

SUPPLEMENTAL MATERIAL**INDEX**

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Table S-1: BTMED Lung Cancer Screening Eligibility Criteria

Entry Variable	≥5 Years of DOE Site or construction trade work or ≥5 Years of work in a job with exposures to asbestos, silica, beryllium, chromium, radiation, or welding	Eligible Age Range	Spirometry FEV₁ >40% Predicted
Smoking 20 pack-years and <u>no restriction</u> on time since last smoked. ^{1,2}	Required	50-79	Required
Smoking 30 pack-years and ≤15 years since quit date. ¹	Not Required	50-79	Required
Chest x-ray with pleural scarring or COPD by spirometry lower limit of normal criteria. Must also meet 20 pack-years smoking criteria.	Not Required	50-79	Required
Chest x-ray parenchymal changes (profusion ≥1/0) even if worker does not meet smoking criteria.	Not Required	50-79	Required

¹ Workers with missing data on smoking history are considered potential eligible pending verification of smoking history by telephone interview.

² Workers are deemed eligible if requirements of any table row are satisfied.

Table S-2: Cumulative Lung Cancer Deaths Stratified by Cohort Entry Characteristics

Characteristic	Category Description	Not Dying of Lung Cancer N (%) ¹	Died of Lung Cancer N (%)	
Sex	Male	15797 (97.9)	336 (2.1)	
	Female	920 (98.3)	16 (1.7)	
Race/Ethnicity	White	14383 (97.8)	315 (2.1)	
	Black	1618 (98.2)	30 (1.8)	
	All Other	716 (99.0)	7 (1.0)	
Smoking Status	Never Smoked	5806 (99.9)	7 (0.1)	
	Former Smoker (<15 Years Quit)	2660 (96.6)	93 (3.4)	
	Former Smoker (15-25 Years Quit)	1825 (97.4)	48 (2.6)	
	Former Smoker (>25 Years Quit)	3107 (98.4)	51 (1.6)	
	Current Smoker	3319 (95.6)	153 (4.4)	
CXR Category ²	Normal	14818 (98.3)	262 (1.7)	
	Pleural Changes	2286 (97.1)	67 (2.9)	
	Parenchymal Profusion Category			
		0/- - 0/0	15881 (98.3)	280 (1.7)
		0/1	166 (93.8)	11 (6.2)
		1/0 - 1/2	591 (91.9)	52 (8.1)
		2/1 - 2/3	64 (90.1)	7 (9.9)
	3/2 - 3/+	15 (88.2)	2 (11.8)	
Spirometry Category	Normal	10036 (98.9)	107 (1.1)	
	Restrictive	4267 (97.5)	109 (2.5)	
	Obstructive	1326 (97.0)	41 (3.0)	
	Mixed	1088 (92.0)	95 (8.0)	
COPD by Spirometry	No COPD	14303 (98.5)	216 (1.5)	
	COPD	2414 (94.7)	136 (5.3)	
Respiratory Symptoms	None	10273 (98.7)	139 (1.3)	
	Cough	1673 (97.8)	38 (2.2)	
	Phlegm	1567 (97.9)	34 (2.1)	
	Cough and Phlegm	3204 (95.8)	141 (4.2)	
Trade Work or DOE Work	< 5 Years	1832 (98.3)	31 (1.7)	
	≥ 5 Years	14885 (97.9)	321 (2.1)	
Beryllium Sensitivity ³	Negative	15449 (97.9)	325 (2.1)	
	Positive	180 (97.3)	5 (2.7)	
Personal History of Cancer	No Cancer History	13879 (98.2)	251 (1.8)	
	Cancer History	2838 (96.6)	101 (3.4)	

¹ Percent values are row percentages.

² CXR categories are not mutually exclusive as workers can have pleural and parenchymal changes.

³ 1110 workers missing data on beryllium sensitivity

Table S-3: Final Cox Lung Cancer Model (In Manuscript)

Risk Predictor¹	Hazard Ratio	95% LCL	95% UCL
Smoking Status (Ref=Never Smoked)			
Current	24.32	10.98	53.85
Former (<15 Years Since Quit)	16.76	7.54	37.27
Former (15-25 Years Since Quit)	10.54	4.70	23.62
Former (>25 Years Since Quit)	5.90	2.66	13.09
Smoking Pack-Years (Increase per pack-year)	1.006	1.002	1.010
CXR B-Reader Category Results²			
Parenchymal Profusion Category ³ (Ref= 0/- - 0/0)			
0/1	2.05	1.11	3.76
1/0 - 1/2	2.33	1.71	3.16
2/1 - 2/3	3.52	1.63	7.63
3/2 - 3/+	10.55	2.58	43.20
Spirometry Category (Ref=Normal)⁴			
Restrictive	1.84	1.40	2.41
Obstructive	1.38	0.95	2.00
Mixed	2.98	2.21	4.01
Respiratory Symptoms (Ref=None)			
Cough	1.07	0.74	1.55
Phlegm	1.38	0.95	2.02
Cough and Phlegm	1.71	1.34	2.20
Years of Trade Work or DOE Work (Ref=<5)⁵			
5+	1.56	1.07	2.26
Body Mass Index (BMI) (Change per BMI unit)	0.972	0.951	0.994
Personal History of Cancer (Ref=No)			
Yes	1.44	1.13	1.83
Model Diagnostics			
AIC	5749.95		
Model C-Statistic	0.880		
Optimism Corrected C-Statistic	0.868		
Grønnesby and Borgan Test p-value	0.4174		

¹ Cox model based on 17,069 workers having data on model covariates, adjusted for age, gender, and race/ethnicity.

² A pleural abnormality was defined as bilateral pleural thickening or plaques, with or without calcification.

³ Parenchymal profusion category by B-read criteria.

⁴ restrictive: $FEV_1/FVC \geq LLN$ AND $FVC < LLN$; obstructive: $FEV_1/FVC < LLN$ AND $FVC \geq LLN$; mixed: $FEV_1/FVC < LLN$ AND $FVC < LLN$; normal: $FEV_1/FVC \geq LLN$ and $FVC \geq LLN$.

⁵ Workers were classified as having 5 or more years of work in a DOE facility or in trade work per current BTMed LDCT eligibility criteria.

Table S-4: Alternate Cox Lung Cancer Model with COPD for Spirometry

Risk Predictor ¹	Hazard Ratio	95% LCL	95% UCL
Smoking Status (Ref=Never Smoked)			
Current	24.47	11.04	54.22
Former (<15 Years Since Quit)	17.50	7.87	38.92
Former (15-25 Years Since Quit)	10.54	4.70	23.64
Former (>25 Years Since Quit)	5.81	2.62	12.91
Smoking Pack-Years (Increase per pack-year)	1.007	1.003	1.011
CXR B-Reader Category Results			
Parenchymal Profusion Category (Ref= 0/- - 0/0) ²			
0/1	1.87	1.02	3.43
1/0 - 1/2	2.26	1.67	3.08
2/1 - 2/3	3.08	1.42	6.68
3/2 - 3/+	12.41	3.04	50.64
COPD by Spirometry (Ref=No)			
Yes	1.67	1.33	2.11
Respiratory Symptoms (Ref=None)			
Cough	1.06	0.74	1.54
Phlegm	1.47	1.01	2.15
Cough and Phlegm	1.86	1.46	2.38
Years of Trade Work or DOE Work (Ref=<5)³			
5+	1.47	1.01	2.14
Body Mass Index (BMI) (Change per BMI unit)			
	0.977	0.956	1.000
Personal History of Cancer (Ref=No)			
Yes	1.42	1.11	1.81
Model Diagnostics			
AIC	5781.70		
Model C-Statistic	0.874		
Optimism Corrected C-Statistic	0.857		
Grønnesby and Borgan Test p-value	0.1645		

¹ Cox model based on 17,069 workers having data on model covariates, adjusted for age, gender, and race/ethnicity.

² Parenchymal profusion category by B-read criteria.

³ Workers were classified as having 5 or more years of work in a DOE facility or in trade work per current BTMed LDCT eligibility criteria.

Table S-5: Alternate Cox Lung Cancer Model using CXR and Spirometry Categories

Risk Predictor ¹	Hazard Ratio	95% LCL	95% UCL
Smoking Status (Ref=Never Smoked)			
Current	24.45	11.04	54.12
Former (<15 Years Since Quit)	16.98	7.64	37.74
Former (15-25 Years Since Quit)	10.52	4.69	23.57
Former (>25 Years Since Quit)	5.98	2.70	13.27
Smoking Pack-Years (Increase per pack-year)	1.006	1.002	1.010
CXR B-Reader Category (Ref=Normal)			
Pleural Only ²	0.75	0.51	1.11
Parenchymal Only ³	2.49	1.76	3.53
Pleural & Parenchymal	2.10	1.34	3.26
Spirometry Category (Ref=Normal)⁴			
Restrictive	1.86	1.42	2.44
Obstructive	1.41	0.87	2.03
Mixed	2.93	2.18	3.95
Respiratory Symptoms (Ref=None)			
Cough	1.10	0.76	1.57
Phlegm	1.40	0.96	2.05
Cough and Phlegm	1.70	1.33	2.18
Years of Trade Work or DOE Work (Ref=<5)⁵			
5+	1.58	1.09	2.29
Body Mass Index (BMI) (Change per BMI unit)			
	0.973	0.951	0.994
Personal History of Cancer (Ref=No)			
Yes	1.42	1.11	1.81
Model Diagnostics			
AIC	5753.20		
Model C-Statistic	0.879		
Optimism Corrected C-Statistic	0.869		
Grønnesby and Borgan Test p-value	0.2412		

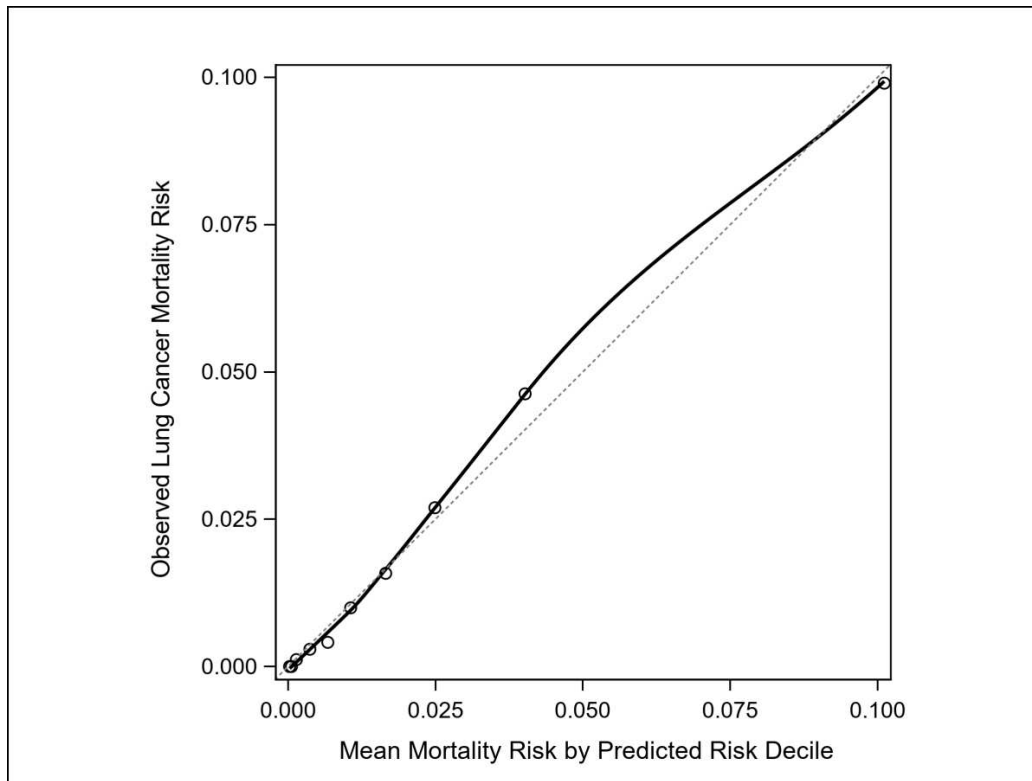
¹ Cox model based on 17,069 workers having data on model covariates, adjusted for age, gender, and race/ethnicity.

² A pleural abnormality was defined as bilateral pleural thickening or plaques, with or without calcification.

³ Parenchymal profusion category $\geq 1/0$ by B-read criteria.

⁴ restrictive: $FEV_1/FVC \geq LLN$ AND $FVC < LLN$; obstructive: $FEV_1/FVC < LLN$ AND $FVC \geq LLN$; mixed: $FEV_1/FVC < LLN$ AND $FVC < LLN$; normal: $FEV_1/FVC \geq LLN$ and $FVC \geq LLN$.

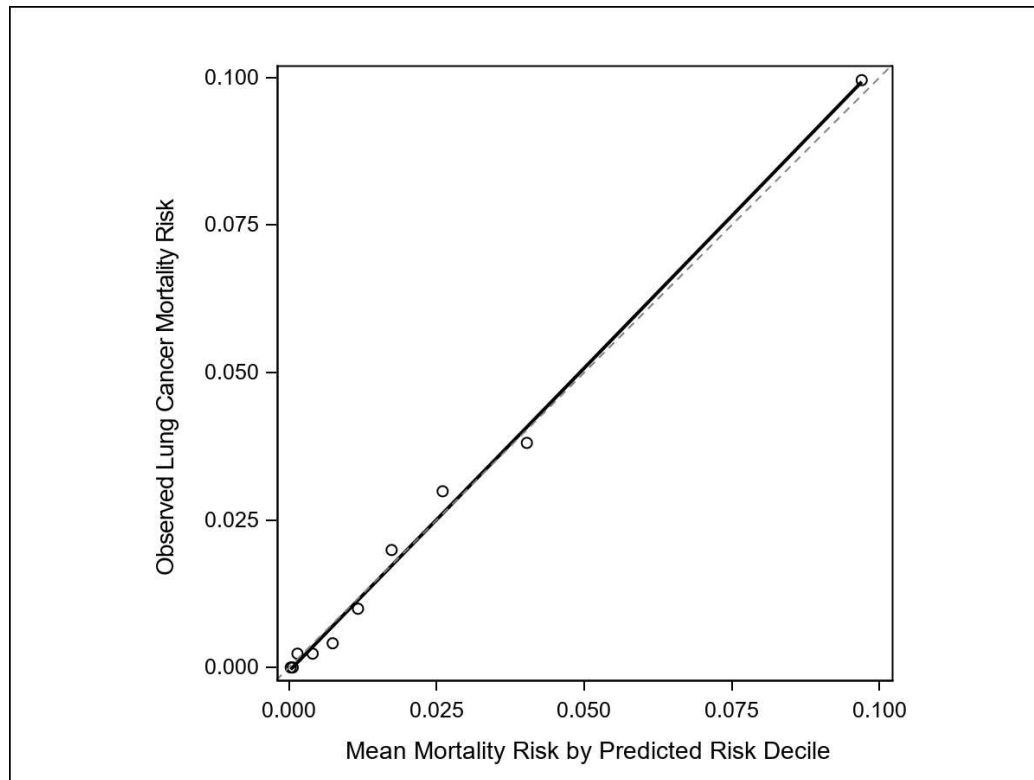
⁵ Workers were classified as having 5 or more years of work in a DOE facility or in trade work per current BTMed LDCT eligibility criteria.

Figure S-1: Calibration Plot, Final Cox Lung Cancer Mortality Model ¹

¹ LOESS regression line fit to data points. Perfect calibration show as --- line.

		Lung Cancer Deaths by Model Predicted Risk Decile									
		0	1	2	3	4	5	6	7	8	9
Predicted Deaths		0.46	1.01	2.43	6.34	11.53	18.16	28.29	42.53	68.64	172.62
Observed Deaths		0	0	2	5	7	17	27	46	79	169

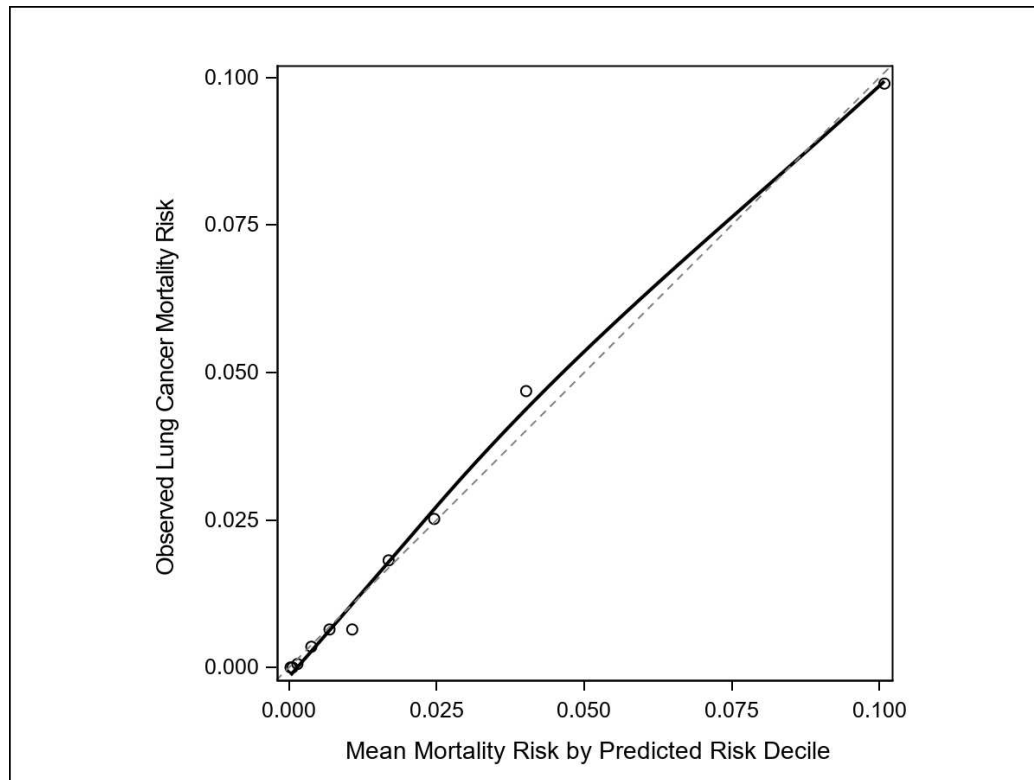
Figure S-2: Calibration, Alternate Cox Lung Cancer Mortality Model with COPD in the Model for Spirometry Results ¹



¹ LOESS regression line fit to data points. Perfect calibration show as --- line.

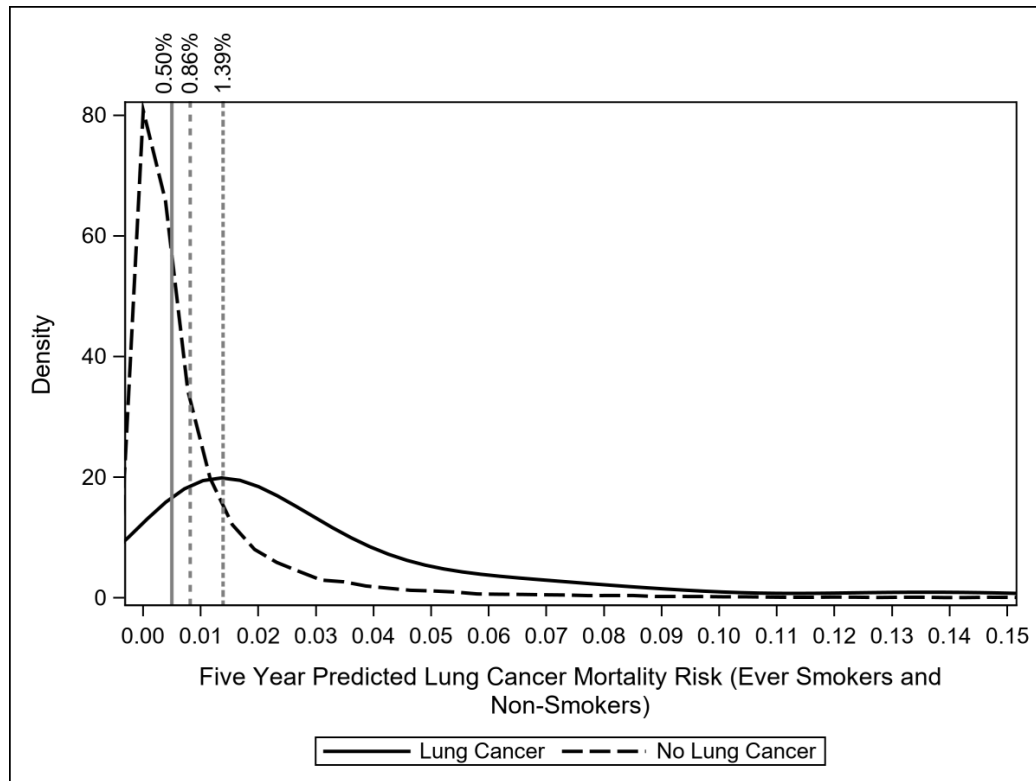
		Lung Cancer Deaths by Model Predicted Risk Decile									
		0	1	2	3	4	5	6	7	8	9
Predicted Deaths		0.51	1.07	2.45	6.84	12.64	19.96	29.68	44.44	68.79	165.62
Observed Deaths		0	0	4	4	7	17	34	51	65	170

Figure S-3: Calibration Plot, Alternate Cox Lung Cancer Mortality Model Using CXR and Spirometry Categories ¹



¹ LOESS regression line fit to data points. Perfect calibration show as --- line.

		Lung Cancer Deaths by Model Predicted Risk Decile									
		0	1	2	3	4	5	6	7	8	9
Predicted Deaths		0.46	1.02	2.44	6.47	11.72	18.29	28.82	42.00	68.59	172.20
Observed Deaths		0	0	1	6	11	11	31	43	80	169

Figure S-4: Final Model Predicted Risk by Lung Cancer Status¹

¹ Model predicted 5-year lung cancer mortality risk for individuals 50-80 years of age and with FEV₁ ≥ 40% of predicted. The distributions are right truncated due to the highly skewed distributions of risk. Risk thresholds for criteria shown in Table 5 are included as vertical reference lines.