 2 (6.2)	<0.001	
Prostatectomy Radiation + hormone Outcome (%) Alive	1973 (57.1) 499 (14.4) 2636 (76.2)	759 (27.1) 710 (25.4) 1714 (61.2)	112 (8.6) 343 (26.2) 619 (47.4)	0 (0.0) 4 (12.5) 8 (25.0)	< 0.001	
Died of OC	665 (19.2)	903 (32.3)	592 (45.3)	21 (65.6)		
Died of PC	157 (4.5)	182 (6.5)	96 (7.3)	3 (9.4)		

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