2020

Sex Bias in the Diagnosis of Chronic Obstructive Pulmonary Disease

Olga Ivan Belitchenko Ryan
Walden University

Walden University

College of Health Sciences

This is to certify that the doctoral study by

Olga Ryan

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

Review Committee
Dr. Vasileios Margaritis, Committee Chairperson, Public Health Faculty
Dr. Jeanne Connors, Committee Member, Public Health Faculty
Dr. Egondu Onyejekwe, University Reviewer, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

Walden University
2020

Abstract

Sex Bias in the Diagnosis of Chronic Obstructive Pulmonary Disease

by

Olga Ivan Belitchenko Ryan

MPH/MBA, Benedictine University, 2015

BS, University of Colorado, 2002

Doctoral Study Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Public Health

Walden University

May 2020

Abstract

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity, mortality, disability, and cost globally and in the United States. Various sources point to women experiencing greater morbidity, increased health care resource use and higher incidence of mortality resultant from COPD. While exact causality is not fully understood, it is possible that social bias towards COPD in women impacting screening and timely diagnosis may be a contributing factor. This current investigation involved the social ecological model. In this cross-sectional secondary analysis of Behavioral Risk Factor Surveillance System, 2017 data, differences in screening through use of breathing testing among 6334 males and females who have knowledge of COPD were assessed through descriptive statistics, Pearson's chi-squared test, and binomial logistic regression (BLR). Bivariate analysis indicated a marginally significant association between sex and participation in breathing tests ($\chi^2 = 3.44$, $p = 0.063$), disproportionately impacting women who used tests less. According to BLR models, females were 15.9% more likely not to take the breathing tests compared to males (*OR* = .841, *CI* 95%: 0.739-0.961) adjusted for COPD symptoms, and females were 11.7% more likely not to take the breathing test when controlling for healthcare coverage, but this result was marginally significant (*OR*=.883 *CI* 95%: .775-1.007). This study can offer insight into the use and patterns of breathing testing among the US population while further describing potential gaps in care, serving as catalyst towards driving necessary education, policy development and broader social change.

Sex Bias in the Diagnosis of Chronic Obstructive Pulmonary Disease

by

Olga Ivan Belitchenko Ryan

MPH, MBA, Benedictine University, 2015

BS, University of Colorado, 2002

Doctoral Study Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Public Health

Walden University

May 2020

Dedication

I humbly dedicate this work to my parents who instilled a passion towards academia and lifelong learning. Their hunger towards contributing to society is unprecedented and through these lessons, I have been privileged to grow up with these philosophies. As an immigrant, I am grateful for their ongoing challenge, support, and sacrifice. Moreover, this study is inspired by my children who continue to share their love for knowledge and wonder. I am equally grateful to my mentors and colleagues who have pushed and challenged me over my career.

Acknowledgments

I want to thank my faculty members for their guidance, patience, and dissemination of knowledge, all contributing to my personal and academic growth.

Table of Contents

List of Tables

List of Figures

Section 1: Foundation of the Study and Literature Review

World Health Organization, global authority in public health, has described chronic obstructive pulmonary disease (COPD) as one of the leading causes of morbidity, mortality, and cost globally and the United States (World Health Organization [WHO], 2017). In 2016, the global burden was estimated at 251 million cases, with a US footprint of roughly 27 million as described by the Centers for Disease Control and Prevention (CDC), US authority in public health (Centers for Disease Control [CDC], 2016). Little is understood about specific variances within the general population; however, mortality due to disease is dense in low-middle income countries, which is hypothesized to be somewhat related to environmental high levels of indoor and outdoor air pollution as well as exposure to tobacco (Quaderi, 2018). The American Thoracic Society suggests the next 15 years will elevate COPD as the primary killer globally when considering current societal exposure to tobacco and indoor air pollution while superimposing an aging population (ATS, 2018).

COPD is known to follow prolonged exposure to noxious particles, complicated by the slow onset of symptoms which progress in severity and persistency over time. For patients, symptoms of shortness of breath and cough take time to be recognized; typically, activity modification is implemented prior to seeking medical attention. These complexities contribute to patients' limited understanding of prevalence and diagnostic patterns; therefore, clinical interaction is necessary for testing and formal assessment. Moreover, COPD was perceived to be an illness mainly observed in men; therefore, inherent biases continue to burden attitudes towards women (WHO, 2019).

This study explored relationship between sex and subsequent diagnostic patterns in COPD to ascertain whether a sex bias, specifically regarding women, towards breathing testing exists. CDC's Behavioral Risk Factor Surveillance System (BRFSS) 2017 dataset was utilized for this secondary analysis to assess occurrence of diagnostic testing between males and females who were told by healthcare providers that they have COPD. This study should guide policymakers, clinicians, researchers, advocacy groups, and patient educators towards recognizing these intrinsic biases, their implication for patients' disease management, and quality of life. Moreover, necessary actions should be taken to reduce time to diagnosis and improvement in outcomes for all patients with COPD.

Section 1 explores rationale for investigation supported by an extensive literature review. Moreover, methodology and application to theory and practice are introduced. The following sections include the *problem statement, purpose of the study, research questions and hypotheses, theoretical foundation for the study, nature of the study, literature search strategy, literature review & variables, definitions, assumptions, scope and delimitations, significance, summary, and conclusions*.

Problem Statement

COPD has recently demanded attention from a multitude of stakeholders on a global and local scale, as burden of illness is alarming. Complicating the issue is the lack of consensus regarding capturing accurate prevalence of COPD prevalence (Diaz-Guzman, 2014). Because the illness is progressive, while symptoms of shortness of breath may have alternate causality, diagnostic testing through the use of pulmonary

function testing is recommended by governing expert panels (GOLD, 2020). Spirometry is a functional breathing assessment with minimal invasiveness; therefore, it is unlikely that early detection initiatives would cause harm. United States Preventative Task Force [USPTF] (2016) suggests that asymptomatic adults should not undergo screening even if at risk; instead, active "case finding" should be practiced by clinicians. Active case finding would prompt a clinician to recommend breathing tests if a patient has active and burdensome symptoms with a known risk factor. Out of the estimated 24 million individuals in the US with signs and symptoms of COPD, only 15.7 million actually have an accurate diagnosis (NIH, 2018). Underdiagnoses is problematic, as patients may be likely to delay treatment, suffering potentially negative outcomes. Chronic Respiratory Disease Collaborators (GBD) (2017) found an increase of over 11% in death causalities due to COPD since 1990, while overall age-related deaths have steadily declined.

American population does not experience COPD homogeneously; in fact, several societal trends are observed. Centers for Disease Control and Prevention (2012) suggests that Hispanics are less likely to report COPD in comparison to non-Hispanic whites and African Americans at 4% vs. 6.3% and 6.1%, respectively. Education level and employment status serve as protective; those with greater degrees of academic achievement and employment experience less disease burden. Disease patterns parallel those of population segments with higher observed incidents of smoking (CDC, 2012). Sex alone is a significant risk factor for both morbidity and mortality in COPD, as women are more likely to die as a result of the illness (Mannino, 2013).

Within the medical community, COPD was historically viewed as a disease predominately affecting Caucasian males (Dransfield, 2006). Within the century, cigarette consumption in the United States experienced rapid uptake by predominately Caucasian males during both world wars and the Great Depression. Following 1964 Surgeon General Report, steady declines in men were observed (U.S. Department of Health and Human Services [DHHS], 2014). In women, prevalence of smoking varied over the same time frame from 5-40%. Use of cigarettes by women, according to multiple surveys, consistently demonstrated a lower consumption rate (Office on Smoking and Health (US, 2001). Aside from social biases and behavioral trends, women are more likely to report symptoms and die as a result of COPD (NIH, 2018). COPD-related mortality decreased in men by 22 % between 2000 and 2014; progress in women decreased by 3.8% over the same period (CDC, 2018). Little evidence is available to describe illnesses specifically experienced by women and access to accurate diagnosis. This gap in understanding of social stigmatization of disease in women warrants further investigation to fully describe societal patterns and ramifications. The intent of this study was to evaluate differences in terms frequency of occurrences of diagnostic testing via breathing tests between men and women.

Purpose of the Study

Considering the immense variabilities in diagnostic patterns of COPD as well as potential impacts of sex bias, the objective of this investigation was to describe these patterns particularly as they relate to women at risk. This quantitative, cross-sectional analysis interrogated the BRFSS 2017 database to describe diagnostic patterns among

men and women; specifically, subjects who have been told by healthcare providers that they have COPD and response to breathing tests construct. Examination of these findings should inform researchers, clinicians, public health practitioners, and policy makers in driving social change. This may include education across societal sectors, working towards population screening, timely diagnosis and intervention for all patients at risk.

Research Questions and Hypothesis

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) promotes spirometry as a necessary diagnostic assessment contributing to the verification of COPD diagnosis. However, societal and organizational dynamics present potential barriers which disproportionally affect women. This study was intended to examine the prevalence of breathing tests among men and women who have been told by healthcare providers that they have COPD. It is hypothesized that less diagnostic testing will be observed in women, with potential greater presence of symptoms and activity limitations.

This study interrogated the 2017 BRFSS cohort, a national database surveying over 500,000 US adults across 50 states, thereby supporting generalizability of the study.

RQ1: Are there differences in terms of use of breathing tests between men and women who have been told by clinicians they have COPD?

H_o1: There are no differences in terms of use of breathing tests between males and females who have been by clinicians told they have COPD.

H_a1: There are difference in terms of use of breathing tests between males and females who have been told by clinicians they have COPD.

RQ2: Are there differences in terms of use of breathing tests between men and women who have been told by clinicians they have COPD and experience cough, phlem, and shortness of breath?

H_o2: There are no differences in terms of use of breathing tests between males and females who have been told they have COPD and experience cough, phlem, and shortness of breath.

H_a2: There are difference in terms of use of breathing tests between males and females who have been told they have COPD and experience cough, phlem, and shortness of breath.

RQ3: Are there differences in terms of use of breathing tests between men and women who have been told by clinicians they have COPD and access to healthcare?

H_o3: There are differences in terms of use of breathing tests between males and females who have been told by clinicians they have COPD and access to healthcare.

H_a3: There are differences in terms of use of breathing tests between males and females who have been told by clinicians they have COPD and access to healthcare.

Theoretical Foundation for the Study

Screening behaviors of clinicians and patients are driven by beliefs and attitudes, further reinforced by social and policy constructs. A model for this work must adequately represent the complexity of COPD diagnostic patterns and societal influences. Social Ecological Model (SEM) was applied to the study. Urie Bronfenbrenner in the 1970s developed the SEM to describe drivers of human development. Later, model further evolved into a theoretical framework delineating external influences on human

beliefs and actions (Kilanowski, 2017). This theoretical framework is grounded on individual attitudes and beliefs towards an idea; recognizing influence of interpersonal, organizational, community, and policy dynamics surrounding phenomena. SEM framework has been applied in many public health research and intervention initiatives to describe various phenomena while stimulating process improvement. The CDC has applied this model towards stimulating and driving participation in the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) for greater participation in screening.

The SEM can be implemented to describe flow of perception within the system involving sex-based trends in COPD screening. Recognizing systemic societal concerns involving COPD as they relate to women is essential.

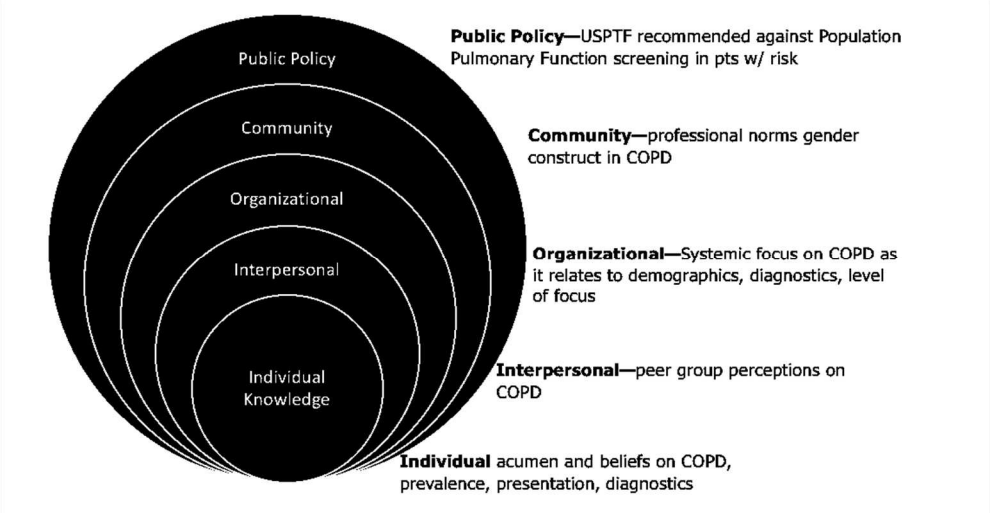

Figure 1. Social Ecological Model applied to societal biases in COPD

Nature of the Study

For this investigation, a cross-sectional, secondary, quantitative methodology was applied. CDC's BRFSS was established in the 1980s with the intent of collecting self-

reported behaviors and risks across the US populace; since its initiation with 15 participating states, data is collected via monthly telephone surveys across 50 states as well as the District of Columbia, American Samoa, Palau, Puerto Rico, US Virgin Islands, and Guam. With more than 500,000 case interviews for this broad population, , this data set is ideal for investigation and observation of potential trends. Participants in the survey were randomly selected adults who were 18 and older. A cross-sectional analysis was selected for this investigation due to the observational nature of the study. A descriptive analysis of the population was completed.

Literature Search Strategy

For this investigation, three primary databases, PubMed, Medline and ProQuest, were used with the assistance of two libraries (AstraZeneca Library Portal and Walden University). Key words used for the literature review were *chronic obstructive pulmonary disease*, *COPD*, *epidemiology*, *morbidity*, *mortality*, *healthcare cost*, *smoking*, *tobacco related illness*, *diagnosis*, *pulmonary function testing*, *sex*, *gender*, *social ecological model*, and *public policy*. I concentrated on recent literature published between 2013 and 2019. Studies describing COPD and diagnostic journeys experienced by women are significantly lacking, as is information about sex-related bias is limited.

Literature Review

Background

COPD is characterized by persistent airflow limitation which predominately results from biological processes subsequent to exposure of the lung to environmental risks, specifically prolonged tobacco smoking and household air pollution (ATS, 2018).

Obstruction of the airway is a product of tissue destruction, inflammation, and bronchial narrowing, all leading to the compromised ability of air to move in and out of the lung. Disease frequently presents as burdensome respiratory symptoms such as shortness of breath, coughing, and production of mucous leading to significant limitation of activity. Moreover, faster decline in lung function in these patients is observed. Exacerbations, periods of disease worsening, are frequent as the airway pathology is altered and can be easily triggered by common viruses and environmental pollutants.

Prevalence

Global burden of obstructive lung disease is estimated at 251 million cases, of which, roughly 27 million are in the United States (WHO, 2017). Generally, those of lower socioeconomic status are more likely to experience disease. Because illness progresses with symptoms developing over time, without advocacy for population wide screening, it is difficult to identify cases early.

The effect of COPD expenditures on US healthcare budget is exorbitant. In the year 2000, there were over 8 million outpatient visits, 1.5 million emergency visits, and 726,000 hospitalizations resulting from COPD (Mannino, 2017). Patients with COPD are also more likely to be re-hospitalized. Because patients with COPD have multiple comorbidities, direct and indirect costs are underestimated; patients may be hospitalized for other reasons which are further complicated by COPD. Patients with COPD have been reported to have a 22.8% burden of disability than those without, 7.3% (Mannino, 2017); as such, total medical expenditure is higher. End of life care for patients with COPD frequently requires intensive care, thereby leading to additional assumed costs.

Small-scale screening interventions have been successful in identifying patients earlier in the disease process. Broad scale screening programs for patients at risk for COPD may incrementally increase costs; however, intervention earlier promises to hinder the already burdensome and expensive trajectories.

Diagnosis and Treatment

GOLD (2018) suggests that patients with known risk and symptoms should undergo lung function testing, confirming diagnosis and establishing degree of airflow obstruction. Because breathing abnormalities can have varied pathologies, pulmonary function testing serves as proper confirmatory procedure. Disease severity is sequentially established based on degree of airflow obstruction, presence and burden of symptoms and risk for exacerbations.

Treatment of illness involves two main goals: reducing symptoms and limiting risks (GOLD, 2018). Nonpharmacologic treatment includes pulmonary rehabilitation as continuance of physical activity has exhibited positive outcomes in patients (McCarthy, 2015). Pharmacologically, vaccines and inhalations therapies for patients have shown both an improvement in lung function, reductions of exacerbations, and slowing of lung function decline (Celli, 2014). Reflecting on pharmacologic treatment patterns in the US, a tremendous opportunity to optimize exists. Diette and colleagues (2015) observed that 45% of COPD population was receiving maintenance therapy while 69% was on rescue treatment. It is possible that underdiagnosis and undertreatment are related as one may lead to the other; however, this is beyond the scope of this investigation. Additional

research is necessary to understand suboptimal treatment patterns across COPD patients, specifically, fragile groups such as women and those of lower socioeconomic status.

COPD and Trends in Women

Reflecting on the experience of women within the healthcare system, disproportionality across therapeutic areas is observed; suggesting that certain chronic diseases are faced to a greater burden and severity in this patient population (Smith 2013). Agency for Healthcare Research and Quality describes disproportionate trends in cardiovascular, metabolic, bone, psychiatric and HIV/AIDS in women, emphasizing nuances detected within female population are unfavorable while calling for much needed awareness, evidence generation and policy change (AHRQ, 2012). Several diseases are observed to present differently in women. For example, cardiovascular disease is the leading killer of men and women alike; however, 42% of women die within the first year following a heart attack in comparison to 24% of men (Agency for Healthcare Research and Quality [AHRQ], 2012). Women are more likely to receive delayed diagnosis and aggressive treatment in comparison to men (AHRQ, 2012). Observance of these important phenomena, both biologically and socially, have led to myriad of questions in multiple therapeutic areas with the intent of understanding causalities and possible opportunities.

Reflecting on current body of evidence specific to COPD patterns, similar distinctions are observed. While respectable gains through the reduction of COPD related mortality have been observed in men, the same target have been stagnant in women (Diaz-Guzman, 2014); COPD is the 4th leading cause of death in the United

States, however, in women, it's the 3rd (CDC, 2018). It is also apparent that women, commonly, have greater morbidity from the illness, defined through a greater utilization of the healthcare system. Mechanistically, some exploration has been done to understand the impact of tobacco exposure to the male and female lung. Certain epigenetic causalities are hypothesized, specifically, maternal exposure to fetus and hormones (Dransfield, 2006). Causality of maternal tobacco exposure to the fetus increases to the risk of offspring developing lung disease, severity is greater in female children. Additionally, certain evidence has pointed to tobacco exposure and sequential pathology. Interestingly, women cultivate disease with less noxious particle 'dose' as compared to men. A study by Nakano et al. utilized computed tomography techniques evaluating lung pathology, determining that women had greater pathology compared to men with similar and even less smoking exposure (Nakano, 2000). These distinctions are important for research as traditionally randomized trials in COPD require subjects 40 years of age and greater with 10-year smoking pack smoking history; this evidence suggests that tobacco exposure for women is potentially less, therefore, a significant proportion of female patients are under-represented in studies.

Publicly, COPD is accompanied by societal bias. Because the illness is considered a product of a health hazardous behavior, a perception of "fault" is not uncommon among society. This sensitivity is potentially detrimental for patients as they are discouraged from and ashamed to seek care and therefore delay interventions. Collectively, this is further complicated by an unspoken bias within the healthcare community possibly affecting both appropriate diagnosis and treatment (Mamary, 2018).

The majority of research continues to regard COPD as a disease primarily observed in men. Chapman and Tashkin (2001) said "only 57% of physicians offered COPD as the most likely diagnosis following presentation of the history and physical examination…[furthermore] COPD was significantly more likely to be offered as the provisional diagnosis for the hypothetical male patient than the hypothetical female patient" (p. 1693). In a recent study by the COPDGene group it was also noted that women generally manifest greater burden of symptoms and earlier in age as compared to males (DeMeo, 2018). It is unknown however how presence of symptoms and risk translate to diagnostic patterns. Aggregating signals point to sex differences in the prevalence, susceptibility to, severity of, and response to treatment and management of chronic obstructive pulmonary disease. This gap may be specifically problematic for women, for example, because they may not be adequately informed of the symptoms of COPD, appropriately screened for the disease, or receive appropriate interventions and treatment.

Definitions

Chronic Obstructive Pulmonary Disease (COPD): A common, preventable, and treatable disease of the respiratory system involving persistent symptoms and airflow limitations due to airway abnormalities typically caused by prolonged exposure to noxious particles and gasses (GOLD, 2018).

Gender: Socially accepted characteristic of males and females which involve physically observable traits, norms, and societal roles (WHO, 2019).

Gender Bias: In the context of healthcare, gender bias is prejudice in terms of perceptions

Health Care Resource Use: Consumed services or goods used by patients resulting from interactions between patients and the healthcare system (Da Silva, 2011).

Pulmonary function testing/Spirometry: A group of breathing tests evaluating air flow, lung volumes, gas exchange, and inflammatory markers (NIH, 2018).

Sex: A biological characteristic typically assigned at birth describing natural chromosomal, internal, and external reproductive organs (APA, n.d.).

Smoking Pack History: A calculation of number of packs smoked per day for the number of years a subject has smoked (GOLD, 2018).

Assumptions

Reflecting on observed prevalence, mortality trends in women, as well as known generalized perceptions about COPD, subjects' sex may have an influence on diagnostic patterns. BRFSS 2017 patient population were queried regarding symptoms of obstructive lung disease and knowledge regarding COPD according to healthcare providers. Additionally, subjects reported undergoing breathing testing suggested use of a screening tool to support the diagnosis as per GOLD recommendations. No known recall bias was described between males and females pertaining to disease and diagnosis history; therefore, it was assumed that trend comparison is acceptable.

Scope and Delimitations

Considering the design of the study and nature of the dataset, this examination was cross-sectional design and descriptive, aiming to determine COPD- related

diagnostic patterns, specifically as they are observed between males and females. The study population included male and female participants who were able to read and write and therefore could self-report their medical history. The BRFSS 2017 queried participants in 50 states across the US, the District of Columbia, American Samoa, Palau, Puerto Rico, US Virgin Islands, and Guam; therefore, the breadth of the patient population allowed deductions to be generalizable at the national level. The original dataset enrolled subjects engaging with the survey team, and therefore no selection bias was observed, and the sample was representative of the general population. For this analysis, participants were male and female respondents who have been told that they have COPD and have responded to breathing tests query. Understanding of illness is complex and can be dependent on perceptions towards disease, access to healthcare, and biases within the healthcare system, and as such, signals within this investigation were intended to be descriptive, rather than point to causality. Further exploration of causality may be warranted, driving potential opportunities for intervention and social change.

Study Boundaries

Selection bias is a significant limitation of this study. As with most secondary analyses, there is little influence on the study population, constructs collected, and methodology utilized for collection and data entry; therefore, variable analysis relies on participant reported history rather than authentic medical record. Original data surveyed subjects across general health, risks and utilization of resources; COPD being a module within the general survey, data is not specific towards a targeted COPD population. It is described that patients may understand, and experience disease differently, therefore may

not be generalizable to the broader population who is symptomatic, yet not engaging within the healthcare system for care. Additionally, because BRFSS 2017 is a US specific dataset, description may only allude to patterns in the US. Utilizing caution when interpreting these is warranted as subject numbers within the specific nations are not balanced.

Generalizability and Scope

BRFSS captured survey responses from the broader population of US and its territories, as such, generalizability of results may be imposed on the general population within surveyed geography. Because this population is gathered in a non-clinical setting, trends may be generalizable to mainstream population, as opposed to limiting to only those seeking care for their illness. Scope of investigation was to subjects who have been told by healthcare provider that they may have COPD, with rest of the cases excluded to focus on relevance to research question. Confounders of study include geographical influences, race-ethnicity, cultural beliefs around COPD, socioeconomic factors, education, and marital status. With the utilization of the 2017 dataset, previous trends were not investigated.

Significance of the Study

Significance to Theory

SEM allows for a deconstruction of an observed phenomena across layers of society. On a macro level, recognizing overall under-diagnosis patterns, particularly as experienced by women, can guide a shift in public policy towards population screening and overall stigmatization of this disease. At the core are individual beliefs by both

clinicians and patients alike. Similarly replacing views of sex bias in prevalence driving towards timely diagnosis stands the capability to impact interpersonal, organizational and community norms. The intent is to drive public acceptance and policy around COPD as it relates to women while synergizing with grass roots efforts on an individual level.

Significance to Practice

Recognizing sheer burden of COPD in the United States, alarming indicator of staggering under-diagnosis, complicated by societal biases towards disease in women warrants further investigations in terms of understanding diagnostic patterns and possible ramifications. Examining time to diagnosis, disease severity upon diagnosis as experienced by male and female patients can offer necessary evidence to guide further research and potential intervention across societal sectors with the intent of changing attitudes and beliefs towards COPD with the anticipated behavior change of timely diagnosis and population wide screening policy.

Significance to Social Change

The USPSTF has been a loud opposing body to COPD screening programs. Following their systematic review, the group recommended against screening asymptomatic patients for COPD, suggesting that benefits do not outweigh risks (USPSTF, 2016). Their work in evaluating currently available data is respectable yet fails to consider success and long-term impact of previously executed programs. The USPSTF, fails to consider the magnitude of undiagnosed COPD patients. An investigation by Martinez and colleagues discovered that patients who don't have a diagnosis have a greater risk of mortality resulting from COPD (Martinez, 2015).

Reflecting on general epidemiologic trends, impact of delays to diagnosis has also been correlated to greater morbidity and lower quality of life (Diaz-Guzman, 2014). It must also be noted that previously executed screening programs in different therapeutic areas have shown capability to halt these trajectories.

Clearly, this particular issue bears a significant magnitude of scientific merit and advocacy, yet, has been less than successful in becoming a political priority. Much of this, possibly, is the discouragement by the USPSTF. Moreover, because screening programs are expensive, political support and therefore fund allocation is necessary. An upstream approach to burdens observed resulting from COPD could provide a long term, sustainable solutions. As such, a consideration and politicization of COPD screening programs is essential.

Borrowing a page from the history of breast cancer, a leading cause of cancer in women, much is to be celebrated in the proposal and adoption of Breast Cancer Screening Programs. Through the work of cross collaborative stakeholders, including the ACS, guideline agencies, and US DHHS, breast cancer screening policies and sequential interventions have been successful in identifying early disease in women. Through the identification of early cases, more women have survived the diagnosis. Similarly, upstream policies encouraging broad screening for COPD, translated in practice by the medical and research communities stand the capability of making an impact on the current trajectories. As is recommended by the GOLD, American Thoracic Society and European Respiratory Society, pulmonary function testing must be offered to patients with a risk factor for COPD. Evidence from this investigation can further elevate the

hypothesized delay to diagnosis as experienced by women, leading awareness, intervention, policy and social change.

Summary

COPD represents a significant problem to society as the prevalence is high, heterogeneously impacting the population. Women have been observed to have greater morbidity and mortality resultant from the illness. Understanding nuances in terms of confirmatory breathing testing between males and females can offer important insights regarding practice patterns and potential biases towards illness. Additionally, the impact of symptoms and healthcare coverage further provides information regarding these important tests. With prevalence and morbidity trends projected to continue increasing, while significantly contributing to the already stretched healthcare expenditure budget, recognizing nuances within the population may serve as a relevant springboard to myriad of stakeholders. Recognizing sex differences and experience with COPD may further guide education and advocacy initiatives, perhaps mitigating or preventing previously engendered societal biases.

Section 2: Research Design and Data Collection

Introduction

COPD prevalence in the United States is underreported, largely due to underdiagnoses and barriers toward screening. While some heterogeneity is apparent within the general population, women continue to experience greater morbidity and mortality. In the United States, more women die as a result of COPD, a trajectory that has increased steadily over the last decade (CDC, 2018). The current study intended to describe use of breathing tests among women who have been told by healthcare providers they had potential COPD. Acknowledging patterns towards lung function testing can describe whether a latent sex bias towards this diagnostic and treatment tool exists, possibly leading towards future exploration and intervention. Section 2 includes; *Research Design and Rationale, Methodology, Population, Sampling and Data Collection Procedures, Instrument and Operationalization of Constructs, Threats to Validity, Ethical Procedures, and a Summary.*

Research Design and Rationale

This study aimed to describe patterns involving breathing testing between males and females who have knowledge of COPD. Because spirometry is a key diagnostic tool and drives treatment decisions, variances based on sex can be instrumental in partially describing disease outcomes. The independent variable in this study was sex as both men and women can develop COPD. The dependent variable was use of breathing tests among the population of subjects who have been told that they may have COPD, emphysema, or chronic bronchitis. Moderating variables were symptoms such as

shortness of breath, cough and production of phlegm. Additionally, sociodemographic factors such as socioeconomic level, education, and presence or absence of healthcare coverage were considered moderating variables as these can impact access to pulmonary function testing.

Methodology

Population

BRFSS 2017, collected by the CDC, was the data source utilized for this secondary analysis. Subjects who had been told they had COPD served as the primary analysis population. Furthermore, responses to breathing tests module and age parameter were imposed. Based on the codebook provided by the CDC, final sample size for this investigation was 6,334 cases.

Sampling and Data Collection Procedures

In order to prevent selection bias, a broad selection strategy was employed by the CDC for outbound calling to subjects targeted by the BRFSS sampling strategy. The entire 2017 data set included 450, 016 cases; of these, 37, 577 were told they had COPD. To further aid in appropriate cohort selection, participants were all older than 35 and had received breathing tests. Subjects within BRFSS- targeted areas had an equal chance of being invited to participate in the survey and give consent for participation. The initial dataset was entered and maintained by the CDC.

Sampling frame. Sampling frame included (a) adults surveyed by BRFSS in 2017, (b) ages 18 years and older, (c) all reported races and ethnicities, and (d) those responding “yes” to “(Ever told) you have chronic obstructive pulmonary disease,

C.O.P.D., emphysema, or chronic bronchitis?" (CDC, 2018). The COPD cohort was extracted from the total population in the database, who have a myriad of non-respiratory diseases and should not undergo spirometric testing. Sample also excluded younger cohort (35 years and less) as COPD is unlikely below this age lacking further pathology (CDC, 2018). Selecting the study population was based on a broad and generic question such as "having been told of COPD", provided the best strategy to eliminate bias introduced by covariates such as severity of disease, incidence of tobacco use, access to care, environmental exposures and behavioral perceptions as the latter should all be equally represented within the chosen analysis set. This specific cohort of subjects underwent described sensitivity testing.

Data accessibility and permission. The BRFSS is an open source dataset and can be accessed through the CDC website (BRFSS, 2018). Data use agreement described by the CDC for research purposes and coordinated by the Institutional Review Board (IRB) at Walden University, described in the ethics section. Primary dataset collected for the purposes of public health surveillance, so, informed consent was exempt.

Power analysis. Since this was a descriptive cross-sectional analysis, all subjects meeting the proposed criteria were analyzed and post hoc power analysis was conducted to confirm that the achieved statistical power was adequate (>80%).

Research Questions and Hypotheses

RQ1: Are there differences in terms of use of breathing tests between men and women who have been told by clinicians they have COPD?

H_o1: There are no differences in terms of use of breathing tests between males and females who have been by clinicians told they have COPD.

H_a1: There are difference in terms of use of breathing tests between males and females who have been told by clinicians they have COPD.

RQ2: Are there differences in terms of use of breathing tests between men and women who have been told by clinicians they have COPD and experience cough, phlem, and shortness of breath?

H_o2: There are no differences in terms of use of breathing tests between males and females who have been told they have COPD and experience cough, phlem, and shortness of breath.

H_a2: There are difference in terms of use of breathing tests between males and females who have been told they have COPD and experience cough, phlem, and shortness of breath.

RQ3: Are there differences in terms of use of breathing tests between men and women who have been told by clinicians they have COPD and access to healthcare?

H_o3: There are differences in terms of use of breathing tests between males and females who have been told by clinicians they have COPD and access to healthcare.

H_a3: There are differences in terms of use of breathing tests between males and females who have been told by clinicians they have COPD and access to healthcare.

Instrumentation

BRFSS is a publicly funded open source database operationalized by the CDC; this study used the 2017 survey. BRFSS is populated by random digital dialing across all

the states and US territories, collecting health related risk behaviors, chronic health conditions and use of preventive services. The BRFSS completed more than 400,000 interviews per year making it the largest continuously conducted health survey. Such a database was the optimal tool to answer the research question within this study, due to its broad US representation, the breadth of captured data and continuous data acquisition, thus making this generalizable across the US. The BRFSS is used by various stakeholders and researchers to evaluate behavioral population trends as well as chronic disease patterns on both state and federal levels.

Operationalization of Variables

Table 1 describes relevant demographic variables explored in this investigation. Account of age, race/ethnicity, marital status, income and education level will offer description of patient population of interest.

Table 1

Demographic Variables of Interest

Name	Type of measurement	Definition	Variable
Age (confounder)	Nominal	Years of life at time of survey	3=35-44 years 4=45-54 years 5=55-64 years 6=65 and up
Race/ethnicity (confounder)	Nominal	Reported race and ethnicity	1=non-Hispanic White 2=non-Hispanic Black 3=Hispanic 4=All Others
Marital Status	Nominal	Marital Status	1=Married

(table continues)

(confounder)			2=Divorced 3=Widowed 4=Separated 5=Never married 6=Unmarried
Income (confounder)	Nominal	Annual household income (all sources)	1=less than $10,000 2=less than $15,000 3=less than $20,000 4=less than $25,000 5=less than $35,000 6=less than $50,000 7=less than $75,000 8= $75,000 of more 77=don't know 99=refused
Education Level (confounder)	Nominal	Highest grade or year of school completed	1=never attended school, only kindergarten 2=grades 1-8, elementary 3=grades 9-11, some high school 4=grade 12 or GED, high school graduate 5=college 1-3 years, some college 6=college 4 years or more,

(table continues)

			college graduate 9=refused

Table 2 describes variables necessary to operationalize research questions. Variables include sex, receipt of breathing tests to diagnose breathing problem, and COPD related symptoms of cough, phlegm, and shortness of breath. Additionally, years of smoking and access to health insurance will be interrogated as cofounders.

Table 2

Operational Definitions of Variables

Name	Type of measurement	Definition	Variable
Sex (independent)	Nominal	Sex of respondent	1=Male 2=Female 9=Refused
Breathing Tests (dependent)	Nominal	Given a breathing tests to diagnose breathing problems	1=Yes 2=No
Cough (covariate)	Nominal	Symptoms of cough on most days in last 3 months	1=Yes 2=No 7=Don't know 9=Refused
Phelm (covariate)	Nominal	Symptoms of phlem on most days in last 3 months	1=Yes 2=No 7=Don't know 9=Refused
Shortness of breath (covariate)	Nominal	Shortness of breath when hurrying on level ground or	1=Yes 2=No 7=Don't know

(table continues)

		walking up hill/stairs	9=Refused
Health Insurance (covariate)	Nominal	Presence of health insurance (HMO/government)	1=Yes 2=No 7=Don't know 9=Refused
Smoking History (covariate)	Nominal	Lifetime years of smoking tobacco products	1-76=Yes 88=Never smoked, less than 1 year 77=Don't know/not sure 99=Refused

Independent Variable. In this study, sex was the independent variable. Sex attributes were obtained directly from the BRFSS database.

Dependent variable. Utilization of breathing tests among the population of subjects who have been told that they may have COPD, emphysema or chronic bronchitis served as the dependent variable. Breathing tests construct was obtained in a binary manner. Cases who had a response of yes or no to this module were selected for analysis

Covariates. The presence of symptoms such as shortness of breath, cough and production of phlegm, were considered as covariates due to potential influence on driving medical decision towards a breathing tests. Additionally, presence/absence of health care coverage can be considered moderating as these can impact access to healthcare sequentially testing. These variables can be analyzed as partially mediating or completely mediating based on the static nature of either the independent or dependent variable.

Study population and missing cases. Study population of subjects with knowledge of COPD, emphysema and chronic bronchitis was isolated from the parent

2017 BRFSS data set, yielding 37, 577 cases for investigation; described in Table 3. Further inclusion criteria of age and response to breathing tests module were applied, Figure 2. Considering no significant missing cases were present within the study population, no additional mitigation procedure was necessary.

Table 3

Subjects with COPD, Emphysema, or Chronic Bronchitis

	Frequency	Percentage	Weighted Percentage
Yes	37,577	8.35	6.51
No	410,141	91.14	93.00
Don't know	2,099	0.47	0.46
Refused	197	0.04	0.03
Not Asked, missing	2	-	-

Data Analysis Plan

Analysis Techniques

All variables used for investigation are nominal, and therefore appropriate techniques were employed to describe the population while evaluating by SPSS 25 statistical software.

Descriptive statistics. The population of interest was described by assessing frequencies, proportions, and percentages within the broad cohort of subjects who have been told they have COPD, emphysema or chronic bronchitis.

Bivariate analysis. I used bivariate chi-square methodology for RQ1, assessing relationships between males and females who have received a breathing tests. The dichotomized phenomena of interest, breathing test, requires Pearson's chi-square test as the primary bivariate analysis (Science Direct, 2019).

Multivariable analysis. Multivariate analysis allows for focus on multiple variables of interest and appropriate methodology for RQ2 & RQ3 in assessing relationship between opportunity of breathing tests among males and females with COPD related symptoms and presence of health insurance, respectively. For this test, BLR was the appropriate methodology (Laerd, 2018).

Rationale for Covariate Inclusion

Inclusion of population demographics such as age, race/ethnicity, income and level of education as it relates to opportunity towards a breathing tests is a confounding factor as these may influence health literary and therefore understanding of necessity to engage with the healthcare system. As important upstream determinants of health, covariates must be considered within the investigation.

Interpretation of Results

Interpretation of results was based on odds ratios of receiving a breathing tests between males and females. Secondarily, odds ratios of receiving breathing tests in the presence/absence of health insurance and applicable symptoms was assessed. Analyses was considered at 95% confidence intervals. All statistical analysis were performed by SPSS version 25 available through Walden University.

Threats to Validity

BRFSS is a comprehensive US generalizable dataset, yet has several limitations requiring notice. Primarily, subject selection methodology is random to non-institutionalized adults 18 years and older selected via outbound calling; subjects wishing not to participate may have unique attributes and are excluded from the dataset. Additionally, because the variables are collected via self-reported survey, validity of recall, non-response, health and literacy, missing information may all impact validity of the investigation.

External Validity

Respective to external validity, broader generalizability of investigation was considered. With a broad subject footprint across BRFSS collection territories, inferences drawn from this investigation may describe breathing tests patterns across the US between males and females while also considering influence by COPD related symptoms and presence of health insurance. Potential threats to external validity include penitential selection bias in the subject population as BRFSS is a wide surveillance instrument, as opposed to a specific COPD focused data set.

Internal Validity

Internal validity assesses the capacity of the data set to accurately support the research question. In this investigation, due to the survey nature of the data set, subject recall bias may have posed a potential threat. Additionally, subjects may fail to accurately understand COPD related questions and either under or over report their

disease as well as testing and symptomatology. Internal validity was confirmed as much as possible by using BLR.

Ethical Procedures

This study underwent an expediated Walden Institutional Review Board review due to the deanonymized nature of the data and lack of active intervention arm (approval # 08-08-19-0628769). Data were collected by the CDC according to the ICH and broad clinic research standards. All data were handled in a sensitive and secure manner. There was no active collection of samples, or identifiable HIPPA protected health information. All data will be kept in two step authenticated electronic media for 5 years. However, this is an open source dataset and the integrity of the data is maintained and cannot be manipulated, creating any additional risk.

Summary

Section 2 described methodological details implicating this investigation. By statistical testing, signal towards receiving a breathing tests between males and females was evaluated. Influence of COPD-related symptoms and presence of health insurance as covariates were assessed. Ethical considerations and mitigations were discussed. In Section 3, a description of the population and study results are presented.

Section 3: Presentation of the Results and Findings

Introduction

COPD is prevalent and burdensome, demanding attention from multiple stakeholders, including patients, families, society, healthcare system, and policy makers. Even though COPD is non-selective in terms of sex, meaning both males and females can develop the illness, morbidity and mortality are experienced differently by women (DeMeo, 2018). In the last decade, there is an observed divergence in mortality resulting from COPD, with women leading in terms of number of deaths (CDC, 2015). Mainly as a byproduct of long-standing societal beliefs and perceptions involving tobacco smoking, females are perceived to be less likely to have COPD then their male counterparts. Section 3 includes bivariate and chi-square analyses assessing breathing tests trends among men and women who have been told by a healthcare provider that they have COPD. Additionally, the influence of common COPD symptoms such shortness of breath, phlem, and coughing and presence of health insurance were evaluated through multivariable analysis. Finally, an explorative quasi-simulation of USPTF spirometric recommendation of active case finding was conducted via chi-square analysis between males and females who admit to having all COPD-related symptoms. Also, in this section, a summary of all findings will be included.

Data Collection of Secondary Data Set

CDC coordinated via random telephone samples health-related behavior and chronic disease data across 50 states and territories by the annual BRFSS. Sampling for

these data sets involved both land and cellular outbound random calls to noninstitutionalized adults who were older than 18. The current study used 2017 data.

Time Frame and Response Rates

Data collection for the 2017 cohort was operationalized between January 1 and December 31, 2017. The Pew Research Center (2012) determined that telephone survey participation rates continue to decline in comparison to live surveys. CDC has managed to produce a dataset with comparable and higher than average participation while balancing representation of landline and cellular participants, with rates of 45.3% for landline and 44.5% for cellular participants. Furthermore, sample-weighing methodologies promote overall population appropriateness and overall generalizability. The total combined BRFSS 2017 sample prior to study cohort extraction was 450,016 cases.

Discrepancies in the Data Set

The original dataset lacked specificity to the research questions respective to participation in breathing tests as diagnostic procedure for COPD in cases who have been told that they have the illness. A specific cohort to support analysis was extracted; inclusion methodologies described in Figure 2.

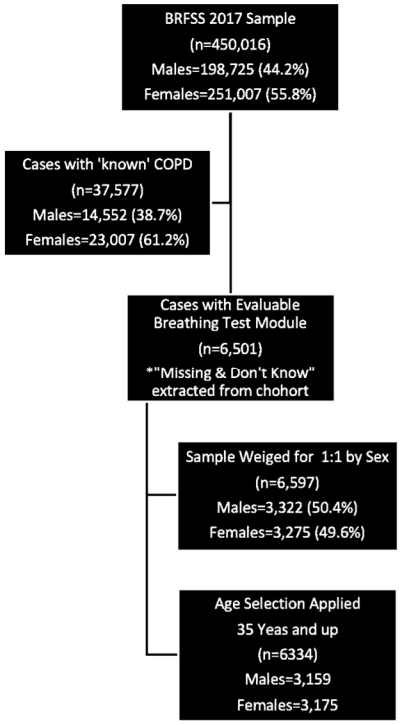

Figure 2. Study cohort selection algorithm

From the initial sample, cases who responded 'yes' to knowledge of COPD yielded 37, 577 cases, or 8.35% of the cohort. Because screening breathing tests is seldomly utilized for reasons aforementioned in general practice, and the research question is anchored on knowledge of this procedure, those cases with the missing/don't know/refused response to 'Have you ever been given a breathing tests to diagnose breathing problems?' were extracted, producing 6,501 evaluable cases. Within this cohort, 61.7% were responses from women; male and female cases were weighed 1:1, giving an equal opportunity for evaluation between the sexes. Because COPD develops in adulthood, pediatric and adolescent cases were removed, only allowing participation of subjects 35 years and older. The final evaluable cohort of n = 6334 was used for analysis.

Descriptive Demographics and Univariate Analysis of Sample

The study sample demographics are described in Table 4. The majority of the sample was over the age of 55 and therefore appropriate for the disease under investigation. While diverse ethnicities are represented, the majority of the sample is Caucasian. Most of the sample is married, divorced, or widowed. Distribution of income is heterogeneous, and the sample represents a diverse socioeconomic cohort. A large proportion of the sample has completed high school and some college.

Table 4

Cohort Demographics

Variable	Males		Females	
	N	%	N	%
Age	(3129)	50.0	(3124)	50.0
35-44 years	178	5.7	180	5.8
45-54 years	378	12.1	439	14.0
55-64 years	926	29.6	847	27.1
65 and up	1647	52.6	1659	53.1
Race/Ethnicity				
White	2538	81.1	2516	80.5
Black	228	7.3	261	8.4
Other, non-Hispanic	104	3.3	100	3.2
Multiracial	83	2.6	66	2.1
Hispanic	103	3.3	113	3.6
dk/refused	74	2.4	68	2.2
Marital Status				
Married	1471	47.0	1038	33.2
Divorced	750	24.0	773	24.7
Widowed	401	12.8	877	28.1
Separated	101	3.2	131	4.2
Never married	317	10.1	223	7.1
Unmarried	75	2.4	61	2.0
Refused	13	0.4	23	0.7
Income				
<$10,000	225	7.2	321	10.3
<$15,000	286	9.1	356	11.4

(table continues)

<$20,000	404	12.9	377	12.1
<$25,000	364	11.6	366	11.7
<$35,000	317	10.1	309	9.9
<$50,000	384	12.3	310	9.9
<$75,000	358	11.4	240	7.7
>$75,000	382	12.2	202	6.5
Don't know	211	6.7	402	12.9
Refused	199	6.3	241	7.7
Education Level				
Never attended school, only kindergarten	4	0.1	6	0.2
Grades 1-8, elementary	157	5.0	131	4.2
Grades 9-11, some high school	318	10.2	346	11.1
Grade 12 or GED, high school graduate	1051	33.6	1075	34.4
College 1-3 years, some college	878	28.0	1006	32.2
College 4 years or more, college	708	22.6	549	17.6
Refused	13	0.4	12	0.4

General health history and access to healthcare coverage is described in Table 5. Few participants described being in excellent health. A larger percentage of the population, ≥ 50% report fair and poor general health. The majority of the cohort, ≥ 90%, acknowledge some presence of healthcare coverage. The type of insurance is beyond the scope of this study.

Table 5

Related Health History

Variable	Males		Females	
	N	%	N	%
General Health	(3129)	50.0	(3124)	50.0
Excellent	121	3.9	97	3.1
Very Good	389	12.4	400	12.8
Good	897	28.7	864	27.6

(table continues)

Fair	930	29.7	994	31.8
Poor	779	24.9	758	24.3
Don't Know	11	0.3	9	0.3
Refused	1	0.0	3	0.1
Health Care Coverage				
Yes	2904	92.8	2910	93.2
No	221	7.1	209	6.7
Don't Know	3	0.1	2	0.1
Refused	1	0.1	2	0.1

Table 6 portrays COPD related history of the sample. Unitarization of smoking tobacco is explained by the lifetime tobacco history of utilization between 1-76 years; 81.3% of males suggest they have smoked within the specified range and only 69.1% of women. Conversely, 26.1% of the women indicate never smoking, or less than 1-year exposure, far less than males. A mere 15.4% fit within this description. While this cohort is all cases who have COPD, far less exposure to tobacco is observed in women.

Table 6

COPD Related History

Variable	Males		Females	
	N	%	N	%
Lifetimes Years of Smoking Tobacco	(3129)	50.0	(3124)	50.0
1-76 years	2545	81.3	2161	69.1
Never smoked/less than 1 year	480	15.4	815	26.1
Don't know	99	3.2	139	4.4
Refused	5	0.2	9	0.3
Previous Diagnosis of Asthma				
Yes	967	30.9	1386	44.4
No	2132	68.1	1719	55.0
Don't Know	30	1.0	19	0.6
Presence of Cough				
Yes	1563	50.0	1733	55.5
No	1555	49.7	1381	44.2

(table continues)

Don' Know	11	0.3	7	0.3
Presence of Shortness of Breath				
Yes	2230	71.3	2428	77.7
No	883	28.2	678	21.7
Don't Know	14	0.5	17	0.5
Refused	1	0.0	1	0.0
Presence of Phlem				
Yes	1489	47.6	1484	47.5
No	1617	51.7	1623	52.0
Don't Know	22	0.7	16	0.5

Far less men, 30.9%, reported a previous diagnosis of asthma in comparison to 44.4% of women. Shortness of breath appears to be the most commonly described COPD symptom among men and women, with over 70% of both sexes reporting. Cough and phlem are experienced by both males and women similarly at over 45% for all.

Representativeness of the Sample

BRFSS 2017 captured landline and cellular phone respondents across all 50 States as well as US Territories. Within this sample, 8.35% of the cases reported having COPD; CDC reports state specific prevalence ranging from 5%-9%. This cohort is representative of national trends. Initial sample overrepresented women, similarly, exhibiting what is commonly observed. Demographics of the cohort specific to age, socioeconomic status, marital status, level of education and access to healthcare are all generalizable to nationally reported data for this patient population (CDC, 2016).

Study Results

Recognizing the observance of COPD related symptoms as well as presence of healthcare coverage within the sample, inclusion of these constructs within the model is

justified. The following subsections include statistical assumptions and results of the three research questions as well as explorative analysis.

RQ1

RQ1 tested for a difference in the utilization of breathing tests between men and women who have been told by a clinician that they have COPD.

Statistical assumptions. For RQ1, Pearson's chi-square test was applied. Six assumptions for a chi-square test are (a) data reported as frequencies or counts, (b) variables are mutually exclusive, (c) each case may only be counted once, (d) study groups are independent, (e) variables are dichotomous and categorical & (f) values of cell expected should be five or more in at least 80% of the cells (McHugh, 2013). All necessary assumptions for this test are met as data are categorical, mutually exclusive, cases independently represented, and more than five cell counts are analyzed.

Crosstab and effect size results. Table 7 displays bivariate analysis for RQ1. Of the overall cohort, 82.56% of the cases have reported participation in a breathing tests. However, there appears to be a difference in utilization of breathing tests between males and females, with chi-square p-value approaching significance of $p<0.063$. To further support findings from the initial chi-square analysis, Fisher's Exact Test (utilized to determine whether a non-random association exists between two categorical variable) suggested a significant $p<0.034$. Cramer's V computation produced an effect size= 0.023, suggesting a moderate association between sex and breathing tests.

Table 7

Bivariate Characteristics of Breathing Tests Procedure

	Received Tests *n (%)*	Not Received Tests *n (%)*	X^2	P-value	Fisher's Exact	Cramer's V
Sex						
Males	2111 (83.4)	518 (16.6)				
Females	2552 (81.7)	573 (18.3)				
			3.444	<0.063	<0.034	0.023 (<0.063)

Figure 3 visually displays responses of males and females respective to experience with breathing tests. There are less women receiving a breathing tests.

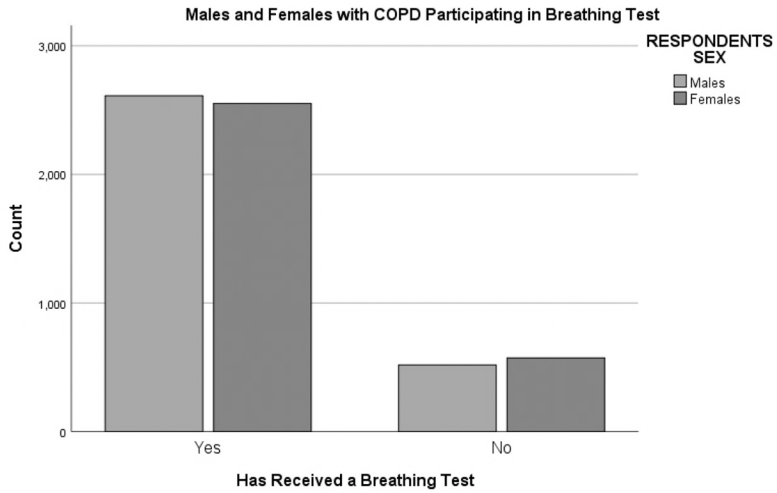

Figure 3. Prevalence of breathing tests between males and females

Hypothesis test results. There is a moderately significant association between independent variable of sex and dependent variable of participation in breathing tests (χ^2 = 3.44, p = 0.063), as displayed in Table 7, thus the null hypothesis for RQ1 is rejected.

Fisher's exact test and effect size further support rejection of the null hypothesis suggesting that there is an association between the variables.

Based on the results of Pearson's chi-square and Fisher's exact test, the null hypothesis is rejected, denotating, there is a difference in terms of use of breathing tests between males and females, with less women participating in the testing.

RQ2 and RQ3

RQ2 assessed for a difference in use of breathing tests between men and women who have been told by a clinician that they have COPD and related symptoms (cough, shortness of breath and phlem).

RQ3 assessed for a difference in use of breathing tests between men and women who have been told by clinicians that they have COPD and have access to healthcare.

Statistical assumptions. For RQ2 and RQ3, BLR models were used to assess relevance of COPD-related symptoms and healthcare insurance in terms of access to breathing tests. These covariates were tested independently and then together to realize the most appropriate model. Six assumptions for BLR include (a) binary dependent variable, (b) independents observations, (c) little or no multicollinearity in the independent variable, (d) linearity of independent variable, and (e) large sample size (minimum of 500; Statistic Solutions, 2019). All of the necessary assumptions for this methodology were met, since dependent variable is dichotomous, cases are independent with no multicollinearity and n=6,334.

BLR results for RQ2. COPD symptoms of cough, shortness of breath and phlem all displayed a positive significant predictive influence of receiving a breathing tests as is

evident by positive regression weight (B) and odds ratio (*OR*), $p<0.000$. Conversely, a patient's sex has a negatively influences receipt of breathing test; females are 15.9% more likely not to have the breathing tests compared to males (*OR*=.841, CI 95%: 0.739-0.961). Nagelkerke R^2=0.044 suggests that model explains roughly 4.4% of the variability of the outcome. Hosmer Lemeshow of the goodness of fit test produces a p=0.000, suggesting that the model is a poor fit.

Table 8

BLR for Breathing Tests with Predictors Sex, Cough, Shortness of Breath, and Phlem

						95% C.I. for OR	
	B	S.E.	Wald	*p* value	OR	Lower	Upper
Sex	-0.173	0.068	6.468	0.011	0.841	0.739	0.961
Cough	0.222	0.065	15.878	0.000	1.249	1.119	1.393
Shortness of Breath	0.485	0.053	84.456	0.000	1.205	1.464	1.800
Phlem	0.187	0.049	14.592	0.000	1.623	1.095	1.327

Answer to RQ2. Analyzing results of the binomial regression model, null hypothesis attached to symptoms of cough, shortness of breath and phelm having no influence on receiving a breathing tests is rejected; all symptoms have a positive odds of increasing testing, while sex, in the same model, displays a negative influence.

BLR results for RQ3. Presence of healthcare coverage significantly increases the odds of breathing tests with $OR = 1.741$, $p < 0.000$. As in the original model, sex displayed a negative influence of $OR = 0.883$, but this is a marginally significant result ($p = 0.064$). Nagelkerke R^2=0.012 suggests that model explains roughly 1.2% of the

variability of the outcome. Hosmer Lemeshow of the goodness of fit test produces a p=0.003, suggesting that the model is a poor fit.

Table 9

BLR for Breathing Tests with Predictors Sex, and Healthcare Coverage

						95% C.I. for OR	
	B	S.E.	Wald	*p* value	OR	Lower	Upper
Sex	-0.124	0.067	3.430	0.064	0.883	0.775	1.007
Health Care Coverage	0.554	0.096	33.679	0.000	1.741	1.444	2.099

Answer to RQ3. Null hypothesis of no difference in utilization of breathing tests in subjects with healthcare coverage is rejected. Health care coverage increases the odds of testing by 74.1% (*OR*=1.741, 95% *CI*: 1.444-.2.099).

Aggregate multivariate regression model. All covariates of sex, COPD-related symptoms, and presence of healthcare coverage were included in the final analysis, with results presented in Table 10. All covariates were significantly associated with breathing tests uptake, with health care coverage having the highest influence (*OR*=1.747, 95% *CI*: 1.448-2.107). Nagelkerke R^2=0.055 suggests that model explains roughly 5.5% of the variability of the outcome. Hosmer Lemeshow of the goodness of fit test produces a p=0.000, suggesting that the model is a poor fit.

Table 10

BLR for Breathing Tests with Predictors Sex, Cough, Shortness of Breath, Phlem, and Healthcare Coverage

						95% C.I. for OR	
	B	S.E.	Wald	*p* value	OR	Lower	Upper
Sex	0.175	0.068	6.544	0.011	0.839	0.074	0.959
Cough	0.224	0.056	15.390	0.000	1.212	1.101	1.335
Shortness of Breath	0.484	0.053	82.957	0.000	1.622	1.462	1.800
Phlem	0.193	0.049	15.390	0.000	1.212	1.101	1.335
Health Care Coverage	0.558	0.196	33.976	0.000	1.747	1.448	2.107

Explorative Analysis

The USPTF (2017) suggested that clinicians should utilize active case finding in patients who have a risk factor for developing COPD and are symptomatic. In this explorative analysis, from the above cohort, only cases responding 'yes' to COPD symptoms of cough, shortness of breath, and phlem were selected. Through this analysis, I was able to assess whether the frequency of breathing tests is higher in symptomatic patients and if the variability in sex is mitigated. Applying supplementary case inclusion criteria, an explorative analysis produced a sample of n=2100.

Statistical assumptions. For this analysis, chi-square methodology was implemented; assumptions were previously described.

Crosstab and effect size results. Out of the original cohort of over 6000 cases, only 2100 reported symptoms of shortness of breath, cough, and phelm. Of these, 88.71% have had a breathing tests. Applying chi-square testing to assess if there a difference in the breathing tests participation between symptomatic males and females yields a non-

significant $p < 0.239$, further analysis described in Table 11 and Figure 4. Fisher's exact test provides a nonsignificant $p < 0.241$. Cramer's V computation produced an effect size of 0.026, suggesting a moderate association between sex and breathing tests.

Table 11

Bivariate Characteristics of Breathing Tests Procedures in Symptomatic Cases

	Received Tests *n (%)*	Not Received Tests *n (%)*	X^2	P-value	Fisher's Exact	Cramer's V
Sex						
Males	893 (89.5)	104 (10.4)				
Females	970 (87.9)	133 (12.05)				
			1.384	<0.239	<0.241	0.026 (<0.239)

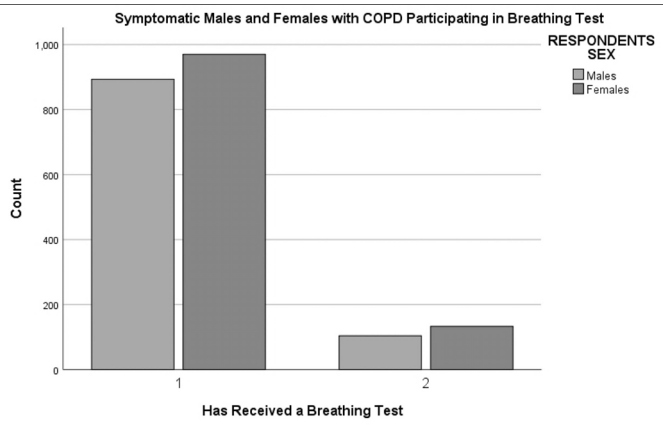

Figure 4. Prevalence of breathing tests between symptomatic males and females

Answer to explorative analysis. Of the symptomatic patients, a higher percentage was observed to participate in a breathing tests. Furthermore, previously

detected differences in terms of tests between males and females was mitigated by the presence of symptoms as suggested by the non-significant $\chi^2 = 1.384$, $p = 0.239$.

Summary

Section 3 included results and findings of this doctorial research. This segment reiterated the study purpose, sample selection schematics, cohort demographics, and COPD-related history and descriptions. This research interrogated the BRFSS 2017 dataset, with participation in breathing tests as the dependent variable and sex, COPD symptoms, and healthcare coverage as independent variables and covariates.

Significant findings involving female sex negatively associating with breathing tests were further supported through binomial regression analysis with inclusion of COPD-related symptoms and presence of health insurance. In a combined model of select independent variables, odds ratio of breathing tests increased, with health insurance and shortness of breath being leading influencers. An explorative analysis of symptomatic adults produced a higher use of breathing tests within this subgroup.

A comprehensive analysis and interpretation of results will be detailed in Section 4. Section 4 offers an overview of analyses, study limitations, recommendations, applications to theory and literature, and opportunities for social change.

Section 4: Application to Professional Practice and Implications for Social Change

Introduction

The purpose of this quantitative cross-sectional investigation was to assess breathing tests patterns between males and females with known COPD status. Inclusion of COPD specific symptoms as well as access to healthcare insurance were also considered in the model as these covariates may be important in terms of recommendation for screening. Moreover, COPD-specific symptoms and healthcare coverage increase the odds of participation in breathing tests in both sexes. Section 4 includes *Key Interpretation of Findings, Limitations of the Study, Recommendations for Future Research, and Implications for Practice and Social Change.*

Interpretation of Findings

Analysis of the BRFSS 2017 data set, cases with known COPD and responses to breathing tests modules, indicated a significant disproportional use of breathing tests between males and females. Sex was a negative influence on the odds of breathing tests (*OR*=0.839, 95% *CI*: 0.0735-0.959), while symptoms and healthcare coverage were both positive significant influencers. This combined model revealed healthcare coverage increasing the odds of breathing tests by 74% (*OR* = 1.747, 95% *CI*: 1.448-2.107), and shortness of breath by 62% (*OR* = 1.622, 95% *CI*: 1.462-1.800). In the following subsections, I will associate findings of the literature and the SEM.

Findings in Literature

An in-depth review of the literature alludes to a broader problem of COPD diagnostic patterns as nearly half of the 24 million Americans with symptoms of

obstructive lung disease remain undiagnosed (NHLBI, 2012). Utilization of a breathing tests as a means of confirmation is similarly deficient. Results of this study propose that sex may have an influence on attaining a breathing tests in a patient with COPD, adversely impacting women. Symptoms and favorable access to healthcare add further weight.

Sex. There is an overall disparity in terms of experience of women with COPD. Multiple analyses confirm a greater proportion of women are burdened with symptoms of COPD, experience morbidity at a younger age then men, as have higher overall mortality due to COPD (DeMeo, 2019). To date, this is the first quantitative analysis explaining differences in terms of use of breathing tests for women. A secondary analysis of the BRFSS 2017 dataset including cases with known COPD and responses to breathing test modules yielded an overall overrepresentation of women with the disease. Cohort was weighted by sex, allowing for an equal chance of selecting male and female responder. Overall use of breathing tests in the study sample was 82.56%, higher than what is reported nationally. Of this group, 83.4% of men received the testing, compared to 81.7% of women.

COPD symptoms. The USPTF (2017) suggested active case finding to be practiced by clinicians with the intent to identify candidates for COPD screening, including process of a breathing tests. Symptoms are objective and generally begin slow, progressing over time; therefore, it may be difficult for the patient to recognize and further attribute symptoms to COPD (Rennard, 2015). Price et al (2016) said that patients will report being asymptomatic when questioned about COPD, yet, report

limitations of activity due to shortness of breath, smoking status, and/or fitness level. While patients' perception regarding symptoms and clinicians' insights involving potential disease may have diverse variability, the current investigation confirms that presence of symptoms increases the odds of breathing tests. This finding is suggests that physician-patient decisions towards spirometry are productive, leading to an increase in use of these important tests.

Healthcare coverage. In 2010, President Barak Obama signed the Patient Protection and Affordable Care Act into Law, intending to expand healthcare coverage to more than 29 million Americans. Those who lack health insurance are less likely to engage with the healthcare system for preventative and screening measures, as these services are expensive within the US health care system. Furthermore, lack of health insurance will lead to delays in sick care, leading to potential detrimental and expensive outcomes (APHA, 2020). With a myriad of professional societies advocating for increases in the use of spirometry to adequately screen for COPD, the literature specific to impact of health insurance on breathing tests is sparse. In this study, presence/absence of health insurance were included as a covariate in the model, yielding $OR = 1.741$, $p < 0.000$ (95% *CI*: 1.444-2.099), suggesting a patient's presence of health insurance increases the probability of receiving breathing tests.

Combined model. Patterns describing receipt of breathing tests to screen for COPD are complex and overlapping. An aggregated model involving relevant covariates of symptoms and healthcare coverage was developed. There is no literature available specifically involving breathing tests; however, results of aggregate multivariable

analyses clearly indicated that the primary construct of sex and covariates of symptoms and healthcare coverage had a significant influence on the breathing tests.

Symptomatic cohort. Little evidence is available on the influence of sex on spirometry. From an older investigation by Chapman et al. (2001) findings described hypothetical female patients with same impairment and risk as males offered less opportunity for breathing tests (Chapman, 2001). Because USPTF *active case finding* is heavily weighed on symptoms, it is of interest if sex biases persist among symptomatic patients. In this study, the symptomatic cohort is smaller (*n=2100)* displayed an overall higher utilization of breathing tests. Moreover, the differences observed between the sexes are no longer significant. This result is different than what was described by Chapman in 2001 in that both symptomatic males and females are equally participating in this procedure. It is promising that nearly 19 years of knowledge and advocacy focused on identifying COPD within population has brought symptoms to the forefront of aiding disease screening.

Findings to Social Ecological Framework

In this study, SEM was implemented to organize attitudes and beliefs towards breathing tests in cases with known COPD. Biases in terms of public policy are beyond the scope of this study; however, trends and inferences can be drawn. On an individual level, at the core of the SEM, patients' beliefs and health literacy may drive their understanding and actions towards engaging with the healthcare system. While the results of this study are not causative, it is apparent that women in the COPD cohort are participating in breathing tests less than males; this may be influenced by differences in

perspectives and action at the individual patient level. For example, women may consider their symptoms to result from being out of shape, possibly neglecting their previous smoking history, while males are more likely to correlate smoking with symptoms, seeking care. Long-standing perceptions of the medical community considering male-dominated diseases may similarly influence recommendations to partake in tests. Broadening the findings to the interpersonal, organizational, and community levels, both individual and societal influences may shape how both patient groups and care providers gather COPD information. Even though COPD is prevalent, burdensome, and costly to the system, wider screening policy is lacking. Early case finding regarding patients at risk with symptoms mitigated sex biases observed in this heterogeneous cohort. This may not serve younger patients and women where symptoms can be correlated with other impairments.

Access to healthcare was explored as a covariate within the study as literature has suggested that absence of health insurance can deter engagement with the healthcare system and decision to screen. These barriers can inhibit individual level decisions, spanning to systemic levels, selecting to recommend testing to patients based on health insurance access. Results from this study suggest presence of health insurance, in simple model with just sex as a construct and those more complex inclusive of COPD symptoms, increase probability of acquisition of breathing tests. Similarly, existence of health insurance may influence multiple levels within the SEM.

Summary of Key Findings and Interpretations

From the BRFSS 2017 survey, a cohort of cases with knowledge COPD and response to breathing tests module produced an overall breathing tests participation rate of 82.56%. Bifurcating these into male and female categories, a moderately significant divergence was identified, negatively affecting women. Introducing COPD-specific symptoms and presence of health insurance into a regression model further reinforced influence of symptoms and presence of health insurance the likelihood of breathing tests. In an explorative analysis, breathing tests participation between males and females among symptomatic cases reveled differences in rates between the sexes were alleviated.

Limitations of the Study

An appreciation of study limitations is necessary as results need be interpreted with caution when considering generalizability, validity, and reliability. An important limitation of this study is the data sample, BRFSS, which is produced from a large population-based survey. As a general random sample, cases are not selected to represent a particular disease, therefore, query concerning specific screening procedure may introduce a challenge with health literacy and recall bias resulting from self-reporting by the participants. Without an exact medical record capturing a diagnosis code and breathing tests procedure code, it is difficult to ascertain whether in fact the tests was performed, and if, upon diagnosis. As such, results are reliant on the subjects' ability to adequately recall, understand disease in question and sequential testing and symptom modules affiliated.

Another limitation of the presents study was that the regression models had a poor fit, based on the values from the Nagelkerke and Hosmer Lemeshow tests. These findings underpin the complexity of the disease, social and medical constructs contributing to the testing decision. Therefore, future research must work towards a larger sample size and consideration of inclusion of additional variables such as type of insurance (Medicare versus private), age and education level of the patient. While these constructs were assessed by descriptive analysis, supplying demographics of the cohort, inclusion of these variables into the research question, and therefore statistical analysis, may offer a potentially closer model on influence towards receiving a breathing tests.

An ecological fallacy is possible as multilevel information is aggregated and the sample is heterogeneous. Furthermore, consideration of the sample size must be noted, following application of inclusion criteria, previously described, a small sample of cases was utilized, therefore interpretation of statistical testing must be hypothesis generating and requiring further investigation in a larger cohort. Finally, the findings of this study should be limited to the US and its territories due to the demographic of the original sample, and therefore may not be generalizable to global trends.

Implications for Professional Practice and Social Change

There are several lessons from this study demanding further investigation and intervention. Recognizing that COPD is burdensome to patients, their families and society at large, its necessary to recognize that varied groups may experience this disease differently; therefore, our approach to improving outcomes must be heterogeneous enough to differentiate and support these nuances. To date, this is one of the first

quantitative studies which has specifically focused on the COPD breathing tests experience of women in comparison with men, adding context to practice and society while laying foundation for future research.

Professional Practice

Learning from historical examples in other therapeutic areas, it is clear that prevention of disease and education on wellness is far more beneficial than battling an established chronic illness. The next best scenario, early identification, allows for education on potential risks, hazards, coaching on lifestyle, habit modification and potential therapeutic intervention. Conversely, a delay in diagnosis may lead to disease progression, morbidity, disability and potentially death. In the case of COPD, the pressing underdiagnosis is concerning, as is the, is the experience of the disease by women. As is signaled by this study, women with COPD are participating in breathing tests less than men; in addition, a presence of symptoms increases the potential of breathing tests. The medical community begins to consider diagnosis of COPD in the middle ages; however, women are far more symptomatic earlier in life (DeMeo, 2019).

Taking lessons from this study, recommendations can be implemented by practitioners, while additional evidence needs to be generated by the research community. Continuing to focus on early disease identification, training modules via continuing medical education (CME) should be updated describing COPD related trends, specifically elevating differences in disease presentation, onset of symptoms while brining attention to potential delay to breathing tests in women. These modules can serve as productive medium to update provider understanding of COPD, elevating

heterogeneity of disease and variability in men and women. Anchoring on the constructive influence of symptoms on probability of receiving breathing tests, utilization of symptom impairment validated questionnaires such as COPD Assessment Test (CAT) can further guide productive discussions between clinicians and patients. Symptom questionnaires can be a helpful tool for both patients and clinicians alike, elevating presence and burden of symptoms, thereby paving the way towards a productive and targeted conversation during a clinical visit.

Additional research is necessary to further explore screening disease patterns in COPD, with a focus on women. Identifying a COPD specific database, ideally one with health care records and claims available, can offer direct analysis of diagnosis and procedure codes, thereby reducing certain limitations and greatly increasing reliability of these findings. Additionally, it would be prudent to also peel away at the causative perceptions of COPD by clinicians and patients, offering greater understanding and opportunities of interventions. Employing qualitative methodologies of direct interviews and focus groups among societal segments of clinicians and patients with and without disease should offer basis of attitudes and beliefs towards COPD and screenings. Finally, a mixed methods approach of interviews with clinicians coupled by analysis of actual practice patterns would be of interest as perceptions and behaviors must be evaluated concurrently, identifying inconsistencies.

Contribution to Social Change

Application of knowledge in the direction of social change stands the capability to alter trajectories for society on a broader scale. In the United States, a general

stigmatization towards COPD exists and is a product of strong rooted beliefs of tobacco utilization. Because the most significant risk factor for developing COPD in the developed world is an ongoing decision to engage in a health hazardous activity of smoking cigarettes, less empathy, sensitivity and ultimately attention may be given to addressing symptoms. Moreover, individuals who have symptoms could be reluctant to elevate these for the fear of guilt and shame that may precipitate. In the case of women, these beliefs are further complicated by previously described entrenched viewpoints on smoking by women and disease patterns. Insights from this study elevate inclinations warranting social attention and change.

While breathing tests participation rates in this COPD cohort was relatively high, over 80%, these results are much higher than what is anticipated in practice. With nearly 12 million Americans with symptoms of obstructive lung disease yet lacking appropriate diagnosis, ongoing and catalyzed advocacy is essential to elevate COPD as an agenda item for health advocates and policy makers. Recognizing that experience of COPD is different in women than men, a change in the perceptions is necessary across societal levels. Starting broadly, society must recognize that COPD, much like any other chronic illness, is burdensome, leading to struggle and disability by the patients while adding a strain on families and the healthcare system. Disassembling biases through the means of education, working towards awareness can reduce the negative stigmatization towards COPD as a whole. Attention heterogeneity of disease and experience of women must similarly take focus and pave the way towards acceptance of prevalence in women. Considering that both males and females have a higher probability for receiving tests if

symptoms are present, a raised focus on awareness of symptoms by the medical community may support more case finding and identification of patients. On a policy level, professional society and USPTF must re-visit definition of active case finding, with potential discussion into the variability of experience by women. Translating these messages to the organizational levels, medical communities should be more vigilant in recognizing that disease may present slightly differently in women therefore both male and female patients at risk with symptoms may be warranted for breathing tests.

Social change stands a better opportunity of success when patients are involved and leading the charge. Working through biases that individual patients may be experiencing, advocacy and education initiatives within patient communities may lift some perceptions, perhaps leading to greater initiative by the patients to screen and have more direct conversations with their providers. Large patient advocacy groups such as the COPD Foundation can engage and message patient communities in that both men and women can develop COPD. Again, because results of this study suggested that when patients have symptoms probability of breathing tests is higher, we must educate patients to have greater awareness of their symptoms, correlate to potential disease, and communicate their experience to the healthcare team. An amalgamation of enhanced awareness and understanding by the healthcare community alongside engaged and health literate patients can be changes necessary to alter trajectories in COPD for all of society.

Conclusion

This study identified differences in rates of breathing tests usage among male and female patients who have knowledge of COPD. When symptoms and healthcare coverage

were added into a multivariate regression model, all had a positive influence on the prevalence of breathing tests. A larger and more targeted COPD sample with access to medical records would offer a comprehensive database for quantitative analysis; specifically, prevalence of breathing tests use among males and females. Furthering testing regarding practice patterns between men and women patients with COPD can offer insights to policy makers, health advocates, practitioners, and community where areas for intervention can offer opportunities to improve identification and ultimately care for this fragile group.

References

Agency for Healthcare Research and Quality. (2012). *Cardiovascular disease and other chronic conditions in women: Recent findings*. Retrieved from https://www.ahrq.gov/sites/default/files/publications/files/womheart.pdf

Alexander, L. K., Lopes, B., Ricchetti-Masterson, K., & Yeatts, K. B. (2015). Cross-sectional Studies. *ERIC Notebook, Vol. 2*, p. 1-5. Retrieved from https://sph.unc.edu/files/2015/07/nciph_ERIC8.pdf

Alspach, J. G. (2012). Is there a gender Bias in critical care? *Critical Care Nurse, 32,* 814. doi:10.4037/ccn2012727

American Psychologic Association (APA). (2015). *Definitions related to sexual orientation and gender diversity in APA documents*. Retrieved from https://www.apa.org/pi/lgbt/resources/sexuality-definitions.pdf

American Public Health Association (APHA). (2020). Why do we need the Affordable Care Act? Retrieved from https://www.apha.org/-/media/files/pdf/topics/aca/why_need_aca_2017.ashx?la=en&hash=3BE48D1C7818F17F4669FEA3B462FFA76CAE8B5B

American Thoracic Society (2018). COPD. Retrieved from https://www.thoracic.org/statements/copd.php

Apps, L. D., Harrison, S. L., Williams, J. E., Hudson, N., Steiner, M., & Morgan, M.D. (2014). How do informal self-care strategies evolve among patients with chronic obstructive pulmonary disease managed in primary care? A qualitative study. *International Journal of Chronic Obstructive Pulmonary Disease, 9*, 257-263.

doi: 10.2147/COPD.S5269

Centers for Disease Control and Prevention (CDC). (2016). *NCHS data brief No. 293: Mortality in the United States, 2016.* Retrieved from https://www.cdc.gov/nchs/data/databriefs/db293.pdf

Centers for Disease Control and Prevention (CDC). (2017). *LLCP 2017 codebook report.* Retrieved from https://www.cdc.gov/brfss/annual_data/2017/pdf/codebook17_llcp-v2-508.pdf

Centers for Disease Control and Prevention. (2018). Chronic Obstructive Pulmonary Diseases (COPD). Retrieved from https://www.cdc.gov/copd/index.html

Centers for Disease Control and Prevention (CDC). (2015). Leading causes of death (LCOD) by race/ethnicity, all females—United States, 2015. Retrieved from https://www.cdc.gov/women/lcod/2015/race-ethnicity/index.htm

Centers for Disease Control and Prevention (CDC). (2014). Summary health statistics for US adults: National health interview survey 2012. *Vital and Health Statistics, 10* (260), 1-118.

Centers for Disease Control and Prevention. (2013). National breast and cervical cancer early detection program. Retrieved from https://www.cdc.gov/cancer/nbccedp/sem.htm

Celli, B. R., & MacNee, W. (2014). Standards for the diagnosis and treatment in patients with COPD: A summary of the ATS/ERS position paper. *European Respiratory Journal*, *23*(6): 932-946. doi: 10.1183/09031936.04.00014304

Chapman, K. R., Tashkin, D. P., & Pye, D. J. (2001). Gender bias in the diagnosis of

COPD. *Chest*, *119*, 1690-1695. Retrieved from http://publications.chestnet.org/

Chronic Respiratory Disease Collaborators (GDB). (2017). Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respiratory Medicine,* 9, 691-706. doi: 10.1016/S2213-2600(17)30293-X.

Dalal A. A., Patel, J., D'Souza, A., Farrelly, E., & Shah, M. (2015). Impact of COPD exacerbation frequency on costs for a managed care population. *Journal of Managed Care Specialty Pharmacy*, *21*, 575-583. doi: 10.18553/jmcp.2015.21.7.575

Da Silva, R., Contandripolous, A. P., Pineault, R., & Tousignant, P. (2011). A global approach to evaluation of health services utilization: Concepts and measures. *Health Policy*, *6*, e106-e117. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3107120/

DeMeo, D. L., Ramagopalan, S., Kavati, A., Vegesna, A., Yadao, A. & Wilcox, T. K. (2018). Women manifest more severe COPD symptoms across the life course. *International Journal of Chronic Obstructive Pulmonary Disease*, *13*, 3021-3092. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6171761/

Diaz-Guzman, E., & Mannino, D. M. (2014).EXACTLE Epidemiology and prevalence of chronic obstructive pulmonary disease. *Clinical Chest Medicine*, *35*, 7–16. doi: 10.1016/j.ccm.2013.10.002.

Diette, G. B., Dalal, A. A., D'Souzsa, A. O., Lunacsek, O. E., & Nagar, S.P. (2015).

Treatment patterns of chronic obstructive pulmonary disease in employed adults in the United States. *International Journal of Chronic Obstructive Pulmonary Disease,* 10, 415-422. doi: 10.2147/COPD.S75034.

Dransfield, M. T., Davis, J. J., Gerald, L. B., & Bailey, W. C. (2016). Racial and gender differences in susceptibility to tobacco smoke among patients with chronic obstructive pulmonary disease. *Respiratory Medicine*, 6, 1110–1116. doi: 10.1016/j.rmed.2005.09.019.

Glanz, K., Rimer, B. K., & Viswanath, K. (2008). *Health behavior and health education theory: Research and practice* (4th ed.). San Francisco, CA: Jossey-Bass.

Global Initiative for Chronic Obstructive Lung Disease (GOLD). (2018). Global strategy for the diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease. Retrieved from https://goldcopd.org/wp-content/uploads/2018/02/WMS-GOLD-2018-Feb-Final-to-print-v2.pdf

Guarascio, A. J., Ray, S. M., Finch, C. F., & Self, T. H. (2013). The clinical and economic burden of chronic obstructive pulmonary disease in the USA. *ClinicoEconomics and Outcomes Research*, *5*, 235-245. doi: 10.2147/CEOR.S34321.

Han, M. K., Postma, D., Mannino, D. M., Giardino, N. D., Buist, S., & Curtis, J. L. (2007). Gender and chronic obstructive pulmonary disease: why it matters. *American Journal of Respiratory Critical Care Medicine* 2007, *176*: 1179–1184. doi:10.1164/rccm.200704-553CC.

Hardin, M. Foreman, M, Dransfield, M. T. Hansel, N. Han, M.K., & Cho, M. H.(2016).

Sex-specific features of emphysema among current and former smokers with COPD. *European Respiratory Journal*, *47*, 104-112. doi: 10.1183/13993003.00996-2015.

Ho, T., Cusack, R., Chaudhary, N., Satia, I. & Kurmi, O.P. (2019). Under-and over-diagnosis if COPD; a global perspective. *European Respiratory Society, Breathe*, *15*,20-35. doi: 10.1183/20734735.0346-2018.

Johnson, K. M., Tan, W. C., Bourbeau, J., Sin, D. D., & Sadatsafavi, M. (2018). The diagnostic performance of patient symptoms in screening for COPD. *Respiratory Research*, 19, 147. doi.org/10.1186/s12931-018-0731-1.

Kilanowski, J. (2017). Breadth of the Socio-Ecological Model. *Journal of Agromedicine*, *4*, 295-297. doi.org/10.1080/1059924X.2017.1358971.

Laerd Statistics. (2018). Binomial Logistic Regression using SPSS Statistics. Retrieved from https://statistics.laerd.com/spss-tutorials/binomial-logistic-regression-using-spssstatistics.php

Mahler, D. A., Ward, J., Waterman, L. A. & Baird, J.C. (2012). Longitudinal changes in patient-reported dyspnea in patients with COPD. *COPD*, *9*, 522-527. doi: 10.3109/15412555.2012.701678.

Mamary, J. A., Stewart, J. I., Kinney, G. L., Kinney, G.L, Hokanson, J, E., & Shenoy, K. (2018). Race and gender disparities are evident in COPD underdiagnoses across all severities of measured airflow obstruction. *Journal of the COPD Foundation*, *5*(3), 177-184. doi: 10.15326/jcopdf.5.3.2017.0145.

Mannino, D. M., Aryal, S. & Diaz-Guzman, E. (2013). COPD and gender differences. *Translational Research,* 162, 208-218. doi: 10.1016/j.trsl.2013.04.003.

Mannino, D. M., & Braman, S. (2017). The epidemiology and economics of chronic obstructive pulmonary disease. *Proceedings of the American Thoracic Society*, 4, 502-506. Retrieved from http://www.atsjournals.org/doi/full/10.1513/pats.200701-001FM#.V5qWEI4_zBQ

Mannino, D. M., Homa D. M., Akinbami L. J., Ford, E. S., & Redd, S. C. (2002) Chronic obstructive pulmonary disease surveillance – United States, 1971–2000. *MMWR Surveillance Summary*, 51, 1–16. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12198919

Martinez, C. H., Mannino, D. M., Jaimes, F. A. Curtis, J. L., Han, M. K., & Hansel, N. N. (2015). Undiagnosed obstructive lung disease in the United States. *Annals of American Thoracic Society*, *12*(12), 1788-1795. doi:10.1513/AnnalsATS.201506-388OC.

Martinez, F. J., Curtis, J. L., Sciurba, F., Mumford, J., Giardino, N. D., & Weinmann, G. (2007). Sex differences in severe pulmonary emphysema. *American Journal of Respiratory and Critical Care Medicine*, 176*,* 243–252. doi: 10.1164/rccm.200606-828OC

McCarthy, B., Casey, D., Devane, D., Murphy, K. Murphy, E., & Lacasse, Y. (2015). Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Systematic Review*, *2*, 176. doi: 10.1002/14651858.CD003793.pub3.

McHugh, M. L. (2013). The chi-square test of independence. *Biochemia Medica. 23(*2), 143-149. doi:10.11613/BM.2013.018

National Heart, Lung, and Blood Institute (NHLBI). (2012). Morbidity & Mortality: 2012 chart book on cardiovascular, lung and blood diseases. Retrieved from https://www.nhlbi.nih.gov/files/docs/research/2012_ChartBook_508.pdf

National Heart, Lung and Blood Institute (NHLBI). (2018). Pulmonary Function Tests. Retrieved from https://www.nhlbi.nih.gov/health-topics/pulmonary-function-tests

National Institutes of Health (NIH). (2018). Chronic obstructive pulmonary disease (COPD) fact sheet. Retrieved from https://report.nih.gov/nihfactsheets/.

Nakano Y., Muro, S., Sakai, H., Hirai, H., Chin, K. & Tsukino, M. (2000). Computed tomographic measurements of airway dimensions and emphysema in smokers. Correlation with lung function. *American Journal of Respiratory and Critical Care Medicine*, *162*, 1102–1108. doi:10.1164/ajrccm.162.3.9907120.

Petty, T. L. (2006). The history of COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, *1*, 3-14. doi: 10.2147/copd.2006.1.1.3.

The Pew Research Center for People and the Press. (2012). Assessing the representativeness of public opinion surveys. Retrieved from http://www.people-press.org/files/legacy-pdf/Assessing%20the%20Representativeness%20of%20Public%20Opinion%20Surveys.pdf.

Prescott, E., Bjerg, A.M., Andersen, P. K., Lange, P., & Vestibo, J. (1997). Gender difference in smoking effects on lung function and risk of hospitalization for COPD: results from a Danish longitudinal population study. *European Respiratory Journal*, 10, 822–827. Retrieved from

https://www.ncbi.nlm.nih.gov/pubmed/9150319

Price, D., Freeman, D., Cleland, J., Kaplan, A., & Cerasoil, F. (2017). Earlier diagnosis and earlier treatment of COPD in primary care. *Primary Care Respiratory Journal*, 20, 15–22. doi: 10.4104/pcrj.2010.00060.

Quaderi, S. A., & Hurst, J. R. (2018). Unmet global burden of COPD. *Global Health, Epidemiology and Genomics, 3*(4), doi: 10.1017/gheg.2018.1.

Rennard, S. I., & Drummond, M.B. (2015). Early chronic obstructive pulmonary disease: definition, assessment, and prevention. *Lancet*, *385*(9979), 1778–1788. doi: 10.1016/S0140-6736(15)60647-X.

Sansores, R. H., & Ramírez-Venegas, A. (2016). COPD in women; susceptibility or vulnerability. *European Respiratory Journal*, *47* (1), 19-22; doi**:** 10.1183/13993003.01781-2015.

Science Direct. (2019). Bivariate analysis. Retrieved from https://www.sciencedirect.com/topics/medicine-and-dentistry/bivariate-analysis

Smith, M. L., Ory, M. G., Ahn, S., & Miles, T. P. (2013). Factors associated with women's chronic disease management: associations of healthcare frustrations, physician support, and self-care needs. *Journal of Aging Research*, 982052. doi.org/10.1155/2013/982052.

Sorheim, I .C., Johannessen, A., Gulsvik, A., Bakke, P. S., Silverman, E. K., & DeMeo, D. L. (2010). Gender differences in COPD: are women more susceptible to smoking effects than men? *Thorax*, *65*, 480–485. doi: 10.1136/thx.2009.122002.

Statistic Solutions. (2019). Assumptions of logistic regression. Retrieved from https://www.statisticssolutions.com/assumptions-of-logistic-regression/

Steyerberg, E. W., & Harrell, F. E. (2016). Prediction model need appropriate internal-external, and external validation. *Journal of Clinical Epidemiology,* 69, 245-247. doi: 10.1016/j.jclinepi.2015.04.005.

Stratelis, G., Jakobsson, P. A., Molstad, S., & Zetterstrom, O. (2014). Early detection of COPD in primary care: screening by invitation of smokers aged 40 to 55 years. *British Journal of General Practice*, *54*, 201-207. Retrieved from http://bjgp.org/content/bjgp/54/500/201.full.pdf

Thun, M. J., Carter, B.D., Feskanich, D., Prentice, R., Lopez, A. D., & Hartge, P. (2013). 50-year trends in smoking-related mortality in the United States. *New England Journal of Medicine*; 368, 351–364. doi: 10.1056/NEJMsa1211127.

US Preventative Services Task Force (USPTF). (2016). Screening for chronic obstructive pulmonary disease US preventive services task force recommendation statement. *Journal of the American Medical Association*, *315*, 1372-1377. doi:org/10.1001/jama.2016.2638.

Wheaton, A. G., Cunningham, T. J., Ford, E. S., & Croft, J. B. (2015). Employment and activity limitations among adults with chronic obstructive pulmonary disease—United States, 2013. *Morbidity Mortality Weekly Report* (MMWR); *64*, 289-295. Retrieved from https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6411a1.htm.

World Health Organization (WHO). (2019). Gender, equity and human rights. Retrieved

from https://www.who.int/gender-equity-rights/understanding/gender-definition/en/

World Health Organization (WHO). (2017). Chronic obstructive pulmonary disease. Retrieved from https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)

World Health Organization (WHO). (2016). Burden of COPD. Retrieved from https://www.who.int/respiratory/copd/burden/en/

World Health Organization (WHO). (2011). Women and men face different chronic disease risk. Retrieved from https://www.paho.org/hq/index.php?option=com_content&view=article&id=5080:2011-women-men-face-different-chronic-disease-risks&Itemid=135&lang=fr

Wullianallur, R., & Raghupathi, V. (2018). An empirical study of chronic diseases in the United States: A visual analytics approach to public health. *International Journal of Environmental Research and Public Health*, *15*, 1-24. doi:10.3390/ijerph15030431.