## {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 our first candidate model based on all predictors, fit in the NHANES training cohort of 7,369 men.

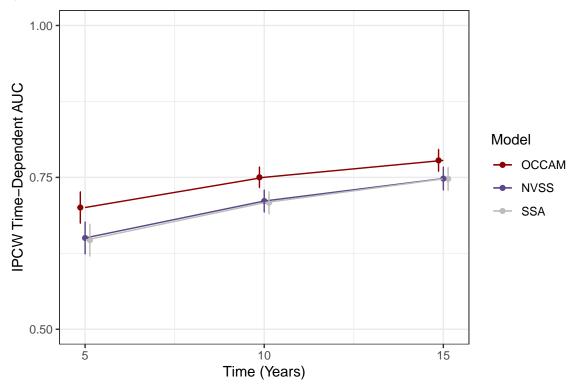
```
## Stratified 1 - level Cluster Sampling design (with replacement)
## With (153) clusters.
## subset(nhanes_svy, inmodel1 == 1)
                                                Age (per 1 year) -
                           Alcohol abuse (ref: no alcohol abuse) -
                                        Anemia (ref: no anemia) -
                                        Arthritis (ref: no arthritis) -
                                        Asthma (ref: no asthma) -
                   Chronic bronchitis (ref: no chronic bronchitis) -
                                      Diabetes (ref: no diabetes) -
                               9th-11th Grade (ref: < 9th grade) -
                                   High School (ref: < 9th grade) -
                                 Some College (ref: < 9th grade) -
                                       College (ref: < 9th grade) -
                              Emphysema (ref: no emphysema) -
                             Hypertension (ref: no hypertension) -
                                        Separated (ref: married) -
                                            Single (ref: married) -
             Previous myocardial infarction (ref: no previous MI) -
                             Liver disease (ref: no liver disease) -
                                     White race (ref: Black race) -
                                     Other race (ref: Black race) -
                             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) -
                                         Angina (ref: no angina) -
                          Congestive heart failure (ref: no CHF) -
                          Coronary heart disease (ref: no CHD) -
              Regular primary care (ref: no regular primary care) -
       Hospitalized in last year (ref: not hospitalized in last year) -
                       High cholesterol (ref: normal cholesterol) -
                                  Health insured (ref: uninsured) -
                         Kidnev disease (ref: no kidnev disease) -
                       No previous military service (ref: veteran) -
                       Prostate cancer (ref: no prostate cancer) -
                                                                                              4.0
                                                                                      2.0
                                                                      0.5
                                                                              1.0
                                                                       Hazard Ratio and 95% CI
                                                                  Model - Unweighted
                                                                                                   Weighted
```

Protective ← → Harmful

eFigure 2: 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.

```
## 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}
```

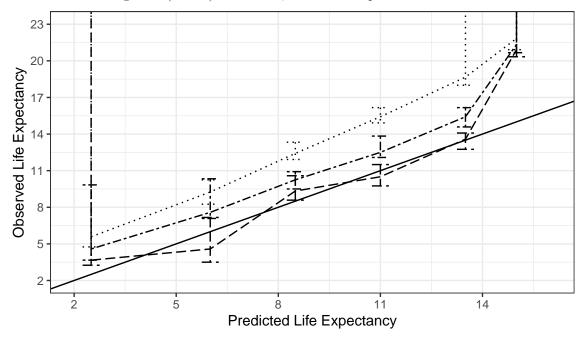
eFigure 2: Externally validated time-dependent area-under-the-curves (AUCs) at 5, 10, and 15 years of our other-cause comorbidity-adjusted mortality (OCCAM) model, the Social Security Administration 2001 actuarial life table predictions (SSA), and the National Vital Statistics System's 2001 life expectancy predictions (NVSS). Models were validated in the Prostate, Lung, Colon, and Ovarian Cancer Screening Trial (PLCO) cohort of 8,220 men with prostate cancer.



```
##
   $p_values_AUC
                         t=60
                                                   t=180
##
                                     t = 120
## Non-adjusted 3.488605e-15 2.005757e-17 3.571423e-09
                7.993606e-15 1.110223e-16 1.468344e-08
   Adjusted
##
##
   $Cor
##
             [,1]
                        [,2]
                                  [,3]
   [1,] 1.0000000 0.5011289 0.2334496
##
  [2,] 0.5011289 1.0000000 0.4769710
## [3,] 0.2334496 0.4769710 1.0000000
## $p_values_AUC
##
                         t=60
                                     t = 120
## Non-adjusted 9.544739e-14 7.701493e-16 4.354698e-09
##
  Adjusted
                1.946221e-13 1.998401e-15 2.321990e-08
##
##
   $Cor
##
             [,1]
                        [,2]
                                  [,3]
## [1,] 1.0000000 0.5002134 0.2324362
  [2,] 0.5002134 1.0000000 0.4778478
## [3,] 0.2324362 0.4778478 1.0000000
## $p_values_AUC
                         t=60
                                     t=120
                                                   t = 180
## Non-adjusted 3.833687e-15 8.676867e-18 5.125878e-09
## Adjusted
                8.215650e-15 0.000000e+00 2.750914e-07
```

```
##
## $Cor
                       [,2]
##
             [,1]
## [1,] 1.0000000 0.5193405 0.2769467
## [2,] 0.5193405 1.0000000 0.5413407
## [3,] 0.2769467 0.5413407 1.0000000
## $p_values_AUC
##
                        t=60
                                    t=120
                                                 t=180
## Non-adjusted 8.173621e-14 1.868094e-16 2.047739e-09
## Adjusted 1.691980e-13 3.330669e-16 4.913563e-09
##
## $Cor
                       [,2]
                                 [,3]
             [,1]
## [1,] 1.0000000 0.5187816 0.2768688
## [2,] 0.5187816 1.0000000 0.5420685
## [3,] 0.2768688 0.5420685 1.0000000
```

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.



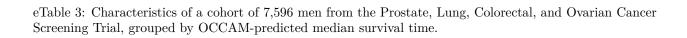
Model -- NHANES-Calibrated OCCAM -- PLCO-Calibrated OCCAM ···· SSA

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, 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.

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