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Racial disparities in lung cancer screening risk factors in an underrepresented safety-net screening population

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RACIAL DISPARITIES IN LUNG CANCER SCREENING RISK FACTORS IN AN UNDERREPRESENTED SAFETY-NET SCREENING POPULATION

by

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ABSTRACT

Background:

The USPSTF (United States Preventive Service Task Force) criteria for lung cancer screening focuses on smoking status and age as the only relevant risk factors for lung cancer screening and does not consider potential racial disparities. Several other risk factors may potentially be predictive of lung cancer. The purpose of this study was to assess other risk factors and to evaluate any racial disparities within these risk factors to create a more comprehensive screening tool.

Methods:

We performed a retrospective chart review of patients who received LDCT screening for lung cancer between 3/1/2015 and 12/31/2019 at Boston Medical Center. Patient demographics and medical histories were collected. A bivariate logistic regression analysis was used to evaluate predictors of lung cancer. A Breslow test was performed to observe if race was an effect modifier.

Results:

A total of 2847 patient charts were reviewed. For white patients, having a history of severe emphysema (adjusted OR 6.25; CI 95% 2.47-15.80), diagnosed with COPD

(Chronic Obstructive Pulmonary Disease) (adjusted OR 1.32; CI 95% 0.76-2.30), a family history of cancer (adjusted OR 3.54; CI 95% 2.17-5.77) and a 50+ pack-year smoking history (adjusted OR 2.47; CI 95% 1.48-4.12) are all significantly associated with developing Lung-RADS4. For black patients, having a history of moderate (adjusted OR 3.29; CI 95% 1.44-7.49) and severe emphysema (adjusted OR 3.66; CI 95% 1.39-9.60), and age older than 65 years (adjusted OR 1.67; CI 95% 1.01-2.75) are significantly associated with Lung-RADS4.

Conclusion:

Current USPSTF screening criteria can be improved by incorporating all relevant risk factors and creating non-biased criteria that account for racial disparities.

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LIST OF ABBREVIATIONS

BMC	Boston Medical Center
BMI	Body Mass Index
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
LDCT	Low-Dose Computed Tomography
LPP	Liverpool Lung Project
LPPi	Liverpool Lung Project Risk Prediction Model
Lung-RADS	Lung Imagine Reporting and Data System
NIH	National Institute of Health
NLST	National Lung Screening Trial
OR	Odds Ratios
PLCOm2012	Modified Prostate Lung Colorectal and Ovarian Cancer Risk-Prediction Model
TSCE	Two-Stage Clonal Expansion
USPSTF	U.S. Preventative Services Taskforce

Chapter I: Introduction

Cancer

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells that can result in death if not treated. Many factors are known to increase the risk of developing cancer, including modifiable behaviors (e.g., tobacco use, alcohol consumption and having an unhealthy diet) and others that are not (e.g., genetic mutations). All known risk factors act by initiating and/or promoting cancer growth. The relative risk of certain cancers among people can be small; however, even small exposures associated with a relatively small excess risk can have a large influence on the number of cancers diagnosed in the population. Some factors have much larger relative risks, such as smoking cigarettes. Men and women who smoke cigarettes are about 25 times more likely to develop lung cancer than people who never smoked. In the United States, it is estimated that 41 out of 100 men and 39 out of 100 women will develop some cancer during their lifetime, however these probabilities may differ for people because of variations in individual exposures and/or genetic susceptibilities.(*Cancer Facts & Figures 2021*, n.d.)

Cancer occurrence throughout the United States varies drastically between different states. This is especially true for cancers tied closely to behavioral factors like smoking. It is reported that the lung cancer incidence rates for black men residing in

southern states are almost double that of northern states due to historic differences in smoking prevalence.(*Cancer Screening 28 Cancer Statistics,* n.d.)

Cancer doesn't just manifest itself; it also comes with a significant financial burden. The cost of cancer can be measured by direct medical costs (total of all health care expenditures) and indirect costs (e.g., lost earnings due to an absence of work or premature death and loss of family income due to the need for caring for a sick family member). "The National Cancer Institute estimates that cancer-related direct medical costs in the US were $183 billion in 2015 and are projected to increase to $246 billion by 2030, a 34% increase based only on population growth and aging. However, the projection is likely an underestimate because of the growing cost of prescription medications, with the list price for many now more than $100,000 annually.(*Cancer Facts & Figures 2021,* n.d.)" Nearly 26 million Americans were uninsured at some point during the 2019 calendar year despite insurance coverage following the implementation of the Affordable Care Act. These uninsured individuals are substantially more likely to be diagnosed with cancer at a later stage due to them not seeking medical attention in a timely fashion by which point treatments are often costlier, more intensive, and less successful.

Cancer is the second leading cause of death in North America with 599,601 cancer deaths reported in 2019. Despite cancer rates dropping 27% from 1999 to 2019, it still has a major impact on our society. According to the National Cancer Institute,

In 2018, there were 18.1 million new cases and 9.5 million cancer-related deaths worldwide… It is predicted that by 2040, the number of new cancer cases per year is

expected to rise to 29.5 million and the number of cancer-related deaths to be 16.4 million. Generally, cancer rates are highest in countries whose populations have the highest life expectancy, education level, and standard of living.(*Cancer Statistics - National Cancer Institute,* n.d.) With cancer mortality rates rising, we need to understand why this is happening. Specifically with regards to lung cancer, problems exist with screening criteria. The currently accepted Low-Dose Computed Tomography (LDCT) model only incorporates age and smoking history as risk factors, yet the National Institute of Health (NIH) lists many other known or suspected risk factors for developing certain cancers. These include Age, Alcohol, Cancer-Causing Substances, Chronic Inflammation, Diet, Hormones, Immunosuppression, Infectious Agents, Obesity, Radiation, Sunlight and Tobacco.(*Risk Factors for Cancer - National Cancer Institute,* n.d.) Some of these factors can't be avoided like age and family history, whereas others can be affected by individual choice. While epidemiological studies on their own cannot prove that a behavior or substance causes cancer, for example a discovery purely based off chance, findings can reveal trends amongst certain population groups which may indicate a possible risk factor for that behavior or substance. This is one of the reasons why we are trying to develop a more accurate model for lung cancer screening that incorporates relevant risk factors other than age and smoking history.

LDCT Screening and Lung-RADS Scoring

The current, widely accepted standard for lung cancer screening is LDCT screening. LDCT technology utilizes a computer algorithm and very low dose radiography to make detailed images of targeted areas inside the body. Multiple images are compiled to create 3-D views of tissues and organs. These images are then analyzed to map the size and determine the type of any unusual masses found during the screening process. These growths are then categorized under the Lung Imaging Reporting and Data System (Lung-RADS), a classification system that standardizes follow-up and management decisions, to determine a patient's risk of malignancy.(*Definition of LDCT - NCI Dictionary of Cancer Terms - National Cancer Institute*, n.d.) Lung-RADS designates four categories of results which are defined as: 1 (no nodules or nodules with specific calcifications, <1% chance of malignancy), 2 (nodules with benign appearance or behavior, <1% chance of malignancy), 3 (probably benign nodules with a low likelihood of becoming a clinically active cancer, 1-2% chance of malignancy), and 4 (suspicious nodules for which additional testing is recommended, 5-15% chance of malignancy).(*Lung-RADS*, n.d.) For patients with a score of RADS4, more advanced imaging (PET/CT) and/or tissue sampling will frequently be conducted depending on the probability of malignancy and comorbidities. RADS scoring is determined by the type of nodule (solid, partly solid, or non-solid) with respect to their relative sizes. When considering the current worldwide population, it is estimated that roughly 90% of people have some type of nodule with a RADS score of 1 or 2. For these patients, annual follow-

ups with LDCT is recommended. For patients with RADS3, which is an estimated 5% of the population, follow-up LDCT screening should be performed every 6-months. For RADS4 patients, an estimated 2% of the population, subsequent diagnostic tests, such as previously described, are indicated.

Studies on LDCT guidelines led to a more definitive study conducted in the United States, the 2002 National Lung Screening Trial (NLST). The NLST is considered the gold standard for current LDCT recommendations. In 2015, Pinsky *et al.* performed a retrospective secondary analysis of the NLST cohort with lung RADS guidelines to determine the efficacy of lung RADS scoring. Results showed that, at baseline, the false-positive result rate for Lung RADS was 12.8% versus 21.8% for the NLST; thus, showing the effectiveness of lung RADS in reducing the false-positive result rate.(Pinsky et al., n.d.)

Screening is one of the keys to improving lung cancer outcome. According to the American Lung Association, in 2020, if every American who was eligible was screened for lung cancer, close to 48,000 lives could have been saved. Only 5.7% of those at high-risk were screened.(Lung Association, n.d.) Lung cancer stages are divided into three categories: early (localized to its primary site), regional (spread to regional lymph nodes) and distant (cancer has metastasized). 23% of diagnoses are early, which carries 59% 5-year survival rate. 22% of diagnoses are regional which has a 32% 5-year survival rate and 47% of diagnoses are distant which carries only a 6% 5-year survival rate. The remaining 8% of diagnoses were unstaged tumors. By improving screening efforts, we can improve lung cancer outcome.

Lung-Cancer Screening Current Model

Cancer is the second leading cause of death for all individuals after heart disease with lung cancer being the leading cause of cancer mortality in North America. In 2021, approximately 608,570 people are expected to die of cancer of which 131,880 will succumb to lung cancer.(*Cancer Facts & Figures 2021,* n.d.) In North America, the current standard for lung cancer screening utilizes LDCT which can detect early-stage disease. In North America and Europe, studies generally included cohorts of high-risk smokers, while in East Asia, they included cohorts of low-risk smokers and never-smokers in addition to their high-risk smoking population.(Pinsky, 2018) These early studies showed promising observational data (LDCT having a roughly three times positive screening result at a baseline than those for chest radiography) which led to a definitive study conducted in the United States, the NLST. The NLST was a randomized trial of over 50,000 high-risk current and former smokers comparing LDCT screening to screening with chest radiography. In 2011, the NLST reported a statistically significant 20% lung cancer mortality relative reduction in the LDCT arm.(Gatsonis et al., 2011) Despite the significant reduction of 20% in lung cancer mortality, the NLST results only showed a cancer detection rate of 1.1% within their study population, thus suggesting the need to investigate possible ways to refine the current screening strategy to improve detection rates. Additionally, dissemination of LDCT screening has been slow with currently less than 5% of those eligible being screened.(Pinsky, 2018)

The U.S. Preventative Services Taskforce (USPSTF) currently recommends asymptomatic people be screened annually for lung cancer with LDCT for adults aged 50-80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years.(Krist et al., 2021) Pack-years are measured by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked.(*Cancer Statistics - National Cancer Institute*, n.d.) The inclusion criteria, although supported by the results of the NLST trial, has areas for improvements. The guidelines were derived from a study population that included only 4% African American smokers, therefore racial differences in smoking patterns were not considered.(Aldrich et al., 2019) Moreover, the only risk factors taken into consideration were age and smoking status. Recent studies suggest that including additional risk factors can increase the sensitivity (positive predictive value) of LDCT screening. Tammemägi *et al.* incorporated additional risk factors in their PLCOm2012 model (modified Prostate, Lung, Colorectal, and Ovarian cancer risk-prediction model) including race, education, body mass index (BMI), pulmonary comorbidities, personal history of cancer and family history of lung cancer.(Tammemägi et al., 2013a) This model based its findings off of the NLST cohort, which not only ignored racial differences amongst their study population but also differed vastly from the general US population. None of these studies adequately evaluated the possibility that amongst different races, various other risk factors and comorbidities can significantly alter their predictive capability of detecting early lung cancer. Boston Medical Center is a safety-net hospital where the demographic composition, education level and prevalence of comorbidities are higher than that of the NLST population. With

this in mind, our goal is to create a screening criterion predictive of lung cancer in our diverse safety-net population to increase screening yield. Our group has recently published on this and so this treatise is an extension of that work which will consider racial differences in those results.(Singh Sarah et al., 2021)

Comparison Between LDCT And Other Models

LDCT has emerged as the national standard for lung cancer screening, yet there remain many other models for lung cancer screening that are still used. Some base their findings off the NLST population whereas others are based off their own study populations. Some of these high-risk prediction models include: the Bach model, the Liverpool Lung Project (LPP) model, the PLCOm2012 model, the Two-Stage Clonal Expansion (TSCE) model for lung cancer incidence, and the Knoke model.(ten Haaf et al., 2017) The Bach model predicts the probability of being diagnosed with lung cancer within the next year. It accounts for the standard criteria of smoking and age, but also takes into consideration asbestos exposure as an additional risk factor.(ten Haaf et al., n.d.) The TSCE and Knoke models consider only age, gender, and smoking exposure as an additional risk factor, while the LPP and PLCOm2012 models consider multiple additional risk factors like race and education.(Seijo et al., 2019; Tammemägi et al., 2013a) Haaf *et al.* performed a comparative analysis of these different screening models based on additional life years gained as well as the number of over-diagnosed cases (false positive cases). This study concluded that while these models considerably averted more

lung cancer deaths, the life years gained using these screening criteria were modest and the number of false positives was considerably high. Overdiagnosis was attributed to having a population of predominately older individuals, most of whom had life expectancies less than 5 years after screening-diagnosis. None of the aforementioned studies have yielded any significant results that have affected the USPSTF guidelines for lung cancer screening. Efficient implementation of lung cancer screening requires an evaluation of each models' strengths and weaknesses to provide a more accurate model which maximizes true positive cases while minimizing false positives; additionally, sensitive selection criteria for study populations is required to reduce overdiagnosis.

Chapter II: Methods

Ethical Approval:

The Boston University/Boston Medical Center Institutional Review Board approved this clinical study.

Study Sample:

Between the dates of March 1st, 2015, and December 31st, 2019, any Boston Medical Center (BMC) patients who went in for LDCT screening for lung cancer under the National Comprehensive Cancer Network and USPSTF guidelines were handpicked from the Lung Cancer Screening Clinical Registry. New USPSTF guidelines indicate that patients between the ages of 50 and 80 years old, with 20+ pack-years are now eligible for screening; however, our data collection and analysis predated the introduction of these new guidelines. During the time period of the study patients underwent their first CT lung cancer screening, and data were collected for each individual. From those patients we completed an eligibility check for patients that were at least 55 years old and had a pack-year of greater than or equal to 30.

Data Collection:

Each variable collected from each of the patients was obtained manually through the BMC electronic medical record and consisted of demographic data (age at date of scan, sex, gender, race, level of education), smoking status (pack-years, start date), personal medical history (Chronic Obstructive Pulmonary Disease (COPD), emphysema, pneumonia, Body Mass Index (BMI), previous non-lung cancer diagnosis), as well as family history of lung cancer.

Outcomes:

Lung-RADS results and lung cancer diagnosis were collected as endpoints for the study. The Lung-RADS tool helps to standardize the reporting of unusual findings from a lung cancer CT screening. It is influential for the quality assurance and registry reporting of these screening exams and allows radiologists to minimize variation when reporting on the detection of lung nodules and their risk. The Lung-RADS results are graded on a scale of 1 to 4: 1 (no lung nodules), 2 (solid nodule with benign appearance, <1% chance of malignancy), 3 (probably benign with 1-2% chance of malignancy), and 4 (suspicious nodules with >5% chance of malignancy). Upon CT report review, emphysema history was collected and categorized into one of four levels: none, mild, moderate, and severe.

Covariates:

We reviewed the literature to identify potential covariates that would influence our analysis (Table 1). We turned age into a categorical variable to create a cutoff for a potential future screening criterion. Race was limited to whites vs blacks since the sample study population contained too few people from other races (Asian, Hispanic, Latino, or Undetermined). Pack-year cutoff was set at 50 pack-years due to our higher age cohort. Level of education was established as graduating high school or not. BMI was defined according to national standards: underweight <18.5%, normal 18.5% – 25%, overweight 25% – 30%, obese >30%. Diagnosed COPD, history of pneumonia, history of emphysema, history of cancer and family history of cancer were determined as a yes or no from recorded patient histories. Smoking status was defined as "Never Smoker," for those who have never smoked cigarettes before, "Former Smoker," for those who quit smoking over 15 years ago and "Current Smoker," for those who actively smoke within the past 15 years.

Statistical Analysis:

Through analysis of Lung-RADS categorical data, a frequency table was generated. In order to observe if race was an effect modifier, a Breslow-test was then performed. For binary variables, logistic regressions were used to evaluate unadjusted

predictors of a Lung-RADS 4 result and Lung-RADS 1 result after stratifying race into white patients and black patients. Adjusted models were designed with respect to Lung-RADS 4 and Lung-RADS 1 by all significant predictors and race, respectively in white patients and black patients. Logistic regressions were then conducted for the cohort to evaluate unadjusted predictors of a Lung-RADS 4 result and a Lung-RADS 1 result. Adjusted models were formed from this data with respect to Lung-RADS 4 and Lung-RADS 1 by all significant predictors. The alpha value was set at 0.05.

Chapter III: Results

There were 208 individuals who did not meet the screening standards and were removed from the analysis, leaving us with a final total of 2,847 patients. The patient's characteristics table (Table 1) was generated for analyzing categorical data with respect to the four groups of Lung-RADS. 152 patients were missing education; 669 patients were missing lung cancer diagnosed; and 250 patients were missing smoking status. Odds ratios (ORs) that did not include one in the 95% confidence interval (CI) were considered statistically significant.

TABLE 1. Patient Characteristics in Lung-RADS Cohort

		Lung-RADS (n=2361)				
Variable	**Category**	**1 (n=401)**	**2 (n=1524)**	**3 (n=282)**	**4 (n=154)**	**Total**
SEX	Female	155 (15.58)	652 (65.53)	121 (12.16)	66 (6.63)	994
	Male	246 (17.96)	872 (63.65)	161 (11.75)	88 (6.42)	1367
AGE	≤65	300 (18.25)	1065 (64.78)	181 (11.01)	94 (5.72)	1640
	>65	101 (13.99)	459 (63.57)	101 (13.99)	60 (8.31)	721
RACE	White Patients	179 (14.83)	785 (65.04)	155 (12.84)	84 (6.96)	1203
	Black Patients	222 (19.17)	739 (63.82)	127 (10.97)	70 (6.04)	1158
Pack-Years	≤50	358 (17.27)	1352 (65.22)	239 (11.53)	119 (5.74)	2068
	>50	43 (14.68)	172 (58.70)	43 (14.68)	35 (11.95)	293
Education-graduated high school	Yes	249 (17.44)	929 (65.06)	160 (11.2)	90 (6.30)	1428
	No	133 (16.99)	502 (64.11)	96 (12.26)	50 (6.39)	781
BMI	Underweight (<18.5)	36 (18.00)	129 (64.50)	24 (12.00)	9 (4.50)	198
	Normal (≥18.5, <25)	97 (15.75)	401 (65.10)	71 (11.53)	47 (7.63)	616
	Overweight (≥25, <30)	125 (16.78)	474 (63.62)	99 (13.29)	45 (6.04)	743
	Obese (≥30)	143 (17.76)	520 (64.60)	88 (10.93)	53 (6.58)	804
Diagnosed COPD	Yes	178 (15.23)	739 (63.22)	150 (12.83)	102 (8.73)	1169
	No	223 (18.65)	785 (65.64)	132 (11.04)	52 (4.35)	1192
History of Pneumonia	Yes	87 (15.37)	354 (62.54)	76 (13.43)	49 (8.66)	566
	No	314 (17.45)	1170 (65.04)	206 (11.45)	105 (5.84)	1795
History of Emphysema	None	156 (19.77)	531 (67.30)	69 (8.75)	29 (3.68)	785
	Mild	201 (15.40)	844 (64.67)	175 (13.41)	85 (6.51)	1305
	Moderate	33 (18.75)	102 (57.95)	21 (11.93)	20 (11.36)	176
	Severe	11 (11.58)	47 (49.47)	17 (17.89)	20 (21.05)	95
History of Cancer	Yes	69 (18.25)	236 (62.43)	41 (10.85)	32 (8.47)	378
	No	332 (16.71)	1288 (64.82)	241 (12.13)	122 (6.14)	1983
Family History of Cancer	Yes	44 (14.47)	184 (60.53)	33 (10.86)	43 (14.14)	304
	No	357 (17.32)	1340 (65.02)	249 (12.08)	111 (5.39)	2057
Lung Cancer Diagnosed	Yes	0	10 (62.50)	6 (37.5)	0	16
	No	0	1418 (84.61)	258 (15.39)	0	1676
Smoking Status	Never Smoker	8 (19.51)	25 (60.98)	6 (14.63)	1 (2.44)	40
	Former Smoker	149 (18.44)	508 (62.87)	100 (12.38)	50 (6.19)	807
	Current Smoker	222 (16.54)	880 (65.57)	150 (11.18)	12 (6.71)	1264

Bivariate logistic regressions were used to evaluate unadjusted predictors of a Lung-RADS 4 result (Table 2). White patients with a history of pneumonia have 1.81 times higher odds of developing Lung-RADS4 than those with no history of pneumonia (unadjusted OR 1.81; 95% CI, 1.14-2.88). White patients with a history of mild emphysema have 2.25 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 2.25; 95% CI, 1.23-4.13). White patients with a history of moderate emphysema have 2.82 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 2.82; CI 95% 1.15-6.95). Black patients with a history of moderate emphysema have 3.84 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 3.84; CI 95% 1.73-8.54). White patients with a history of severe emphysema have 9.27 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 9.29; CI 95% 4.00-21.58). Black patients with a history of severe emphysema have 5.06 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 5.06; CI 95% 2.02-12.69).

With regards to COPD in both white patients and black patients a positive diagnosis is significantly associated with Lung-RADS4 ($p=0.0007$ and $p=0.0127$) at a 95% confident interval. White patients with diagnosed COPD have 2.32 times higher odds of developing Lung-RADS4 than white patients without diagnosed COPD (unadjusted OR 2.32; CI 95% 1.42-3.77). Black patients with diagnosed COPD have 1.87 times higher odds of developing Lung-RADS4 than those who have never been diagnosed with COPD (unadjusted OR 1.87; CI 95% 1.14-3.06).

A personal history of cancer has a significant association with Lung-RADS4 ($p=0.014$) for black patients at a 95% confidence interval. Black patients who have a personal history of cancer have 2.05 times higher odds of developing Lung-RADS4 than those with no personal history of cancer (unadjusted OR 2.05; CI 95% 1.16-3.64).

Likewise, a positive family history carries a significant association with Lung-RADS4 ($p<0.0001$) for white patients at a 95% confidence interval. White patients that have a family history of cancer have 3.4 times higher odds of developing Lung-RADS4 than those who don't have family history of cancer (unadjusted OR 3.60; CI 95% 2.26-5.75).

White patients with 50+ pack-years have 2.87 times higher odds of developing Lung-RADS4 than those who have less than 50 pack-years (unadjusted OR 2.87; CI 95% 1.77-4.64). The pack-years category shows significant association with Lung-RADS4 ($p<0.0001$) in white patients at a 95% confidence interval. Similarly, pack-years is significantly associated with Lung-RADS4 ($p=0.0063$) in black patients at a 95% confidence interval. Black patients older than 65 have 1.97 times higher odds of developing Lung-RADS4 than black patients who are 65 years old or younger (unadjusted OR 1.97; CI 95% 1.21-3.20).

TABLE 2. Unadjusted Odds Ratios for Lung-RADS 4 vs. 1-3

	WHITE PATIENTS				BLACK PATIENTS			
Independent Variable	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**
History of Pneumonia	Yes vs. No	1.81	(1.14, 2.88)	0.01	Yes vs. No	1.20	(0.69, 2.10)	0.51
History of Emphysema	Mild vs. None	2.25	(1.23, 4.13)	0.01	Mild vs. None	1.43	(0.77, 2.66)	0.25
	Moderate vs. None	2.82	(1.15, 6.95)	0.02	Moderate vs. None	3.84	(1.73, 8.54)	0.001
	Severe vs. None	9.29	(4.00, 21.58)	<.001	Severe vs. None	5.06	(2.02, 12.69)	0.001
Diagnosed COPD	Yes vs. No	2.32	(1.42, 3.77)	0.001	Yes vs. No	1.87	(1.14, 3.06)	0.01
Personal History of Cancer	Yes vs. No	1.01	(0.57, 1.80)	0.97	Yes vs. No	2.05	(1.16, 3.64)	0.01
Family History of Cancer	Yes vs. No	3.60	(2.26, 5.75)	<.001	Yes vs. No	1.85	(0.92, 3.73)	0.09
Education-graduated high school	Yes vs. No	1.05	(0.61, 1.79)	0.87	Yes vs. No	0.93	(0.57, 1.52)	0.77
Pack-years	>50 vs. ≤50	2.87	(1.77, 4.64)	<.001	>50 vs. ≤50	1.22	(0.54, 2.74)	0.63
Age	>65 vs. ≤65	1.18	(0.73, 1.91)	0.49	>65 vs. ≤65	1.97	(1.21, 3.20)	0.01
BMI	Underweight vs. Normal	0.64	(0.27, 1.54)	0.32	Underweight vs. Normal	0.47	(0.11, 2.02)	0.31
	Overweight vs. Normal	0.82	(0.45, 1.52)	0.53	Overweight vs. Normal	0.75	(0.41, 1.34)	0.33
	Obese vs. Normal	1.24	(0.70, 2.20)	0.45	Obese vs. Normal	0.56	(0.31, 1.02)	0.06
Smoking Status	Former Smoker vs. Never Smoker	1.08	(0.14, 8.47)	0.94	Former Smoker vs. Never Smoker	n/a*	n/a*	0.21
	Current Smoker vs. Never Smoker	1.24	(0.16, 9.58)	0.83	Current Smoker vs. Never Smoker	n/a*	n/a*	0.21
Sex	Male vs. Female	0.86	(0.55, 1.33)	0.49	Male vs. Female	1.13	(0.69, 1.85)	0.64

After adjusting for covariates, the association between a history of emphysema, diagnosed COPD, a family history of cancer, pack-year history and age all with respect to Lung-RADS4 were all maintained. The association between a history of emphysema and a personal history of lung cancer with respect to Lung-RADS4 was not maintained.

Adjusted models were created with respect to Lung-RADS 4 (Table 3) by all significant predictors and race, respectively in white patients and black patients. In white patients, history of severe emphysema ($p=0.0001$), family history of cancer ($p<0.0001$) and pack-years category ($p=0.0005$) are significantly associated with Lung-RADS4, after adjusting for other risk factors in the model. White patients with a severe history of emphysema have 6.25 higher odds of developing Lung-RADS4 than patients without a history of emphysema (adjusted OR 6.25; CI 95% 2.47-15.80). White patients with diagnosed COPD have 1.32 higher odds of developing Lung-RADS4 than white patients without a COPD diagnosis (adjusted OR 1.32; CI 95% 0.76-2.30). White patients with a family history of cancer have 3.54 times higher odds of developing Lung-RADS4 than white patients without a family history of cancer (adjusted OR 3.54; CI 95% 2.17-5.77). White patients with a pack-year history greater than 50 have 2.47 times higher odds of developing Lung-RADS4 than white patients with a pack-year history less than 50 (adjusted OR 2.47; CI 95% 1.48-4.12). There is evidence of joint confounding by a history of pneumonia, diagnosed COPD, family history of cancer and pack-years category in the estimation of the relationship of history of severe emphysema to Lung-RADS4. In the estimation of relationship of pack-years category and Lung-RADS4, there

is evidence of joint confounding by history of pneumonia, history of emphysema, diagnosed COPD and family history of cancer.

In black patients, having a history of moderate (p=0.0064) or severe emphysema (p=0.0085) and age category (p=0.0452) are significantly associated with Lung-RADS4 at a 95% confidence interval after adjusting for other risk factors. Black patients with a history of moderate emphysema and severe emphysema have 3.29 times higher odds (adjusted OR 3.29; CI 95% 1.44-7.49) and 3.66 times higher odds (adjusted OR 3.66; CI 95% 1.39-9.60) than those with no history of emphysema respectively. There is evidence of joint confounding by diagnosed COPD, personal history of cancer and age category in the estimation of the relationship of history of moderate and severe emphysema to Lung-RADS4.

Black patients older than 65 have 1.67 times higher odds of developing Lung-RADS4 than those who are 65 years old and younger (adjusted OR 1.67; CI 95% 1.01-2.75). In the estimation of relationship of age category and Lung-RADS4, there is evidence of joint confounding by history of emphysema, diagnosed COPD and personal history of cancer.

TABLE 3. Adjusted Odds Ratios for Lung-RADS 4 vs. Lung-RADS 1-3

	WHITE PATIENTS				BLACK PATIENTS			
Independent Variable	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**
History of Pneumonia	Yes vs. No	1.41	(0.86, 2.33)	0.18	Yes vs. No			
History of Emphysema	Mild vs. None	1.62	(0.85, 3.10)	0.14	Mild vs. None	1.31	(0.70, 2.46)	0.41
	Moderate vs. None	1.77	(0.68, 4.60)	0.24	Moderate vs. None	3.29	(1.44, 7.49)	0.005
	Severe vs. None	6.25	(2.47, 15.80)	0.001	Severe vs. None	3.66	(1.39, 9.60)	0.01
Diagnosed COPD	Yes vs. No	1.32	(0.76, 2.30)	0.001	Yes vs. No	1.40	(0.83, 2.37)	0.20
Personal History of Cancer	Yes vs. No				Yes vs. No	1.77	(0.99, 3.19)	0.06
Family History of Cancer	Yes vs. No	3.54	(2.17, 5.77)	<.001	Yes vs. No			
Pack-years	>50 vs. ≤50	2.47	(1.48, 4.12)	0.001	>50 vs. ≤50			
Age	>65 vs. ≤65				>65 vs. ≤65	1.67	(1.01, 2.75)	0.045

Bivariate logistic regressions were used to evaluate unadjusted predictors of Lung-RADS1 (Table 4) after race was stratified into white patients and black patients. In white patients, history of mild emphysema versus none (p=0.021) and age category (p=0.0086) are significantly associated with Lung-RADS1. White patients with no history of emphysema have 0.67 times higher odds of having Lung-RADS1 than those who have a mild history of emphysema (unadjusted OR 0.67; CI 95% 0.48-0.94). White patients older than 65 have 0.59 times higher odds of having Lung-RADS1 than those who are 65 years old and younger (unadjusted OR 0.59; CI 95% 0.40-0.88).

TABLE 4. Unadjusted Odds Ratios for Lung-RADS 1 vs. 2-4

	WHITE PATIENTS				BLACK PATIENTS			
Independent Variable	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**
History of Pneumonia	Yes vs. No	0.77	(0.52, 1.13)	0.18	Yes vs. No	0.97	(0.68, 1.38)	0.85
History of Emphysema	Mild vs. None	0.67	(0.48, 0.94)	0.02	Mild vs. None	0.80	(0.58, 1.10)	0.17
	Moderate vs. None	0.57	(0.28, 1.15)	0.12	Moderate vs. None	1.31	(0.77, 2.23)	0.32
	Severe vs. None	0.51	(0.20, 1.33)	0.17	Severe vs. None	0.55	(0.23, 1.34)	0.19
Diagnosed COPD	Yes vs. No	0.80	(0.58, 1.10)	0.18	Yes vs. No	0.80	(0.60, 1.08)	0.14
Personal History of Cancer	Yes vs. No	1.25	(0.84, 1.86)	0.27	Yes vs. No	1.03	(0.68, 1.56)	0.90
Family History of Cancer	Yes vs. No	0.90	(0.58, 1.39)	0.63	Yes vs. No	0.79	(0.45, 1.37)	0.40
Education-graduated high school	Yes vs. No	1.03	(0.72, 1.48)	0.87	Yes vs. No	1.10	(0.81, 1.49)	0.54
Pack-Years	>50 vs. ≤50	0.69	(0.43, 1.12)	0.13	>50 vs. ≤50	1.17	(0.70, 1.93)	0.55
Age	>65 vs. ≤65	0.59	(0.40, 0.88)	0.01	>65 vs. ≤65	0.81	(0.59, 1.11)	0.20
BMI	Underweight vs. Normal	1.24	(0.72, 2.14)	0.43	Underweight vs. Normal	1.31	(0.63, 2.70)	0.47
	Overweight vs. Normal	1.04	(0.68, 1.61)	0.85	Overweight vs. Normal	1.13	(0.77, 1.68)	0.53
	Obese vs. Normal	1.10	(0.71, 1.69)	0.68	Obese vs. Normal	1.20	(0.83, 1.74)	0.34
Smoking Status	Former Smoker vs. Never Smoker	0.67	(0.21, 2.11)	0.49	Former Smoker vs. Never Smoker	1.24	(0.41, 3.74)	0.70
	Current Smoker vs. Never Smoker	0.51	(0.16, 1.59)	0.24	Current Smoker vs. Never Smoker	1.21	(0.41, 3.58)	0.74
Sex	Male vs. Female	1.13	(0.82, 1.57)	0.44	Male vs. Female	1.22	(0.91, 1.65)	0.19

After adjusting for covariates, the association between having no history of emphysema and having an age less than 65 years with respect to Lung-RADS1 were both maintained.

Adjusted models were created with respect to Lung-RADS1 (Table 5) by all significant predictors and race respectively in white patients and black patients. Having a mild history of emphysema is statistically significantly associated with Lung-RADS1 (p=0.0200) at a 95% confidence interval after adjusting for age category. White patients with a history of mild emphysema have 0.67 times higher odds of having Lung-RADS1 than those with no history of emphysema in the adjusted model (adjusted OR 0.67; CI 95% 0.48-0.94). Age category is statistically significantly associated with Lung-RADS1 (p=0.0093) at a 95% confidence interval after adjusting for history of emphysema. White patients older than 65 have 0.59 times higher odds of having Lung-RADS1 than those that are 65 years old and younger (adjusted OR 0.59; 0.40-0.88).

TABLE 5. Adjusted Odds Ratios for Lung-RADS 1 vs. 2-4

	WHITE PATIENTS				BLACK PATIENTS			
Independent Variable	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**
History of Emphysema	Mild vs. None	0.67	(0.48, 0.94)	0.02	Mild vs. None			
	Moderate vs. None	0.57	(0.28, 1.16)	0.12	Moderate vs. None			
	Severe vs. None	0.54	(0.21, 1.43)	0.22	Severe vs. None			
Age	>65 vs. ≤65	0.59	(0.40, 0.88)	0.01	>65 vs. ≤65			

Bivariate logistic regressions were conducted for the cohort to evaluate unadjusted predictors of a Lung-RADS 4 result and Lung-RADS 1 result (Table 6). Race is significantly associated with Lung-RADS1 (p=0.005) at a 95% confidence interval. Black patients have 1.36 times higher odds of having Lung-RADS1 than white patients (unadjusted OR 1.36; CI 95% 1.10-1.69). Patients with a history of mild emphysema have 0.74 times higher odds than patients with no history of emphysema of having Lung-RADS1 (unadjusted OR 0.74; CI 95% 0.59-0.93). Patients with diagnosed COPD have 0.78 times higher odds than those with no diagnosed COPD of having Lung-RADS1 (unadjusted OR 0.78; CI 95% 0.63-0.97). Patients older than 65 have 0.73 times higher odds of having Lung-RADS1 than patients who are 65 years old and younger (unadjusted OR 0.73; CI 95% 0.57-0.93).

Patients with a history of pneumonia have 1.53 times higher odds of developing Lung-RADS4 than those with no history of pneumonia (unadjusted OR 1.53; CI 95% 1.07-2.18). Patients with a history of mild emphysema have 1.83 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 1.83; CI 95% 1.19-2.81). Patients with a history of moderate emphysema have 3.36 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 3.36; CI 95% 1.85-6.09). Patients with a history of severe emphysema have 6.99 times higher odds of developing Lung-RADS4 than those with no history of emphysema (unadjusted OR 6.99; CI 95% 3.78-12.95). Patients with diagnosed COPD have 2.1 times higher odds of developing Lung-RADS4 than those with no diagnosed COPD (unadjusted OR 2.10; CI 95% 1.49-2.97). Patients with a family history of cancer

have 2.89 times higher odds of developing Lung-RADS4 than patients with no family history of cancer (unadjusted OR 2.89; CI 95% 1.99-4.21). Patients who smoke more than 50 pack-years have 2.23 times higher odds of developing Lung-RADS4 than those smoke 50 pack-years or less (unadjusted OR 2.23; CI 95% 1.50-3.32). Patients older than 65 years old have 1.5 times higher odds of developing Lung-RADS4 than patients who are 65 years old or younger (unadjusted OR 1.50; CI 95% 1.07-2.09).

TABLE 6. Unadjusted Odds Ratio for Lung-RADS 4 and Lung-RADS 1

	Unadjusted Variables for Lung-RADS 4 vs. 1-3				Unadjusted Variables for Lung-RADS 1 vs. 2-4			
Independent Variable	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**
Race	Black patients vs. White patients	0.86	(0.62, 1.19)	0.37	Black patients vs. White patients	1.36	(1.10, 1.69)	0.01
Sex	Male vs. Female	0.97	(0.69, 1.34)	0.84	Male vs. Female	1.19	(0.95, 1.48)	0.13
History of Pneumonia	Yes vs. No	1.53	(1.07, 2.18)	0.02	Yes vs. No	0.86	(0.66, 1.11)	0.25
History of Emphysema	Mild vs. None	1.83	(1.19, 2.81)	0.01	Mild vs. None	0.74	(0.59, 0.93)	0.01
	Moderate vs. None	3.36	(1.85, 6.09)	<.001	Moderate vs. None	0.94	(0.62, 1.42)	0.76
	Severe vs. None	6.99	(3.78, 12.95)	<.001	Severe vs. None	0.53	(0.28, 1.02)	0.06
Diagnosed COPD	Yes vs. No	2.10	(1.49, 2.97)	<.001	Yes vs. No	0.78	(0.63, 0.97)	0.03
Personal History of Cancer	Yes vs. No	1.41	(0.94, 2.12)	0.09	Yes vs. No	1.11	(0.84, 1.48)	0.46
Family History of Cancer	Yes vs. No	2.89	(1.99, 4.21)	<.001	Yes vs. No	0.81	(0.58, 1.13)	0.22
Education-graduated high school	Yes vs. No	0.99	(0.69, 1.41)	0.94	Yes vs. No	1.03	(0.82, 1.30)	0.79
Pack-years	>50 vs. ≤50	2.23	(1.50, 3.32)	<.001	>50 vs. ≤50	0.82	(0.59, 1.16)	0.27
Age	>65 vs. ≤65	1.50	(1.07, 2.09)	0.02	>65 vs. ≤65	0.73	(0.57, 0.93)	0.01
BMI	Underweight vs. Normal	0.57	(0.27, 1.19)	0.13	Underweight vs. Normal	1.18	(0.77, 1.79)	0.45
	Overweight vs. Normal	0.78	(0.51, 1.19)	0.25	Overweight vs. Normal	1.08	(0.81, 1.44)	0.61
	Obese vs. Normal	0.85	(0.57, 1.28)	0.45	Obese vs. Normal	1.16	(0.87, 1.55)	0.31
Smoking Status	Former Smoker vs. Never Smoker	2.64	(0.36, 19.54)	0.32	Former Smoker vs. Never Smoker	0.93	(0.42, 2.06)	0.86
	Current Smoker vs. Never Smoker	2.88	(0.39, 21.16)	0.28	Current Smoker vs. Never Smoker	0.82	(0.37, 1.79)	0.61

After adjusting for covariates, the association between a history of emphysema, a family history of cancer and pack-year with respect to Lung-RADS4 were all maintained. The association between race, history of pneumonia, diagnosed COPD and age with respect to Lung-RADS4 was not maintained. The association between race, history of emphysema and age with respect to Lung-RADS1 was maintained. The association between COPD with respect to Lung-RADS1 was not maintained.

Adjusted models were formed with respect to Lung-RADS 4 and Lung-RADS 1 by all significant predictors (Table 7). Having a history of moderate ($p=0.004$) or severe ($p<0.0001$) emphysema, family history of cancer ($p<0.0001$) and pack-years category ($p=0.0071$) are significantly associated with the outcome of interest Lung-RADS4, adjusting for other variables in the model. In the estimation of the relationship between history of emphysema and Lung-RADS4, there is evidence of joint confounding by race, history of pneumonia, diagnosed COPD, family history of cancer, pack-years, and age category. In the estimation of relationship between pack-years category and Lung-RADS4, there is evidence of joint confounding by race, history of pneumonia, history of emphysema, diagnosed COPD and family history of cancer and age category. Race is significantly associated with the outcome of interest Lung-RADS1 ($p=0.0042$), after adjusting for history of emphysema, diagnosed COPD and age category. Having a history of mild emphysema is significantly associated with the outcome of interest Lung-RADS1 ($p=0.0101$), after adjusting for race, diagnosed COPD and age category. Age category is

significantly associated with the outcome of interest Lung-RADS1 (p=0.0117), after adjusting for race, history of emphysema, diagnosed COPD.

TABLE 7. Adjusted Odds Ratios for Lung-RADS 4 and Lung-RADS 1

	Adjusted Variables for Lung-RADS 4 vs. 1-3				Adjusted Variables for Lung-RADS 1 vs. 2-4			
Independent Variable	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**	**Category (n)**	**Odds Ratio**	**Confident Interval**	**P-value**
Race	Black patients vs. White patients	1.02	(0.73, 1.45)	0.89	Black patients vs. White patients	1.37	(1.11, 1.71)	0.004
History of Pneumonia	Yes vs. No	1.20	(0.83, 1.75)	0.33	Yes vs. No			
History of Emphysema	Mild vs. None	1.46	(0.93, 2.29)	0.10	Mild vs. None	0.77	(0.60, 0.98)	0.01
	Moderate vs. None	2.48	(1.34, 4.61)	0.004	Moderate vs. None	0.99	(0.64, 1.51)	0.95
	Severe vs. None	4.48	(2.30, 8.75)	<.001	Severe vs. None	0.61	(0.31, 1.19)	0.14
Diagnosed COPD	Yes vs. No	1.42	(0.97, 2.08)	0.07	Yes vs. No	0.78	(0.70, 1.11)	0.27
Family History of Cancer	Yes vs. No	2.69	(1.82, 3.98)	<.001	Yes vs. No			
Pack-years	>50 vs. ≤50	1.78	(1.17, 2.72)	0.01	>50 vs. ≤50			
Age	>65 vs. ≤65	1.34	(0.94, 1.90)	0.11	>65 vs. ≤65	0.73	(0.57, 0.93)	0.01

Chapter IV: Discussion

Since the landmark National Lung Screening Trial, several lung cancer prediction models have been proposed with the goal of analyzing a wide range of both clinical and demographic risk factors. The most notable being the LPP / Liverpool Lung Project Risk Prediction Model (LLPi) and the PLCOm2012 Model.(Cassidy et al., 2008; Cronin et al., 2006; Hoggart et al., 2012; Marcus et al., 2015; Spitz et al., 2007; Tammemägi et al., 2013b; Wilson & Weissfeld, 2015) One limitation amongst all these models is that they fail to incorporate racial disparities amongst their study populations. Whether they use NLST data or their own similar populations, no model compares risk-factors between racial groups, or rather, they only identify if the risk-factor is significant in general. As a safety-net institution, our BMC cohort differs significantly when compared to the NLST population. Patients in our safety-net cohort were older, had less advanced educational backgrounds and included significantly higher proportions of racial and ethnic minorities. Additionally, these patients had significantly higher proportions of comorbidities previously identified as potential risk factors for lung cancer, including COPD and emphysema. The purpose of our study was to analyze these risk factors and determine which, if any of them are significant and shared based on racial differences.

It is our contention that the current USPSTF criteria for lung cancer screening can be improved. Our results indicate that there are several additional risk factors that not only create a more inclusive patient screening population but can also show how certain risk factors affect races differently. White people with a severe history of emphysema,

diagnosed chronic obstructive pulmonary disease (COPD), a family history of cancer and pack-years history greater than 50 have a significant association with having Lung-RADS4; Black people with a moderate or severe history of emphysema or who are older than 65 have a significant association with having Lung-RADS4. Additionally, White patients with no history of emphysema or who are less than 65 years of age have a significant association with having Lung-RADS1. These findings indicate that the current USPSTF screening criteria can be revised and new criteria that appropriately adjust levels of risk based on how each significant risk factor affects whites versus blacks can be implemented.

Pack-year

With regards to pack-year smoking history, it is interesting to note that only white patients have a significant association with Lung-RADS4 for a greater than 50 pack-year history. The current USPSTF guidelines for lung cancer screening are based off the NLST cohort and they do not distinguish racial disparities within their screening criteria. In the same article from Aldrich *et al*, which explores racial disparities in the NLST cohort, they found the population of those diagnosed with lung cancer contained a significantly lower percentage of African American smokers eligible for screening when compared to white smokers. “The lower percentage of eligible lung cancer cases in African American smokers was primarily associated with fewer smoking pack-years among African American vs white smokers… Lowering the smoking pack-year

eligibility criteria to a minimum 20-pack-year history was associated with an increased percentage of screening eligibility of African American smokers and with equitable performance of sensitivity and specificity compared with white smokers across all ages.(Aldrich et al., 2019)" Although our study does not determine if lowering the eligibility criteria of the current USPSTF guidelines will increase the screening eligibility of African Americans, our data does show that a high pack year history is only significantly associated with white people.

Age

The current USPSTF guidelines recommend annual screening for people between the ages of 50 and 80, however we contend that this standard is outdated as our evidence suggests that a stricter criterion for different racial groups could potentially increase screening yield as well as reduce over screening. Unlike each model previously mentioned, our research focused on age as a distinct variable between races rather than as a whole like the PLCOm2012 model. Our results show that black patients with a pack-year history over 50 was insignificant. Additionally, white people less than 65 years of age had a significant association with having Lung-RADS1 indicating that there are no nodules present during CT screening; a Lung-RADS1 score is indicative of a negative screening result. With this knowledge, we should consider raising the screening age criteria for white people as well as decreasing the screening age for black people to increase screening yield. Our study is limited in that we did not determine what the ideal

age cutoff should be for screening; further studies will have to be conducted, looking at 5-year intervals, to determine what age cutoff is appropriate for each race when looking at age as an independent risk factor and when considering other potential confounding risk factors, like emphysema or pack-year smoking history. The ideal scenario would be to create a formula that incorporates all significant risk factors for each race to create a more precise screening tool.

Emphysema

In recent literature, emphysema has been marked as a probable risk-factor associated with lung cancer. Li *et al*. have found positive correlations between severity of emphysema and a lung cancer diagnosis. They found that mild emphysema (0%-5% emphysema on CT films) correlated with a an approximate 3-fold increase in lung cancer diagnoses and moderate to severe emphysema (5%-10% and 10%+ respectively of emphysema on CT films) correlated with an approximate 4-fold increase in lung cancer diagnoses. The caveat with their study was that their population was predominantly Caucasian (95.6%) with very little non-Caucasian representation.(Li et al., 2011)

From our data, we found that a history of emphysema in both white and black populations was significantly associated with a Lung-RADS4 scoring on LDCT exams. Specifically for white patients, any presence of emphysema (mild, moderate, or severe) increased the risk of a Lung-RADS4. Though the risk increases depending on the severity of emphysema, this study shows that white patients over 55 years of age with an

emphysema diagnosis are more likely to have a radiologic diagnosis of multiple suspicious nodules compared to those with no history of emphysema. Similar to white patients, black patients also had an increased risk for a RADS4 scoring with emphysema history. However, the severity of the emphysema is more telling in this population. A diagnosis of mild emphysema had no significant correlation with a Lung-RADS4 scoring for black patients, leading us to deduce that black patients under the USPSTF criteria may not need to be screened as frequently if their history of emphysema is mild or nonexistent. A history of moderate to severe emphysema for this population is still significantly associated with a Lung-RADS4 score and should continue to be screened similarly.

Family History of Cancer

Family history of disease can have a large impact on our predisposition to develop similar issues. From previous models, a family history of cancer has been significantly linked to the development of cancer. The PLCOm2012 model showed a significant association between lung cancer diagnosis and a family history of cancer with an odds ratio of (OR, 1.80; 95% CI, 1.47–2.20).(Tammemägi et al., 2013b) The LPPi model also showed a higher incidence of lung cancer in participants who had a family history of lung cancer (HR, 1.68; 95% CI, 1.04–2.72).(Marcus et al., 2015)

As genetic predisposition plays a major role in this finding, we hypothesized that a family history of cancer would be significantly correlated with a Lung RADS4 score for

both black and white patients as seen in previous models. This is due to the idea that genetic information is passed on through generations, factoring out covariates that may otherwise impact the development of cancer. However, we found that a family history of cancer was only significantly associated with a RADS4 score in our white population. Due to our original thoughts on this risk factor, we still believe that family history of cancer is an important variable to consider for screening in both populations. Nonetheless, due to the significance only of the white subjects in our study, we recommend that this population be screened at a higher rate if they meet USPSTF criteria and have a relevant history of cancer in their family.

Race and Education

Similar to the findings from Aldrich *et al.*, African American race and education were not significantly associated with lung cancer in our cohort. This contradicts previous studies which suggest that African Americans are more likely to develop lung cancer compared to whites.(*Cancer Screening 28 Cancer Statistics,* n.d.) Additionally, our results indicate that age is only significantly associated with African Americans who are older than 65 years of age, which supports Aldrich's findings that younger African Americans (in comparison to whites) are not more susceptible to lung cancer. There are several possible explanations for this finding. First, there is the possibility that our study may be underpowered, only being a single institution collecting data over a four-year period. Another possible explanation may have to do with the makeup of our study

population, as our entire cohort represents a safety-net population that contains a higher percentage of African American individuals and persons of lower socioeconomic status. Therefore, our study had the unique ability to compare racial background at a 51:49 ratio of white patients to black patients. Current literature indicates there is significance when comparing African Americans and lower educational background with a lower socioeconomic status. However, due to the majority of our population being characterized as lower socioeconomic status, these factors were not found to hold any significance in our research. Unlike other studies, our diverse population allowed us to obtain a more in-depth comparison between races, leading us to discover that the overall incidence of lung cancer for our population was 2.5% compared to the 1.1% seen in the NLST study. This variation supports the inclusion of more diverse populations into clinical studies of lung cancer to help mitigate the development of racially biased clinical models.

COPD

Previously discussed models showed that COPD is a significant risk factor for the development of lung cancer and RADS4 scoring on a lung screening CT scan. Our study is the first to assess racial disparities with COPD, unlike other models such as the PLCOm2012 model and LPPi model.(Marcus et al., 2015; Tammemägi et al., 2013b) While these studies showed an association between COPD and an increased risk of developing lung cancer, their analyses were too generalized. With this knowledge, we

expected to see significance in the development of a RADS4 score for both white and black patients diagnosed with COPD. However, from Table 3, we see there was only significance for white patients with diagnosed COPD to present as RADS4. Therefore, we recommend white patients that meet USPSTF screening criteria should be screened at a higher rate if they have been diagnosed with COPD in the past. It was interesting to find that COPD held no significance for the black population in our study. From the same table, we see that over the age of 65, black patients have a significant association with a RADS4 score, yet between the ages of 50 and 65 there is no correlation. This should make us consider narrowing screening criteria for black patients that meet USPSTF criteria and are between the ages of 50 and 65. Within this age range, the lack of significance of a COPD diagnosis for the black population may permit us to put less weight on these diagnoses if the patient has no other risk factors present.

Pneumonia

Pneumonia has been recognized as an insignificant risk factor for the development of lung cancer. Similarly, we hypothesized that the effects of pneumonia would have an insignificant impact on both black and white populations due to the relatively low number of individuals in our cohort with this type of respiratory condition as well as similar findings from current literature. Specifically, when we look at the LPPi model, the incidence of lung cancer was higher for individuals who had a prior history of pneumonia in conjunction with other risk factors discussed in this paper.(Marcus et al.,

2015) Through univariate analysis, the LPPi model found that this prior diagnosis of pneumonia was significant. However, when the LPPi model was adjusted through multivariate analysis, they found that pneumonia was not considered to be a significant independent risk factor for lung cancer. This correlates closely with our univariate and multivariate analyses. Whereas our unadjusted model showed that a history of pneumonia was significant for white patients and not black patients, our adjusted model showed that pneumonia was not a significant risk factor for the development of lung RADS4 score for either population. This parallel between our model and others in circulation had led us to predict that a history of pneumonia is not a prominent indicator for individuals meeting USPSTF criteria to score a RADS4 and go on to develop lung cancer.

Personal History of Cancer

Individuals who have been diagnosed with cancer in the past have been labelled as ‘at risk’ due to their previous ability to develop a neoplasm. Secondary cancers can form from a late effect of an individual’s first cancer, the treatment, or could be completely unrelated to the first cancer. It is estimated that 1 in 6 individuals diagnosed with cancer have had a previous cancer in the past.(*Lung Cancer - Non-Small Cell: Statistics | Cancer.Net*, n.d.) This knowledge led us to predict that there would be a significant association between a personal history of cancer and a RADS4 score. From other models we see a significant correlation between a previous cancer diagnosis and current lung cancer diagnoses. The LPPi model showed that lung cancer incidence was

noticeably higher for individuals with a previous diagnosis of malignancy.(Marcus et al., 2015) Unadjusted analysis (HR, 4.18; 95% CI, 3.15–5.55) and adjusted analysis (HR, 3.09; 95% CI, 2.33–4.11) showed a significantly increased risk for cancer when a patient had been diagnosed with cancer in the past. This suggests that there should be an addition to the current screening criteria such that people with a prior history of personal cancer are at a higher risk of developing Lung-RADS4. Further studies could clarify whether this classification applies to all cancer diagnoses or is specific to only certain cancers.

Strengths and Limitations

Our study had several strengths. It is unique in that it is one of the first to evaluate lung cancer risk factors between different racial groups. Additionally, our data were collected from Boston Medical Center where the demographic composition differs drastically from the NLST population in that it contains a more diverse population than seen in other studies. However, one limitation this creates is in the generalizability of our study. As our population was formulated from a unique safety net population out of a singular site, our data may not be applicable to other populations across the US. Another limitation comes from our method of data collection. All of the patient information was pulled directly from EPIC chart review which is a successful method for obtaining sex, age, and BMI, but may not be as reliable for smoking history, pulmonary comorbidities, or family history of cancer as these variables are generally not captured with high accuracy. For example, COPD diagnoses are many times not captured due to the low

frequency of PFTs ordered for patients when such tests are required to diagnose COPD. For this reason, our study may have displayed inaccuracies when looking at the prevalence of COPD in our population. Obtaining information from EPIC chart review alone is also a limitation depending on the frequency that patient charts are updated, reviewed, and corrected.

CHAPTER V: Conclusion

The purpose of our study was to identify possible racial disparities in risk factors for lung cancer screening. Based on our analysis, it can be concluded that emphysema, COPD, a family history of cancer, and pack-year smoking history are all important factors that need to be considered when calculating a relative risk of developing Lung-RADS4 and Lung-RADS1. While our study population limits the generalizability of our results, our findings provide new insights not only into which risk factors are significantly associated with developing Lung-RADS4, but also which risk factors specifically affect Blacks versus Whites. Further research is needed to determine the relative weights each risk factor contributes to determining the risk of developing Lung-RADS4 as well as to determine appropriate age ranges for screening to create a comprehensive non-biased formula to determine lung cancer risk.

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