CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN U.S. VETERANS: COMORBIDITY, OCULAR PATHOLOGY, AND COST OF CARE

by

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ABSTRACT

CHARLES N. DAVIS JR. Chronic Obstructive Pulmonary Disease in U.S. Veterans: Comorbidity, Ocular Pathology, and Cost of Care (Under the direction of DR. WILLIAM BRANDON)

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality among veterans. The present study investigated the identified comorbidities, ocular diagnoses, and the cost and utilization of care for veterans diagnosed with COPD compared to veterans without COPD. The study included the population of veterans that were enrolled for primary care at the Salisbury Veteran Affairs Health Care Center from January 1, 2016 to December 31, 2018. This case-control study comprised veterans between the ages of 50 years and 90 years. Structured Query Language (SQL) was used to identify the eligible study subjects, the sociodemographic variables, and the select ICD-9-CM and ICD-10-CM specific diagnoses. Statistical analyses used multivariant logistic models for the comorbidities and ocular diagnoses, and multivariant conditional quantile regression models for the cost and utilization of care. Veterans with COPD were shown to have greater odds for 15 systemic diagnoses compared to veterans without COPD. Cases were shown to be at significantly greater odds for exudative macular degeneration compared to control. Healthcare costs and utilization among veterans with COPD was approximately four times higher than those for veterans without COPD.

DEDICATION

This dissertation is dedicated to my wife, Nance, for her unwavering patience and understanding through this academic journey.

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CHAPTER 1: INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a persistent respiratory ailment and a major cause of morbidity and mortality. Worldwide, the deaths from COPD have steadily risen for the past 30 years. [1] In addition, COPD is detrimental to the patients' reported quality of life. [2,3] The prevalence of COPD varies according to how it is defined, the diagnostic standards, and the geographic region. [4] A 2010 national survey revealed that in the United States COPD affects approximately 5.4% of all adults aged 18 and older. [5] Between 1970 and 2002, the reported deaths from heart disease and stroke declined substantially, but the reported mortality related to COPD increased by 100%. [6]

The definition of COPD continues to evolve and inspire discussion. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) first proposed a definition of COPD severity that relied on the findings from spirometry. Spirometry measures pulmonary function over a time interval, i.e., the forced expiratory volume in one second over the forced vital capacity (FEV1/FVC), but this definition fails to consider patient symptoms and sometimes lacks diagnostic accuracy. [7] In 2018, the GOLD report expanded the definition to emphasize an individual's "persistent respiratory symptoms," or subjective complaints of a chronic cough or dyspnea, as a meaningful characteristic of COPD. [8]

Veterans represent a special population. Military service creates unavoidable psychological and physical hazards. For example, veterans are often exposed to dust, sand, smoke, fine particulates, and toxic chemicals that injure the lungs. Researchers have demonstrated that burn pit exposures cause respiratory disease in veterans. [9] In response, Congress authorized the U.S. Institute of Medicine to study the impact of burn pit exposure on veterans' respiratory health. [10] As a result, in 2022 President Biden signed into law the

Promise to Address Comprehensive Toxins Act, or the PACT Act. The PACT act provides veterans with potential compensation for respiratory injury as a result of military service.[336]

The research reported here investigates the relationships between systemic comorbidities, ocular pathologies, and the cost of care for veterans with COPD compared to veterans without COPD. The study used veterans' data found in the electronic and administrative files at the Bill Hefner Salisbury Health Care System (SVAHCS). The research relied on the eligible population of veterans enrolled in primary care at the Salisbury VAHCS over a 3-year period, from January 1, 2016 to December 31, 2018.

The research began with an epidemiological assessment of the prevalence and patterns of comorbidities diagnosed in veterans with COPD as compared to veterans without COPD, or the cases compared with the controls. This work relied on descriptive, nonparametric, and multivariant logistic regression analysis to characterize the patterns and associations of socio-demographic and systemic comorbidities found among the population of veterans.

The next phase entailed the study of the prevalence and patterns of ocular pathologies found in the cases and controls. Again, the epidemiological assessment utilized descriptive, nonparametric, and multivariant logistic regression techniques to understand the patterns and associations of ocular pathologies found in veterans with and without COPD.

The final phase focused on a comparison of healthcare utilization and cost of care for eligible veterans with and without COPD. The concluding study used the population of eligible veterans that were enrolled in primary care at the SVAHCS from January 1, 2016 to December 31, 2018. For each veteran, the relative value units (RVUs) and average cost per exam per year for care delivered at the SVAHCS was extracted from the national database. The Department of Veterans Affairs (DVA) defined RVUs and average cost of care from January 1, 2016 to

December 31, 2018 across four clinical categories: primary care visits, pulmonology care visits, emergency department visits, and the days of acute hospitalization. The researcher compared the RVU values and cost of care for veterans with and without COPD across each clinical category and for the total values over the 36-month timeline. The analysis used descriptive, nonparametric, and multivariant conditional quantile regression to compare the utilization and the cost of care for the eligible population of veterans with and without COPD.

For clinical care delivered from January 1, 2016 through December 31, 2018, specific ICD-9 and ICD-10 diagnostic and procedure codes were taken from eligible veterans' electronic medical records for clinical encounters at the SVAHCS. Both ICD-9 and ICD-10 codes were used because the SVAHCS was transitioning to the ICD-10 codes at the time of the study. Structured Query Language (SQL) programming applications were used to capture information about select variables, including the patients' sociodemographic characteristics, specific diagnoses, frequency of visits, generated RVUs and cost of care for primary care, pulmonology care, emergency department care, and days of acute hospitalization for veterans with and without COPD.

Specific Aims

1. To describe and analyze the epidemiological prevalence and associations of select comorbidities recorded for veterans with and without COPD.

2. To describe and analyze the epidemiological prevalence and associations of vision-threatening ocular pathologies recorded for veterans with and without COPD.

3. To contrast and compare the utilization and cost of care for veterans with and without COPD across four cost categories: primary care, pulmonology care, emergency department care, and days of acute hospitalization.

Chapter 2 provides background information on the topic, including a general review of the literature about COPD, known risk factors for COPD, the epidemiology of COPD, the classification of COPD disease severity, and a description of COPD overlap syndromes. Chapter 3 then turns to specific comorbidities associated with COPD among veterans. Chapter 4 reviews the literature on specific ocular pathologies associated with COPD among veterans, and Chapter 5 examines the healthcare utilization and cost for veterans with COPD. Finally, Chapter 6 summarizes the research conclusions and discusses the implications for future research.

CHAPTER 2: LITERATURE REVIEW

COPD is a major cause of morbidity and mortality in the United States (U.S.). In a 22-year national sample of hospital discharges across the U.S., 21% of the hospitalizations listed COPD as the primary diagnosis. The specific study concluded that a recorded COPD diagnosis increased both the likelihood of hospitalization and the likelihood of death from other comorbidities for patients with COPD compared to those without COPD. [11]

In 2015, the Centers for Disease Control and Prevention (CDC) analyzed a Behavioral Risk Factor Surveillance System (BRFSS) dataset with regards to COPD. The BRFSS data indicated that in the United States around 15.5 million adults aged 18 and older had been diagnosed with COPD. The same analysis found that 335,000 adults with COPD, 65 and older, used Medicare for hospitalization. In addition, the CDC study noted that rural residents had a higher age-adjusted prevalence of COPD and associated mortality compared to residents of metropolitan areas. [12]

Patients with COPD present with an array of systemic illnesses, [13] but research is needed to understand how COPD relates clinically to other comorbidities. [14] For example, there is little knowledge on COPD's association with systemic and ocular morbidities. This is particularly true for the connection between COPD and comorbidity, healthcare utilization, and costs of care for veterans.

Classification and Definition of COPD

The definition of COPD continues to evolve. Early COPD definitions centered on the signs and symptoms that differentiated emphysema and chronic bronchitis, both considered obstructive respiratory conditions, which were then labeled type-A and type-B COPD. [15] COPD is an "obstructive" respiratory disease because the lungs are not expelling respiratory

gases. Umbrella terms found in past publications for obstructive respiratory diseases include "chronic bronchitis," "emphysema," and "asthmatic bronchitis," to name a few. [16]

Perhaps the most recognized classification of COPD comes from the classification by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). The GOLD classification is spirometer-based. Spirometry quantifies gas movement in the lungs over a defined time interval through the use of a post-bronchodilator inhaler. [7] Clinicians measure the forced volume of air expelled in one second, divided by the total air forced from the lungs over a time interval. The result is labeled the FEV1/FVC ratio, and the ratio is used to define COPD severity. The recognized stages of COPD are mild, moderate, severe, and very severe. Determined by spirometry findings, the defined stages are: Stage 1 with an FEV1 $\geq$ 80% predicted value with symptoms; Stage 2 with an 50% $\leq$FEV1 $\leq$ 80% predicted value; Stage 3 with an 30% $\leq$ FEV1 $\leq$50% predicted value; and Stage 4 with an FEV1 $\leq$ 30% predicted value. [8,17]

The American Thoracic Society (AST), the European Respiratory Society (ERS), and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) represent clinical organizations whose mission it is to promote respiratory research and education. Around 25 years ago, each of these organizations proposed parallel COPD definitions, but with separate features. The ATS defined COPD as "a disease state characterized by the presence of airflow limitation due to chronic bronchitis or emphysema; the airflow obstruction is generally progressive, may be accompanied by airway hyperreactivity, and may be partially reversible." [18] The GOLD report defined COPD as "a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases." [19] In contrast, the ERS considered COPD

to have a "reduced maximum expiratory flow and slow forced emptying of the lungs, which is slowly progressive and mostly irreversible to present medical treatment." [20]

Each statement includes the ideas of limited airflow, disease progression, and incomplete reversibility as distinguishing concepts of COPD. In 2004, the ATS and ERS updated the COPD definition to read as follows: "Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking." [21]

Researchers have recognized that using specific cut-off values for the FE1/FVC ratios causes problems with diagnostic accuracy. [22] In response, the ATS and ESR recommended using the spirometry lower limit of normality (LLN) to define early COPD. [21] Statistically, the LLN embodies the test values at the lower fifth percentile of the frequency distribution of a normal population. [17] The FEV1/FCV ratio and the LLN produce differing sensitivity and specificity measures. In a prospective cohort study that lasted almost 5 years, researchers found that the FEV1/FCV diagnostic criteria produced more false positives for COPD, while the LLN criteria produced more false negatives for COPD diagnoses. [7]

The CanCOLD study, a population-based, cross-sectional study in Canada, explored the best approach for diagnostic accuracy of COPD. The authors recommended using spirometer values for the FEV1/FVC ratio or the LLN, along with the measured FEV1 value. They concluded that whenever a low FEV1/FVC ratio corresponds with a low FEV1 value, the COPD diagnostic accuracy improves. [23] In a systematic literature review, investigators examined how the FEV1/FVC ratio and the LLN compare for accurate COPD diagnosis. The authors concluded

that more longitudinal research was needed to determine which diagnostic strategy, the FEV1/FVC or LLN, yields the more precise COPD diagnosis. [17]

The international GOLD association published three COPD classification systems over a 10-year period from 2007 to 2017. [24] In 2007, the GOLD COPD classification system emphasized spirometry findings and labeled COPD disease severity as Stage 1 through 4, from mild to moderate, severe, and very severe. The 2007 classification system was clinically attractive because it offered a uniform approach by which to measure the severity of COPD. [19]

In 2011, the GOLD initiative proposed a classification system based on the patient's spirometry findings combined with the patient's symptoms and frequency of exacerbations, known as the "ABCD" management classification system. [25] The researchers placed patients into one of four groupings: Group A or Stage 1 severity, with few symptoms and good lung health; Group B or Stage 2 severity, with more symptoms and fair lung health; Group C or Stage 3 severity, with few symptoms and poor lung health; and Group D or Stage 4 severity, with more symptoms and worse lung health. The diagnoses relied on spirometry testing. The 2011 GOLD classification system offered an initial pharmacological treatment algorithm in accordance with the ABCD classification. [25] The aim was for clinicians to inquire of patients' symptoms in addition to the spirometry findings. [19]

Similarly, the 2017 GOLD classification system assigned patients to one of four treatment groups, labeled ABCD, but without an emphasis on spirometry test findings. COPD diagnosis relied on spirometry, but the classification assignment was based on patient symptoms and the frequency of COPD exacerbations, which were associated with increased severity and hospitalizations. The 2017 GOLD guidelines included a recommended pharmacological treatment algorithm that corresponded with the COPD classification. [26]

There are still questions about the clinical implications of the different GOLD guidelines. Investigators used a retrospective, cross-sectional study to examine how the GOLD ABCD classifications and the GOLD Stage 1–4 disease severity levels are related to patients' cost of care and health-related quality of life. The investigators concluded that the GOLD ABCD classifications had a stronger relationship with the cost of care and the patient's health-related quality of life than the GOLD Stage 1–4 severity levels. [27]

Researchers in Norway conducted a 15-year longitudinal study on how the GOLD ABCD management classification and GOLD Stage 1–4 disease severity classifications were related to mortality. They concluded that the GOLD 1–4 disease severity classification system was a better predictor of COPD mortality than the GOLD ABCD classification. [28]

A retrospective study in Poland examined how the different GOLD classifications (2007, 2011, 2017) affected COPD treatment practices. The researchers found that from 2007 to 2017 there was a significant reduction in the use of inhaled corticosteroid medications and short-acting bronchodilators. These medications were replaced with long-acting bronchodilators from the beta-2 and muscarinic antagonist groups. The study found that the number of adverse drug interactions declined with use of the 2017 GOLD classification guidelines. [29]

COPD and Pathophysiology

COPD is a chronic, progressive respiratory syndrome. Smoking behaviors, increased age, occupational exposures, asthma, prior respiratory infections, and a family history of respiratory illness are known risk factors for COPD. [30] COPD symptoms, particularly breathlessness, appear to have a diurnal variability with a tendency for symptoms to be heightened in the morning. [31]

The mammalian pulmonary structure, or respiratory tree, is a branching system of respiratory tubes, and each distal branch decreases in diameter. Air moves from the nasal cavity to the trachea and to the primary bronchi along bifurcations of the bronchial tree to the terminal bronchioles. From the terminal bronchioles, air then moves along the respiratory bronchioles to the alveolar duct and alveolar sac, the site of gas exchange. [32]

Specialized respiratory epithelium is present along the entire respiratory tree and serves multiple functions in maintaining pulmonary health. The respiratory epithelium acts as a physical barrier to inhaled pathogens and irritants and plays a critical role in the innate immune response to environmental injury. [33] Epithelial cell types vary histologically from the proximal to the distal regions of the lungs, with pseudostratified epithelium proximally and simple columnar epithelium along the distal airways. [34] At the most distal respiratory area, the site of gas exchange, there are two types of specialized epithelial cells: type I alveolar epithelium and type II alveolar epithelium. The type I cells are essential to gas exchange, and the type II cells secrete surfactants that keep the air spaces open. [35] COPD is associated with injured respiratory epithelium, thickened walls of the smaller airway passages, excess mucus production, and elevated levels of systemic inflammation. [36]

About 60 years ago, emphysema was recognized as a respiratory finding associated with COPD. [37] Emphysema is defined as an "abnormal, permanent enlargement of the air spaces distal to the terminal bronchiole accompanied by destruction of their walls" and "without obvious fibrosis." [38] Emphysema can be located throughout the lungs, but specific patterns of pulmonary emphysema are common. Emphysema causes airflow obstruction in air spaces less than 2 mm in size and is accompanied by injury to the adjacent pulmonary vasculature. Tissue damage is correlated with a chronic inflammatory process. [39] Chronic inflammation stimulates

disproportionate proteolytic activity, a loss of the extracellular matrix, a damaged alveolar wall, and pulmonary tissue fibrosis. [40] The resultant cellular alterations obstruct the exchange of respiratory gases.

Chronic bronchitis is under the diagnostic umbrella for COPD, but the pathological findings for chronic bronchitis differ from those for emphysema. The definition for chronic bronchitis is "the presence of cough and sputum production for ≥ 3 months in each of least two consecutive years." [41] Researchers estimate that around 30% of COPD cases are the result of chronic bronchitis. [42] Chronic bronchitis is characterized by an over-production of mucus by respiratory goblet cells. Inflammation triggers a chemical cascade, leading to mucous metaplasia, mucous hypersecretion, epithelial thickening, and luminal constriction. [43] The excess mucus promotes wheezing, coughing, and blocks the smaller respiratory passages. [44]

COPD and Inflammation

An amplified inflammatory response is recognized as a key factor in COPD's pathogenesis. The COPD narrative involves chronic inflammation, an antigenic immune response, and tissue remodeling. The small airway spaces collect inflammatory cells, including macrophages, B-cells, neutrophils, lymphoid cells, and specialized T-cells. Researchers have identified an array of inflammatory responses linked with COPD. [45]

Respiratory cells, particularly goblet cells, produce a mucous mixture of lipids, proteins, ions, mucin, and water and keep the lungs healthy. The mucous traps pathogens and particulates, which the ciliated epithelium then removes with an elaborate mucociliary clearance process; this is part of the lung's innate immune system. With COPD, the goblet cells produce excess mucous that becomes dehydrated and highly viscous. The ciliated epithelium cannot clear the thickened mucous, and it begins to block the pulmonary pathways, obstructing gas exchange. Patients then

cough, wheeze, and experience dyspnea. [46] The viscous mucous triggers an inflammatory cascade, tissue remodeling, and a progressive decline in pulmonary function. [47]

The chronic inflammatory response is known to promote tissue remodeling of the lungs. Cigarette smoke or inhaled environmental particulates injure the specialized respiratory epithelium. The damage to the epithelium then causes a release of inflammatory mediators, including cytokines, chemokines, and cellular growth factors. The inflammatory response further alters the structure of respiratory smooth muscle and the adjacent extracellular matrix. Consequently, activated local fibroblasts and myofibroblasts generate fibrotic tissue that impairs lung function. [47,48] The small respiratory bronchioles then obstruct respiratory gas exchange, which is the hallmark of COPD. [49]

COPD Phenotypes

The Merriam-Webster medical dictionary defines phenotype as "the observable characteristics or traits of an organism that are produced by the interaction of the genotype and the environment: the physical expression of one or more genes." [50] In 2010, scholars proposed a definition for a COPD phenotype as, "a single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression, or death)." The scholars recommended that this proposed definition for a COPD phenotype could guide forthcoming research. [51]

COPD presents as a heterogenous disease with variable clinical characteristics. Researchers have sought to identify COPD phenotypes with the purpose of adapting individual treatments for improved outcomes. [52] Investigators continue to propose new COPD phenotypes, but the goal of phenotypically specific treatments remains elusive.

In 1959, proceedings from the CIBA symposium grouped COPD into three phenotypes: emphysema, chronic bronchitis, and certain asthmas. [53] In 2008, Marsh et al. conducted research to determine the prevalence of COPD for each of these categories and found that, among the subjects in their study, 30% had emphysema, 55% had asthma, and 32% had chronic bronchitis. [54]

COPD–Eosinophilia Phenotype

Investigators are still working to identify the dominant COPD phenotypes. In a retrospective study, researchers examined blood fibrinogen and eosinophil levels in 370 patients diagnosed with COPD. The researchers found that elevated fibrinogen and eosinophil levels were associated with COPD severity and frequency of exacerbations. The authors proposed that elevated levels for fibrinogen and eosinophils represented a specific COPD phenotype. [55]

In another retrospective study, researchers reviewed emergency department records for patients with confirmed COPD exacerbations. The COPD exacerbations were categorized as an *infectious* or *noninfectious* etiology based on exam findings and the white blood cell count. The researchers noted that some patients with noninfectious exacerbations had elevated counts for a specific white blood cell, the eosinophile. Elevated eosinophilia counts were significantly more prevalent among patients with noninfectious exacerbations compared to infectious exacerbations. The authors suggested that elevated eosinophilia counts are a unique finding for patients with noninfectious COPD exacerbations. [56]

In a randomized controlled trial with a cross-over design, investigators treated COPD patients with elevated sputum eosinophil levels with 30 milligrams of oral prednisone. The investigators found that these patients benefited from the short-term prednisone treatment. The

authors proposed that COPD patients with elevated sputum eosinophil levels signified a unique COPD phenotype. [57]

COPD–Asthma Phenotype

Some respiratory patients display findings of both asthma and COPD, with comparable symptoms. Clinically, this presentation is considered an "asthma–COPD overlap syndrome," or ACOS. [58] Asthma and COPD are both inflammatory diseases that affect the small airways, but the conditions differ. Asthma usually presents prior to age 25, whereas COPD typically appears in individuals older than 40. Asthma symptoms include wheezing, coughing, and shortness of breath. Airway obstruction with asthma involves spasms of the smooth muscle, the obstruction is reversible, and the disease is not considered progressive. COPD obstructions involve tissue remodeling and excess mucous production at the site of gas exchange. Unlike asthma, COPD is a chronic, progressive, and nonreversible condition. [59]

In 2014, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and Global Initiative for Asthma (GINA) committees published a statement listing the features of ACOS. Patients with ACOS are usually diagnosed with asthma prior to age 40, and the COPD characteristics develop later. Presently, a uniform definition for ACOS is lacking. [60] Investigators have proposed a preliminary definition of ACOS by incorporating three clinical characteristics. Patients with ACOS have the following traits: nonreversible and persistent airway limitations per spirometry findings, a significant history of exposure to smoke from cigarettes or biomass, and a medical diagnosis for asthma prior to 40 years of age. [61]

COPD–Sleep Apnea Phenotype

COPD and sleep apnea are common respiratory conditions with different etiologies. While COPD involves airflow obstruction, or impaired gas exchange in the lower respiratory

system, sleep apnea is caused by the physical restriction of the upper airway passages. [62] Unfortunately, some individuals suffer from both COPD and sleep apnea, and this is considered a "COPD–sleep apnea overlap syndrome" (OSAS). [63]

An epidemiological analysis taken from the Sleep Heart Health Study dataset found that OSAS was not common with mild COPD but was more likely with a decline in the spirometry-measured FEV1/FVC ratio. Patients with OSAS and reduced FEV1/FVC values experienced more frequent reductions in oxygen saturation levels compared to those without OSAS. [64]

COPD and sleep apnea are each associated with heightened systemic inflammation. The elevated inflammation is believed to damage organ systems, including the lungs. Those with OSAS are at greater risk for atherosclerosis, heart disease, and pulmonary hypertension compared to those without OSAS. [65] A retrospective chart review of 30 patients with OSAS found that hyperinflation of the lungs, a measure of COPD severity, was associated with reduced sleep efficiency. [66] In addition, those with OSAS reported poorer sleep quality and reduced quality-of-life measures compared to those with COPD alone. [67]

COPD–Bronchiectasis Phenotype

Non-cystic fibrosis bronchiectasis, or bronchiectasis, is a pulmonary condition characterized by widened bronchi, chronic inflammation, respiratory wall thickening, airway obstruction, and repeated infections. COPD and bronchiectasis share comparable symptoms that consist of a chronic cough, excess sputum production, dyspnea, and rhinosinusitis. [68] Computerized tomography (CT) is required for a definitive diagnosis of bronchiectasis. Since CT imaging is often used to diagnose COPD, bronchiectasis is frequently diagnosed as a COPD-linked comorbidity. A systematic literature review revealed that bronchiectasis was labeled as idiopathic 45% of the time, but the illness was associated with COPD in about 4% of cases. [69]

Recent studies suggest that bronchiectasis is commonly found in patients with COPD. In a prospective study of 92 patients with moderate or severe COPD, researchers found that bronchiectasis was present in near 58% of the subjects. [70] In another study on 69 subjects with moderate or severe COPD, the investigators found bronchiectasis in 48% of the subjects. [71] Additional studies are needed to determine the prevalence of bronchiectasis among patients with moderate or severe COPD.

Patients with either COPD or bronchiectasis experience frequent respiratory infections, and the repeated infections may represent the connection for the coexisting conditions. [72] Clinical findings show that patients with COPD and bronchiectasis have more exacerbations and poorer outcomes compared to those with COPD or bronchiectasis alone. [73] This has led some clinicians to propose that COPD combined with bronchiectasis represents a specific COPD phenotype. [74]

COPD and Comorbidities

Clinicians have long recognized that patients with COPD present with comorbidities. People with COPD often appear feeble compared to their cohorts. Using the National Health and Nutrition Examination Survey (NHANES) national survey data from 2003–2006, investigators calculated the prevalence of frailty among those with COPD to be 58%. In addition, they found that frail persons with COPD had more comorbidities compared to those without COPD. [75] In a systematic literature review exploring the relationship between COPD and frailty, researchers noted that the pooled prevalence for COPD-associated frailty was 19% and that the odds of frailty with COPD were almost 2 times that of cohorts without COPD. The authors proposed that frailty and COPD were most likely bidirectional in nature. [76]

There is a need to better understand how COPD relates to comorbidities. [77] When studying healthcare outcomes, researchers have focused on select conditions, or specialties, and they have failed to apply uniform groupings for comorbidities. [78] Clinical outcomes tend to be misinterpreted or misunderstand because there is variability among the diagnostic definitions, the assigned treatment regiments, and the research designs. [79] In a policy statement, respiratory specialists identified COPD related comorbidities as a priority for medical research. [14]

Age, smoking history, environmental exposures, and genetic predispositions influence the relationship between COPD and comorbidities. [80] In an epidemiological literature review, the authors identified 10 different comorbidities commonly associated with COPD. [81] A review of 20 years of national hospital discharge data found that about 21% of discharges logged COPD as the primary diagnosis and that the associated in-hospital mortalities were correlated to common comorbidities including heart disease and cancer. [11]

COPD and Cardiovascular Disease

COPD and cardiovascular disease often present together because the organ systems are physiologically coupled and suffer biological insults with age. [82] Researchers acknowledge that acute COPD exacerbations correlate with harmful cardiovascular events. [83] A COPD diagnosis due to declining spirometry values is predictive of large vessel atherosclerosis, aneurysms, and cardiovascular disease. [84,85] Hospitalization for COPD exacerbations is related with adverse cardiovascular events within 30 days of discharge. [86]

Congestive heart failure (CHF), a serious vascular condition, is related to COPD. Approximately 20% of patients with CHF are diagnosed with COPD. [87] A retrospective study of patients hospitalized with CHF found that about 36% also had a diagnosis for COPD. [88]

Those with COPD are significantly more likely to develop CHF and to report a prior heart attack compared to those without COPD. [89] A finding for CHF confounds a COPD diagnosis because the symptoms intersect. Dyspnea occurs with CHF because the measured FEV1 is reduced. Clinicians must rely on the reduced FEV1/FVC ratio rather than the FEV1 alone to reliably differentiate COPD from CHF. [90] Unfortunately, coexisting COPD and CHF significantly increase the overall mortality risk. [91]

Atrial fibrillation (AF), a common cardiac arrhythmia, also frequently coexists with COPD. In a systematic literature review, researchers found that the odds of AF progression with COPD was almost 2 times greater than those for AF without COPD. [92] A retrospective study of Japanese subjects found that AF was independently associated with COPD and that the association increased with the COPD severity. [93] The cellular and molecular evidence shows that COPD promotes heart disease via an accelerated aging of the respiratory system. [94,95] Regrettably, patients with AF and COPD experience more symptoms and a diminished quality of life compared to patients with AF alone. [96]

Acute coronary syndrome (ACS) is an expansive term for any condition that results in signs and symptoms of reduced blood flow to the heart tissue, or myocardial ischemia. ACS results from a partial or full thrombotic occlusion of a coronary artery. [97] In a prospective multinational study, investigators found that about 16% of patients had a non-fatal heart attack or died within six months following an episode of ACS. [98]

COPD and ACS often coexist in patients. In a prospective multinational study of Middle Eastern patients, investigators found that 5% of patients hospitalized with ACS had a COPD diagnosis. These patients had lengthier hospital stays, additional bleeding complications, and a higher risk for heart failure than patient with ACS alone. [99] Researchers conducted pulmonary

screening prior to discharge on 137 hospitalized patients who smoked and had ACS. The researchers identified undiagnosed COPD in 29% of the 137 patients. [100] In a Swedish study of 407 hospitalized patients admitted for ACS and who completed pulmonary screening prior to discharge, the researchers found that undiagnosed COPD coexisted with ACS in 11% of the subjects. The Swedish authors concluded that COPD is often underdiagnosed or misdiagnosed in patients with ACS. [101]

COPD and Autoimmune Conditions

The biological markers for chronic systemic inflammation are elevated in the presence of both COPD and in a range of autoimmune conditions. [102,103] Contemporary research findings point to shared inflammatory pathways that hypothetically link COPD to different autoimmune disorders. [104,105]

A retrospective case-control study conducted in Israel studied the relationship between COPD and psoriasis in roughly 37,000 subjects. The researchers observed that the prevalence of COPD was significantly associated with psoriasis (OR=1.63). The authors advised that individuals with psoriasis should be consulted for a pulmonary evaluation. [106]

In a systematic review and meta-analysis, researchers examined the relationship between psoriasis and COPD in patients with both conditions compared to patients with COPD alone. Seven observational studies met the inclusion criteria. The investigators found a statistically significant pooled risk ratio for COPD with psoriasis (RR=1.51) and noted that the COPD prevalence was higher in those with psoriasis. [107]

Rheumatoid arthritis (RA) is another often-diagnosed autoimmune condition. A systematic review and meta-analysis of cohort studies investigated the risk of COPD among those diagnosed with RA. The researchers pooled the findings from four studies and concluded

that the pooled relative risk (RR) for patients with COPD and RA was 1.99, compared to those without RA. [108]

Korean researchers analyzed data from a national survey to study the prevalence of COPD in patients with RA. The researchers noted that the prevalence of RA coexisting with COPD was substantial. COPD was more prevalent in Korean men with RA (OR = 2.16) compared to men without RA. The association failed to reach that level of statistical significance for Korean women. [109]

Danish investigators used 12 years of data from the Danish National Patient Registry to explore the mortality risk of patients with COPD and RA. The investigators produced Kaplan-Meier mortality curves with more than 33,000 subjects with a RA diagnosis. The investigators found that the adjusted hazard ratio (HRR) for risk of death within 10 years was greater for those with COPD and RA (HRR =2.1) compared to those with RA alone. [110]

Inflammatory bowel disease is an acknowledged autoimmune condition. Researchers have postulated a link between COPD and inflammatory bowel disease because both diseases involve the chronic inflammation of mucosal tissue. [111] Inflammatory bowel disease is known to affect the lungs as well as other organ systems. [112] Patients with inflammatory bowel disease and COPD have been shown to be at greater risk of death compared to those with inflammatory bowel disease alone. [113] A retrospective study found that the odds of having a diagnosis for inflammatory bowel disease was significantly greater if there was a known respiratory diagnosis, excluding asthma. [114]

COPD and Psychological Health

Chronic illnesses, such as COPD, impact an individual's psychological well-being. Researchers conducted a systemic literature review covering 46 years of publications that

reported the prevalence of anxiety in patients with COPD. Ten articles met the defined inclusion criteria. The researchers found that the prevalence for anxiety with COPD among out-patients ranged from 13% to 46%. The study concluded that diagnosed anxiety was quite prevalent in those with COPD and that primary care providers should screen for anxiety as a COPD related comorbidity. [115]

A study with a modest sample size, 93 patients with COPD and 15 without COPD, compared the presence of anxiety between the two groups. The authors observed that the presence of anxiety was similar between the two groups, but that in the COPD group anxiety was closely related to the reported COPD symptoms. Interestingly, the degree of COPD severity in terms of airflow limitations did not appear to be correlated with the presence of anxiety in the study. [116]

A study with a larger sample size of over 1,200 cases and 300 controls used multivariant analysis and found that COPD was significantly associated with anxiety (OR=1.85). Patients with COPD and anxiety performed poorer on physical tests and reported more functional limitations compared to those without anxiety. The authors recommended that all patients with COPD would benefit from the medical management of anxiety. [117]

Many people with COPD also experience depression. One population-based study used a decade of national data from the United Kingdom to explore the relationship between COPD and depression. The researchers used a nested case-control design with over 70,000 subjects and found a positive association between COPD and a diagnosis for depression. The risk of a depression diagnosis increased with the level of COPD severity. [118]

In a systematic literature review and meta-analysis, investigators studied the combined prevalence of depressive symptoms in those with COPD compared to those without COPD.

Eight studies were included in the meta-analysis. The investigators found that there was a significant association between depressive symptoms and a diagnosis for COPD compared to those without COPD (pooled OR = 2.81). [119]

In another systematic literature review and meta-analysis, researchers examined the variability in the estimated prevalence for depression coexisting with COPD. The authors used eight studies in the meta-analysis. The authors proposed that the application of differing research methodologies accounted for the wide variability for the prevalence estimates. The authors found the pooled prevalence for depression coexisting with COPD to be 27%, compared to 10% prevalence for depression among the those without COPD. [120]

Researchers used retrospective Medicare data (2006 to 2012) to study the relationship between COPD, depression, and healthcare utilization among over 16,000 subjects. The researchers noted that depression frequently coexisted with COPD and that compliance with COPD and depression therapies reduced healthcare utilizations. Patients adherent to COPD and depression treatments report more frequent emergency department visits, but fewer episodes of acute hospitalizations. [121]

Illness is linked with chronic pain. [122] A study comparing chronic pain in patients with COPD to patients without COPD found that 50% of those with COPD reported chronic pain, often described as chest and lower back pain, compared to 26% of those without COPD. The authors suggested that primary care practitioners actively screen patients with COPD for chronic pain. [123]

A systematic literature review and meta-analysis evaluated 39 publications that explored the prevalence of reported pain with COPD. The prevalence of reported pain with COPD ranged from 32% to 60%. The researchers noted that pain prevalence was linked with moderately severe

COPD. One theme from the meta-analysis was that the COPD-related pain directly impacted the patient's quality of life. [124]

A systematic literature review assessed the published COPD clinical practice guidelines to see how often the guidelines referenced pain. Out of 41 reviewed standards, 25 clinical practice guidelines mentioned pain. The reviewers concluded that COPD associated chronic pain was common and negatively impacts the patients' daily activities and quality of life. [125]

COPD and Ocular Associations

COPD causes harm to the peripheral and central nervous system. Electrodiagnostic testing in a sample of 89 patients with COPD found abnormal peripheral nerve conduction in 44% of the subjects. [126] COPD also injures the central nervous system. Scientists have documented that cognitive function declines in patients with COPD. [127] The ocular system is an extension of the central nervous system, is highly vascularized, and is theoretically susceptible to damage from COPD.

The visual-evoked potential (VEP) is a recognized electrodiagnostic test for evaluations of optic nerve function and the visual pathway. [128] In a prospective case-control study, researchers tested the visual function of 40 patients with COPD and 40 healthy age-matched controls using the VEP. The study found that 55% of the participants had abnormal P100 latency measured with the electrophysiologic assessment. The researchers postulated that chronic hypoxemia, smoking, hypercapnia, or COPD treatment regiments promote optic neuropathy in those with COPD. [129]

Aras et al. used VEP to evaluate the visual function of 41 COPD patients and 41 healthy age-matched patients. The researchers found that 57% of COPD patients recorded abnormal VEP

results compared to those without COPD. The findings of this case-control study indicated that neuropathy of the visual system was associated with COPD. [130]

COPD causes chronic hypoxemia and generates vascular stress. The eye is a highly vascular structure. Researchers used spectral-domain optical coherence tomography (SD-OCT) to study the retinal nerve fiber layer and retinal vessels in patients with COPD. The study evaluated 43 patients with COPD and 31 controls with SD-OCT. The researchers found that the mean retinal venule width was significantly greater in patients with COPD compared to the controls and suggested that chronic hypoxia and chronic inflammation caused the retinal vascular alterations noted in patients with COPD. [131]

Researchers used color doppler ultrasonography to study blood flow in the major ocular vessels in 45 patients with COPD and 17 healthy subjects without COPD. The COPD patients were grouped into three categories based on COPD severity (mild, moderate, severe). The researchers found that COPD was associated with abnormal retrobulbar hemodynamics compared to the ocular blood flow of the patients without COPD. [132]

Blindness or low vision are potential comorbidities associated with COPD. A retrospective study in the Netherlands used the primary care providers' electronic medical records of over 14,000 patients to catalogue the comorbidities associated with COPD. The researchers found that 13% of the patients with COPD had a diagnosis for blindness or low vision registered as a comorbidity. [133]

Another study used the United Kingdom General Practice Research Database, a national dataset, to identify the frequency of comorbidities in patients with newly diagnosed COPD. The researchers compared about 2,700 patients with COPD to matched controls without COPD. The study grouped comorbidities by organ systems, including the eye. The researchers observed that

the relative risk (RR) for eye disorders, including cataracts and glaucoma, was 30% greater for those with COPD compared to cohorts without COPD. [134]

COPD and Cost of Care

Healthcare for chronic conditions is costly, and COPD is no exception. From 2013–2014, the Canadian healthcare system spent over CAN $235 million caring for approximately 109,000 people with COPD in Alberta, Canada. This means that, on average, from 2013–2014, Canada spent $2,156 CAN dollars per person diagnosed with COPD in Alberta. Exacerbation-related hospitalizations comprised the majority, or 55%, of the COPD-related expenditures in the region. [135]

Economists conducted a systematic literature review including 70 studies published between 2000 to 2012. The objective was to estimate Canada's cost of care associated with COPD. The economists reported that COPD patients used more healthcare resources than those without COPD, and the estimated average total cost per patient diagnosed with COPD was between CAN $2,444 and $4,391. [136]

Investigators used national, retrospective data from the 2017–2018 Medical Expenditure Panel Survey (MEPS) to estimate the direct cost of care for patients with COPD in the United States. The researchers used a sample of more than 23,000 COPD patients over a 2-year span. Through an incremental expenditure method, the calculations revealed that the average annual COPD-related costs per patient was over $3,900. These cost estimates reflected the economic burden that COPD places upon the U.S. healthcare system. [137]

Acute COPD exacerbations, or a sudden worsening of COPD symptoms, include severe shortness of breath, coughing, plus excess phlegm, and the symptoms can last for days. COPD exacerbations represent a major cause for hospitalizations, and the associated costs are

substantial. For instance, researchers retrospectively analyzed the 2006 data from the Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample. The in-patient cost of care and mortality figures for patients 40 and older hospitalized for COPD exacerbations were summarized. In 2006, more than 1.25 million hospitalization events were recorded. The average cost per episode of care for COPD exacerbations was $9,545 (±12,700), the total cost was about $12 billion, and the in-patient mortality rate was greater than 4%. [138]

Patients with severe COPD are at a greater risk for pneumonia-associated mortality. [139] Scientists retrospectively analyzed a 5% sample of fee-for-service Medicare beneficiary claims (2005–2007) comparing the incidence and cost of care of pneumonia in those with and without COPD. The scientists found that Medicare beneficiaries with COPD had about six times the incidence rate for pneumonia compared to those without COPD (RR = 5.7). Also, those hospitalized for COPD-associated pneumonia had over $22,000 greater 1-year direct medical costs than patients with pneumonia alone. [140]

Veteran Health Administration

The Veterans Health Administration (VHA) is the arm of the DVA that provides medical care for eligible veterans. The VHA is the largest integrated health delivery system in the United States and provides healthcare for some nine million enrolled veterans. Nationally, there are 171 medical facilities and 1,112 community-based out-patient clinics that serve veterans. [141]

The emergent policies expanding medical care for U.S. veterans paralleled the nation's military involvements and military conflicts. For example, on June 22, 1944, Congress passed the G.I. Bill, a key piece of legislation that greatly impacted veterans and their families. After World War II, General Omar Bradley and Major General Paul Hawley moved to reorganize and expand access to medical care for some 12 million veterans. In 1988, President Reagan signed

Public Law 100-527, or the Department of Veteran Affairs Act, into effect. The passage of Public Law 100-527 elevated the Veterans Administration to a Cabinet-level department within the federal government. [142] Veterans' healthcare services evolved and expanded with each major military episode beginning from the Civil War and extending to today. [143]

Active-Duty Military Health Status

Department of Defense (DoD) Directive number 1308.1, issued June 30, 2004, authorized the military branches to define the enlistment, induction, and qualification standards for members of the Armed Service. Section 4.1.1 of 1308.1 states:

> The Military Services shall design physical fitness training and related physical activities consistent with established scientific principles of physical conditioning that enhance fitness and general health essential to combat readiness. Individual Service members must possess the cardio-respiratory endurance, muscular strength, and muscular endurance, together with desirable levels of body composition to successfully perform in accordance with their Service-specific mission and military specialty.

To qualify, candidates must be between the ages of 17 and 39 and pass a pre-enlistment physical exam and background check. Pre-existing chronic conditions may exclude the individual from military service. As a result, the enlistees possess a consistent grade of health, and the service members are expected to engage in health-promoting behaviors that maintain their base level of physical well-being. [144]

Military service, unlike many occupations, involves rigorous exercise, severe environmental conditions, interrupted sleep, physical prerequisites, and possibly life-risking assignments. [145] The veteran's likelihood of physical or psychological injury is considerable. A retrospective study of the 2010 Behavioral Risk Factor Surveillance Survey (BRFSS) compared self-reported health outcomes of active-duty military, veterans, and civilian men on primary health indicators. The researchers found that active-duty military reported higher rates of smoking or tobacco use, alcohol consumption, and anxiety disorders compared to civilians or

veterans. Active-duty military were less likely to report “fair or poor health” and more likely to consistently exercise compared to civilians or veterans. [146]

For veterans, combat has both near-term and long-term risks. Researchers conducted a longitudinal study looking at the effects of combat on 328 World War II veterans and found an association between combat and the veterans’ physical decline or death within 15 years of military service. The study found that World War II combat veterans trended toward poorer health status following military combat. [147]

Active-duty military members are at risk for post-traumatic stress disorder (PTSD) if they suffer life-threatening injury or extreme violence. Scholars studied the incidence of PTSD in active-duty military over a 17-year period. The scholars estimated that the incidence of PTSD among active-duty military had risen from 1.24 per 1,000 in 2001 to about 13 per 1,000 by 2016, a 10-fold increase. PTSD was more common in members of the Army between the ages of 20 to 24 years and among those who were married and White. [148]

Investigators used a self-report survey methodology to examine how PTSD impacted the mental and physical well-being of 366 active-duty military members. The survey revealed that PTSD negatively affected the participants’ mental health but not their physical functioning at the time of the survey. [149]

Active-Duty Military and Smoking Behavior

Smoking is a recognized risk factor for COPD. [150] There is a record of the tobacco industry’s vigorous promotion of tobacco products to active-duty service members. [151] The tobacco industry targetd military personnel with brand development and price promotions in the hope of capturing future customers. [152] Evidence shows that military service has served as a major underlying stimulus for smoking behavior later in life. [153]

In 1980, approximately 50% of all active-duty military personnel smoked, but by 2008 this percentage had declined to around 24%. [154] The decline in smoking paralleled the public health efforts to educate the public regarding the hazards of smoking. Scientists have shown that smoking increases when military personnel are placed in high-stress environments. [155] Historically, cigarettes were proposed as a mechanism for stress reduction, but research suggests that smoking is not only ineffective in managing stress, but may actually heighten stress. [156] Military deployments, particularly lengthy operations, are significantly associated with the initiation of smoking and smoking recidivism for those with combat exposure. [157]

Veterans and Respiratory Illness

Military combat has long been associated with respiratory injury. For example, mustard gas, a chlorine-containing compound, was employed with deadly effectiveness as a chemical warfare agent during World War I. [158] The psychological threat of mustard gas attacks generated panic among the troops. [159] A retrospective study spanning 36 years of medical records of soldiers exposed to mustard gas poisoning during World War I found that mustard gas increased the risk for lung cancer in these veterans. [160]

More recently, mustard gas was used from 1980 to 1988 during the Iran-Iraq war. A literature review of recent publications reported that mustard gas exposure promotes serious respiratory complications years after exposure. The authors found that mustard gas exposure is linked with pulmonary fibrosis, chronic bronchitis, asthma, emphysema, and other forms of COPD. [161]

World War II naval ships used asbestos as an insulating material around pipes and pumps. [162] As early as 1939, the Navy recognized asbestos exposure as a respiratory hazard and recommended precautions to minimize breathing asbestos fibers. [163] U.S. Navy veterans

exposed to asbestos often developed respiratory ailments that included pulmonary fibrosis, pleural plaques, and lung cancer. [164]

Vietnam veterans suffered adverse respiratory effects from exposure to the herbicidal defoliant Agent Orange which contained the contaminate dioxin. Scientists compared the self-reported health status of Vietnam veterans exposed to Agent Orange to unexposed veterans. The scientists reported that a greater percentage of veterans who sprayed Agent Orange self-reported respiratory problems compared to the unexposed veterans. Veterans that sprayed Agent Orange were 41% more likely to report respiratory problems compared to veterans that never sprayed Agent Orange. [165] In another survey, veterans that sprayed Agent Orange were asked if they had received a physician's diagnosis for COPD. Veterans that sprayed Agent Orange were statistically more likely to report receiving a physician's diagnosis for COPD compared to non-sprayers (OR = 1.82). [166]

Veterans of the Iraq and Afghanistan wars risked respiratory injury from dust, fine particulate matter, exhaust fumes, and smoke from burn pits. Such irritants are known to trigger a sustained inflammatory response within the lungs. [167] One study examined a sample of 24 veterans previously stationed in Iraq or Afghanistan for the occurrence of exercise-induced bronchoconstriction. From this sample, 58% reported a chronic cough and near 38% reported shortness of breath. The investigators observed exercise-induced bronchoconstriction in near 17% of the veterans. [168]

Respiratory specialists evaluated 94 Iraq and Afghanistan veterans that reported respiratory symptoms. The specialists conducted detailed tests of pulmonary function and found that 12% of the veterans had asthma or chronic bronchitis and that 31% of the veterans had

pulmonary vascular disorders. The specialists noticed an association between the length of military deployment and the abnormal vascular findings. [169]

A retrospective, case-control study investigated the respiratory ailments of Gulf War veterans. Researchers compared a total of over 360,000 deployed Gulf War veterans to about 323,000 active but non-deployed veterans to estimate the 10-year-period prevalence rates (PR) of respiratory conditions. COPD and chronic airway obstruction were among the five most prevalent respiratory diagnoses when comparing cases to controls. Compared to non-deployed veterans, the deployed Gulf War veterans were 9% more likely to develop COPD and 19% more likely to be diagnosed with chronic bronchitis. [170]

Respiratory specialists published a descriptive case series of the findings from the comprehensive respiratory evaluations of 80 veterans deployed in Iraq and Afghanistan. The 80 veterans all reported diminished exercise tolerance and dyspnea following deployment. Overall, 49 of the 80 veterans underwent lung biopsies with 48% of the veterans receiving a diagnosis for constrictive bronchiolitis, an uncommon obstructive respiratory disorder. [171]

Congress proposed legislation for the creation of a burn pit registry to monitor the respiratory health of Iraq and Afghanistan veterans exposed to environmental hazards while deployed. [172,173] In response, the Veterans Administration Office of Public Health developed the Airborne Hazards and Open Burn Pit Registry to monitor respiratory illness in Iraq- and Afghanistan-era veterans. [174] The DoD and the VA issued plans and guidance for collaborative participation in developing the official Open Burn Pit Registry. [175] As a result of research findings and healthcare policy, in 2022 President Biden signed into law the Promise to Address Comprehensive Toxins Act, or the PACT Act. The PACT act provides veterans with potential compensation for respiratory injury as a result of military service.[336]

Veterans and Comorbidities

Researchers are interested in how veterans' health equates to the health of non-veterans. Scholars used the 2010 Behavioral Risk Factor Surveillance System (BRFSS), a comprehensive health survey, and multivariant logistic regression to contrast the health of male veterans with active-duty service members and citizens. The authors found that for the included measures veterans had worse health compared to non-veterans and that veterans reported more diabetes, more smoking, and higher alcohol consumption compared to non-veterans. [146]

In 2015, the RAND corporation published a VA-sponsored report on the characteristics and projected healthcare needs of the veteran population. The report was extensive and contrasted and compared the veteran population to non-veterans across various groupings. The veterans' health status was found to be poorer than that of non-veterans on several measures. For instance, veterans had a statistically greater prevalence for diabetes, COPD, PTSD, hearing loss, and cancers. However, veterans fared better than non-veterans financially and were more likely to have health insurance. Veterans who relied solely on the VA for medical care tended to be older, sicker, and have a diminished income compared to veterans with an outside source of care. Finally, veterans with higher income levels enjoyed better over-all health compared to veterans with a lesser income. [176]

Researchers used the national 2018 BRFSS to contrast and compare the health status of veterans with non-veterans. The survey indicated that veterans had a statistically greater risk for numerous comorbidities compared to non-veterans. Veterans were more likely to report a diagnosis for diabetes (OR = 1.61), a history of stroke (OR = 1.86), diagnosed coronary heart disease (OR = 2.63), and a diagnosis for COPD (OR = 1.52), compared to those without military service. [177]

Scientists reexamined the BRFSS responses over a 16-year time span (2003–2019) comparing the reported health of veterans with non-veterans. Veterans reported poorer health on several comorbidities compared to non-veterans. The researchers applied statistical age adjustments and estimated the representative values for the combined years 2011–2019. The findings revealed that these veterans had higher rates of diabetes, stroke, cancer, heart disease, and COPD, but less reported mental illness compared to non-veterans. [178]

Investigators analyzed responses from the (SF-36) Health Status Quality of Life measure to compare the health status of veterans with non-veterans in the Boston, Massachusetts region. The responses from over 2,400 male veterans receiving care at the VA was compared with those of about 1,300 non-veterans receiving care in the community. The investigators found that the overall health of the veterans was significantly worse than that of non-veterans in the study. The veterans' poor health was attributed to service-connected disabilities and income inequalities. [179]

Scholars used VA clinical data to investigate how clusters of comorbidities have a bearing on the veterans' 5-year mortality rate. The analysis used 11 chronic conditions including COPD. Data from over 740,000 veterans between the ages of 55 and 64 was included in the cohort study. After the allotted time interval, the scholars calculated the 5-year mortality rates and found that veterans with four or more chronic conditions had a 17% mortality rate, while only 6% of the veterans with one chronic condition died within 5 years. [180]

Investigators were interested to learn how moving from the ICD-9 diagnostic codes to the ICD-10 diagnostic codes impacted the VA's reported prevalence rate for chronic conditions. The researchers randomly pulled one million veteran records from the VA administrative database and measured the chronic condition prevalence rate for the 2014 to 2016 fiscal years. The

researchers then compared the prevalence for chronic conditions as recorded in the International Classification of Diseases, Ninth Revision (ICD-9) compared to the International Classification of Diseases, Tenth Revision (ICD-10). The condition prevalence estimates were similar for most conditions with the coding transition. For 2016, hypertension (54%), diabetes (28%), and lower back pain (23%) were the most common diagnoses. The researchers found that the estimated ICD-10 condition prevalence for veterans with a COPD diagnosis was near 11%. [181]

Veterans and Ocular Health Status

Increased age carries an amplified risk for sensory impairment. VA researchers explored the prevalence of veterans with dual sensory impairment (DSI), defined as decreased hearing plus decreased vision, through a random review of 400 electronic medical records. The researchers found that the prevalence of DSI increased with age and ranged from 0% for veterans under age 65 to 20% for veterans over 85 years. The calculated prevalence for vision impairment, including blindness, in the sample of veterans was greater than 7%. [182]

VA clinicians also conducted a retrospective chart review of over 600 medical records to measure the prevalence of ocular pathology among veterans presenting for routine eye exams. The clinicians found that 25% of the veterans needed additional evaluation as glaucoma suspects, 5% were diagnosed with macular degeneration, and 6% were diagnosed with cataracts. The clinicians concluded that the rate of ocular pathology was sizable in the veteran population. [183]

Scientists conducted a retrospective study to estimate the prevalence of ocular diseases diagnosed in veterans cared for at the VA Capital Healthcare Network by extracting ocular diagnoses from the electronic health records. Records from 2007-2011 were reviewed. The prevalence of “all types” of ocular disease was over 20% in 2007 but had increased to over 23% by 2011. Veterans’ prevalence for diabetic eye disease increased from nearly 10% in 2007 to

over 12% by 2011. For veterans 65 years and older, the 2011 prevalence for glaucoma was just under 10%. The prevalence for cataracts was nearly 7% in 2007 but increased to nearly 12% by 2011. The authors concluded that both the prevalence for ocular diseases and the demand for needed eye care services increased among veterans from 2007 to 2011. [184]

Clinicians retrospectively collected the prevalence of ocular diseases in veterans with serious mental illness (SMI) compared to veterans without SMI. The veterans received care in the VA Capital Healthcare Network in 2011. The clinicians evaluated charts for over 6,000 veterans with SMI and over 137,000 veterans without SMI. Of the veterans with SMI, the prevalence of any type of ocular disease diagnosis was near 23% while veterans without SMI had a 35% prevalence of an ocular disease diagnosis. The veterans with SMI reported a higher prevalence of glaucoma and cataracts compared to veterans without SMI. [185]

A retrospective study reviewed the electronic health records of diabetic veterans who had completed either an in-person eye examination or a tele-retinal screening in 1998. Examination findings for about 430,00 veterans with diabetes were captured in the study. In this national sample, greater than 4% of the veterans had vision-threatening diabetic retinopathy, 11% were diagnosed with glaucoma, and 18% were diagnosed with cataracts. Furthermore, some 3% of the veterans were legally blind. [186]

VA investigators at the VA Caribbean Healthcare System (VACHCS) in Puerto Rico retrospectively reviewed over 800 eye exam records of legally blind veterans for a ten-year period (1997- 2007). The investigators were interested in identifying the causes for legal blindness in these veterans. The investigators reported that 43% of the veterans were blind from glaucoma, 27% were blind from diabetic retinopathy, and 11% were blind from age-related

macular degeneration. The investigators estimated the ten-year prevalence of blindness among all veterans at the VACHCS to be near 1 out of 200 veterans. [187]

VA researchers were interested how a dry eye diagnosis might be associated with a diagnosis for chronic pain conditions. Over 3.2 million veterans' records spanning a four- year time interval (2010-2014) were used in the retrospective study. The authors used the ICD-9 codes for dry eye syndrome and non-ocular pain to identify and tabulate the diagnoses. The researchers found that 29% of veterans had a diagnosis for dry eye syndrome. The likelihood of a diagnosis for dry eye syndrome was related to the frequency of the non-ocular pain diagnoses. The authors concluded that dry eye syndrome among veterans was associated with chronic pain conditions. [188]

Veterans and the Cost of Care

In 1990, Congress passed PL 101-576, the Chief Financial Officers Act, to improve the efficiency and accuracy of federal accounting and financial management. The goals of the Chief Financial Officers Act were to deter fraud, reduce waste, and assist the executive and legislative branches in evaluating federal systems. [189] Around the same time, the DVA created an accounting system known as the Decision Support System (DSS) to meet the provisions of the Chief Financial Officers Act. DSS combined fiscal and clinical information to calculate budget allocations relative to costs. The DVA piloted DSS in 1986 and launched its systemwide application in 1994. [190] DSS uses "bottom-up" accounting system that cross-references information from the facility payroll and general ledger with each departments' employee cost and productivity. The DVA uses relative value units (RVUs) to assign values to "intermediate products" but not charges. For example, RVUs are associated with six product categories, which include: physicians, nurses, equipment, supplies, contract labor, and any other labor. [191]

Administrative and overhead costs are assigned to departments using a "step down" approach. Episodes of clinical care are assigned values for RVUs. The RVU is a function of time and clinical complexity. Clinical care often involves intermediate products, such as imaging, transfusions, or emergency room visits. The intermediate products are bundled as part of the patient episode-of-care. RVUs are assigned to each step in the care pathway, including each intermediate product, based on the associated resources needed for each episode of care. Every DVA facility can adjust the RVU figures to match variations in care. The cost of the episode of care includes the departmental RVUs mathematically combined with the RVUs from the intermediate products. [192]

Today, the DSS is known as the DVA Managerial Cost Accounting System (MCA). The MCA collects cost data and apportions costs so that the price of individual care episodes can be estimated for the medical department and facility. MCA is an activities-based cost distribution accounting system. The service fixed and variable costs are mapped to intermediate products (imaging, lab, social work, and so on), and costs are assigned to intermediate departments and aggregated to determine the average cost of patient encounters. The MCA relies on pre-existing DVA databases to track specific information on details defining episodes of care for the individual veteran. The data is combined with unit cost estimates to calculate the average cost of hospital stays and out-patient visits. [193]

The DVA sponsored a systematic literature review for a technical report that categorized the cost techniques scholars use to research the DVA's cost of care. The review included over 250 articles published between 1980 and 2012. The publications were grouped into one of four costing methods:1) HERC average cost (top-down); 2) MCA activity costs (bottom-up); 3) direct costs (micro-costing); and 4) community care cost comparison. The authors found that the direct

cost method and the MCA activity cost methods were used over 90% of the time. The top-down approach and the community care comparison approach were infrequently used. [194]

Policy analysts are interested in veterans' costs of care because the DVA represents a nationally integrated system where clinical decisions are not propelled by profit incentives. [195] For example, scholars used the 2010 DVA national data base to study the relationship between costs of care, comorbidities, and care utilization among veterans. The cross-sectional study pulled data from the electronic medical records of over 5.2 million veterans who received in-patient or out-patient care in 2010. Veterans with costs in the top 5% of the population were labeled "high cost" veterans. The scholars found that "high cost" veterans were responsible for 47% of the VA-incurred costs of care for 2010. In addition, 41% of the "high cost" veterans had five or more chronic conditions with an average cost per veteran of about $64,000 for that year. The remaining 95% of veterans had far fewer chronic diagnoses and reported an average cost of about $5,200 per veteran for 2010. [196] This means that the "high cost" veterans on average consumed 12 times the cost compared to other veterans in 2010.

Researchers were also interested in the DVA cost of care for lower limb amputations for veterans with diabetes. The study mined national DVA data for the in-patient and out-patient costs of care for lower limb amputations in 2004 for comparison with the costs from 2010. A total of 3,381 lower limb amputations were completed in 2004, compared to 3,403 for 2010. The researchers calculated that for 2004 the mean cost of care for diabetic veterans with lower limb amputations was over $50,000, but the expenditures rose to over $60,000 by 2010. The in-patient surgical cost represented about 90% of the cost for lower limb amputations in 2004 and about 88% of the cost for lower limb amputations in 2010. [197]

Cost studies have been conducted to compare the total cost of care for veterans with COPD to that of veterans without COPD. For example, a study used a bottom-up or MCA activity cost method to analyze cost and utilization data mined from the VISN 16 data warehouse. The researchers collected retrospective data for a 7-year timeline (1997-2004). The study compared the total cost of care of about 60,00 veterans with COPD to over 117,000 veterans without COPD. The study reported that the total healthcare utilizations and total cost of care was significantly higher in veterans with COPD compared to the controls. The mean total cost of care was estimated to be 10 times greater for those with COPD compared to veterans without COPD. [198]

Veterans and the Salisbury Health Care Center

The Salisbury VA Health Care Center (SVAHCS) is part of the VISN-6 healthcare network and provides care to veterans over a 21-county catchment area across the Central Piedmont region of North Carolina. The major metropolitan areas are connected by the I-85 expressway and include the municipalities of Greensboro, High Point, Winston-Salem, and Charlotte, North Carolina. [199]

The SVAHCS has four physical locations: the Kernersville Health Care Center (HCC), the South Charlotte HCC, the North Charlotte Community Based Outpatient Clinic (CBOC), and the 'Bill Hefner 'Salisbury VA Medical Center . The Kernersville HCC and the Charlotte HCC opened in 2016 and are two of the largest such DVA facilities in the nation. The 'Bill Hefner' Salisbury VA Medical Center, the administrative hub for the SVAHCS, was opened in 1953. [199]

The SVAHCS has a total of 484 beds that include 159 hospital beds, 270 nursing home beds, and 55 psychiatric substance abuse treatment beds. The SVAHCS is affiliated with the

Wake Forest University School of Medicine and the Edward Via Virginia College of Osteopathic Medicine. There are a total of 17 specialty clinical programs that include ambulatory care, pulmonary care, imaging, mental health, nuclear medicine, psychiatric care, and advanced low vision, to name a few. The in-patient services provided include acute medicine, surgery, psychiatry, cardiology, and physical rehabilitation, among others. Primary and specialty out-patient services are provided across various disciplines, including audiology, optometry, neurology, physical therapy, sleep medicine, and dermatology, to name a few. [200]

At the end of the 2019 physical year, there were a total of 102,909 veterans enrolled for care at the SVAHCS, although the number had decreased to 102,309 veterans by 2020. In 2019, the SVAHCS provided over 1.43 million encounters, or care-related interactions, to veterans, but the number of encounters declined in 2020 because of the COVID-19 pandemic.

Regarding the demographic characteristics of the SVAHCS veterans in 2019, 75% of veterans were 50 years of age or older, 39% were between 60 and 79 years of age, and 25% were younger than age 50. Male veterans made up 91% of the enrolled veterans in 2019. In terms of ethnicity, 25% of the veterans identified as Black, 63% as White, and 12% as Multiracial/Other. In 2019, 44% of veterans had no service-connected disability, 23% had between 50% and 90% service-connected disability, and 11% of the veteran had 100% service-connected disability. Approximately 70% of veterans lived in a designated urban zone, while 30% lived in a designated rural region. The SVAHCS-enrolled veterans represented a wide range of military eras: 39% served in the Persian Gulf War, 37% served in the Vietnam War, 14% were from the post-Vietnam Era, just over 4% served in the Korean War, 4% served during the post-Korean War era, and just less than 2% served during World War II.

CHAPTER 3: FINDINGS ON COPD AND COMORBIDITIES

There is a gap in the knowledge regarding the relationships between the comorbidities and epidemiological disease patterns among veterans with chronic obstructive pulmonary disease (COPD). Prior work has shown that veterans struggle with complex clusters of systemic comorbidities, which include respiratory ailments. [201] A national, retrospective study describing comorbidities diagnosed in Iraq War veterans assigned to Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) observed that 18% of veterans with post-traumatic-stress disorder (PTSD) had a respiratory disease diagnosis. [202] The association between PTSD and respiratory disease is a concern since the prevalence of PTSD among veterans ranges from 4–17%. [203,204]

Published findings show that veterans diagnosed with COPD often have an assortment of comorbidities. A retrospective case-control study observed that veterans hospitalized with a COPD diagnosis were much more likely to have a diagnosis for congestive heart failure (CHF), coronary artery disease, and atrial fibrillation (AF) compared to veterans without COPD. [205] Anxiety and depression are common psychological comorbidities that accompany the veteran's COPD diagnosis. [206] Veterans with frequent episodes of COPD-associated dyspnea are more likely to suffer chronic pain than veterans without COPD. [207] A national, retrospective review of hospital records found that veterans discharged with a COPD diagnosis were seven times more likely to suffer with pulmonary hypertension compared to non-hospitalized veterans. [208] Veterans with advanced COPD reported a diminished health-related quality of life (HRQL), had more frequent primary care visits, and were more frequently admitted to the hospital compared to veterans with other respiratory diseases. [209]

The present study investigated the frequencies and associations between COPD and comorbidities found in veterans from the Piedmont region of North Carolina. The cases and

controls received primary care at the Salisbury VA Health Care System (SVAHCS). In contrast to previously published case-control studies of veterans, the study reported here was more recent, specific to veterans from North Carolina, and assessed a wider range of comorbidities. [205,210,211]

The objectives of this study were as follows:

Objective 1: To describe the frequencies and prevalence of select comorbidities recorded for veterans with COPD compared to veterans without COPD.

Objective 2: To statistically analyze the associations between sociodemographic characteristics and select comorbidities recorded for veterans with COPD compared to veterans without COPD.

The goal of the study was to provide a contemporary understanding of the relationships found between COPD and systemic comorbidities in veterans enrolled in primary care at the Salisbury VAHCS.

Methods

Study Design

The present study used a retrospective, case-control design to contrast, compare, and analyze the frequencies and associations of comorbidities diagnosed in veterans with and without COPD. The dependent and independent variables were pulled from the electronic medical records based on select ICD-9 and ICD-10 diagnostic codes (see Appendix A). Both ICD-9 and ICD-10 codes were used because the Salisbury VAHCS transitioned to the ICD-10 codes during the study's timeline. The diagnostic codes represented variables categorized as psychological, cardiovascular, metabolic, pulmonary, autoimmune, and renal comorbidities.

Select variables were collected from the electronic health records of a cohort of U.S. veterans that received primary care at the SVAHCS. Structured Query Language (SQL) programming was used to identify the population of veterans enrolled for primary care services between January 1, 2016 and December 31, 2018. The SVAHCS Institutional Review Board (IRB) approved this study (IRB project number 19-016).

Veterans enrolled for primary care services with a minimum of two recorded primary care visits during the 3-year study period comprised the population of eligible subjects. Veterans with two recorded visits were considered more likely to rely on the SBYVAHCS for their care. The veterans needed to be 50 or older as of January 1, 2016 to be included in the study. Veterans younger than 50 years were excluded from the study because of a generally low COPD prevalence below age 50. The study excluded veterans who developed COPD or who died during the study period. Thus, the veterans had the same diagnostic classification as cases or controls throughout the study. The control subjects lacked a diagnosis of COPD, while the case subjects all had a COPD diagnosis in the electronic medical record before January 1, 2016. Veterans with fewer than two completed primary care visits during the study period were not included in the study. Veterans with a diagnosis of human-immuno-virus (HIV) were excluded because HIV represents a protected research category per DVA research guidelines.

Data

Structured Query Language (SQL) programming applications were used to query the VHA Decision Support System (DSS) and the VISN 6 Data Warehouse, a regional databank of electronic records, to identify all veterans who met the inclusion criteria. Once the population of eligible veterans were identified, the subjects' recorded information about sociodemographic and clinical diagnoses were collected from the electronic medical records.

COPD is an umbrella term that includes specific diagnostic codes. The study's dichotomous dependent variable was defined by established ICD-9-CM and ICD-10-CM diagnostic codes for COPD (see Appendix A). Both ICD-9-CM and ICD-10-CM codes were used because the medical facility was transitioning to ICD-10-CM codes during the study's timeline. The diagnostic codes encompassed chronic bronchitis, emphysema, bronchiectasis, and chronic airway obstruction. Veterans with these diagnostic codes in their electronic health records represented the case subjects and veterans without these diagnostic codes were the controls.

The independent variables were selected following an extensive literature review. The independent variables used for the multiple logistic regression analysis included dyspnea, a prominent symptom of COPD, 19 systemic diagnoses, and eight sociodemographic variables. The sociodemographic variables included age, marital status, sex, race, smoking history, rural or urban residence, the service connection level (SC)≥50%, and the designation as a military combat veteran. The percentage service level connection reflects injuries the veteran suffered while enlisted. Age was broken into four interval groups (50–59, 60–69, 70–79, and over 79) with *50-59* as the reference group. Marital status included four coded categories with *married* as the reference group. Race included three categories with *White* as the reference group. Sex was coded with *male* as the reference group. For smoking history, *never smoked* was the reference group. Regarding residence, urban or rural, *urban* was the reference group. For service connection, service connection *(SC)<50%* was the reference group. For combat veterans, *no combat* was the reference group. And for reported dyspnea, *no dyspnea* was the reference group.

Specific ICD-9-CM or ICD-10-CM definitions for the 19 systemic conditions were used to measure the increased prevalence of comorbidities in COPD cases compared with the

background prevalence of these conditions in the DVA population without COPD (see Appendix A). The select conditions were representative of psychological, cardiovascular, metabolic, pulmonary, autoimmune, and renal comorbidities.

Data Analysis

The data analysis used STATA, version 16, and SPSS statistical software, version 27.0. The frequencies of the variables were expressed as numeric values (percentages) and descriptively compared relative to the cases and controls. The mean and median value for age, the only continuous variable, was calculated for comparisons between groups using the *t*-test and the Mann–Whitney *U*-test. A tetrachoric correlations table was constructed for the dichotomous variables and used it to identify any variables with correlations ≥0.8. The presence of multi-collinearity was investigated by calculating the variance inflation factors (VIF). Variables with VIF>5 were defined as highly correlated (see Table 3.1). Adjustments were made for the highly correlated variables alcohol and drug abuse.

Table 3.1. VIF for Each of the 23 Comorbid Diagnoses

Variable	VIF
Alcohol	5.359
Drug	5.467
PTSD	1.117
Smoking	1.625
Depression	1.235
Anxiety	1.117
Chronic pain	1.02
Dementia	1.015
Coronary artery	1.093
Ischemic heart	1.061
Atrial fib	1.056
Congestive heart	1.061
Stroke	1.022
Diabetes	1.063
High cholesterol	1.002
Rheumatoid	1.002
Asthma	1.013
Sleep apnea	1.271
Reported dyspnea	1.223
Diagnosed pneumonia	1.011
Peripheral vascular	1.061
Renal	1.052
Cancer	1.008

A bivariate analysis was used to identify the independent variables significantly associated with COPD. Chi-square (χ^2)-calculations were employed to evaluate the association between each dichotomous variable and COPD. The χ^2 significance threshold was set at $p < 0.01$. Race had three categories and marital status had four categories. Age was broken into four ordinal categories to evaluate the impact of age relative to the odds for COPD. The 28 independent variables were entered simultaneously into a multivariable logistic regression model to determine the independent variables' relationship with the presence or absence of COPD. A post-estimation analysis of the model was conducted to examine model fit and included the sensitivity-specificity classification, the area under the receiver-operator-curve (ROC), and the Hosmer–Lemeshow test, where a p value > 0.05 indicated an acceptable model fit.

The present study's population included 33,639 veterans, representing over 1,100 subjects per independent variable. A study population of this magnitude means the multiple logistic regression model risked excess statistical power. [212] Consequently, the meaningful independent variables were identified using multiple logistic regression along two separate criteria based upon the calculated *p*-values and the effect size, or odds ratios (ORs). The independent variables were retained with $p \leq 0.025$ if the OR ≤ 0.70 or ≥ 1.30. In other words, these variables were defined as clinically significant given a 0.30 effect size as demonstrated by the absolute value of the OR. The second criteria applied to the independent variables with a $p \leq 0.01$ and the OR ≤ 0.80 or ≥ 1.20, meaning that the absolute value of the effect size was a minimum of 0.20 with the more stringent p-value. Variables with $p > 0.025$ and an effect size < 0.30 were dismissed from the model. Variables were also dropped when the absolute value of the effect size was < 0.20

Results

Of 33,639 veterans in the study, 5,079 (15%) were diagnosed with COPD and the remaining 85% lacked a COPD diagnosis. This represents a ratio of 5.7 controls per case. As stated, age was broken into four intervals: 50–59, 60–69, 70–79, and 80 or older. Table 3.2 lists the reference age characteristics of the study population.

Table 3.2. Frequency of Veteran Age by Category

Age Interval	Frequency	Percentage
50–59	5,424	16.1%
60–69	9,598	28.5%
70–79	13,616	40.5%
80 and older	5,001	14.8%
Total	33,639	100%

The age distribution was skewed slightly to an older age, with 55% of the study population aged 70 and older. The mean age for the veteran population was 69.6 years, with a range from 50 to 90 years. The median age for the veteran population was 70 years. The mean age for the cases was 71.8 years, while the mean age for the controls was 69.2 years. An independent sample *t*-test revealed a statistically significant difference comparing the mean age of cases versus controls, with the cases significantly older than the controls (t = -18.391; $p <$ 0.001, CI[-2.845 to -2.297]). Likewise, the Mann-Whitney *U*-test revealed that the median age for the cases was statistically different from that expected for the controls (χ^2 = 144.899, df 1, $p <$ 0.001).

Table 3.3 provides descriptive information for the age distribution of veterans with and without COPD. It also showed that the frequency of the COPD diagnosis increases with age and peaks between the ages of 70 to 79 years.

Table 3.3. Age Distribution by Categories of Veterans With and Without COPD

Age Category	No COPD	Yes COPD	Total
50–59 years	5,122 (94.4%)	302 (5.6%)	5,424 (100%)
60–69 years	8,079 (84.2%)	1,519 (15.8%)	9,598 (100%)
70–79 years	11,226 (82.4%)	2,390 (17.6%)	13,616 (100%)
80 and older	4,133 (82.6%)	868 (17.4%)	5,001 (100%)
Total	28,560 (84.9%)	5,079 (15.09%)	33,639

Table 3.4 provides descriptive information on the race of veterans in the study. Of the participants, 66% were White, 30% were Black, and just under 4% identified as

Multiracial/Other. Black veterans were over-represented in this population compared to the census data for the proportion of Black residents in North Carolina. [213] Table 3.4 reveals the percentage of cases and controls within each category of race. A substantially greater percentage of White veterans compared to Black and Multiracial/Other veterans had a diagnosis for COPD. Fewer Black veterans were diagnosed with COPD compared to the other racial groups.

Table 3.4. Percentages of Controls and Cases by Veteran Race

COPD Diagnosis	White	Black	Multiracial/Other	Total
Controls	18,462 (83%)	9,023 (90%)	1,075(88%)	28,560 (85%)
Cases	3,928(17%)	1,008 (10%)	143 (12%)	5,079 (15%)
Grand Total	22,390 (100%)	10,031 (100%)	1,218 (100%)	33,639

Marital status was categorized as *married*, *divorced*, *widowed*, or *unknown*. The reference category was *married*. Out of a population of 33,639 veterans, slightly over 62% were married, 21% were divorced, just under 5% were widowed, and about 12% failed to report their marital status. Table 3.5 provides the frequency of the cases and controls associated with the marital status of the veterans within each group.

Table 3.5. Percentages of Cases and Controls by Veteran Marital Status

COPD Diagnosis	Married	Divorced	Widowed	Unknown	Total
Controls	18,051 (86%)	5,846 (83%)	1,258(76%)	3,405 (86%)	28,560
Cases	2,925 (14%)	1,248 (17%)	316 (24%)	590 (14%)	5,079
Grand Total	21,381(100%)	7,369 (100%)	1,339 (100%)	3,995 (100%)	33,639

Of those who were divorced, the overall prevalence of COPD was slightly over 17%. This compared to a COPD prevalence of about 14% for married veterans, near 20% for widowed veterans, and just over 14% for veterans with no report regarding their marital status.

The veterans in the study were predominately male. Males comprised about 95% of the study population and the remaining veterans were female. Regarding sex and COPD diagnosis,

4,951 (15%) male veterans were diagnosed with COPD compared to 195 (10%) of female veterans.

The veterans were recorded as having either an *urban* or *rural* residence. Just under 70% (24,105) of the veterans had an urban designation, and nearly 30% (10,423) were designated as rural, with two records that had missing data. Table 3.6 shows the frequency of cases and controls recorded as urban or rural.

Table 3.6. Frequency of COPD by Urban or Rural Residency

COPD Diagnosis	Urban	Rural	Missing	Total
Control	20,857 (87%)	8,525 (82%)	2	28,560
Case	3,248 (13%)	1,898 (18%)	0	5,079
Grand Total	24,105 (100%)	10,423 (100%)		33,639

The frequency count for veterans' smoking history, designated as *never smoked* or *previous or current smoker,* was retrieved. Again, *never smoked* was the reference category. Out of 33,639 veterans, 8,357 (25%) were designated as previous or current smokers and 25,282 (75%) as never smoked. Of those veterans who had never smoked, 2,513 (10%) were diagnosed with COPD compared to 2,565 (31%) of the previous or current smokers with a COPD diagnosis.

The frequency count for veterans with verified service-related injuries, defined as service connection, was retrieved from the records. The veterans were categorized as either having a serviced connection of less than 50% (SC < 50%) or a service connection greater than or equal to 50% (SC ≥ 50%). A total of 20,749 (62%) veterans had SC < 50% and 12,890 (38%) had SC ≥ 50%. About 15% of veterans SC < 50% were diagnosed with COPD compared to 15% of veterans with SC ≥ 50%.

Table 3.7 shows the population frequency of each comorbidity found in both cases and controls. A review of the frequency table for specific comorbidities revealed that the cases had a greater frequency across 18 of the 20 systemic illnesses compared to the controls. Only the metabolic ailments diabetes and hypercholesteremia recorded similar frequencies when comparing cases to controls.

Table 3.7. Frequencies of Categorical Study Variables

Variable		Total		No COPD		Yes COPD	
		N	**%**	***N***	**%**	***N***	**%**
Sex	Male	31,892	94.8	26,996	84.6	4,896	15.4
	Female	1,747	5.2	1,564	89.5	183	10.5
Race	White	22,390	66.5	18,462	82.5	3,928	17.5
	Black	10,031	29.8	9,023	90.0	1,008	10.0
	Other	1,218	3.6	1,075	88.3	143	11.7
SC ≥ 50%	No	20,749	61.7	17,646	85.0	3,147	15.0
	Yes	12,890	38.3	10,914	84.7	1,999	15.3
Rural/Urban	Urban	23,442	69.7	20,241	86.3	3,248	13.7
	Rural	10,195	30.3	8,317	81.6	1,898	18.4
Marital Status	Married	20,976	61.4	18,051	86.1	2,925	13.9
	Divorced	7,094	21.1	5,846	82.4	1,248	17.6
	Widowed	1,574	4.7	1,258	79.9	316	20.0
	Unknown	3,995	11.9	3,405	85.2	590	14.8
COPD	No	28,560	84.9	-	-	-	-
	Yes	5,079	15.1	-	-	-	-
Alcohol	No	25,755	76.6	22,733	88.3	3,022	11.7
	Yes	7,884	23.4	5,827	73.9	2,057	26.1
Drug	No	26,976	80.2	23,704	87.9	3,274	12.1
	Yes	6,661	19.8	4,856	72.9	1,805	27.1
PTSD	No	27,272	81.1	23,273	85.3	3,999	14.7
	Yes	6,367	18.9	5,287	83.0	1,080	17.0
Smoking	No	25,282	75.2	22,768	90.0	2,514	10.0
	Yes	8,357	24.8	5,792	69.3	2,565	30.7
Depression	No	24,072	71.6	20,747	86.2	3,325	13.8
	Yes	9,567	28.4	7,813	81.7	1,754	18.3
Anxiety	No	27,796	82.6	23,803	85.6	3,993	14.4
	Yes	5,843	17.4	4,757	81.4	1,086	18.6
Chronic Pain	No	32,647	97.1	27,807	85.2	4,840	14.8
	Yes	992	2.9	753	75.9	239	24.1
Dementia	No	32,657	97.1	27,775	85.0	4,882	15.0
	Yes	982	2.9	785	79.9	197	20.1
CorArtDz	No	27,777	82.6	23,892	86.0	3,885	14.0
	Yes	5,862	17.4	4,668	79.6	1,194	20.4
IschHtDz	No	31,520	93.7	26,893	85.3	4,627	14.7
	Yes	2,119	6.3	1,667	78.7	452	21.3
Atrial fib	No	30,221	89.8	25,828	85.5	4,393	14.5
	Yes	3,418	10.2	2,732	79.9	686	20.1
CongHt Dz	No	32,428	96.4	27,696	85.4	4,732	14.6
	Yes	1,211	3.6	864	71.3	347	28.7

Table 3.7 continued

Variable		Total		No COPD		Yes COPD	
		N	**%**	***N***	**%**	***N***	**%**
Stroke	No	32,383	96.3	27,572	85.1	4,811	14.9
	Yes	1,256	3.7	988	78.7	268	21.3
Diabetes	No	21,318	63.4	18,051	84.7	3,267	15.3
	Yes	12,321	36.6	10,509	85.3	1,812	14.7
Cholesterol	No	33,343	96.2	27,444	84.9	4,899	15.1
	Yes	1,296	3.8	1,116	86.1	180	13.9
Rheumatoid	No	33,192	98.7	28,207	85.0	4,985	15.0
	Yes	447	1.3	353	79.0	94	21.0
Asthma	No	31,640	94.1	27,156	85.8	4,484	14.2
	Yes	1,999	5.9	1,404	70.2	595	29.8
Sleep apnea	No	25,489	75.8	21,832	85.7	3,657	14.3
	Yes	8,150	24.2	6,728	82.6	1,422	17.4
Dyspnea	No	30,387	90.3	26,028	85.7	4,359	14.3
	Yes	3,252	9.7	2,532	77.9	720	22.1
Pneumonia	No	33,006	98.1	28,215	85.5	4,791	14.5
	Yes	633	1.9	345	54.5	288	45.5
PVD	No	30,699	91.3	26,484	86.3	4,215	13.7
	Yes	2,940	8.7	2,076	70.6	864	29.4
Renal Dz	No	29,712	88.3	25,289	85.1	4,423	14.9
	Yes	3,927	11.7	3,271	83.3	656	16.7
Cancer	No	33,311	99.0	28,335	85.1	4,976	14.9
	Yes	328	1.0	225	68.6	103	31.4
DiabRet	No	33,199	98.7	27,870	84.8	4,998	15.2
	Yes	440	1.3	690	89.5	81	10.5
Glaucoma	No	30,463	90.6	25,860	84.9	4,603	15.1
	Yes	3,176	9.4	2,700	85.0	476	15.0
ExARMD	No	33,339	99.1	28.345	85.0	4,994	15.0
	Yes	300	0.9	215	71.7	85	28.3
NonARMD	No	32,877	97.7	27,986	85.1	4,891	14.9
	Yes	762	2.3	574	75.3	188	24.7
NA-AION	No	33,515	99.4	28,452	84.9	5,063	15.1
	Yes	124	0.6	108	87.1	16	12.9
LowVision	No	32,531	96.7	27,596	84.8	4,935	15.2
	Yes	1,108	3.3	964	87.0	144	13.0
RetVeinOccl	No	33,383	99.2	28,346	84.9	5,037	15.1
	Yes	256	0.8	214	83.6	42	16.4

Table 3.8 shows the bivariate associations via the χ^2 test between the dependent variable and 26 dichotomous variables. Only four of the 26 dichotomous variables failed to demonstrate a significant χ^2 association with a diagnosis for COPD. These four variables were labeled as

combat veteran status, SC ≥ 50%, diagnosis for diabetes, and diagnosis for hypercholesterolemia. The five variables of alcohol abuse, smoking history, asthma, pneumonia, and peripheral vascular disease each yielded particularly robust positive χ^2 associations among the cases compared with the controls.

Table 3.8. Chi-Square Test Results for Variables by COPD Diagnosis

Variable	χ^2	**df**	***p***
Sex	37.739	1	< 0.001
Rural/Urban	128.654	1	< 0.001
Alcohol	973.808	1	< 0.001
Drug	934.733	1	< 0.001
PTSD	21.855	1	< 0.001
Smoking	2129.827	1	< 0.001
Depression	113.291	1	< 0.001
Anxiety	70.227	1	< 0.001
Chronic pain	67.873	1	< 0.001
Dementia	19.064	1	< 0.001
Coronary artery	163.674	1	< 0.001
Ischemic heart	71.481	1	< 0.001
Atrial fib	75.665	1	< 0.001
Congestive heart	184.556	1	< 0.001
Stroke	40.246	1	< 0.001
Rheumatoid	17.180	1	< 0.001
Asthma	363.053	1	< 0.001
Sleep apnea	48.937	1	< 0.001
Reported dyspnea	145.241	1	< 0.001
Diagnosed pneumonia	468.642	1	< 0.001
CCI peripheral vascular	518.625	1	< 0.001
CCI Renal	10.745	1	= 0.001
CCI Cancer	102.501	1	< 0.001

Table 3.9 shows the tetrachoric correlation values for the variables in the present study. Excess correlation between the variables is not a problem except for the relationship between the diagnosis for alcohol abuse and drug abuse.

Table 3.9. Tetrachoric Correlation Matrix for Comorbid Diagnoses

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	–														
2	1.00	–													
3	0.24	0.21	–												
4	0.82	0.84	0.09	–											
5	0.32	0.29	0.48	0.18	–										
6	0.18	0.17	0.29	0.11	0.52	–									
7	0.20	0.22	0.17	0.17	0.33	0.23	–								
8	0.02	0.00	0.07	-0.03	0.15	0.04	0.01	–							
9	-0.10	-0.08	-0.03	-0.03	-0.04	-0.03	0.02	0.08	–						
10	-0.04	-0.01	-0.04	-0.03	-0.03	-0.03	-0.02	0.12	0.45	–					
11	-0.14	-0.13	-0.12	-0.14	-0.10	-0.06	-0.04	0.10	0.26	0.20	–				
12	0.01	0.02	0.00	-0.04	0.04	0.00	0.04	0.10	0.27	0.27	0.45	–			
13	0.05	0.05	-0.01	0.07	0.07	0.01	0.08	0.33	0.15	0.21	0.14	0.15	–		
14	-0.08	-0.06	0.05	-0.08	0.05	-0.03	0.04	0.07	0.20	0.18	0.07	0.24	0.13	–	
15	0.00	0.01	-0.02	-0.03	-0.01	0.01	-0.04	0.08	0.06	0.12	0.02	-0.04	0.07	0.04	–

Table 3.9, continued

	16	17	18	19	20	21	22
16	–						
17	0.11	–					
18	0.00	0.19	–				
19	0.03	0.16	0.74	–			
20	0.10	0.19	0.06	0.12	–		
21	0.04	-0.09	0.00	0.06	0.11	–	
22	0.04	-0.02	0.07	0.08	0.08	0.21	–
23	0.05	-0.02	-0.03	0.04	0.14	0.09	0.11

Note: (1) Alcohol, (2) Drug, (3) PTSD, (4) Smoking, (5) Depression, (6) Anxiety, (7) Chronic pain, (8) Dementia, (9) Coronary artery, (10) Ischemic heart, (11) Atrial fib, (12) Congestive heart, (13) Stroke, (14) Diabetes, (15) High cholesterol, (16) Rheumatoid, (17) Asthma, (18) Sleep apnea, (19) Reported dyspnea, (20) Diagnosed pneumonia, (21) CCI peripheral vascular, (22) CCI Renal, (23) CCI Cancer

Table 3.10 lists the findings from the multiple logistic regression model. The variables representing demographic characteristics, 19 select systemic illnesses, and one symptom (dyspnea) were entered simultaneously into the logistic regression model. The systemic illnesses included diagnoses for cardiovascular, psychological, pulmonary, autoimmune, renal, and metabolic disorders. The multiple logistic regression analysis allowed for the estimation of the

associations between the given independent variables and the outcomes, holding all other variables constant; this thereby precluded the possibility that an apparently significant finding might be associated with a different independent variable. Thus, the findings that follow did not result from age, sex, or other control variables because the regression eliminated the differences in all other independent variables.

Table 3.10. Logistic Regression Results for Comorbidities Among Cases Versus Controls

COPD Variable	**Odds Ratio**	**Std. Err.**	***Z***	**P>|z|**	**[95% Conf. Interval]**
Age (≤ 59 reference)					
60–69	2.985	0.2029	16.09	0.000	2.613–3.411
70–79	4.051	0.2787	20.33	0.000	3.540–4.636
>79	5.621	0.4552	21.32	0.000	4.796–6.588
Marital Status (married reference)					
Divorce	1.306	0.0547	6.38	0.000	1.203–1.418
Widow	1.280	0.0921	3.43	0.001	1.111–1.474
Unknown	1.267	0.0704	4.27	0.000	1.137–1.413
Sex (male reference)					
Female	0.769	0.0671	-3.00	0.003	0.6482–0.9128
Race (White reference)					
Black	0.5702	0.0253	-12.66	0.000	0.5227–0.6220
Other	0.7248	0.0692	-3.37	0.001	0.6009–0.8741
Alcohol	1.321	0.0593	6.21	0.000	1.210–1.443
PTSD	1.013	0.0487	0.28	0.780	0.9222–1.113
Combat	0.9743	0.0782	-0.32	0.746	0.8324–1.140
Smoke	4.094	0.1781	32.39	0.000	3.759–4.458
SC ≥ 50	1.094	0.0433	2.29	0.022	1.012–1.183
Country	1.206	0.0427	5.31	0.000	1.125–1.293
Depress	1.228	0.0485	5.20	0.000	1.136–1.327
Anxiety	1.176	0.0513	3.72	0.000	1.079–1.281
Dementia	1.086	0.0962	0.94	0.348	0.0913–1.292
Pain	1.373	0.1162	3.75	0.000	1.63–1.621
Coronary	1.183	0.0197	4.01	0.000	1.090–1.285
Isch. Heart	1.132	0.0701	2.01	0.044	1.003–1.278
A Fib	1.123	0.0580	2.26	0.024	1.015–1.243

Table 3.10, continued

COPD Variable	Odds Ratio	Std. Err.	*Z*	P>|z|	[95% Conf. Interval]
CHF	1.856	0.1388	8.28	0.000	1.603–2.149
Diabetes	0.8532	0.0303	-4.46	0.000	0.7957–0.9148
Cholesterol	0.8250	0.0723	-2.19	0.028	0.6948–0.9796
Arthritis	1.393	0.1739	2.66	0.008	1.091–1.779
Asthma	3.399	0.1963	21.19	0.000	3.035–3.806
Apnea	1.194	0.0515	4.11	0.000	1.097–1.299
Dyspnea	1.493	0.0872	7.25	0.000	1.340–1.665
Pneumonia	3.576	0.3250	14.02	0.000	2.993–4.273
PVD	1.587	0.0775	9.47	0.000	1.442–1.747
Renal	0.9909	0.0506	-0.18	0.859	0.8964–1.095
Cancer	2.089	0.2785	5.53	0.000	1.609–2.713
_cons	0.0189	0.0014	-52.03	0.000	0.0612–0.0219

Note: Number of obs = 33,639; LR $\chi^2(33) = 4392.56$; Prob > $\chi^2 = 0.000$; Log likelihood = -12341.304; Pseudo R2 = 0.1511

The multiple logistic regression model was executed using 28 independent variables on 33,639 veterans, with 5,079 cases and 28,560 controls. Of the 28 independent variables, five variables dropped out of the model with an estimated $p > 0.025$. These five independent variables included combat veteran status, diagnosis for PTSD, dementia diagnosis, prior stroke, and renal disease diagnosis. Eight independent variables dropped out of the model with an effect size less than 0.20 and/or the $p > 0.01$. These variables were: service connection (SC) ≥ 50%, diagnoses for ischemic heart disease, atrial fibrillation, hypercholesteremia, diabetes, anxiety, coronary artery disease, and sleep apnea. So, 13 of the 28 independent variables dropped from the model, and 15 were retained.

Table 3.11 lists the independent variables excluded, along with the exclusion criteria.

Table 3.11. Independent Variables Omitted from the Regression Model

Exclusion Criteria	Independent Variable
Calculated $p > 0.025$	Combat veteran, PTSD, dementia, stroke, renal disease
Effect size (OR) < 0.20	SC ≥ 50%, ischemic heart disease, atrial fibrillation hyper-cholesterol, anxiety, diabetes, coronary heart disease, sleep apnea

The logistic regression results identified six sociodemographic variables that were statistically significant for the model. Four variables had a positive relationship, suggesting a greater likelihood of also having a COPD diagnosis, and two had a negative relationship for cases compared to controls, meaning that they were more often observed in COPD-free veterans (controlling for all other factors).

Age was positively related to the COPD diagnosis. The odds ratio (OR) for COPD sharply increased at each of the age categories, such that veterans aged 70–79 were over four times more likely to have COPD (OR = 4.05, $p < 0.001$), and veterans 80 and older were over five times as likely to have COPD (OR = 5.63, $p < 0.001$), compared to veterans under 60. Marial status was a significant demographic variable. Divorced veterans (OR = 1.30, $p < 0.001$), widowed veterans (OR = 1.29, $p = 0.001$), and those of unknown marital status (OR = 1.27, $p < 0.001$) were more likely to be diagnosed with COPD compared to married veterans. It is notable that this finding is robust, independently of the veterans' age, sex, or smoking history.

Race also proved to be a meaningful demographic variable in this study. Black veterans (OR = 0.57, $p < 0.001$) and veterans with race listed as Multiracial/Other (OR = 0.71, $p = 0.001$) were significantly less likely to have a COPD diagnosis than White veterans. Sex was another important demographic variable. Female veterans (OR = 0.78, $p < 0.004$) were less likely to have COPD compared to male veterans. Smoking history was positively related to a COPD diagnosis. Veterans who had previously or who currently smoked were much more likely to be diagnosed

with COPD (OR = 4.11, $p < 0.001$) compared to veterans who had never smoked. The place of residence, urban versus rural, was also positively related to the COPD diagnosis. Veterans designated as having a rural residence were 21% more likely to have a COPD diagnosis compared to veterans residing in urban areas.

A total of nine diagnostic variables met the defined *p*-value and effect size criteria for significance in the model. A subjective symptom, shortness of breath or dyspnea, was positively related to a COPD diagnosis. Veterans with COPD were more 51% more likely to report dyspnea compared to the controls (OR = 1.51, $p < 0.001$). Veterans with a diagnosis for alcohol abuse (OR = 1.33, $p < 0.001$) were also at greater odds of a COPD diagnosis.

Congestive heart disease (CHF) and peripheral vascular disease (PVD) were the only cardiovascular diagnoses that were significant in the present study. Veterans with CHF were at greater odds of a COPD diagnosis compared to other veterans (OR = 1.94, $p < 0.001$). Peripheral vascular disease had a positive relationship with a COPD diagnosis. Cases were significantly more likely to have peripheral vascular disease (PVD) than controls (OR = 1.58, $p < 0.001$). The remaining four cardiovascular conditions failed to achieve an effect size of 0.20.

Of the four psychological diagnoses, only depression and chronic pain were retained in the model. Veterans with COPD were 24% more likely to have a diagnosis for depression compared with veterans without COPD. Also, veterans with COPD were more likely to experience chronic pain compared to the controls (OR = 1.39, $p < 0.001$).

Rheumatoid arthritis (RA) and metastatic cancer were considered autoimmune conditions. Veterans with RA were 41% more likely to have COPD diagnosis compared to controls. Likewise, there was a robust positive relationship between COPD and the diagnosis for metastatic cancer (OR = 2.23, $p < 0.001$) in cases compared to controls.

Asthma, sleep apnea, and pneumonia were considered pulmonary comorbidities in this study. Each diagnoses had a positive association with the COPD diagnosis, but sleep apnea failed to report an effect size ≥ 0.20 (OR = 1.19, $p < 0.001$). Asthma was shown to have a robust positive relationship with the COPD diagnosis (OR = 3.50, $p < 0.001$). Veterans with a diagnosis for COPD were more likely to have a diagnosis for asthma compared to the controls. Pneumonia also had a strong positive relationship with the COPD diagnosis (OR = 3.57, $p < 0.001$). Veterans with COPD had pneumonia more frequently compared to the controls.

Post-estimation procedures for the logistic regression model were conducted for the final model. The model had a pseudo-R2 = 0.151. The model was acceptable, with a calculated ROC = 0.7701. Measures of accuracy revealed that sensitivity was marginal, at 11.87%, and the specificity was higher, at 98.50%, yielding an overall model accuracy of 85.59%. The logistic regression model did not predict the veterans with COPD as much as desired, but it performed well in predicting those without COPD. The computed ROC value indicated that the model did a fair job in discriminating between cases and controls. The Hosmer-Lemeshow goodness-of-fit test was satisfactory, with the Hosmer-Lemeshow $\chi^2(10) = 15.87$, Prob > $\chi^2 = 0.1035$.

Study Limitations and Strengths

All the subjects in this study were veterans, so the findings may not be generalizable to the non-veteran population. The population of veterans was comprised of subjects 50 years and older, so the findings may not be applicable to younger veterans. The study population was also predominately White male veterans, so the findings may vary with larger samples of females and non-White veterans. This becomes important as retirees from the U.S. military branches come to be more multi-cultural and multi-racial in the future.

All the veterans were enrolled for primary care at the Salisbury VAHCS, had a minimum of two recorded primary care visits, and lived in the SVAHCS catchment area; consequently, the findings may not apply to veterans who do not use the DVA for services or who reside in different geographical regions. Many primary care providers serve the regional VA population, so practice patterns, data entry behaviors, and data entry errors may vary among primary care providers. As such, it is possible that some veterans were mislabeled relative to the COPD diagnostic classification and subject to selection bias.

There were notable strengths to this study. The population size for cases and controls was large enough to support the generalizations of the findings. The cost and time associated with data extraction and analysis was minimal compared to other study designs. There was minimal missing data among the study variables, and only two cases were discarded. The data was in numerical form, permitting me to apply recognized analytical techniques. The dataset represented the entire population of veterans who met the inclusion requirements and who received care at the SVAHCS. The data were readily assessable, consistent, and available in the electronic health records with the use of SQL programming, thereby making replication at a DVA medical center easy. The statistical relationships among the variables were suitable for analysis. The data were sufficiently robust to enable the identification and description of complex relationships among the variables, and the study design allowed me to analyze multiple risk factors or associations at once. The retrospective, case-control design was efficient because COPD has a relatively long latency period between exposure and disease manifestation.

Discussion

The present study benefitted from the detailed coding practices primary care providers use to input ICD-9-CM and ICD-10-CM diagnostic codes into veterans' electronic medical

records. Missing data was not a barrier. Consequently, the present study provided significant findings for the comparative influence of sociodemographic factors and select diseases identified among veterans with and without COPD. The results from this study revealed some unforeseen and significant relationships between the independent variables and the risk for COPD among veterans within the Salisbury VAHCS.

Veterans are reported to suffer significantly greater comorbidity compared to the general public. [214,215,216] A total of 26 dichotomous variables were evaluated via bivariate analysis applying χ^2 calculations. The χ^2 findings revealed that the cases had stronger associations with 19 of 21 illnesses compared with each illness' association in the controls. The diagnosis for alcohol abuse was included in the model, but not the diagnosis for drug abuse because the two diagnoses were highly correlated. The final multiple logistic regression model included 19 systemic disorders.

The results of the model revealed that nine out of 19 ailments were significantly more likely to occur in veterans with COPD. This is not to say that those without COPD enjoyed outstanding health. For example, 36% of the controls had diabetes, which was three times the estimated national prevalence for diabetes in 2020. [217] Also, 7% of the controls were diagnosed with peripheral vascular disease, a percentage greater than the 1999–2004 estimated U.S. prevalence of 4.1% to 5.9%. [218,219] Likewise, 27% of veterans without COPD had a diagnosis for depression. A 2015–2018 national survey on depression estimated the U.S. prevalence for depression to be about 11%. [220] The present Salisbury study found that veterans enrolled in primary care at the SVAHCS with a COPD diagnosis experienced significantly higher rates of depression than veterans without COPD.

A 2011 national survey estimated the overall U.S. prevalence for COPD to be about 6.3%. [221] The COPD prevalence for eligible subjects in the present study at the SVAHCS was nearly 15%. The lower COPD prevalence found in the 2011 national survey reflected a wider age of those surveyed. The population of SVAHCS veterans in the present study was older with a median age of 70. COPD prevalence is known to increase with age. Further evidence is needed to distinguish COPD prevalence between veterans and non-veterans.

A prior study retrospectively analyzed 2004–2011 national survey data on the prevalence of COPD among U.S. workers aged 55 to 70. The survey asked the interviewees to report if they had been clinically diagnosed with COPD in the form of emphysema or chronic bronchitis. Some 5.13% of respondents reported a diagnosis for COPD. [222] The lower COPD prevalence among U.S. workers can be explained in several ways: first, the estimated prevalence relied upon respondent memory; second, the average age of the respondents in the national survey was lower than that of the Salisbury veterans studied here; and third, the COPD diagnosis among Salisbury veterans was independent of the patients' memory because it was captured directly from medical records. More importantly, cohort studies among workers have been shown to suffer from a type of selection bias labeled the "healthy worker effect." The idea is that active workers enjoy a greater level of health compared to non-working cohorts, so the measures of population illness may be underestimated via selection bias. [223,224] In addition, studies have demonstrated that, in the absence of spirometry, COPD is often underdiagnosed. [225,226] Consequently, the 2004–2011 national survey likely underestimated the true prevalence of COPD among U.S. workers. The Salisbury study used the COPD diagnosis in the electronic medical records rather than spirometry findings to select cases. Further study is needed to contrast and compare the veterans' COPD diagnosis with respiratory symptoms and spirometry findings.

In another study, investigators used retrospective CDC survey data from the 2009 Behavioral Risk Factor Surveillance System (BRFSS) to study the prevalence and characteristics of COPD in North Carolina residents. The analysis estimated the COPD prevalence for adults 65 years and older to be around 10%. The COPD prevalence was higher for North Carolina seniors in nursing homes, those who smoked, and those with lower incomes. [227] While the 2009 survey included an age-appropriate cohort like the veterans in the present study, the reliance upon survey data raises questions about the validity of the COPD prevalence estimate for the same reasons enumerated for the survey of U.S. workers.

Published studies have estimated the COPD prevalence among veterans. In 2010, researchers conducted a retrospective study of veterans enrolled at the Boise Veteran Affairs Medical Center (VAMC) to explore the relationship between smoking history and a COPD diagnosis. The study included records of about 20,000 veterans of all age groups from January 1, 1999 through May 30, 2006. The average age of veterans in the Boise VAMC study was 61 years. The overall prevalence of COPD in veterans at the Boise VAMC was about 9%, but the prevalence for smokers rose to 14%. [228] The lower COPD prevalence reported in the Boise VAMC study compared to that in the present Salisbury study can be explained by the younger average age of veterans in the Boise VAMC study and by differences in the sociodemographic characteristics of the two regions.

Results from a retrospective study of over 53,000 veterans who received care across the Veterans Integrated Service Network 5 (VISN 5) was published as a poster presentation at a national conference in San Diego, California. The investigators were interested in the prevalence of COPD-overlap syndromes across VISN 5. The results from pulmonary function testing were used to classify the veterans as *pure COPD* or *COPD accompanied by an overlap syndrome*. The

investigators found that some 12% of veterans had COPD without overlap and an additional 6% were diagnosed with a COPD-overlap syndrome. The total prevalence for all categories of COPD combined in this study was about 18%. [229]

The present Salisbury study used the COPD diagnostic codes found in the electronic medical records to identify cases, while the VISN 5 study employed pulmonary function testing to label cases. The present Salisbury study included appropriate diagnostic codes to identify case subjects with asthma and sleep apnea diagnoses. For example, at the SVAHCS, 600 veterans had a diagnosis for asthma and COPD. Regarding sleep-apnea, over 1,400 veterans had a diagnosis for both sleep-apnea and COPD recorded in their medical records. So, of the total cases in Salisbury study about 39% of the cases qualified as having with one of these two COPD-overlap syndromes. Clearly, the estimated prevalence of COPD-overlap syndromes among Salisbury veterans with COPD was significantly higher than that reported in the VISN 5 study. Additional research is needed to better understand the different prevalence estimates in the two studies.

The estimates from the multiple logistic regression model revealed that the Salisbury cases were significantly more likely to have asthma–COPD overlap syndrome (OR = 3.42, $p < 0.001$) than the controls. Likewise, there was a clear trend for the cases to have sleep apnea overlap syndrome (OR = 1.20, $p < 0.001$) compared to the controls. Pulmonary function testing on controls with asthma and sleep apnea would help refine the estimated COPD prevalence. It is reasonable to hypothesize that with pulmonary function testing the computed COPD prevalence would be greater than 15% for the Salisbury study.

Researchers analyzed the 2017 Behavioral Risk Factor Surveillance System (BRFSS) national survey data to estimate the COPD prevalence and smoking behavior of veterans and non-veterans using over 450,000 survey responses. The survey respondents were asked if a

medical professional had previously told them that they had COPD. The investigators concluded that veterans had a higher prevalence of COPD (14.2%) than non-veterans (11.1%). [230] The 15% COPD prevalence for the eligible subjects found in the population of Salisbury veterans paralleled the estimated COPD prevalence for veterans from the 2017 national BRFSS survey.

Researchers conducting a retrospective case-control study of all veterans enrolled for care in the Veterans Integrated System Network-16 (VISN 16) estimated the 7-year COPD prevalence for VISN-16 veterans to be about 8%. The researchers labeled veterans with a primary or secondary ICD-9-CM diagnosis code for COPD as cases. [198] The lower VISN-16 prevalence for COPD compared to the calculated Salisbury veterans' COPD prevalence (15%) can be explained by a younger, healthier veteran population. For example, the veterans in the VISN 16 study included all ages and reported lower rates for diabetes, metastatic cancer, peripheral vascular disease, renal disease, dementia, and rheumatoid disease compared to the comorbidity rates found in the Salisbury veteran study population.

A decline in pulmonary function accompanies increased age. [231] Consequently, mortality is correlated with an increased prevalence of COPD. [232] The present study found that increased age was highly associated with a COPD diagnosis. The probability for a COPD diagnosis at age 80 and older was around 6 times more likely than that for veterans younger than 60. One explanation for this finding has to do with the multi-system decline that accompanies age. Octogenarians show a steady decline in physical activity and cardiac output that impairs pulmonary function. Other publications have documented the increased risk for COPD in older veterans. [75,198,210]

The COPD literature reports a relationship between race and COPD, but the findings remain ambiguous. In a prospective cohort study of 1200 patients enrolled with the Kaiser

Permanente Medical Care Program (KPMCP), scientists studied the relationship between select sociodemographic variables and COPD severity. The scientists aimed to identify the sociodemographic variables related to COPD disease severity. After controlling for socio-economic status and other variables, the scientists concluded that there was no difference in COPD disease severity for Black versus White patients. The scientists hypothesized that the socio-economic status and the levels of educational attainment were the primary determining factors related to COPD disease severity in this population of northern California residents. [233]

In the COPDGene study, investigators used computer tomography imaging to compare COPD severity as evidenced by the degree of emphysema in Black and White patients. All the images were from patients with COPD, and all the patients had similarly impaired pulmonary function. The researchers compared the images from 863 White subjects to those of 200 Black subjects. The images for White subjects revealed more severe emphysema compared to the Black subjects, despite comparable pulmonary function. The authors concluded that other factors not measured by computer tomography likely explained the poor pulmonary function of Black patients with COPD. [234]

As mentioned, in the present Salisbury study, 67% of the veterans self-identified as White, 30% as Black, and 3% as Multiracial. The study, which controlled for age and other confounding variables, found that veterans who identified as Black or Multiracial were significantly less likely to be diagnosed with COPD compared to White veterans. Black veterans demonstrated a 43% reduced risk (OR = 0.569, $p < 0.001$), and veterans who identified as Multicultural demonstrated a 28% reduced risk (OR = 0.724, $p = 0.001$) for COPD compared to White veterans. Previous studies have reported similar findings regarding race and the odds for COPD. [198,235]

The present study's results regarding race and risk of COPD raise several questions. For instance, how can the lower risk for COPD among Black veterans be explained? There are plausible reasons. One possibility is that the findings represent a clinician bias or health disparity around the diagnosis of COPD for minorities. Perhaps primary care providers question minority veterans less often for signs or symptoms of COPD. Published studies have explored this notion. Researchers examined the patterns of smoking cessation treatment offered to veterans who smoked and who were hospitalized with COPD. The researchers found that veterans with COPD who were Black, older, had elevated comorbidity, or who had a diagnosed psychosis were significantly less likely to be counseled and prescribed appropriate medications for smoking cessation compared to younger, healthier, White veterans. [236] These findings justify additional study but suggest that a provider's approach to care may reflect biases.

It is also possible that veterans who identify as Black and Multiracial are less likely to develop COPD compared to White veterans for reasons yet to be determined. In a national sample of veterans, researchers studied the chronic conditions and cost for the high utilizers of healthcare. Ethnicity was a variable of interest. The researcher extracted data on the descriptive characteristics and chronic conditions of over 237,000 veterans who consumed the upper 5% of medical resources in the DVA system for the 2010 fiscal year. The study inspected the comorbidities diagnosed in these very sick veterans. The study-wide COPD prevalence was 20%, but Black veterans were 41% less likely to have a diagnosis for COPD compared to White veterans (RR = 0.59). [237] These outcomes support the findings on race and the odds of COPD for veterans in the present study. For the Salisbury veterans, the multiple logistic regression model found that Black veterans were 43% less likely to have a COPD diagnosis (OR = 0.57, $p <$

0.001) compared to White veterans. The relationship between the identified race and the risk for COPD merits additional study.

Marital status influences the likelihood for both a COPD diagnosis and disease progression, as reported in two studies of the general population. In a cohort study that spanned 11 years with over 2,600 subjects, investigators found that remarriage after divorce or bereavement was associated with a decreased risk of COPD. Subjects who remarried had a reduced incidence for COPD (HR = 0.51) compared to those not married. The investigators hypothesized that marriage generates psychosocial support such that lifestyle and behavioral decisions abated the risk of COPD. [238]

Another research group used an exploratory mixed-methods design to study the factors related to suicidal ideation in patients with advanced COPD. One variable measured was the percentage of participants with advanced COPD who were married, unmarried, or living with another. The researchers found that suicidal ideation was frequent but that those who were married had a lowered prevalence of suicidal ideation compared to those who were unmarried or living with a significant other. [239] Again, one hypothesis is that married veterans benefit from greater levels of social support compared to unmarried veterans.

Like those findings from the general population, in the present Salisbury study, the veterans who were married were significantly less likely to be diagnosed with COPD compared to unmarried veterans. The divorced veterans (OR = 1.31, $p < 0.001$), widowed veterans (OR = 1.28, $p = 0.001$), and those with an unreported marital status (OR = 1.27, $p < 0.001$) were at increased odds for COPD. Again, other publications have considered the relationship between marital status and COPD. [210][240] One possible theory for these trends is that married

veterans enjoy an enhanced financial and social support system that encourages healthy behaviors which reduce the odds for COPD.

The present study found that female veterans were at a decreased likelihood of being diagnosed with COPD compared to male veterans (OR = 0.77, $p < 0.001$). This contrasts with recent trends in the literature where findings indicate that the rate of COPD in women is similar to that in men. [241][242][243] The explanation for the sex effect in the Salisbury study may involve several factors. First, only 5% of the study population identified as female. The small number of females in the study may have influenced the findings. Second, the cohort or behavioral differences of male to female veterans might explain the likelihood of COPD in female veterans. Female enlistment has increased for the past 30 years, while fewer women enlisted in World War II, the Korean War, and the Vietnam War. The number of women in the military increased with the adoption of an all-volunteer military force after the Vietnam War. [244][245] The present study included a large percentage of males from the Vietnam War. Perhaps the male veterans enrolled for care at the SVAHCS, especially unmarried males, adopted negative health behaviors that promoted the development of COPD. Larger age-matched studies comparing the prevalence of COPD among male and female veterans are justified.

Researchers have also been interested in how a preferred residence in the city versus the countryside impacts a person's health. One retrospective study used 2018 national BRFSS data to address this question. The researchers found that rural residents had a higher rate of COPD, suffered greater poverty, and had increased levels of comorbidity compared to urban residents. [246] According to a federal report generated from the 2015 BRFSS, the overall COPD prevalence for rural residents was near 8%, compared to just under 5% for urban residents. States

with large percentages of rural residents, such as Arkansas, West Virginia, Kentucky, and Mississippi, recorded significantly higher numbers of residents with COPD. [247]

The DVA classifies a veteran's residence as urban or rural because travel distance impacts access to care. In the present study, urban veterans comprised about 70% of the study population. Key demographic characteristics of the rural veterans were associated with a positive COPD diagnosis. Regarding race, 85% of the rural residents were White, 12% were Black, and 3% identified as Multiracial/Other. The rural veterans were significantly older: about 61% of rural veterans were over 69 years, compared to 52% of urban veterans. In addition, 68% of rural veterans had a positive smoking history, compared to 32% of urban veterans. In sum, rural veterans were more likely to be older, White, with a positive smoking history, which are all known risk factors for COPD. Overall, the Salisbury study discovered that rural veterans were 21% more likely to have a COPD diagnosis compared to urban veterans when holding other variables constant (OR = 1.21, $p < 0.001$). The Salisbury findings are supported by other studies. [248][249] Researchers have proposed that factors like race, poverty, health literacy, and gaps in follow-up care modify the health outcomes for rural residents with COPD. [250][251] The present Salisbury study did not capture measures for income and health literacy. Additional study is needed on the relationship between COPD, social determinants of health, and health disparities among rural veterans.

Smoking is a recognized risk factor for COPD. [232][252] Unfortunately, the prevalence of smoking among veterans is greater than among non-veterans. [253] The present study categorized smoking as *never smoked* and *previous or current smoker*. A total of 75% of veterans reported that they had never smoked, while 25% reported previously or currently smoking. A slightly larger but nonsignificant percentage of female veterans with COPD smoked

(26%) compared to male veterans (25%). Smoking prevalence varied by race, with 23% White, 29% Black, and 20% Multiracial/Other classified as previous or current smokers. The results of the present study indicated that the classification as previous or current smoker significantly increased the odds of a COPD diagnosis (OR = 4.09, $p < 0.001$). The findings associated with a positive smoking history were noteworthy given that the odds of COPD were lower in Black veterans, but Black veterans also recorded a slightly higher percentage as *previous or current smokers* compared to White veterans. One explanation for this finding may relate to the duration and intensity of the smoking history. It is possible that the White veterans were heavier smokers for longer durations than the Black veterans. The present study did not capture information about smoking frequency and smoking duration. Another issue involves changes in smoking behavior with knowledge on smoking-related health risks across cohorts over time. Smoking was socially more acceptable among older veterans prior to changes in social norms. For example, researchers found that the comparative risk for cardiovascular mortality across age groups was modified by the knowledge of smoking-related health risks over time. [254] Another study found that the higher smoking rates over the past eight decades were associated with decreased life expectancy in older adults. [255] Future study into the relationship between race, smoking behavior, and risk for COPD is needed.

Dyspnea is a common symptom of cardio-pulmonary conditions, including COPD. [256] In the present study, about 9% of the controls reported dyspnea, compared to 14% of the cases. Episodes of dyspnea trigger psychological worries. Scientists have shown that dyspnea is associated with increased anxiety among veterans with COPD. [257] In the present study, about 9% of veterans without dyspnea were diagnosed with anxiety, compared to 13% of veterans with dyspnea. Veterans with frequent episodes of dyspnea are more likely to be diagnosed with

chronic pain. [207] The relationship was evident in the present study. About 3% of veterans without dyspnea reported chronic pain, compared to 4% with dyspnea. In a systematic literature review, researchers connected dyspnea and COPD exacerbations with heightened anxiety and depression. [258] Veterans with moderate to severe COPD more often reported dyspnea and comorbid depression compared to veterans without COPD. [259] The present study found that veterans with dyspnea were 49% more likely to have a COPD diagnosis (OR = 1.49, $p < 0.001$). Primary care providers should therefore arrange COPD evaluations for veterans with reported dyspnea and probe for symptoms of chronic pain, depression, or anxiety.

Studies show that alcoholism is a common comorbidity among men with COPD. [260][261] Although alcohol offers a socially acceptable means for "self-medication" when in distress, alcohol carries inherent risks to health. In the present study, 24% of the veterans had a history for alcohol abuse. Cases (41%) more frequently reported alcohol abuse in the record compared to controls (21%). Men recorded a slightly higher percentage of cases with alcohol abuse compared to women (24% versus 22%). In the present study, a history of alcohol abuse had a moderately positive association with a diagnosis for COPD (OR = 1.32, $p < 0.001$). For veterans with COPD, alcohol abuse raises concerns because alcohol may cause immunological and biochemical injury to the lungs. [262][263][264] It is reasonable to hypothesize that alcohol abuse may promote COPD disease progression. Veterans with a COPD diagnosis should be counseled regarding alcohol consumption. Conversely, it is reasonable that older veterans with known alcohol abuse be screened for COPD.

The logistic regression model retained two psychological variables: depression (OR = 1.226, $p < 0.001$) and chronic pain (OR = 1.370, $p < 0.001$). Publications document the positive relationship between depression and COPD in veterans. A retrospective study of 180 veterans

with COPD found that 86% met the criteria for depression under the DSM-IV criteria. [265] A published poster presented by researchers from the Boston VAMC compared the accuracy of medical record diagnoses with self-reported diagnoses for depression in veterans with COPD. The researchers estimated that 29% of veterans with COPD suffered depression. [266] The present Salisbury study found that nearly 35% of veterans diagnosed with COPD had a diagnosis for depression, compared to 28% of veterans without COPD. The risk for depression concurrent with COPD may be greater in older, rural, unmarried veterans. It is reasonable that primary care providers would proactively screen and treat depression in veterans with COPD.

Chronic pain is a recognized risk factor for suicidality in patients with inadequate psychosocial support. [267] The analysis here found that veterans diagnosed with COPD suffered with chronic pain at a significantly greater frequency than veterans without COPD (5% versus 3%). The present Salisbury study observed that 43 out of 100 veterans with chronic pain were divorced or widowed, more often White (67%), between the ages of 60–79 (71%), and likely men (90%). Primary care providers should recognize the special needs for veterans with COPD and chronic pain. Ideally, for veterans with COPD, clinicians would endeavor to manage the chronic pain, screen for the risk of suicide, and inquire about the veteran's psychosocial support systems.

The present study categorized rheumatoid arthritis and metastatic cancer as autoimmune conditions. The multiple logistic regression model found that veterans with rheumatoid arthritis were 39% more likely to have COPD compared to those without COPD. (OR = 1.39, $p < 0.008$) There was also a robust relationship between COPD with metastatic cancer (OR = 2.08, $p < 0.001$). Smoking serves as a common inflammatory link that connects rheumatoid arthritis and metastatic cancer with COPD. [268][269] About 51% of the cases had a positive smoking

history. Primary care providers may wish to screen veterans with COPD, particularly those who smoke, for rheumatoid arthritis and cancer. Veterans with COPD who smoke should be educated about the inherent risk for rheumatoid arthritis and cancer. Additional study on COPD and the connection with autoimmune conditions is desirable.

Congestive heart disease and peripheral vascular disease are known comorbidities for COPD. [81][270] In addition, congestive heart disease and peripheral vascular disease are often concomitant conditions with a shared pathogenesis. [271] Congestive heart disease (OR = 1.85, $p < 0.001$) and peripheral vascular disease (OR = 1.58, $p < 0.001$) proved to be significant comorbidities in veterans diagnosed with COPD. Unfortunately, congestive heart failure and COPD share common symptomology, such as fatigue, chronic cough, and dyspnea. [272][273] It is possible that COPD and congestive heart disease act synergistically to promote disease progression. The findings of the present study suggest that veterans with congestive heart failure and peripheral vascular disease may benefit from pulmonary function testing. Conversely, veterans with COPD should be screened for cardiovascular disease.

Two comorbid pulmonary diagnoses recorded a robust relationship with COPD and remained in the multiple logistic regression model. These comorbid conditions were asthma (OR = 3.40, $p < 0.001$) and pneumonia (OR = 3.56, $p < 0.001$). The disease interaction between asthma and COPD progression is unclear. The present study found that 600 cases, or 12% of cases, had a diagnosis for both asthma and COPD, or an asthma–COPD overlap syndrome. This percentage differs from that reported in other published findings. For example, a retrospective study conducted in Norway estimated the prevalence of asthma–COPD overlap syndrome in those > 60 years to be about 3%. [274] A retrospective study using 2008–2010 U.S. survey data (MEPS) found that for adults between the ages of 40 and 85 the prevalence of asthma–COPD

overlap syndrome was about 17%. [275] In a cross-sectional study of veterans who had undergone pulmonary function testing, investigators found that among older veterans who were heavy smokers (45 pack/years on average) about 26% of the veterans had an asthma–COPD overlap syndrome. [276] A precise diagnosis for asthma–COPD overlap syndrome relies on pulmonary function testing. The present Salisbury study did not capture the veterans' results for pulmonary function testing from the electronic medical records.

In the present Salisbury study, the veterans with a COPD diagnosis were significantly more likely to develop pneumonia compared to veterans without COPD. Of the 638 veterans diagnosed with pneumonia 45% had a diagnosis for COPD. The demographic characteristics offer a picture of the Salisbury veterans diagnosed with pneumonia. Overall, 74% of the veterans with pneumonia were White, 60% were older than 69 years, and 37% had a positive smoking history.

A retrospective study on veterans with COPD from VISN 16 produced similar findings regarding pneumonia as a comorbid condition. The VISN 16 study spanned 12 years (2000–2012) and compared characteristics and mortality rates across three groups of veterans: those hospitalized with COPD exacerbation, those hospitalized with pneumonia but without COPD, and those hospitalized with COPD and pneumonia. The study found that veterans hospitalized with COPD and pneumonia were more likely to be older White males, with increased comorbidity, prior or current smokers, and on home-oxygen therapy. [277] Primary care providers have a duty to educate veterans with COPD regarding the increased risk for pneumonia and offering the pneumonia vaccine. Veterans with COPD who smoke should be offered smoking cessation support and advised regarding the signs and symptoms of pneumonia.

Conclusion

The present Salisbury study used a retrospective, case-control design with multiple logistic regression modeling to better understand how select sociodemographic characteristics and disease diagnoses differ between veterans with COPD compared to veterans without COPD. The study's time frame spanned 36 months and included a population of over 33,000 veterans. A total of 28 variables representing sociodemographic and systemic diagnoses were used in logistic regression model. The present study identified marital status, race, and place of residence (urban versus rural) as important sociodemographic variables in need of further research. Veterans with a COPD diagnosis were more likely to be diagnosed with specific comorbidities across distinct health categories including the psychological, cardiovascular, autoimmune, and pulmonary domains compared to veterans without COPD. The present Salisbury study revealed that cases were more likely to be diagnosed with 9 out of 19 major systemic illnesses compared to controls. Each of these conditions alone is troublesome, but when concomitant with COPD the added comorbidities can be overwhelming for the veteran.

The study produced curious results that either supported previous publications or that identified topics for future research on veterans and COPD; such as the role of marriage in decreasing the risk for a COPD diagnosis in veterans, the protective role of race in decreasing the risk for COPD for Black veterans, the relationship between COPD and the increased risk for the veteran's cancer diagnosis, and the relationship between certain psychological diagnoses and a diagnosis of COPD among veterans, to name a few.

The findings around race and the risk for COPD were especially intriguing. Why did White veterans demonstrate a significantly increased risk for COPD compared to Black veterans? Additional research is needed to better understand the effect of race on the risk for

COPD among veterans. The study also found that rural or country-dwelling veterans were more likely to develop COPD than urban or city-dwelling veterans, but the reasons for this difference are yet to be determined. Are there variations in health behaviors or health literacy that might place rural veterans at greater risk of COPD?

The present study reinforced the fact that depression and chronic pain are commonly diagnosed in veterans with COPD. Each of these illnesses adversely impacts the veteran's quality of life. The findings support the notion that clinicians should screen and offer treatment for depression and chronic pain for veterans with a diagnosis for COPD.

Cardiovascular conditions are often associated with the diagnosis of COPD. In the present study, congestive heart failure and peripheral vascular disease were more prevalent among the cases compared to the controls. One recommendation from the study findings would be that veterans with either of these cardiovascular conditions be evaluated for possible COPD. Further research to better understand how these conditions interact with and influence COPD health outcomes among veterans is needed.

Overall, veterans enrolled for primary care services at the Salisbury Veteran Affairs Health Care System (SBYVAHCS) are diagnosed with a significant number of illnesses. That said, the findings from the present study show that veterans with COPD are diagnosed with a greater number of comorbidities as compared to veterans without a COPD diagnosis.

CHAPTER 4: FINDINGS ON OCULAR MORBIDITIES ASSOCIATED WITH COPD AMONG VETERANS

Of the five senses, vision is both predominant and vital for navigating the physical world. Consequently, fear frequently accompanies conditions linked with visual impairment. Research findings show that blindness relates to depression, anxiety, and the risk for suicide. [278] It should be no surprise that visual impairment is a recognized public health concern. The Healthy People 2030 goals include over a dozen objectives intended to mitigate visual impairment in children and adults. [279]

Visual impairment from blast-related injuries is a known occupational hazard for members who served active-duty military. [280] Congress, as the agency that appropriates funds for the DVA, routinely reviews reports about the veterans' health regarding blast related injuries. Those reviews led Congress to require the DVA and DoD to establish a collaborative research center, named the Vision Center of Excellence, in the National Defense Authorization Act of 2008 (NDAA). The Vision Center of Excellence investigates the prevalence and treatment of combat-related visual trauma among veterans. [281]

Respiratory injury is another documented occupational hazard for those who serve active-duty in the military. Significant exposure to dust, smoke, exhaust fumes, and airborn particulate matter promotes respiratory disease among military personnel. This fact gained nationwide attention as combat veterans returning from the Middle East were diagnosed with respiratory illness from toxic burn pit exposures. In response, Congress drafted legislation, known as the S.437-Veterans Burn Pit Exposure Recognition Act of 2021, to ensure that veterans exposed to burn pits would receive disability benefits and medical care from the DVA for the subsequent respiratory illness. [282,283]

Few studies explore how ocular morbidity may be related to COPD, especially among veterans. This paper, the ocular morbidity and COPD study, explores the frequency and associations of six vision-threatening ocular morbidities in veterans with and without COPD. The study begins with a brief literature review discussing pertinent topics, including the observable ocular effects of hypoxia from COPD, some published findings that link ocular morbidity with the COPD diagnosis, and the reported prevalence of select ocular diseases within the veteran population. Next, the six ocular diagnoses that comprised the dependent variables were introduced. The ocular diagnoses represent recognized causes for potentially serious visual impairment. The six dependent variables represented select ocular diagnoses as recorded in veterans' electronic medical records, these included: vision-threatening diabetic retinopathy, defined as diagnosed macular edema, severe diabetic retinopathy, and proliferative diabetic retinopathy; any diagnosis for glaucoma; a diagnosis for exudative macular degeneration; a diagnosis for retinal vein occlusion; a diagnosis for ischemic optic neuropathy; and a diagnosis for low vision where the best corrected acuity was recorded as 20/50 or worse Snellen visual acuity.

Unadjusted logistical regression models were then used to investigate the relationship between these six ocular diagnoses and COPD. The ocular diagnoses that had a statistically significant relationship with COPD in the unadjusted logistic regression models became the dependent variables for additional study, while ocular diagnoses that lacked significance in the unadjusted logistic regression models were not included for analysis. The present study aimed to answer the questions: "Are veterans with a COPD diagnosis more likely to be diagnosed with one of these six vision-threatening diagnoses?" and "What are the odds of COPD among veterans with one of the select vision-threatening ocular diagnoses?"

COPD's Impact on the Eye

Scientists have utilized clinical devices to investigate how the eye responds to COPD. Studies have shown that the retinal blood vessel diameter varies, or compensates, in response to systemic hypoxia from COPD. [131] Researchers have also used optical coherence tomography (OCT) to identify retinal nerve fiber thinning, or a loss of retinal tissue, in patients with COPD. [284] In addition, electrodiagnostic testing revealed that COPD induces an aberrant optic nerve conduction defect similar to that found with multiple sclerosis. [285] While the evidence links COPD with impaired ocular functioning, questions remain about the association between COPD and vision-threatening ocular diagnoses among veterans.

Investigators have used diagnostic codes from medical records to study the relationship between COPD and ocular diseases. For example, in 1998, academics in the United Kingdom extracted diagnostic codes for comorbidities found in patients hospitalized with COPD. The scientists reviewed almost 2,700 patients records and found that a COPD diagnosis was associated with a 30% increased risk for glaucoma (RR = 1.3). [134]

A retrospective, population-based study from Taiwan (2000–2012) found that those newly diagnosed with COPD were at a marginally increased risk for macular degeneration (HR = 1.2) compared to the matched controls. [286] Another retrospective study from Taiwan reviewed 12 years of data (2001–2013) and found that, among patients with diabetic retinopathy about 21% had a diagnosis for COPD, compared to 19% of patients without COPD. [287]

Researchers have also used National Health and Nutrition Examination Survey (NHANES) data from 1999–2008 to study comorbidities associated with COPD. In a sample of over 14,000 subjects aged 45 and older, investigators found that those with COPD more often reported visual impairment (14%) compared to those without COPD (10%). [288] While these

few studies suggested an association between ocular comorbidities and COPD, the evidence linking COPD to ocular pathologies is sparse. Especially lacking are studies of veterans with their unique history of risk exposure.

Recognized Causes for Vision Loss

Three well-known and common causes for vision loss among adults include exudative macular degeneration, vision-threatening diabetic retinopathy, and glaucoma. [289,290] Other recognized but less frequent causes for significant visual impairment include retinal vein occlusions and ischemic optic neuropathy. [291,292] Low vision is a general diagnosis used when functional vision is reduced to 20/70 Snellen acuity or worse in the best-seeing eye as a result of any ocular pathology. [293]

Exudative macular degeneration is a retinal pathology where aberrant retinal neovascularization disrupts macular function, causing potentially profound vision loss. [294] A recently developed treatment with anti-vascular endothelial growth factors has greatly improved the visual prognosis given judicious management, but treatment success is not guaranteed. [295] Older age is the greatest risk factor for exudative macular degeneration, and the retinal condition presents more often among Caucasians compared to other ethnicities. [296]

Diabetic retinopathy involves metabolic injury to the retina from damaged retinal capillary structure. Diabetic retinopathy progresses in stages from non-proliferative retinopathy to the vision-threatening stages that include severe retinopathy, proliferative retinopathy, and macular edema, which often cause lasting vision loss. [297,298]

Glaucoma is considered a progressive optic neuropathy with multi-factorial etiologies that cause a loss of peripheral vision and potential blindness. [299] Glaucoma has a recognized

worldwide prevalence of about 3.5% in those 40 years and older and is a leading cause of irreversible vision loss. [300]

Retinal vein occlusions (RVO) originate from an impaired venous return of the retinal capillary system. The RVO may vary by the retinal location, the area of retinal involvement, and severity. A central RVO impacts the retina's overall venous outflow and carries a poorer visual prognosis. [291]

Finally, ischemic optic neuropathy results from impaired vascular flow to either the anterior or posterior segment of the optic nerve. Abnormal flow to the anterior segment of the optic nerve is more common, presents with visible optic nerve edema, and often results in visual field defects with diminished visual acuity. Either category of ischemic optic neuropathy causes irreversible damage to the eye. [301]

Patients with a Snellen visual acuity worse than 20/50 in the best-seeing eye or functionally constricted visual fields are deemed visually impaired or as having low vision. [302,303] Worldwide, the number of people with low vision increased significantly from 1990 to 2015. [304]

Veterans and Ocular Pathology

Veterans often suffer from ocular disease. Researchers have published estimates for the prevalence of ocular pathology among veterans. A 2011 study compared the prevalence of ocular disease among veterans with and without mental illness and found that the overall prevalence of glaucoma was between 7.1–10.2% in that population. In addition, the same study found that about 2% of these veterans were diagnosed with diabetic eye disease. [185] A retrospective, 24-month study (2006–2008) of veterans at a Connecticut VAMC found a prevalence of approximately 2.4% for exudative macular degeneration over the study duration. [305] Another

retrospective study of veterans across VISN 5 (2007–2011) found that the prevalence of glaucoma was about 7% and that the prevalence of diabetic ophthalmic complications was about 2%. [184] A retrospective prevalence study (June 2004–May 2005) at the Mountain Home VAMC in Tennessee estimated the prevalence of low vision among veterans to be about 7%. [182] Nationally, it was projected that approximately one million veterans suffered with visual impairment or low vision in 2007. [306]

In this study, the Salisbury ocular pathology and COPD study, the frequencies and associations between six vision-threatening ocular diseases (the dependent variables) and select comorbidities (the independent variables) found in veterans at the Salisbury Veteran Affairs Health Care System (SVAHCS) were statistically analyzed with logistic regression modeling.

The objectives of the study were as follows:

Objective 1: To describe the frequencies of select comorbidities, with an emphasis on COPD, recorded for veterans with vision-threatening ocular diagnoses compared to veterans without vision-threatening ocular diagnoses.

Objective 2: To statistically analyze the associations between select vision-threatening ocular conditions and common systemic diseases including COPD for cases compared to controls.

The goal of the study was to provide a contemporary understanding of the relationships uncovered between six vision-threatening ocular diseases and COPD diagnoses in veterans from the Piedmont region of North Carolina.

Methods

Study Design

In the present study, a retrospective, case-control design was employed to contrast, compare, and analyze the frequencies and associations of six vision-threatening ocular diseases (the dependent variables) diagnosed in veterans with select sociodemographic and comorbid diagnoses (the independent variables). The relationship between the dependent variables and COPD received special attention. The dependent and independent variables were extracted from the electronic medical records based upon select ICD-9-CM and ICD-10-CM diagnostic codes (see Appendix A). Both the ICD-9-CM and ICD-10-CM diagnostic codes were used because the medical center transitioned to the ICD-10-CM codes during the study. The extracted information represented variables specific for systemic illnesses including COPD, and for vision-threatening ocular diseases.

The study variables were captured from the electronic health records of a population of U.S. veterans who received primary care at the Salisbury VAHCS using Structured Query Language (SQL) programming. The population was comprised of veterans enrolled for primary care services between January 1, 2016 and December 31, 2018. The SVAHCS IRB approved this study (IRB project number 19-016).

Veterans enrolled for primary care services with a minimum of two recorded primary care visits during the 3-year study period comprised the population of eligible subjects. The decision to select subjects with two recorded visits meant that the subjects were more likely to rely on the SVAHCSV for care. Veterans younger than 50 years were excluded from the study because of a generally low COPD prevalence below age 50. The subjects were 50 and older as of January 1, 2016. The study excluded veterans who developed COPD or who died during the

study period. Thus, the veterans had the same diagnostic classification for COPD throughout the study. The control subjects lacked a diagnosis for one of the six vision-threatening ocular diagnoses, while the case subjects all had a diagnosis for one of the six vision-threatening ocular diagnoses in the electronic medical record at the time of data extraction.

Veterans with fewer than two completed primary care visits during the study period were excluded, as well as veterans with a diagnosis of HIV, as HIV belongs to a protected category per DVA research guidelines.

Data

Structured Query Language (SQL) programming applications were used to query the VHA Decision Support System (DSS) and the VISN 6 Data Warehouse, a regional databank of electronic records, to identify all veterans who met the inclusion criteria. After having identified the population of eligible veterans, the subjects' sociodemographic and clinical diagnoses were placed into an Excel spreadsheet.

The study's dependent variables included the diagnoses for six vision-threatening ocular conditions as defined by established ICD-9-CM and ICD-10-CM codes. Vision-threatening conditions included the following: exudative macular degeneration, vision threatening diabetic retinopathy (severe retinopathy, proliferative retinopathy, and diabetic macular edema), glaucoma, central retinal vein occlusion, ischemic optic neuropathy, and low vision. Each of these dichotomous dependent variables were defined by established ICD-9-CM and ICD-10-CM diagnostic codes for ocular diagnoses (see Appendix A). Both ICD-9-CM and ICD-10-CM codes were used because the medical facility transitioned to the ICD-10-CM codes during the study timeline. Veterans diagnosed with one of the six ocular diseases represented cases for that condition, while the veterans without the ocular disease diagnosis were the controls.

The study's dichotomous independent variable of foremost interest, or COPD, was defined by established ICD-9-CM and ICD-10-CM diagnostic codes for COPD. The codes included those specific to chronic bronchitis, emphysema, bronchiectasis, and chronic airway obstruction.

A total of 22 independent variables were selected for the study following an extensive literature review. Along with COPD, the study included seven sociodemographic variables: age by intervals, marital status, sex, race, smoking history, rural or urban residence, and service connection level (SC) ≥ 50%. The SC level reflects recognized injuries or illnesses the veteran suffered while enlisted. Age was broken into four interval groups (50–59, 60–69,70–79, and over 79) with *50–59 years* as the reference group. Marital status included four coded categories, with *married* as the reference group. Race included three categories, with *White* as the reference group. Other reference groups were as follows: sex = *male* ;smoking history = *never smoked*; rural or urban = *urban* and service -connected level = *SC < 50%*

ICD-9-CM or ICD-10-CM diagnostic codes as found in Appendix A were used to capture the frequency of the select systemic conditions recorded for the study population. The select conditions were representative of psychological, cardiovascular, metabolic, pulmonary, autoimmune, and renal comorbidities. A total of 15 disease specific independent variables were included for analysis.

Data Analysis

The data was analyzed using STATA, version 16, and SPSS statistical software, version 27.0. The frequencies of the variables were calculated as numeric values (percentages) for the population. Age was segmented into four intervals (50–59, 60–69, 70–79, 80 and older) to better evaluate the impact of age on the dependent variables. The age *category 50-59* was the reference

group. Pearson correlations for the variables were calculated to identify any variables with correlations ≥ 0.80. Multi-collinearity was evaluated by calculating the variance inflation factors (VIF). Variables with VIF > 5 were considered highly correlated and necessary adjustments were applied. For the highly correlated variables of alcohol and drug abuse, only the variable *alcohol abuse* was used to maximize the precision of variance and confidence intervals.

A bivariate analysis using chi-square (χ^2) calculations was completed to evaluate the association between the independent variables and each of the six dependent variables. The χ^2 significance threshold was $p < 0.01$.

Six unadjusted logistic regression models were executed using the six vision-related diagnoses as the dependent variables and COPD as the sole independent variable. The goal was to identify which vision-related diagnoses had a meaningful statistical relationship with COPD based upon the calculated *p*-value. Any visual diagnoses with a *p*-value ≤ 0.05 was significant and later used in the adjusted multiple logistic regression models, while visual diagnoses with a *p*-value > 0.05 was not used for further analysis.

Then, 22 independent variables, including COPD, were entered simultaneously into the multiple logistic regression models. The calculated the odds ratios (OR) and 95% confidence intervals for the relationships between the vision-related diagnoses and the independent variables were estimated using STATA. Post-estimation analysis of the model was completed to examine model fit. The post-estimation analysis included the sensitivity-specificity classification, the area under the receiver-operator-curve (ROC), and the Hosmer–Lemeshow test where a *p* value > 0.05 indicated an acceptable model fit.

This study was based on a population of 33,639 veterans (N) or about 1,150 subjects per independent variable. This large *N* meant that the logistic multiple regression models risked

excess statistical power. [212] Adjustments were needed to correct for the over-powered models. Consequently, independent variables were considered significant under two conditions: if they had a $p \leq 0.01$ and the effect size as measured by the absolute value of the odds ratio (OR) was ≥ 0.30; and if the $p \leq 0.025$ and the effect size as measured by the absolute value of the OR was ≥ 0.60. Independent variables that did not meet these criteria were not included in the statistical model.

Results

Table 4.1 reports the frequency of categorical variables calculated for the population of veterans. From a total of 33,369 veterans, there were 5,079 (15%) veterans diagnosed with COPD, the independent variable of emphasis, and 28,560 (85%) without COPD.

Table 4.1. Frequencies of Categorical Study Variables Among Veterans With and Without COPD

Variable		Total		No COPD		Yes COPD	
		N	**%**	***N***	**%**	***N***	**%**
Sex	Male	31,892	94.8	26,996	84.6	4,896	15.4
	Female	1,747	5.2	1,564	89.5	183	10.5
Race	White	22,390	66.6	18,462	82.5	3,928	17.5
	Black	10,031	29.8	9,023	90.0	1,008	10.0
	Other	1,218	3.6	1,075	88.2	143	11.8
SC ≥ 50%	No	20,749	61.7	17,646	85.0	3,103	15.0
	Yes	12,890	38.3	10,914	84.7	1,976	15.3
Marital Status	Married	20,976	62.4	18,051	86.1	2,925	13.9
	Divorced	7,094	21.1	5,846	82.4	1,247	17.6
	Widowed	1,574	4.6	1,258	79.9	316	20.1
	Unknown	3,995	11.9	3,405	85.2	599	14.8
COPD	No	28,560	84.9	-	-	-	-
	Yes	5,079	15.1	-	-	-	-
Alcohol	No	25,755	76.6	22,733	88.3	3,022	11.7
	Yes	7,884	23.4	5,827	73.9	2,057	26.1
Drug	No	26,978	80.2	23,704	87.9	3,274	12.1
	Yes	6,661	19.8	4,856	72.9	1,805	27.1
PTSD	No	27,272	81.0	23,273	85.3	4,057	14.7
	Yes	6,367	19.0	5,287	83.0	1,089	17.0
Smoking	No	25,282	75.2	22,768	90.1	2,514	09.9
	Yes	8,357	24.8	5,792	69.3	2,565	30.7
Depression	No	24,072	71.6	20,747	86.2	3,367	13.8
	Yes	9,567	28.4	7,813	81.7	1,779	18.3

Variable		Total		No COPD		Yes COPD	
		N	**%**	***N***	**%**	***N***	**%**
Anxiety	No	27,796	82.6	23,803	85.6	3,993	14.4
	Yes	5,843	17.4	4,757	81.4	1,086	18.6
Chronic Pain	No	32,647	97.1	27,807	85.2	4,840	14.8
	Yes	992	2.9	753	75.9	239	24.1

Table 4.1, continued

Variable		Total		No COPD		Yes COPD	
		N	**%**	***N***	**%**	***N***	**%**
Coronary Dz	No	27,777	82.6	23,892	86.0	3,885	14.0
	Yes	5,862	17.4	4,668	79.6	1,194	20.4
Isch. Heart	No	31,520	93.7	26,893	85.3	4,627	14.7
	Yes	2,119	6.3	1,667	78.7	452	21.3
Atrial fib	No	30,221	89.8	25,828	85.5	4,393	14.5
	Yes	3,418	10.2	2,774	79.9	686	20.1
CongHt Dz	No	32,428	96.4	27,696	85.4	4,732	14.6
	Yes	1,211	3.6	864	71.3	347	28.7
Stroke	No	32,383	96.3	27,527	85.1	4,811	14.9
	Yes	1,256	3.7	988	78.7	269	21.3
Diabetes	No	21,318	63.4	18,051	84.7	3,267	15.3
	Yes	12,321	36.6	10,509	85.3	1,812	14.7
Cholesterol	No	32,343	96.2	27,444	84.9	4,899	15.1
	Yes	1,296	3.8	1,116	86.1	180	13.9
Rheumatoid	No	33,192	98.7	28,207	85.0	4,484	15.0
	Yes	447	1.3	353	79.0	94	21.0
Asthma	No	31,640	94.1	27,156	85.8	4,546	14.2
	Yes	1,999	5.9	1,404	70.2	595	29.8
Sleep apnea	No	25,489	75.8	21,832	85.7	3,657	14.3
	Yes	8,150	24.2	6,728	82.6	1,422	17.4
Dyspnea	No	30,387	90.3	26,028	85.7	4,359	14.3
	Yes	3,252	9.7	2,532	77.9	720	22.1
Pneumonia	No	33,006	98.1	28,215	85.5	4,791	14.5
	Yes	633	1.9	345	54.5	288	45.5
PVD	No	30,699	91.3	26,484	86.3	4,215	13.7
	Yes	2,940	8.7	2,076	70.6	864	29.4
Renal Dz	No	29,712	88.3	25,289	85.1	4,423	14.9
	Yes	3,927	11.7	3,271	83.3	656	16.7
Cancer	No	33,311	99.0	28,335	85.1	4,976	14.9
	Yes	328	1.0	225	68.6	103	31.4
DiabRet	No	33,199	98.7	28,612	84.8	5,037	15.2
	Yes	440	1.3	398	90.5	42	9.5
Glaucoma	No	30,463	90.6	25,860	84.9	4,603	15.1
	Yes	3,176	9.4	2,700	85.0	476	15.0
ExARMD	No	33,339	99.1	28,345	85.0	4,994	15.0
	Yes	300	0.9	215	71.7	85	28.3
CrNPalsy	No	34,421	99.4	28,389	84.9	5,042	15.1
	Yes	208	0.60	172	82.2	37	17.8

Variable		Total		No COPD		Yes COPD	
		N	%	*N*	%	*N*	%
LowVision	No	32,531	96.7	27,596	84.8	4,935	15.2
	Yes	1,108	3.3	964	87.0	144	13.0
RetV.Occl	No	33,383	99.2	28,346	84.9	5,037	15.1
	Yes	256	0.8	214	83.6	42	16.4
NA-AION	No	33,515	99.6	28,452	84.9	5063	15.1
	Yes	124	0.4	108	87.1	16	12.9

Table 4.2 lists the frequency for COPD, the independent variable of emphasis, as diagnosed among veterans with each of the ocular diagnoses that comprised the six dependent variables. Note that the frequencies for cases and controls were very similar for three of the six ocular diagnoses. Only diabetic retinopathy and exudative age-related macular degeneration (ARMD) recorded dissimilar frequencies for cases compared to controls.

Table 4.2. Population Frequency of Visual Diagnoses With and Without COPD

Dependent Variable	Without COPD (%)	With COPD (%)
Diabetic Retinopathy	401 (1.4%)	42 (0.8%)
Glaucoma	2,734 (9.3%)	478 (9.3%)
Exudative ARMD	217 (0.7%)	85 (1.7%)
Low Vision	991 (3.4%)	146 (2.8%)
NA-AION	111 (0.4%)	16 (0.3%)
Retinal Vein Occlusion	218 (0.7%)	42 (0.8%)

Table 4.3 provides a summary of the four age intervals. Around 55% of the study population was aged 70 and older. The mean age for the veteran population was 69.6 years, with a range from 50 to 90 years. The median age for the veteran population was 70 years.

Table 4.3. Frequency of Veteran Age by Age Category

Age Interval	Frequency	Percentage
50–59	5,424	16.1%
60–69	9,598	28.5%
70–79	13,616	40.5%
80 and older	5,001	14.9%

Total	33,369	100%

In addition to age, the present study included other sociodemographic variables: marital status, sex, race, service connection (SC) ≥ 50%, and rural versus urban residence. Marital status had four categories (married, divorced, widowed, and unknown status) and race had three categories (White, Black, and Other).

Table 4.4 provides a descriptive summary of the veterans by marital status. The data shows that approximately 62 of 100 veterans were married, approximately 21 out of 100 were divorced, and 5 out of 100 were widowed.

Table 4.4. Frequency and Percentage of the Veterans' Marital Status

	Frequency	**Percent**
Married	20,976	62.4%
Divorced	7,094	21.1%
Widowed	1,574	4.7%
Unknown	3,995	12.0%
Total	33,639	100.0%

Table 4.5 lists the summary information regarding race. While approximately 66 out of 100 veterans identified as White, those veterans who identified as Black constituted near 30% of the veteran population. Black veterans were well-represented in this study population.

Table 4.5. Frequency of Veterans by Race

Group	**Frequency**	**Percent**
White	22,865	66.2%
Black	10,405	30.1%
Other	1,260	3.6%
Total	33,639	100.0%

Table 4.6 summarizes the frequencies for the remaining four sociodemographic variables: sex, rural versus urban, SC ≥ 50%, and smoking history. Some generalities emerge from these

sociodemographic variables. The veterans were more likely to be male, to live in an urban setting, were service connected less than 50%, and reported a negative history for past or present smoking behavior.

Table 4.6. Frequency of Select Sociodemographic Characteristics

Variable	Frequency	Percent
Sex		
Male	31,892	94.8%
Female	1,747	5.2%
Residence		
Rural	10,195	30.3%
Urban	23,442	69.7%
SC ≥ 50%		
Yes	12.890	38.3%
No	20,749	61.7%
Smoking History		
Yes	8,357	24.9%
No	25,282	75.1%

The first stage of the analysis involved evaluation of the Pearson correlations and the χ^2 statistics. The purpose of this stage of the analysis was to sort out which independent variables were significantly associated with each of the ocular dependent variables.

Table 4.7 shows the Pearson correlation values between the sociodemographic, systemic, and ocular variables in the study. A review of the correlation values revealed that none of the variables had correlations that approach the value ≥ 0.80; hence, there were no problems with highly correlated variables in the present study. A review of the chi-square calculations identified select variables that were significantly associated to the ocular diagnoses (dependent variables) of interest. This summary of Table 4.8 is shown in Table 4.9, which lists each of the variables with the largest and significant χ^2 associations for each of the ocular diagnoses.

Table 4.7. Calculated Pearson Correlation Values Between Sociodemographic, Systemic, and Ocular Variables

VARIABLE	Marital	Sex	Race	Alcohol	PTSD	Smoker	SC 50	Countr	Depress	Anxiety	Art-Dz	A-Fib	CongHF	Cholest	Glauc	RetVein
Martial	1.0000															
Sex	0.1243	1.0000														
Race	0.1588	0.1055	1.0000													
Alcohol	0.1654	-0.0120	0.1076	1.0000												
PTSD	-0.0171	0.0373	0.0907	0.1303	1.0000											
Smoker	0.1403	0.0080	0.0367	0.5852	0.0193	1.0000										
SC > 50	-0.0745	0.0521	0.1033	0.0343	0.4498	-0.0229	1.0000									
Country	-0.0830	-0.0572	-0.2164	-0.0224	-0.0035	0.0216	0.0056	1.0000								
Depression	0.0660	0.1210	0.0683	0.1861	0.2852	0.1041	0.2108	-0.0285	1.0000							
Anxiety	0.0285	0.0668	-0.0307	0.0966	0.1549	0.0548	0.1109	0.0027	0.3087	1.0000						
Art-Dz	-0.0738	-0.0848	-0.1301	-0.0451	-0.0142	-0.0131	0.0342	0.0578	-0.0204	-0.0128	1.0000					
A-Fib	-0.0414	-0.0596	-0.1082	-0.0558	-0.0458	-0.0546	-0.0242	0.0222	-0.0426	-0.0219	0.1214	1.0000				
CongHF	-0.0042	-0.0283	-0.0113	0.0041	0.0001	-0.0113	0.0163	0.0053	0.0116	0.0000	0.0960	0.1736	1.0000			
Cholest	-0.0177	-0.0051	-0.0317	0.0007	-0.0052	-0.0104	0.0043	0.0181	-0.0022	0.0019	0.0179	0.0061	-0.0070	1.0000		
Glaucoma	-0.0038	-0.0299	0.0474	-0.0200	0.0138	-0.0371	0.0288	-0.0096	-0.0002	-0.0203	0.0100	0.0119	0.0218	0.0082	1.0000	
Ret Vein	-0.0049	-0.0081	-0.0040	-0.0010	-0.0042	-0.0022	0.0054	0.0018	0.0009	-0.0045	0.0155	0.0077	0.0214	-0.0068	0.0794	1.0000
ExMacDeg	-0.0116	-0.0148	-0.0516	-0.0185	-0.0118	-0.0066	-0.0097	0.0168	-0.0047	0.0029	0.0250	0.0390	0.0241	0.0024	0.0395	0.0062
Low Vision	0.0113	-0.0196	0.0127	-0.0092	-0.0211	-0.0046	-0.0152	-0.0252	-0.0039	-0.0113	-0.0004	0.0086	0.0191	-0.0087	0.0639	0.0252
NAION	-0.0004	-0.0065	-0.0013	0.0012	0.0063	-0.0118	0.0094	0.0080	0.0074	0.0050	0.0105	0.0100	0.0091	0.0029	0.0464	0.0224
Diab Ret	-0.0081	-0.0177	0.0187	-0.0112	-0.0062	-0.0187	0.0229	0.0041	0.0087	-0.0135	0.0267	0.0005	0.0395	-0.0066	0.0636	0.0437
Ret. Art Dz	-0.0057	-0.0046	-0.0081	0.0017	-0.0036	0.0047	0.0007	0.0084	0.0043	-0.0059	0.0027	-0.0030	0.0112	0.0030	0.0319	0.0401
Rhem. Art	-0.0128	0.0178	-0.0051	-0.0021	0.0061	0.0026	0.0107	0.0067	0.0215	0.0034	0.0001	0.0058	0.0065	0.0086	0.0115	-0.0043
Asthma	0.0065	0.0909	0.0172	-0.0048	0.0350	-0.0284	0.0488	-0.0062	0.0487	0.0374	-0.0110	0.0033	-0.0046	-0.0080	-0.0001	-0.0005
Sleep Apnea	-0.0509	-0.0127	-0.0061	-0.0127	0.1374	-0.0407	0.1679	0.0176	0.1525	0.0771	0.0376	0.0375	0.0588	-0.0023	0.0246	0.0054
COPD	0.0215	-0.0331	-0.0885	0.1680	0.0251	0.2483	0.0063	0.0610	0.0573	0.0451	0.0688	0.0468	0.0731	-0.0059	-0.0002	0.0031
PVD	-0.0082	-0.0468	-0.0462	0.0751	-0.0053	0.1285	-0.0004	0.0206	-0.0010	-0.0040	0.1489	0.0611	0.0705	0.0017	0.0121	0.0316
Renal Dz	-0.0109	-0.0500	0.0203	-0.0274	-0.0179	-0.0339	0.0229	-0.0029	-0.0150	-0.0190	0.0854	0.0585	0.1123	0.0061	0.0546	0.0201

Table 4.7, continued

VARIABLE	Ex Mac Deg	Low Vision	NAION	Diab Ret	Ret Art Dz	Rhem Art	Asthma	Apnea	COPD	PVD	Renal Dz
Ex Mac Deg	1.0000										
Low Vision	0.0716	1.0000									
NAION	0.0148	0.0612	1.0000								
Diab Ret	0.0059	0.0511	0.0441	1.0000							
Ret Art Dz	0.0174	0.0100	0.0105	0.0707	1.0000						
RhemArt	-0.0028	-0.0115	0.0013	-0.0043	0.0115	1.0000					
Asthma	-0.0010	-0.0048	-0.0030	-0.0099	-0.0034	0.0192	1.0000				
Apnea	-0.0074	-0.0247	0.0063	0.0224	0.0032	0.0006	0.0775	1.0000			
COPD	0.0349	-0.0107	-0.0039	-0.0174	0.0045	0.0223	0.1025	0.0377	1.0000		
PVD	0.0308	0.0038	0.0051	0.0299	0.0141	0.0065	-0.0232	-0.0001	0.1225	1.0000	
Rhenal Dz	0.0178	0.0200	0.0261	0.0904	0.0148	0.0080	-0.0054	0.0320	0.0176	0.0847	1.0000

Table 4.8 shows the calculated χ^2 values for each of the six ocular diagnoses (the dependent variables) and the 22 independent variables included in the present study**.**

Table 4.8. Calculated Chi-Square Associations for the Six Dependent Variables and the Independent Variables

Vision-Threatening Diabetic Retinopathy				
Variable	**Chi Square**	**df**	**P value**	**Phi value**
Sex	10.838	1	P< 0.001	-0.018
Race	21.520	2	P< 0.001	0.025
Marital Status	6.843	3	P = 0.077	0.014
COPD Diagnosis	10.403	1	P = 0.001	-0.017
Alcohol Abuse	4.423	1	P = 0.038	-0.011
PTSD	1.306	1	P = -.253	-0.006
Smoking	12.030	1	P < 0.001	-0.019
SC > 50%	18.052	1	P < 0.001	0.023
Rural vs Urban	0.574	1	P = 0.449	0.004
Depression	2.596	1	P = 0.107	0.009
Anxiety	6.298	1	P = 0.012	-0.014
Coronary Disease	24.586	1	P < 0.001	0.027
Atrial Fib	0.008	1	P= 0.927	< 0.001
Congestive HF	53.824	1	P < 0.001	0.039
Cholesterol	1.481		P = 0.224	-0.007
Glaucoma	139.694	1	P < 0.001	0.064
Retinal Vein	65.801	1	P < 0.001	0.044
Exudative ARMD	1.192	1	P= 0.275	0.006
Low Vision	90.055	1	P < 0.001	0.051
NAION	67.114	1	P < 0.001	0.044
Rheum. Arth	0.629	1	P = 0.428	-0.004
Asthma	3.412	1	P = 0.065	-0.010
Sleep Apnea	17.268	1	P < 0.001	0.022
PVD	30.868	1	P < 0.001	0.030
Renal Disease	282.108	1	P < 0.001	0.090
Glaucoma				
Variable	**Chi Square**	**Df**	**P value**	**Phi Value**
Marital Status	8.117	3	P = 0.044	0.015
Sex	30.959	1	P < 0.001	-0.030
Race	168.395	2	P < 0.001	0.070
Alcohol Abuse	13.561	1	P < 0.001	-0.020
PTSD	6.490	1	P = 0.011	0.014
Smoking	47.714	1	P < 0.001	-0.037
SC > 50%	28.424	1	P < 0.001	0.029
Rural or Urban	3.199	1	P = 0.074	-0.010

Table 4.8, continued

Glaucoma				
Variable	**Chi Square**	**Df**	**P value**	**Phi Value**
Depression	0.00	1	P = 0.995	< 0.001
Anxiety	14.331	1	P < 0.001	-0.020
Coronary Art Dz	3.400	1	P = 0.065	0.010
Atrial Fib.	4.895	1	P = 0.027	0.012
Cong Heart Dz	16.443	1	P < 0.001	0.022
Cholesterol	2.303	1	P = 0.129	0.008
Diabetic Ret	139.694	1	P < 0.001	0.064
Ret Vein Occl	217.518	1	P < 0.001	0.079
Exudative Mac Degeneration	53.935	1	P < 0.001	0.040
Low Vision	140.672	1	P < 0.001	0.064
NAION	74.422	1	P < 0.001	0.046
Rheumatoid Art	4.558	1	P = 0.033	0.011
Asthma	0.000	1	P = 0.987	0.00
Sleep Apnea	21.170	1	P < 0.001	0.025
Glaucoma	0.001	1	P = 0.972	0.00
PVD	5.036	1	P = 0.025	0.012
Renal Disease	102.836	1	P < 0.001	0.055
COPD	0.001	1	P = 0.972	< 0.001
Exudative Macular Degeneration				
Variable	**Chi Square**	**Df**	**P Value**	**Phi Value**
Marital Status	66.632	3	P < 0.001	0.044
Sex	7.544	2	P = 0.006	-0.015
Race	111.600	2	P < 0.001	0.057
Alcohol	11.789	1	P < 0.001	-0.018
PTSD	4.800	1	P = 0.028	-0.012
Smoking	1.525	1	P = 0.217	-0.007
SC > 50%	3.232	1	P = 0.072	-0.010
Rural or Urban	9.776	1	P = 0.002	0.017
Depression	0.751	1	P = 0.386	-0.005
Anxiety	0.301	1	P = 0.583	0.003
Coronary Dz	21.512	1	P < 0.001	0.025
Atrial Fib	52.653	1	P < 0.001	0.039
Cong Heart Dz	20.085	1	P < 0.001	0.024
Cholesterol	0.205	1	P = 0.651	0.002
Diabetic Ret.	5.799	1	P = 0.016	0.013
Low Vision	176.821	1	P < 0.001	0.072
NAION	7.610	1	P = 0.006	0.015
Rheumatoid Art	0.266	1	P = 0.606	-0.003
Asthma	0.038	1	P =0.846	-0.001
Ret. Vein Occlus	1.332	1	P = 0.248	0.006

Table 4.8, continued

Exudative Macular Degeneration				
Variable	**Chi Square**	**Df**	**P Value**	**Phi Value**
Glaucoma	53.935	1	P < 0.001	0.040
Sleep Apnea	1.916	1	P=0.166	-0.007
COPD	42.130	1	P < 0.001	0.035
Renal Disease	10.955	1	P < 0.001	0.018
Low Vision				
Variable	**Chi Square**	**Df**	**P Value**	**Phi Value**
Marital Status	17.006	3	P < 0.001	0.022
Sex	13.231	1	P < 0.001	-0.020
Race	9.317	2	P = 0.009	0.016
Alcohol Abuse	2.931	1	P = 0.087	-0.009
PTSD	15.427	1	P < 0.001	-0.021
Smoking	0.733	1	P = 0.392	-0.005
SC > 50%	7.935	1	P = 0.005	-0.015
Rural or Urban	29.894	1	P < 0.001	-.0.025
Exudative	176.82	1	P<0.001	0.072
ARMD	0.531	1	P = 0.466	-0.044
Depression				
Anxiety	4.388	1	P = 0.036	-0.011
Corn Art Dz	0.005	1	P = 0.945	-< 0.001
Atrial Fib	2.571	1	P = 0.109	0.009
Cong Heart Dz	12.655	1	P < 0.001	0.019
Cholesterol	2.634	1	P = 0.105	-0.009
Diabetic Ret	73.967	1	P < 0.001	0.046
Glaucoma	140.612	1	P < 0.001	0.064
Retinal Vein Occlusion	21.979	1	P < 0.001	0.025
NAION	129.222	1	P < 0.001	0.061
Rheum. Art	4.592	1	P = 0.032	-0.012
Asthma	0.798	1	P = 0.372	-0.005
Sleep Apnea	21.044	1	P < 0.001	-0.025
COPD	3.943	1	P = 0.047	-0.011
Renal Disease	13.762	1	P < 0.001	0.020
Non-Arteritic Ischemic Optic Neuropathy (NA-AION)				
Variable	**Chi Square**	**df**	**P Value**	**Phi Value**
Marital Status	3.474	3	P =0.324	0.010
Sex	1.454	1	P=0.228	-0.006
Race	1.882	2	P=0.390	0.007
Alcohol Abuse	0.049	1	P=0.825	0.001
PTSD	1.350	1	P = 0.245	0.006
Smoking	4.784	1	P =0.029	-0.012
SC > 50%	3.084	1	P = 0.079	0.009

Table 4.8, continued

Non-Arteritic Ischemic Optic Neuropathy (NA-AION)				
Variable	**Chi Square**	**Df**	**P Value**	**Phi Value**
Rural or Urban	2.202	1	P = 0.138	0.008
Depression	1.869	1	P = 0.172	0.007
Anxiety	0.865	1	P = 0.352	0.005
Corn Art Dz	3.773	1	P = 0.052	0.010
Atrial Fib	3.436	1	P =0.064	0.010
Diabetic Ret	67.114	1	P < 0.001	0.044
Glaucoma	74.422	1	P < 0.001	0.046
Ret. Vein Occl	17.293	1	P < 0.001	0.022
Exudative ARMD	7.610	1	P = 0.006	0.015
Low Vision	129.222	1	P < 0.001	0.061
Rheum. Arthritis	0.057	1	P = 0.811	0.001
Asthma	0.313	1	P = 0.576	0.003
Sleep Apnea	1.377	1	P = 0.241	0.006
COPD	0.534	1	P = 0.465	-0.004
PVD	0.906	1	P = 0.341	0.005
Renal Disease	23.496	1	P < 0.001	0.026
Congestive HF	2.853	1	P=0.091	0.009
Cholesterol	0.292	1	P =0.589	0.003
Retinal Vein Occlusion				
Variable	**Chi Square**	**df**	**P Value**	**Phi Value**
Marital Status	2.964	3	P = 0.397	0.009
Sex	2.278	1	P = 0.131	-0.008
Race	1.371	2	P = 0.504	0.006
Alcohol Abuse	0.037	1	P = 0.848	-0.001
PTSD	0.612	1	P = 0.434	-0.004
Smoking	0.160	1	P = 0.689	-0.002
SC > 50%	1.026	1	P = 0.311	0.005
Rural or Urban	0.116	1	P = 0.733	0.002
Depression	0.026	1	P = 0.872	0.001
Anxiety	0.708	1	P = 0.400	-0.005
Coronary Art Dz	8.299	1	P = 0.004	0.016
Atrial Fib	2.059	1	P = 0.151	0.008
Congestive HF	15.836	1	P < 0.001	0.021
Cholesterol	1.610	1	P = 0.204	-0.007
Diabetic Ret.	65.801	1	P < 0.001	0.044
Glaucoma	217.518	1	P < 0.001	0.079
Exudative ARMD	1.332	1	P = 0.248	0.006
Low Vision	21.979	1	P < 0.001	0.025
Rheumatoid Art	0.632	1	P = 0.427	-0.004
Asthma	0.007	1	P = 0.934	< 0.001

Table 4.8, continued

Retinal Vein Occlusion				
Variable	**Chi Square**	**df**	**P Value**	**Phi Value**
Sleep Apnea	0.993	1	P = 0.319	0.005
COPD	0.323	1	P = 0.570	0.003
PVD	34.432	1	P < 0.001	0.032
Renal Disease	13.891	1	P < 0.001	0.020

A review of the chi-square calculations identified select independent variables that were significantly associated to the ocular diagnoses. This summary of Table 4.8 is shown in Table 4.9, which lists each of the variables with the largest and significant chi-square associations for each of the ocular diagnoses.

Table 4.9. Variables with Significant Association to the Ocular Diagnoses by χ^2 Calculations

Ocular Diagnosis	**Significant Variables by Chi-Square**
Diabetic Retinopathy	Race, Smoking History, Coronary Artery Disease, Congestive Heart Failure, Glaucoma, Renal Disease, Low Vision, NA-AION
Glaucoma	Race, Smoking History, Diabetic Retinopathy, Renal Disease, Retinal Vein Occlusion, Low Vision, NA-AION,
Exudative ARMD	Marital Status, Race, A-fib, Low Vision, Glaucoma, COPD
Low Vision	Marital Status, Rural/Urban, NA-AION, Diabetic Retinopathy, Glaucoma, Retinal Vein Occlusion, Exudative ARMD
Retinal Vein Occlusion	Congestive HF, Diabetic Retinopathy, Low Vision, Glaucoma, PVD
NA-AION	Diabetic Retinopathy, Low Vision, Renal Disease, Retinal Vein Occlusion

Note: The ocular diagnoses are included to compare the relationships among the dependent variables.

The second stage of the multi-staged analysis required discovering which of the six visual diagnoses qualified for further analysis by determining the relation of each to COPD independent of the influence of other variables. The first step in this stage involved unadjusted logistic regression models which were calculated with COPD as the sole independent variable along with each of the six visual diagnoses as the dependent variables. The summary results for the six unadjusted logistic regression models are found in Table 4.10.

Table 4.10. Unadjusted Logistic Regression Models with COPD as a Predictor of Visual Diagnoses

Visual Diagnosis	**N**	**Odds Ratio**	**95% Confidence Interval**	***P* Value**
Diabetic Retinopathy				
No	33,199	(Reference)	(Reference)	(Reference)
Yes	440	**0.590**	(0.429, 0.812)	$p = 0.001$
Glaucoma				
No	30,463	(Reference)	(Reference)	(Reference)
Yes	3,176	0.990	(0.894, 1.10)	0.854
Exudative ARMD				
No	33,339	(Reference)	(Reference)	(Reference)
Yes	300	**2.244**	(1.754, 2.880)	< 0.001
NA-AION				
No	33,515	(Reference)	(Reference)	(Reference)
Yes	124	0.832	(0.492, 1.408)	0.495
Retinal Vein Occlusion				
No	33,383	(Reference)	(Reference)	(Reference)
Yes	256	1.104	(0.792, 1.539)	0.558
Low Vision				
No	32,531	(Reference)	(Reference)	(Reference)
Yes	1,108	0.835	(0.699, 0.998)	0.047

Among the unadjusted logistic regression models, only vision-threatening diabetic retinopathy, and exudative age-related macular degeneration (ARMD) had significant findings. (As explained in the methods section, a threshold of $p \leq 0.01$ to define statistical significance was necessary to compensate for the excess statistical power generated by the large number of

subjects.) COPD appeared to be protective against vision-threatening diabetic retinopathy with an OR = 0.59 ($p = 0.001$). Exudative macular degeneration was found to be significantly related to COPD with an OR = 2.24 ($p < 0.001$). These two ocular conditions were chosen to be the focus of the third phase of analysis.

In the last phase of the analysis, two multivariant logistic regression models were run using vision-threatening diabetic retinopathy and exudative ARMD as the dependent variables while simultaneously loading the 22 independent variables.

The results for the logistic regression model for vision-threatening diabetic retinopathy are found in Table 4.11. A total of 10 independent variables were significant (effect size = 0.30 with $p \leq 0.01$ or effect size = 0.60 with $p \leq 0.025$), while holding all other variables constant.

Table 4.11. Logistic Regression Results for Vision-Threatening Diabetic Retinopathy

Threat. Diabetic Retinopathy	**Coef.**	**St.Err.**	***z*-value**	***p*-value**	**[95% Conf**	**Interval]**	**Sig**
50-59 years	1.000	.	.	.	.	.	
60-69 years	1.240	0.213	1.25	0.210	0.886	1.735	
70-79 years	1.198	0.207	1.04	0.297	0.853	1.680	
80 and older	**0.528**	0.124	-2.73	0.006	0.333	0.835	**
White	1.000	.	.	.	.	.	
Black	**1.424**	0.167	3.01	0.003	1.132	1.793	**
Multiracial/Other	1.030	0.298	0.10	0.919	0.584	1.817	
Married	1.000	.	.	.	.	.	
Divorced	0.782	0.106	-1.81	0.071	0.599	1.021	
Widowed	0.789	0.203	-0.92	0.356	0.477	1.305	
Other	0.912	0.149	-0.56	0.573	0.663	1.256	
Sex	0.486	0.168	-2.08	0.037	0.247	0.958	*
PTSD	**0.626**	0.092	-3.20	0.001	0.469	0.834	***
Smoke History	0.723	0.114	-2.06	0.040	0.531	0.985	*
Service Connected	1.310	0.144	2.46	0.014	1.056	1.626	*
Rural/Urban	1.218	0.135	1.79	0.074	0.981	1.513	
Depression	1.298	0.151	2.24	0.025	1.033	1.631	*
Anxiety	0.718	0.109	-2.19	0.029	0.533	0.966	*
Coronary Art Dz.	**1.389**	0.165	2.76	0.006	1.100	1.753	**
Atrial Fib	0.808	0.136	-1.27	0.204	0.581	1.123	

Table 4.11, continued

Threat. Diabetic Retinopathy	**Coef.**	**St.Err.**	***z*-value**	***p*-value**	**[95% Conf**	**Interval]**	**Sig**
Cong Heart	**1.905**	0.339	3.62	0.000	1.344	2.699	***
High Cholesterol	0.687	0.204	-1.26	0.207	0.383	1.231	
Glaucoma	**2.611**	0.307	8.16	0.000	2.074	3.287	***
Low Vision	**3.133**	0.508	7.05	0.000	2.281	4.305	***
Rhem. Arthritis	0.683	0.348	-0.75	0.455	0.251	1.856	
Asthma	0.687	0.174	-1.48	0.139	0.418	1.130	
Sleep Apnea	1.236	0.136	1.93	0.054	0.996	1.533	
COPD Diagnosis	**0.595**	0.102	-3.01	0.003	0.425	0.834	**
PVD	**1.695**	0.240	3.73	0.000	1.284	2.236	***
Renal Dz.	**3.647**	0.390	12.09	0.000	2.957	4.498	***
Alcohol Abuse	0.958	0.149	-0.27	0.784	0.707	1.299	
Constant	0.006	0.001	-27.05	0.000	0.004	0.009	***

Mean dependent var	0.013	SD dependent var	0.114
Pseudo r-squared	0.097	Number of obs	33637.000
Chi-square	455.897	Prob > chi2	0.000
Akaike crit. (AIC)	4292.537	Bayesian crit. (BIC)	4536.815

NOTE: *** $p \leq 0.001$ ** $p \leq 0.01$ * $p < 0.05$

Table 4.12 lists the 10 variables with the calculated OR and *p*-values.

Table 4.12. Logistic Regression: Significant Independent Variables for Vision Threatening Diabetic Retinopathy

Variable	**OR**	***p*-value**
Black (Race)	1.42	$p = 0.003$
PTSD	0.65	$p = 0.003$
Smoke	0.71	$p = 0.009$
Coronary Art	1.39	$p = 0.006$
Congestive HF	1.90	$p < 0.001$
Glaucoma	2.61	$p < 0.001$
Low Vision	3.13	$p < 0.001$
COPD	0.59	$p = 0.003$
PVD	1.69	$p < 0.001$
Renal Disease	3.65	$p < 0.001$

The post-estimation procedures for the vision-threatening diabetic multiple logistic regression model were completed. The model had a pseudo-R2 = 0.097. The model was

satisfactory, with a calculated receiver operator curve (ROC) value = 0.7588. Measures of accuracy revealed that sensitivity was poor, at 0.23%, but specificity was very high, near 100%, yielding an overall model accuracy of 98.72%. Thus, the logistic regression model did not perform well at predicting those with vision-threatening diabetic retinopathy, but it did perform very well at predicting those without vision-threatening diabetic retinopathy. The poor measure on model sensitivity and specificity is a recognized finding with a highly unbalanced pairing of cases and controls. [307,308] With imbalanced data categories, the ROC curve calculation served as a meaningful and reliable measure of model performance. [309,310]

The computed ROC value indicated that the model performed reasonably well in discriminating between the cases and controls. The Hosmer-Lemeshow goodness-of-fit test was satisfactory, with the Hosmer-Lemeshow $\chi^2(8) = 7.05$, Prob > $\chi^2 = 0.530$. The Hosmer-Lemeshow goodness-of-fit test compares the observed and expected frequencies of events and non-events, or the predicted cases versus the controls. When the Hosmer-Lemeshow goodness-of-fit test has a larger chi-square value and a *p*-value significantly greater than 0.05, then the model fit is acceptable.

The logistic regression model for exudative macular degeneration used 22 independent variables loaded simultaneously. Table 4.13 shows the results for the model. A total of four independent variables achieved the specified effect sizes (OR) with the *p*-values for discussion. Table 4.14 lists the four independent variables with the defined OR and *p*-values.

Table 4.13. Logistic Regression Results for Exudative Macular Degeneration

Exudative ARMD	**Coef.**	**St. Err.**	***t*-value**	***p*-value**	**[95% Conf**	**Interval]**	**Sig**
Age: 50-59 years	1.000	.	.	.	.	.	
60-69 years	3.465	2.615	1.65	0.100	0.789	15.208	
70-79 years	**14.566**	10.487	3.72	0.000	3.552	59.730	***
≥80 years	**57.914**	42.007	5.60	0.000	13.976	239.990	***
White	1.000	.	.	.	.	.	
Black	**0.163**	0.052	-5.71	0.000	0.088	0.304	***
Multiracial/Other	**0.357**	0.163	-2.25	0.024	0.146	0.874	*
Married	1.000	.	.	.	.	.	
Divorced	1.173	0.206	0.91	0.364	0.832	1.653	
Widowed	1.430	0.266	1.92	0.055	0.993	2.061	
Other	0.963	0.274	-0.13	0.894	0.551	1.683	
Sex	1.481	0.636	0.91	0.361	0.638	3.438	
PTSD	1.131	0.228	0.61	0.543	0.761	1.680	
Smoking History	1.553	0.306	2.23	0.026	1.055	2.286	*
Service Con 50%	1.246	0.184	1.50	0.135	0.934	1.664	
Rural/Urban	1.133	0.140	1.01	0.312	0.890	1.442	
Depression	1.390	0.210	2.18	0.030	1.033	1.869	*
Anxiety	1.278	0.209	1.50	0.134	0.927	1.762	
Coronary Art Dz	0.981	0.133	-0.14	0.890	0.752	1.281	
Atrial Fib	1.262	0.186	1.57	0.116	0.945	1.686	
Congestive Heart	1.276	0.290	1.07	0.283	0.818	1.992	
High Cholesterol	0.876	0.254	-0.46	0.648	0.496	1.548	
Glaucoma	**2.073**	0.308	4.91	0.000	1.550	2.773	***
Low Vision	**4.879**	0.814	9.49	0.000	3.517	6.767	***
Rhem Arthritis	0.641	0.378	-0.75	0.451	0.202	2.037	
Asthma	0.976	0.255	-0.09	0.925	0.584	1.629	
Sleep Apnea	0.993	0.153	-0.05	0.962	0.734	1.343	
COPD Diagnosis	**1.590**	0.227	3.25	0.001	1.202	2.103	***
PVD	**1.451**	0.232	2.33	0.020	1.061	1.986	*
Renal Disease	0.996	0.160	-0.02	0.981	0.727	1.364	
Alcohol Abuse	0.720	0.156	-1.51	0.130	0.471	1.101	
Constant	0.000	0.000	-11.09	0.000	0.000	0.001	***
Mean dependent var		0.009	SD dependent var			0.094	
Pseudo r-squared		0.171	Number of obs			33637.000	
Chi-square		587.968	Prob > chi2			0.000	
Akaike crit. (AIC)		2899.108	Bayesian crit. (BIC)			3143.386	

**** p≤ 0.001, ** p ≤0.01 * p < 0.05*

Table 4.14. Logistic Regression Significant Independent Variables for Exudative Macular Degeneration

Variable	Odd Ratio	*p*-value
Age		
70–79	11.3	$p < 0.001$
80 and older	46.9	$p < 0.001$
Race		
Black	0.18	$p < 0.001$
Low Vision	5.3	$p < 0.001$
Glaucoma	2.1	$p < 0.001$
COPD	1.6	$p = 0.001$

Note: Smoking History had $p > 0.025$ and PVD had effect size < 0.60, so the variables were not included in Table 4.14.

Again, the post-estimation procedures for the exudative macular degeneration multiple logistic regression model were completed. The model had a pseudo-R2 = 0.171. The model performed well, with a calculated ROC = 0.8416. Measures of accuracy revealed that sensitivity was very poor, approaching 0%, but specificity was very high, at near 100%, yielding an overall model accuracy of 99.13%. Again, the problem with the classification of sensitivity and specificity reflected the significant data imbalance between the cases and controls. The poor measure on model sensitivity and specificity is a recognized finding with an unbalanced pairing of cases and controls. [307,308] The logistic regression model did not perform well at predicting the sensitivity and specificity for those with exudative macular degeneration, but it did perform very well at predicting those without exudative macular degeneration. Again, with imbalanced data categories, the ROC curve calculation (ROC = 0.8416) served as a satisfactory and reliable measure of model performance. [309,310] The computed ROC value indicated that the model performed well at discriminating between cases and controls. The Hosmer-Lemeshow goodness-of-fit test was satisfactory, with the Hosmer-Lemeshow $\chi^2(8) = 7.05$, Prob > $\chi^2 = 0.530$.

In summary, the three stages of analysis revealed meaningful findings. The results from the multivariant logistical regression models for vision-threatening diabetic retinopathy and

exudative ARMD identified significant independent variables based on the defined criteria for the effect sizes and the *p*-values (effect size = 0.30 with $p \leq 0.01$ or effect size = 0.60 with $p \leq 0.025$). A total of 10 variables were significantly related to veterans with vision-threatening diabetic retinopathy. Of note, veterans with vision-threatening diabetic retinopathy were significantly less likely to have a diagnosis for COPD. A total of four variables were significantly related to veterans with exudative ARMD. Veterans with a diagnosis for COPD were statistically more likely to have a diagnosis for exudative ARMD, while holding other variables constant.

Study Limitations and Strengths

All the subjects in this study were veterans, so the findings may not be generalizable to the non-veteran population. The population of veterans was 50 years and older, so the findings may not be applicable to younger veterans. The studied population was predominately White male veterans, so the findings may not be representative of females and non-White veterans. This becomes important if retirees from the U.S. military branches become more multi-cultural and multi-racial in the future.

All the veterans were enrolled for primary care at the SVAHCS, had a minimum of two recorded primary care visits, and lived in the Salisbury VAHCS catchment area; consequently, the findings may not apply to veterans who do not use the DVA for services or who reside in a different geographic region. Many primary care providers serve the regional VA population, so practice patterns, data entry behaviors, and data entry errors may vary among primary care providers. As such, it is possible that some veterans were mislabeled relative to the COPD diagnostic classification and subject to selection bias.

There were notable strengths to this study. The population size for cases and controls was large enough to support the generalizations of the findings. The cost and time associated with data extraction and analysis was minimal compared to other study designs. There was minimal missing data among the variables. Only two cases were discarded. The data was in numerical form suitable for statistical analysis. The dataset represented the entire population of veterans who met the inclusion requirements and who received care at the SVAHCS. The data were readily assessable, consistent, and available in the electronic health records with the use Structured Query Language (SQL) programming, thereby making replication at a VA medical center straightforward. The statistical relationships among the variables were suitable for analysis. The data were sufficiently robust to enable the identification and description of complex relationships among the variables. The study design allowed the analysis of multiple risk factors or associations at once. The retrospective, case-control design was efficient because COPD has a relatively long latency period between exposure and disease manifestation.

Discussion

The present study explored the frequency and associations of six ocular diagnoses, the dependent variables of interest, among veterans with and without COPD. The unadjusted logistic regression models revealed a significant relationship between both vision-threatening diabetic retinopathy and exudative ARMD with COPD, but not the other four ocular diagnoses.

Studies have conflicted regarding how diabetes impacts pulmonary function. Scientists have hypothesized that diabetes promotes microvascular damage and chronic inflammation that impairs pulmonary function. [311] On the other hand, the Gutenberg Health Study, a large, German cohort study of 5,000 pre-diabetic patients, found no association between diabetic retinopathy and COPD. [312]

The relationship between vision-threatening diabetic retinopathy and COPD has not been well studied among veterans. Interestingly, the present study found that COPD was statistically protective in association to vision-threatening diabetic retinopathy, while holding other variables constant. Overall, 90% of veterans with vision-threatening diabetic retinopathy did not have a COPD diagnosis, compared to about 10% of veterans with a COPD diagnosis. In other words, veterans with COPD were significantly less likely to have vision-threatening diabetic retinopathy compared to veterans without COPD, while holding all other variables constant (OR = 0.59, $p < 0.001$). This finding raised the question, "Why is the risk of vision-threatening diabetic retinopathy significantly reduced in the Salisbury veterans with COPD?"

Vision-Threatening Diabetic Retinopathy and COPD

Italian researchers conducted a retrospective study of hospitalized patients to examine the relationship between systemic diabetes and COPD and found that of 493 patients with COPD, only 19% had a diagnosis for systemic diabetes. The researchers found that the diagnosis for systemic diabetes was more common in younger, obese patients and was associated with advanced stages of COPD. [313] In the SVAHCS case-control study, measures of obesity were not collected. In addition, the measure of the veterans' COPD disease severity was not collected. It is possible that variations in both obesity and COPD disease severity influenced the prevalence of vision-threatening diabetic retinopathy among the cases and controls in the present study.

The development of diabetic retinopathy and COPD involves diverse pathogenic mechanisms. With diabetic retinopathy, elevated glucose levels, or hyperglycemia, trigger retinal vascular alterations over time that damage the vascular integrity of the retina. [314] The years lived with diabetes, or disease duration, is a recognized risk factor associated with the development of vision-threatening diabetic retinopathy. [315] Perhaps the most critical risk

factor associated with the progression of diabetic eye disease is glucose control, or hemoglobin A1c levels. Poor control of hemoglobin A1c levels often results in vision-threatening diabetic retinopathy. [316] In addition, progressive diabetic retinopathy is associated with the inadequate control of hypertension and cholesterol levels. [317] Information about the veterans' duration of diagnosed diabetes, the hemoglobin A1c control, and the control of blood pressure was not available for the present study. It is possible that the Salisbury veterans with COPD and diabetes had recently been diagnosed with diabetes, had achieved a better level of diabetic control, had made healthier behavioral choices, or had better control of blood pressure and cholesterol levels, compared to the veterans with diabetes but without COPD.

Vision-Threatening Diabetic Retinopathy and Cardiovascular Disease in Veterans

In the present study, the multiple logistic regression model for vision-threatening diabetic retinopathy identified significant relationships with three cardiovascular diagnoses. Systemic diabetes is known to be associated with cardiovascular diseases such as coronary artery disease, peripheral vascular disease, and congestive heart failure. [318,319] In the present study, veterans with vision-threatening diabetic retinopathy were significantly more likely to be diagnosed with congestive heart failure (OR = 1.90, $p < 0.001$), peripheral vascular disease (OR = 1.69, $p < 0.001$), and coronary artery disease (OR = 1.39, $p = 0.006$)) compared to the controls, while holding all other variables constant.

Vision-Threatening Diabetic Retinopathy and Kidney Disease

Diabetes is known to be promote chronic kidney disease. [320] Veterans with a diagnosis for vision-threatening diabetic retinopathy were more likely to have a diagnosis for kidney disease (OR= 3.64, $p<0.001$), while holding other variables constant. The present study's findings support the known relationship between diabetic retinopathy and kidney disease.

Vision-Threatening Diabetic Retinopathy and Other Ocular Diagnoses

The ocular diagnoses for low vision and glaucoma were included as independent variables in the present study. Both diagnoses had a significant relationship with vision-threatening diabetic retinopathy. As expected, vision-threatening diabetic retinopathy was predictive for the diagnosis of low vision (OR = 3.13, $p < 0.001$) because visual acuity is often negatively impacted with vision-threatening diabetic retinopathy. Of interest, vision-threatening diabetic retinopathy was highly associated with a diagnosis for glaucoma among the Salisbury VAHCS veterans (OR = 2.61, $p < 0.001$), while holding other variables constant. The relationship between diabetic retinopathy and glaucoma remains contested. [321] A detailed chart review of other relevant clinical findings for the Salisbury VAMC veterans with concomitant vision-threatening diabetic retinopathy and glaucoma would be necessary to better understand the nature of the association. Additional research is needed into how diabetic retinopathy is related to glaucoma in the veteran population.

Exudative Macular Degeneration and COPD

The published literature on the relationship between exudative age-related macular degeneration (ARMD) and COPD is sparse, particularly regarding veterans. A retrospective cohort study in Taiwan used insurance data from 2000 to 2012 to match patients with COPD to those without COPD. The investigators found that Taiwanese patients with COPD were significantly more likely to be diagnosed with exudative ARMD compared to those without COPD (HR = 1.49). [286] The Beaver Dam Eye Study, a longitudinal study spanning 15 years, found that patients diagnosed with emphysema during the study period were at a significantly increased risk for exudative macular degeneration compared to those without emphysema (OR = 3.65). [322] In a related longitudinal study, researchers followed Beaver Dam patients who had

been diagnosed with emphysema and gout at reference for the development of exudative macular degeneration. The researchers found that patients with a diagnosis for emphysema were at greater risk for exudative macular degeneration (RR = 5.12) compared to those without emphysema. [323] Chronic inflammation serves as one common denominator connecting emphysema with exudative ARMD. [324,325]

Exudative ARMD and COPD in Veterans

From the population of 33,369 veterans at the Salisbury VAMC, exudative macular degeneration was diagnosed in 300 veterans over the study duration, averaging about nine cases per 1,000 veterans. Of the 300 Salisbury veterans with a diagnosis for exudative macular degeneration, 85 (28%) had a concomitant diagnosis for COPD. The multiple logistic regression model found a significant relationship between exudative macular degeneration and COPD in veterans (OR = 1.51, $p < 0.001$), while holding all other variables constant. For the Salisbury veterans, a COPD diagnosis was a contributing factor for exudative age-related macular degeneration.

Exudative ARMD and Age of Veterans

One of the most noticeable relationships in the multiple logistic regression model was the increased odds for exudative ARMD with progressive age. Advanced age is a clear and recognized risk factor for exudative ARMD. [326] In the present Salisbury study, the odds for exudative macular degeneration in veterans rose dramatically compared to the reference group (50–59 years), by over 14-fold by age 70–79 (OR = 14.6, $p < 0.001$) and over 57-fold if 80 years or older (OR = 57.9, $p < 0.001$), while holding all other variables constant. Approximately 56% of all Salisbury veterans with a diagnosis for exudative macular degeneration were older than 79

years. Additional research is needed to better understand how the aging process influences the risk for exudative macular degeneration among veterans.

Exudative ARMD and Race of Veterans

Another noteworthy variable identified from the multiple logistic regression model was the relationship between race and the odds for an exudative ARMD diagnosis. Compared to the reference group, or White veterans, the Black veterans and multiracial veterans were much less likely to be diagnosed with exudative ARMD. In the present study, out of 300 veterans with an exudative macular degeneration diagnosis, only 11 (4%) were Black while 286 (95%) were White. Black veterans had 87% reduced odds of being diagnosed with exudative ARMD compared to White veterans (OR = 0.133, $p < 0.001$), while holding all other variables constant. Veterans with race labeled as Multiracial reported 49% reduced odds (OR = 0.510, $p = 0.022$) of a diagnosis for exudative ARMD compared to White veterans, while holding all other variables constant. Publications have noted that macular degeneration is most often a condition found in people of Northern European ancestry. [327] A large retrospective study used a network insurance database of over 1.7 million enrollees to analyze 6 years of diagnostic codes (2001–2007), exploring the relationship between race and exudative macular degeneration. The study found that White patients over the age of 70 were around three times more likely to be diagnosed with exudative ARMD compared to Black patients. [328] Additional research is needed to better understand the bio-molecular and genetic mechanisms that provide protection from macular degeneration in Black and multiracial veterans.

Exudative ARMD and Smoking History of Veterans

While the variable “smoking history” did not reach the level of statistical significance in the present study, it merits discussion because the topic pervades the literature as a risk factor for

macular degeneration. For example, an extensive systematic review and meta-analysis found that the cumulative odds ratio for exudative macular degeneration with active smokers in case-control studies was OR = 1.78 (95% CI 1.52-2.09). [329] A more recent systematic review found that former smokers had an estimated increased risk for exudative macular degeneration that was 1.54 times greater than non-smokers. [296] In the present Salisbury study, 66 (22.0%) of the 300 veterans with a diagnosis for exudative ARMD were listed as previous or current smokers, but 78.0% of veterans without exudative ARMD were listed as non-smokers. The odds for an exudative ARMD diagnosis in the Salisbury veterans who previously or currently smoked was OR = 1.55, $p = 0.026$, while holding all other variables constant.

Several factors may explain the statistically marginal impact of smoking history on risk for exudative ARMD in the present study. Public health promotions in the United States from the 1960s forward changed smoking behaviors and led to a factual decrease in the prevalence of smoking. [330] Measures for smoking behavior by veterans at the Salisbury VAHCS appear more conservative than expected. This may reflect a tendency for veterans to under-report their true smoking behavior. The generational differences in smoking behavior across the military service eras must be considered in the present study. It is likely that the Salisbury VAMC veterans over 70 years of age, a significant percentage of the population, had a positive smoking history that was not reported. Also, estimates for tobacco consumption such as “pack-years” and smoking duration were not included in the present study. The definition for smoking behavior, *nonsmoker* versus *past or present smoker*, lacked the granularity to accurately measure the relationship between the risk for exudative ARMD and the veterans’ smoking behavior.

Exudative ARMD and Ocular Diagnoses

It is not surprising that exudative ARMD would be related to a diagnosis for low vision since exudative ARMD significantly impairs visual acuity. This was true in the present Salisbury VAHCS study. Veterans with a diagnosis for exudative ARMD were significantly more likely to be diagnosed with low vision compared to other veterans (OR = 4.87, $p < 0.001$), while holding other variables constant.

What was more surprising was the association between exudative ARMD and a diagnosis for glaucoma (OR = 2.07, $p < 0.001$), while holding all other variables constant. The risk for exudative ARMD and glaucoma both increased with advanced age. Recent studies have shown an increased risk for glaucoma associated with ocular injections used for the treatment of exudative ARMD. [331] In a retrospective study, investigators identified a tendency to underdiagnose glaucoma in patients with exudative ARMD. [332] A retrospective study in Taiwan (2017) mined an insurance database and found that the odds for exudative ARMD in patients diagnosed with glaucoma was significant (OR = 2.45). [333] Additional research is needed to explore the relationship between exudative ARMD and glaucoma in the veteran population.

Conclusion

The present Salisbury VAHCS study explored the relationships between six ocular diseases and 22 select independent variables, with COPD as the key independent variable of interest. An unadjusted logistic regression model was executed with each ocular diagnosis as the dependent variable and the COPD diagnosis as the sole independent variable. The purpose of the unadjusted logistic regression models was to identify the ocular diagnoses that had a statistically significant relationship with COPD. From the unadjusted logistic regression results, vision-

threatening diabetic retinopathy and exudative ARMD were significantly associated with COPD. These two ocular diagnoses served as the dependent variables for two distinct multiple logistic regression models that included the diagnosis for COPD and 21 other independent variables.

The relationship between vision-threatening diabetic retinopathy and COPD has not been well studied, particularly among veterans. Interestingly, the present study found that COPD was statistically protective in association to vision-threatening diabetic retinopathy, while holding all other variables constant. This finding was unexpected and likely influenced by important measures that were not included in the present study. For example, the present study did not extract measures for the duration of diabetes, obesity, the level of hyperglycemic control, the level of blood pressure control, the cholesterol control, the duration of COPD, and the severity of COPD. Each of these variables could influence the severity of diabetic retinopathy diagnosed in the Salisbury veterans.

The published literature on the relationship between exudative ARMD and COPD is sparse, particularly regarding veterans. In the present study, the multiple logistic regression model calculated a significant relationship between exudative macular degeneration and a diagnosis for COPD. Veterans with COPD were more likely to be diagnosed with exudative ARMD compared to veterans without COPD.

The present study corroborated the robust relationship between increased age and the odds for a diagnosis for exudative ARMD. In addition, the present study confirmed that the odds for exudative macular degeneration are significantly influenced by race, with Black and multiracial veterans at a much-reduced risk for exudative ARMD compared to White veterans.

Veterans place themselves at increased risk for respiratory injury during active duty. The environmental conditions often include smoke, dust, and chemical exposures that damage the

lungs, the cardiovascular system, and thus the ocular health of the veterans. Future studies are needed to better understand how respiratory illness may be related to ocular pathologies in veterans.

CHAPTER 5: FINDINGS ON COST AND UTILIZATION OF CARE BY VETERANS WITH COPD

The cost of healthcare in the United States has long been a topic of wide-ranging interest. [334] Well-organized chronic disease management represents one feasible strategy to restrain healthcare costs. Chronic obstructive pulmonary disease (COPD) is a prevalent and chronic respiratory disease associated with significant cost of care. [335] Consequently, research into the cost of care for patients with COPD needs no justification.

In 2013, Congress directed the Department of Veteran Affairs (DVA) to establish a registry of Gulf War veterans who had been exposed to toxic smoke from burn pits because thousands of veterans were reporting respiratory illnesses. [334] On August 10, 2022, President Biden signed into law the Promise to Address Comprehensive Toxins Act, or the PACT Act. This legislation listed respiratory illness, among others ailments, as a service-connected condition for veterans exposed to toxic burn pits. [336] COPD is listed as a presumptive diagnosis that qualifies eligible veterans for service-connected disability under the PACT Act. [335] Subsequently, the DVA must commit the necessary financial and clinical resources to meet the requirements of the PACT Act. Thus, the cost and utilization of care for veterans with COPD is now a topic of foremost interest for the DVA. Strangely, however, little research has been conducted on the cost of care or the VA measure of providers' work in treating COPD.

Estimates for the clinical cost and the utilization of care for services in the DVA can be retrieved from administrative files found in the Decision Support System (DSS). The DSS uses an activity-based-costing (ABC) method to calculate the average clinical cost of care for provided services. The ABC method determines expenses by assigning costs to specific clinical activities or services based upon resources consumed. By identifying the services and resources consumed, and tracking the expenses, the costs can then be calculated for the care provided for

the veterans. The accuracy of the ABC method depends upon complete and precise cost data that correctly reflects the care and resources provided to the patient. [337]

The cost estimates from the DSS are generated from a "bottom up" accounting method. With the bottom-up accounting method, managers for each organizational unit track and reports various expenses. Overhead costs are assigned using a step-down method that incorporates direct costs. This information is then aggregated up the chain of command for evaluation and planning purposes. The bottom-up accounting method offers detailed information, but can be time consuming, lack flexibility, and lack accuracy if all elements of care are not captured.[191]

The DVA uses RVUs as published by Centers for Medicare & Medicaid Services (CMS) to evaluate the productivity of the clinical staff. [337] In addition, the CMS- issued RVUs are used by the DVA in determining payments made to community- based providers, the non-VA clinicians that also provide care for veterans. [338]

Relative value units (RVUs) also play a role in the DVA's bottom-up accounting system for calculating the cost of care. The DVA uses the RVUs to assign weights to the intermediate products (e.g., lab tests, imaging, hospital days, prosthetics). The sum of the intermediate products utilized are used to estimate the cost of the clinical encounter. So, RVUs are combined with other cost and utilization data to calculate the cost of clinical care services provided. [191]

The VA monitors two parameters for assessing the care it provides: Cost using dollars and "resource consumption" focused on physician labor as measured in units of resource-based relative value (RBRV). The cost of care is a facility-specific, Salisbury Veteran Affairs Medical Center (SBYVAMC), dollar average for the type of care (e.g., primary care, pulmonary care, emergency room, acute hospitalization). This average is very general, because all quite different clinical procedures provided in a year are lumped together in one average for each type of care.

Moreover, the dollar averages may also be somewhat arbitrary, because the VA's annual budget categories do not reflect the categories that are used to allocate costs of care.

Much more complex than the VA's measure of cost is the resource based relative value unit (RBRV)—a scale that was adopted for Medicare reimbursement in the Omnibus Budget Reconciliation Act of 1989 (P.L. 101-239) and is now also widely used by commercial insurers. The central core idea is that the physicians' work can be meaningfully measured by determining the relative (1) time, (2) mental effort and judgment, (3) technical skill and physical effort, and (4) stress involved. Dimensions two through four can be considered the relative intensity of the work during the time it takes. [339] (Time, without consideration of those additional factors, is the most common basis for paying workers in industrial economies.) Total work includes pre- and post-service work as well as the health providers' contact with patient. William Hsiao and colleagues, who developed the RBRV scale also thought it necessary to incorporate practice costs and the amortization of medical training over a physician's professional career. [340] RBRV is a *relative* scale: Its units are related to a standard clinical experience in each select medical specialty that is assigned the value 1.0. (The standard for internal medicine and family practice is a "follow-up visit of a 55-year-old man following β-blocker/thiazide regimen for management of hypertension, mild fatigue" and for general surgery is an "uncomplicated indirect inguinal hernia repair in a 45-year-old man.") [339, Table 1, p. 2364] Values relative to the specialty standard are determined for each of the thousands of the Current Procedural Terminology (CPT) codes used to record specific medical services and procedures. Medicare adopted the RB-RVS framework with some adjustments for use in reimbursing physicians. Equating the relative value of some medical service or procedure with a dollar value involves selecting a dollar value per RVU and multiplying this "conversion factor" with the total RVUs

resulting from a patient-provider encounter.

VA health providers use CPT codes to record interactions with patients and its health information systems use those CPT codes and the corresponding RVUs developed by Medicare (perhaps with some VA specific modifications) to measure clinical productivity. [Steve Patel, Salisbury Chief of Fiscal, personal communication, May 2023.] Because VA care is not generally reimbursed, RVUs are not translated into dollars or used for billing. Thus, the RBRV contrasts with the absolute numbering system that measures costs in dollars. The VA uses RBRV units to measure provider productivity and dollars to measure costs. This article explores how the two measurement systems describe COPD care compared with the care received by veterans without COPD.

The present study involved extracting data for 36-months (2016-2018) from the Salisbury, North Carolina Veteran Affairs Medical Center (SBYVAMC) electronic medical records, the SBYVAMC administrative files, and from the DVA's national managerial cost accounting system, known as the Decision Support System (DSS). The goal was to contrast and compare both the cost of care and the resource utilization of veterans with COPD compared to veterans without COPD. All veterans were enrolled in primary care at the Salisbury VAMC. Both the cost of care and the relative value units (RVUs) reported for individual veterans over the study duration were captured from four categories: primary care, pulmonology care, emergency department care, and acute hospitalization care. The total cost of care was the sum of each veteran's average total cost of care for episodes of care across the four clinical cost categories for the study duration. The total RVUs were calculated from the sum of the veteran's total RVUs mined for each episode of care from the same four clinical categories over the study duration.

The goal of the study was to address the following questions: “Is the cost of care for veterans with COPD more or less than the cost of care for veterans without COPD?” and “Do veterans with COPD utilize more or less care as measured by RVUs compared to veterans without COPD?”

The objectives of the study were as follows:

Objective 1: To contrast and compare via appropriate statistical techniques the cost of care for veterans diagnosed with COPD receiving care at the Salisbury VAMC to other Salisbury VAMC veterans without a COPD diagnosis.

Objective 2: To contrast and compare using appropriate statistical techniques the work effort in providing the health care represented by the total RVUs recorded for veterans diagnosed with COPD receiving care at the Salisbury VAMC to other Salisbury VAMC veterans without COPD.

Methods

Study Design

The present study used a retrospective, case-control design to contrast, compare, and analyze the total cost of care and total RVUs reported for cases and controls. The frequency of visits, the total cost of care, and the total RVUs for eligible veterans for episodes of care provided at the Salisbury VAMC between January 1, 2016 and December 31, 2018 were pulled from the electronic records. The dependent and independent variables were captured from the DVA’s national managerial accounting system, the DSS, as well as the Salisbury VAMC administrative records and the veterans’ electronic medical records. Both ICD-9 and ICD-10 diagnostic codes were used because the SBYVAMC transitioned from the ICD-9 codes to the ICD-10 codes within the study timeline (see Appendix A). The extracted variables represented

specific sociodemographic characteristics, select systemic illnesses, including COPD, the veteran's frequency of visits, the average cost of care per episode of care for the clinical visits, and the veteran's recorded RVUs for the episodes of care over the study duration.

The variables were collected using Structured Query Language (SQL) from the electronic health records of a population of U.S. veterans who received primary care at the SBYVAMC. The population was comprised of veterans enrolled for primary care services between January 1, 2016 and December 31, 2018. The Salisbury VAMC Institutional Review Board (IRB) approved this study (IRB project number 19-015).

Veterans enrolled for primary care services with a minimum of two recorded primary care visits during the 3-year study period were included in the study because these veterans were more likely to rely upon the Salisbury VAHCS for care. Veterans 50 years and older were included in the study because the prevalence of COPD is minimized with younger ages. The subjects were 50 and older as of January 1, 2016. The study excluded veterans who developed COPD or who died during the study period. Thus, the veterans had the same diagnostic classification for COPD throughout the study. The control subjects lacked a diagnosis for COPD before or during the study duration. A total of 33,639 veterans comprised the population of veterans eligible for the study. Veterans with a diagnosis of HIV were excluded from the study as HIV belongs to a protected category per DVA research guidelines and was therefore not available for this study.

Data

SQL programming applications were used to query the VHA Decision Support System (DSS) , the Veteran Integrated Service Network (VISN 6) Data Warehouse, and the SBYVAMC databank of medical records, to identify the population of veterans who met the inclusion

criteria. For the eligible veterans, the recorded frequency of visits for each fiscal year and the average cost of care per episode of care for that year was collected across four clinical categories (primary care, pulmonary care, emergency department (ER), and acute hospitalization (AH)). The patient's reported RVUs for episode of care for the same four clinical categories, plus select sociodemographic variables, and select clinical diagnoses were mined from the national DSS electronic records and the SBYVAMC administrative files.

The study had two dependent variables: the veterans' total cost of care and the veterans' total RVUs recorded for the study duration. The average cost of care per clinical episode of care was captured from the DSS records for the span of 36 months. The yearly average cost of care recorded by the DSS for the episode of care for each of the four clinical cost categories varied from year to year because of the bottom-up cost accounting methods used by the DVA. The individual veteran's frequency of visits for each year for the four clinical categories was multiplied by the specific yearly average cost of care for the clinical cost categories, producing the individual veteran's total cost of care. Each individual veteran's cost of care was summed, yielding a total average cost of care for primary care, pulmonary care, ER visits, and AH. The total average cost for each of the four cost categories was then summed, yielding the grand total average cost of care for all veterans in the present study. The grand total average cost of care, or the cost, was inflation adjusted to the 2022 dollar value, with the adjustment calculated using the U.S. Department of Labor consumer price index (CPI) calculator. [341] The CPI percentage adjustment factor for the total cost of care was 1.25, or 25%, when adjusted to the year 2022.

The present study used 20 independent variables. The independent variables included seven sociodemographic variables (age by intervals, sex, marital status, race, alcohol abuse, smoking history, service connection $\geq$ 50%) and 13 systemic comorbidities, including COPD.

The comorbidities included the following diagnoses: depression, ischemic heart disease, atrial fibrillation, congestive heart failure, cerebrovascular accident (stroke), rheumatoid arthritis, asthma, pneumonia, diabetes (type I and type II), peripheral vascular disease, renal disease, cancer, and COPD. The list of the ICD-9-CM or ICD-10-CM codes for the disease-related independent variables are in Appendix A.

The values of the dichotomous independent variable of chief interest, COPD, were established by the presence of ICD-9-CM and ICD-10-CM diagnostic codes for COPD (see Appendix A). The presence of the diagnostic codes for chronic bronchitis, emphysema, bronchiectasis, and chronic airway obstruction also constituted the codes to signal the presence of COPD. Again, ICD-9-CM and ICD-10-CM codes were used because the medical center was transitioning to the ICD-10-CM codes during the study timeline.

Regarding service connection (SC) designation, the SC level reflects injuries or illnesses the veteran suffered while enlisted. Veterans were classified into two groups, as an SC level of < 50% (as reference) or ≥ 50%, labeled SC50. Race included three categories: *White* (reference), *Black*, and *Multiracial/Other*. Marital status included four categories: *married* (reference), *divorced*, *widowed*, and *other*. Alcohol abuse was defined as a *past* or *present* diagnosis for alcohol abuse or absence of the diagnosis with *absence* as the reference. Smoking history was defined as having *never smoked* (reference) or reporting a positive history for *past or present smoking behavior*. Cancer represented a diagnosis for metastatic cancer, with *none* as the reference. Peripheral vascular disease diagnosis was coded as PVD, with *none* as the reference. Age was transformed into four interval groups (*50–59* (reference), 60–69,70–79, and over 79).

Data Analysis

STATA, version 16, and SPSS statistical software, version 27.0 were used for data analysis. The variables' frequency counts were tabulated as percentages. As stated, the total cost of care and total RVUs for the four clinical categories were retrieved from the information collected from the DSS. The distributions of dependent variables were evaluated with common descriptive measures. A Pearson correlation method was used to calculate the correlation matrix for the study variables. If two variables were highly correlated (≥0.80), only one of the variables was included in the analysis.

The dependent variables, the CPI-adjusted total cost of care and total RVUs, were not normally distributed, as evidenced by the variables' distributional characteristics (Table 5.1).

Table 5.1. Characteristics of CPI-Adjusted Total Cost of Care and Total RVUs (Years of Study)

Variable	Observations	Mean	Median	Std. Dev.	Skewness	Kurtosis
Total Cost of Care	33,639	$4,934	$2,959	$9,594	13.35	325.38
Total RVUs	33,639	11.3	7.9	14.0	10.5	228.2

All but three of the independent variables were dichotomous and the dependent variables lacked homoscedasticity. Linear regression (OLS) techniques are known to frequently mis-specify the regression model when applied to dichotomous independent variables and homoscedasticity is an assumption for OLS [342] The data distribution for the present study lacked homoscedasticity. Given this, the decision was made to adopt a statistical technique other than the traditional OLS regression for the current study.

Since valuable information about the veteran's cost and utilization of care are revealed in outliers, the choice was made to use a statistical technique that fostered the evaluation of the associations between the dependent variables and the independent variables at select points

across the range of the dependent variables. Multiple conditional quantile regression techniques were developed to serve this purpose. [343,344] With multiple conditional quantile regression, it was possible to model the changes for the dependent and independent variables at specific points of the curve, thereby uncovering the outliers' impact on the cost and utilization of care.

The multiple conditional quantile regression models were used to study the shift in the independent variables' coefficients for the CPI-adjusted total cost of care, or simply the total cost, and the utilization, as measured by total RBRV units, across the 40th, 50th, 75th, and 90th quantiles, with emphasis on cases versus controls. The 20 independent variables were entered simultaneously into the multiple, conditional quantile regression models with bootstrapping techniques available with STATA (version 16). Bootstrapping is a recognized statistical technique that increases the accuracy of the confidence intervals and reduces the bias of the model's estimated parameters when the data includes outliers. [345,346] The significant coefficients ($p < 0.01$) were then assessed from the lower to higher quantiles for both the cost of care models and the utilization models. The idea was to explore the gaps or shift in the total cost of care and the RVUs across the quantiles.

Results

Descriptive Characteristics of the Veteran Population

The study population consisted of 33,639 veterans. Of these veterans 5,079, about 15%, had a diagnosis for COPD, and the balance lacked a diagnosis for COPD. The population's age was normally distributed, with a mean age of 69.7 years and a median age of 70 years. The veterans' reported race was as follows: 67% White, 30% Black, and near 4% Multiracial/Other. Regarding sex, 95% of the veterans identified as male and 5% as female. Most veterans, about

62%, were married, 21% were divorced, about 5% were widowed, and 12% did not identify their marital status (treated as unknown).

Table 5.2 provides the mean and median values for the veterans' CPI-adjusted cost of care for the four cost categories (primary care, pulmonary care, ER, and AH) plus the total cost of care.

Table 5.2. CPI-Adjusted Total Cost for Clinical Cost Categories

Department	Veterans	Mean Cost	Median Cost	Std. Dev.
Primary Care	33,639	$3,024	$2,594	$2,092
Pulmonary Care	33,639	$205	0	$785
ER	33,639	$627	0	$1,308
Acute Hospitalization	33,639	$1,078	0	$8,285
Total Cost	33,639	$4,934	$2,959	$9,594

Table 5.3 provides the total RVUs or utilization for episodes of care for the same four clinical categories. The table reflects the influence of outliers upon the total RVUs or utilization of care.

Table 5.3. Total RVUs Per Clinical Utilization Category

Department	Veterans	Mean RVUs	Median RVUs	Std. Dev.
Primary Care	33,639	7.6	7.0	4.2
Pulmonary Care	33,639	0.6	0	2.5
ER	33,639	1.9	0	5.2
Acute Hospitalization	33,639	1.0	0	9.9
Total RVUs	33,639	11.3	8.0	14.1

Table 5.4 shows the value of the total RVUs at these specific percentiles for the four clinical care categories. The progression in total RVUs was calculated for the 25th, 50th, 75th, 90th, and 99th quantiles. Note the impact of outliers on values from the 25th to the 99th quantiles.

Table 5.4. Total RVUs Per Selected Quantile

Department	25th	50th	75th	90th	99th
Primary Care	4.8	6.9	9.5	12.4	20.5
Pulmonary Care	0	0	0	1	12.2
ER	0	0	1.3	6.4	24.6
Acute Hospitalization	0	0	0	0	30.3

Table 5.5 provides the frequency of veterans' visits to each of the four clinical care section. Note that veterans recorded significantly fewer visits to the specialty clinics compared to primary care, and only 5% of veterans had acute hospitalizations.

Table 5.5. Percentage of Veterans with Visits to Clinical Categories

Cost Category	No Visits (%)	Yes Visits (%)
Primary Care	0	33,639 (100%)
Pulmonology	29,168 (86.7%)	4,397 (13.3%)
ER	23,752(70.6%)	9,887 (29.4%)
Acute Hospitalization	32,107(95.4%)	1,532 (4.6%)

Table 5.6 reveals the frequency of the veterans' clinical visits over the study duration by quantile. As expected, the veterans visited primary care clinics more frequently than specialty care clinics.

Table 5.6. Frequency of Veteran Visits to Clinical Cost Categories Over 36 Months

Variable	Obs.	Mean	50th quantile	75th quantile	90th quantile	99th quantile	Std. Dev.	Min	Max
Primary Care	33,639	7.1	6 visits	9 visits	13 visits	24 visits	4.9	2	159
Pulmonology	33,639	0.4	0 visits	0 visits	1 visit	8 visits	1.5	0	22
ER	33,639	0.9	0 visits	1 visit	3 visits	11 visits	2.4	0	91
AH	33,639	0.2	0 days	0 days	0 days	6 days	1.8	0	84

Note: Episodes of acute hospitalization were recorded in days. Thus, the value represents total days of hospitalization for all episodes of hospitalization.

The frequency for the independent variables comparing the percentage of veterans with and without COPD are recorded in Table 5.7.

Table 5.7. Frequencies of Categorical Study Variables Among Veterans With and Without COPD

Variable		Total		No COPD		Yes COPD	
		N	**%**	***N***	**%**	***N***	**%**
Sex	Male	31,892	94.8	26,996	84.6	4,896	15.4
	Female	1,747	5.2	1,564	89.5	183	10.5
Race	White	22,390	66.6	18,462	82.5	3,928	17.5
	Black	10,031	29.8	9,023	90.0	1,008	10.0
	Multi/Other	1,218	3.6	1,075	88.3	143	11.7
SC ≥ 50%	No	20,749	61.7	17,646	85.0	3,103	15.0
	Yes	12,890	38.3	10,914	85.0	1,976	15.0
Marital Status	Married	20,976	62.4	18,051	86.1	2,925	13.9
	Divorced	7,094	21.1	5,846	82.6	1,258	24.7
	Widowed	1,574	4.7	1,258	79.9	316	20.1
	Unknown	3,995	12.0	3,405	85.2	590	14.8
COPD	No	28,560	84.9	-	-	-	-
	Yes	5,079	15.1	-	-	-	-
Alcohol	No	25,755	76.6	22,733	88.3	3,022	11.7
	Yes	7,884	23.4	5,827	73.9	2,057	26.1
Smoking	No	25,282	75.2	22,768	90.0	2,514	10.0
	Yes	8,357	24.8	5,792	69.3	2,565	30.7
Depression	No	24,072	71.6	20,747	86.2	3,325	13.8
	Yes	9,567	28.4	7,813	81.7	1,754	18.3
Isch.-Hrt.	No	31,520	93.7	26,893	85.3	4,627	14.7
	Yes	2,119	6.3	1,667	78.7	452	21.3
Atrial Fib	No	30,221	89.8	25,823	85.5	4,393	14.5
	Yes	3,418	10.2	2,732	79.9	686	20.1
CHF	No	32,428	96.4	27,696	85.4	4,732	14.6
	Yes	1,221	3.6	864	71.3	347	28.7
Stroke	No	32,383	96.3	27,572	85.1	4,811	14.9
	Yes	1,256	3.7	988	78.7	268	21.3
Diabetes	No	21,318	63.4	18,051	84.7	3,267	15.3
	Yes	12,321	36.6	10,509	85.3	1,812	14.7
Arthritis	No	33,192	98.7	28,207	85.0	4,985	15.0
	Yes	447	1.3	353	79.0	94	21.0
Pneumonia	No	33,006	98.1	28,215	85.5	4,791	14.5
	Yes	633	1.9	345	54.5	288	45.5

Table 5.7, continued

Variable		Total		No COPD		Yes COPD	
		N	**%**	***N***	**%**	***N***	**%**
PVD	No	30,699	91.3	26,484	86.3	4,215	13.7
	Yes	2,940	8.7	2,076	70.6	864	29.4
Renal	No	29,712	88.3	25,289	85.1	4,423	14.9
	Yes	3,927	11.7	3,271	83.3	656	16.7
Cancer	No	33,311	99.0	28,335	85.1	4,976	14.9
	Yes	328	1.0	225	68.6	103	31.4
Asthma	No	31,640	94.1	27,156	85.8	4,484	14.2
	Yes	1,999	5.9	1,401	70.2	595	29.8
PTSD	No	27,272	81.1	23,273	85.3	3,999	14.7
	Yes	6,367	18.9	20,241	86.3	3,201	13.7
Urban/Rural	No	10,195	30.3	6,637	83.0	1,080	17.0
	Yes	23,442	69.7	8,317	81.6	1,878	18.4
Anxiety	No	27,796	82.7	23,803	85.6	3,993	14.4
	Yes	5,843	17.3	4,757	81.4	1,086	18.6
Cholesterol	No	32,343	96.2	27,444	84.9	4,899	15.1
	Yes	1,296	3.8	1,116	86.1	180	13.9
Coronary Art.	No	27,777	82.6	23,892	86.0	3,885	14.0
	Yes	5,852	17.4	4,668	79.6	1,194	20.4
Sleep Apnea	No	25,489	75.8	21,832	85.7	3,657	14.3
	Yes	8,150	24.2	6,728	82.6	1,422	17.4

The frequency of veteran age by category was recorded in Table 5.8. Note that a greater percentage of veterans were between the ages of 70 to 79 years.

Table 5.8. Frequency of Veteran Age by Age Category

Age Interval	Frequency	Percentage
50–59	5,424	16.1%
60–69	9,598	28.5%
70–79	13,616	40.5%
80 and older	5,001	14.9%
Total	33,639	100%

Table 5.9 and Table 5.10 show the variability and range of the CPI- adjusted total cost of care and total RVUs for the veteran population across quantiles.

Table 5.9. Descriptive Statistics for Total Cost and Total RVUs

Variables	Obs.	Min	1%	Median	Mean	99%	Max	Std Dev.
Total Cost	33,639	$730	$818	$2,959	$4,915	$39,995	$45,300	$9,594
Total RVUs	33,639	1.6	2.3	8.0	11.3	62.3	580.1	14.1

Table 5.10 identifies the four diagnoses that consumed the most dollars and RVUs from among the 13 systemic diagnoses. Of the four most costly diagnoses, COPD ranked fourth for both cost and RVUs consumed. Veterans with COPD were more likely to be diagnosed with pneumonia, congestive heart failure (CHF), or cancer than veterans without COPD. In fact, the odds of these three most costly conditions among cases compared to controls were as follows: pneumonia (OR = 4.92), congestive heart failure (OR = 2.35), and cancer (OR = 2.61).

Table 5.10. Diagnoses with Highest Total Cost and Total RVUs (N= 33,639)

Diagnosis	40th quantile	50th quantile	75th quantile	90th quantile
COPD				
Cost	$671	$900	$1,784	$3,140
RVUs	1.7	2.3	4.9	8.9
Pneumonia				
Cost	$2,037	$2,799	$7,697	$21,441
RVUs	4.4	5.8	11.4	18.8
CHF				
Cost	$750	$972	$2,094	$7,548
RVUs	1.8	2.1	4.6	8.9
Cancer				
Cost	$1,239	$1,318	$1,911	$3,943
RVUs	3.3	3.8	5.8	10.9

Conditional Quantile Regression Results for Total Cost and Total RVUs

Four multivariant conditional quantile regression models (q40, q50, q75, q90) were executed for each of the two dependent variables. Regression attempts ≤ 35th quantiles failed to converge because of the decidedly skewed distributions. The independent variables were entered into the models simultaneously. Not all independent variables were deemed significant for discussion purposes based upon the p-values. Four variables consistently lacked significance (sex, smoking history, ischemic heart disease, and rheumatoid arthritis) and are not included for discussion.

Table 5.11 summarizes the results from the four multivariant conditional quantile regression models. Several points are worth noting from the findings. First, from the 40th through the 90th quantile, except for three variables (smoking, age greater than 69, and race other than White), the total cost of care consistently increased with each quantile. Oddly, cost of care for cancer increased at each quantile but lost significance at the 90th quantile. By the 90th quantile, the cost of COPD-related care increased over four-fold compared to the lowest quantile. Veterans with COPD at the 40th quantile reported a cost of care about $671 dollars more than veterans without COPD at the same quantile, while veterans with COPD at the 90th quantile reported a cost of care $3,140 more than veterans without COPD at the same quantile.

Table 5.11. Quantile Regression Total Costs ($) for Select Variables

Variables	**40th quantile**	**50th quantile**	**75th quantile**	**90th quantile**	***p*-value**
COPD	$671	$900	$1,784	$3,1340	***
Pneumonia	$2,037	$2,790	$7,696	$21,441	***
CHF	$750	$9712	$2,094	$7,548	***
Cancer	$1,239***	$1,318***	$1,911 **	($3,993)	
Asthma	$ 610	$819	$1,442	$2,226	***
Renal Disease	$365	$427	$813	$2,132	***
Depression	$519	$631	$1,144	$2,134	***
Stroke	$402	$504	$961	$1,782	***
SC50%	$572	$673	$1,025	$1,452	***
Diabetes	$530	$599	$849	$1,605	***
PVD	$341	$453	$699	$1,981	***
Atrial Fib.	$223	$340	$678	$1,566	***
Alcohol Abuse	$177	$216	$444	$1,302	***
Smoking	$88 **	$80 **	($139)	($ -18)	
Married (ref.)					
Divorced	$ 297	$385	$635	$1,395	***
Widowed	$ 215	$ 365	$620	$1,790	***
Other	$176	$257	$512	$1,331	***
Age (ref: <59)					
60-69 years	$257	$264	$568	$690	***
70-79 years	$ -85**	$ -144***	($-147)	$ -509***	
≥ 80 years	$-301	$ -494	$ -680	$ -1,301	***
Race (ref: White)					
Black	$ 148**	$ 197**	$ 256**	($118)	
Multiracial/Other	$ -126*	$-121*	$ -423 ***	$ -748***	

Note: Significance: $p \leq 0.001$ = ***, $p \leq 0.015$ = **, $p \leq 0.025$ = *.
The ( ) means $p > 0.025$ for the variable value at that quantile.
The *p*-value column with *** means all quantile points in the row for that variable had $p \leq 0.001$.

Table 15.12 shows the conditional quantile regression results for the total RVUs for each independent variable from the 40th to the 90th quantile. Table 15.12 shows that veterans

diagnosed with COPD steadily utilized more care from the 40th to the 90th quantile. Veterans with COPD at the 90th quantile consumed almost five times more RVUs compared to veterans at the 40th quantile, holding all other variables constant. Veterans with a COPD diagnosis at the 40th quantile consumed 1.7 RVUs more than veterans without COPD at the same quantile. Cases at the 90th quantile consumed 8.9 more RVUs than controls at the same quantile. For 14 of the 17 independent variables, the RVUs consumed progressively increased from the 40th to the 90th quantile. Only smoking behavior, age, and race failed to demonstrate this pattern for RVU utilization when comparing cases to controls.

Table 5.12. Quantile Regression Results for Utilization (RVUs) for Select Variables

Variables	**40th quantile**	**50th quantile**	**75th quantile**	**90th quantile**	***p*-value**
COPD	1.8	2.1	4.6	8.9	***
Pneumonia	4.4	5.8	11.4	18.8	***
CHF	1.8	2.1	4.6	8.9	***
Cancer	3.3	3.8	5.8	10.9	
Asthma	1.4	1.9	3.8	5.5	***
Renal Disease	0.7	0.9	1.7	3.7	***
Depression	1.2	1.4	2.4	4.6	***
Stroke	0.9	1.0	1.4	2.0	***
SC50%	1.4	1.6	2.2	3.3	***
Diabetes	1.4	1.6	2.2	3.3	***
PVD	0.9	1.1	1.8	2.9	***
Atrial Fib.	0.7	0.9	1.5	3.1	***
Alcohol Abuse	0.4	0.3	1.0	2.5	***
Smoking	0.2***	0.4***	0.3**	(-0.0)	
Married (ref.)					
Divorced	0.6	0.8	1.2	2.0	***
Widowed	0.4	0.5	1.1	2.2	***
Other	0.3*	0.4***	0.9***	1.3***	
Age (ref: <59)					
60-69 years	0.6	0.7	1.0	1.5	***
70-79 years	(-0.1)	(-0.2)	-0.4*	-1.0*	
≥ 80 years	-0.9	-1.0	-2.0	-3.2	***

Table 5.12, continued

Variables	40th quartile	50th quartile	75th quartile	90th quartile	*p*-value
Race (ref: White)					
Black	(-0.1)	(-0.1)	-0.4*	-0.8**	
Multiracial/Other	-0.4	-0.5	-1.2	-1.8	***

Note: Significance: $p \leq 0.001$ = ***, $p \leq 0.015$ = **, $p \leq 0.025$ = *.
The ( ) means $p > 0.025$ for the value at that quantile.
The *p*-value column with *** means all quantile points in the row for that variable had $p \leq 0.001$.

Study Limitations and Strengths

All the subjects in the present study were veterans, so the findings may not be generalizable to the non-veteran population. The study veterans were 50 years and older, so the findings may not be applicable to younger veterans and younger non-veterans. The studied population was predominately White male veterans from central North Carolina, so the findings may not be representative of females and non-White veterans from other geographic regions. This becomes important if retirees from the U.S. military branches become more multi-cultural, multi-racial, and establish residence in North Carolina in the future.

A significant number of DVA-eligible veterans have public or private health insurance. These veterans make use of private healthcare services as well as services within the DVA. In other words, these veterans are "dual-users" of healthcare, sometimes using the DVA and other times using private providers. The present study did not capture the information about the cost or utilization of care by veterans outside the DVA system. The absence of cost and utilization information about the veterans who are dual- users generates ambiguity when interpreting the findings from the present study.

The Salisbury VAMC (SBYVAMC) has service care agreements with regional, tertiary care centers for the provision of high acuity care to the seriously ill veterans. Veterans in need of high intensity care not offered by the SBYVAMC are referred out to these tertiary care facilities.

Information regarding the diagnoses, cost, and utilization of care provided to veterans referred to the tertiary care centers was not captured in the present study. This means that information specific tertiary care provided for the sickest of veterans was not included in the present study.

Veterans diagnosed with COPD during the 36-month study period or veterans that died during the study period were excluded from the study. The exclusion of these veterans effectively decreased the values for the total cost and total RVUs, thereby introducing uncertainty into the findings.

There were notable strengths to this study. The population size for cases and controls was large enough to support the generalizations of the findings. The cost and time associated with data extraction and analysis was minimal compared to other study designs. The dataset represented the entire population of veterans who met the inclusion requirements and who received care at the Salisbury VAHCS. The data were readily assessable, consistent, and available in the electronic health records with the use of SQL programming, thereby making replication at other DVA medical centers straightforward. The data were sufficiently robust to enable the identification and description of complex relationships among the variables.

Discussion

The present SBYVAMC study is one of the first studies to use multiple conditional quantile regression models to investigate the cost and utilization of care by veterans diagnosed with COPD. The study's goal was to contrast and compare the cost of care and healthcare utilization for veterans with COPD (cases) to those without COPD (controls).

Key themes are relevant to the present SBYVAMC study and warrant discussion to place the findings in perspective. Included below is a review of the origin and definition of relative

value units (RVUs). The elements associated with physician reimbursement are also introduced. Likewise, a segment introducing conditional quantile regression analysis is presented . Of course, the study's main theme is to evaluate the way in which costs and RVUs were consumed by SBYVAMC veterans diagnosed with COPD.

An Introduction to RVUs

Resource-based relative value units (RBRVUs) originated from work conducted by the Harvard public health economists, Dr. William Hsiao, and colleagues. The goal is to define the doctor's work output by a measurable unit, the RBRVU. The formula as proposed by Dr. Hsiao for the RBRVU incorporates the sum of three factors: the resource value unit (RVU) for physician's work, the RVU for overhead costs, and the RVU for cost of training. Key features of physician work involve the provider's total time and the clinical complexity. Each of the three factors are multiplied by a specific geographic cost adjustment. To calculate reimbursement for a specific medical service the grand total is multiplied by a conversion factor that represents the number of dollars allotted per RVU. The formula determines the reimbursement factor used by Medicare and many health insurance companies to pay health providers for an episode of care. Of interest, an early drawback Dr. Hsiao recognized is the probable ambiguity for the estimates that connected the work associated RVUs allotted for the physician's time. [343,344]

Overview of Physician Reimbursements

Physician reimbursements require three crucial pieces of information: the suitable disease linked diagnostic code based upon the systematic ICD-10-CM; the current procedure terminology code, or CPT code, published by the American Medical Association (AMA); and the assigned Medicare value for the RBRVU. When the RVUs are used in private contracts for physician reimbursement, the RVUs are built around a factor of the Medicare RVU. The ICD-

10-CM lists over 120,000 diagnostic codes for distinct diseases, and the codes are grouped by disease related groups, or DRGs. [348] The CPT codes are annually revised and are central to determining physician reimbursement. [349] The conversion factor for the RBRVU plays a vital role in calculating the Medicare physician reimbursement rates. [350]

RVUs Within the DVA

A primary use of RVUs within the DVA is to monitor provider productivity and offer a metric for use with annual employee evaluations. [337] Patient bills are not habitually generated in caring for veterans. Also, physicians employed with the DVA purchase malpractice insurance at their own discretion since they work at a federal facility which limits the malpractice exposure.[351] The DVA and DSS do make use of RVUs in estimating the average cost of clinical care for managerial purposes. The clinic specific RVUs serve as a measure for the quantity of resources used by the clinical department. RVU calculations begin with the Centers for Medicare & Medicaid RVUs, then a DVA-specific formula incorporates intermediate products (salaries, imaging, lab work, etc.) and other practice costs into the RVU. [352] In the present study, the reported RVUs for the four clinical categories were pulled from the national DSS data files, which incorporated those intermediate products and practice costs.

In the present study, problems arose when trying to interpret how the costs of care relate to the reported RVUs. The DVA collects and reports cost and utilization measures using RVUs very differently from reporting by the for-profit healthcare organizations depending on fee-for-service reimbursement, because the DVA operates with congressional funding which is not based on measures of service. A past conference attended by economists and DVA researchers concluded that the DVA intertwines a combination of micro and macro costs to estimate the clinical cost of care.[353] Each service chief, in coordination with their local fiscal service, is

responsible for tracking costs. This practice raises questions regarding the role of service chiefs in estimating the cost of care because of the unmeasured variability in both staff productivity and the inputs at the individual level of clinical care.

The DSS uses an activity-based cost system whereby indirect and direct costs are aggregated from the "bottom up" to determine each department's overall costs. A ratio of the sum of the total department costs divided by the total captured clinical encounters, or the volume of care, are used to calculate the aggregate "average cost of care" for that clinical category at that facility and region. This represents a "bottom-up" approach to cost-of-care estimation. The bottom-up approach to fiscal reporting is considered practical if the local variation in cost of care is being examined.[191] That said, it does not appear that the RVUs as reported by the DVA serve to firmly connect the utilization of care to the cost of care. This represents a significant weakness for researchers interested in investigating details of how the DVA's cost of care relates to the utilization of care.

It is recognized that outliers significantly impact cost-of-care estimates because unanticipated treatments with longer lengths of stay may be required. [350,351] Ordinary least square (OLS) regression works well when the statistical assumptions are met and outliers are addressed, but what if the outliers contain information of interest? This was the case with the present study since the outliers contained valuable information regarding the cost and utilization of care delivered at the Salisbury VAMC.

Multivariant Conditional Quantile Regression

A statistical procedure was advanced around 1978 by Koenker and Bassett specifically for analysis of non-normal distributions with outliers, called multivariant conditional quantile regression. Unlike OLS, which minimizes the sum of errors around the means, the multivariant

conditional quantile regression estimates the parameters of the model by minimizing the sum of the absolute deviations between the observations and the predicted quantiles using a weighting function. The conditional quantile regression technique is not constrained by the same assumptions as OLS regression. [356] Multivariant conditional quantile regression permits the comparison of the change in the coefficient's values at different points along the distribution. This reveals how the coefficients shift across the distribution and reveals valuable information about the influence of outliers. The interpretation of the conditional quantile coefficients is like that of OLS coefficients except that the quantile regression coefficient measures the change in the dependent variable for a one-unit increase in the independent variable, specifically at a select quantile of the dependent variable. In practical terms, this analytical technique has several advantages: 1) the technique is robust to outliers; 2) the technique is flexible since it can estimate the conditional distribution of the response variable at any percentile of the distribution; and 3) the technique permits a more nuanced understanding of the relationships between the dependent and independent variables. COPD-related articles have been published that used multivariant conditional quantile regression, but oddly few that investigated COPD in veterans. [353,354]

Cost and Utilization of Care for Veterans with COPD

The regression findings show that the total cost of care and the total RVUs for cases increased significantly from the 40th quantile to the 90th quantile when compared to controls. Veterans with COPD at the 90th quantile cost over 4.5 times more dollars and required five times more total RVUs of care compared to cases at the 40th quantile. These findings reflect the influence of clinical outliers on medical resource consumption.

A study was conducted at the Cincinnati VAMC that investigated the cost of care and utilization of care of veterans with COPD. The retrospective study examined the cost of care and

utilization of care for veterans over a 12-month period (2008). The researchers found that COPD-related hospitalizations accounted for 87% of the total COPD-related costs of care. The same study estimated the veterans' median cost of COPD care to be $1,004 per year, while the average cost for COPD care rose to $6,546 per veteran per year. [210]

The Cincinnati VAMC COPD study had significant design differences compared with the present Salisbury COPD study. The Cincinnati VAMC study only included veterans with COPD diagnosed by prior spirometry results and the study did not include control subjects. The Cincinnati VAMC study only calculated costs specific for COPD related care. In contrast, the present Salisbury study used the COPD diagnostic codes found in the electronic health records to identify subjects and a control group was included. In addition, the present Salisbury study examined total costs across four clinical categories without regard as to whether the care was explicitly for complications related to COPD.

In the Salisbury VAMC study, veterans with COPD at the 40th quantile reported a cost of care about $671 dollars more than veterans without COPD at the same quantile, while cases at the 90th quantile reported a cost of care about $3,140 more than veterans without COPD at the same quantile. Cases at the 90th quantile consumed 8.93 more RVUs than controls at the same quantile. Again, the regression finding for cost of care and total RVUs demonstrated that veterans with COPD consumed more medical care than veterans without COPD.

Comorbid Diseases and COPD

Disease comorbidity is a recognized factor associated with an increased cost of care for COPD. [355,356] The degree of comorbidity diagnosed among the case subjects in the present study was notable. The prevalence of COPD in the study population was around 15%. In the study population, the percentages with costly diagnoses were as follows: 1.8% pneumonia; 3.6%

congestive heart failure; 11.7% renal disease; 8.74% peripheral vascular disease; and 1% with cancer, to name a few. Pneumonia, CHF, and cancer were the three leading diagnoses related to higher cost and utilization of care among veterans with COPD. Other publications have reported a significant relationship between COPD and these three diagnoses. [355,357]

Significant Findings for Sociodemographic Variables

In the present study, noteworthy findings were revealed regarding some of the sociodemographic variables. This was true relative to the veteran's race. The comparison group for race was White veterans. From the 40th quantile through the 75th quantile, the total cost of care for Black veterans was positive, statistically significant, and slowly increased. This means that from the 40^{th} to the 90^{th} quantile Black veterans generated more cost than White veterans and the Black-White difference increased. Oddly, at the 90th quantile the total cost of care for Black veterans, while still higher than cost of care provided to White veterans, lost statistical significance ($p = 0.281$). The nonsignificant finding at the 90^{th} quantile for Black veterans is most likely caused by a variable that was not included in the present study, or from an interaction effect between race and variables yet to be identified. Black veterans recorded an interesting utilization pattern as measured by the total RVUs. At the 40^{th}, 50^{th}, and 75th quantiles, the total RVUs consumed by Black veterans compared to White veterans was not statistically significant, but at the 90th quantile the variable recorded significance ($p = 0.001$) with a negative coefficient, or -0.86 RVUs, meaning that they received fewer RVUs of care than Whites at that high quantile. This finding could have three causes: 1) the number of Black veterans who consumed high levels of care were too small to yield meaningful results; 2) Black veterans in need of complex care were triaged to regional, tertiary care facilities; or 3) seriously ill Black veterans have sought care closer to home and outside the VA system, thereby utilizing

VA healthcare at a lower rate than White veterans for these more intensive healthcare conditions. The finding that Black veterans receive less of the most complex care is consonant with the point made earlier. Veterans who are very sick may seek care outside of the VA system and therefore the care is not recorded in the VA medical records. Also, lower income minority patients may find it more difficult than white patients to arrange transportation to often distant regional sites where VA care is available. Additional research is needed to better understand the effect of race on the utilization of VA services for more complex health conditions.

From Tables 5.11 and 5.12, it is noted that cost and utilization of care varied by age groups. Compared to the reference group of similarly aged but COPD-free veterans with COPD aged 60–69 showed a positive, significant pattern of increased total cost of care and increased total RVUs across the quantiles. Veterans aged 70–79 had negative coefficients for the total average cost of care and total RVUs for all four quantiles. Veterans 80 and older had consistently increasing negative coefficients for the total cost of care and total RVUs at each of the four quantiles. These results mean that veterans 70 years and older were less likely to use the Salisbury VA for advanced levels of care. These findings could be explained by three influences. First, eligibility for Medicare insurance begins at age 65, and older veterans likely depend on Medicare for coverage outside the VA for more complex care. Second, travel and proximity to care become problematic and inconvenient for very old veterans because of frailty and infirmity. And third, the Salisbury VAMC offers limited categories of specialty care. Older veterans with serious conditions may find that the needed specialty care is outside the Salisbury VAMC. Veterans over 65 years of age with Medicare insurance are less reliant on the DVA for healthcare compared to younger veterans without Medicare. [176]

Marital status influences the total cost of care and the total RVUs consumed by veterans. Tables 5.11 and 5.12 show that, compared to married veterans, divorced veterans consume more resources, while holding other variables constant. Interestingly, at the 90th quantile the widowed veterans overtake the divorced veterans relative to the total cost of care and total RVUs (divorced =$1,395 and 1.2 RVUs, widowed = $1,791 and 1.9 RVUs). One hypothesis was that divorced veterans and widowed veterans have limited social and financial support compared to married veterans. Additional research is warranted regarding the influence of social support systems upon cost of care and healthcare utilization by veterans with COPD.

Asthma and COPD in Veterans

Asthma and COPD represent pulmonary conditions with similar symptoms, such as dyspnea and wheezing, but with a different pathophysiology. That said, veterans are often diagnosed with COPD and asthma, or a COPD–asthma overlap syndrome. [59] In the Salisbury VAMC study, approximately 30% of the veterans with a COPD diagnosis had the COPD–asthma overlap syndrome. The measures of cost and the RVUs consumed by veterans with the COPD-asthma overlap syndrome could not be calculated because the cost and RVUs of care for COPD and asthma were only recorded separately.

For the 40th, 50th, and 75th quantiles, the total cost of care and total RVUs for asthma and COPD increased at similar rates, but at the 90th quantile, the total cost of care for COPD began to diverge and increase from that of asthma ($2,225 versus $3,240). The total RVUs at the 90th quantile for asthma and COPD reflected the increased utilization of care for COPD compared to asthma (COPD = 8.93 and asthma = 5.49). One might hypothesize that veterans with the COPD-asthma overlap syndrome would display a higher acuity of respiratory disease such that these veterans would consume more dollars and RVUs of care compared to veterans

with COPD alone. It is not clear what role COPD–asthma overlap syndrome plays in cost of care. Research is warranted to investigate how veterans with the COPD–asthma overlap syndrome vary in cost and utilization of care compared to veterans with a COPD diagnosis alone.

Conclusion

From the present study, the multivariant conditional quantile regression models revealed that veterans with COPD consumed greater healthcare resources as measured by the total cost of care and the total RVUs representing more health provider work than veterans without COPD. The high cost of care is most likely a reflection of the significant comorbidity among veterans with COPD.

The present study demonstrated that COPD was among the four most costly diagnoses for veterans. Only three diagnoses consumed more healthcare resources than COPD: congestive heart failure, cancer, and pneumonia. Unfortunately, each of these serious comorbid conditions is recognized to be associated with a COPD diagnosis. [355,357] For a veteran diagnosed with COPD, there is a real likelihood that they will develop congestive heart failure, cancer, or pneumonia, thereby critically elevating the costs and RVUs of care. Additional research is needed to better understand how to manage COPD in veterans to minimize the risk for costly comorbidities.

CHAPTER 6: CONCLUSION

Chronic obstructive pulmonary disease (COPD) is a prevalent, chronic respiratory condition associated with increased morbidity and mortality. The prevalence of COPD varies according to how it is defined, the diagnostic standards, and the geographic region. [4] In 2014–2015, the estimated prevalence of COPD in the United States averaged around 5.9%, but the prevalence varied by state, with West Virginia's COPD prevalence estimated at 12%. [362]

The three research studies reported here investigated the relationships between systemic comorbidities, ocular pathologies, and the cost and utilization of care for veterans with COPD compared to veterans without COPD. The studies used veterans' data mined from the national and local administrative files and the medical records at the Bill Hefner Salisbury VA Health Care System (SVAHCS). The research relied on the eligible population of veterans aged 50 and older and enrolled in primary care at the Salisbury HCS over a 3-year period, from January 1, 2016 to December 31, 2018.

The Salisbury veteran COPD study discovered more than a few findings that have expanded the understanding of how a COPD diagnosis impacted the population of veterans at the Salisbury VAHCS. For example, at the start of the study, the prevalence of COPD among veterans 50 and older enrolled for primary care, except for those who died of any cause (including COPD) during the study duration, was notably high at 15%. The Promise to Address Comprehensive Toxic Act, or the PACT Act of 2022, a federal law, places a spot light on the respiratory health of veterans by recognizing that military service inherently places veterans at greater risk for respiratory problems compared to most other professions.[363] Consequently, this expansion of eligibility of VA care is expected to result in heightened levels of clinical surveillance and a significant increase in the prevalence of COPD among veterans. Thus, the

expansion raises important policy questions about the future costs of care, the utilization of care, and resource allocations for veterans diagnosed with COPD.

The studies presented here identified some noteworthy relationships between veterans' sociodemographic characteristics and the odds for a COPD diagnosis. The risk for COPD increased markedly with age, specifically for veterans 80 and older. What was most surprising was the relationship between the risk for COPD and race. White veterans were disproportionately diagnosed with COPD at a higher rate compared to Black veterans. For reasons yet unknown, Black veterans at the SVAHCS were much less likely to be ill with COPD. The veteran's marital status was also related to the odds of a COPD diagnosis. Married veterans were significantly less likely to have developed COPD compared to divorced or widowed veterans. This finding raised questions as to just how marital status influenced the odds for a COPD diagnosis. Future research is needed to better understand how race and marital status influence the risk for a diagnosis of COPD.

Three Empirical Studies

Each of the three drafts of potential journal articles delve into some aspect of health or health care bearing on COPD. Moreover, each are based on the same population of veterans treated in the Salisbury VA region between January 1, 2016 and December 31, 2018. However, each article has its own distinctive focus, which requires different research designs and analytical approaches.

Study Designs and Analysis

The first article was an observational study with a straightforward question answered by a familiar and clear-cut analytical approach, multivariant logistic regression. The article utilized a case-control design to explore how select comorbid diagnoses were related to veterans with and

without COPD. From the first article we learned that a COPD diagnosis was associated with some serious, chronic comorbidities among veterans.

The second article required a more intricate strategy with six dependent variables, each corresponding to a known ocular pathology associated with visual infirmity. A two-step process was required. First, an unadjusted logistic regression model was employed to identify which of the dependent variables had a statistically significant relationship with the independent variable of utmost interest, a diagnosis for COPD. The unadjusted regression models identified vision-threatening diabetic retinopathy and exudative macular degeneration as the two ocular pathologies that were of foremost interest. Second, these two ocular pathologies then became the dependent variables used for multivariant logistic regression modeling whereby 22 independent variables (including COPD) were statistically analyzed.

The third and final article proved to be the most intricate because it moved into the world of social science involving clinical decisions and human behaviors. Complex measures and administrative data created by accountants, health service researchers, and economists were used to explore the troublesome problems of human institutions and the difficult questions of healthcare value and cost. Multiple conditional quantile regression modeling was employed to address these questions. From this statistical approach, we learned how the cost and utilization of care varied with intensity of care for specific sociodemographic and comorbid illnesses

.*Principal Findings*

The first study (Chapter 3) identified some noteworthy relationships between the veteran's sociodemographic characteristics and the odds for a COPD diagnosis. The risk for COPD increased markedly with age, specifically for veterans 80 and older. What was most surprising was the relationship between the risk for COPD and White veterans compared to

Black veterans. For reasons yet unknown Black veterans at the SVAHCS were much less likely to be ill with COPD. The veteran's marital status was related to the odds of a COPD diagnosis. Married veterans were significantly less likely to develop COPD compared to divorced or widowed veterans. This finding raised questions as to just how marital status influenced the odds for a COPD diagnosis.

Future research is needed to better understand how race and marital status influence the risk for a diagnosis for COPD.

Chapter 3 also revealed that veterans diagnosed with COPD reported excessive levels of comorbidity compared with similar veterans without COPD. For example, SVAHCS veterans diagnosed with COPD were at greater odds for congestive heart failure and peripheral vascular disease compared to veterans without COPD. In addition, these same veterans had significantly greater odds of suffering from pneumonia, metastatic cancer, asthma, and sleep apnea. Regarding psychological diagnoses, the SVAHCS veterans diagnosed with COPD were at greater odds for depression and chronic pain compared to veterans without COPD. The directionality of the comorbidities relative to the COPD needs further study. For example, it is not clear how varying levels of congestive heart failure impact pulmonary function prior to a diagnosis for COPD. Would the more effective clinical management of congestive heart failure decrease the likelihood of a COPD diagnosis? Conversely, would the improved clinical management of COPD decrease the odds for congestive heart failure? Similar questions can be raised regarding asthma and sleep apnea among veterans with COPD.

This research is among the first to investigate the relationship between COPD and select ocular diagnoses in a veteran population as Chapter 4 reported. Six ocular diagnoses known to cause potentially severe vision loss were modeled using multivariant logistic regression models.

These ocular diagnoses included vision-threatening diabetic retinopathy, glaucoma, exudative age-related macular degeneration (ARMD), central retinal vein occlusion, non-arteritic anterior ischemic optic neuropathy (NA-AION), and low vision. Two of the ocular diagnoses, vision threatening diabetic retinopathy and exudative ARMD revealed a significant relationship with a COPD diagnosis.

Vision-threatening diabetic retinopathy appeared to be *protective* against COPD. One explanation for this finding could be that the Salisbury veterans received outstanding primary care, made good behavioral health choices, and achieved a high level of diabetic control, thereby avoiding or delaying the onset of vision-threatening diabetic retinopathy Another explanation could be that for veterans with COPD the duration of diabetic disease was brief, without the necessary time for ocular disease progression.

Exudative ARMD was shown to have a significant relationship to a diagnosis for COPD. One common factor shared by both conditions is that the risk increases as the patients age. White veterans were at a much greater risk for both COPD and exudative ARMD compared to Black and multiracial veterans. In the present study, Black veterans were rarely diagnosed with exudative ARMD. This finding was notable and deserves further study to explain the determinative influences.

The cost of care and utilization of care for veterans with and without COPD was evaluated in Chapter 5 using multivariant conditional quantile regression models at the 40th, 50th, 75th, and 90th quantiles. Costs were updated using consumer price index (CPI) dollars adjusted to 2022 dollars. Resource based relative value units (RBRVUs) provided a measure of care utilization, especially physicians' work. The findings in Chapter 5 demonstrated that from the 40th through the 90th quantiles veterans with a COPD diagnosis consumed significantly

more dollars and utilized more clinical RBRVUs- approximately 4.5 times more than veterans without COPD.

In addition, the present study produced interesting results about the way in which the DVA used RBRVUs as a managerial tool. Unlike healthcare organizations receiving fee-for-service reimbursement for physician services, DVA uses the RBRVU measures as a macro-economic gauge to assess intra-agency and inter-agency productivity and the utilization of resources in the belief that they measure utilization of resources in providing clinical care. Future research is needed to explore ways in which the DVA might use RBRVUs in a more granular manner that would more closely reflect the quality and process of care provided.

Several caveats should be noted in interpreting and generalizing the findings from the three empirical chapters. The population of Salisbury veterans was predominantly White and above the age of 69. Thus, the studies' findings may not apply to a younger, diverse veteran population with more recent military experience, or future conflicts. Likewise, the Salisbury veteran populations is predominately male, and the findings may not reflect the health care needs of more gender diverse cohorts in the future. Moreover, VA data systems do not capture care received outside of the nationwide VA networks of hospitals, nursing homes, and other clinical facilities. Therefore, patient data used in these three studies cannot be assumed to constitute the totality of health care received by the study population during the three years of the study. Finally, the DVA's process for calculating costs and RBRVUs differ from the protocols for determining costs and RBRVUs in mainstream fee-for-service organizations. Economic and policy-oriented investigators find it difficult to compare the DVA's cost and utilization of care with nonfederal healthcare organizations, especially in regard to the VA's quite different use of RBRVUs.

Potential Policy Impacts

Some of the more notable findings from the present studies had to do with the veterans' race and COPD. Black veterans were 43% less likely to have a diagnosis for COPD compared to White veterans (OR = 0.57, Table 3.10) even though a greater percentage of Black veterans reported a positive smoking history. Black veterans were 87% less likely to have a diagnosis for exudative age-related macular degeneration (ARMD), a visual condition linked with a COPD diagnosis, when compared to White veterans. In addition, the multiple conditional quantile regression model found that Black veterans consumed significantly fewer RBRVUs for the complex levels of care (90^{th} quantile) compared to White veterans. The discoveries raise questions about the racial discrepancies between the disease prevalence of illness and utilization of care, particularly the delivery of complex care for Black veterans. How might these racial differences between disease diagnosis and health care delivery be explained, and what actions would minimize clinically unjustified disparities? A variety of explanations and associated responses are worth investigating.

- Occupational exposures influence the likelihood of developing COPD. It is possible that on average the Black veterans selected occupations that carried a lower risk for COPD compared to White veterans. Information about the veterans' occupations was not collected for the present studies.
- Providers are prone to biases. It is possible that on average the Salisbury primary care providers solicit respiratory symptoms from White veterans more frequently than from Black veterans, thereby diagnosing COPD more frequently in White veterans. Studies have demonstrated the ways in which biases can influence clinical care decisions. [236]

- Social and cultural factors influence both healthcare seeking behaviors and risk for disease. Providers are prone to diagnose illnesses based upon symptoms. White veterans may be more vocal discussing respiratory symptoms with their doctor compared to Black veteran.
- Biological or genetic factors may protect Black veterans from COPD and exudative ARMD. A national study with hospitalized veterans who were at the 95th percentile for healthcare consumption found that Black veterans were significantly less likely to have a diagnosis for COPD compared to White veterans. [237] Regarding exudative ARMD, genetic studies have demonstrated that a greater risk for exudative ARMD is associated with northern European descent. [364]
- The fact that Black veterans consumed fewer RBRVUs for high intensity care (90th quantile) at the SVAHCS when compared to White veterans merits study. It is important to analyze and understand this finding to remedy the source of the racial health disparity in patients suffering from COPD.

Six policy recommendations aimed at decreasing health disparities in the diagnosis of COPD in Black veterans are worth considering. 1) Primary care providers should be made aware of the health disparity in COPD diagnosis between Black and White veterans. That awareness would encourage physicians to search more carefully for symptoms of COPD among Black veterans. 2) There could be an increased use of pulmonary function tests and chest x-rays for at risk veterans. 3) A structured educational campaign could be developed to better educate veterans, particularly Black veterans, about the risks, signs, and symptoms of COPD. 4) Black veterans with comorbid conditions that often accompany COPD, such as congestive heart failure, peripheral vascular disease, asthma, sleep apnea, and increased age could be identified and proactively screened for COPD. 5) Black veterans could be screened for dyspnea with the

use of standardized questionnaires. 6) Veterans with a positive history for occupational exposures known to promote COPD could be screened for respiratory illness.

A thorough study of SVAHCS care for black and white veterans is probably the best way to evaluate and then implement the various strategies suggested above. A comprehensive strategy with a team approach seems critical in any attempt to determine what are best practices for the COPD population and then adopt them. The steps for studying the healthcare disparities might include: clearly defining the questions to be addressed; reviewing the literature to identify current ideas and potential causes for the healthcare disparities; collecting and analyzing electronic health records to understand the process of care delivery; conducting interviews or focus groups with stakeholders to better understand the differences in critical care delivered to Black veterans compared to White veterans; identifying contributing factors that can cause healthcare disparities such as cultural differences, socioeconomic influences, institutional policies, structural barriers, and access issues; unmasking system level factors that promote disparity such as staff training, hospital policies, DVA regulations, and clinical care protocols; and developing and implementing an action plan that can be evaluated. Healthcare changes can address health care disparities among and between Black and White veterans, but real improvements take time and organizational commitment.

In addition to the implications for racial disparities revealed in the three empirical studies, a second focus emerging from Chapter 5 is worth highlighting. Whereas the discussion of racial disparities is part of the current society-wide attention to racial and social justice associated with the death of George Floyd, the New York Times and Nikole Hannah-Jones' 1619 Project, and numerous recent expressions in the health literature, the other policy opportunity is a little-noticed, somewhat technical change that has the potential of improving VA efficiency and

effectiveness. Changing the ways that RBRVUs, which were explained in the last chapter, are used in the DVA health system could improve quality of care for veterans.

Three factors compose the whole RBRVU value: a work-RVU, a practice expense-RVU, and the professional liability-RVU. The work RVU is the primary component (51%) of the whole RVU and represents the key attributes (time, intensity, complexity) of the clinical services provided. [365] In fee-for-service health care delivery systems the RBRVU can result in the payment for services with minimum value. [366]

Since the DVA is funded by Congress without direct reference to the services to be provided, RBRVU are not used in calculating practice expense. Also, federal tort laws shield DVA clinical providers from the malpractice risks experienced by nonfederal providers. [367] Without the shackles of the fee-for-service milieu, and little need for provider malpractice coverage, DVA could develop a work-RBRVU system that embraces meaningful performance and quality measures. A reform that assigns numerical value to specific clinical actions associated with improved clinical outcomes in order to foster meaningful research on healthcare utilization by economic and policy analysts.

For example, a RAND study found that while the DVA performed well in delivering mental health and substance abuse counseling, improvement was needed in providing pharmacotherapy to veterans with alcohol abuse. [368] If work-RBRVU values were increased specifically for the desired clinical action (such as provision of pharmacotherapy in this instance) the RBRVU would measure improved quality of care. The idea for modifying work-RVUs for better clinical outcomes is not new. Stecker and Schroeder provided several examples where RVU values could be adjusted to align clinical care for improved quality of care. [369]

The DVA is in a unique position regarding work-RVUs. It is not constrained by the pressures of profit maximization or professional medical liability. This means that DVA could design and beta-test a new system for work-RVUs that would simultaneously accomplish two meaningful goals: serve as a driver to promote healthcare utilization for improved outcomes and offer a mechanism for economists and health policy specialists to better study the utilization of care in the DVA.

Conclusion

In summary, Chapter 3 aimed to address the question, "Do veterans with a diagnosis for COPD experience more comorbidity than veterans without COPD?" The results from Chapter 3 show that veterans with COPD are generally sicker than those without COPD. Chapter 4 was one of the few studies that explored the relationship between six vision threatening ocular diagnoses and COPD in a veteran population. The results from Chapter 4 revealed that exudative age-related macular degeneration was positively associated with a diagnosis for COPD; but oddly, COPD was somehow protective for vision-threatening diabetic retinopathy. Finally, Chapter 5 intended to answer the question, "Do veterans with a COPD diagnosis consume more health care dollars and utilize more care than veterans without a COPD diagnosis?" Chapter 5 revealed that health care costs and utilization of care for veterans is highly skewed, but that veterans with COPD do indeed require more costs and consume more RVUs of care compared to veterans without COPD. The results from Chapter 5 also pointed out differences in the cost and utilization of the high intensity care consumed by Black veterans compared to White veterans, and veterans over 70 years of all races. Less money and fewer resources were expended on high intensity care (90^{th} quantile) for Black veterans compared to White veterans. Additional study is needed to better understand and remedy what appears to be a racial disparity in care delivered for Black

veterans. As for veterans over age 70, research is warranted to clearly understand what factors cause older veterans to consume high intensity care outside the SVAHCS facility.

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APPENDIX A: ICD9 AND ICD10 CODES

Variables

Age	No ICD 9 or 10 Codes
Marital Status	No ICD 9 or 10 Codes
Sex	No ICD 9 or 10 Codes
Race	No ICD 9 or 10 Codes
Substance Abuse with Alcohol	
ICD9Code	
303.0 – 304.0	Alcohol dependence syndrome
304.0 – 305.0	Drug dependence
305.0 – 306.0	Nondependent abuse of drugs
ICD10Code	
F10 – F11	Alcohol related disorders
F11 – F12	Opioid related disorders
F12 – F13	Cannabis related disorders
F13 – F14	Sedative, hypnotic, or anxiolytic related disorders
F14 – F15	Cocaine related disorders
F15 – F16	Other stimulant related disorders
F16 – F17	Hallucinogen related disorders
F18 – F19	Inhalant related disorders
F19 – F20	Other psychoactive substance related disorders
Substance Abuse without Alcohol	
ICD9Code	
304.0 – 305.0	Drug dependence
305.0 – 306.0	Nondependent abuse of drugs
ICD10Code	
F11 – F12	Opioid related disorders
F12 – F13	Cannabis related disorders
F13 – F14	Sedative, hypnotic, or anxiolytic related disorders
F14 – F15	Cocaine related disorders
F15 – F16	Other stimulant related disorders
F16 – F17	Hallucinogen related disorders
F18 – F19	Inhalant related disorders
F19 – F20	Other psychoactive substance related disorders
Post-Traumatic Stress Disorder (PTSD)	
ICD9Code	
309.81 – 309.82	POSTTRAUMATIC STRESS DIS
V11.4 – V11.5	HX COMBAT/STRESS REACTN
ICD10Code	
F43.10 – F43.11	Post-traumatic stress disorder, unspecified
F43.11 – F43.12	Post-traumatic stress disorder, acute
F43.12 – F43.13	Post-traumatic stress disorder, chronic
Combat Veteran Designation	No ICD 9 or 10 Codes

Smoking

ICD9Code	
305.1 – 305.2	Tobacco use disorder
649.0 – 649.1	Tobacco use disorder complicating pregnancy, childbirth, or the puerperium
989.84 – 989.85	Toxic effect of tobacco
E869.4 – E869.5	Second hand tobacco smoke
V15.82 – V15.83	Personal history of tobacco use
ICD10Code	
F17.21 – F17.22	Nicotine dependence, cigarettes
O99.33 – O99.34	Tobacco use disorder complicating pregnancy, childbirth, and the puerperium
T59.81 – T59.82	Toxic effect of smoke
T65.22 – T65.23	Toxic effect of tobacco cigarettes
Z71.6 – Z71.7	Tobacco abuse counseling
Z72.0 – Z72.1	Tobacco use
Deceased	No ICD 9 or 10 Codes
Rurality (Rural/Urban)	No ICD 9 or 10 Codes

Psychological Variables

Depression

ICD9Code	
296.3 – 296.4	Major depressive disorder recurrent episode
296.5 – 296.6	Bipolar disorder, most recent episode (or current) depressed
296.82 – 296.83	Atypical depressive disorder
301.12 – 301.13	Chronic depressive personality disorder
309.0 – 309.1	Adjustment disorder with depressed mood
309.1 – 309.2	Prolonged depressive reaction
309.28 – 309.29	Adjustment disorder with mixed anxiety and depressed mood
311 – 312	Depressive disorder, not elsewhere classified
ICD10Code	
F06.31 – F06.32	Mood disorder due to known physiological condition with depressive features
F32 – F33	Major depressive disorder, single episode
F33 – F34	Major depressive disorder, recurrent
F43.21 – F43.22	Adjustment disorder with depressed mood
F43.23 – F43.24	Adjustment disorder with mixed anxiety and depressed mood

Anxiety Disorder

ICD9Code

293.84 – 293.85	Anxiety disorder in conditions classified elsewhere
300.0 – 300.1	Anxiety states
309.21 – 309.22	Separation anxiety disorder
309.24 – 309.25	Adjustment disorder with anxiety
309.28 – 309.29	Adjustment disorder with mixed anxiety and depressed mood

ICD10Code

F06.4 – F06.5	Anxiety disorder due to known physiological condition
F40 – F41	Phobic anxiety disorders
F41 – F42	Other anxiety disorders
F43.22 – F43.23	Adjustment disorder with anxiety
F43.23 – F43.24	Adjustment disorder with mixed anxiety and depressed mood
F93.0 – F93.1	Separation anxiety disorder of childhood

Dementia

ICD9Code

290 – 291	Dementias
291.2 – 291.3	Alcohol-induced persisting dementia
292.21 – 292.22	DEMENTIA ASSOCIATED WITH ALCOHOLISM, MILD
292.82 – 292.83	Drug-induced persisting dementia
294.1 – 294.2	Dementia in conditions classified elsewhere
294.2 – 294.3	Dementia, unspecified
331.19 – 331.20	Other frontotemporal dementia
331.82 – 331.83	Dementia with lewy bodies

ICD10Code

F01 – F02	Vascular dementia
F02 – F03	Dementia in other diseases classified elsewhere
F03 – F04	Unspecified dementia
F10.27 – F10.28	Alcohol dependence with alcohol-induced persisting dementia
F10.97 – F10.98	Alcohol use, unspecified with alcohol-induced persisting dementia
F13.27 – F13.28	Sedative, hypnotic or anxiolytic dependence with sedative, hypnotic or anxiolytic-induced persisting dementia
F13.97 – F13.98	Sedative, hypnotic or anxiolytic use, unspecified with sedative, hypnotic or anxiolytic-induced persisting dementia
F18.17 – F18.18	Inhalant abuse with inhalant-induced dementia
F18.27 – F18.28	Inhalant dependence with inhalant-induced dementia

Dementia, continued

F18.97 – F18.98	Inhalant use, unspecified with inhalant-induced persisting dementia
F19.17 – F19.18	Other psychoactive substance abuse with psychoactive substance-induced persisting dementia
F19.27 – F19.27	Other psychoactive substance dependence with psychoactive substance-induced persisting dementia
F19.97 – F19.97	Other psychoactive substance use, unspecified with psychoactive substance-induced persisting dementia
G31.0 – G31.1	Frontotemporal dementia
G31.83 – G31.84	Dementia with Lewy bodies

Chronic Pain Diagnosis

ICD9Code

338.21 – 338.22	CHRONIC PAIN DUE TO TRAUMA
338.29 – 338.30	OTHER CHRONIC PAIN
338.4 – 338.5	CHRONIC PAIN SYNDROME

ICD10Code

G89.21 – G89.22	Chronic pain due to trauma
G89.4 – G89.5	Chronic pain syndrome
G89.29 – G89.30	Other chronic pain

Cardiovascular Diagnoses

Coronary Artery Disease

ICD9Code

414.2 – 414.3	CHRONIC TOTAL OCCLUSION OF CORONARY ARTERY
414.06 – 414.07	CORONARY ATHEROSCLEROSIS, OF NATIVE CORONARY ARTERY OF TRANSPLANTED HEART
414.12 – 414.13	DISSECTION OF CORONARY ARTERY
746.85 – 746.86	CORONARY ARTERY ANOMALY, CONGENITAL

ICD10Code

I21.0 – I21.1	Elevation (STEMI) myocardial infarction of anterior wall
I21.1 – I21.2	ST elevation (STEMI) myocardial infarction of inferior wall
I21.21 – I21.22	ST elevation (STEMI) myocardial infarction involving left circumflex coronary artery
I25.1 – I25.2	Atherosclerotic heart disease of native coronary artery
I25.4 – I25.5	Coronary artery aneurysm and dissection
I25.7 – I25.8	Atherosclerosis of coronary artery bypass graft(s) and coronary artery of transplanted heart with angina pectoris
I25.81 – I25.82	Chronic total occlusion of coronary artery

Coronary Artery Disease, continued

I25.82 – I25.83	Chronic total occlusion of coronary artery
T82.21 – T82.22	Mechanical complication of coronary artery bypass graft
T82.855 – T82.856	Stenosis of coronary artery stent

Ischemic Heart Disease

ICD9Code

411.8 – 411.9	OTHER ACUTE AND SUBACUTE FORMS OF ISCHEMIC HEART DISEASE
411.89 – 411.90	OTHER ACUTE AND SUBACUTE FORMS OF ISCHEMIC HEART DISEASE
414.8 – 414.9	OTHER SPECIFIED FORMS OF CHRONIC ISCHEMIC HEART DISEASE
414.9 – 415.0	CHRONIC ISCHEMIC HEART DISEASE, UNSPECIFIED

ICD10Code

I24.8 – I24.9	Other forms of acute ischemic heart disease
I24.9 – I25.0	Acute ischemic heart disease, unspecified
I25.89 – I25.90	Other forms of chronic ischemic heart disease
I25.9 – I26.0	Chronic ischemic heart disease, unspecified

Atrial Fibrillation Diagnosis

ICD9Code

427.31 – 427.32	ATRIAL FIBRILLATION

ICD10Code

I48.0 – I48.1	Paroxysmal atrial fibrillation
I48.1 – I48.2	Persistent atrial fibrillation
I48.2 – I48.3	Chronic atrial fibrillation
I48.91 – I48.92	Unspecified atrial fibrillation

Cerebrovascular Accident or Stroke

ICD9Code

436 – 437	Acute, but ill-defined, cerebrovascular disease
437.1 – 437.2	Other generalized ischemic cerebrovascular disease
437.8 – 437.9	Other ill-defined cerebrovascular disease
437.9 – 438.0	Unspecified cerebrovascular disease
438.0 – 438.1	Late effects of cerebrovascular disease, cognitive deficits
438.1 – 438.2	Speech and language deficits
438.2 – 438.3	Hemiplegia/hemiparesis
438.3 – 438.4	Monoplegia of upper limb
438.4 – 438.5	Monoplegia of lower limb
438.50 – 438.51	Late effects of cerebrovascular disease, other paralytic syndrome affecting unspecified side
438.51 – 438.52	Late effects of cerebrovascular disease, other paralytic syndrome affecting dominant side
438.52 – 438.53	Late effects of cerebrovascular disease, other paralytic syndrome affecting nondominant side

Cerebrovascular Accident or Stroke

438.81 – 438.82	Other late effects of cerebrovascular disease, apraxia
438.82 – 438.83	Other late effects of cerebrovascular disease, dysphagia
438.89 – 438.90	Other late effects of cerebrovascular disease
438.9 – 439.0	Unspecified late effects of cerebrovascular disease
674.01 – 674.02	Cerebrovascular disorders in the puerperium, delivered, with or without mention of antepartum condition
674.02 – 674.03	Cerebrovascular disorders in the puerperium, delivered, with mention of postpartum complication
997.02 – 997.03	Iatrogenic cerebrovascular infarction or hemorrhage

ICD10Code

I67.81 – I67.82	Acute cerebrovascular insufficiency
I67.89 – I67.90	Other cerebrovascular disease
I67.9 – I68.0	Cerebrovascular disease, unspecified
I68.8 – I68.9	Other cerebrovascular disorders in diseases classified elsewhere
I69.8 – I69.9	Sequelae of other cerebrovascular diseases
I69.9 – I70.0	Sequelae of unspecified cerebrovascular diseases
I97.81 – I97.82	Intraoperative cerebrovascular infarction
G46.3 – G46.4	Brain stem stroke syndrome
G46.4 – G46.5	Cerebellar stroke syndrome

Congestive Heart Failure

ICD9Code

428.0 – 428.1	CONGEST HEART FAIL UNSPECIFIED
428.1 – 428.2	LEFT HEART FAILURE
428.20 – 428.21	UNSPEC SYSTOL HEART FAILURE
428.21 – 428.22	ACUTE SYSTOLIC HEART FAILURE
428.22 – 428.23	CHRONIC SYSTOLIC HEART FAILURE
428.30 – 428.31	UNSPEC DIASTOL HEART FAILURE
428.31 – 428.32	ACUTE DIASTOLIC HEART FAILURE
428.32 – 428.33	CHRON DIASTOL HEART FAILURE

ICD10Code

I50.1 – I50.2	Left ventricular failure, unspecified
I50.20 – I50.21	Unspecified systolic (congestive) heart failure
I50.21 – I50.22	Acute systolic (congestive) heart failure
I50.22 – I50.23	Chronic systolic (congestive) heart failure
I50.23 – I50.24	Acute on chronic systolic (congestive) heart failure
I50.30 – I50.31	Unspecified diastolic (congestive) heart failure
I50.31 – I50.32	Acute diastolic (congestive) heart failure
I50.32 – I50.33	Chronic diastolic (congestive) heart failure
I50.33 – I50.34	Acute on chronic diastolic (congestive) heart failure
I50.9 – I50.9	Heart failure, unspecified

Metabolic Related Diagnoses

Diabetes

ICD9Code

250 – 251	Diabetes mellitus

ICD10Code

E10 – E11	Type 1 diabetes mellitus
E11 – E12	Type 2 diabetes mellitus
E13 – E14	Other specified diabetes mellitus

Hypercholesterolemia

ICD9Code

272.0 – 272.1	Pure hypercholesterolemia

ICD10Code

E78.0 – E78.1	Pure hypercholesterolemia

Vision

Vision Diabetic Retinopathy

ICD9Code

362.01 – 362.02	DIABETIC RETINOPATHY NOS
362.02 – 362.03	PROLIF DIAB RETINOPATHY
362.03 – 362.04	NONPROLF DB RETNOPH NOS
362.04 – 362.05	MILD NONPROLF DB RETNOPH
362.05 – 362.06	MOD NONPROLF DB RETINOPH
362.06 – 362.07	SEV NONPROLF DB RETINOPH
362.07 – 362.08	DIABETIC MACULAR EDEMA

ICD10Code

E10.311 – E10.312	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10.321 – E10.322	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E10.331 – E10.332	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E10.339 – E10.340	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E10.341 – E10.342	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E10.349 – E10.350	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E10.351 – E10.352	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema

Vision Diabetic Retinopathy, continued

E10.359 – E10.360	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema
E11.311 – E11.312	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E11.321 – E11.322	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E11.331 – E11.332	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E11.339 – E11.340	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E11.341 – E11.342	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E11.349 – E11.350	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E11.351 – E11.352	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema
E11.359 – E11.360	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema
E13.311 – E13.312	Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema
E13.321 – E13.322	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E13.331 – E13.332	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E13.339 – E13.340	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E13.341 – E13.342	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E13.349 – E13.350	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E13.351 – E13.352	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema
E13.359 – E13.360	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema

Vision-Threatening Retinopathy

ICD9Code

362.02 – 362.03	PROLIF DIAB RETINOPATHY
362.06 – 362.07	SEV NONPROLF DB RETINOPH
362.07 – 362.08	DIABETIC MACULAR EDEMA

ICD10Code

E10.311 – E10.312	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10.321 – E10.322	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E10.331 – E10.332	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E10.341 – E10.342	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E10.349 – E10.350	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E10.351 – E10.352	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema
E10.359 – E10.360	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema
E11.311 – E11.312	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E11.321 – E11.322	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E11.331 – E11.332	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E11.341– E11.342	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E11.349 – E11.350	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E11.351 – E11.352	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema
E11.359 – E11.360	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema
E13.311 – E13.312	Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema

Vision-Threatening Retinopathy, continued

E13.321 – E13.322	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E13.331 – E13.332	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E13.341 – E13.342	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E13.349 – E13.350	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E13.351 – E13.352	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema
E13.359 – E13.360	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema

Vision Mild Retinopathy

ICD9Code

362.05 – 362.06	MOD NONPROLF DB RETINOPH

ICD10Code

E10.339 – E10.340	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E11.339 – E11.340	Type 2 miabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E13.339 – E13.340	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema

Vision Glaucoma

ICD9Code

365 – 366	Glaucoma

ICD10Code

H40 – H43	Glaucoma

Vision Retinal Artery Occlusion

ICD9Code

362.30 – 362.31	RETINAL VASC OCCLUS NOS
362.31 – 362.32	CENT RETINA ARTERY OCCLU
362.32 – 362.33	ARTERIAL BRANCH OCCLUS
362.34 – 362.35	TRANSIENT ARTERIAL OCCLU
362.81 – 362.82	RETINAL HEMORRHAGE
362.82 – 362.83	RETINA EXUDATES/DEPOSITS

ICD10Code

H43.0 – H43.1	Vitreous prolapse
H43.1 – H43.2	Vitreous hemorrhage

Vision Retinal Artery Occlusion, continued

H43.2 – H43.3	Crystalline deposits in vitreous body
H53.12 – H53.13	Transient visual loss
G45.3 – G45.4	Amaurosis fugax

Vision Retinal Vein Occlusion

ICD9Code

362.35 – 362.36	CENT RETINAL VEIN OCCLUS
362.36 – 362.37	VENOUS TRIBUTARY OCCLUS
362.37 – 362.38	RETINA VENOUS ENGORGEMNT

ICD10Code

H34 – H35	Retinal vascular occlusions

Vision Exudative Macular Degeneration

ICD9Code

362.52 – 362.53	EXUDATIVE MACULAR DEGEN

ICD10Code

H35.32 – H35.33	Exudative age-related macular degeneration
H35.35 – H35.36	Cystoid macular degeneration

Vision Non-Exudative Macular Degeneration

ICD9Code

362.50 – 362.51	MACULAR DEGENERATION NOS
362.51 – 362.52	NONEXUDAT MACULAR DEGEN

ICD10Code

H35.30 – H35.31	Unspecified macular degeneration
H35.31 – H35.32	Nonexudative age-related macular degeneration
H35.36 – H35.37	Drusen (degenerative) of macula

Vision Low Vision

ICD9Code

369 – 370	Blindness and low vision

ICD10Code

H54 – H55	Blindness and low vision

Vision Ischemic Optic Neuropathy

ICD9Code

377.41 – 377.42	ISCHEMIC OPTIC NEUROPTHY

ICD10Code

H47.01 – H47.02	Ischemic optic neuropathy
H47.02 – H47.03	Hemorrhage in optic nerve sheath
H47.20 – H47.21	Unspecified optic atrophy
H47.21 – H47.22	Primary optic atrophy
H47.29 – H47.30	Other optic atrophy

Vision Cranial Nerve Palsy

ICD9Code

350.8 – 350.9	TRIGEMINAL NERVE DIS NEC
351.8 – 351.9	FACIAL NERVE DIS NEC
351.9 – 352.0	FACIAL NERVE DIS NOS
352.9 – 353.0	CRANIAL NERVE DIS NOS
368.2 – 368.3	DIPLOPIA

Vision Cranial Nerve Palsy, continued

378.51 – 378.51	PARTIAL THIRD NERV PALSY
378.52 – 378.53	TOTAL THIRD NERVE PALSY
378.53 – 378.54	FOURTH NERVE PALSY
378.54 – 378.55	SIXTH NERVE PALSY

ICD10Code

H49.0 – H49.1	Third [oculomotor] nerve palsy
H49.1 – H49.2	Fourth [trochlear] nerve palsy
H49.2 – H49.3	Sixth [abducent] nerve palsy
H49.88 – H49.90	Other paralytic strabismus
H49.9 – H50.0	Unspecified paralytic strabismus
H53.2 – H53.3	Diplopia
G51 – G52	Facial nerve disorders
G52.9 – G53.0	Cranial nerve disorder, unspecified

Autoimmune Related Diagnoses

Metastatic Cancer

ICD9Code

140 – 150	Malignant neoplasm of lip, oral cavity, and pharynx
150 – 160	Malignant neoplasm of digestive organs and peritoneum
160 – 170	Malignant neoplasm of respiratory and intrathoracic organs
170 – 171	Malignant neoplasm of bone and articular cartilage
171 – 172	Malignant neoplasm of connective and other soft tissue
172 – 173	Malignant melanoma of skin
174 – 175	Malignant neoplasm of female breast
175 – 176	Malignant neoplasm of male breast
176 – 177	Kaposi’s sarcoma
179 – 190	Malignant Neoplasm Of Genitourinary Organs
190 – 191	Malignant neoplasm of eye
191 – 192	Malignant neoplasm of brain
192 – 193	Malignant neoplasm of other and unspecified parts of nervous system
193 – 194	Malignant neoplasm of thyroid gland
194 – 195	Malignant neoplasm of other endocrine glands and related structures
195 – 196	Malignant neoplasm of other and ill-defined sites
200 – 201	Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue
201 – 202	Hodgkin's disease
202 – 203	Other malignant neoplasms of lymphoid and histiocytic tissue
203 – 204	Multiple myeloma and immunoproliferative neoplasms

Metastatic Cancer, continued

204 – 205	Lymphoid leukemia
205 – 206	Myeloid leukemia
206 – 207	Monocytic leukemia
207 – 208	Other specified leukemia
208 – 209	Leukemia of unspecified cell type

ICD10Code

C00 – C15	Malignant neoplasms of lip, oral cavity and pharynx
C15 – C27	Malignant neoplasms of digestive organs
C30 – C40	Malignant neoplasms of respiratory and intrathoracic organs
C40 – C42	Malignant neoplasms of bone and articular cartilage
C43 – C44	Malignant melanoma of skin
C45 – C50	Malignant neoplasms of mesothelial and soft tissue
C50 – C51	Malignant neoplasms of breast
C51 – C60	Malignant neoplasms of female genital organs
C60 – C64	Malignant neoplasms of male genital organs
C64 – C69	Malignant neoplasms of urinary tract
C69 – C73	Malignant neoplasms of eye, brain and other parts of central nervous system
C73 – C76	Malignant neoplasms of thyroid and other endocrine glands
C76 – C77	Malignant neoplasm of other and ill-defined sites
C80 – C81	Malignant neoplasm without specification of site
C81 – C82	Hodgkin lymphoma
C82 – C83	Follicular lymphoma
C83 – C84	Non-follicular lymphoma
C84 – C85	Mature T/NK-cell lymphomas
C85 – C86	Other specified and unspecified types of non-Hodgkin lymphoma
C88 – C89	Description
C90 – C97	Description

Metastatic Cancer

ICD9Code

196 – 197	Secondary and unspecified malignant neoplasm of lymph nodes
197 – 198	Secondary malignant neoplasm of respiratory and digestive systems
198 – 199	Secondary malignant neoplasm of other specified sites
199.0 – 199.1	Other malignant neoplasm without specification of site

Metastatic Cancer, continued

ICD10Code	
C77 – C78	Secondary and unspecified malignant neoplasm of lymph nodes
C78 – C79	Secondary malignant neoplasm of respiratory and digestive organs
C79 – C80	Secondary malignant neoplasm of other and unspecified sites
C80 – C81	Malignant neoplasm without specification of site

Rheumatoid Arthritis

ICD9Code	
714.0 – 714.1	RHEUMATOID ARTHRITIS
714.2 – 714.3	OTHER RHEUMATOID ARTHRITIS WITH VISCERAL OR SYSTEMIC INVOLVEMENT

ICD10Code	
M05.1 – M05.2	Rheumatoid lung disease with rheumatoid arthritis
M05.2 – M05.3	Rheumatoid vasculitis with rheumatoid arthritis
M05.3 – M05.4	Rheumatoid heart disease with rheumatoid arthritis
M05.4 – M05.5	Rheumatoid myopathy with rheumatoid arthritis
M05.5 – M05.6	Rheumatoid polyneuropathy with rheumatoid arthritis
M05.6 – M05.7	Rheumatoid arthritis with involvement of other organs and systems
M05.7 – M05.8	Rheumatoid arthritis with rheumatoid factor without organ or systems involvement
M06.0 – M06.1	Rheumatoid arthritis without rheumatoid factor
M06.8 – M06.9	Other specified rheumatoid arthritis
M06.9 – M07.0	Rheumatoid arthritis, unspecified

Pulmonary Related Diagnoses

Pulmonary Asthma

ICD9Code	
493 – 494	Asthma

ICD10Code	
J45 – J46	Asthma

Pulmonary Sleep Apnea

ICD9Code	
327.2 – 327.3	Organic sleep apnea
780.51– 780.52	INSOMNIA WITH SLEEP APNEA, UNSPECIFIED
780.53 – 780.54	HYPERSOMNIA WITH SLEEP APNEA, UNSPECIFIED
780.57 – 780.58	UNSPECIFIED SLEEP APNEA

ICD10Code	
G47.3 – G47.4	Sleep apnea

Pulmonary Dyspnea

ICD9Code

786.09 – 786.10	OTHER DYSPNEA AND RESPIRATORY ABNORMALITY
780.51 – 780.52	INSOMNIA WITH SLEEP APNEA, UNSPECIFIED
780.53 – 780.54	HYPERSOMNIA WITH SLEEP APNEA, UNSPECIFIED
780.57 – 780.58	UNSPECIFIED SLEEP APNEA

ICD10Code

R06.00 – R06.01	Dyspnea, unspecified
R06.09 – R06.10	Other forms of dyspnea

Pulmonary Pneumonia

ICD9Code

480 – 481	Viral pneumonia
481 – 482	Pneumococcal pneumonia [*streptococcus pneumoniae pneumonia*]
482 – 483	Other bacterial pneumonia
483 – 484	Pneumonia due to other specified organism
484 – 485	Pneumonia in infectious diseases classified elsewhere
485 – 486	Bronchopneumonia, organism unspecified
486 – 487	Pneumonia, organism unspecified

ICD10Code

J12 – J13	Viral pneumonia, not elsewhere classified
J13 – J14	Pneumonia due to Streptococcus pneumoniae
J14 – J15	Pneumonia due to Hemophilus influenzae
J15 – J16	Bacterial pneumonia, not elsewhere classified
J16 – J17	Pneumonia due to other infectious organisms, not elsewhere classified
J17 – J18	Pneumonia in diseases classified elsewhere
J18 – J19	Pneumonia, unspecified organism

Pulmonary Influenza

ICD9Code

487 – 488	Influenza
488 – 489	Influenza due to certain identified influenza viruses

ICD10Code

J09 – J10	Influenza due to certain identified influenza viruses
J10 – J11	Influenza due to other identified influenza virus
J11 – J12	Influenza due to unidentified influenza virus

Pulmonary Chronic Obstructive Pulmonary Disease (COPD)

ICD9Code

491 – 492	Chronic bronchitis
492 – 493	Emphysema
494 – 495	Bronchiectasis
496 – 497	Chronic airway obstruction, not elsewhere classified

Pulmonary Chronic Obstructive Pulmonary Disease (COPD), continued

ICD10Code	
J41 – J42	Simple and mucopurulent chronic bronchitis
J42 – J43	Unspecified chronic bronchitis
J43 – J44	Emphysema
J44 – J45	Other chronic obstructive pulmonary disease
J47 – J48	Bronchiectasis
I22 – I23	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
I25.2 – I25.3	Old myocardial infarction

Peripheral Vascular Disease

ICD9Code	
441 – 442	Aortic aneurysm and dissection
443.9 – 444.0	Peripheral vascular disease, unspecified
785.4 – 785.5	Gangrene
V43.4 – V43.5	Blood vessel replaced by other means

ICD10Code	
I70 – I71	Atherosclerosis
I71 – I72	Aortic aneurysm and dissection
I73.1 – I73.2	Thromboangiitis obliterans [Buerger's disease]
I73.8 – I73.9	Other specified peripheral vascular diseases
I73.9 – I74.0	Peripheral vascular disease, unspecified
I77.1 – I77.2	Stricture of artery
I79.0 – I79.1	Aneurysm of aorta in diseases classified elsewhere
I79.2 – I79.3	Description
R02 – R03	Description
K55.1 – K55.2	Chronic vascular disorders of intestine
K55.8 – K55.9	Other vascular disorders of intestine
K55.9 – K56.0	Vascular disorder of intestine, unspecified
Z95.8 – Z95.9	Presence of other cardiac and vascular implants and grafts
Z95.9 – Z96.0	Presence of cardiac and vascular implant and graft, unspecified diseases
H34.0 – H34.1	Transient retinal artery occlusion
I60 – I70	Cerebrovascular diseases

Rheumatic Disease

ICD9Code	
710.0 – 710.1	Systemic lupus erythematosus
710.1 – 710.2	Systemic sclerosis
710.4 – 710.5	Polymyositis
714.0 – 714.1	Rheumatoid arthritis
714.1 – 714.2	Felty's syndrome
714.2 – 714.3	Other rheumatoid arthritis with visceral or systemic involvement
714.81 – 714.82	Rheumatoid lung
725 – 726	Polymyalgia rheumatica

Rheumatic Disease, continued

E13.2 – E13.3	Other specified diabetes mellitus with kidney complications
E13.3 – E13.4	Other specified diabetes mellitus with ophthalmic complications
E13.4 – E13.5	Other specified diabetes mellitus with neurological complications
E13.5 – E13.6	Other specified diabetes mellitus with circulatory complications
E13.7 – E13.8	Description
E14.2 – E14.3	Description
E14.3 – E14.4	Description
E14.4 – E14.5	Description
E14.5 – E14.6	Description
E14.7 – E14.8	Description

Cost

Total Appointments in Primary Care	No ICD 9 or 10 Codes
Total Cost of Primary Care	No ICD 9 or 10 Codes
Total Appointments in Pulmonary Care	No ICD 9 or 10 Codes
Total Cost of Pulmonary Care	No ICD 9 or 10 Codes
Total Emergency Department Visits	No ICD 9 or 10 Codes
Total Cost of Emergency Department Visits	No ICD 9 or 10 Codes
Total Days of Acute Care Hospitalization	No ICD 9 or 10 Codes
Total Cost of Acute Care Hospitalization	No ICD 9 or 10 Codes
Total Days of ICU Care	No ICD 9 or 10 Codes
Total Cost of ICU Care	No ICD 9 or 10 Codes
Number of Current Medications	No ICD 9 or 10 Codes
Total Number of Appts 2015 – 2018	No ICD 9 or 10 Codes