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I dedicate this work to:

- The memory of my late parents Lydie and Abel Youmbi who are sleeping in the Lord, I hope to see them again when our Redeemer, Jesus-Christ returns.
- My children and grandchildren.

Abstract

Due to elevated readmission costs, the Affordable Care Act established the Hospital Readmission Reduction Program in 2012 to curb the 30-day readmission rates. COPD and schizophrenia are two very expensive diseases, COPD national medical costs is projected to be $49.0 billion in 2020; the cost of schizophrenia was 155.7 billion in 2013. The main objective of this study was to determine if schizophrenia is a significant predictor of 30-day readmission following hospitalization for acute exacerbation of COPD after adjusting for age, gender, anxiety, smoking status, T2DM, chronic ischemic heart disease, and GERD. Methods: A retrospective cohort design was used to request data from the South Carolina RFA. Data were from January 1, 1996 to September 30, 2015 with primary or secondary diagnosis of ICD 9 491.21 or 491.22. The RFA created a unique identifier for each patient. Schizophrenia was defined as and ICD 9 diagnostic code of 295.XX. Calculations were initially made in R, then in SPSS. Results: Unadjusted and adjusted analyses per the robust GEE matrix revealed that schizophrenia was not a significant indicator for 30-day COPD readmission ($p = 0.105$ and 0.054 respectively). However, GEE model-based method indicated that schizophrenia was a significant predictor of 30-day readmission for COPD in both the unadjusted analysis ($p = 0.019$) and the adjusted analysis ($p = 0.002$). Conclusion: Although not quite statistically significant per the more reliable robust matrix, the results raise the possibility that schizophrenia could be a predictor of readmission. Further studies using a prospective approach are recommended.

Keywords: COPD, schizophrenia, 30-day readmission.

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CHAPTER 1

Description of the Problem

Chronic obstructive pulmonary disease (COPD) is a progressive disorder characterized by airflow limitation not fully reversible, caused by chronic inflammation of the airways and lung parenchyma (GOLD, 2018, Sutherland & Cherniack, 2005). Individuals suffering from COPD also have some substantial extrapulmonary effects, and important comorbidities that may contribute to the severity of the disease (Rabe et al., 2007). About 90% of COPD cases are caused by cigarette smoking; other risk factors include advanced age and genetic factors such as α-1 antitrypsin deficiency (Epocrates, 2016). COPD is an expensive disease responsible for roughly 750,000 hospitalizations in the US, and the cost associated with the care of patients with COPD was estimated to approximated 24 billion dollars in 1993 (Sullivan & Ramsey, 2000). In 2008, the combined cost of COPD and asthma was 68 billion, including 53.7 billion in direct cost; mortality rate was 14.3% (NHLBI, 2012). There were 7.3 million emergency department visits (CDC, 2015).National medical costs are projected to increase from $32.1 billion in 2010 to $49.0 billion in 2020 (Ford, Murphy, Khavjou, Giles, Holt, & Croft, 2015). COPD is also a life-threatening condition; according to Barnes (2000), the World Health Organization predicted that worldwide, COPD would be the third leading cause of mortality and the fifth leading cause of disability by 2020.

Schizophrenia is a scarce; but very serious mental disorder affecting more males than females (WHO, 2016). Worldwide in 2009, about one percent of the population was diagnosed with schizophrenia, and approximately 1.2% of Americans (3.2 million) had the disorder (Nemade & Dombeck, 2009). Still in 2009, about 1.5 million people were diagnosed with

schizophrenia worldwide, translating to about 100,000 Americans diagnosed; in other words, 7.2 people per 1,000 or about 21,000 people within a city of 3 million were likely to be suffering from schizophrenia (Nemade & Dombeck, 2009). Despite its scarcity, schizophrenia is affecting more and more people and the statistics are still alarming; in 2016, more than 21 million people worldwide suffer from it; 12 million males and 9 million females (WHO, 2016). In 2013, schizophrenia was ranked as the 11th leading cause of disability worldwide (Global Burden of Disease Study 2013 Collaborators, 2015).

Most people with schizophrenia are mentally disabled, and their disability can in turn affect their educational and occupational performance (WHO, 2016). Schizophrenia is often associated with stigma, discrimination and violation of human rights of people who have it (WHO, 2016). Additionally, it is very costly for families and society. The number of emergency departments (ED) visits related to schizophrenia was estimated to 382,000 from 2009 to 2011. Of these visits, 32.7% resulted in a hospital admission, a higher percentage compared with ED visits not related to schizophrenia (10.3%). Similarly, 16.7% of ED visits related to schizophrenia resulted in a transfer to a psychiatric hospital, versus 0.7% of the ED visits not related to schizophrenia (CDC, 2015b). In 2002, the overall cost of schizophrenia was estimated to be $62.7 billion, with $22.7 billion in excess direct healthcare cost in the following categories: $7.0 billion outpatient, $5.0 billion drugs, $2.8 billion inpatient, and $8.0 billion long-term care (Wu et al., 2005). Cloutier et al. (2016) reported that the cost associated with schizophrenia in 2013 was estimated at $155.7 billion 2013 and included excess direct health care costs of $37.7 billion (24%), direct non–health care costs of $9.3 billion (6%), and indirect costs of $117.3 billion (76%) compared to individuals without schizophrenia. The majority of expenses were associated with unemployment (38%), productivity loss due to caregiving (34%), and direct health care

costs (24%). These elevated costs do not unfortunately translate in decreased mortality; in fact, people with schizophrenia are still 2 to 2.5 times more likely to die prematurely than the general population, due to physical illnesses such as cardiovascular, metabolic and infectious diseases (WHO, 2016).

The National Institute for Mental Health (NIMH, n.d.) defines schizophrenia as a chronic, severe and debilitating mental disorder that alters thoughts, behavior, feelings and perception in people affected by it. Onset of schizophrenic symptoms is usually in early adulthood, although there are rare pediatric schizophrenias. Symptoms are classified as positive, negative or cognitive. Positive symptoms include delusion, hallucinations, thoughts disorders, and catatonia. Negative symptoms are self-neglect, demotivation, affective flattening, anhedonia, and impoverished or disorganized speech and language or alogia. Cognitive symptoms include attention deficit, poor executive functioning and poor working memory. It is thought that their poor working memory is due to a specific deficit in their prefrontal cortex function, as evidenced by their poor performance on continuous Performance Test measured on magnetic resonance imaging (Barch, Carter, Braver, Sabb, MacDonald III, Noll, & Cohen, (2001). Diagnosis of schizophrenia is made on the basis of co-occurrence of at least two of the listed symptoms occurring for a significant period of at least one month associated with ongoing problems for at least 6 months; at least one of the symptoms must be a positive symptom (APA, 2013).

Individuals with schizophrenia are likely to suffer multiple co-morbid conditions that could potentially lead to hospitalizations. Olfson, Gerhard, Huang, Crystal, & Stroup (2015) sought to describe the overall cause of mortality and the specific mortality rates and standardized mortality ratios (SMRs) for adults with schizophrenia in the United States. They calculated mortality rates per 100,000 person-years and the mean years of potential life lost per death and

found that adults with schizophrenia were more than 3.5 times (all-cause SMR, 3.7; 95% CI, 3.7-3.7) as likely to die in the follow-up period as were adults in the general population.

Problem Statement or Purpose and Development of PICO Question.

COPD is a preventable and manageable chronic condition; but individuals with schizophrenia have the tendency not to adhere to their prescribed regimen (Lacro, Dunn, Dolder, Leckband, & Jeste, 2002). Cahoon, Mcginty, Ford, & Daumit (2013) sought to determine if individuals with schizophrenia were at higher risk for ambulatory care sensitive (ACS) hospitalizations due to the nature of their disease, barriers to high quality primary care, lack of social support, and fragmentation of healthcare delivery services. Overall, acute, and chronic ACS hospitalizations were higher for admissions with secondary diagnosis of schizophrenia compared to those without (OR 1.34; 95% CI: 1.31, 1.38). Unadjusted ORs of the majority of chronic ACS conditions measured, including congestive heart disease (CHF), COPD, asthma, diabetes mellitus (DM), long and short-term complications, and uncontrolled diabetes were higher for hospitalizations with schizophrenia, versus without secondary diagnosis of schizophrenia.

Ho, Tsai, Ruan, Huang, & Lai (2014) sought to determine in-hospital mortality and one-year mortality for patients with COPD and their predictors in patients hospitalized for first-ever disease exacerbations. Older and hospitalized COPD patients had more comorbidities such as congestive heart failure (CHF), malignancies or stroke, and were more likely to die (OR: 1.08 per point; 95% CI: 1.01–1.15). A greater number of COPD survivors had hyperlipidemia. Angiotensin II receptor blockers (ARBs), beta blockers and statins were more frequently prescribed to patients who survived. Also, hospital length of stay was longer for non-survivors (hazard ratio 1.01 per day; 95% CI: 1.01–1.01), they experienced more cardiac events, and they

were more likely to be admitted to ICU for mechanical ventilation (HR: 1.33; 95% CI: 1.03–1.73). As far as one-year outcome was concerned, concomitant liver cirrhosis and malignancy, and length of stay and ICU admissions during the index hospitalization were significant independent predictors of mortality.

Additionally, Guerrero et al. (2016) found that 20% of COPD patients were readmitted for acute exacerbation of COPD (AECOPD) within 30-days of discharge. They found that 30-day readmission for AECOPD correlated with increasing long-term mortality risk; more precisely, the absolute increase in mortality rate was 4% at 30 days, 17% at 6 months, 19% at one year, and 24% at 3 years. Guerrero et al. also found that 30-day readmission was an independent risk factor for mortality at one year (HR 2.48; 95% CI, 1.10-5.59).

Furthermore, previous hospital admission, increased PaCO2, low forced expiratory volume in one second (FEV1), dyspnea, oral corticosteroids, long term use of oxygen therapy, poor health related quality of life or inability to perform activities of daily living, and absence of routine physical examination by a primary care provider were found to be significant risk factors for admissions and readmissions to the hospital of AECOPD (Bahadori & Fitzgerald, 2007). Conversely, regular physical activity and higher quality of life were associated with reduced admission risk at a statistically significant level. The Lung Health Study also demonstrated that exacerbations contribute to decline in FEV1 (Donaldson & Wedzicha, 2006)).

In regard to schizophrenia, Jørgensen (2017) examined the association between schizophrenia and the quality and predictors of care for diabetes, heart failure and COPD in Danish populations, as well as the clinical outcomes of heart failure and COPD among patients with schizophrenia. She found that COPD patients with schizophrenia had a lower probability of meeting certain process-performance measures for COPD, CHF and diabetes mellitus.

Additionally, patients with schizophrenia were more likely to die after an admission for AECOPD.

Furthermore, a comprehensive database search from January 1990 to June 2014 indicated that a number of studies supported the hypothesis that patients with mental disorders are more likely to be readmitted if they have co-occurring medical conditions (Šprah, Dernovšek, Wahlbeck, & Haaramo, 2017). In fact, co-occurring physical and mental disorders can worsen a patient's course of illness leading to hospital readmission not related to their psychiatric condition. Medical diagnoses such as chronic lung diseases, hepatitis C virus infection, and hypertension were associated with readmission for substance abuse disorder and schizophrenia.

Due to elevated costs associated with readmissions, the Affordable Care Act (ACA) established the Hospital Readmission Reduction Program (HRRP) in 2012 with the aim to curb the 30-day readmission rate. Under the HRRP, hospitals are penalized if their 30-day readmission rates are greater than expected for acute myocardial infarction, CHF, pneumonia, elective total hip arthroplasty, total knee arthroplasty, and acute exacerbation of COPD (McIlvennan, Eapen, & Allen, 2015). Additionally, institutions such as the Veterans Health Administration (VHA) uses the 30-day readmission rate as a SAIL (Strategic Analytics for Improvement and Learning) measure. The SAIL combines private sector key metrics and metrics specific to the VHA to address access to care, quality of mental health care, employee perception about the organization, nursing turnover and efficiency (U.S. Department of Veterans Affairs, 2016).

The studies summarized above are evidence of an existing link between mental illnesses such as schizophrenia and increased mortality, hospitalization and rehospitalization odds. Research to examine if the coexistence of schizophrenia would increase 30 day-readmission rates

of South Carolinians with COPD is rather slim or nonexistent. If the diagnosis of schizophrenia correlates with greater hospitalization and readmission rates as seen in the literature, hospitals in South Carolina can scheme specific medical and social services for this fringe of vulnerable population.

Based on the current research on the coexistence of schizophrenia and COPD as it relates to hospital readmission, the principal key objectives of this research study is to determine if schizophrenia is a significant predictor for 30-day COPD readmission after adjusting for the other covariates age, gender, anxiety, smoking status, T2DM, chronic ischemic heart disease, and GERD). A secondary objective is to suggest lifestyle approaches to manage both COPD and schizophrenia. This approach would have a significant impact given that neuroleptic used for schizophrenia management are highly associated with the development of type 2 diabetes mellitus (Bobo et al., 2013). The PICO question for this research study is as follows: "In the hospitalized South Carolinians with COPD (P), how does having schizophrenia (I) compared to not having schizophrenia (C) influence the 30-day readmission rate (O)? The project is an investigational project which aims to improve the quality of care provided to South Carolinians with schizoaffective disorders/schizophrenia and COPD. If schizophrenia is a significant predictor for COPD readmission, since schizoaffective disorders are a worldwide problem, healthcare providers could benefit from the results and suggestions of the research findings.

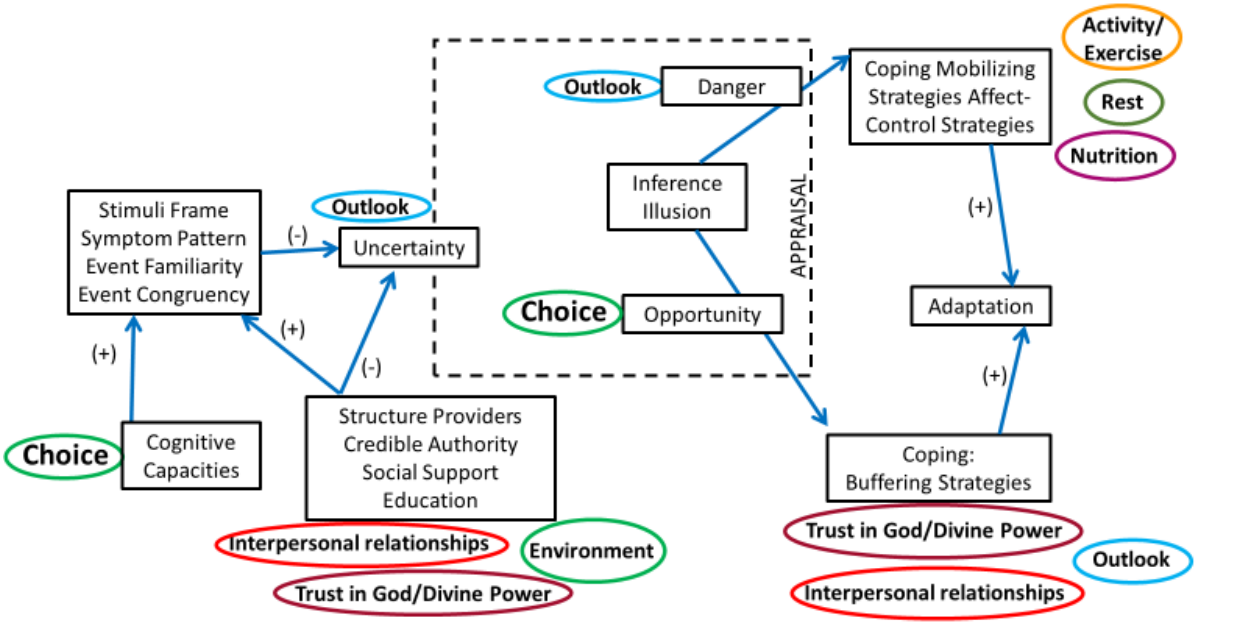
Theoretical Framework

The uncertainty in illness theory (UIT), the reconceptualized uncertainty in illness theory (RUIT), and the CREATION Health theory will be used as framework for this project. Mishel (2014) developed the UIT in 1988 to address "uncertainty during the diagnosis and treatment phases of an illness or an illness with a determined downward trajectory" (p. 53). She defined

uncertainty as "the inability to determine the meaning of illness-related events." Mishel subsequently developed the RUIT "to address the experience of living continuous uncertainty in either a chronic illness requiring ongoing management or an illness with a possibility of recurrence" (p. 53). UIT is centered around three principal themes: antecedents of uncertainty, appraisal of uncertainty, and coping with uncertainty without a desired outcome of returning to the previous level of adaptation or functioning. Mishel added the concepts of self-organization and probabilistic thinking to create the RUIT with the desired outcome of growth to a new value system (p. 53). Due to its irreversible nature, COPD can trigger lots of anxiety and uncertainty in people affected by this disease. COPD and schizophrenia both have uncertain trajectories; nurse practitioners can help patients who have these conditions by implementing nursing actions to help them prevent, predict and manage acute episodes. In conclusion, healthcare providers can use UIT and RUIT in various ways and settings not only to predict and manage COPD and schizophrenia exacerbations, but also to educate families and patients on the trajectories of these diseases.

The approach to this study would have a unique conceptualization due to the introduction of the CREATION Health (Edgerton, 2014) model as a novel framework to manage both COPD and schizophrenia. The CREATION Health (Edgerton, 2014) model would simultaneously shed light on the etiology of some symptoms and provide long term solutions to symptoms management. It would be practically impossible to manage the schizophrenic patient with COPD outside of his/her psychotic disorder. Although the etiology of schizophrenia is not well known, it is now known that genetic, perinatal and environmental factors as well as cannabis play an important part in psychosis/schizophrenia development (Frankenburg, 2017). Some epigenetic studies have demonstrated that methamphetamine that causes psychosis in humans alters DNA

methylation as well as expression of genes in brain regions that are thought to be involved in schizophrenia (Numachi et al. 2004). Schizophrenia treatment should no longer be limited to pharmacological approaches; non-pharmacological management including psychosocial interventions and nutrition have been proven to be effective in treating schizophrenia (Álvarez-Jiménez, Hetrick, González-Blanch, Gleeson, & McGorry, 2008). The CREATION Health approach to lifestyle advocates that proper nutrition preserves lung function and leads to healthy brains. Individuals with healthy frontal lobe would make good choices and avoid cigarette smoking, one of the primary causes of COPD. There is evidence that pulmonary rehabilitation and regular physical activity -regardless of the level of physiologic decline- can improve the quality of life (Seemungal, Hurst, & Wedzicha, 2009, p. 213). In fact, all the aspects of the CREATION Health model are important in managing both COPD and schizoaffective disorders (see Figure1). Controlling COPD symptoms, adopting healthy lifestyles and having proper interpersonal relationships would improve the 30-day readmission rate of the schizophrenic South Carolinians with COPD.



Combined Model of Perceived Uncertainty in Illness and Creation Health Model

Adapted from Mishel, M. H. (1988). Uncertainty in illness. Image: The Journal of Nursing Scholarship, 20(4), 225-232.

CHAPTER 2

Literature Review

A review of literature related to chronic obstructive pulmonary disease (COPD), schizophrenia, COPD and schizophrenia, as well as medical, pharmacological, and non-pharmacological management of COPD and schizophrenia was made. Resources used include medical databases at the McKee Library and the Veterans Administration National Library, as well as internet search in PubMed-NCBI, Google Scholar, and Open Access Journal Search Engine.

COPD

In a retrospective population-based cohort, Ho, Tsai, Ruan, Huang, & Lai (2014) sought to determine in-hospital mortality and one-year mortality for patients with COPD and their predictors in patients hospitalized for first-ever disease exacerbations. Patients who were older and hospitalized had more comorbidities such as congestive heart failure (CHF), malignancies, stroke, were more likely to die (OR: 1.08 per point; 95% CI: 1.01–1.15) than survivors. A greater number of survivors had hyperlipidemia. Hospital length of stay was longer for non-survivors (HR 1.01 per day; 95% CI: 1.01–1.01), they experienced more cardiac events, and they were more likely to be admitted to the ICU for mechanical ventilation (HR: 1.33; 95% CI: 1.03–1.73). At one-year, concomitant liver cirrhosis, malignancy, length of stay and ICU admissions during the index hospitalization were significant independent predictors of mortality.

Shams, Ajorlou, & Yang (2015) determined that various models intended to predict and reduce hospital readmission rates were not accurate enough and did not incorporate timing of readmission in their predictions. They developed a new readmission metric that can identify potentially avoidable readmissions from all other types of readmissions. Shams et al. also

proposed a tree-based classification method to estimate the predicted probability of readmission that can directly incorporate patient's history of readmission and risk factors changes over time. They applied their new readmission metric by retrospectively examining 7200 records corresponding to 2985 different adult patients with principal (or secondary) discharge diagnoses of heart failure (HF), acute myocardial infarction (AMI), pneumonia (PNA), and COPD in veterans seeking care at various Veterans Administration (VA) hospitals in the state of Michigan from 2011-2012. Their model was effective at predicting the reduction of 30-day avoidable readmissions of patients with HF, AMI, PNA, and COPD. Their results showed increased discrimination power compared to the literature (c-statistics > 80%) and good calibration. However, Shams et al.'s study was limited to the state of Michigan (Veterans Integrated Service Network [VISN] 11) comprising mostly male veterans. Furthermore, it did not include laboratory results and vital signs which could also contribute to readmissions.

Schizophrenia

Individuals with schizophrenia are likely to suffer multiple co-morbid conditions that could potentially lead to hospitalizations. Olfson, Gerhard, Huang, Crystal, & Stroup (2015) sought to describe the overall cause of mortality and the specific mortality rates and standardized mortality ratios (SMRs) for adults with schizophrenia in the United States. They used mortality rates and mortality ratios standardized to the general population by age, sex, race/ethnicity, and geographic region to characterize and stratify the burden and excess mortality from common medical problems. They calculated mortality rates per 100,000 person-years and the mean year of potential life lost per death. The cohort included 1,138,853 individuals, 4,807,121 years of follow-up, and 74,003 deaths, of which 65,553 had a known cause. Adults with schizophrenia were more than 3.5 times (all-cause SMR, 3.7; 95% CI, 3.7-3.7) as likely to die in the follow-up

period as were adults in the general population. Cardiovascular disease had the highest mortality rate (403.2 per 100,000 person-years) and an SMR of 3.6 (95% CI, 3.5-3.6). Among the six selected cancers, lung cancer had the highest mortality rate (74.8 per 100,000 person-years) and an SMR of 2.4 (95% CI, 2.4-2.5). SMRs were remarkably elevated for COPD (9.9; 95% CI, 9.6-10.2) and influenza pneumonia (7.0; 95% CI 6.7-7.4). Accidental deaths (119.7 per 100,000 person-years) were more than twice as many as suicidal deaths (52.0 per 100,000 person-years). Non-suicidal substance-induced death, mostly from alcohol or other drugs, was also a leading cause of death (92.2 per 100,000 person-years). Olfson et al. concluded that nicotine use and other modifiable cardiovascular risks were the reasons for excess cardiovascular and respiratory deaths in people with schizophrenia.

Davydow et al. (2016) found that in individuals with serious mental illnesses (SMIs) such as schizophrenia or bipolar disorder were at increased risk for hospitalizations for ambulatory care-sensitive conditions (ACSCs) and rehospitalization for the same or another ACSC within 30 days. Among individuals with ambulatory care-sensitive condition, serious mental illness was associated with increased risk for hospitalizations for angina (Incidence rate ratios [IRR]: 1.14, 95% CI, 1.04–1.25), COPD/asthma exacerbation (IRR: 1.87; 95% CI, 1.74–2.00), congestive heart failure exacerbation (IRR: 1.25; 95% CI, 1.16–1.35), and diabetes (IRR: 1.43; 95% CI, 1.31–1.57), appendiceal perforation (IRR: 1.49; 95% CI, 1.30–1.71), pneumonia (IRR: 1.72; 95% CI, 1.66–1.79), and urinary tract infection (IRR: 1.70; 95% CI, 1.62–1.78). SMI was also associated with increased risk for rehospitalization within 30 days for the same (IRR: 1.28; 95% CI, 1.18–1.40) or for another ACSC (IRR: 1.62; 95% CI, 1.49–1.76).

Burke, Donzé, & Schnipper (2013) aimed to determine the independent contribution of psychiatric illness and substance abuse to all-cause and potentially avoidable 30-day

readmissions in medical patients. They followed 6,987 patients discharged from a large teaching hospital from July 1, 2009 to June 30, 2010, measured 30-day all-cause and potentially avoidable readmissions (PAR). Burke et al. found that of the 6,987 discharged patients, 1260 were readmitted within 30 days (18.0%); 388 readmissions were potentially avoidable (5.6%). Patients treated for depression and schizophrenia while hospitalized were found to be at higher risk for potentially avoidable 30-day readmissions; on the other hand, those prescribed more psychiatric medications as outpatients are at increased risk for all-cause readmissions.

Mai, Holman, Sanfilippo, & Emery (2011) examined mental illness-related disparities in potentially preventable hospitalizations (PPHs). They sought to answer the four specific following questions: 1) do mental health clients (MHCs) have more PPHs than non-MHCs; 2) which PPH category/medical condition has the highest relative risk; 3) do the associations vary by category of mental disorders; and 4) what would be the potential savings in hospital admissions if MHCs had received the 'same' quality of primary care as non-MHCs? They discovered that PPHs accounted for more than ten percent of all hospital admissions in mental health clients (MHCs). Diabetes and its complications, adverse drugs events, COPD, convulsions and epilepsy, and congestive heart failure (CHF) were the common causes. Ali et al. also found that compared with non-MHCs, MHCs with any mental disorders were more likely to experience a PPH than non-MHCs (overall ARR 2.06, 95% CI 2.03-2.09). Furthermore, adjusted rate ratios of potentially preventable hospitalizations were highest for convulsions and epilepsy, nutritional deficiencies, COPD and adverse drugs events. The ARR of a PPH was highest in mental health clients with alcohol/drug disorders, affective psychoses, other psychoses and schizophrenia.

Brown, Inskip, & Barraclough (2000) investigated the standardized mortality ratio (SMR) and the reasons for excess mortality in a community cohort of 370 schizophrenic individuals

aged 16-65. They followed the cohort for 13 years and found that the SMRs were 298 for all causes of death, 232 for natural causes, and 1273 for unnatural deaths. These SMRs were significantly higher than those to be expected in the general population: three-fold increase for all causes of death, two-fold increase for natural cause mortality, and 12 times increase for unnatural deaths. The SMRs for diseases of the circulatory, digestive, endocrine, nervous and respiratory systems, suicide and undetermined health were also significantly higher than those to be expected in the general population. Finally, fatal diseases from cigarette smoking were more conspicuous than in the general population. Brown, Inskip, & Barraclough (2000) concluded that since the mechanisms of excess schizophrenia-related mortality are known for the most part, thus should be controlled with current guidelines. Of utmost importance, psychiatrists and mental health providers should stay up-to-date with guidelines recommendations and be assertive in addressing smoking, alcohol use, diet and other modifiable lifestyle factors.

Cahoon, Mcginty, Ford, & Daumit (2013) examined the association of schizophrenia with acute and chronic ambulatory care sensitive (ACS) hospitalizations. They defined ACS as hospitalizations potentially preventable by timely primary care. Cahoon et al. used the Prevention Quality Indicators (PQIs) developed by the Agency for Healthcare Quality and Research (AHRQ) to identify ACS hospitalizations and analyze hospital discharge data from the Nationwide Inpatient Sample (NIS). They found that schizophrenia was associated with increased odds of hospitalization for acute ACS conditions (OR = 1.34; 95% CI: 1.31, 1.38), as well as for chronic ACS conditions (OR 1.04, 95% CI 1.01-1.06). Hospitalization for acute ACS conditions were remarkable for COPD (OR 1.52, 95% CI 1.46-1.59), asthma (OR 1.14, 95% CI 1.08-1.20), diabetes mellitus short-term complications (OR 1.42, 95% CI 1.33-1.50), and uncontrolled diabetes (OR 2.34, 95% CI 2.20-2.50). Nonetheless, schizophrenia was associated

with decreased odds of hospitalization for congestive heart failure, diabetes mellitus long-term complications, angina without procedure, and diabetes related lower- extremity amputations. Schizophrenia was not associated with hospitalization for hypertension.

In a meta-analysis study intended to investigate factors influencing readmission in depression or schizophrenia, Bridge & Barbe (2004) found five principal factors that seemed to influence the risk of rehospitalization: (1) patient factors: sex, marital status, age, and involuntary first admission; (2) clinical factors such as psychiatric diagnosis, global functioning, the degree and type of symptoms; (3) comorbid psychiatric disorders, such as substance abuse disorders, history of past psychiatric hospitalization; (4) number of previous admissions; and (5) a poor discharge prognosis. Concomitantly, they found that strategies with great potential to reduce hospital readmissions for depression and schizophrenia included: (1) Medication Event Monitoring System to ensure medication adherence or compliance; (2) linkage with outpatient care; (3) disease management programs; (4) psychoeducation, and (5) psychiatry advance directives.

Using a framework of specific care recommendations, Tsan et al. (2012) sought to determine whether there were particular types and patterns of routine outpatient care that were associated with improved survival for male veterans aged 50 years and older, diagnosed with schizophrenia seeking care from the VA. They identified three groups. First, the high-consistent care group, the largest (n= 20,854), with an average of 5.4 types of care annually. This group included veterans with the most comorbidities; the unadjusted mortality rate of 26%. Second, the moderate-consistent care group averaged 3.8 types of care; the unadjusted mortality rate was 36% (n = 18,218). Third, the poor-decreasing care group averaged 1.9 types of care across all years; this group comprised the oldest veterans (but with a wider variation in age, with SD = 10

years); however, it had the least comorbidity. The unadjusted mortality rate was 31% (n = 10,101). In the multivariable adjusted model, the hazard ratio (HR) for the moderate-consistent group indicated a 41% increase in the mortality rate (HR = 1.41, 95% CI 1.36 to 1.47) relative to the high-consistent group. However, patients in the poor-decreasing group experienced a 6% decrease in mortality rate (HR = 0.94; 95% CI 0.90 to 0.99) relative to the high-consistent group.

COPD and Schizophrenia

In a retrospective record linkage study, Hoang, Stewart, & Goldacre (2011) desired on one hand to investigate whether the mortality gap had reduced from 1999 to 2006 between people with schizophrenia or bipolar disorder and the general population; and on the other hand, to describe the relative contribution from natural death and unnatural causes of death. They calculated mortality in 3 broad age groups after hospital discharge as age and sex standardized mortality ratios, comparing mortality in people with schizophrenia or bipolar disorder with mortality in the general population of England. The age groups were: <45, 45-64, and 65-84. Patients aged 85 and over were excluded from analysis due to their small numbers. Poisson test was used to investigate whether there was a significant trend in standardized mortality ratio over time. Hoang et al. made the following findings: (1) from 1999 to 2006, the mortality gap had widened overtime, and standardized mortality ratios in the psychiatric cohorts were about double the population average; (2) for people discharged with schizophrenia, the ratio was 1.6 (95% confidence interval 1.5 to 1.8) in 1999 and 2.2 (2.0 to 2.4) in 2006 (P< 0.001 for trend); for bipolar disorder, the ratios were higher for unnatural than for natural causes; they were 1.3 (1.1 to 1.6) in 1999 and 1.9 (1.6 to 2.2) in 2006 (P= 0.06 for trend). Nonetheless, about three quarters of all deaths were certified as natural, and increases in ratios for natural causes, especially

circulatory and respiratory diseases, were the main components of the increase in all-cause mortality.

Strid, Christiansen, Olsen, & Qin (2014) examined the risk of suicide among patients hospitalized with COPD and profiled differences according to sex, age, psychiatric history, recency and frequency of COPD hospitalization. They studied 19,869 cases who died from suicide between ages 40–95 years from the year 1981 through 2006 and 321,867 matched controls randomly selected from a 25% representative sample of the national population. They used conditional logistic regression to estimate the association between hospitalization for COPD and risk for subsequent suicide. Wald test was used to test differences in OR estimates between groups and to examine interactions between COPD and sex, age and previous psychiatric illness. Strid et al. found that the majority of suicide cases were men (n=12 548; 63.2%) and aged 40 to 60 years (n=10 877; 54.7%). In the study population, 3% (n=592) of suicide cases had a history of hospitalization for COPD by the date of suicide compared with 1% (n=3087) of population controls. Overall, hospitalization for COPD increased suicide risk significantly more in individuals with no recorded history of psychiatric illness (OR 2.6, 95% CI 2.3 to 2.9) than it did for individuals with a psychiatric history (OR 1.2, 95% CI 1.0 to 1.5) after having controlled for the main effect of psychiatric illness and the effects of socioeconomic factors. Regardless of sex and age, COPD was a significant risk factor for suicide in people without a psychiatric history. For individuals with a prior hospital contact because of psychiatric illness, the additional risk of suicide associated with COPD remained highly significant only in female participants and in patients above 60 years.

Partti et al. (2015) sought to determine if the respiratory health of individuals with psychosis is different than that of the general population. They designed a two-stage cluster

quasi-experimental study comprising 8028 participants aged 30 or over 3637 men (45.3%) and 4391 women (54.7%) stratified to represent the Finland's adult population. Among other dependent variables, psychosis was identified by DSM-IV-TR; lung function was measured by spirometry; asthma was diagnosed if participants reported being diagnosed by a physician and was taking anti-asthmatic medication(s); COPD was diagnosed as such if the participants had been admitted to a hospital with COPD or had a spirometry result indicative of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria; and smoking was objectively quantified with serum cotinine (S-Cot) levels. The most striking results of this study were: (1) self-reported daily smoking and heavy smoking were significantly more common in participants with schizophrenia compared with participants without psychosis; (2) participants with schizophrenia had significantly higher serum cotinine (S-Cot) levels compared with participants without psychosis, even after adjusting for age and gender (b=127.6 ng/mL, 95% CI 31.4–223.9 ng/mL, P=0.009) in a linear regression model; (3) participants with schizophrenia as well as those with other non-affective psychoses had statistically significantly lower FEV1 and FVC values but a normal FEV1/FVC ratio compared with participants without psychosis, suggesting a restrictive ventilatory pattern. Overall, participants with schizophrenia and other non-affective psychosis had significantly lower lung function values compared with the general population, and the association remained significant for schizophrenia after adjustment for smoking and other potential confounders. Schizophrenia was associated with increased odds of pneumonia (odds ratio (OR) = 4.9), COPD, (OR = 4.2), chronic bronchitis (OR=3.8), and with high cotinine levels.

Copeland et al. (2007) wanted to determine the risk associated with schizophrenia for common pulmonary illnesses (pneumonia and COPD) during the last year of veterans' lives.

From the VA electronic database, they identified 27,798 deceased veterans in 2002 and analyzed four parameters: pulmonary disease diagnosed in the final year of life, pulmonary disease diagnosed in the final hospitalization where death occurred, final-year diagnosis of pneumonia, and final-year diagnosis of COPD. They found that among the deceased, 943 (3.4% of 27,798) had schizophrenia, 3% were women, most were white (76%) or African–American (18%), and average age at death was 72.4 years (SD 11.5). For the primary outcome in the multivariable model, schizophrenia nearly doubled the odds of pulmonary disease in the last year of life (OR=1.9, 95% CI 1.6–2.2), after controlling for covariable effects. Odds of pulmonary disorders were also greater for patients engaged in outpatient care or diagnosed with tobacco dependence or other mental illness and increased slightly with age and Charlson comorbidity score. Non-white race, female gender, never-married status, diagnosis with substance abuse disorders, and having minimal hospital days in the last year of life were negatively associated with the diagnoses of COPD or pneumonia. Copeland et al. concluded that VA inpatient decedents with schizophrenia were at increased risk for pneumonia and COPD, independent of smoking indicators.

Medical and Pharmacological management of COPD

Adamson, Burns, Camp, Sin, & van Eeden (2016) sought to determine the impact of an individualized care package (CP) on early readmission rates following a hospital admission due to acute exacerbation of COPD (AECOPD). They reviewed data of patients admitted for AECOPD to two inner-city teaching hospitals. The control group consisted of 271 patients whose index AECOPD occurred the year before the comprehensive program, and the experimental group consisted of 191 patients who received the comprehensive care. The primary outcome measure was the total number of readmissions in 30- and 90-day post index

hospitalizations. Secondary outcome measures included the length of time between the index admission and first readmission and all-cause mortality. The CP team comprised a nurse, a respiratory therapist and a physiotherapist. This team enrolled patients during hospitalization; upon discharge, the team made post discharge phone calls, home visits, ensured that patients followed up with their primary care providers and had the community resources needed; the team also identified and addressed individual risk factors. The Student's t-test and Fisher's exact test were used to analyze the two groups. The analysis of variance test with a post hoc Tukey test and the chi-square test were used for comparison between four groups. Length of time until first readmission was evaluated using the Student's t-test. All-cause mortality was assessed through the Kaplan–Meier estimate, using the log-rank test to determine significance. Adamson et al. found that the CP significantly reduced 90-day readmission rates in females (P=0.0205, corrected for age, BMI, number of comorbidities, substance abuse, and mental illness) but not in males or in the whole group (P > 0.05). The average times between index admission and first readmission were not different between the two groups. Post hoc multivariate analysis showed that substance abuse (P < 0.01) increased 30- and 90-day readmissions (corrected for age, sex, BMI, number of comorbidities, and mental illness). The 90-day all-cause in-hospital mortality rates were significantly less in the care package group (2.67% versus 7.97%, P=0.0268). Overall, CP for patients admitted to the hospital for AECOPD did not reduce 30- and 90-day readmission rates for both genders but did reduce their 90-day total mortality; nonetheless, it reduced 90-day readmission rate in females.

In order to better understand the reasons why patients with COPD poorly adhere to their medication regimen, Huetsch, Uman, Udris, & Au (2012) sought, on one hand, to identify the characteristics of patients who adhere to their inhaled medications; and the other hand to assess

whether adherence to one medication class was associated with the adherence to the other medication classes in patients who have multiple inhalers. Study participants were 2,730 veterans in VISN 20 selected from the VA electronic databases diagnosed with COPD by pulmonary function testing between January 2003 and December 2007. Huetsch et al. used pharmacy records to estimate adherence to inhaled corticosteroids (ICS), ipratropium bromide (IP), and long-acting beta-agonists (LABA) over two consecutive six-month periods. Veterans were said to be adherent if they had refilled their medications to have 80% of drug available over the time period. Covariates were demographics, behavioral habits, COPD severity, and comorbidities. The most remarkable findings were that: (1) adherence was poor, with 19.8 % adherent to ICS, 30.6 % adherent to LABA, and 25.6 % adherent to IP; (2) predictors of adherence to inhaled therapies were inconsistent and dependent on the medication being examined; (3) in adjusted analysis, being adherent to a medication at baseline was the strongest predictor of future adherence to that same medication [(Odds ratio, 95 % confidence interval) ICS: 4.79 (3.22–7.12); LABA: 6.60 (3.92–11.11); IP: 14.13 (10.00–19.97)], but did not reliably predict adherence to other classes of medication. Additionally, Huetsch et al. found that: (1) gender, race, and smoking status were not associated with medication adherence; (2) overall, there was no association between medication adherence and the presence of particular comorbid conditions, nor with the number of total drug classes that patients had received; (3) older age and fewer missed clinic visits were associated with LABA adherence only; (4) a previous diagnosis of lung cancer or asthma was associated with decreased adherence to LABA, while a diagnosis of acute coronary syndrome or depression was associated with decreased adherence to IP.

Moy et al. (2016) examined the effects of a 12-month Internet-mediated, pedometer-based walking intervention called Taking Healthy Steps by randomizing 239 veterans with

COPD in a 2:1 ratio to the intervention or wait-list control. The primary outcome was health-related quality of life (HRQL) assessed by the St George's Respiratory Questionnaire Total Score (SGRQ-TS), the secondary outcome was daily step count. Linear mixed-effect models were used to evaluate the effect of intervention at 4, 8 and 12 months. They found that between-group difference in daily step count was maximal and statistically significant at month 4 (P<.001) but approached zero in months 8-12. Also, at 12 months, there were no significant between-group differences in SGRQ-TS or daily step count. Within the intervention group, mean 76.7% (SD 29.5) of 366 days had valid step-count data, which decreased over the months of study (P<.001). They concluded that an Internet-mediated, pedometer-based PA intervention, although efficacious at four months, did not maintain improvements in HRQL and daily step counts over time.

Pharmacological and Nonpharmacological Management of Schizophrenia

Berger et al. (2012) studied adherence to second generation antipsychotic medications such as aripiprazole, quetiapine, and ziprasidone, as prescribed following hospitalization for schizophrenia and bipolar disorder. They used a database linking hospital admission records to health insurance claims and identified 43 patients hospitalized for schizophrenia, and 84 patients with bipolar disorder between January 1, 2001 and September 30, 2008. During the 6-month period following hospitalization, patients with schizophrenia received an average of 101 therapy-days with the second-generation antipsychotic agent prescribed at discharge. Mean medication possession ratio (MPR) at 6 months was 55.1% for schizophrenia patients, and 37.3% for patients with bipolar disorder; roughly 25% of patients switched to another agent over this period. These findings are indicative of poor adherence to treatment with aripiprazole, quetiapine, or ziprasidone at hospital discharge.

Wildgust & Beary (2010) searched the literature to examine the impact of modifiable risk factors on excess schizophrenia mortality and to what extent these factors can be managed. Using the search terms schizophrenia and mortality and modifiable (OR reduction OR intervention), Wildgust and Beary searched Medline, Embrase, and PsycInfo from 1987 to January 2010 and found 974 articles related to excess mortality in schizophrenia, modifiable risk factors in the general population, modifiable mortality risk factors in schizophrenia, non-modifiable mortality risk factors in schizophrenia, review of studies in schizophrenia designed to reduce mortality, and can one reduce the mortality risk factors in schizophrenia? The literature revealed the following: (1) patients with schizophrenia have high levels of the top six modifiable risk factors identified by the World Health Organization: hypertension, smoking, elevated glycemia, physical inactivity, obesity, and dyslipidemia; (2) a small number of studies showed successful interventions to improve these risk factors, but prospective long-term studies were not available to show their impact on mortality; (3) a number of studies supported that premature deaths in patients with schizophrenia could be due to health disparities in this category of patients; (4) suboptimal cardiorespiratory fitness and muscle strength were among the strongest predictors of all-cause mortality in the general population; (5) cigarette smoking was still one of the largest risk factors for premature all-cause mortality; (6) lifestyle intervention programs addressing exercise, smoking cessation and compliance with medication were likely to significantly decrease mortality in schizophrenia; (7) ultimately, decreasing mortality in schizophrenic patients would inevitably require having people who advocate for them and ensure that they receive treatments needed, avoiding prejudice, and establish fitness standards in schizophrenia care.

Conclusion

The majority of literature reviewed indicates that the mechanisms of COPD and schizophrenia are well known and the rate of mortality in individuals with schizophrenia is greater than that of the general population. Individuals with schizophrenia are likely to suffer multiple co-morbid conditions that could potentially lead to hospitalizations, and COPD is one of those comorbid conditions. As a matter of facts, one VA study found that schizophrenia nearly doubled the odds of pulmonary disease (pneumonia and COPD) in the last year of life. Moreover, a study demonstrated that individuals with schizophrenia and other non-affective psychosis have significantly lower lung function values, compared with the general population. It is also documented that individuals with serious mental illnesses (SMIs) such as schizophrenia or bipolar disorder, have an increased risk for hospitalizations for ambulatory care-sensitive conditions and rehospitalization for the same or another ACSC within 30 days. Likewise, patients treated for depression and for schizophrenia while hospitalized are at higher risk for potentially avoidable 30-day readmissions. An effective model to predict the reduction of 30-day avoidable readmissions of patients with HF, AMI, PNA, and COPD was developed for VISN 11 of the VA. Nonetheless, there is gap in the literature regarding schizophrenia in general, and predisposition of schizophrenic South Carolinians in particular, to be readmitted within 30 days after being treated for AECOPD.

CHAPTER 3

Methodology

Purpose, objectives, and design of project

The purpose of this study was to examine if the coexistence of schizophrenia would increase 30 day-readmission rates among South Carolinians with COPD. Its two key objectives were: (1) to determine if schizophrenia is a significant predictor for 30-day COPD readmission after adjusting for the other covariates (age, gender, anxiety, smoking status, T2DM, GERD and chronic ischemic heart disease); (2) to suggest lifestyle approaches to manage both COPD and schizophrenia. The PICO question for the research study was as follows: "In the hospitalized South Carolinians with COPD (P), how does having schizophrenia (I) compared to not having schizophrenia (C) influence the 30-day readmission rate (O)?

Since individuals with schizophrenia are likely to suffer multiple comorbid conditions that could potentially lead to hospitalizations (Olfson, Gerhard, Huang, Crystal, & Stroup, 2015), this study sought to investigate a possible relationship between the coexistence of COPD-schizophrenia and 30-day readmission for COPD in South Carolinians. To better achieve this goal, a retrospective cohort design was chosen because the study will be done on a preexisting population. Cohort studies are designed by selecting a group of exposed individuals and a group of nonexposed individuals and follow them with the aim to compare the incidence of a disease or the mortality rate from a disease (Gordis, 2014, p. 179). A cohort study is said to be retrospective when historical data are used, reason why this type of study is also called historical cohort or nonconcurrent prospective study. In application to the current study, it looked at data related to a group of South Carolinians hospitalized in the past, from 1996 to 2015. Contrary to classic

epidemiological study, the 30-day readmission rate of a group of South Carolinians with acute exacerbation of COPD (AECOPD) and schizophrenia was compared to the one of a different group of South Carolinians without schizophrenia. Based on the PICO question detailed above, the dependent variable (DV) or outcome variable was "30-day readmission." There was one major independent (factor variable) with two levels:

1. South Carolinians with underlying schizophrenia, admitted in the hospital for AECOPD.
2. South Carolinians without schizophrenia, admitted in the hospital for AECOPD.

The other covariates (CV) are:

1. Gender (male/female)
2. Age group (< 65 years/≥ 65 years)
3. Anxiety
4. Smoking status
5. T2DM
6. GERD
7. Chronic ischemic heart disease.

Procedure

Following IRBs approval, an *Application for Encounter Data* and a signed Data Use Agreement was sent to the South Carolina Revenue and Financial Affairs Office (RFA). This retrospective study included dates of hospital discharge from January 1, 1996 to September 30, 2015. The following ICD 9 were sent as variables and values to be used for record selection:

491.21: AECOPD/Obstructive chronic bronchitis with exacerbation

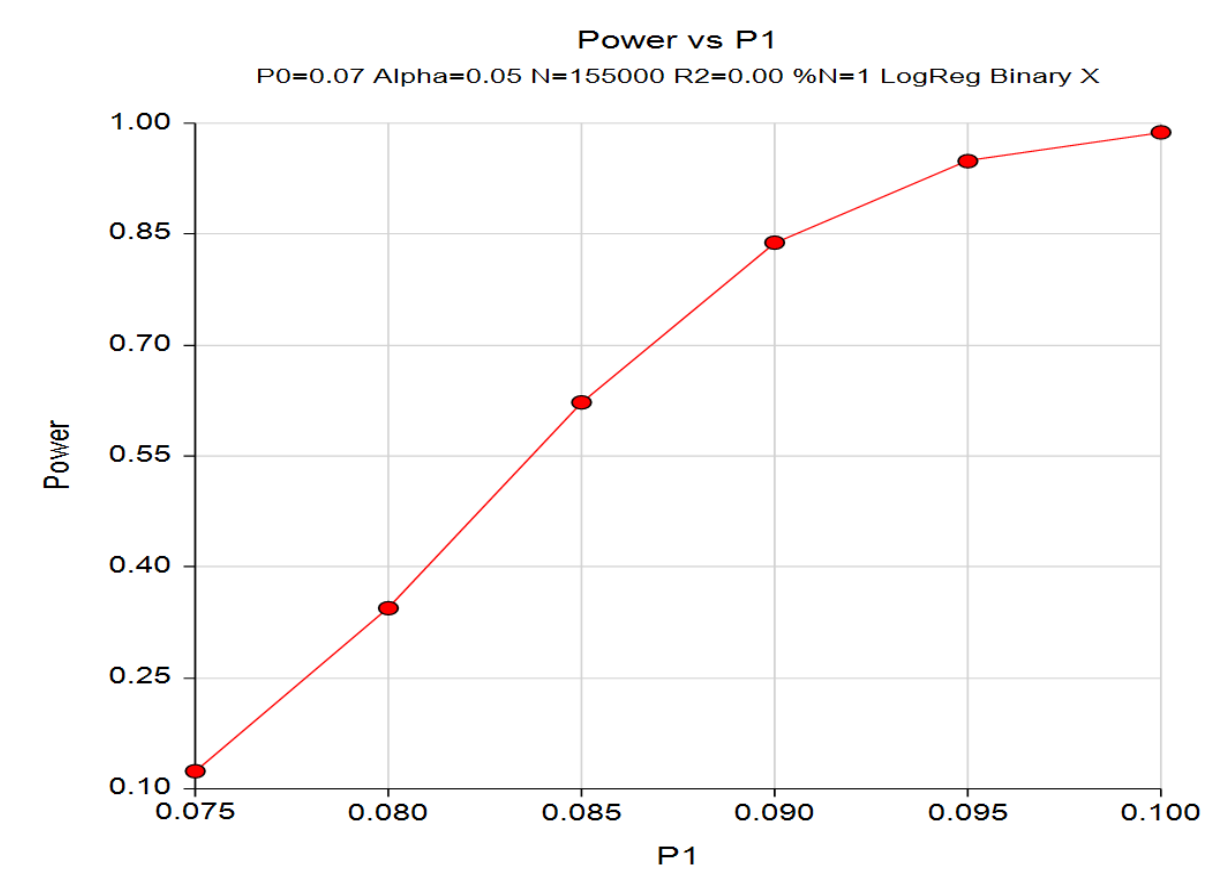
491.22: Obstructive chronic bronchitis with acute bronchitis

Primary and Secondary diagnoses.

RFA was also asked to create a dichotomous schizophrenia variable indicating whether the patient has any inpatient or outpatient diagnosis of schizophrenia (ICD 9: 295.XX) during the time frame. Preparatory research performed by the RFA indicated that there were approximately 155,000 discharges that met the inclusion criteria of this study and a baseline readmission proportion of 0.07. As Figure 1 below from PASS 14 sample size software showed, a readmission proportion of about 0.09 or greater in schizophrenics would result in ≥ 80% power to show a statistically significant difference between the two groups using a two-sided alpha of 0.05. Figure 1 did not reflect the increase in power which usually occurs with the addition of needed covariates to the logistic model. According to Mackinnon (2013), the addition of one or two good covariates undeniably improves statistical power without complicating a statistical model.

Figure 1

Relationship between power and readmission proportion of schizophrenic patients for AECOPD.



Protection of human subjects

Although there was no direct contact with study participants, approval of Southern Adventist University's Internal Review Boards (IRBs) was obtained. In the data application, a patient unique identifier was requested because the outcome variable is "30-day readmission". The unique identifier for each patient was also intended to prevent any one, including the principal investigator of this study, would be able to discover patients' identity. To ensure additional confidentiality, only the year and month of initial and subsequent discharges of each patient were requested, rather than asking for the date. Alternatively, the RFA was asked to

identify the initial discharge of a given patient, and then give the time in days to any subsequent discharges.

Description of measures

After receiving the data from the RFA, measurements and calculations were done in three phases, univariate analysis, bivariate analysis and multivariate analysis. In the univariate analysis phase, descriptive analysis was completed on each IV and CV. Because of the clustered readmission, a series of GEE models was used. Bivariate analyses consisted of running a series of GEE regressions with 30-day readmission as the outcome, entering individual CVs. Multivariate analyses consisted in performing a series of GEE regressions analyses to determine the association of schizophrenia and the covariates each with 30-day AECOPD exacerbation readmission. Covariates chosen were age, gender, smoking status, anxiety, ischemic heart disease, type 2 diabetes mellitus, gastroesophageal reflux disease (GERD), pulmonary hypertension. These covariates were chosen based on their association – in the literature- with hospital readmission of individuals suffering from mental illnesses such as schizophrenia, bipolar disease and depression. All statistics tests were run in R, then SPSS. In the multiple regression phase, SPSS displayed the odds ratio and confidence interval to aid in determining the statistical significance of association found between an independent variable and the outcome variable.

Evaluation plan

The absence of randomization is an undeniable weakness of cohort studies, including this one. Nonetheless, Figure 1 suggested an association between 30-day readmission and schizophrenia in patients with AECOPD. Another disadvantage was the inability to establish causation or generate incidence rate and risk as also seen in case-control studies (PennState, 2017; Lewallen & Courtright, 1998). Similarly, comorbidities and other co-existing psychiatric

disorders, medication compliance, family support, and the complexity of schizophrenia's etiology were real threats to the internal validity of this study. Some advantages included cost effectiveness, the ease to conduct the study, and the potential to be powerful. Selection and information biases seen in classic cohort studies were not applicable to this study's unique design.

CHAPTER 4

Results

Univariate Analyses

The data received from the South Carolina Revenue and Financial Affairs Office (RFA) included 325,780 observations and 70 variables. The following data were excluded: patients under the age of 15 years, patients with unknown gender, negative span days and admissions where it was uncertain whether a 30-day readmission occurred, mainly, the September 2015 admissions. The resulting data set was 323,237 observations.

Additional variables were created to run descriptive, binary and regression analyses. Those variables included schizophrenia, inclusion criteria, exacerbation, acute bronchitis, 30-day readmission, other mental illnesses, and severity of disease as illustrated by ICU admission. Bipolar disease, T2DM, and GERD had strong preliminary generalized estimating equation (GEE) and were included in the analysis. The covariate age was dichotomized in ages < 65, and ≥ 65 years. Because admissions are clustered within patients, a p value was calculated, rather than running a chi square test. GEE is another way to estimate the parameters of a logistic regression model. The maximum likelihood estimation (MLE) would be another way. The difference between GEE and MLE is that GEE is able to take the within subject variance in consideration, which MLE does not. It does not require to know the variance or covariance structure in order to model the mean response. The same patient could have been admitted more than once, and the data do not reflect that.

Table 1 indicates the baseline characteristics of the patients by schizophrenia status. Of the 323,237 COPD patients for whom data were collected, 3,812 (1.18%) had a diagnosis of schizophrenia. Of the total sample, 152, 624 (47.22%) were males; 201,692 (62.4%) were age 65

years or more. Since GEE automatically calculated p values, Table 1 also indicates that age group significantly predicts schizophrenia status ($p < 0.001$); but gender does not ($p = 0.061$). While initially, it was the intent to collect data related to race, this data was not available. Other mental illnesses were recorded. Including tobacco and substance abuse which are common in COPD and schizophrenic patients, there were 122,131 (37.78%) of the total group with mental health diagnoses. Excluding tobacco use but including other substance abuse diagnoses, there were 59,999 (18.56%) with mental health diagnoses. There were significantly more comorbid mental health diagnoses in patients with schizophrenia than in the COPD patients without schizophrenia, as can be seen in Table 1. Mental illnesses ($p < 0.001$), anxiety ($p = 0.001$), bipolar disorder ($p = 0.002$), personality disorder ($p = 0.028$), smoking status ($p < 0.001$), admission to ICU ($p = 0.002$), and T2DM ($p <0.001$) are the other covariates that significantly predicted schizophrenia status. There were 36,683 (11.4%) COPD admissions with secondary diagnosis of anxiety, 5,229 (1.6%) with bipolar disease, 447 (0.1%) with personality disorder, 87,910 (27.2%) with nicotine use, 53,388 (16.5%) admissions or transferred to ICU, and 60,930 (18.8%) with T2DM. Depression, eating disorder, attention deficit disorder, ischemic heart disease, congestive heart failure, pulmonary hypertension, and GERD were not significant predictors of schizophrenia status.

Table 1

*Baseline Characteristics by Schizophrenia Status**

Variable	All Admissions (n=323,237)	Schizophrenic (n=3,812)	Not Schizophrenic (n=319,425)	P-value**
Male Gender	152,624 (47.2%)	1,708 (44.8%)	150,916 (47.2%)	0.061
Age ≥ 65 years	201,692 (62.4%)	1,179 (30.9%)	200,513 (62.8%)	<0.001
Other Mental Illness***	122,131 (37.8%)	2,176 (57.1%)	119,955 (37.6%)	<0.001
Other Mental Illness****	59,999 (18.6%)	1,049 (27.5%)	58,950 (18.5%)	<0.001
Depression	1816 (0.6%)	36 (0.9%)	1780 (0.6%)	0.952
Anxiety	36683 (11.4%)	294 (7.7%)	36689 (11.5%)	0.001
Eating Disorder	28 (0.0%)	2 (0.0%)	26 (0.0%)	0.501
Attention Deficit Disorder	124 (0.04%)	2 (0.1%)	122 (0.0%)	0.798
Bipolar Disorder	5229 (1.6%)	498 (13.1%)	4731 (1.5%)	0.002
Personality Disorder	447 (0.1%)	31 (0.8%)	416 (0.1%)	0.028
Smokers	87910 (27.2%)	1762 (46.2%)	86148 (27%)	<0.001
Admitted to ICU	53388 (16.5%)	827 (21.7%)	52561 (16.5)	0.002
Type 2 Diabetes Mellitus	60930 (18.8%)	907 (23.8%)	60023 (18.9%)	<0.001
Ischemic Heart Disease	576 (0.1%)	5 (0.1%)	571 (0.2%)	0.346
Congestive Heart Failure	1592 (0.5%)	12 (0.3%)	1580 (90.5%)	0.205
Pulmonary Hypertension	1228 (0.4%)	9 (0.2%)	1219 (0.4%)	0.314
GERD	56777 (17.6%)	583 (15.3%)	56194 (17.6%)	0.368

*Counts (%) **By simple GEE logistic regression ***Includes tobacco use disorder and other substance abuse **** Does not include tobacco use disorder, but does include other substance abuse

Table 2 indicates the comparison of selected characteristics by readmission status. Of the total sample of 323,237 patients in this sample, 36,035 (11.15%) were readmitted within 30 days of discharge. Of the 152,624 (47.2%) males, 17,870 (49.6%) were readmitted, and 22,223 (61.7%) of patients 65 years or older out of 201,692 (62.4%) were readmitted. Of the 122,131 (37.8%) admitted patients with tobacco use disorder and other substance abuse, 14,290 (39.7%) were readmitted, while 7,853 (21.8%) out of 59,999 (18.6%) of patients without tobacco use but with other mental illnesses were readmitted. Patients with mental health diagnoses were a significant proportion of the 30-day readmission sample. Still, gender ($p < 0.001$), age 65 years or older ($p < 0.001$), comorbid mental illnesses ($p = 0.006$), anxiety ($p < 0.001$), T2DM ($p = 0.002$), GERD ($p < 0.001$) significantly predicted readmission within 30 days after admission for AECOPD. There were 5,338 (14.8%) out of 36,983 (11.1%) COPD readmissions with secondary diagnosis of anxiety, 7,264 (20.2%) out of 60,930 (18.8%) with T2DM, and 6,983 (19.4%) from a total of 56,777 (17.6%) with GERD. Depression, eating disorder, attention deficit disorder, bipolar disorder, personality disorder, nicotine use, admission in the ICU, ischemic heart disease, congestive heart failure, and pulmonary hypertension were not significant predictors of 30-day readmission.

Table 2

*Comparison of Selected Characteristics by Readmission**

Variable	All Admissions (n=323,237)	Readmitted (n=36,035)	Not Readmitted (n=287,202)	P-value**
Male Gender	152,624 (47.2%)	17,870 (49.6%)	134,754 (46.9%)	<0.001
Age≥65 years	201,692 (62.4%)	22,223 (61.7%)	179,469 (62.5%)	<0.001
Other Mental Illness***	122,131 (37.8%)	14,290 (39.7%)	107,841 (37.5%)	0.006
Other Mental Illness****	59,999 (18.6%)	7,853 (21.8%)	52,146 (18.2%)	0.006
Depression	1,816 (0.6%)	216 (0.6%)	1,600 (0.6%)	0.795
Anxiety	36,983 (11.4%)	5,338 (14.8%)	31,645 (11%)	<0.001
Eating Disorder	28 (0%)	2 (0%)	26 (0%)	0.861
Attention Deficit Disorder	124 (0%)	6 (0%)	118 (0%)	0.469
Bipolar Disorder	5,229 (1.6%)	663 (1.8%)	4,566 (1.6)	0.128
Personality Disorder	447 (0.1%)	65 (0.2%)	382 (0.1%)	0.416
Smokers	87,910 (27.2%)	9,684 (26.9%)	78,226 (27.2%)	0.815
Admitted to ICU	53,388 (16.5%)	6,232 (17.3%)	47,156 (16.4%)	0.319
Type 2 Diabetes Mellitus	60,930 (18.8%)	7,264 (20.2%)	53,666 (18.7%)	0.002
Ischemic Heart Disease	576 (0.2%)	61 (0.2%)	515 (0.2%)	0.355
Congestive Heart Failure	1,592 (0.5%)	185 (0.5%)	1,407 (0.5%)	0.781
Pulmonary Hypertension	1,228 (0.4%)	142 (0.4%)	1,086 (0.4%)	0.795
GERD	56,777 (17.6%)	6,983 (19.4%)	49,794 (17.3%)	<0.001

*Counts (%), readmitted within 30 days for COPD exacerbation **By simple GEE logistic regression ***Includes tobacco use disorder and other substance abuse **** Does not include tobacco use disorder, but does include other substance abuse.

Hypothesis Testing and Bivariate Analyses

The PICO question for this research study is: "In the hospitalized South Carolinians with COPD (P), how does having schizophrenia (I) compared to not having schizophrenia (C) influence the 30-day readmission rate (O)? It was hypothesized that South Carolinians with COPD and schizophrenia were likely to be readmitted more frequently 30 days after being hospitalized for an AECOPD. Thus, bivariate chi square analysis was done to determine if there

is a difference in readmission rates for those with schizophrenia versus those without. No significant difference was found ($\chi^2(1) = 2.628$, p = 0.105) as shown in Table 3 (only consider the p value in the Test of Model Effects). There were significant differences in readmission based on:

- Gender; for males ($\chi^2(1) = 37.518$, p = 0.000) as seen in Table 4 - Appendix A.
- Age ($\chi^2(1) = 406.220$, p = 0.000) as shown in Table 5 - Appendix A.
- Anxiety ($\chi^2(1) = 111.187$, p = 0.000) as revealed in Table 6 - Appendix A.
- T2DM ($\chi^2(1) = 23.561$, p = 0.014) as illustrated in Table 7 - Appendix A.
- GERD ($\chi^2(1) = 55.594$, p = 0.000) as seen in Table 8 - Appendix A.

There was no statistical significant difference in 30-day readmission based on smoking status ($\chi^2(1) = 0.130$, p = 0.719) as revealed in Table 9 - Appendix A, and on chronic ischemic heart disease ($\chi^2(1) = 1.928$, p = 0.165) as illustrated 10 - Appendix A.

Table 3

Thirty-Day Readmission Based on Schizophrenia Status (Model-based)

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	2904.374	1	0.000
Schizophrenia	2.628	1	0.105

Dependent Variable: Readmission30b
Model: (Intercept), Schizophrenia

Parameter Estimates

			95% Wald Confidence Interval		Hypothesis Test			95% Wald Confidence Interval for Exp(B)		
Parameters	B	Std Error	Lower	Upper	Wald Chi-Square	df	Sig	Exp(B)	Lower	Upper
Intercept	2.069	0.0971	1.878	2.259	453.712	1	0.000	7.915	6.543	9.574
Schizophrenia =No	0.617	0.0981	0.425	0.809	39.566	1	0.000	1.853	1.529	2.246
Schizophrenia =Yes	0[a]							1		
Scale	1									

Multivariate Analysis

Using the GENLIN function in SPSS, the logic link, the Fisher method with full likelihood, and exchangeable correlation type, exploratory multivariate data analysis was done using the variables in the data set to create a model for predicting readmission within 30 days for COPD patients. Because of the categoric nature of the dependent variable, multiple logistic regression procedures were used. Several models were created. The odds ratio and their respective 95% confidence intervals were included. Since GEE is a semiparametric method which relies solely on the data to inform the user, there were no constraints of meeting assumptions. The first model used eight independent variables analyzed per the robust method (Table 4). This model resulted in six significant predictors of readmission: Gender ($\chi^2(1) = 77.151$, $p = 0.046$); Anxiety ($\chi^2(1) = 31.318$, $p = 0.000$); Age ($\chi^2(1) = 272.996$, $p = 0.000$); T2DM ($\chi^2(1) = 5.982$, $p = 0.014$); Smoking Status ($\chi^2(1) = 4.867$, $p = 0.027$); and GERD ($\chi^2(1) = 14.126$, $p = 0.000$).

Schizophrenia was slightly below significance level (p = 0.054), chronic ischemic disease was not significant (p = 0.332)

Table 11

Logistic Regression Output- Robust Method

Tests of Model Effects			
Source	Type III		
	Wald Chi-Square	df	Sig.
Intercept	405.025	1	0.000
Schizophrenia	3.705	1	0.054
SEX	77.151	1	0.000
Anxiety	31.318	1	0.000
AGRP65	272.996	1	0.000
Chronic Ischemic Heart dz	0.941	1	0.332
T2DM	5.982	1	0.014
Smoking Status	4.867	1	0.027
GERD	14.126	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), Smoking Status, Schizophrenia, SEX2, Anxiety, AGRP65, Chronic.Ischemic.Heart.dz, T2DM, GERD

Parameter Estimates

Parameters	B	Std Error	95% Wald Confidence Interval		Hypothesis Test				95% Wald Confidence Interval for Exp(B)	
			Lower	Upper	Wald Chi-Square	df	Sig	Exp(B)	Lower	Upper
Intercept	-2.708	0.0162	-2.740	-2.676	27783.892	1	0.000	0.067	0.065	0.069
Schizophrenia = Yes	.213	.1108	-0.004	.430	3.705	1	0.054	1.238	0.996	1.538
Schizophrenia = NO	0[a]							1		
SEX2 = Male	0.120	0.0150	0.091	0.150	64.558	1	0.000	1.219	1.095	1.162
SEX2 = Female	0[a]							1		
Anxiety = YES	0.198	0.0355	0.129	0.268	31.318	1	0.000	1.219	1.138	1.307
Anxiety = NO	0[a]					1				
AGRP65 = Less than 65 years	-.385	0.0233	-0.430	-0.339	272.996	1	0.000	0.681	0.650	0.712
AGRP65 = 65 years or older	0[a]					1				
Chronic ischemic heart dz = YES	0.205	0.2116	-0.209	0.620	0.941	1	0.332	1.228	0.811	1.859
Chronic ischemic heart dz = NO	0[a]					1				
T2DM = YES	0.072	0.0296	0.014	0.130	5.982	1	0.014	1.075	1.041	1.139
T2DM = NO	0[a]					1				
Smoking status = YES	0.061	0.0275	0.007	0.115	4.867	1	0.027	1.063	1.007	1.121
Smoking status = NO	0[a]					1				
GERD =YES	0.110	0.0293	0.053	0.168	14.126	1	0.000	1.117	1.054	1.183
GERD = NO	0[a]					1				
Scale	1									

Dependent Variable: Readmission30b
Model (Intercept). Schizophrenia, SEX2, Anxiety, AGRP65, Ischemic Heart dz, T2DM, Smoking Status, GERD
[a] Set to zero because this parameter is redundant.

Interpretation of the strength of association between the predictors and readmission:

- ***Schizophrenia***: Holding the other predictors constant, a patient with schizophrenia would have an odds ratio of readmission of 1.238, that is a 23.8% increase in the odds of readmission compared to a person without schizophrenia; with a 95% confidence interval between 0.996 and 1.538. That is, we are 95% confident that the odds of readmission for a schizophrenic is between 0.4% lower and 53.8% higher than the same odds in a non-schizophrenic. The unadjusted schizophrenia odds ratio is not significantly different from 1 at the 0.05 level.
- ***Anxiety***: Holding the other predictors constant, a patient with anxiety would have an odds ratio of readmission of 1.219, that is a 21.9% increase in the odds of readmission compared to a person without anxiety; with a 95% confidence interval between 1.138 and 1.307, or an increase of odds between 13.8% and 30.7%.).
- ***AGRP65***: Holding the other predictors constant, a patient less than 65 years old would have an odds ratio of readmission of 0.319, that is a 31.9% decrease in the odds of readmission compared to a patient who is at least 65 years old, with a 95% confidence interval between 0.288 and 0.35, or a decrease of odds between 28.8% and 35%.).
- ***Chronic ischemic heart disease***: Holding the other predictors constant, a patient with chronic ischemic heart disease would have an odds ratio of readmission of 1.228, that is a 22.8% increase in the odds of readmission compared to a person without chronic ischemic disease; with a 95% confidence interval between 0.811 and 1.859. In other words, we are 95% confident that the odds for readmission with a patient with ischemic heart disease is between 18.9% lower and 85.9% higher than the same odds

in a patient without ischemic heart disease. The unadjusted ischemic heart disease odds ratio is not significantly different from 1 at the 0.05 level.

- ***T2DM***: Holding the other predictors constant, a patient with T2DM would have an odds ratio of readmission of 1.075, that is a 7.5% increase in the odds of readmission compared to a person without T2DM, with a 95% confidence interval between 1.014 and 1.139, or an increase of odds between 1.4% and 13.9%.
- ***Smoking status***: Holding the other predictors constant, a patient who has smoking disorder would have an odds ratio of readmission of 1.063%, that is a 6.3% increase in the odds of readmission compared to a person without smoking disorder, with a 95% confidence interval between 1.007 and 1.121, or an increase of odds between 0.7% and 12.1%.).
- ***GERD***: Holding the other predictors constant, a patient with GERD would have an odds ratio of readmission of 1.117%, that is 11.7% increase in the odds of readmission compared to a patient without GERD, with a 95% confidence interval between 1.054 and 1.183, or an increase of odds between 5.4% and 18.3%.).

Additional comments on the associations:

- All IVs have a positive relationship with the DV except age less than 65 in other words, all IVs as coded are risk factors for readmission (odds ratio >1), except for the age group variable where age less than 65 years is protective.
- Age is the biggest contributing factor, followed by anxiety, then, gender, GERD, T2DM, and smoking status.

Comments on the statistical significance of the associations:

- The six significant predictors of readmission: Gender ($\chi^2(1) = 77.151$, p = 0.046); Anxiety ($\chi^2(1) = 31.318$, p = 0.000); Age ($\chi^2(1) = 272.996$, p = 0.000); T2DM ($\chi^2(1) = 5.982$, p = 0.014); Smoking Status ($\chi^2(1) = 4.867$, p = 0.027); and GERD ($\chi^2(1) = 14.126$, p = 0.000).

Statement of the regression equation:

- The regression equation for the robust (GEE) model:

$$\log\{P(Y=1) / [1 - P(Y=1)]\} = \beta_0 + \beta_1*SEX2 + \beta_2*Anxiety + \beta_3*AGRP65 + \beta_4*T2DM + \beta_5*Smoking\ Status + \beta_6*GERD.$$

Where P(Y=1) is the probability of readmission, β_0 is the intercept, β_1 is the coefficient for SEX2, β_2 is the coefficient for Anxiety, β_3 is the coefficient for AGRP65, β_4 is the coefficient for T2DM, β_5 is the coefficient for Smoking Status, and β_6 is the coefficient for GERD.

Log is the natural logarithm.

SEX2 = 1 if the patient is MALE, 0 if FEMALE.

Anxiety = 1 if the patient has an anxiety diagnosis, 0 otherwise.

AGRP65 = 1 if age<65, 0 otherwise.

T2DM = 1 if the patient has a diagnosis of T2DM, 0 otherwise.

Smoking Status = 1 if the patient has a diagnosis of nicotine use disorder, 0 otherwise.

GERD =1 if the patient has a diagnosis of GERD, 0 otherwise.

Alternative regression analyses using a model-based method as opposed to the prior robust method resulted in one additional variable (schizophrenia) being included as a significant

predictor of readmission, as illustrated in Table 12 of Appendix B. Smoking Status ($\chi^2(1) = 13.750$, $p = 0.000$); Schizophrenia ($\chi^2(1) = 9.283$, $p = 0.002$); SEX2 ($\chi^2(1) = 44.420$, $p = 0.000$); Anxiety ($\chi^2(1) = 102.552$, $p = 0.000$); Age ($\chi^2(1) = 388.340$, $p = 0.000$); T2DM ($\chi^2(1) = 17.003$, $p = 0.000$); and GERD ($\chi^2(1) = 42.213$, $p = 0.000$).

CHAPTER 5

Discussion

Schizophrenia was not found to be a predictor of 30-day readmission after discharge from an acute exacerbation of chronic obstructive pulmonary disease ($p = 0.105$, OR=1.172, 95% CI [0.967, 1.421]. After adjusting for the other covariates (age, gender, anxiety, smoking status, T2DM, chronic ischemic heart disease, and GERD), schizophrenia was not significantly different from 1 at the 0.05 level, although the odds ratio was 1.238, increasing the odds of readmission of a schizophrenic patient by 23.8% compared to a non-schizophrenic patient 95% CI [0.996, 1.538].

Interestingly, GEE logistic regression univariate analysis using the model-based method showed significance ($p = 0.002$). Likewise, schizophrenia was a significant predictor for 30-day readmission at the multivariate level. When all the other predictors were held constant, a patient with schizophrenia would have an odds ratio of readmission of 1.238, that is a 23.8% increase in the odds of readmission compared to a patient without schizophrenia, with a 95% confidence interval between 1.079 and 1.420, or an increase of odds between 7.9% and 42%.). When model-base GEE regression analysis was done, the matrix assumed that the covariance structure was accurate. In case of misspecification, the odds ratios and the confidence intervals would be off. Because the robust p-values are still consistent and unbiased in case of misspecification of the working correlation matrix, more weight is put in these results compared to the p-values obtained by the model-based method. Although not quite statistically significant, the results still raise the possibility that schizophrenia can be a predictor of readmission and further studies using a prospective approach are recommended.

Patients treated for depression and schizophrenia while hospitalized were at higher risk for potentially avoidable 30-day readmissions (Burke, Donzé, & Schnipper, 2013). The unadjusted ORs of the majority of chronic conditions such as CHF, COPD, asthma, diabetes mellitus (DM), long and short-term complications, and uncontrolled diabetes were higher for hospitalizations of people with schizophrenia, versus those without a secondary diagnosis of schizophrenia (Cahoon, McGinty, Ford & Daumit, 2013). It is thus not surprising that T2DM was significant predictor for 30-day readmission, and significantly contributed to all regression models created. Similarly, Jørgensen (2017) found that COPD patients with schizophrenia had a lower probability of meeting certain process-performance measures for COPD, CHF and diabetes mellitus; these patients were also more likely to die after an admission for AECOPD. This scholarly project revealed that mental illnesses are significant predictors for 30-day readmission; which is consistent with the findings that co-occurring physical and mental disorders can worsen patient's course of illness leading to hospital readmission not related to their psychiatric condition (Šprah, Dernovšek, Wahlbeck, & Haaramo, 2017). Individuals with serious mental illnesses such as schizophrenia or bipolar disorder were at increased risk for hospitalization for COPD/asthma exacerbation (IRR: 1.87; 95% CI [1.7, 2.00], Davydow et al., 2016).

Surprisingly, smoking status was not a significant predictor for 30-day readmission for AECOPD; yet nicotine use is known as the most predictor for COPD and schizophrenic patients are usually nicotine-dependent. Cigarette smoking nearly doubled the odds of pneumonia and COPD in the last year of veterans' lives (Copeland, Mortensen, Zeber, Pugh, Restrepo, & Dalack, 2007). Nicotine use and other modifiable cardiovascular risks were the reasons for excess cardiovascular and respiratory deaths in people with schizophrenia (Olfson, Gerhard,

Huang, Crystal, & Stroup, 2015). Patients with schizophrenia and other non-affective psychosis had significantly lower lung function values compared with the general population (Partti et al., 2015). Copeland et al. (2007) concur with this finding in that VA inpatient decedents with schizophrenia were at increased risk for pneumonia and COPD, independent of smoking indicators. Conversely, GERD was a significant predictor. These odds findings can be explained by the fact that the data set were billing data, among other plausible reasons.

Strengths and Limitations

The strengths of this study include its great power from examining 10 years of data, its cost effectiveness and the ease to conduct it. Using the robust method for binary regression offset the GEE limitations caused by the misspecification of the variance-covariance correlation as mentioned below. The robust method enabled achievement of reliable and efficient estimations (Khajeh-Kazemi, Golestan, Mohammad, Mahmoudi, Nedjat, & Pakravanc, 2011).

Despite the strengths, there are a number of limitations. Proxy data were used; in fact, they were billing data, so, it was not possible to have all the desired covariates. There were no records related to the September 2015 admissions; because it was the last month of data collection, there was no 30 days in the index admission to see if they were readmitted. The GEE used for statistical analyses has its own limitations. Parameter estimates could be inefficient in case the working correlation is misspecified. The consistency of the estimated parameters depends only on the accurate specification of the mean model; but there is no universally accepted test for the goodness-of-fit for mean model that extend above binary dependent variable (Khajeh-Kazemi, Golestan, Mohammad, Mahmoudi, Nedjat, & Pakravanc, 2011). Additionally, the parameters are sensitive to outliers; if the data is contaminated, the consistency of estimators

is affected (Khajeh-Kazemi et al., 2011). Model selection is not easy to perform in GEE, as evidenced by the difficulties encountered with this study.

It would have been interesting to see what role racial groups play in the 30-day readmission; but the data set obtained from the SC RFA did not contain that information. Factors other than schizophrenia, the complexity of this disease itself, and the fact that some patients had multiple readmissions were ignored in the analysis. The absence of randomization, the fact that data were created for insurance purpose, comorbidities and other co-existing psychiatric disorders, medication compliance, family support or lack thereof, and the complexity of schizophrenia etiology are some of the threats to the internal validity of this study. Further exploratory and supplemental studies will be needed to refine this pioneer work.

Implication for Advanced Practice

This scholarly project addressed the important subject of 30-day readmission of schizophrenic patients following an acute exacerbation of COPD and raised the possibility that schizophrenia can be a predictor of readmission in South Carolina. There are two compelling observations that emanate from this scholarly project. First, although COPD is the third leading cause of death in the US, it does not receive as much attention as other chronic diseases such as CHF, CAD, MI, or CVA (COPD Foundation (2012). Second, schizophrenic patients are known to be neglected worldwide (WHO,2016); in 2013, schizophrenia was ranked as the 11th leading cause of disability worldwide (Global Burden of Disease Study 2013 Collaborators, 2015). Third, hypertension, nicotine use disorder, hyperglycemia/diabetes, physical inactivity, obesity and dyslipidemia are the top six modifiable global mortality risk factors, respectively, per the 2009 World Health Organization report on global health risk (Wildgust & Beary, 2010). Individuals with schizophrenia have high levels of all these risk factors (Wildgust & Beary,

2010). This scholarly project found that of those factors, smoking status and diabetes mellitus significantly contributed to the 30-day readmission of schizophrenic patients, ($p = 0.027$, $p = 0.014$ respectively). Moreover, literature supports the hypothesis that lifestyle intervention programs targeting exercise, smoking cessation and compliance with medication are likely to have significant impact on mortality in schizophrenia (Wildgust & Beary, 2010). It would thus be appropriate to design comprehensive models of care for schizophrenic patients, models encompassing lifestyle modification and patient advocacy. In addition to targeting nicotine use disorder and diabetes, lifestyle modification would also help these patients achieve a state of overall well-being. Patients advocates will ascertain that the treatments they receive is unbiased and prejudice-free.

A “need-based” individualized care package with the intent to reduce 30 and 90-day readmission following an admission for AECOPD was developed by Adamson, Burns, Camp, Sin, & van Eeden (2016). This model measured mortality rates as well as the length of time until first readmission for their population. A multidisciplinary COPD Outreach Team (OT) was created to provide a care package (CP). The OT consisted of a nurse practitioner, a respiratory therapist, and a physiotherapist. The CP intended to provide patient-specific disease management based on comprehensive clinical and needs assessment. The ultimate goals of the CP was to: (1) facilitate continuous care from the hospital to the community; (2) educate patients on their specific diseases and empower them on the management of those disease; (3) identify and address individual risk factors; and (4) mobilize appropriate community resources and coordinate care providers (Adamson et al., 2016). The CP comprised four phases: (1) initial contact, (2) post-discharge phone-call/contact, (3) home visit; and (4) continued care. Upon admission to the hospital for AECOPD, patients were enrolled in the program by a member of the OT. Each

member of the team provided expertise care over the first two to four weeks following patients discharge The nurse practitioner educated the patients on their disease processes and performed medication reconciliation. The physiotherapist encouraged mobility while teaching patients safe mobility techniques to prevent falls. The respiratory therapist assessed breathing, reviewed breathing techniques and instructed on proper use of inhalers.

Adamson et al. found that although the CP for patients admitted to the hospital for AECOPD reduced 90-day total mortality and 90-day readmission rate in female patients, it did not reduce 30 or 90-day readmission rate. For this scholarly project, what could be done differently would be to add a psychologist and a social worker to the OT. The psychologist would address the specificities of schizophrenia since it is such a complex disease. The social worker would address the patients' social needs, advocate for them and ensuring that they receive bias-free care. Moreover, the nurse practitioner of the OT will be one who is proficient in lifestyle medicine interventions. He/she would be tasked to oversee the patients' care while using motivational interviewing to help them perceive the need to modify the behaviors (nicotine use, sedentary life/lack of exercise) that perpetrate their current disease state or make them susceptible to diseases, and adopt those leading to long term health benefits. In this scholarly project, bivariate analysis indicated that gender, age, anxiety, T2DM and GERD were significant predictors of 30-day readmission. In the multivariate analysis, smoking status emerged as another predictor of 30-day readmission for COPD. While gender and age are not modifiable, the other covariates are. All members of the OT would need to visit male patients and patients aged 65 at least more often than female and patients less than 65 years old, since these individuals are more likely to be readmitted. The suggested frequency would be twice a week over the first two weeks, then weekly thereafter. During these visits, members will pay special attention to

additional risk factors that could be in their environment and address them when found. The nurse practitioner (NP) would put emphasis on modifying factors that contributes to anxiety, T2DM and GERD. To address anxiety, the NP would seek to determine the root of the anxiety through motivational interviewing (MI). Eventually, the NP could suggest MTHFR mutation testing because it has been implicated in anxiety (Lynch, 2012). Cognitive behavioral therapy (CBT) and aerobic exercise produce anxiolytic effects (Gaudlitz, Plag, Dimeo & Ströhle, 2015), thus can be effectively utilized to relieve anxiety. While finances may be a limiting factor for certain patients, exercise requires very little investment in good pair of walking shoes. The NP would keep in mind that patients may have limited functional lung capacity; in which case the physiotherapist would collaborate with him/her to design the best exercise plan for them. For T2DM, the NP would visit every three days for the first three weeks, ascertain the patients understand how, why and how often they are taking the antidiabetic medications prescribed at discharge. The patients would have to keep taking their medications while the NP teaches them how to remain normoglycemic by making healthy food choices and exercise regularly, keeping in mind their functional limitations. The NP may do several other things including, presenting to his/her patients a very simplified pathophysiology of the disease, shopping with them and teaching them how to shop in the periphery rather than the center of a grocery store; while shopping, the NP would also teach the patients how to read food labels. The NP would also teach the patients how to cook simple but delicious nutrient-dense meals. In case they want to eat out, advise the patients to call the restaurant ahead of time about the ingredients that they would rather not have, and request healthy alternatives. After four weeks, the NP would check the patients' glycated hemoglobin to measure the effectiveness of his/her interventions. For GERD, by explaining the side effects of proton pump inhibitors (osteoporosis, nephritis, leaky guts and

certain autoimmune diseases), the NP might be more successful at getting the patient to abide by the following rules: proper food mastication, avoiding lying down within two or three hours post prandial, avoiding offenders such as caffeine, alcohol, and spicy foods. Raw potatoes juice is very effective in neutralizing gastric PH without interfering with gastric parietal cells or the proton pump mechanism (Pamplona-Roger, 2004, p. 203). Success would be measured by self-reporting. Motivational interviewing and coaching would be of utmost importance in promoting smoking cessation. The NP would guide each patient in finding what healthy thing they can do when the urge to smoke arises; going for a short walk or eating an apple for instance. Weekly discussion on achievement, failures, barriers to making and implementing healthy choices would be helpful and encouraging for both the patient and NP.

Rather than limiting their interventions to the first two to four months following discharge, the social worker and psychologist would continue to see the patients as needed; the nurse practitioner would also be a strong patient advocate and continue to work with the patients until their treatment goals are met, or the patients terminate the relationship. This multidisciplinary team approach would address some of the factors that increase the probability of readmission: premature discharge, inadequate post-discharge support, insufficient follow-up, therapeutic errors, adverse drug events and other medication related issues, failed handoffs, post-procedural complications, nosocomial infections, pressure ulcers, and patient falls (O'Malley, Greenwald, Aronson, & Park, L., 2015).

This novel model of care has not been tested, and further studies will be needed to achieve this. It may not, as in Adamson et al.'s study, reduce the 30-day readmission rate of schizophrenic patients after hospitalization for AECOPD; but it may reduce their morbidity and mortality rates. More than anyone else, today's nurse practitioners are in a position to

strategically take on and implement proven effective strategies to reduce 30-day readmissions. They can efficiently head care transition teams. More and more states are giving nurse practitioners full practice authority, this will unleash their natural propensity to provide care where and when it is needed, to the fullest of their ability and within the boundary of their qualifications. Nurse practitioners can also play an important role in destigmatizing schizophrenia and other mental diseases by their commitment to social justice and respect for human dignity (ANA, 2015).

Conclusion

This study is a pioneer in seeking a correlation between schizophrenia and COPD readmission in South Carolina. It has augmented the literature and the hope is that future studies will build on this ground work with the aim to improve the health of schizophrenic individuals. Schizophrenic individuals are cognitively impaired, self-negligent, and usually lack family and social support necessary to remind or encourage them to stay healthy by practicing primary preventive care. This leads not only to avoidable hospitalizations and readmissions; but also to premature death. The integration of biblical-based lifestyle practices to their care would aid them in making better choices, keep them mentally sharp and increase their probability of being productive citizens. These lifestyle practices would also decrease the economic burden of their disease by decreasing their antipsychotic use for instance. These medications carry multiple risks including extrapyramidal symptoms, sudden death, significant cardiac risk (QT prolongation, torsades de pointes, arrhythmias, hypotension) and diabetes. Medications used to control extrapyramidal symptoms (Cogentin for instance) are not innocent. Cardiovascular, metabolic, and infectious diseases are responsible for the 2 to 2.5-fold increased odds of premature death of schizophrenic patients. In addition to the adoption of the eight principles of CREATION health,

medical models such as described in this study will allow to continue Christ's ministry of healing and caring for the voiceless or the "least of Jesus' brothers".

References

Adamson, S. L., Burns, J., Camp, P. G., Sin, D. D, & van Eeden, S. F. (2016). Impact of individualized care on readmissions after a hospitalization for acute exacerbation of COPD. *International Journal of COPD*, 11, 61–71. doi: 10.2147/COPD.S93322

Álvarez-Jiménez, M., Hetrick, S. E., González-Blanch, C., Gleeson, J. F., McGorry, P. D. (2008). Non-pharmacological management of antipsychotic-induced weight gain: systematic review and meta-analysis of randomised controlled trials. *The British Journal of Psychiatry, 193*(2), 101-107. doi: 10.1192/bjp.bp.107.042853

American Psychiatric Association (2013). Schizophrenia spectrum and other psychotic disorders [excerpt]. *Diagnostic and statistical manual of mental health disorder (DSM-5)*. Washington, DC: American Psychiatric Publishing. doi: 10.1176/appl.books.9780890425596.dsm02

American Nurses Association (2015). *Code of ethics for nurses with interpretive statements*. Silver Spring, MD: Nursesbooks.org.

Bahadori, K., & Fitzgerald, J. M. (2007). Risk factors of hospitalization and readmission of patients with COPD exacerbation – systematic review. *International Journal of COPD*, *2*(3), 241–251.

Balter, M. S., & Grossman, R. F. (2012). Respiratory failure part IV: Chronic obstructive pulmonary disease. In J. M. Rippe (Ed.), *Lifestyle medicine* (pp. 525-533). Boca Raton, FL: CRC Press.

Barch, D. M., Carter, C. S., Braver, T. S., Sabb, F. W., MacDonald III, M. A., Noll, D. C., & Cohen, J. D. (2001). Selective deficits in prefrontal cortex function in medication-

naïve patients with schizophrenia. *Archives of General Psychiatry, 58*(3), 280-288. doi:10.1001/archpsyc.58.3.280

Barnes, P. J. (2000). Chronic obstructive pulmonary disease. The *New England Journal of Medicine, 343*, 269-280. doi: 10.1056/NEJM200007273430407

Berger, A. Edelsberg, J., Sanders, K. N., Alvir, J. M. J., Mychaskiw, M. A. & Oster, G. (2012). Medication adherence and utilization in patients with schizophrenia or bipolar disorder receiving aripiprazole, quetiapine, or ziprasidone at hospital discharge: A retrospective cohort study. *BMC Psychiatry, 12(*99). doi:10.1186/1471-244X-12-99

Bobo, W. V., Cooper, W. O., Stein, C. M., Olfson, M., Graham, D., Daugherty, …, Ray, W. A. (2013). Antipsychotics and the risk of Type2 diabetes mellitus in children and youth. *JAMA Psychiatry, 70*(10), 1067-1075. doi:10.1001/jamapsychiatry.2013.2053

Bridge, J. A., & Barbe, R. P. (2004). Reducing hospital readmission in depression and schizophrenia: current evidence. Current Opinion in Psychiatry, 17(6), 505-511. doi: 10.1097/00001504-200411000-00015

Brown, S. Inskip, H., & Barraclough, B. (2000). Causes of the excess mortality of schizophrenia. *The British Journal of Psychiatry*, *177*(3), 212–217. doi.org/10.1192/bjp.177.3.212

Burke, R. E, Donzé, J., & Schnipper, J. L. (2013). Contribution of psychiatric illness and substance abuse to 30-day readmission risk. *Journal of Hospital Medicine, 8*(8), 450-455. doi: 10.1002/jhm.2044

Cahoon, E. K., Mcginty, E. E., Ford, D. E., & Daumit, G. L. (2013). Schizophrenia and potentially preventable hospitalizations in the United States: a retrospective cross-sectional study. *BMC Psychiatry, 13* (37). doi: 10.1186/1471-244X-13-37

Centers for Disease Control (2015a). National Hospital Ambulatory Medical Care Survey: 2015 Emergency Department Summary Tables. Retrieved from https://www.cdc.gov/nchs/data/nhamcs/web_tables/2015_ed_web_tables.pdf

Centers for Disease Control (2015b). Emergency department visits related to schizophrenia among adults aged 18–64: United States, 2009–2011. Retrieved from https://www.cdc.gov/nchs/data/databriefs/db215.htm

Cloutier, M., Aigbogun, M. S., Guerin, A., Nitulescu, R., Ramanakumar, A. V., Kamat, S. A., … Wu, E. (2016). The economic burden of schizophrenia in the United States in 2013 [Abstract]. *The Journal of Clinical Psychiatry, 77*(6), 764-771.doi: 10.4088/JCP.15m10278

COPD Foundation (2012): Impact of COPD on healthcare costs. Retrieved from https://www.copdfoundation.org/pdfs/Impact%20on%20Costs.pdf

Copeland, L. A., Mortensen, E. M., Zeber, J. E., Pugh, M. J., Restrepo, M. I., & Dalack, G. W. (2007). Pulmonary disease among inpatient decedents: Impact of schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 31*(3), 720-726. doi: 10.1016/j.pnpbp.2007.01.008

Davydow, D. S., Ribe, A., R. Pedersen, H. S., Fenger-Grøn, M., Cerimele, J. M., Vedsted, P. &

Donaldson, G. C., & Wedzicha, J. A. (2006). COPD exacerbations. 1: Epidemiology. *Thorax*, *61*, 764–768. doi.10.1136/thx.2005.041806

Edgerton, R. (2014). CREATION Health: God's 8 principles for living life to the fullest seminar personal study guide. Orlando, FL: Florida Hospital.

Epocrates (2016). Chronic obstructive pulmonary disease. In Epocrates Premium (Version 17.1) [Mobile application software]. Retrieved from https://www.epocrates.com

Ford, E. S, Murphy, L. B., Khavjou, O., Giles, W. H., Holt, J. B., & Croft, J. B (2015). Total and State-specific medical and absenteeism costs of COPD among adults aged 18 years in the United States for 2010 and projections through 2020 [Abstract]. *Chest, 147*(1), 31-45. doi: https://doi.org/10.1378/chest.14-0972

Frankenburg, F. R. (2017). Schizophrenia. Retrieved from http://emedicine.medscape.com/article/288259-overview#a4

Gaudlitz, K., Plag, J., Dimeo, F., & Ströhle, A. (2015). Aerobic exercise training facilitates the effectiveness of cognitive behavioral therapy in panic disorder. *Depression and Anxiety, 32*(3), 221-228. doi:10.1002/da.22337

Global Burden of Disease Study 2013 Collaborators (2015). Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet, 386*(9995), 743–800. doi:10.1016/S0140-6736(15)60692-4

Global Initiative for Chronic Pulmonary Obstructive Lung Disease (2018). 2019 Global strategy for prevention, diagnosis, and management of COPD. Retrieved from https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf

Gordis, L. (2014). *Epidemiology*. Philadelphia, PA: Elsevier Saunders.

Guerrero M, Crisafulli E, Liapikou A, Huerta A, Gabarrús A, Chetta A, … Torres, A. (2016) Readmission for acute exacerbation within 30 Days of discharge is associated with a subsequent progressive increase in mortality risk in COPD patients: A long-term observational study. *PLoS ONE, 11*(3), e0150737. doi:10.1371/journal.pone.0150737

Ho, T., Tsai, Y., Ruan, S., Huang, C., & Lai, F. (2014). In-hospital and one-year mortality and their predictors in patients hospitalized for first-ever chronic obstructive pulmonary disease exacerbations: A nationwide population-based study. *PLOS ONE*. doi.org/10.1371/journal.pone.0114866

Hoang, U., Stewart, R., & Goldacre, M. J. (2011). Mortality after hospital discharge for people with schizophrenia or bipolar disorder: retrospective study of linked English hospital episode statistics, 1999-2006. *BMJ (Clinical research ed.)*, *343*, d5422. doi: 10.1136/bmj.d5422

Huetsch, J. C., Uman, J. E., Udris, E. M., & Au, D. H. (2012). Health predictors of adherence to inhaled medications among veterans with COPD. *Journal of General Internal Medicine, 27*(11), 1506-1512. doi: 10.1007/s11606-012-2130-5

Jørgensen, M. (2017). Quality of care for medical comorbidities among patients with schizophrenia: A Danish nationwide perspective. Aalborg Universitetsforlag. (Ph.d.-serien for Det Sundhedsvidenskabelige Fakultet, Aalborg Universitet). DOI: 10.5278/vbn.phd.med.00082

Khajeh-Kazemi, R., Golestan, B., Mohammad, K., Mahmoudi, M., Nedjat, S., & Pakravanc, M. (2011). Comparison of generalized estimating equations and quadratic inference functions in superior versus inferior Ahmed glaucoma valve implantation. *Journal of*

Research in Medical Sciences: The official Journal of Isfahan University of Medical Sciences, *16*(3), 235-44. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3214328/

Lacro, J. P., Dunn, L. B., Dolder, C. R., Leckband, S. G., & Jeste, D. V. (2002). Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *The Journal of Clinical Psychiatry, 63*(10), 892-909.

Lewallen, S. & Courtright, P. (1998). Epidemiology in practice: Case-control studies. Community Eye Health, *11*(28), 57–58. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1706071/

Lynch, B. (2012). Improving patients outcomes: identifying common methylation polymorphisms. Retrieved from https://www.youtube.com/watch?v=QRHif2aVPvw&feature=youtu.be

Mackinnon, S. (2013). Increasing statistical power in psychological research without increasing sample size. Retrieved from http://osc.centerforopenscience.org/2013/11/03/Increasing-statistical-power/

Mai, Q., Holman, C. D. J., Sanfilippo, F. M., & Emery, J. D. (2011). The impact of mental illness on potentially preventable hospitalisations: A population-based cohort study. *BMC Psychiatry*, *11,* (163). doi: 10.1186/1471-244X-11-163

McIlvennan, C. K., Eapen, Z., & Allen, L. A. (2015). Hospital readmissions reduction program. Circulation, 131, 1796-1803. doi: 10.1161/CIRCULATIONAHA.114.010270

Mishel, M. H. (2014). Theories of uncertainty in illness. In M. J. Smith & P. R. Liehr (Eds.), *Middle range theory for nursing* (pp. 53-86). New York, NT: Springer Publishing Company, LLC.

Moy, M. L., Martinez, C. H., Kadri, R., Roman, P., Holleman, R. G., Kim, H. M., … Richardson, C. R. (2016). Long-term effects of an Internet-mediated pedometer-based walking program for chronic obstructive pulmonary disease: Randomized controlled trial. *Journal of Medical Internet Research, 18*(8), 35-48.

National Heart, Lung, and Blood Institute (2012). Morbidity & Mortality: 2012 chartbook on cardiovascular, lung and blood diseases. Retrieved from https://www.nhlbi.nih.gov/research/reports/2012-mortality-chart-book

National Institute of Mental Health (n. d.). Schizophrenia. Retrieved from https://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml

Nemade, R. & Dombeck, M. (2009). Schizophrenia symptoms, patterns and statistics and patterns. Retrieved from https://www.mentalhelp.net/articles/schizophrenia-symptoms-patterns-and-statistics-and-patterns/

Numachi, Y., Yoshida, S., Yamashita, M., Fujiyama, K., Naka, M., Matsuoka, H., … Sora, I. (2004). Psychostimulant alters expression of DNA methyltransferase mRNA in the rat brain [Abstract]. *Annals of the New York Academy of Sciences*. doi: 10.1196/annals.1316.013

Olfson, M., Gerhard, T, Huang, C., Crystal, S., & Stroup T. S. (2015). Premature mortality among adults with schizophrenia in the United States. *JAMA Psychiatry, 72*(12), 1172-1181. doi:10.1001/jamapsychiatry.2015.1737

Pamplona-Roger, G. D. (2004). *Encyclopedia of foods and their healing power- A guide to food science and diet therapy*. Volume 2. Hagerstown, MA: Review and Herald Publishing Association.

Partti, K., Vasankari, T., Kanervisto, M., Perälä, J., Saarni, S. I., Jousilahti, P., … Souvisari, J. (2015). Lung function and respiratory diseases in people with psychosis: Population-based study. *British Journal of Psychiatry*, *207*(1), 37-45. doi: 10.1192/bjp.bp.113.141937

PennState (2017). Case-control study design. Retrieved from https://onlinecourses.science.psu.edu/stat507/node/48

Rabe, K., Hurd, S., Anzueto, A., Barnes, P., Buist, S., Calverley, P., … Zielinski, J. (2007). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *American Journal of Respiratory and Critical Care Medicine, 176*(6), 532-555. doi: 10.1164/rccm.200703-456SO

Seemungal, T. A. R., Hurst, J. R., & Wedzicha, J. A. (2009). Exacerbation rate, health status and mortality in COPD - A review of potential interventions. *International Journal of Chronic Obstructructive Pulmonary Disease*, *4*, 203–223. https://doi.org/10.2147/COPD.S3385

Shams, I., Ajorlou, S., & Yang, K. (2015). A predictive analytics approach to reducing 30-day avoidable readmissions among patients with heart failure, acute myocardial infarction, pneumonia, or COPD. *Health Care Management Science, 18*, 19–34. doi: 10.1007/s10729-014-9278-y

Šprah, L., Dernovšek, M. Z., Wahlbeck, K., & Haaramo, P. (2017). Psychiatric readmissions and their association with physical comorbidity: a systematic literature review. *BMC Psychiatry*,

17(1), 2. https://doi.org/10.1186/s12888-016-1172-3

Strid, J. M. C., Christiansen, C. F., Olsen, M., & Qin, P. (2014). Hospitalisation for chronic obstructive pulmonary disease and risk of suicide: a population-based case-control study. *BMJ Open, 4*(11), e006363. doi: 10.1136/bmjopen-2014-006363

Sullivan, S. D, & Ramsey, S. D. (2000). The economic burden of COPD. [Abstract; Supplement] *Chest* (2). doi: 10.1378/chest.117.2_suppl.5S

Sutherland, E. R., & Cherniack, R. M. (2005). Management of chronic obstructive pulmonary disease. The *New England Journal of Medicine, 350*, 2689-2697. doi: 10.1056/NEJMra030415

Tsan, J. Y., Stock, E. M., Gonzalez, J. M., Greenawalt, D. S., Zeber, J. E., Rouf, E. & Copeland, L. A. (2012). Mortality and guideline-concordant care for older patients with schizophrenia: A retrospective longitudinal study. *BMC Medicine, 10* (147). doi: 10.1186/1741-7015-10-147

U.S. Department of Veterans Affairs (2016). Strategic Analytics for Improvement and Learning (SAIL). Retrieved from https://www.va.gov/QUALITYOFCARE/measure-up/Strategic_Analytics_for_Improvement_and_Learning_SAIL.asp

Vestergaard, M. (2016). Serious mental illness and risk for hospitalizations and rehospitalizations for ambulatory care-sensitive conditions in Denmark: A nationwide population-based cohort study. *Medical Care, 54*(1), 90-97. doi: 10.1097/MLR.0000000000000448

Wildgust, H. J., & Beary, M. (2010). Are there modifiable risk factors which will reduce the excess mortality in schizophrenia [Supplemental material]. *Journal of Psychopharmacology, 24*(11), 37-50. doi: 10.1177/1359786810384639

World Health Organization (2016). Schizophrenia. Retrieved from http://www.who.int/mediacentre/factsheets/fs397/en/

Wu, E. Q., Birnbaum, H. G., Shi, L., Ball, D. E., Kessler, R. C., Moulis, M., & Aggarwal, J. (2005). The economic burden of schizophrenia in the United States in 2002 [Abstract]. *The Journal of Clinical Psychiatry, 66*(9), 1122-1129.

Appendix A

Bivariate analyses output per the robust method

Table 4

Thirty-Day Readmission Based on Gender

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	77418.170	1	0.000
Gender	37.518	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), SEX2

Table 5

Thirty-Day Readmission Based on Age

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	65653.280	1	0.000
AGRP65	406.220	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), AGRP65

Table 6

Thirty-Day Readmission Based on Anxiety

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	46678.109	1	0.000
Anxiety	111.187	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), Anxiety

Table 7

Thirty-Day Readmission Based on T2DM

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	5717.471	1	0.000
T2DM	5.464	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), T2DM

Table 8

Thirty-Day Readmission based on GERD

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	57299.315	1	0.000
GERD	55.594	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), GERD

Table 9

Thirty-Day Readmission Based on Smoking Status

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	5717.471	1	0.000
Smoking Status	5.464	1	0.719

Dependent Variable: Readmission30b
Model: (Intercept), Smoking Status

Table 10

Thirty-Day Readmission Status Based on Chronic Ischemic Heart Disease

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	5717.471	1	0.000
Ischemic.Heart.dz	5.464	1	0.165

Dependent Variable: Readmission30b
Model: (Intercept), Ischemic.Heart.dz

Appendix B

Model-based method and related output

Table 12

Logistic Regression Output- Model-Based Method

Tests of Model Effects

	Type III		
Source	Wald Chi-Square	df	Sig.
Intercept	991.377	1	0.000
Smoking.Status	13.750	1	0.000
Schizophrenia	9.283	1	0.002
SEX2	44.420	1	0.000
Anxiety	102.552	1	0.000
AGRP65	388.440	1	0.000
Chronic.Ischemic Heart.dz	2.315	1	0.128
T2DM	17.003	1	0.000
GERD	42.213	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), Smoking.Status, Schizophrenia, SEX2, Anxiety, AGRP65, Chronic.Ischemic.Heart.dz, T2DM, GERD

Parameter Estimates

Parameters	B	Std Error	95% Wald Confidence Interval		Hypothesis Test			95% Wald Confidence Interval for Exp(B)		
			Lower	Upper	Wald Chi-Square	df	Sig	Exp(B)	Lower	Upper
(Intercept)	-2.709	0.0165	-2.742	-2.677	26936.826	1	0.000	0.067	0.064	0.069
Smoking Status = Yes	0.061	0.0164	0.029	0.093	13.750	1	0.000	1.063	1.029	1.097
Smoking Status = NO	0[a]							1		
Schizophrenia = Yes	0.213	0.0700	0.076	0.350	9.283	1	0.002	1.238	1.079	1.420
Schizophrenia = No	0[a]							1		
SEX2 = Male	0.122	0.0198	0.083	0.161	38.052	1	0.000	1.130	1.087	1.174
SEX2 = Female	0[a]							1		
Anxiety = Yes	0.198	0.0196	0.160	0.237	102.552	1	0.000	1.219	1.174	1.267
Anxiety = No	0[a]							1		
AGRP65 = Less than 65 years	-0.385	0.0195	-0.423	-0.346	388.440	1	0.000	0.681	0.655	.707
AGRP65 = 65 Years or older	0[a]							1		
Chronic Ischemic Heart dz	0.205	0.1349	-0.059	0.470	2.315	1	0.128	1.228	0.943	1.600
Chronic Ischemic Heart dx = NO	0[a]							1		
T2DM = YES	0.072	0.0176	0.038	0.107	17.003	1	0.000	1.075	1.039	1.139
T2DM = NO	0[a]							1		
GERD =YES	0.110	0.0170	0.077	0.144	42.213	1	0.000	1.117	1.080	1.154
GERD = NO	0[a]							1		
Scale	1									

Dependent Variable: Readmission30b
Model (Intercept). Schizophrenia, SEX2, Anxiety, AGRP65, Ischemic Heart dz, T2DM, Smoking Status, GERD.
[a] Set to zero because this parameter is redundant.

Interpretation of the strength of association between the predictors and readmission:

- Smoking status: Holding the other predictors constant, a patient who has smoking disorder would have an odds ratio of readmission of 1.063, that is a 6.3% increase in the odds of readmission compared to a patient without smoking disorder, with a 95% confident interval between 1.029 and 1.097, or an increase of odds between 2.9% and 9.7%.).
- Schizophrenia: Holding the other predictors constant, a patient with schizophrenia would have an odds ratio of readmission of 1.238, that is a 23.8% increase in the odds of readmission compared to a patient without schizophrenia, with a 95% confident interval between 1.079 and 1.420, or an increase of odds between 7.9% and 42%.).
- SEX2/Gender: Holding the other predictors constant, a male patient would have an odds ratio of readmission of 113%, that is 13% increase in the odds of readmission, with a 95% confident interval between 1.087 and 1.174, or an increase of odds between 8.7% and 17.4%.).
- Anxiety: Holding the other predictors constant, a patient with anxiety would have an odds ratio of readmission of 1.219, that is a 21.9% increase in the odds of readmission compared to a patient without anxiety, with a 95% confident interval between 1.174 and 1.267, or an increase of odds between 17.4% and 26.7%.).
- AGRP65: Holding the other predictors constant, a patient less than 65 years old would have an odds ratio of readmission of 0.319, that is a 31.9% reduction in the odds of readmission, with a 95% confident interval between 0.293 and 0.345 or a decrease of odds between 29.3% and 34.5%.
- Chronic ischemic heart disease: Holding the other predictors constant, a patient with chronic ischemic heart disease would have an odds ratio of readmission of 1.228, that

is a 22.8% increase in the odds of readmission compared to a person without chronic ischemic disease; with a 95% confident interval between 0.057 and 1.6, or an increase of odds between 5.7% and 60%.). Nonetheless, chronic ischemic disease was not significantly different from 1 at the 0.05 level.

- T2DM: Holding the other predictors constant, a patient with T2DM would have an odds ratio of readmission of 1.075, that is a 7.5% increase in the odds of readmission compared to a patient without T2DM, with a 95% confident interval between 1.039 and 1.113, or an increase of odds between 3.9% and 11.3%.).
- GERD: Holding the other predictors constant, a patient with GERD would have an odds ratio of readmission of 1.117%, that is 11.7% increase in the odds of readmission compared to a patient without GERD, with a 95% confident interval between 1.080 and 1.154, or an increase of odds between 8% and 15.4%.).

Additional comments on the associations:

- All IVs have a positive relationship with the DV except age less than 65 in other words, all IVs as coded are risk factors for readmission (odds ratio >1), except for the age group variable where age less than 65 years is protective.
- Age is the biggest contributing factor, followed by schizophrenia, then anxiety, gender, GERD, T2DM, and smoking status.

Comments on the statistical significance of the associations:

The six significant predictors of readmission: Smoking Status ($\chi^2(1) = 13.750$, $p = 0.000$); Schizophrenia ($\chi^2(1) = 9.283$, $p = 0.002$); SEX2($\chi^2(1) = 44.420$, $p = 0.000$); Anxiety

($\chi^2(1) = 102.552$, p = 0.000); Age ($\chi^2(1) = 388.340$, p = 0.000); T2DM ($\chi^2(1) = 17.003$, p = 0.000); and GERD ($\chi^2(1) = 42.213$, p = 0.000).

Statement of the regression equation:

- The regression equation for this model-based model:

$$\log\{P(Y=1) / [1 - P(Y=1)]\} = \beta_0 + \beta_1*SEX2 + \beta_2*Anxiety + \beta_3*AGRP65 + \beta_4*T2DM + \beta_5*Smoking\ Status + \beta_6*GERD.$$

Where P(Y=1) is the probability of readmission, β_0 is the intercept, β_1 is the coefficient for SEX2, β_2 is the coefficient for Anxiety, β_3 is the coefficient for AGRP65, β_4 is the coefficient for T2DM, β_5 is the coefficient for Smoking Status, and β_6 is the coefficient for GERD.

Log is the natural logarithm.

SEX2 = 1 if the patient is MALE, 0 if FEMALE.

Anxiety = 1 if the patient has an anxiety diagnosis, 0 otherwise.

AGRP65 = 1 if age<65, 0 otherwise.

T2DM = 1 if the patient has a diagnosis of T2DM, 0 otherwise.

Smoking Status = 1 if the patient has a diagnosis of nicotine use disorder, 0 otherwise.

GERD =1 if the patient has a diagnosis of GERD, 0 otherwise.

Tables 13-20 illustrate bivariate analyses related to the model-base method; they are similar to those of the robust output, except for schizophrenia.

Table 13

Thirty-Day Readmission Based on Schizophrenia Status

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	5717.471	1	0.000
Schizophrenia	4.464	1	0.019

Dependent Variable: Readmission30b
Model: (Intercept), Schizophrenia

Table 14

Thirty-Day Readmission Based on Gender

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	77418.170	1	0.000
Gender	37.518	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), SEX2

Table 15

Thirty-Day Readmission Based on Age

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	65653.280	1	0.000
AGRP65	406.220	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), AGRP65

Table 16

Thirty-Day Readmission Based on Anxiety

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	46678.109	1	0.000
Anxiety	111.187	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), Anxiety

Table 17

Thirty-Day Readmission Based on T2DM

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	5717.471	1	0.000
T2DM	5.464	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), T2DM

Table 18

Thirty-Day Readmission based on GERD

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	57299.315	1	0.000
GERD	55.594	1	0.000

Dependent Variable: Readmission30b
Model: (Intercept), GERD

Table 19

Thirty-Day Readmission Based on Smoking Status

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	5717.471	1	0.000
Smoking Status	5.464	1	0.719

Dependent Variable: Readmission30b
Model: (Intercept), Smoking Status

Table 20

Thirty-Day Readmission Status Based on Chronic Ischemic Heart Disease

Test of model Effects			
Source	Wald Chi-Square	Type III df.	Sig.
(Intercept)	5717.471	1	0.000
Ischemic.Heart.dz	5.464	1	0.165

Dependent Variable: Readmission30b
Model: (Intercept), Ischemic.Heart.dz