2019

A COST CONTROL MODEL FOR INPATIENT MEDICATIONS AMONG ADULTS WITH MENTAL AND BEHAVIORAL HEALTH DISORDERS

Huanan Li

University of the Pacific, phoenix03qinze@gmail.com

A COST CONTROL MODEL FOR INPATIENT MEDICATIONS AMONG ADULTS WITH MENTAL AND BEHAVIORAL HEALTH DISORDERS

By

Huanan Li

A Dissertation Submitted to the

Graduate School

In Partial Fulfillment of the

Requirements for the Degree of

DOCTOR OF PHILOSOPHY

Thomas J. Long School of Pharmacy and Health Sciences
Pharmaceutical and Chemical Sciences

University of the Pacific
Stockton, California

2019

A COST CONTROL MODEL FOR INPATIENT MEDICATIONS AMONG ADULTS WITH MENTAL AND BEHAVIORAL HEALTH DISORDERS

By

Huanan Li

APPROVED BY:

Dissertation Advisor: William A. Kehoe, Pharm.D., M.A., FCCP, BCPS

Committee Member: Michelle M. Amaral, Ph.D.

Committee Member: Patrick N. Catania, Ph.D., R.Ph.

Committee Member: Eric G. Boyce, Pharm.D.

Committee Member: Jacquelyn Cituk, Pharm.D.

Department Chair: William A. Kehoe, Pharm.D., M.A., FCCP, BCPS

A COST CONTROL MODEL FOR INPATIENT MEDICATIONS AMONG ADULTS WITH MENTAL AND BEHAVIORAL HEALTH DISORDERS

By

Huanan Li

DEDICATION

This dissertation is dedicated to Professor William A. Kehoe in honor of his retirement from active teaching after 34 years on the faculty.

ACKNOWLEDGEMENTS

There are many people that have earned my gratitude for their contribution to my time in the pharmacy school for the past seven years.

First, I am indebted to my dissertation advisor, Dr. William Kehoe. Since my first day in graduate school, Bill believed in me like nobody else and gave me endless support. It all started in Fall 2012 when he offered me such a great opportunity to join this program.

On the academic level, Bill taught me fundamentals of conducting scientific research. Under his supervision, I learned how to define a research problem and find a solution to it. Particularly, I could not literally stand here to present these valuable results without his effort to letting me have the data form the St. Joseph Behavioral Health Center. On a personal level, Bill inspired me by his hardworking and passionate attitude. I would give Bill most of the credit for becoming the kind of researcher I am today.

Besides my advisor, I would like to thank the rest of my dissertation committee members for their great support and invaluable advice. I am thankful to Dr. Amaral, an expert in econometrics for her crucial remarks that shaped my final dissertation. I am also grateful to Dr. Boyce for his insightful comments during the proposal defense. I am quite appreciative of Dr. Catania for agreeing to serve on my dissertation committee and his passion involved in academic project even if he is already retired. I also want to show gratitude for Dr. Cituk to serve as a great committee member and a wonderful clinical pharmacist in Dignity health.

I want to thank Dr. Patel for teaching me Pharmacoeconomics and letting me work with him on several great projects. Thank Dr. Herrin from department of economics letting me audit his econometric class, also Dr. Hilsenrath from school of business to teach me Health Insurance.

Last but not least, I would like to express my deepest gratitude to my family and friends. This dissertation would not have been possible without your warm love, continued patience, and endless support. Thank you, my beloved husband Woody, you are my life the only heart; my dear parents, you are my life eternal light; my three wonderful sons, the most precious gifts I have ever received.

God Almighty, I would like to thank You for giving me knowledge, ability, strength, and opportunity to undertake this dissertation study. Without Your blessing, this achievement would not have been possible. We know that in all things God works for the good of those who love him, who have been called according to his purpose (Roman 8:28).

A COST CONTROL MODEL FOR INPATIENT MEDICATIONS AMONG ADULTS WITH MENTAL AND BEHAVIORAL HEALTH DISORDERS

Abstract

by Huanan Li

University of the Pacific
2019

Pharmaceutical expenditures are an important part of the entire hospital operating budget, and inpatient pharmaceuticals denote one of the highest costs in hospital care. Predictions for medication budgets based on the types of patients have been largely undertaken in medical hospitals and not psychiatric facilities. According to several previous studies, gender, age, diagnosis, comorbidity and length of stay (LOS) affect the general inpatient treatment expenditures. However, whether or not the impact of these factors differs in psychiatric hospitals remains to be investigated. To that end, the current study examines medication costs for mental and behavioral health disorder as well as the primary chronic diseases commonly comorbid with mental and behavioral health disorders that suggest formulary management control might be helpful. Multiple regression models were developed to determine the leading drivers associated with the growing inpatient hospital medication costs among patients admitted to an acute psychiatric hospital. We also analyzed LOS using a Poisson model in order to determine whether it is a proxy for psychiatric inpatient medication costs.

Our finding selected 51 medications (14% of the 364 total medications consumed 90% of the total medication cost) under A category (AV, AE, and AN) and B category (BV, BE, and BN) in order to develop a medication list (MUC, medication under control) that suggested cost control measures based on cost and clinical criticality could be important. This study

demonstrated that comorbidity, principal and secondary diagnoses, LOS, and MUC are associated with higher inpatient medication costs than other factors, including age, gender, insurance type, and month admitted. Our study also observed that the principal ICD-10-CM codes F10 (Alcohol related disorders) is associated with high inpatient medication cost. Secondary diagnosis related groups (DRGs) 203 (Bronchitis & asthma), 192 (Chronic obstructive pulmonary disease, COPD), 201 (pneumothorax), 639 (Diabetes), 642 (Inborn and other disorders of metabolism), 645 (Endocrine disorders), 641 (Nutritional & miscellaneous metabolic disorders), 690 (Kidney & urinary tract infections), 675 (Other kidney & urinary tract procedures), 699 (Other kidney & urinary tract diagnoses), and 700 (Other kidney and urinary tract diagnoses), 305 (Hypertension), 310 (Cardiac arrhythmia & conduction disorders), 303 (Atherosclerosis), 293 (Heart failure & shock), and 316 (Other circulatory system diagnoses) were found to be associated with higher inpatient medication costs. In addition, LOS can be used as an indicator (proxy) for inpatient medication cost when patients present with a secondary DRG 639 (diabetes) and 690 (kidney & urinary tract infections) in an acute psychiatric hospital.

Viewed collectively, this study would enable executives of acute psychiatric hospitals to identify the most important factors that are associated with high inpatient medication costs, thereby assisting in the development of the hospital pharmaceutical budget using a novel and scientific approach.

TABLE OF CONTENTS

LIST OF TABLES

Table

LIST OF FIGURES

Figure

LIST OF ABBREVIATIONS

ABC	Always Better Control
ACS	Acute Coronary Syndrome
AMI	Any Mental Illness
BD	Bipolar Disorder
BEA	Bureau of Economic Analysis
CAD	Coronary Artery Disease
CC	Complication or Comorbidity
CDC	Center for Disease Control and Prevention
CMS	the Center for Medicare and Medicaid Services
COPD	Chronic Obstructive Pulmonary Disease
CVD	Cardiovascular Disease
DRGs	Diagnosis-Related Groups
FGAs	First-Generation Antipsychotics
HCUP	Healthcare Cost and Utilization Project
HIV/AIDS	Human Immunodeficiency Virus, Acquired Immunodeficiency Syndrome
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
IMS	Intercontinental Marketing Services
IPS	Inpatient Psychiatric Facility
IRB	Institutional Review Board
LAI	Long-Acting Injectable

LOS	Length of Stay
MBD	Mental and Behavioral Disorder
MCC	Major Complication or Comorbidity
MI	Myocardial Infarction
MS-DRGs	Medical Severity Diagnosis-Related Groups
MUC	Medications Under Control
NB	Negative Binomial
NIMH	National Institute of Mental Health
NSDUH	National Survey on Drug Use and Health
OTC	Over the Counter
P&T	Pharmacy and Therapeutic
PBM	Pharmacy Benefit Managers
PPS	Prospective Payment System
PTSD	Post-Traumatic Stress Disorder
R&D	Research and Development
RA	Rheumatoid Arthritis
RR	Readmission Rate
RW	Relative Weight
SAMHSA	Substance Abuse and Mental Health Services Administration
SGAs	Second-Generation Antipsychotics
SMDC	Secondary Major Diagnostic Category
SUD	Substance Use Disorder

TD	Tardive Dyskinesia
VEN	Vital, Essential, and Non-essential
WHO	World Health Organization
WHS	World Health Survey

CHAPTER 1: INTRODUCTION

1.1 Background

The ever-increasing number of patients with mental disorders, and the concomitant increasing occurrence of chronic diseases have significantly increased healthcare expenditures over the past decade. Among hospital stays related to mental health and substance abuse, schizophrenia, mood disorders, depression, and bipolar disorder had the highest discharges in 2014 [1]. By 2016, 8.6 million inpatient stays were involved with at least one mental disorder or substance use disorder diagnosis, thereby accounting for 32% of the total inpatient stays [2]. Medication expenditures contribute a high portion of the overall hospital operating budget, and inpatient medications represent one of the highest expenditures in hospitals [3]. Between 2013 and 2015, the costs of inpatient pharmaceutical increased 23.4% on average annually. The increase in expenditures for inpatient medications surpassed the increase in spending on retail medications, which only grew by approximately 10% [4]. A survey conducted in 2017 from a healthcare industry group revealed that 96% of healthcare executives reported significant growth in inpatient medications costs over the past five years. Along with mounting prescription rates as a leading driver of budget increases (95% of surveyed organizations or institutions reported), followed by increased use of specialty medications (91%) and increased patient acuity (64%), it can be inferred that the cost of prescription medications assume significance in the context of the United States market, surpassing other healthcare sectors [5]. By 2020, medication expenditures are expected to account for 11.1% of the total national health expenditures [6-8]. Moreover, the three most common strategies that hospital leaders used to manage growing medication expenditures were increased use of generic medications (89%), tightening up the

hospital's medication formulary (82%), as well as asking pharmacists to identify expensive medication use patterns and to suggest alternative medication treatments (75%) [9].

In fact, the data from hospital pharmacies are powerful tools that can help reduce medication-related expenditures. In addition to medication costs, evaluating other healthcare data may help identify the causes of mounting medication expenditures today. As opposed to investigating only medication costs per patient, evaluating medication cost per diagnosis-related group (DRG), may be able to align expense analysis by reimbursement groups. In addition, evaluating the length of stay (LOS), and other similar measures that reflect overall medication costs may be helpful. For this reason, identifying medication cost savings through utilization-based data may be helpful. Although medication cost containment has gradually spread across most hospitals in the United States, only 29% of hospitals monitor formulary compliance, which can lead to inefficiencies in medication utilization. Analyzing medication use patterns, ensuring proper management of the medication formulary, identifying top medication cost drivers, as well as forecasting medication expenditures may be useful methods of controlling hospital medication costs [10].

1.1.1 Inpatient Medication Cost

During a hospitalization, medications including antidepressants, anti-anxiety medications, anxiolytics, stimulants, mood stabilizers, and antipsychotics play a pivotal and potentially life-altering role in treating patients presenting with a variety of mental disorders. With constant growth in the usage of psychotropic medication, the medication expenditures for these types of patients constitutes a significant portion of the psychiatric hospital operating budget [11]. Over nine-tenths of the surveyed general acute care hospitals reported that inpatient medication cost increases had a moderate to severe effect on their ability to control the budget. However,

psychiatric hospitals were excluded from this survey, and similar studies have not been conducted in this setting.

1.1.2 Hospital Reimbursement Systems

Under existing reimbursement systems, hospitals are paid by government sponsored or private insurance companies. Under certain scenarios, hospitals may be reimbursed less than the actual amount spent on treatment, particularly in bundled reimbursement systems. Hospitals are required to develop plans to lower treatment costs in order to manage budgets. In this context, Prospective Payment System (PPS) denotes a method whereby Medicare payment is made based on a predetermined, fixed amount that only focuses on the conditions being treated. Under this model, the payment amount is derived based on the classification system of a particular service, such as diagnosis-related groups (DRGs) for inpatient hospital services [12]. In 2011, the Centers for Medicare and Medicaid Services (CMS) expanded this concept of "bundled payment" to provide incentives in order to enable a more efficient and high-quality healthcare delivery [13, 14]. Under bundled payment, patients are charged a flat fee for an inpatient DRG episode, regardless of the actual cost, which takes into consideration the frequency as well as variance of the episode (an episode of care is defined as a single stay in hospital) cost [15-17]. When reimbursement rates fail to keep up with the input costs, such as medications, hospitals are compelled to assimilate a certain amount that remains uncovered [18]. Since the bundled payment is a fixed amount, hospitals will no longer bear the difference and can make a profit if costs such as those of medications can be reduced. Therefore, serious attention must be paid to research-based and actionable efforts to contain inpatient pharmaceutical costs.

A problem arises owing to the strong possibility that the cost of inpatient medications prescribed for mental/behavior disorders (MBDs) increases the hospital budget assigned to the

pharmacy department. This, in turn, leads to an inevitable financial burden on acute psychiatric hospitals. To this end, lowering inpatient medication costs, exploring the leading drivers of growing medication costs, and ameliorating the hospital's financial burden are the most challenging facets of hospital pharmacy management, particularly in the context of mental and behavioral health treatment facilities. Additionally, forecasting future medication cost trends for MBDs and chronic diseases, as well as monitoring and reacting to trends, is also a serious issue that merits attention.

1.2 Review of Literature

The drivers of medication spending patterns are both diverse and complex. From the hospital's perspective, the most challenging task is to accurately estimate future expenditures for medications. However, in order to attain this objective, the primary endeavor is to determine the most critical reasons for high medication expenditures in hospitals.

Patients and market factors are random, inconsistent, and unpredictable factors. In this regard, patient demographic factors (gender, age, etc.), and clinical factors, such as length of stay (LOS), diagnosis-related groups (DRGs), major diagnostic categories (MDC), comorbidities, etc., are not controllable factors. Market factors, such as medication shortages and the emergence of innovative medications are also not amenable to change. However, continuous monitoring of these factors is something that is indeed feasible.

Although the aforementioned factors are uncontrollable, some solutions do exist that can help control costs through the implementation of hospital control mechanisms. These include periodic formulary reviews conducted by the hospital pharmacy and therapeutic (P&T) committee and regular medication usage education prepared for physicians. Research has

demonstrated that educational interventions have been successfully implemented to improve prescribing competencies. Within this context, the World Health Organization (WHO) Guide to Good Prescribing has credible evidence that supports its use as an encouraging model to design targeted prescription behaviors [19].

1.2.1 External Factors

1.2.1.1 Inpatient medication utilization. Uncontrollable demographic changes in the United States are an example of an external factor that has contributed to the rise in medication usage and costs. More than 10,000 Americans above the age of 65 years enroll in the Medicare program every day. Inexorably, this puts a tremendous strain on the entire system. The Census Bureau forecasted the number of Americans aged 65 years and above will exceed the proportion of minors by 2030. This means that one in five Americans will be a senior citizen for the first time in American history [20].

Such a large aging population is accompanied by a corresponding increase in chronic illness and disease. This has further increased medication usage and cost a higher order phenomenon that is beyond the control and management of pharmacy and hospital leaders [21]. According to data published from the Healthcare Cost and Utilization Project (HCUP), many patients treated for issues related to mental health and substance abuse in United States hospitals seek recurring treatment. The study published in 2014 showed that 12.8% of mental disorder discharges and 9.9% of substance abuse-related discharges were readmitted for the same type of diagnosis within a span of 30 days.[21, 22] Therefore, it is evident that uncontrollable drivers, such as increased hospital stays attributed to an aging population, can lead to possible increases in inpatient medication cost.

1.2.1.2 Medication shortages. The United States has been confronted with an increasingly serious problem of medication shortages over the past two decades, despite a functional warning system for impending products facing shortages [22]. It is notable, that medication shortages are not a new phenomenon and have led to difficulties for physicians, health care facilities, patients, and federal regulators [23]. Medication shortages are attributed to many reasons including manufacturing issues, regulatory problems, difficulties in acquiring raw materials, business decisions, as well as several other disturbances within the supply chain. Medication shortages adversely affect patient care by causing replacement of safe and effective therapies with substitute treatments, which may not be optimal. Moreover, it also imposes a significant burden on providers and health care facilities [24]. In fact, most medication shortages observed in the United States involve generic medications [25], which are likely due to few financial incentives to produce off-patent medications from manufacturers [22].

Findings from a national survey conducted in 2017 suggested that vital medications which impacted many service lines were affected by medication shortages, including those for neurology (18%), allergy and asthma care (15%), psychiatry (10%), endocrinology (10%), and ophthalmology (5%) treatment [26].

Medication shortage statistics show that there were 186 new shortages in 2018 including anesthetics, antibiotics, cancer drugs and much more. As of June 2019, the top 5 drug classes with active shortages included antimicrobials, chemotherapy, cardiovascular, central nervous system, and electrolytes/nutrition/fluids. Many of these are critical for patients with serious illnesses [27]. Much time and effort are spent in managing medication shortages, such as inventory tracking and seeking alternative supply chains. More alarmingly, some vendors are involved in price gouging when selling medications in short supply to hospitals [28].

1.2.1.3 New and innovative medications. Another largely inconsistent and uncontrollable external factor is an issue that is faced on a more practical level: the high cost of new and innovative medications. The United States is the world's leader in biopharmaceutical investment and innovation [29]. Although Americans have access to many of the most innovative medications worldwide, they are becoming increasingly difficult to afford.

In 2015, a study conducted by Tufts Center for the Study of Drug Development announced it had calculated that it costs pharmaceutical companies $2.6 billion to develop a new medication up from the $802 million the Center estimated in 2003 [30]. Meanwhile a survey on the research and development (R&D) costs of 106 new medications showed that the estimated average out-of-pocket cost per approved new medications is $1.39 billion. The study also estimated an increase in post-approval R&D costs, bringing the total cost estimate to $2.87 billion [31].

An example pertinent to an acute psychiatric hospital would be valbenazine for tardive dyskinesia (TD) a severe condition that can affect almost one out of four patients on previous or existing antipsychotic treatment, which is inclusive of both first-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs) [32]. Although the prevalence is fewer than 200,000 per year in the United States, the cost of medication treatment is still high in terms of the monthly cost. Depending on the wholesaler used, velbenazine imposes costs from $5,000 to $6,000 per month, meaning that patients diagnosed with TD may demonstrate significantly higher healthcare utilization and costs [33].

In May 2018, the Trump administration created the "American Patient First" blueprint in order to take a proactive step towards solving this problem. As per the blueprint, the government will encourage greater competition between pharmaceutical companies and reduce the regulatory

burden. This, in turn, will allow new medications to enter the market faster and at cheaper prices. This blueprint will also remove large numbers of intermediaries, such as pharmacy benefit managers (PBM) and insurance companies. Doing this will expedite the approval process for over-the-counter (OTC) drugs, thereby allowing patients to get cheaper options without a prescription. In addition, the government will take drastic action to punish pharmaceutical manufacturers that use patent law in order to stifle competitors, especially for generic medications [34, 35] [36].

1.2.1.4 Patient factors. Patients in a psychiatric hospital with additional medical conditions may incur higher costs for their medications. Equally, psychiatric hospitals are also required to treat the medical conditions the patient also suffers from. Arthritis, as a chronic condition, as well as depression, as a mental health illness, are both perceived to be some of the leading causes of disability worldwide [37, 38]. To illustrate, a patient with severe rheumatoid arthritis may be on an immunomodulatory treatment that is necessary, but also very expensive. Many other linkages have been found to exist between mental illness and cardiovascular diseases, in addition to diabetes, obesity, asthma [39].

Patients - Psychotropic medication and mental disorders. The 2015 National Survey on Drug Use and Health (NSDUH) observed that approximately 43.4 million adults (18% of the population) in the United States have suffered from some kind of mental illness in the past year (including mental, behavioral, or emotional disorders, but excluding developmental and substance use disorders) [40]. The latest self-report study published in 2017 shows that 1 in 6 U.S. adults reported taking psychotropic medications on at least one occasion. However, these numbers may have been underestimated because the prescriptions were self-reported, and the estimates of long-term use were confined to a single survey year [3, 41] [42]. Meanwhile

antidepressants are the most frequently prescribed medications for treating depression, anxiety and other MBDs [25]. In 2005, antidepressants surpassed antihypertensive agents to become the most commonly prescribed class of medications in office-based and hospital outpatient–based medical practices [43, 44]. The data for antidepressants used in inpatient settings are rarely reported. From 1999 to 2010, a significant growth was reported in the long-term use of antidepressant medications in the United States, which may explain the overall increasing trend in use [45]. Individuals treated with antidepressants with inadequate responses, became more likely to receive additional treatment with more costly antipsychotic medications which increased treatment costs [46]. However, there are very few reports for inpatient-based psychotropic medication use patterns as well as cost data published during the past decade among adults in the United States.

Patient gender. The 2014 NSDUH survey results indicated that mental illness was more prevalent among women (21.2%) as compared to men (14.3%). In addition, this study observed that when compared to men, women were 50% to 70% more likely to be diagnosed with major depression (43.2% vs. 27.2%, $p < 0.001$) or anxiety disorders (41.8% vs. 24.4%, $p < 0.001$) [40].

Among previously published studies on the age and gender patterns of antipsychotic use, women between the ages of 25 and 84 years had recorded a high rate of use as compared to men in the same age range [25]. Furthermore, the Intercontinental Marketing Services (IMS) data showed that anxiolytics were also proportionately more commonly prescribed to antipsychotic-treated women in comparison to men. Similarly, other studies also suggest that women are 2.5 times more likely to take antidepressants than men and that almost a quarter of women between 40 and 59 take antidepressants, more than in any other age-gender group [47]. Although the prevalence of social anxiety is found to be equal in both men and women, the lifelong diagnostic

rate for anxiety is found to be higher in women in comparison to men. Additionally, women suffering from a lifetime diagnosis of one type of anxiety disorder were more likely to be diagnosed with an additional anxiety disorder than men [48-50]. For this reason, women are more likely to receive two or more classes of psychiatric medications than men, which increases medication-related expenses [51, 52].

Evidence seems to suggest that there is a difference between men and women in terms of prevalence of mental illness and patterns relating to psychotropic medication usage. It is important to note that gender may be one significant driver of rising medication costs in an acute psychiatric hospital. Thus far, no research has been published to determine whether or not there is a linkage between the patient's gender and the inpatient cost of medications for MBDs. This association between gender and inpatient cost of psychotropic medications, as well as the medications for other chronic diseases, continues to be a subject that necessitates further research.

Patient age. Mental illness occurs among more than 20% of adults aged 18 to 49, and 14% of the adults aged 50 and older, which is inclusive of Alzheimer's disease. Between 2008 and 2015, the percentage of adults with any mental illness remained generally stable, with the highest prevalence among those who were aged 26 to 49, and the lowest among those aged 50 and older, which included patients with Alzheimer's disease [12]. Males and females aged 40 and above were more likely to take antidepressants in comparison to patients belonging to other age groups [53]. It was found that the percentage of adults who were prescribed both antipsychotics and mood stabilizers tended to decline with age. Similar declines with age were observed for antipsychotic-treated men and women who were prescribed two or three of the other psychotropic medication classes (antidepressant, anti-anxiety medication, and mood

stabilizer) [54]. Meanwhile a study carried out among psychotropic medication prescriptions suggested that antipsychotic use varies by patient age within a retail setting [55]. It was found that in two age groups namely, 18 to 39 and 40 to 64, affective psychoses (F39) and schizophrenia (F20) contributed nearly 70% of atypical antipsychotic usage. By contrast, the two diagnoses represent only 41% of the usage among patients aged between 1 and 17, and 36% among patients whose age was at least 65 years. For this reason, it is necessary to examine the relationship between the age of the patient and their medication use and cost within an acute psychiatric hospital setting.

Patient medical insurance. Medicare has been the most common payer for hospitalizations involving only MBD diagnoses (37% of aggregate hospital expenses). On the other hand, Medicaid was found to be the most frequent payer for Substance Use Disorders (SUD) diagnoses only (29% of aggregate hospital expenses). When viewed collectively, Medicaid was found to cover 56.0% of all inpatient stays with primary MBDs or SUDs, including those with co-occurring MBDs/SUDs. However, Medicare accounted for the largest proportion (46%) of aggregate hospital costs [56]. More than 50% of all psychiatric hospitalizations were paid by Medicare or Medicaid, which may be linked to an individuals' ability to maintain employment [57, 58]. The study that examined the costs/payments for psychiatric treatment (inpatient) in community hospitals suggested that the costs were 2.5 times higher as compared to the reported costs of the hospitals in delivering care. It was found that the average cost for delivering care was the lowest for the uninsured and highest for Medicare: $5,707 for 7.4 days and $8,509 for 11.1 days, respectively for schizophrenia treatment; $4,356 for 5.5 days and $7,593 for 9.4 days for bipolar disorder treatment; $6 $3,616 for 4.4 days and ,990 for 8.4 days for depression treatment; $3,422 for 3.7 days and $4,591 for 5.2 days for

medication use disorder treatment; and $4,147 for 3.8 days and $5,908 for 6.2 days for alcohol usage disorder treatment. Therefore, understanding the relationship between insurance type and inpatient medication cost among psychiatric hospitals is worthy of exploration as one of the leading factors.

Patient clinical factors – Comorbidity. Patients are often comorbid for MBDs and chronic medical illnesses. Nearly one out of four American adults aged 18 years and older suffer from a diagnosable mental disorder in a given year [59]. In 2009, 145 million people, which account for almost 50% of all Americans, were living with a chronic medical condition [60]. In 2018, the Center for Disease Control and Prevention (CDC) indicated that six out of ten adults in the United States suffer from a chronic medical disease, and four out of ten have two or more, which contributed $3.3 trillion toward annual health care costs [61]. Investigators are yet to determine if having a chronic disease can increase the prevalence of depression or depression increases the risk of having a chronic medical disease. Nevertheless, the linkage between mental health and chronic medical disease cannot be ignored. Medication treatment for mental illness combined with chronic medical diseases may increase hospital medication expenditures [62-66]. However, it is difficult to forecast when patients with both MBDs and chronic medical diseases will be admitted, which will make forecasting medication costs a very challenging task.

Many associations have been found to exist between mental illness and cardiovascular diseases [53], as well as diabetes [67, 68], obesity [69, 70], asthma [71-73], and arthritis [74, 75] [76, 77]. A common research finding shows that patients who suffer from chronic diseases are more likely to also suffer from depression [59]. Depression is found to co-occur in 17% of cardiovascular cases, 23% of cerebrovascular cases, 27% of diabetes cases and more than 40% of individuals with cancer [78] [52] [79]. Depression, anxiety, impulsive eating disorders, as well

as substance use disorders were found to have significant associations with the subsequent diagnosis of hypertension [80]. In this regard, a study conducted in China showed that there is a linkage between anxiety and heightened risk of hypertension [81]. According to a systematic review, depression is a common phenomenon in patients suffering from rheumatoid arthritis (RA) and is associated with poor prognosis [82]. In addition, higher rates of cardiovascular disease (CVD) and diabetes are also observed in patients suffering from schizophrenia. In most nations, the standardized rate of mortality in schizophrenia is around 2.5, which results in a reduced life expectancy between 15 and 20 years. To this end, CVD is a significant contributor of increased mortality in schizophrenia; it was found that mortality in schizophrenia ranged from 40 to 50% with CVD in the majority of the studies [83].

Since several studies have demonstrated a meaningful relationship between mental health and chronic diseases, it can be inferred that the medication treatment of mental illness combined with chronic diseases will greatly increase hospital medication spending [47-51]. Therefore, comorbidity is another factor that needs to be duly considered. So far, few studies have considered this issue and did not break down the pharmaceutical expenses.

Clinical factors involving MBDs. Hospital care for patients with mental disorders in the United States has changed tremendously over the last several decades in the wake of numerous factors. This includes the passage of the Social Security Act of 1965, which enacted the Medicare and Medicaid programs. Notably, these programs made considerable progress in achieving parity in private insurance coverage for patients with mental disorders, creating competition within an increasingly specialized mental disorder workforce, as well as innovations in the services and treatment [84]. Since the mid-1960s, treatment for mental disorders has departed from a system characterized by care in state-owned facilities to one that is driven by

market forces. Between 1971 and 2001, the share of spending on specialty mental disorder services dropped by nearly 70% for state mental hospitals; however, this expenditure on specialty mental disorder dropped by 65% for general hospitals and 366% with regard to private psychiatric hospitals [85-87]. Although many patients with mental disorders can be treated successfully in ambulatory care settings, inpatient treatment continues to be a key component of care [88]. The increasing number of hospitalized patients and longer hospital stays will lead to a continued increase in inpatient medication usage and cost. Therefore, paying attention to the trends of use and costs of medication prescribed in psychiatric hospitals can play an important role in controlling psychiatric hospital pharmacy budgets.

Length of Stay (LOS). LOS is one of the factors that contributes to rising pharmaceutical expenses across hospitals [89]. Among hospital stays related to MBDs and substance abuse, discharges were observed to be the highest for schizophrenia, mood disorders, depression, as well as bipolar disorder in 2014 [90] [91]. As noted earlier, 12.8% of mental disorder discharges and 9.9% of substance abuse-related discharges were readmitted for the same type of diagnosis within a period of 30 days [92].

Length of Stay (LOS) as a proxy of inpatient medication cost. Comorbidity is another key determinant of longer LOS. A study conducted among coronary artery disease (CAD) patients with mental disorders showed that comorbid mental disorders are associated with higher healthcare utilization with regard to longer LOS and higher hospital readmission rates (RR) [93]. Longer LOS and higher RR are also associated with mental disorders in patients admitted with myocardial infarction (MI) [94]. Also, patients with acute coronary syndrome (ACS) and depression were found to have longer LOS in emergency departments [95]. To that end, a study conducted in New Zealand showed that depression, as opposed to anxiety, is related to the

number and length of cardiac-related hospitalizations in patients with CAD [96]. A more recent study published in 2018 among readmitted patients showed that treatment-resistant bipolar disorder (BD) often accounts for longer hospitalization stays [97]. Atypical antipsychotics, anticonvulsants, antidepressants, and lifetime alcohol dependence predicted LOS for 68.2% of admissions for use ($p = 0.042$) [97].

LOS with MBD/Substance Use Disorder (SUD). Nationwide, in 2016, approximately 10 million inpatient stays were found to involve at least one MBD or SUD diagnosis, which accounted for 27.8% of the total inpatient stays. Among all MBD and SUD, depressive disorder, alcohol-related disorders, and schizophrenia were the most common primary diagnoses. The average LOS for all MBD/SUD stays were higher as compared to all other stays (6.4 vs. 4.2 days). However, the average costs for MBD/SUD stays were found to be 50% lower than for all other stays ($7,100 vs. $11,500) [87]. This cost was not broken down to separate out the inpatient medication cost. Therefore, LOS might be a feasible alternative indicator of the inpatient medication cost among MBD/SUD patients.

1.2.2 Internal Factors

Increasing medication expenditures are a financial burden on hospitals, patients and the government. Notably, the factors affecting medication expenditures within the health system are usually determined by the scope and nature of the care provided. To some extent, they can be controlled by the pharmacy manager. One example is to replace expensive new medications with newly approved generics. Such an approach is within the purview of pharmacy and therapeutics committees. Although the current predicament of mounting medication expenditures cannot be addressed in a short span of time, the internal factors mentioned in the subsequent sub-sections can help control expenditure to some extent.

1.2.2.1 Hospital medication expenditure control strategies. Although external factors such as inpatient medication utilization, medication shortages, patient clinical factors, new and innovative medications, comorbidity, patient medical insurance, patient age and patient gender are uncontrollable for medication costs in a hospital pharmacy, there is still a way to control costs by implementing hospital control mechanisms (C) and reviewing prescribing practices (D) (Figure 1.1). Effective medication cost control strategies are known to vary in inpatient settings as compared to managed care and ambulatory care settings. To that end, four primary factors drive growth in overall medication expenditures in the hospital setting: (1) high existing price of medications, (2) medication utilization, (3) rising costs of new medications, and (4) newly approved medications [98, 99] (Figure 1.2). Rising medication costs pose a challenge for hospital budgets, insurance plans, and out-of-pocket spending for consumers. Moreover, steeply rising medication prices are not a new predicament for hospital pharmacies, which have been making difficult formulary choices for several years [100].

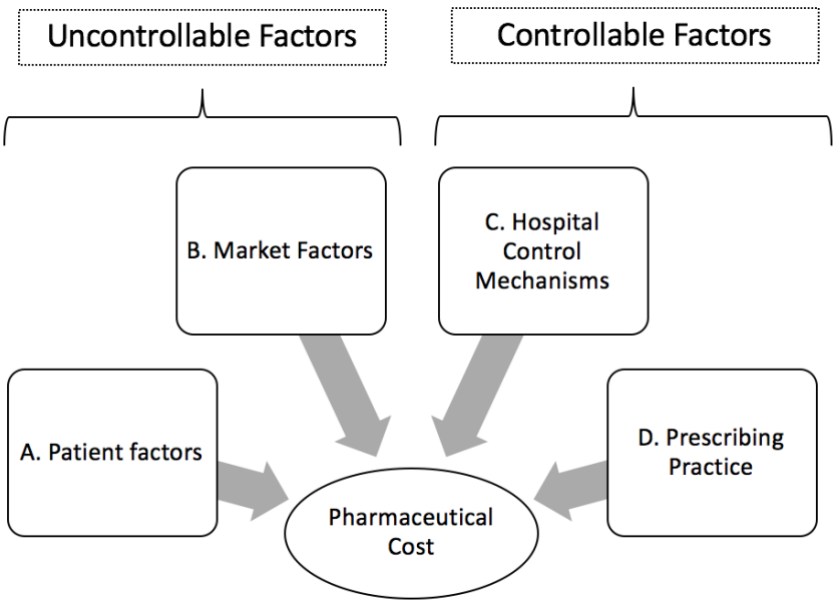

Figure 1.1 Factors impacting pharmaceuticals cost to hospitals.

In most hospital pharmacy budgets, 20% of medications (high priority medications) typically account for 80% of hospital medication budgets. Therefore, budgeting and cost-containment efforts should ideally focus on those high cost medications, and cost-management plans should especially concentrate on those top medications for which prescribing patterns may be changed. When medication cost growth in hospitals is attributed to increasing prices of medications, a cost-containment tactic could involve a change in a preferred formulary medication or a new therapeutic category to something less expensive yet as effective [101]. It has been found that it is possible to adopt an ABC-VEN matrix analysis in order to pinpoint medications demanding strict management control for effective utilization of hospital funds and reduction of out-of-stock situations in hospital pharmacies [102, 103]. ABC analysis combined with VEN analysis provides an organized common coding of potentially cost-effective medications [104]. In addition, recent findings suggest that a relatively small number of medications account for most of the funds allocated by hospitals. Moreover, non-essential medications represent nearly 45% of studied items and account for around 26% of the total hospital funds [105]. However, ABC analysis, VEN analysis, and ABC-VEN matrix analyses are rarely applied to studies conducted in acute psychiatric hospitals among adults with MBD [106, 107].

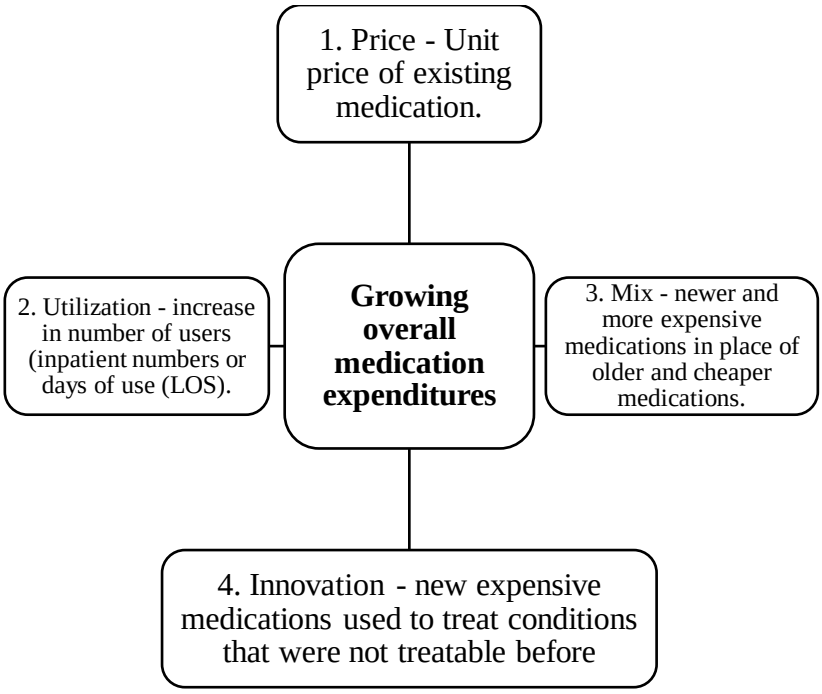

Figure 1.2 Four primary factors drive growth in overall medication expenditures in hospital setting.

There is a reasonable and applicable cost-containment opportunity in moderating the trend in increasing expenditures, which means mitigating the rate of increase for high-priority medications. Moderating the growing trend and avoiding unnecessary cost is as relevant as actual cost reduction. A large number of studies and data demonstrated that hospitals bear heavy financial burdens from high-cost medications [108-110]. To that end, one study suggested that reducing high-volume medications could be more effective in optimizing the hospital medication budget than concentrating solely on reducing high-cost medications.[111] Medications with high volume in the acute psychiatric hospital have been examined to determine whether strict medication management control can be useful. These findings are important in the context of this study which aims to fill the gap in extant literature on examining LOS as a predictor as well as outcome variable.

On a related note, a systematic study needs to be conducted in order to fill the research gap in examining how factors such as age, gender, length of stay, DRGs (MBDs and chronic diseases), insurance, and comorbidity can influence inpatient prescription medication costs. By combining all patient factors impacting inpatient psychotropic medication usage patterns and cost, an important task of the current study is to develop a regression model that can determine the most important drivers of medication costs to hospitals and how a hospital can monitor and react to changing trends.

1.2.2.2 Physicians. Personal experience, government regulatory approval, and guidelines are the three main factors guiding clinicians' decision-making regarding treatment of psychiatric diseases, which inevitably involves prescription of psychotropic medications, the affordability/lack thereof could be a key factor in determining health outcomes for patients. Among them, personal experience is the key factor guiding clinical decision-making. For example, most psychiatrists use second-generation oral antipsychotics (SGAs), in the treatment of schizophrenia, and they are costly. Meanwhile long-acting injectable (LAI) SGAs were prescribed to one-third of schizophrenic patients. It was found that the psychiatrists following the higher percentage of schizophrenic patients were associated with a higher use of LAI antipsychotics and a lower use of oral SGAs [112]. Thus, the discernment of physicians can help determine the cost of psychotropic medications that for patients and shape prescription decisions.

This was confirmed by a survey which found that 88% of physicians believe the cost of medications is an important consideration in the prescribing decision, and 71% are willing to sacrifice some extent of efficacy in order to make medications more affordable for patients. However, 80% of physicians are unaware of the actual medication costs; only 13% had been formally educated about medication costs [113]. Since a sizeable portion of physicians feel that

medication cost is an important issue for the patient, there is a strong possibility that physicians can prescribe less expensive medications with equivalent efficacy. Hence, the prescribing decision of a physician can play a very critical role in containing hospital inpatient medication costs.

1.2.2.3 Pharmacy and therapeutic (P&T) committee and formulary management issues. The Pharmacy and Therapeutics (P&T) Committee typically oversees the various facets of medication therapy in an institution. More specifically, they are required to ascertain the costs benefits of all medications and determine the ones that have the greatest efficacy per dollar. Furthermore, P&T committees adopt an evidence-driven strategy to effect changes in the health systems through re-evaluation of existing policies and an emphasis on latest research to support decision-making. It is comprised of actively practicing physicians, other prescribers, pharmacists, nurses, administrators, quality-improvement managers, and other health care professionals who participate in the medication-use process [114].

To be an efficient and successful P&T committee, it is important to generate a timeline for formulary reviews to set periodical expectations, as well as a process for formulary requests. Also, collaboration with hospitals that fall under and comply with drug-prescription related practices under a single cohesive system can potentially help facilitate successful formulary standardization. When developing a P&T committee or standardizing a formulary system, evidence-based data and rationales need to be provided to all departments in the hospital to support formulary changes [115].

In the field of medical management, it is becoming increasingly evident that robust executive practice is crucial for effective delivery of inpatient care. Hospital pharmacies deliver significant supportive services that embrace planning, designing, and organization, leading to

proficient clinical and administrative services. The endeavor to contain costs with improved efficiency requires adopting a scientific method for undertaking hospital medication inventory management in order to attain better outcomes for the stated purpose (cost containment) [116]. ABC analysis and VEN Analysis have been used successfully to narrow down the group of medications that require strict monitoring and facilitate optimization of medication formularies [102, 104, 105, 117-119].

In most hospital pharmacy budgets, 10 – 20% of medications (high cost) account for 80% of hospital medication budgets. Budgeting and cost-containment efforts should focus on those medications, and the cost-management plan should concentrate on those top medications for which changes in prescribing patterns can be realistic.

1.2.2.4 Generic products. For economic reasons, substituting brand medications with generic medications is common and encouraged. Using alternatives are based on the concept of bioequivalence, which deemed equal to therapeutic equivalence. Brand medications require long-term research and testing that take substantial investments, but generic medications only need to be shown to be bioequivalent to the brand product saving research expenditures and reducing purchase costs. Therapeutic equivalence has been challenged for certain psychotropic medications by case reports and retrospective studies [120]. However, a study conducted among patients taking risperidone found no difference in the use of healthcare services between switchers and non-switchers of the brand versus the generic group [121].

By understanding the external and internal drivers of health spending, researchers can analyze specific utilization patterns and expenditures of medication in order to develop a robust and accurate budget forecast.

1.2.3 Important Drivers for Psychiatric Hospitals

1.2.3.1 Newly approved psychiatric medications. Since the year 2015 prices of newly approved psychiatric medications have risen drastically. It is a known fact that new psychiatric medications are often very expensive [122]. For example, injectable Invega Sustenna costs roughly $1,500 per injection. In 2015, there were three new psychiatric medications approved by the FDA, which are Aristada, an extended-release injectable medication that is for treatment of schizophrenia; Rexulti, once daily oral for the treatment of depression and schizophrenia; and Vraylar, a once-daily oral medication for the treatment of schizophrenia and bipolar disorder.

In 2016, no new medications were approved in psychiatry, but two new medications for neurology were approved. Briviact was approved for the treatment of partial onset seizures related to epilepsy. Carnexiv was approved for replacement therapy when oral administration is not feasible for adults with seizures.

In 2017, Austedo and Ingrezza were approved for the treatment of tardive dyskinesia, and in July 2018, Perseris, a once-monthly extended-release injectable was approved for treatment of schizophrenia in adults.

In 2019, Spravato (esketamine), a nasal spray has been approved for treatment of resistant depression in adults; Zulresso (brexanolone) was approved for the treatment of postpartum depression.

Over the past five years, an average of two new medications were approved on a yearly basis for patients with MBD (including 2018). In addition, a large number of new medications for other chronic medical conditions annually still imposes a burden on psychiatric hospitals.

1.2.3.2 Other medical conditions and medications. Psychiatric hospitals are also tasked with treating any additional medical conditions the patient may have. Many such medications are new and only available as the brand name until they come off patent. For instance, a psychiatric patient with severe rheumatoid arthritis may be on an immunomodulatory medication, which is needed, but also very expensive. In 2017, Zilretta (triamcinolone acetonide extended-release injectable suspension), an extended-release injectable suspension, was approved by the FDA for the treatment of osteoarthritic knee pain. More examples of new medications for the treatment of chronic diseases are also emerging [123]. Over the past five years, fifteen new medications were approved for diabetes, three medications for asthma, two medications for hypertension, one for the treatment of chronic obstructive pulmonary disease (COPD), and one for high cholesterol. Similarly, the FDA approved three new medications for cardiovascular abnormalities over the past three years. New medications such as these can add significantly to the pharmacy budget.

Due to the significant association between MBD and chronic diseases, medication treatment of mental illness combined with chronic diseases, may dramatically impact hospital medication expenditures. Therefore, comorbid conditions requiring expensive medications may significantly impact the medication budget. However, there is no plausible way to predict when one of these patients with comorbidities will be admitted. This uncertainly makes forecasting very challenging.

1.3 Research Objective

In order to expand the empirical research examining the association between high inpatient medication cost in psychiatric hospitals and its leading factors, ABC-VEN matrix

analysis was conducted as a preliminary study to examine mental and behavioral health disorder medications and the primary chronic disease medications associated with mental and behavioral health disorders that demand strict formulary management control. In chapter 3, multiple regression models were designed and analyzed to determine the leading drivers associated with growing inpatient hospital medication costs among patients admitted to a mental and behavioral health disorder hospital. One primary focus of the chapter was to determine if secondary major diagnoses codes (SMDC) had a significant impact on inpatient medication costs and if they did, which specific SMDC had an impact. Moreover, length of stay (LOS) was used as a proxy for inpatient medication cost allowing the use of count data regression models, like Poisson and Negative Binomial, to be analyzed.

CHAPTER 2: MEDICATION FORMULARY MANAGEMENT STUDY

2.1 Introduction

Cost containment has emerged as the most pertinent consideration when it comes to healthcare delivery. It has been found that efficient management targeted on the accessibility and availability of essential drugs, along with alternative medications in pharmacy practice, are imperative [118, 124]. Hospital pharmacies deliver a very significant supportive service that includes designing, planning, and delivering the pharmaceutical services which leads to proficient clinical and administrative services [99]. Cost containment with improved efficiency requires addressing the needs of hospital drug inventory management using scientific methods for improved outcomes. A variety of tools have been utilized for inventory management; the combination of VEN analysis, ABC analysis, and ABC-VEN matrix analysis has been successfully approved in order to narrow down the group of drugs that require strict monitoring and optimization of drug formulary.

ABC analysis refers to a method to determine which drugs are classified into Class A items (10-20% of items account for approximately 70-80% of cumulative drug cost), Class B items (10-20% of items account for a further 15-20% of the cumulative drug cost) and Class C items (the remaining 60-80% of items explains 5-10% of the total drug cost). When making drug selection and purchasing decisions, ABC analysis will be used to prioritize Class A items [116]. The result of drug selection (Class A items) provided an important platform to target the most expensive DRGs and ICD-10-CM codes (ICD, International Classification of Diseases; CM, Coordination and Maintenance Committee) after the commencement of study on the factors of excessive drug expenditure. However, ABC analysis of our fundamental study has certain limitations. It is based solely on the rate of consumption and the monetary value of the item. An

item of low cost and consumption does not mean that the item is not important or even lifesaving in an acute psychiatric hospital. Their importance cannot be ignored simply because they are excluded from the list under category A [117]. In light of this situation, another tool involved in inventory management was introduced to our study, namely, VEN analysis.

The drugs, in consonance with certain standards, can be classified into three categories: V, E, and N. Vital medicines (V) are indispensable in saving the lives or the provision of basic health care, such as fluoxetine 10mg; essential medicines (E) are effective for less severe but important diseases. They provide substitutes for vital products, such as imipramine 10mg; necessary medicines (N) meanwhile are also known as non-essential for minor or self-limiting diseases, such as loratadine 10mg. The drugs in this category have a relatively high cost for additional therapeutic value. In the hospital pharmacy management, VEN analysis is adopted to identify the most consumed and the largest number of therapeutic drugs, as well as to identify drugs that are over-consumed or inconsistent use with regard to the number of cases. Historically, it has been found that VEN analysis can be combined with the ABC analysis to discuss the removal of the "N" class of drugs from the high cost / high consumption of "A" resulting from the ABC analysis.

ABC-VEN matrix analysis takes the two aforementioned analyses into consideration, ensuring that the result is not only based on economic value, but also on the clinical value [105]. In addition, it gives us a clear picture of the classified drugs in accordance with the priority of their control mechanisms. The resulting ABC-VEN matrix analysis can help ensure the complete and successful selection of high-cost drugs. Furthermore, it provides a ‘double guarantee’ to target the most expensive DRGs and ICD-10-CM codes after starting the study on the factors of excessive drug expenditure.

In our study, we examined/identified the MBD medications and associated chronic disease medications prescribed in an acute psychiatric hospital that may benefit from strict formulary management control by conducting ABC analysis, VEN analysis, as well as ABC-VEN matrix analysis.

2.2 Study Design and Methodology

Medication usage aggregate data sources, including procurement records, warehouse medicine records, pharmacy stock and dispensing records, adverse drug reaction (ADR), medication error reports, as well as patient medical records have been used [125]. In the current study, patient data were collected during a continuous time period by using patient medical records (coding and summary reports). These expensive medications can be highlighted through aggregate data analysis on medicine usage and expenditure.

This study was conducted in a 35-bed, licensed, not-for-profit acute psychiatric hospital. In this regard, all admitted patients diagnosed with psychiatric and chemical dependency disorders were provided with comprehensive behavioral health services. The consumption data were retrieved from the Coding and Summary Report of 400 patients. These patients were enrolled between March 16th and July 27th, 2018 thus collecting approximately 4-month medication consumption data. Among the 400 patients, six patients did not take any medication during the hospitalization, whereas three patients' data could not be tracked during the study period because of incomplete records. Therefore, a total of nine patients were excluded from ABC analysis, VEN analysis, and ABC-VEN Matrix analysis.

For each patient the individual drug list with an exact item quantity during hospitalization was created and stored in the Excel sheet. Subsequently, inpatient drug cost data were retrieved

from McKESSON Purchasing Detail Reports for the hospital. Drug cost data were collected with the assistance of the inpatient pharmacist in the acute psychiatric hospital (McKESSON Report data selection: 11/01/2017 to 03/31/2018).

The drug prices recorded in McKESSON purchasing report displayed the price per item (for example: acyclovir 800mg tab, 100 tablets). The price per bottle is $50.19, and per tablet is $0.50) or package (for example: fentanyl 12mcg/hr). For five patches, the package price is $60.57 and per patch is $12.11. It was found in the McKESSON purchasing report that a drug with a certain dosage came at more than one price. To illustrate: clonazepam 0.5mg tab (100 tablets) contains three different prices: $1.30 per 100 tabs ($0.013 per tab), $4.05 per 100 tabs ($0.041 per tab), and $3.90 per 100 tabs ($0.039 per tab). Accordingly, the final price per clonazepam 0.5mg tab, $0.03, was calculated by taking the average of the three prices shown in the parentheses for further analysis. During the four-month period, the total drug consumption quantity of clonazepam 0.5mg tab was 107 tablets. Therefore, the single unit and total cost of this drug are $0.03 (price per unit) and $3.21 ($0.03*107=$3.21, price per drug), respectively. These data were then used for further study by implementing ABC analysis, VEN analysis, and ABC-VEN matrix analysis.

A drug cost per patient Excel sheet and total drug cost Excel sheet were created in order to obtain and analyze the inpatient drug costs of each patient's hospitalization during the study period. Drug cost per patient was calculated by multiplying the cost per tablet, capsule, patch, etc. with the quantity of those that were consumed by each patient. For another data set, total drug cost was obtained by integrating the drug cost per patient into an all-inclusive drug consumption and cost data, which includes complete drug items consumed by 391 patients, cost

per tablet, capsule, or patch, etc. as well as quantity of those for each drug item along with the total drug cost of all drugs during the four-month study period.

2.2.1 ABC Analysis

ABC analysis can be applied to patient drug consumption or drug purchase data over a one-year period or shorter [125]. In this study, a total of 364 medication items (27678 medication units) used for inpatient treatment in the acute psychiatric hospital (during the four-month study period) were arranged in descending order in accordance with the total drug expenditure and cumulative expenditure for each item. Furthermore, the cumulative percentage of items and cumulative percentage of expenditures (4 months) were calculated. Next, the drug items were divided into three categories based on the cumulative cost percentage: Class A (72%), Class B (18%), and Class C (10%).

2.2.2 VEN Analysis

The VEN analysis of all 4-month drug items used for inpatient treatment was conducted by classifying all items into vital (V), essential (E), and non-essential (N) categories. The VEN drug list was developed by a clinical pharmacist and a clinical psychopharmacology consultant with expertise in medically treating patients presenting with mental and behavioral disorders. The VEN drug list was created on the basis of criticality in line with the World Health Organization (WHO) lists of essential medicines (2017) [126] and VEN category assignment criteria [125], before being finalized with justification by the inpatient pharmacist.

2.2.3 ABC-VEN Matrix Analysis

ABC-VEN matrix analysis was implemented by generating a crosstab of two individual analyses. After creating nine different subgroups, they were further divided into three different

categories: I, II, and III (Table 2.1). Category I consists of sub-categories AV, AE, AN, BV and CV (The first letter indicates the position of the item in the ABC analysis, while the second letter indicates the position of the product in the VEN analysis). Category II consists of sub-categories BE, CE and BN and Category III only contains sub-category CN. The existence of statistically significant differences among nine different subgroup categories under all three classes was examined in order to confirm the significance of performing ABC-VEN matrix analysis. In order to establish the foundation for the cost drivers regression analysis in Chapter 3, the difference in drug cost among nine different groups: AV, AE, AN, BV, BE, BN, CV, CE, and CN were also explored in this chapter.

Table 2.1

The ABC-VEN Matrix

Category I	The category consists of drug items belong to AV, AE, AN, BV and CV
Category II	The category consists of drug items belong to BE, CE and BN
Category III	The category consists of drug items belong to CN

2.2.4 Statistical Analysis

Cumulative cost data of drugs obtained from the McKESSON purchasing detail report were checked to ensure completeness and accuracy. Data were analyzed using the Microsoft Excel spreadsheet (Version 16.20, 2018) and Stata, 2017 (Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC). In order to compare the difference in drug cost among the aforementioned nine subgroups under ABC-VEN matrix analysis, a parametric statistical test, one-way ANOVA, and multiple comparison (post hoc) tests were applied. The level of statistical significance was set at $p < 0.05$.

2.3 Results and Discussion

2.3.1 ABC Analysis

After performing the necessary analysis of the drug consumption and expenditure data obtained from the acute psychiatric hospital, the drug units were grouped on the basis of ABC analysis. Table 2.2 depicts the result of the ABC analysis which categorizes 27,678 drug units consumed by 391 patients between March and July 2018 within the acute psychiatric hospital. As per the findings, 585 (2.11%), 5439 (19.65%) and 21654 (78.24%) drug units were found to account for $50,168.95 (71.97%), $12,869.05 (18.46%), and $6,673.60 (9.57%), respectively of four-month inpatient drug expenditures. These results are also graphically illustrated in Figure 2.1 in order to provide a clearer picture of the cumulative percentage of drug units' amount and expenditure. The cut-offs were not exactly equal to 70%, 20%, and 10%, which is acceptable according to the theory of ABC analysis [102, 104, 118, 127, 128].

Table 2.2

ABC Analysis

Category	Total Units	% of Units	Cumulative % Units	4-Month Expenditures (Us $)	% Of 4-Month Expenditures	Cumulative % Expenditure
A	585	2.11	2.11	50,168.95	71.97	71.97
B	5439	19.65	21.76	12,869.05	18.46	90.43
C	21654	78.24	100.00	6,673.60	9.57	100.00
Total	27678	100.00		69,711.60	100.00	

Note. Unit cost is not equal to the item cost. One unit includes any of the following dosage forms: Tablet, capsule, patch, bottle, and ampule[129]. Different dosage forms or dosages of the same drug can be considered as a different drug. (For example: ziprasidone 20mg cap, ziprasidone 40mg cap, ziprasidone 40mg cap, and ziprasidone 20mg vial are regarded as four different drug items).

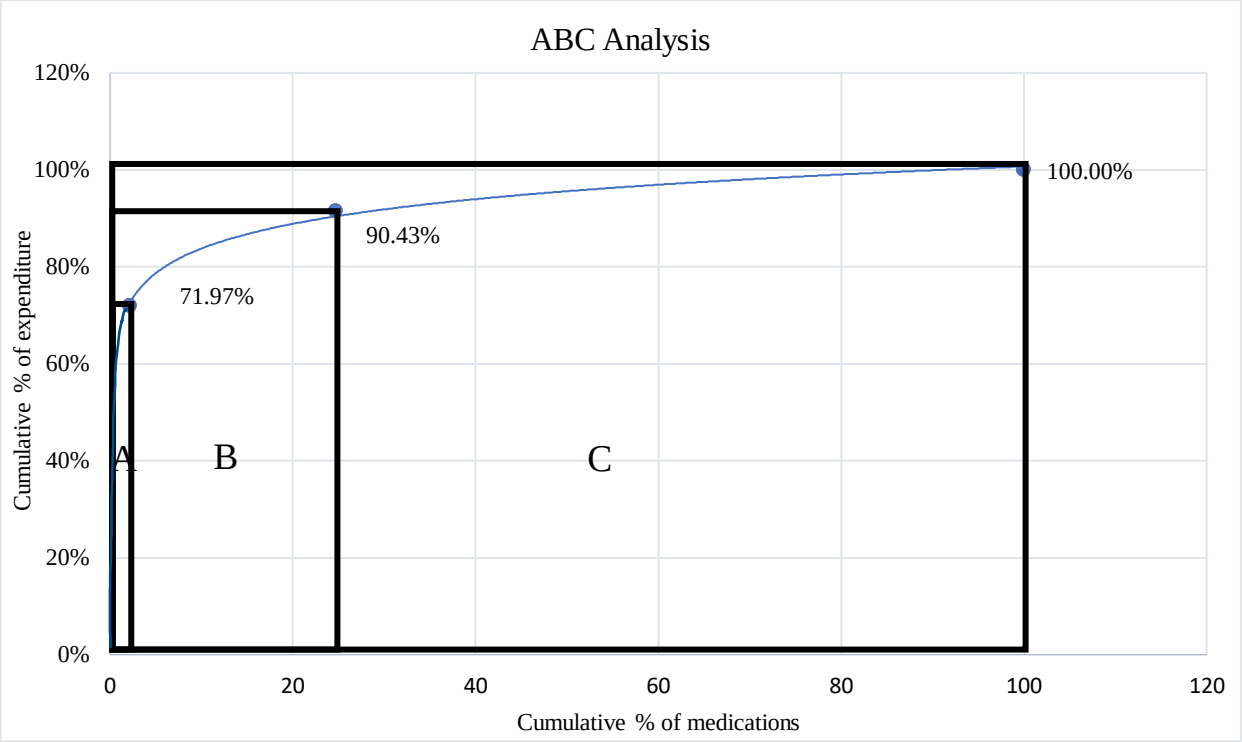

Figure 2.1 Cumulative curve of ABC analysis

2.3.2 VEN Analysis

The results of the VEN analysis are depicted in Table 2.3. Accordingly, it can be seen that 12,604 (45.54%) of drug units in the vital category consumed $28,296.06 (40.59%), 13681 (49.53%) drug units in the essential category consumed 53.08% ($37,006.29), and 1393 (5.03%) in the non-essential category consumed 6.32% ($4,409.25) of the four-month inpatient drug expenditures.

Table 2.3

VEN Analysis

Category	*Total units*	*% of units*	*Cumulative% units*	*4-month expenditures (US $)*	*% of 4-month expenditures*	*Cumulative% expenditure*
V	12,604	45.54	45.54	28,296.06	40.59	40.59
E	13,681	49.43	94.97	37,006.29	53.08	93.67
N	1,393	5.03	100.00	4,409.25	6.32	100.00
Total	27,678	100.00		69,711.60	100.00	

Note. In this study, the specified VEN drug list were created in accordance with the World Health Organization's Essential Drug List, 2017 and a clinical pharmacist from the acute psychiatric hospital (study samples source). Different dosage forms and dosages of the same drug can be regarded as a single drug (Example: ziprasidone 20mg cap, ziprasidone 40mg cap, ziprasidone 40mg cap, and ziprasidone 20mg vial are considered as four drug items).

2.3.3 ABC-VEN Matrix Analysis

The results of ABC-VEN matrix analysis are displayed in Table 2.4. Nine different subcategories were further grouped into three main categories: I, II, and III. There were 12,705 (45.90%) drug units in category I, 13,603 (49.15%) drug units in category II, and 1,370 drug units in category III. This, in turn, accounted for 86.06% ($59,996.27), 13.43% ($9,361.72), and 0.51% ($353.61), respectively of four-month inpatient drugs expenditures.

Table 2.4

ABC-VEN Matrix Analysis

Matrix Classification	Total Units	% Of Units	4-Month Drug Expenditures (US$)	% of 4-Month Drug Expenditures
Category I: AV, AE, AN, BV and CV	12,705	45.90	59,996.27	86.06
Category II: BE, CE and BN	13,603	49.15	9,361.72	13.43
Category III: CN	1,370	4.95	353.61	0.51
Total	27,678	100.00	69,711.60	100.00

Thus far, ABC and VEN matrix analyses have been rarely applied to the study of drug formulary management in psychiatric hospitals. According to literature reviews, other studies, which examined similar cases that were not limited to psychiatric hospitals showed a variety of results in the drug use and cost percentages of vital, essential, and non-essential items, as well as percentage of A, B and C items, as depicted in Table 2.5.

Table 2.5

Comparison of ABC, VEN, and ABC-VEN Matrix Study Results

Hospital Type	***Acute Psychiatric Hospital (2019) Current study***		***Private Hospital (2018)****[130]*, ***India***		***Government Medical College (2017), India*** *[131]*		***Tertiary Care hospital (2015)*** *[119]*, ***India***		***Neuropsychiatry Hospital (2013)****[132]*, ***India***	
Category	% of drugs	% of 4 months drug expenditure	% of drugs	% of Annual drug expenditure	% of drugs	% of Annual drug expenditure	% of drugs	% of Annual drug expenditure	% of drugs	% of Annual drug expenditure
A	2.11	71.97	5.05	70.08	16.8	70	6.77	70.03	3.45	70.50
B	19.65	18.46	10.11	19.88	21.8	20.1	19.27	19.98	6.9	19.68
C	78.24	9.57	84.84	10.04	61.4	9.9	73.59	9.98	89.65	9.83
V	45.54	40.59	29.12	44.42	35.3	34.3	13.14	19.00	32.41	70.90
E	49.43	53.08	51.32	47.06	50.4	49.5	56.37	68.00	61.38	28.72
N	5.03	6.32	19.56	8.52	14.3	16.2	30.49	13.00	6.2	0.38
I	45.90	86.06	32.75	82.55	47.9	82.3	21.00	69.45	33.80	92.33
II	49.15	13.43	49.01	15.66	43.7	16.5	51.17	24.35	60.00	7.29
III	4.95	0.51	18.24	1.79	8.4	1.2	27.83	6.2	6.2	0.38

Note. Hospital data used for comparison purposes focused on annual drug use and expenditures in hospital pharmacies. This included both inpatient and outpatient drug prescriptions. Findings of our study were from the four-month actual inpatient drug use and cost in the acute psychiatric hospital.

According to the ABC analysis, the percentage of category A in our study is similar to the findings of the Neuropsychiatry Hospital [132]. However, a significant difference was found in the percentage of drugs in Category B, which showed a similar percentage of drug expenditure. Our study also revealed that if we only take VEN analysis into consideration, the vital and/or essential drug items can be successfully controlled which accounted for 93.67% of 4-month inpatient drug expenditures [119, 130-132]. These diverse results might be attributed to the differing hospital types and medical specialties at each facility. Only one study which applied ABC, VEN, and ABC-VEN matrix analysis conducted in a Delhi-based neuropsychiatry hospital showed that the vital and essential items accounted for 99.62% (93.79% of drugs) of annual drug expenditures of the hospital medical store, while 6.2% (non-essential drugs) accounted for only 0.38% of annual drug expenditures. These results included both inpatient and outpatient drug costs [132].

In contrast, the results of our study showed that 5.03% of drugs (non-essential drugs) consumed 6.32% of 4-month inpatient drug cost. Due to the relatively high cost percentage in non-essential drugs as compared to the results from similar hospital types, this finding provided a partial explanation of keeping drugs listed in the N category under A and B groups for further drug monitoring selection.

2.3.4 Drug Monitoring Selection

In this study, all nine subgroups (Table 2.6) were kept in order to generate the drug list. Notably, this drug list needs strict control, with the exception of the subgroup CV, CE, and CN. Based on the findings of previous ABC-VEN matrix analyses conducted under the environment of general hospitals (non-specialized), the drugs in Category I (AV, AE, AN, BV, and CV as shown in Table 2.1) can be seen to be expensive, but important for patients' treatment. Due to

these factors, Category I drugs require strict and careful monitoring [17][133]. Therefore, after conducting ABC-VEN matrix analysis, the following subcategories within Category I drugs were selected for composing the drug list that required strict drug cost control: AV, AE, AN, BV. Category II drugs (BE, CE, and BN; refer to Table 2.1) are deemed less important, considering the expenditure and patient treatment. In our study, subgroups BE and BN were kept for the further regression study, but the subgroup CE was excluded. Although the subgroup BN contains drugs of less importance in terms of patient treatment, it does contain drugs of moderate importance for expenditure. Since the guiding concept of the entire study is intended to help acute psychiatric hospitals save money on inpatient drug costs, we kept the subgroup BN in the drug list that needs strict control. In addition, 5.03% of drugs consumed 6.32% of the four-month drug cost under N category, which is sufficient enough to attract attention in order to determine specific drugs under this category that contribute to the uncommon results, especially when compared to a similar study conducted in a neuropsychiatric hospital (in N category, 6.2% of drugs consumed 0.38% of the annual drug cost). Large differences were found between drug cost percentages (see Table 2.6).

Table 2.6

ABC-VEN Nine Subgroups

Subgroups	*Total Units*	*% of Units*	*4-Month Drug Expenditures (US$)*	*% of 4-Month Drug Expenditures*	*Average Cost per Unit (US$)*
AV	484	1.75	18,468.74	26.49	385.16
AE	99	0.36	28,744.17	41.23	290.35
AN	2	0.01	2,956.04	4.24	1478.02
BV	2,921	10.55	6,404.66	9.19	2.19
BE	2,497	9.02	5,364.79	7.70	2.15
BN	21	0.08	1,099.60	1.58	52.36
CV	9,199	33.24	3,422.66	4.91	0.37
CE	11,085	40.05	2,897.33	4.16	0.26
CN	1,370	4.95	353.61	0.51	0.26
Total	27678	100.00	69,711.60	100.00	2.52

The reason for not selecting subgroup CV from Category I and CE from Category II, as the drugs that need strict control, are supported by the data. Table 2.6 depicts that CV (33.24% of total drug units over a four-month period) and CE (40.05% of the total units over the four-month period) were only accountable for 4.91% and 4.16% of the total 4-month drug cost, respectively. Even if the usage percentage of drugs in CV (33.24%) and CE (40.05%) were found to be among the top two in all subgroups, the low drug cost (73.29% of the total drug units consumed 9.07% of 4 months drug cost) was not a compelling enough reason to include these drugs for further analysis. Therefore, it can be inferred that even a large number of drugs used under the subgroups CV and CE will not have a significant impact on inpatient drug costs. In contrast, a large number of drugs used under in other subgroups in Category I (AV, AE, AN, and BV) and Category II (BE and BN) will impose a major financial burden on the hospital.

One-way ANOVA was performed to explore the cost differences among these nine subgroups. However, subgroups AN (one drug item) and BN (two drug items) could not be included due to the small sample size within each subgroup. In order to further support the reason behind not selecting subgroups CV and CE, post hoc tests (Bonferroni) were used to determine the differences between AV, AE, CV, and CE. According to the results, a statistically significant difference was found in the inpatient drug cost between the "AV-CV" group ($p<0.05$), the "AV-CE" groups ($p<0.05$), the "AE-CV" group ($p<0.05$), as well as the "AE-CE" group ($p<0.05$). However, no difference was found between the "CV-CE" group ($p=1.000$). Therefore, it can be concluded that both groups can be excluded.

The CN subgroup was excluded because it is the only subgroup under Category III that included drugs of low importance, both in terms of drug cost and patient treatment. Hence, we retained drugs under category AV, AE, AN, and BV, BE, and BN based on the specific study concept and hospital type. The 51 drugs from subgroup AV, AE, AN, and BV, BE, and BN were selected in order to enter the medications under control (MUC) list, as shown in Table 2.7.

Table 2.7

M*edications Under Control (MUC) List*

	VEN	*Drug Information*	*Unit*	*Unit Cost (US$)*	*Cost (US$)*	*ABC*
1	V	aripiprazole 400mg/2ml susp	5	1935.21	9676.05	A
2	V	aripiprazole 5mg tab	353	8.13	2869.89	A
3	V	fluticasone 110mcg inh	9	205.57	1850.13	A
4	V	lurasidone 20mg tab	46	34.10	1568.60	A
5	V	fluticasone-vilanterol 100-25mcg inh	14	101.79	1425.06	A
6	V	olanzapine 10mg tab	57	18.93	1079.01	A
	Total		484		18468.74	
7	E	insulin lispro 100 units/1ml 3ml syr	32	490.61	15699.52	A
8	E	insulin glargine 100units/ml 100units/1ml 3ml syr	28	320.12	8963.36	A
9	E	tuberculin, purified protein derivative	35	67.67	2368.45	A
10	E	risperidone 25mg syr	4	428.21	1712.84	A
	Total		99		28744.17	
11	N	paliperidone 156mg 1.5ml syr	2	1478.02	2956.04	A
	Total		2		2956.04	
12	V	lurasidone 40mg tab	16	33.49	535.84	B
13	V	apixaban 5mg tab	83	5.80	481.40	B
14	V	umeclidinium 62.5mcg inh	10	47.93	479.30	B
15	V	albuterol 90mcg inh	25	18.94	473.50	B
16	V	lurasidone 80mg tab	14	33.49	468.86	B
17	V	quetiapine XR 50mg tab	56	7.49	419.44	B
18	V	quetiapine 100mg tab	1461	0.25	365.25	B
19	V	fluticasone 220mcg inh	1	317.02	317.02	B
20	V	quetiapine XR 200mg tab	23	13.36	307.28	B
21	V	desvenlafaxine 50mg tab	29	10.51	304.79	B
22	V	divalproex ER (24hr) 500mg tab	141	2.16	304.56	B
23	V	duloxetine 30mg cap	157	1.56	244.92	B
24	V	rivaroxaban 20mg tab	23	9.48	218.04	B
25	V	pregabalin 75mg cap	31	7.02	217.62	B
26	V	asenapine 5mg tab	12	17.30	207.60	B
27	V	linagliptin 5mg tab	19	10.64	202.16	B
28	V	sitagliptin 25mg tab	16	12.57	201.12	B

(Table 2.7 Continued)

29	V	ziprasidone 20mg vial	45	4.18	188.10	B
30	V	divalproex ER (24hr) 250mg tab	112	1.46	163.52	B
31	V	benztropine mesylate 1mg tab	626	0.25	156.50	B
32	V	pregabalin 50mg cap	21	7.04	147.84	B
	Total		2921		6404.66	
33	E	chlorpromazine 50mg tab	116	8.16	946.56	B
34	E	neomycin/polymyxin b/hydrocort	14	66.76	934.64	B
35	E	nicotine transdermal 21 mg patch	449	1.41	633.09	B
36	E	mag/alum hydrox simethicone 30ml liq	227	1.90	431.30	B
37	E	oxycodone ER 20mg tab	59	6.33	373.47	B
38	E	haloperidol decanoate 100mg/1ml 1ml	6	37.51	225.06	B
39	E	ketoconazole 2% topical cream	11	20.32	223.52	B
40	E	nicotine transdermal 14 mg patch	141	1.53	215.73	B
41	E	risperidone 2mg tab	601	0.31	186.31	B
42	E	bimatoprost 0.01% ophthalmic solution	1	163.31	163.31	B
43	E	chlorpromazine 25mg/1ml 2ml	6	26.71	160.26	B
44	E	clozapine 100mg tab	168	0.94	157.92	B
45	E	lorazepam 2mg/1ml 1ml	96	1.53	146.88	B
46	E	risperidone 1mg tab	544	0.27	146.88	B
47	E	fluphenazine 2.5mg tab	54	2.64	142.56	B
48	E	gatifloxacin zymaxid 0.5% ophthalmic solution	3	46.31	138.93	B
49	E	insulin NPH 30 unit 0.3ml	1	138.37	138.37	B
	Total		2497		5364.79	
50	N	dalfampridine ER 10mg tab	20	36.02	720.40	B
51	N	rifaximin 550mg tab	1	379.20	379.20	B
	Total		21		1099.60	

Note. The tuberculin skin test involves monitoring the immune reaction to an injection of Purified Protein Derivative (PPD) insulin NPH 30 unit 0.3ml [134]. NPH stands for neutral protamine Hagedorn. NPH insulin starts lowering blood glucose within 1 to 2 hours after injection. Its strongest effect is felt 6 to 10 hours after injection but keeps working about 10 hours after injection. It is also referred to as N insulin.
Abbreviation: cap, capsule; tab, tablet; susp, suspension; inh, inhaler; syr, syringe; liq, liquid;

In the present study, 51 drug items (14.01% of the 364 total drug items) consumed 90.43% of the four-month drug cost. ABC-VED matrix analysis allowed the application of

stringent managerial control measures to all the 51 drug items under the following categories: AV, AE, AN, and BV, BE, and BN, all of which are expensive and vital/essential, or expensive and non-essential subgroups. Traditionally, drugs in the Category I (AV, AE, AN, BV, and CV) among ABC-VEN matrix studies are always kept for cost control. However, CV was excluded from further study due to its low-cost percentage (on the basis of high use percentage). This study is unique in that subgroups BE and BN were kept under Category II (BE, BN, and CN) for future analysis. Additionally, CN was also excluded from the study due to its low cost percentage. Meanwhile BN was retained. due to its extremely low percentage of drug use and relatively high average cost per unit ($52.36 - see Table 2.6). As compared to the average cost per unit of CV ($0.37), CE ($0.26), and CN ($0.26), we have a more compelling reason to retain BN. If the same proportion of drug use is increased in BN, CV, and CE, the drug cost growth of the subgroup BN will be much larger than that of the subgroups CV and CE owing to its higher average unit cost. The importance of the MUC list lies in the fact that the secondary diagnosis groups (DRGs) will be generated by the assistance of 51 medications.

2.4 Limitation

The empirical results reported herein should be considered in light of some limitations, which could be addressed in future research. First, this study focused only on four-month drug expenditure data while other similar studies usually collect data of annual drug costs. Second, this study did not utilize the annual drug storage data to generate ABC, VEN, and ABC-VEN analysis results. Instead, it used actual inpatient drug consumption data to perform the same analysis. The resulting comparison is depicted in Table 2.5. The difference between our study and the one conducted in another neuropsychiatric hospital might be attributed to the different

time span of data (4 months vs. 12 months) different data resources (actual inpatient drug usage and cost data vs. annual drug storage data), or different hospital and patient types (inpatient drug costs in the acute psychiatric hospital vs. inpatient and outpatient drug cost in either psychiatric hospitals or general hospitals).

2.5 Conclusion

The application of scientific inventory management tools is necessary for optimizing the management of pharmacy budgets in acute psychiatric hospitals. It is imperative that the purchasing and supervision of drug items be done based on the importance in terms of treatment and cost. ABC-VEN matrix analysis can be applied in psychiatric hospitals to select the drugs that require strict management control for efficient utilization of hospital funds and resources

Based on the results of this study, stringent drug cost control applied to acute psychiatric hospital drugs under subgroups AV, AE, AN, and BV, BE, and BN may be beneficial. It is important to note that drugs under AV, AE, BV, and BE are either vital or essential, and are generally kept in the inventory. In light of the high cost of drugs under AV, AE, and AN, strict control should be exercised on the prescription and utilization patterns of these medications. In addition, dedicated efforts are needed for medications under subgroup AN, BN, which make up a significant part of the pharmacy budget in the acute psychiatric hospital, such as looking for better pricing structure, identifying therapeutic alternatives, and allowing patients to bring their home medications for use during the admission. However, it must also be considered that such attempts must not compromise the quality of health care services. Drugs under subgroups CV and CE should receive lower or moderate controls considering their low percentage on inpatient drug cost.

This study applied the concept of pharmacy formulary management tool, ABC analysis, VEN analysis, as well as ABC-VEN matrix analysis to select 51 drugs requiring strict control on the basis of cost and clinical criticality. In addition, this study can be deemed as a fundamental research that details underlying factors for the regression analysis on high drug cost, which is discussed in Chapter 3.

CHAPTER 3: LEADING DRIVERS STUDY

3.1 Introduction and Motivation

With an increased emphasis on value-based care, healthcare organizations are increasingly striving to provide consistent, high quality, and safe medical services, while appropriately reducing costs in healthcare. However, the United States spent approximately 18% of its gross domestic product on health care, and the cost of hospital care amounted to 33% of the overall cost in 2017 [135]. With reduced reimbursements for hospital inpatient care by private health insurance, Medicare, and Medicaid [136], unnecessary practices must be identified and minimized [137, 138].

Under the current U.S. healthcare model, Medicare payments are made based on a predetermined, fixed amount. This means, hospitals are reimbursed using a Prospective Payment System (PPS). The cost of a particular service is derived from service-related classification systems, such as diagnosis-related groups (DRGs) for inpatient hospital services [58]. In particular, the Center for Medicare and Medicaid Services (CMS) uses separate PPSs for reimbursement in acute inpatient hospitals, such as Inpatient Psychiatric Facility PPS (IPF PPS) [139]. Meanwhile the IPF PPS provides patient-level reimbursement adjustments on the basis of patient age, medical severity diagnosis-related groups (MS-DRGs), and selected comorbidity categories. Every hospital has a unique payment rate per individual. This rate can also be referred to as the “base payment rate”. Each DRG is assigned a relative weight (RW) according to the average recourses consumed by each hospital to care for the patient assigned to each DRG. In order to be profitable under this model, hospitals need to provide treatment for illnesses that requires less spending than the DRG-based reimbursement they receive. Otherwise, hospitals are

held responsible for any costs that exceed the reimbursement amount. Therefore, hospitals are developing processes to help the scenarios where cost exceeds reimbursement. Under such a circumstance, the current study was aimed to help assess this issue from the perspective of medication costs in an inpatient setting of acute psychiatric hospitals.

Inpatient mental health treatment is aimed at helping people who require stabilizing mental and behavioral symptoms. Many patients with mental disorders, including but not limited to schizophrenia, bipolar disorder, major depression, schizoaffective disorder, and post-traumatic stress disorder (PTSD) experience flare ups. When serious mental illness occurs (also known as acute mental illness), inpatient hospitalization may be needed [140]. While medication usage and cost pattern data in acute psychiatric hospital settings have rarely been reported, a large number of studies on inpatient medication costs in other settings have been undertaken in the past decade [4, 21, 141-144].

In an inpatient setting, pharmacy expenditures comprise approximately 20% of the total operating budget and are commonly considered as the top area to prioritize potential savings [145]. Unlike other countries, the United States does not regulate medication prices; pharmacy benefit managers (PMBs) use their negotiating power to secure better price and discounts from pharmaceutical companies. However, it does not necessarily lower the price for patients or the inpatient pharmacy. This may be the result of the complicated market structures combined with the decreasing competition among PMBs [146]. For instance, the number of PBMs reduced from 60 to 30 from 2003 to 2016 [147, 148]. Even though many findings suggest the desire for a more concerted effort to reduce medication prices and administrative costs, policy constraints only provide short-term curtailment [135]. Our study proposed that ascertaining the leading

drivers of increasing inpatient medication cost in psychiatric hospitals can be a pivotal component of cost control management in psychiatric hospital pharmacies.

In the Chapter 2, the medication cost management study demonstrated how medication cost management can be applied in acute psychiatric hospital settings. Following a systematic ABC-VEN matrix analysis, 51 medication items, also known as medications under control (MUC) were selected and added to a list of medications that need strict control.

This study informed the search for effective cost management strategies and predictions for medication budget within the acute psychiatric hospital setting in a novel manner. The goal of this study was to identify a relationship between potential factors including patient demographics, diagnosis , length of stay (LOS), MUC, insurance type and increasing inpatient medication costs (dependent variable) in an acute psychiatric hospital. The potential factor, diagnosis, which contains principal diagnosis (ICD-10-CM codes) and secondary diagnosis (secondary major diagnostic categories, SMDC) were included in the regression model. A regression model was used to identify the relationship between diagnosis categories and cost while controlling for other factors.

The factors used in the cost regression model are displayed below. In addition, LOS can be considered as a proxy for hospital medication cost per patient through the application of "count outcome" regression modeling, a method that has been rarely used in psychiatric hospital pharmacy setting.

Cost regression model:

Cost = f (patient demographics, diagnosis category, LOS, MUC,
insurance type, and month admitted)

3.2 Literature Justification of Selecting Factors in Regression Model

3.2.1 The Demographic Factor-Age/Gender-MBD

National Institute of Mental Health (NIMH) data showed that out of 44.7 million adults with any mental illness (AMI), 19.2 million (43.1%) received mental health treatment. The National Survey on Drug Use and Health (NSDUH) defines mental health treatment as having received inpatient treatment/counseling or outpatient treatment/counseling, or having used prescription medications for problems with emotions, nerves, or mental health. Older adults are not in a better mental health than younger adults [149]. The percentage of adults with AMI aged 50 and older (71.5%) is among the highest age group as compared to 18-25 years young adults (51.5%) and 26-49 years adults (66.1%) [150]. The definition of AMI excluded patients with a developemtal or substance use disorder. Notably, 67% of adults with major depression received mental health treatment. Among these, 80.9% are 50 years of age and older. This is followed by individuals who are 26-49 years of age (67.4%) and 18-25 years of age (46.8%). With the increasing age, the elderly continue to accept the challenges associated with additional health problems beyond their mental health. It is important to note that untreated mental health problems are linked to poor physical health outcomes. This includes an increase in disability and chronic disease, as well as lower quality of life. The elderly may be prone to anxiety, depression, or using alcohol or medications to manage their mood [151]. In addition, gender differences have been reported [152]. In the United States, mental illness was more prevalent among women (21.2 %) in comparison to men (14.3 %). Women were also 50-70% more likely to be diagnosed with major depression (43.2 vs. 27.2 %, $p < 0.001$) or anxiety disorders (41.8 vs. 24.4 %, $p < 0.001$) [153]. In this study, we examined whether age and gender differences in mental patients have an impact on their inpatient medication costs.

3.2.2 Mental Illnesses - Other Chronic Illnesses

3.2.2.1 Depression. According to the World Health Survey (WHS), as compared to patients only diagnosed with either depression or chronic disease, a comorbid diagnosis involving depression and chronic disease affects patient health incrementally [154]. This study enables one to observe whether patients with comorbidities generate higher inpatient medication costs in acute psychiatric hospitals.

People with chronic diseases, specially chronic conditions that are not a mental-health diagnosis, are known to have a higher risk of depression [39, 155]. A common explanation for this is that the chronic conditions trigger anxiety and stress that can also generate symptoms of depression [156]. Common chronic illnesses among people with depression include cancer, coronary heart disease, diabetes, rheumatoid arthritis, epilepsy, multiple sclerosis, stroke, Alzheimer's disease, human immunodeficiency virus, acquired immunodeficiency syndrome (HIV/AIDS), Parkinson's disease, and Systemic lupus erythematosus, and others. Studies have demonstrated that people with depression and other diseases tend to exhibit more severe symptoms of both diseases. Historically, individuals with both a chronic medical condition and depression have faced higher medical expenses than those that did not suffer from depression [157].

Beyond patients with other chronic diseases being more likely to suffer from depression, people with depression had a higher likelihood of developing other chronic diseases. The primary reason behind this is that many patients with depression may not seek medical services. In addition, they may experience more difficulties addressing their health, such as seeking appropriate medical care and adhering to prescription medications [158]. As an example of the challenges for adherence, antidepressants are commonly used to treat depression and usually take

two to four weeks to work, which can negatively impact adherence. Several different antidepressant medications may need to be prescribed before finding one that improves the symptoms and has manageable side effects [159][146]. In this scenario, the cost of medications for depression treatment are increased.

3.2.2.2 Other mental illnesses. Inpatient medication cost for patients with schizophrenia has historically been expensive. Schizophrenia is not as common as other mental illnesses, but the symptoms of this ailment can be very disabling. Interactions between genes and aspects of an individual's growth environment contribute to the development of schizophrenia, but there is no evidence to suggest that chronic disease can trigger the symptoms of schizophrenia [160]. Since the causes of schizophrenia are still being investigated, treatments mainly focus on eliminating the symptoms [161]. Antipsychotic medications are usually taken orally, and some antipsychotics are injected once or twice per month, or in some instances every 6 to 8 weeks. For example, risperidone injection 25mg is generally given once every two weeks. Patients may also need to take risperidone by mouth in tablet or liquid form during the first three weeks of injections. The cost of risperidone injection 25mg is $428.21 per injection or nearly one thousand dollars per month, which excludes the cost of oral antipsychotic medications used by patients during this treatment period. Expensive medications such as the long-acting injectable antipsychotics may not make up a high percentage of medications used, but the cost of them can be very significant.

Unlike Schizophrenia , bipolar disorder, also known as manic-depressive illness, is one of the most common mental illnesses. This disorder causes unusual changes in mood, energy, and activity level. People with bipolar disorder are also at higher risk for migraine headaches, thyroid disease, heart disease, diabetes, obesity, and several other chronic conditions. As is the

case with depression, patients often need to try several different medications before finding the ones that work best to help alleviate symptoms. Mood stabilizers, atypical antipsychotics, and antidepressants are generally given to treat bipolar disorder [162].

3.2.3 Comorbidity

Diagnosis of a physical disease has been found to have a profound impact on the mental health of an individual. The impact of chronic disease on mental health also leads to increased substance abuse rates [163]. Meanwhile, excessive alcohol use can also increase the risk of developing diabetes, particularly for women [164, 165]. The life-threatening disease cirrhosis can be caused by any substance abuse, which is particularly prevalent with abuse of alcohol, steroids, inhalant, and heroin [166]. When a patient is suffering from heart disease, the use of medications can affect the heart rate and exacerbate symptoms, resulting in a higher chance of having a heart attack or stroke [167-169]. Chronic obstructive pulmonary disease (COPD), chronic bronchitis, asthma, and emphysema are lung diseases that can be triggered or otherwise affected by substance abuse [170]. Patients with chronic diseases have a high rate of mental health issues, which has been demonstrated in a large review from the Substance Abuse and Mental Health Services Administration (SAMHSA) [171].

3.2.4 Major Diagnostic Categories (MDC)/Diagnosis Related Groups (DRGs)

MDC are formed by dividing all possible principal diagnoses from ICD-10-CM (ICD, International Classification of Diseases; CM, Coordination and Maintenance Committee) into 25 mutually-exclusive diagnosis areas [172]. The DRG codes are also mapped or grouped into MDC codes. MDC 1 to MDC 23 are grouped in accordance with the principal diagnoses. MDC 19 is assigned to Mental Diseases and Disorders. DRG codes 876 to 887 are grouped into MDC

19. In this study, hospital pharmacies can explore which specific DRGs have the highest impact on medication cost by analyzing the relationship between the medication cost and DRGs.

3.2.5 Primary Diagnosis and Principal Diagnosis

In an inpatient setting, the primary diagnosis is related to the most serious and/or resource-intensive condition. Both the primary and principal diagnoses are typically the same, but that is not always the case. According to the ICD-10-CM official guidelines for Coding and Reporting, principal diagnosis refers to the condition which causes admission into the hospital. Principal diagnosis denotes what resulted in the reason, and not necessarily the condition that brought the patient into the emergency room [173]. The inpatient report used for data collection in this study only contains the information of principal diagnosis (principal ICD-10-CM codes)

3.2.6 Secondary Diagnosis

Secondary diagnoses are comprised of conditions that coexist at the time of admission, develop subsequently, or affect the patient care during the current episode. This condition needs to involve one of the listed medical services in order to constitute a secondary diagnosis: clinical evaluation, therapeutic treatment, diagnosis studies, an extended LOS, or increased nursing care [174]. In this study, any secondary codes that yielded medication treatment were identified as a secondary diagnosis.

3.2.7 Medications Under Control (MUC)

MUC is one of the leading factors of higher medication cost and longer LOS shown by results of the ABC, VEN, and ABC-VEN matrix analysis in study 1. MUC comprises 51 medications (including 21.77% of total medication units) that accounted for nearly 91.43% of four-month inpatient medication costs.

3.2.8 Determinants of Length of Stay (LOS) for Patient with Mental Illness

LOS has been a key indicator of hospital efficiency and quality of care [175]. However, longer stays result in higher treatment costs and extra cost burdens to hospitals. From the perspective of clinical and hospital financial management, LOS has become one of the most watched indicators in all hospitals and medical systems [176-179]. Substantial studies conducted in general medical hospitals have focused on how LOS is affected by hospital for-profit status, hospitalists, physicians and nursing involvement, hospital volumes, and patient insurance status [180-184].

According to a review of regression analyses to determine the contributing factors of the determinants to LOS for adults in the United States, female gender, larger hospital sizes, and psychosis (ICD-10-CM code: F20–29), were associated with a longer LOS [185]. Another study conducted in the United Kingdom pointed out that a diagnosis of psychosis (ICD-10-CM code: F20–29) and male gender identity was associated with a longer LOS as compared to the reference groups [186].

Factors that are tentatively associated with LOS have been studied in a university-affiliated, not-for-profit psychiatric hospital. Diagnoses including schizophrenia, schizoaffective disorder, bipolar disorder, major depressive disorder, other psychoses, and other affective disorders are important predictors of LOS. The number of psychiatric conditions was also linked to longer stays. Comorbidity was weakly associated with longer stays [187]. In our study, principal and secondary diagnosis information was included in the form of ICD-10-CM codes and secondary major diagnosis categories (MDC) in the count regression model in order to evaluate the association with LOS. In addition, comorbidity was also tested in order to explore its association with LOS.

3.2.9 Insurance

Many studies have revealed a strong association between insurance type and LOS [188-190]. Patients with Medicaid or Medicare were hospitalized an average of 14 days, while those with private insurance had a median LOS of 10 days [187]. However, uninsured have rarely been compared with Medicare, Medicaid and private insurance. According to one study conducted in a community hospital concerning the psychiatric stays, publicly paid hospitalizations (Medicare and Medicaid) were found to be significantly longer than those covered by private or uninsured payers among five diagnoses: (1) schizophrenia; (2) bipolar disorder; (3) depression; (4) drug use disorder; and (5) alcohol use disorder [57].

3.2.10 Month Admitted

Mental and behavioral disorders have been considered to have seasonal variation. According to a six-year study, there were statistically significant peaks of admission in the spring and fall among patients with mental disorders. Moreover, alcoholism-related admission also showed an increase in spring [191]. Exploration of the admitted month may help ascertain the seasonal variation in an acute psychiatric hospital. Similar to variable insurance, month admitted was also added as controls in order to better isolate the relationship between clinical variables (ICD-10-CM codes, SMDC, MUC) and LOS.

3.3 Data and Empirical Methods

400 consecutive, adult patients admitted with a mental health condition as their primary diagnosis that were then hospitalized in a 35-bed, licensed, not-for-profit acute psychiatric hospital between March 16th and July 27th were enrolled in this study. Patients' data were collected from the patient report entitled Coding and Summary in the electronic record.

Descriptive statistics can be found in Table 3.1. There were fewer patients in the age group 76 years old and over than other age groups. However, there was no statistically significant differences between medication costs among different age groups. There were slightly more male patients (51.73%) than female patients (48.27%), but not a statistically significant difference in their medication cost. In addition, no significant difference existed in cost among different insurance groups. Medicare beneficiaries represented 60% of the sample but only 18.21% of the sample is over 65 years of age (66-75, 15.03%; 76 and over, 3.18%). This suggests a large fraction that qualifies for Medicare based on disability rather than age. In addition, Medicaid beneficiaries could not be identified in the sample due to the unavailability of specific insurance information shown in the report of Coding and Summary. For length of stay. we found that 78.32% of patient stayed in the hospital less than seven days.

During the data collection period, six patients did not take any medication during the hospitalization, and data of three patients were not available due to a software issue (MUC list was generated from 391 patients in Chapter 2, see Table 2.1). Because a primary goal of this analysis was to determine if SMDC was associated with higher inpatient medication costs, 45 patients without a secondary diagnosis were excluded from the analysis. Therefore, regression results reported below are based on a sample of 346 patients.

Patients' private information, including demographic and clinical data involved in this study were all de-identified and no intervention was given to the patients for any research purpose, therefore this study was exempt from Institutional Review Board (IRB) review of the University of the Pacific. Data collected from the patient report of Coding and Summary included the following: age, gender, principal and secondary diagnosis code (ICD-10-CM code), comorbidity, LOS, patient admission and discharge date, and insurance type.

Using SMDC as a potential factor allowed observation of which specific Secondary major diagnoses contributed to higher inpatient medication costs. Adding comorbidity status helped to identify which type of comorbidity resulted in a higher inpatient medication cost. In this study, comorbidity status was determined using the principal diagnosis code and secondary diagnosis code. The category of comorbidity was developed based on the structure of "principal diagnosis + secondary diagnosis". Six subgroups were listed: (1) no comorbidity; (2) Psych (psycho diagnosis) + Med (medical diagnosis); (3) Psych (psycho diagnosis) + Psych (psycho diagnosis); (4) Psych (psycho diagnosis) + SUD (substance use disorder diagnosis); (5) SUD (substance use disorder diagnosis) + Med (medical diagnosis); and (6) SUD (substance use disorder diagnosis) + SUD (substance use disorder diagnosis). Table 3.1 showed that the portion of Psycho + Med is much more than the portion of other comorbidity groups. Comorbidity, as a potential factor, may enable one to see if the six combinations of diagnosis structure yield the statistically different results for inpatient medication costs. Thus, comorbidity was used to examine the extent of impact on inpatient medication costs.

MUC, as defined and discussed in Chapter 2, is hypothesized to be a significant factor as discussed in Chapter 2. Accordingly, MUC contains 51 medications (including 21.77% of total medication units) that accounted for nearly 91.43% of four months of inpatient medication costs. These 51 medications were a significant factor in the finalization of the secondary ICD-10-CM code for each patient.

The descriptive statistics in Table 3.1 showed patients who took medications under MUC had a statistically significant higher cost than patients that did not.

Table 3.1

Descriptive Statistics for Admissions. (n=346)

Variable	*No. of Patient*	*Proportion (%)*	*Cost (US$ 65,169.76)*			
			Total (US$)	Mean (US$)	Std. Dev	p value*
Age (n=346)						0.108
18-25	47	13.58	5203.78	110.718	268.601	
26-35	49	14.16	12239.70	249.790	604.603	
36-45	63	18.21	8304.73	131.821	242.688	
46-55	48	13.87	5820.09	121.252	218.377	
56-65	76	21.97	22350.12	294.081	510.512	
66-75	52	15.03	9677.44	186.105	445.287	
76 and over	11	3.18	1573.00	143.082	172.742	
Gender (n=346)						0.301
Female	167	48.27	27489.47	164.608	357.625	
Male	179	51.73	37680.29	210.504	456.296	
Insurance type (n=346)						0.808
Private (including Medicaid)	136	39.31	22590.72	166.108	425.159	
Medicare	206	59.54	42023.75	203.999	406.126	
Uninsured	2	0.58	81.66	40.83	3.394	
Dual eligible (Medicare and Medicaid)	2	0.58	473.63	236.815	303.766	
MUC (n=346)						<0.05
Present	261	75.43	64133.80	245.723	4459.641	
Absent	85	24.57	1035.96	12.188	23.456	
Comorbidity (n=346)						0.051
No comorbidity	11	3.18	572.10	52.009	133.956	
Psych + Med	234	67.63	55074.88	235.363	461.612	
Psych + Psych	36	10.40	3593.39	99.816	351.482	
Psych + SUD	36	10.40	1413.38	39.261	54.526	
SUD + Med	28	8.09	4514.31	161.225	295.495	
SUD + SUD	1	0.29	1.70	1.7	N/A	
Length of stay (LOS) (n=346)						<0.05
One weeks	271	78.32	37590.16	138.709	328.971	
Two weeks	49	14.16	13874.44	283.152	514.610	
Three weeks	15	4.34	4892.60	326.173	470.390	
Three weeks +	11	3.18	8812.56	801.142	889.959	

(Table 3.1 Continued)

Month Admitted (n=346)						0.226
March	1	0.29	554.89	554.890	N/A	
April	16	4.62	5365.80	335.363	588.134	
May	128	36.99	28461.24	222.353	459.715	
June	122	35.26	16699.77	136.883	294.280	
July	79	22.83	14088.06	178.330	438.631	
Principal diagnosis (ICD-10-CM code) (n=346)						0.365
F03. Unspecified dementia	1	0.29	2.43	2.430	N/A	
F10. Alcohol related disorders	26	7.51	3594.85	138.264	273.992	
F11. Opioid related disorders	6	1.73	498.34	83.057	108.907	
F12. Cannabis related disorders	2	0.58	501.17	250.585	238.005	
F15. Other stimulant related disorders	2	0.58	17.59	8.795	10.034	
F19. Other psychoactive substance related disorders	2	0.58	838.65	419.325	588.263	
F20. Schizophrenia	55	15.90	9559.46	173.808	357.286	
F22. Persistent delusional disorder	1	0.29	1.86	1.860	N/A	
F23. Acute and transient psychotic disorder	1	0.29	32.03	32.030	N/A	
F25. Schizoaffective disorders	42	12.14	16803.87	400.092	692.676	
F29. Unspecified nonorganic psychosis	19	5.49	3092.79	162.778	369.583	
F31. Bipolar affective disorder	78	22.54	11013.49	141.199	283.559	
F32. Major depression disorder, single episode	10	2.89	3276.31	327.631	616.138	
F33. Major depression disorder, recurrent	96	27.75	15495.73	161.414	391.537	
F39. Unspecified mood [affective] disorder	1	0.29	2.85	2.850	N/A	
F41. Other anxiety disorders	3	0.87	14.91	4.970	2.957	
F60. Specific personality disorders	1	0.29	423.43	423.430	N/A	

(Table 3.1 Continued)

Secondary major diagnostic Categories (n=346)						<0.05
1. Nervous System (020-103)	18	5.20	3092.69	171.816	417.240	
2. Eye (113-125)	1	0.29	1780.22	1780.220	N/A	
4. Respiratory System (163-208)	33	9.54	6328.40	191.770	198.608	
5. Circulatory System (215-316)	42	12.14	4834.91	115.117	255.749	
6. Digestive System (326-395)	9	2.60	2441.37	271.263	631.715	
7. Hepatobiliary System and Pancreas (405-446)	2	0.58	391.35	195.675	262.513	
8. Musculoskeletal System and Connective Tissue (453-566)	14	4.05	2420.30	172.879	513.639	
9. Skin, Subcutaneous Tissue and Breast (573-607)	2	0.58	57.18	28.590	4.865	
10. Endocrine, Nutritional and Metabolic System (614-645)	53	15.32	21616.65	407.861	614.248	
11. Kidney and Urinary Tract (652-700)	14	4.05	5068.67	362.048	581.201	
12. Male Reproductive System (707-730)	1	0.29	0.56	0.560	N/A	
13. Female Reproductive System (734-761)	1	0.29	1.96	1.960	N/A	
19. Mental Diseases and Disorders (876-887)	56	16.18	4660.86	83.230	289.120	
20. Alcohol/Drug Use or Induced Mental Disorders (984-897)	31	8.96	1065.11	34.358	41.441	
21. Injuries, Poison and Toxic Effect of Drugs (901-923)	1	0.29	38.07	38.070	N/A	
23. Factors Influencing Health Status and Other Contacts with Health Services (939-951)	68	19.65	11371.46	167.227	364.152	

Note. I25, B34, and O99 were excluded from the principal diagnosis. Principal diagnosis I25, Chronic ischemic heart disease, B34; Viral infection of unspecified site; and O99; other maternal diseases were classifiable elsewhere, but complicating pregnancy, childbirth and the puerperium

(Table 3.1 Continued)
were excluded in this study. The category of comorbidity was based on the "principal diagnosis + secondary diagnosis": no comorbidity, Psych + Med, Psych + Psych, Psych + SUD, SUD + Med, and SUD + SUD). This table was generated from the data collected from 346 patients. *One-way ANOVA was conducted to determine if inpatient medication cost was different under the subgroups of each variable.

During the early stages of data collection, we found that individuals had multiple secondary ICD-10-CM codes and that one individual had up to 26 secondary ICD-10-CM codes. More than 25% of patients (of 391 patients) had more than 10 secondary ICD-10-CM codes. All secondary ICD-10-CM codes were collapsed in order to capture the most expensive secondary ICD-10-CM code for each patient. Table 3.2 depicts the process of generating one secondary ICD-10-CM code for each patient. The five-code condensing process follows.

Table 3.2

Secondary ICD-10-CM Codes Condensing Process

Step	Description	Criteria
1	Deleting Code Z	Categories Z00-Z99 are provided for occasions when circumstances other than a disease, injury or external cause classifiable to categories A00-Y89 are recorded as 'diagnoses' [174].
2	Deleting Code V-Y	V00-Y99. Environmental events and circumstances as the cause of injury, and other adverse effects [15].
3	Deleting Code S-T	S00-T88. Injury, poisoning and certain other consequences of external causes [15].
4	Keeping Code under MUC	MUC-Chapter 2. 1. Reviewed each patient's medication consumption list and found out the medications listed under the MUC 2. Targeted medications that were not used for the principal ICD-10-CM codes but under MUC 3. Checked those medications' indications, and then located the most matched ICD-10-CM codes [15][192, 193]. 4. If the situation of two matched ICD-10-CM codes existed under one patient, the most expensive one was retained and recorded as the final secondary ICD-10-CM codes for the patients
5	What if no medications under MUC	The indication of the most costly medications was checked [29][193] andthe most matched ICD-10-CM code was then located [15].
	A total of 346 patients with secondary ICD-10-CM code were recorded (all retained secondary ICD-10CM-code must be related to medication treatment and contribute to medication cost).	

Note. Three patients contained code Z23, encounter for immunization. Since it may possibly yield the medication expenditure on immunization purchase in the acute psychiatric hospital, the code Z23 was retained in the first step for patients with this code.

In the process of condensing secondary ICD-10-CM codes, codes S, T, W, Y, Z as described in Table 3.2 were deleted from all 391 patients with the exception of Z23 (Z23, encountered for immunization was identified as a medication cost related code) after following steps 1 to 3. Subsequently, indications were checked by referring to the book: Applied Therapeutics: The Clinical Use of Drugs and Food and Drug Administration (FDA) drug insert (online) during step 4 and 5 [15][192, 193]. Forty-five of 391 patients were not found to have an assigned secondary ICD-10-CM codes (three patients did not have secondary ICD-10-CM codes

in the original patient coding and summary report; 42 patients' secondary ICD-10-CM codes that were not found to be related to medication treatment were excluded). Therefore, the assigned secondary ICD-10-CM codes for 346 patients was recorded. Next, secondary DRGs and secondary MDC (SMDC) for a total 346 patients were generated in Table 3.3 using the ICD-10-CM code and DRGs conversion tool [194, 195].

Table 3.3

Secondary Major Diagnostic Categories SMDC and Diagnosis Related Groups (DRGs) Mapping in this Study

SMDC No.	SMDC (DRGs Range)	Secondary DRGs (frequency)	Total Frequency
23	Factors Influencing Health Status and Other Contacts with Health Services (939-951)	951 (68)	68
19	Mental Diseases and Disorders (876-887)	880 (10), 881 (4), 882 (12), 883 (14), 884 (1), 885 (13), 886 (1), 887 (1)	56
10	Endocrine, Nutritional and Metabolic System (614-645)	638 (1), 639 (22), 641 (1), 642 (18), 645 (11)	53
05	Circulatory System (215-316)	293 (1), 303 (4), 305 (30), 310 (6), 316 (1)	42
04	Respiratory System (163-208)	192 (12), 201 (3), 203 (18)	33
20	Alcohol/Drug Use or Induced Mental Disorders (984-897)	897 (31)	31
01	Nervous System (020-103)	057 (1), 060 (1), 074 (2), 093 (9), 101 (4), 103 (1)	18
08	Musculoskeletal System and Connective Tissue (453-566)	546 (1), 547 (1), 552 (4), 554 (5), 556 (3)	14
11	Kidney and Urinary Tract (652-700)	675 (4), 690 (6), 699 (2), 700 (2)	14
06	Digestive System (326-395)	392 (9)	9
07	Hepatobiliary System and Pancreas (405-446)	434 (2)	2
09	Skin, Subcutaneous Tissue and Breast (573-607)	603 (1), 607 (1)	2
02	Eye (113-125)	125 (1)	1
12	Male Reproductive System (707-730)	726 (1)	1
13	Female Reproductive System (734-761)	759 (1)	1

(Table 3.3 Continued)

21	Injuries, Poison and Toxic Effect of Drugs (901-923)	914 (1)	1

Note. In total, 346 patients had secondary DRGs. SMDC was included in the regression analysis as a potential contributing factor of inpatient medication cost and LOS.

3.3.1 Determinants of Inpatient Medication Costs

A model explaining inpatient medication costs using information from categories of predictor variables has been justified using the information from categories of predictor variables listed in equation (1)

$$\text{cost} = f(\text{patient demographics, diagnosis category, comorbidity, LOS, MUC, insurance type, month admitted}) \quad (1)$$

In order to better explain the dependent variable inpatient medication cost, the natural log of the medication cost variable was adopted. During regression analysis, the natural logarithm of a variable is commonly used and is a convenient method of transforming a highly skewed variable into one that is more approximately normal [196]; Figure 3.1 below illustrates two histograms of inpatient medication costs. The histogram on the left illustrates a positively skewed distribution having a value of 3.3608, which implies there is a group of patients bunched at lower medication cost. Under this scenario, the cost data skewed to the right indicates the mean of cost is greater than the median of cost. The histogram on the right depicts how taking a log-transformation of the cost variable brings the widely-spread data points from the right tail towards the rest of the data. The skewness value of the right histogram is 0.2449 and the

distribution looked similar to a normal distribution. This dependent variable will distribute the drug cost more normally.

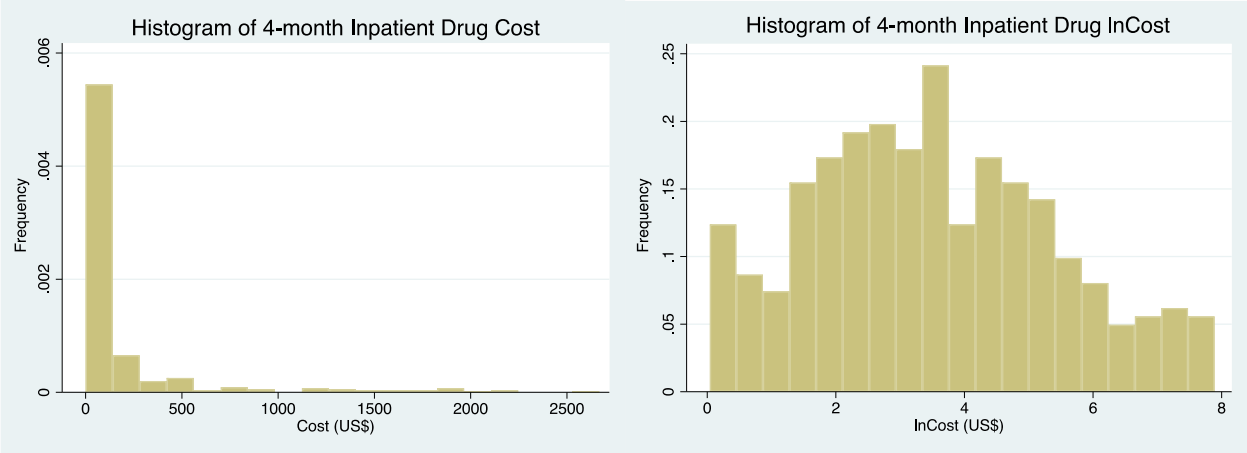

Figure 3.1 Original and natural log transformed cost histogram graph

Therefore, rather than using the actual medication cost as the outcome variable, a linear regression is hypothesized between a log transformed outcome variable and a group of predictor variables. This relationship can be shown in the equation (2)

$$\ln(y_i) = \beta_0 + \beta_1 x_{1i} + \cdots + \beta_k x_{ki} + e_i \qquad (2)$$

where y denotes the outcome variable, medication cost and $x_1, \cdots, x_k$ are the control variables coming from the categories in equation (1). It is assumed that y is log-normal condition on all covariates. The expected change in ln(y) is interpreted with respect to a one-unit increase in x_1 holding all predictor variables at any fixed value. Therefore, the inpatient medication cost is modelled by using the information from categories of predictor variables listed in equation (3) below:

$$\ln(\text{cost}) = f(\text{patient demographics, diagnosis category, comorbidity, LOS, MUC, insurance type, and month admitted}) \quad (3)$$

Table 3.4 identified, defined, and provided summary statistics for the specific variables included in the model. The table also includes the predicted sign when appropriate. Diagnosis and medication treatment attributes denote the set of four variables: comorbidity, principal ICD-10-CM code, SMDC, and MUC. Demographics contain two variables. We included the age of patient in order to capture the association between age and the propensity for higher inpatient medication expenditures. It is known that an increasing number of seniors with heart disease, diabetes, and other chronic illnesses tend to have mental illness, and may lead to more inpatient services, which is inclusive of medication treatment [197]. Demographics also contained an indicator of the gender of patients, as evidence has been given to support the correlation between this factor and the incidence of mental illness [150]. Insurance type was indicated as private, Medicare, uninsured, or dual-eligible (Medicare and Medicaid). Months admitted indicated March, April, May, June, and July.

Table 3.4

Variable Definition and Summary Statistics for Regression (n = 346)

Variable	*Definition*	*Mean [S.D.]*	*Expected Sign*
Outcome variables			
Cost	Total cost of four months inpatient medication in the acute psychiatric hospital (US $)	188.352 [411.689]	
lnCost	Log transformed of total four months inpatient medication cost in the acute psychiatric hospital	3.665 [1.822]	
LOS	Length of stay in acute psychiatric hospital	6.185 [6.399]	
Control variables			
Age	Patient age	47.777 [16.785]	(+)
Age^2	The square of Age	2563.592 [1624.023]	?
Gender	Indicator variable = 1 if patient gender is female, 0 otherwise	0.483 [0.500]	(?)
LOS	Length of stay in acute psychiatric hospital	6.185 [6.399]	(+)
MUC (Medications under control)	Indicator variable = 1 if patient did not take the d medication s that included in the 51 medications (including 21.77% of total medication units) that consumed about 91.43% of 4 months inpatient medication costs), 0 otherwise	0.754 [0.431]	(+)
Comorbidity	Set of 5 binary variables indicating the status of comorbidity. (Psych-Med omitted*)	0.861 [0.346]	(+)
Principal diagnosis (ICD-10-CM code$_j$)	Set of 16 binary variables indicating principal diagnosis code in which the patient was assigned. (F33. Major depression disorder, recurrent omitted*)	N/A	N/A
Secondary Diagnosis (SMDC$_j$)	Set of 16 binary variables indicating secondary major diagnostic category in which the patient was assigned (Mental Diseases and Disorders omitted*)	N/A	N/A
Admission Month$_j$	Set of 4 binary variables indicating the month in which the patient was admitted (June omitted*)	N/A	N/A
Insurance$_j$	Set of 3 binary variables indicating the insurance type that patient had during the hospitalization (Private omitted*)	N/A	N/A

Note. omitted variables are also known as reference variables. The results were discussed based on the comparison between the reference variable and other variables.

LOS is a proxy for the inpatient medication cost, which has not been commonly studied in acute psychiatric hospitals. It captures, albeit imperfectly, the impact of longer hospital days on inpatient medication cost. A number of studies have justified and provided evidence for the use of LOS as a proxy for inpatient medication cost [176-179] [185] [186] [187]. Previous studies have examined the reasons why count data, like LOS, can be explained by a count outcomes regression model [198][51].

The construction of variables that were used in the count outcomes regression (Poisson regression) were the same as the variables in the multiple linear regression (medication cost as outcome variable) and follows their description. In particular, we model acute psychiatric hospitalization days in equation (4) as a Poisson-distribution since it counts the number of times an event occurs in a given period. The study of hospitalization data demonstrates the statistical reasons as to why this type of variable needs to be explained by implementing a count outcome regression model [199]. Poisson modeling has been applied to health issues. To illustrate, Poisson modeling was applied to explain the incidence of schizophrenia as well as to study the number of days ill in a given month [200, 201]. An appropriate regression model for count data often follows a Poisson distribution or one of its variants. One of the rarely met assumptions of a Poisson model is that the mean must equal the variance. When the conditional variance is found to be greater than the mean, overdispersion may occur [202-204]. An over-dispersed Poisson model produces incorrect variance estimates that are biased downwards, which is when a negative binomial (NB) model, which does not constrain the conditional variance to equal the mean, is preferred over a Poisson model [205]. Our study used both the Poisson and NB regression model.

We modelled LOS in equation (4) as Poisson-distributed given that it counts the number of events (hospital days) in an interval.

$$\text{LOS} = f(\text{patient demographics, diagnosis category, comorbidity, MUC, insurance type, and month admitted}) \quad (4)$$

Theoretically, the mean and variance of Poisson-distributed variables are equal [206]; however, Table 3.4 shows that the variance of days ($40.95 = 6.399^2$) is more than six times its mean (6.185) in our study sample. This implies a higher dispersion in the predicted number of hospital days than what has been allowed by the Poisson distribution. This indicates that the Poisson underestimates the standard errors of the estimated coefficients. The Poisson estimates the expected number of hospital days for the ith patient, $\mu_i(X)$, which is conditional upon the set of explanatory variables, X. By definition, $u_i(X) \equiv e^{\alpha+\Sigma_j \beta_j x_{ij}}$ is the mean number of hospital days for i given its value for each predictor variable x_{ij}. Notably, this definition guarantees that the mean number of hospital days is positive.

The underestimated dispersion is corrected by redefining the expected number of days as $u_i(X) \equiv e^{\alpha+\Sigma_j \beta_j x_{ij}+\varepsilon}$, which includes the error term, ε that allows for unobserved heterogeneity beyond what is captured by the set of predictors [207]. Adding ε shows that all hospital days are negative binomial-distributed, which is a generalization of the Poisson distribution.

A formal examination for overdispersion is then conducted by comparing the NB estimation with the Poisson estimation using a likelihood ratio test. This likelihood comparison is computed as $\chi^2 = 2(\ln L_{NB} - \ln L_P) = 2(-887.7870+1035.7035) = 295.833$, where L_{NB} and L_P denote the natural logs of the likelihood functions for the NB and Poisson regressions (see Table

3.5). Therefore, the null hypothesis (no overdispersion) was rejected. Accordingly, we used a NB regression to estimate equation (4) more accurately. The results of NB estimation are depicted.

Table 3.5

Comparison Between Negative Binomial Regression and Poisson Regression (Outcome Variable: Length of Stay (LOS), n = 346). Statistically Significant Estimates Are Highlighted

Variable	*Negative binomial (n=346)*			*Poisson (n=346)*	
	Length of stay (LOS)			*Length of stay (LOS)*	
	Coefficient	*I.R.R.*[b]	*Number of patients*	*Coefficient*	*I.R.R.*[b]
	Robust [S.E.][a]	*[LOS, Mean=6.185]*		*Robust [S.E.]*[a]	*[LOS, Mean=6.185]*
Comorbidity (Reference group: psych-medi, n=234)					
No comorbidity	0.3327 [0.2369]	1.3947 [2.4412]	11	0.2016 [0.2426]	1.2234 [1.3818]
Psych-Psych	**0.3780*** **[0.1911]**	**1.4594** **[2.8412]**	36	0.3144 [0.2007]	1.3695 [2.2853]
Psych-Sub	0.3850 [0.2189]	1.4696 [2.9045]	36	0.4198 [0.2446]	1.5216 [3.2262]
Sub-Medi	-0.0179 [-0.0179]	0.9822 [-0.1099]	28	0.0907 [0.1929]	1.0950 [0.5875]
Sub-Sub	-0.3344 [-0.3344]	0.7158 [-1.7580]	1	-0.2230 [0.4307]	0.8001 [-1.2363]
SMDC (Reference: 19. Mental Diseases and Disorders (876-887) (n=56)					
1. Nervous System (020-103))	**0.5383*** **[0.2220]**	**1.7130** **[4.4102]**	**18**	0.4374 [0.2329]	1.5487 [3.3935]
2. Eye (113-125)	**1.0543**** **[0.2493]**	**2.8699** **[11.5655]**	**1**	**0.9899**** **[0.2739]**	**2.6910** **[10.4587]**
4. Respiratory System (163-208)	0.1812 [0.1991]	1.1986 [1.2285]	33	0.0859 [0.2094]	1.0897 [0.5546]
5. Circulatory System (215-316)	0.3115 [0.2115]	1.3654 [2.2600]	42	0.2214 [0.2250]	1.2479 [1.5331]
6. Digestive System (326-395)	0.1557 [0.2293]	1.1685 [1.0423]	9	0.0320 [0.2411]	1.0325 [0.2012]

(Table 3.5 Continued)

7. Hepatobiliary System and Pancreas (405-446)	**-0.9162** [0.2732]**	**0.4000 [-3.7108]**	**2**	**-1.0166** [0.2938]**	**0.3618 [-3.9470]**
8. Musculoskeletal System and Connective Tissue (453-566)	0.2639 [0.2799]	1.3020 [1.8678]	14	0.1797 [0.3086]	1.1968 [1.2175]
9. Skin, Subcutaneous Tissue and Breast (573-607)	**0.4687* [0.2035]**	**1.5980 [3.6984]**	2	0.3828 [0.2177]	1.4664 [2.8845]
10. Endocrine, Nutritional and Metabolic System (614-645)	**0.5193** [0.1856]**	**1.6808 [4.2109]**	**53**	**0.4264* [0.1974]**	**1.5317 [3.2886]**
11. Kidney and Urinary Tract (652-700)	**0.5074* [0.2470]**	**1.6609 [4.0879]**	**14**	0.4066 [0.2398]	1.5017 [3.1030]
12. Male Reproductive System (707-730)	**-1.1589** [0.2499]**	**0.3138 [-4.2440]**	**1**	**-1.2940** [0.2769]**	**0.2742 [-4.4893]**
13. Female Reproductive System (734-761)	0.0449 [0.2393]	1.0459 [0.2841]	1	-0.0156 [0.2499]	0.9846 [-0.0956]
20. Alcohol/Drug Use or Induced Mental Disorders (984-897)	0.1777 [0.2222]	1.1945 [1.2028]	31	0.0705 [0.2454]	1.0731 [0.4520]
21. Injuries, Poison and Toxic Effect of Drugs (901-923)	0.2524 [0.2095]	1.2871 [1.7758]	1	0.1880 [0.2136]	1.2069 [1.2795]
23. Factors Influencing Health Status and Other Contacts with Health Services (939-951)	**0.7752** [0.2040]**	**2.1711 [7.2431]**	**68**	**0.7104** [0.2074]**	**2.0347 [6.3998]**
ICD-10-CM codes (Reference: F33. Major depression disorder, recurrent) (n=96)					
F03. Unspecified dementia	**-0.4855** [0.1692]**	**0.6154 [-2.3789]**	**1**	**-0.4275* [0.1913]**	**0.6522 [-2.1514]**

(Table 3.5 Continued)

F10. Alcohol related disorders	0.0609 [0.2014]	1.0628 [0.3884]	10	-0.0830 [0.2328]	0.9204 [-0.4925]
F11. Opioid related disorders	-0.1105 [0.2084]	0.8954 [-0.6470]	6	-0.2577 [0.2425]	0.7728 [-1.4050]
F12. Cannabis related disorders	**0.7998** [0.2725]**	**2.2250 [7.5767]**	**2**	**0.6787** [0.2431]**	**1.9713 [6.0074]**
F15. Other stimulant related disorders	-0.3862 [0.2473]	0.6797 [-1.9813]	3	-0.5056 [0.2793]	0.6032 [-2.4545]
F19. Other psychoactive substance related disorders	0.4558 [0.7743]	1.5774 [3.5712]	2	0.2007 0.8141	1.2223 [1.3748]
F20. Schizophrenia	0.2599 [0.1461]	1.2968 [1.8360]	64	0.2053 [0.1694]	1.2279 [1.4093]
F22. Persistent delusional disorder	**0.8664** [0.1817]**	**2.3783 [8.5246]**	**1**	**0.8517** [0.1899]**	**2.3436 [8.3102]**
F23. Acute and transient psychotic disorder	-0.1842 [0.1652]	0.8318 [-1.0406]	1	-0.1276 [0.1928]	0.8802 [-0.7412]
F25. Schizoaffective disorders	**0.4633** [0.1448]**	**1.5893 [3.6451]**	**47**	**0.4409** [0.1543]**	**1.5541 [3.4271]**
F29. Unspecified nonorganic psychosis	**0.3876** [0.1408]**	**1.4734 [2.9281]**	**24**	**0.3550* [0.1489]**	**1.4262 [2.6361]**
F31. Bipolar affective disorder	0.2022 [0.1236]	1.2240 [1.3857]	83	0.1813 [0.1398]	1.1988 [1.2294]
F32. Major depression disorder, single episode	-0.1250 [0.1477]	0.8825 [-0.7267]	12	-0.1425 [0.1646]	0.8672 [-0.8216]
F39. Unspecified mood [affective] disorder	0.2790 (p=0.105) [0.1720]	1.3219 [1.9907]	1	0.2134 [0.2076]	1.2379 [1.4716]
F41. Other anxiety disorders	0.3299 [0.2078]	1.3908 [2.4172]	3	0.3557 [0.2074]	1.4272 [2.6425]
F60. Specific personality disorders	**-0.3907* [0.1756]**	**0.6766 [-2.0003]**	**1**	**-0.4474* [0.1859]**	**0.6393 [-2.2309]**
MUC (Reference: absent) (n=85)	**0.2982** [0.1027]**	**1.3474 [2.1489]**	**261**	**0.3136** [0.1104]**	**1.3683 [2.2778]**

(Table 3.5 Continued)

Age	-0.0196 [0.0124]	0.9806 [-0.1200]		-0.0166 [0.0132]	0.9835 [-0.1018]
Age^2 (n=346)	**0.0003*** **[0.0001]**	**1.0003** **[0.0017]**		**0.0002** **[0.0001]**	**1.0002** **[0.0015]**
Gender (Reference: Male) (n=179)	0.0782 [0.0937]	1.0813 [0.5030]	167	0.0336 [0.1116]	1.0342 [0.2116]
Insurance (Reference: Private, n=122)					
Medicare	0.1421 [0.1041]	1.1526 [0.9441]	206	0.1512 [0.1192]	1.1632 [1.0097]
Uninsured	**0.6143*** **[0.2697]**	**1.8483** **[5.2470]**	**2**	**0.6438*** **[0.2721]**	**1.9037** **[5.5892]**
Dual	0.5380 [0.4082]	1.7125 [4.4070]	2	0.5772 [0.3957]	1.7811 [4.8311]
Month admitted (Reference: June 135) (n=122)					
March	**1.9793**** **[0.2308]**	**7.2379** **[38.5815]**	**1**	**1.9885**** **[0.2385]**	**7.3047** **[38.9949]**
April	**0.8247**** **[0.1864]**	**2.2812** **[7.9242]**	**16**	**0.8048**** **[0.1798]**	**2.2362** **[7.6459]**
May	0.1592 [0.1045]	1.1726 [1.0675]	128	0.1833 [0.1226]	1.2012 [1.2445]
July	-0.1748 (p=0.107) [0.1085]	0.8397 [-0.9917]	79	-0.2121 [0.1193]	0.8089 [-1.1819]
Constant	0.8954* [0.4032]	2.4484 [8.9585]		0.9441* [0.4308]	2.5706 [9.7140]
Log likelihood	-887.7870		*Log likelihood*		-1035.7035
p-value	<0.05		*p-value*		<0.05
Dispersion χ^2	295.833[c]		*Likelihood of ratio χ^2*		591.86[d]
Pseudo R2	0.0854			0.2222	
LR chi^2	165.79			591.86	

Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level; [a] Standard error clustered at the patient level; [b] Shows the relative impact of a unit change in the predictor; [c] Test H_0: no overdispersion; [d] Test H_0: all days of hospitalization is Poisson-distributed.

3.3.2 Statistical Analysis

Data were analyzed using the Microsoft Excel spreadsheet (Version 16.20, 2018) and Stata, 2017 (Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC). Figures were generated by Stata 15 and GraphPad Prism 8. The level of statistical significance was set at $p < 0.01$ or $p < 0.05$ for all regression analyses.

3.4 Results and Discussion

In this study, different results were obtained for the relationship between inpatient medication cost and different principal diagnosis (psychiatric diagnosis), as well as the relationship between cost and secondary diagnoses (psychiatric diagnosis and other chronic diagnoses). Demographic factors, comorbidity, insurance type, patient admission month, and 51medications (MUC) that required strict control were also included as key factors in cost regression modeling. Thus far, analysis of LOS as a proxy for medication cost to identify the contributing factors has been sparsely studied in acute psychiatric hospitals.

3.4.1 Outcome Regression

A cost-transformed multiple regression was performed in order to determine the leading factors of inpatient medication costs from gender, age, comorbidity, MUC, insurance, month admitted, LOS, ICD-10-CM diagnosis codes, as well as secondary major diagnostic categories (SMDC). Negative binomial regression was performed to examine if LOS could be used as a proxy for cost. Further results analyses are presented from Table 3.6 to Table 3.13.

Table 3.6

Regression Results – Comorbidity

Variable		*lnCost*	*Length of Stay*	
		ln-transformed regression (n=346)	*Negative binomial regression (n=346)*	
	Number of patients	*Coefficient*	*Coefficient*	*I.R.R. (Incidence Rate Ratio)*[b,1]
		Robust [S.E.][a]	*Robust [S.E.]*[a]	*Extra days*[2] *[LOS, Mean=6.185]*
Comorbidity (Reference group: Psych + Med, n=234)				
No comorbidity	11	-0.1390 [0.5473]	0.3327 [0.2369]	1.3947 [2.4412]
Psych + Psych	36	0.0938 [0.4075]	**0.3780*** **[0.1911]**	**1.4594** **[2.8412]**
Psych + SUD	36	-0.5853 [0.7223]	0.3850 [0.2189]	1.4696 [2.9045]
SUD + Med	28	**-1.0960*** **[0.4918]**	-0.0179 [-0.0179]	0.9822 [-0.1099]
SUD + SUD	1	-0.8923 [1.1779]	-0.3344 [-0.3344]	0.7158 [-1.7580]

Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level; [a] Standard error clustered at the patient level; [b] Shows the relative impact of a unit change in the predictor.

The negative coefficient for comorbidity in Table 3.6 suggests that the inclusion of SUD + Med is associated with, on average, a 110% decrease in inpatient medication costs as compared to a patient with Psych + Med (reference group), holding everything else in the model constant. No significant difference is found in inpatient medication cost between Psych + Med and Psych + Psych.

1 I.R.R is incidence rate ratio. It expresses the incident rate as the relative change in the dependent variable when patient in the specific subgroup compared to the reference group.

2 Extra days mean additional hospital days yield when patient in the specific subgroup compared to the reference group. Under variable comorbidity, the reference group is Psych + Med.

The results also show that patients whose principal and secondary diagnoses are both psychiatric disorders have on average a 45.94% longer LOS, roughly 3 extra days, compared to the patients with Psych + Med, holding everything else in the model constant. This supports the theoretical predication that the number of psychiatric conditions is associated with longer LOS. Notably, patients with psychiatric conditions may result in a longer LOS.

Table 3.7

Regression results - Principal Diagnosis

Variable		*lnCost*	*Length of Stay*	
		ln-transformed regression (n=346)	*Negative binomial regression (n=346)*	
		Coefficient	*Coefficient*	*I.R.R. (Incidence Rate Ratio)*[b]
	Number of patients	*Robust [S.E.]*[a]	*Robust [S.E.]*[a]	*Extra days [LOS, Mean=6.185]*
ICD-10-CM codes (Reference: F33. Major depression disorder, recurrent) (n=96)				
F03. Unspecified dementia	1	**-0.8047**** **[0.2519]**	**-0.4855**** **[0.1692]**	**0.6154** **[-2.3789]**
F10. Alcohol related disorders	10	**1.0022*** **[0.4965]**	0.0609 [0.2014]	1.0628 [0.3884]
F11. Opioid related disorders	6	1.2483 [0.6946]	-0.1105 [0.2084]	0.8954 [-0.6470]
F12. Cannabis related disorders	2	0.8264 [0.9537]	**0.7998**** **[0.2725]**	**2.2250** **[7.5767]**
F20. Schizophrenia	64	-0.0464 [0.2628]	**0.2599** **[0.1461]**	**1.2968** **[1.8360]**
F22. Persistent delusional disorder	1	**-1.5945**** **[0.3310]**	**0.8664**** **[0.1817]**	**2.3783** **[8.5246]**
F23. Acute and transient psychotic disorder	1	**0.8390*** **[0.3230]**	-0.1842 [0.1652]	0.8318 [-1.0406]
F25. Schizoaffective disorders	47	0.1509 [0.2818]	**0.4633**** **[0.1448]**	**1.5893** **[3.6451]**
F29. Unspecified nonorganic psychosis	24	-0.0697 [0.3136]	**0.3876**** **[0.1408]**	**1.4734** **[2.9281]**
F60. Specific personality disorders	1	**1.9560**** **[0.2883]**	**-0.3907*** **[0.1756]**	**0.6766** **[-2.0003]**

(Table 3.7 Continued)
Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level; [a] Standard error clustered at the patient level; [b] Shows the relative impact of a unit change in the predictor.

The findings from the regression shown in Table 3.7 suggest that having a principal diagnosis of alcohol related disorder (F10) is associated with, on average, a 100% increase in inpatient medication costs, holding everything else in the model constant.

We find that LOS are a 59% higher, or roughly 4 extra days in patients with schizoaffective disorders (F25). A 47% higher LOS, or about 3 extra inpatient days with unspecified nonorganic psychosis compared to a patient with major depression disorder was observed.

Although the results show statistically significant differences among unspecified dementia (F03), cannabis related disorders (F12), persistent delusional disorder (F22), and specific personality disorders (F60) when compared to the reference group, these are not practically that significant despite their statistical significance, due to the small sample size.

According to our findings, principal diagnoses schizoaffective disorder, unspecified nonorganic psychosis, and major depression disorder, recurrent are important predictors of LOS (refer to Table 3.7). This moderately supports the similar findings of prior studies conducted in hospitals [187].

Table 3.8

Regression Results - Secondary Diagnosis (Secondary Major Diagnosis Categories, SMDC)

Variable		*lnCost*	*Length of Stay*	
		ln-transformed regression (n=346)	*Negative binomial Regression (n=346)*	
	Number of patients	*Coefficient*	*Coefficient*	*I.R.R. (Incidence Rate Ratio)[b]*
		Robust [S.E.][a]	*Robust [S.E.][a]*	*Extra days [LOS, Mean=6.185]*
SMDC (Reference: 19. Mental Diseases and Disorders (876-887) (n=56)				
Nervous System (020-103))	18	0.6884 [0.5219]	**0.5383* [0.2220]**	**1.7130 [4.4102]**
Eye (113-125)	1	**3.7810** [0.4977]**	**1.0543** [0.2493]**	**2.8699 [11.5655]**
Respiratory System (163-208)	33	**1.5274** [0.4331]**	0.1812 [0.1991]	1.1986 [1.2285]
Circulatory System (215-316)	42	**0.8929* [0.4197]**	0.3115 [0.2115]	1.3654 [2.2600]
Hepatobiliary System and Pancreas (405-446)	2	**2.2310** [0.6786]**	**-0.9162** [0.2732]**	**0.4000 [-3.7108]**
Skin, Subcutaneous Tissue and Breast (573-607)	2	-0.2199 [0.4488]	**0.4687* [0.2035]**	**1.5980 [3.6984]**
Endocrine, Nutritional and Metabolic System (614-645)	53	**1.3729** [0.4292]**	**0.5193** [0.1856]**	**1.6808 [4.2109]**
Kidney and Urinary Tract (652-700)	14	**1.1498* [0.5516]**	**0.5074* [0.2470]**	**1.6609 [4.0879]**
Male Reproductive System (707-730)	1	-0.6113 [0.4798]	**-1.1589** [0.2499]**	**0.3138 [-4.2440]**
Factors Influencing Health Status and Other Contacts with Health Services (939-951)	68	0.5039 [0.4339]	**0.7752** [0.2040]**	**2.1711 [7.2431]**

Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level; [a] Standard error clustered at the patient level; [b] Shows the relative impact of a unit change in the predictor.

When considering secondary diagnoses in Table 3.8, the findings indicate that having a secondary diagnosis for the respiratory system is associated with, on average, a 153% increase in costs, holding everything else in the model constant. Having the secondary diagnosis in the

circulatory system is associated with, on average, an 89% increase in costs when everything else in the model is held constant. Also, having a secondary diagnosis in endocrine, nutritional and metabolic system, and in kidney and urinary tract is, respectively, associated with, on average, a 137% and a 115% increase in medication costs, holding everything else in the model constant.

The finding shows that LOS are 71.3% higher, or roughly 4 extra days, in patients with secondary diagnoses in the nervous system. LOS are 68.08% higher, or roughly 4 extra days, in patients with secondary diagnosis in the endocrine, nutritional and metabolic systems. LOS are 66.09% higher, or roughly 4 extra days, in patients with secondary diagnoses in the kidney and urinary tract. Also, LOS are 117% higher, or about 7 extra days, in patients with secondary diagnosis in having factors influencing health status and other contacts with health services.

In the category of SMDC, the inclusion of a secondary diagnosis of an eye condition or a hepatobiliary system and pancreas condition has been associated with, on average, a 378% and 223% increase in costs, respectively, holding others constant. It must be reiterated that there was only one patient with an eye condition, while two patients had been diagnosed with hepatobiliary system and pancreas conditions. Mathematically, they are statistically significant. From these results, we can question the practical significance of the coefficient generated from the small sample size until a larger sample size is studied. Therefore, it would be premature to draw the conclusion of significant association among these secondary diagnostic groups. The same explanation is also applicable to the variable ICD-10-CM codes (principal diagnosis): unspecified dementia (F03), persistent delusional disorder (F22), acute and transient psychotic disorder (F23), and specific personality disorders (F60), as well as to the variable month admitted in Table 3.13.

Table 3.9

Regression Results – Gender, Age, MUC, and LOS

Variable		*lnCost*	*Length of stay (LOS)*	
		ln-transformed regression (n=346)	*Negative binomial regression (n=346)*	
		Coefficient	*Coefficient*	*I.R.R. (Incidence Rate Ratio)*[b]
	Number of patients	*Robust [S.E.]*[a]	*Robust [S.E.]*[a]	*Extra days [LOS, Mean=6.185]*
Gender (Reference: Male) (n=179)	167	0.0945 [0.1671]	0.0782 [0.0937]	1.0813 [0.5030]
Age (n=346)	346	0.0393 [0.0272]	-0.0196 [0.0124]	0.9806 [-0.1200]
Age^2 (n=346)	346	-0.0004 [0.0003]	**0.0003* [0.0001]**	**1.0003 [0.0017]**
MUC (Reference: absent) (n=85)	261	**2.0058** [0.1835]**	**0.2982** [0.1027]**	**1.3474 [2.1489]**
LOS (n=346)	346	**0.0966** [0.0179]**	N/A	N/A

Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level; [a] Standard error clustered at the patient level; [b] Shows the relative impact of a unit change in the predictor.

MUC and LOS are also worth emphasizing. The results from the cost regression in Table 3.9 indicates that having medications in MUC is associated with, on average, a 201% increase in medication costs, holding everything else in the model constant. The extra hospital day is associated with 10% higher medication costs.

The results from negative binomial regression indicate that a patient taking medications in MUC have, on average, a 35% longer LOS, or roughly 2 additional hospital days, holding everything else in the model constant. This indicates that taking medications in the MUC list is associated with longer LOS compared to patients who do not take medications in MUC.

The results also show that gender is not associated with higher impatient medication costs in the acute psychiatric hospital studied. The variable Age was squared to better explore if there is a non-linear association between this variable and inpatient medication cost and LOS. The result shows that Age was not associated with inpatient medication costs but was associated with LOS.

Table 3.10 illustrates that the average LOS for the 26-35 years of age group is 5.10 days. As the patient's age increases, the average LOS decreases to 2.09 days (35-45 age group) and 2.53 days for the (46-55) year age group. This reduction reflects the change of IRR value within the age category in the regression model (Table 3.9). However, the average LOS of patients increases to 3.87 days and 3.58 days in the 56-65 and 66-75 age groups. It is notable that the average LOS increased significantly to 13 days in the age group of 76 and above. At this point, square of age (Age^2) was intruoduced into the regression model to help delineate the realtionship between Age and LOS. In Table 3.9, it is observed that Age^2 significnatlly ($p<0.05$) impact LOS.

Table 3.10

Descriptive Statstics of Patient Age

Age (n=346)	*Number of patients (n=346)*	*Total LOS*	*Average LOS*
18-25	47	110.72	2.36
26-35	49	249.79	5.10
36-45	63	131.82	2.09
46-55	48	121.25	2.53
56-65	76	294.08	3.87
66-75	52	186.10	3.58
76 and over	11	143.00	13.00

The equation (5) demonstrates that the relationship between patient's age and LOS is U-shaped (Figure 3.2). The graph was generated by GraphPad Prism 8. The graph shows that when a patient's age is 33, the LOS is the lowest at approximatley a half day. When the patient is less than or equal to 33 years of age, they have shorter length of stays. After the age of 33, the length of stay for a patient increases. It was observed that patients who were 65 years or older were likely to be admitted to a mental hospital and stay longer than other age groups in several countries [208]. A systematic review showed that while young adults (18-35 years old) do experience mental disorders frequently, they do not tend to seek help or hospitalization [209]. The result is consistent with the findings of our study.

Age and LOS equation:

$$\begin{aligned} \mathrm{Y(LOS)} &= 0.0003\mathrm{X(Age)}^2 - 0.0196\mathrm{X(Age)} + 0.8954 \\ &= 0.0003(\mathrm{X} - 32.67)^2 + 0.5754 \end{aligned} \tag{5}$$

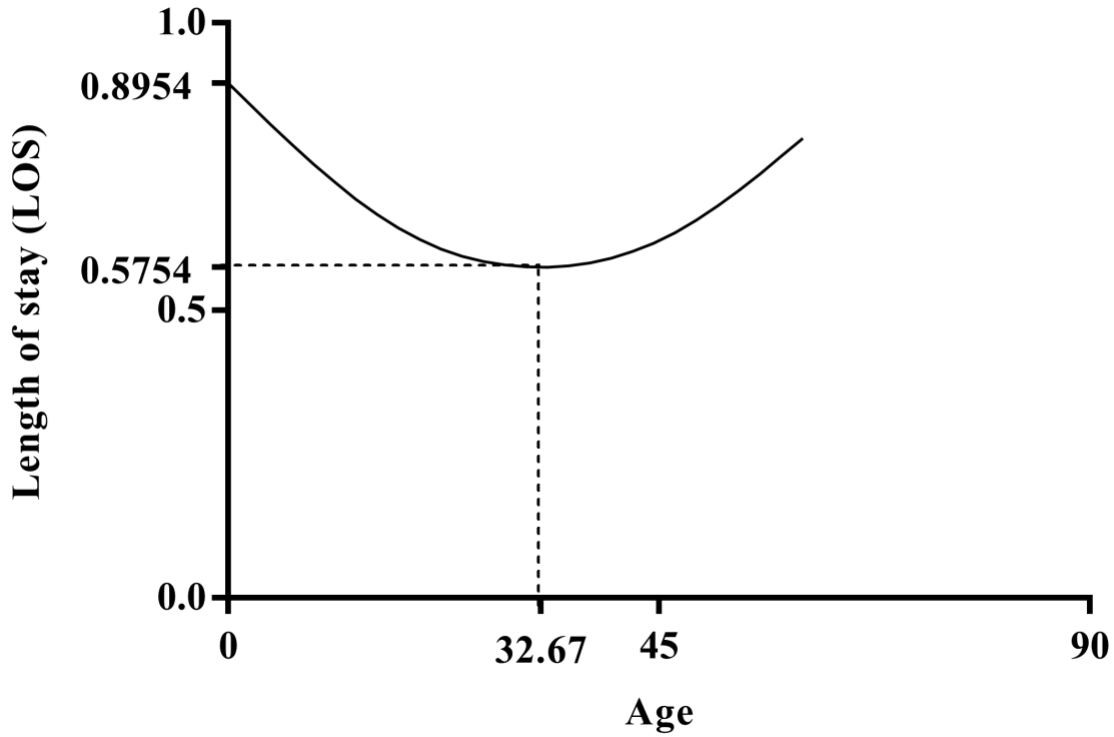

Figure 3.2 The relationship between age and LOS

Table 3.11

Regression Results – Insurance Type

Variable		*lnCost*	*Length of stay (LOS)*	
		ln-transformed regression (n=346)	*Negative binomial regression (n=346)*	
		Coefficient	*Coefficient*	*I.R.R. (Incidence Rate Ratio)*[b]
	Number of patients	*Robust [S.E.]*[a]	*Robust [S.E.]*[a]	*Extra days [LOS, Mean=6.185]*
Insurance (Reference: Private, n=136)				
Medicare	206	0.0526 [0.1897]	0.1421 [0.1041]	1.1526 [0.9441]
Uninsured	2	0.1609 [0.7689]	**0.6143* [0.2697]**	**1.8483 [5.2470]**
Dual (Medicare and Medicaid)	2	-0.1631 [0.4689]	0.5380 [0.4082]	1.7125 [4.4070]

Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level; [a] Standard error clustered at the patient level; [b] Shows the relative impact of a unit change in the predictor.

Table 3.12

Number of ICD-10-CM Codes in Private Insurance and Medicare

Insurance	*ICD-10-CM codes*					
	Number of Patients	*Number of codes*	*mean*	*Maximum*	*Minimum*	*p value*
Private	136	838	6.16	18	1	<0.05
Medicare	206	1679	8.15	26	1	
Total	342	2517				

Note. Independent T-test was run to show the significant difference between private insurance and Medicare.

Statistically significant differences were found in the number of secondary ICD-10-CM codes between priavate insurance and Medicare (refer to Table 3.12). Medicare patients have been found to have more ICD-10-CM codes than paitent with private insurance ($p<0.05$).

However, there were no statistically significant difference on both cost and LOS among patients with different insurance types: Medicare, uninsured, and Dual (Medicare and Medicaid), see Table 3.11.

Table 3.13

Regression results – Month Admitted

Variable		*lnCost*	*Length of stay (LOS)*	
		ln-transformed regression (n=346)	*Negative binomial regression (n=346)*	
		Coefficient	*Coefficient*	*I.R.R. (Incidence Rate Ratio)*[b]
	Number of patients	*Robust [S.E.]*[a]	*Robust [S.E.]*[a]	*Extra days [LOS, Mean=6.185]*
Month admitted (Reference group: June, n=122)				
March	1	**-2.6068** [1.0296]**	**1.9793** [0.2308]**	**7.2379 [38.5815]**
April	16	0.2849 [0.3993]	**0.8247** [0.1864]**	**2.2812 [7.9242]**
May	128	0.1903 [0.1885]	0.1592 [0.1045]	1.1726 [1.0675]
July	79	0.0636 [0.2003]	-0.1748 [0.1085]	0.8397 [-0.9917]

Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level; [a] Standard error clustered at the patient level; [b] Shows the relative impact of a unit change in the predictor.

In the variable of month admitted, April was associated with, on average, an 82.3% increase (7.9 extra days, $p<0.05$) in LOS, holding everything else in the model constant when compare to the month of June. This result demonstrates that month or season of the year may impact hospital stays, although the short time span studied limits generalizability to other time periods or hospitals.

In the light of the above statistical findings, we demonstrate that the presence of MUC, LOS, and comorbidity were associated with higher inpatient medication costs. In addition, we observed that the principal diagnosis code, alcohol related disorders (F10) may contribute toward explaining the fluctuation in inpatient medication costs. Moreover, patients with diseases of the respiratory system, circulatory system, endocrine, nutritional and metabolic system, as well as kidney and urinary tract may be associated with higher inpatient medication costs. Other predictors such as gender, age, insurance type, and month admitted are statistically associated with higher medication costs in the regression model.

The secondary DRGs associated with higher inpatient medication costs, in comparison to the reference group (mental disease and disorder), are shown in Table 3.14. The most expensive secondary DRGs were among four systems: respiratory, endocrine, nutritional and metabolic systems, kidney and urinary tract, and circulatory system. DRG203 (bronchitis & asthma w/o cc/mcc), DRG192 (chronic obstructive pulmonary disease w/o cc/mcc, COPD), and DRG 201 (pneumothorax without cc/mcc) are included in the respiratory system; meanwhile DRG639 (diabetes w/o cc/mcc), DRG642 (inborn and other disorders of metabolism), DRG645 (endocrine disorders w/o cc/mcc), DRG638 (Diabetes w cc), and DRG641 (nutritional & miscellaneous metabolic disorders w/o mcc) are included in endocrine, nutritional and metabolic system; on the other hand, DRG690 (Kidney & urinary tract infections w/o mcc), DRG675 (other kidney & urinary tract procedures w/o cc/mcc), DRG699 (other kidney & urinary tract diagnoses w cc), and DRG700 (other kidney and urinary tract diagnoses without cc/mcc) are included in the kidney and urinary tract; similarly, DRG305 (hypertension w/o mcc), DRG310 (cardiac arrhythmia & conduction disorders w/o cc/mcc), DRG303 (atherosclerosis w/o mcc), DRG293

(heart failure & shock w/o cc/mcc), and DRG316 (other circulatory system diagnoses w/o cc/mcc) are included in the circulatory system.

Table 3.14

The Most Expensive Secondary DRGs

Ranking	*Secondary MDC*	*Secondary DRGs*	*Frequency*
1	*Respiratory System***	203. Bronchitis & asthma w/o cc/mcc[3]	18
		192. Chronic obstructive pulmonary disease w/o cc/mcc	12
		201. Pneumothorax without cc/mcc	3
2	*Endocrine, nutritional and metabolic system***	639. Diabetes w/o cc/mcc	22
		642. Inborn and other disorders of metabolism	18
		645. Endocrine disorders w/o cc/mcc	11
		638. Diabetes w cc	1
		641. Nutritional & miscellaneous metabolic disorders w/o mcc	1
3	*Kidney and urinary tract**	690. Kidney & urinary tract infections w/o mcc	6
		675. Other kidney & urinary tract procedures w/o cc/mcc	4
		699. Other kidney & urinary tract diagnoses w cc	2
		700. Other kidney and urinary tract diagnoses without cc/mcc	2
4	*Circulatory system**	305.Hypertension w/o mcc	30
		310. Cardiac arrhythmia & conduction disorders w/o cc/mcc	6
		303.Atherosclerosis w/o mcc	4
		293. Heart failure & shock w/o cc/mcc	1
		316. Other circulatory system diagnoses w/o cc/mcc	1

[3] A complication or comorbidity (CC) or a major complication or comorbidity (MCC) when used as a secondary diagnosis

(Table 3.14 Continued)
Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level.

Table 3.15 shows that the secondary MDC (Factors Influencing Health Status and Other Contact with Health Services > Nervous System > Endocrine, Nutritional and Metabolic System > Kidney and Urinary Tract > Mental Diseases and Disorders) was also a key predictor of LOS. Meanwhile the secondary DRGs associated with longer LOS are listed in Table 3.15.

Table 3.15

The Longest LOS Secondary DRGs

Ranking	*Secondary MDC*	*Secondary DRGs*	*Frequency*
1	*Factors Influencing Health Status and Other Contact with Health Services***	951. Other factors influencing health status	68
2	*Nervous System**	093. Other disorders of nervous system w/o cc/mcc	9
		101. Seizures w/o mcc	4
		074. Cranial & peripheral nerve disorders w/o mcc	2
		125. Other disorders of the eye w/o mcc	1
		057. Degenerative nervous system disorders w/o mcc	1
		060. Multiple sclerosis & cerebellar ataxia w/o cc/mcc	1
		103. Headaches w/o mcc	1
3	*Endocrine, Nutritional and Metabolic System***	639. Diabetes w/o cc/mcc	22
		642. Inborn and other disorders of metabolism	18
		645. Endocrine disorders w/o cc/mcc	11
		638. Diabetes w cc	1
		641. Nutritional & miscellaneous metabolic disorders w/o mcc	1

(Table 3.15 Continued)

4	*Kidney and Urinary Tract**	690. Kidney & urinary tract infections w/o mcc	6
		675. Other kidney & urinary tract procedures w/o cc/mcc	4
		699. Other kidney & urinary tract diagnoses w cc	2
		700. Other kidney and urinary tract diagnoses without cc/mcc	2
10	*Mental Diseases and Disorders*	883. Disorders of personality and impulse control	14
		885. Psychoses	13
		882. Neuroses except depressive	12
		880. Acute adjustment reaction and psychosocial dysfunction	10
		881. Depressive neuroses	4
		884. Organic disturbances and mental retardation	1
		886. Organic disturbances and mental retardation	1
		887. Other mental disorder diagnoses	1

Note. * Identifies statistical significance at the 5% level; ** identifies statistical significance at the 1% level.

In most hopsitals, cost contaiment efforts have focused on interventions that reduce LOS as a way to reduce the cost of inpatient medications [210]. The results show that the leading factors are not the same between two different regression models. Patients with dieases in endocrine, nutritional and metabolic system as well as kidney and urinary tract are signifcantlly associated with both higher inpaitent medication cost and longer LOS as comapred to the reference group, mental diseases and disorders.

In addition, we found that patients who take medications in MUC are associated with both higher inpaitent medication cost and longer LOS. Our findings does not show any realtionship between insurance and cost or between insurance and LOS.

We also recognize that inpaitent medication costs in acute psychiatirc hospitals do not occur in a linear ralationship over the lenth of hospital stays. Shortened LOS may help lower inpaitent medication costs to some extent, but they will not be signiicantly impacted by eliminaing the last couple of days from a given admission due to the high number of medications taken early on in the admisson [210].

3.5 Conclusion and Limitations

This study uses patient demographic and diagnostic data, medication usage and cost data, as well as data of insurance type and admission month from a single acute psychiatric hospital in order to identify multiple relationships between the potential leading factors and inpatient medication costs. In this regard, LOS was applied as a proxy to indicate the possible leading factors.

In this study, we found several statistically significant correlations between patient diagnosis and inpatient medication cost, but there is one that is distinguished from the others. The association of MUC with inpatient medication cost is higher than any other factors. The estimates are robust across different models, including the count model (negative binomial regression) which uses LOS as a proxy for cost. However, this finding is not surprising and supports the results from the ABC-VEN matric analysis carried out in Chapter 2. Our findings also show that LOS is associated with higher inpatient medication costs.

Comorbidity appears to have an impact on higher medication cost when patients experience their first diagnosis of a psychiatric disorder and secondary diagnosis with another chronic disorder or other psychiatric disorder. In addition, patients with the secondary diagnosis in respiratory system, circulatory systems, endocrine, nutritional and metabolic system, as well as kidney and urinary tract are associated with higher inpatient medication costs than the reference group - patients with mental disease and disorders. Under principal diagnosis, patients with alcohol related disorder have higher medication cost when compared to the reference group - major depression disorder, recurrent.

When LOS is used as a proxy for inpatient medication costs, our findings demonstrate the impact of comorbidity on longer LOS. A diagnosis of psych-psych is associated with long LOS as compared to psych-medi group. Meanwhile patients with disorders in the nervous system, nutritional and metabolic systems, kidney and urinary tract as secondary diagnoses, along with factors influencing health status and other contacts with health services, are associated with longer LOS as compared to those with mental disorders. Under principal diagnosis, patient with schizoaffective disorders, unspecified nonorganic psychosis, and bipolar affective disorder are found to have a correlation with longer LOS as compared to the reference group - major depression disorder, recurrent. Furthermore, young adults (age 18-35) and the elderly (age 65 and above) are associated with longer LOS. Under the existing medical system in the United States, increasing medication costs are imposing a major financial burden on hospital budgets. Identifying the most expensive diagnoses may help with preparing for inpatient medication budget.

In this context, our study revealed that ICD-10-CM code F10 (Alcohol related disorders) were associated with higher inpatient medication costs. Meanwhile with secondary diagnosis,

DRG 203 (bronchitis & asthma w/o cc/mcc), DRG 192 (chronic obstructive pulmonary disease w/o cc/mcc, COPD), DRG 201 (pneumothorax without cc/mcc), DRG639 (diabetes w/o cc/mcc), DRG 642 (inborn and other disorders of metabolism), DRG 645 (endocrine disorders w/o cc/mcc), DRG 638 (diabetes w cc), DRG 641 (nutritional & miscellaneous metabolic disorders w/o mcc), DRG 690 (kidney & urinary tract infections w/o mcc), DRG675 (other kidney & urinary tract procedures w/o cc/mcc), DRG 699 (other kidney & urinary tract diagnoses w cc), DRG 700 (other kidney and urinary tract diagnoses without cc/mcc), DRG 305 (hypertension w/o mcc), DRG 310 (cardiac arrhythmia & conduction disorders w/o cc/mcc), DRG 303 (atherosclerosis w/o mcc), DRG 293 (heart failure & shock w/o cc/mcc), as well as DRG 316 (other circulatory system diagnoses w/o cc/mcc) are linked to higher inpatient medication costs.

Our study also found that ICD-10-CM codes F25 (schizoaffective disorders), F29 (unspecified nonorganic psychosis), F31 (bipolar affective disorder), and F33 (major depression disorder, recurrent) are the four principal diagnoses that are found to have a strong correlation with longer LOS. Moreover, DRG 951 (other factors that influence health status), DRG 639 (diabetes /o cc/mcc), DRG 690 (kidney & urinary tract infections w/o mcc), DRG 883 (disorders of personality and impulse control), DRG 305 (hypertension w/o mcc), DRG 554 (bone diseases & arteriopathies w/o mcc), DRG 203 (Bronchitis & asthma w/o cc/mcc), DRG 897 (alcohol/drug abuse or dependence w/o rehabilitation therapy w/o mcc), as well as DRG 392 (esophagitis, gastroenteritis and miscellaneous disorders w/o mcc) are the nine secondary DRGs that make a significant contribution to longer LOS.

Toward this end, our work can serve as a useful guide during the formulation of inpatient medication budgets. However, this study did have some limitations that must be addressed. First, the analysis of predictors correlating with the cost of inpatient medication and LOS was

based on data sourced from a single acute psychiatric hospital. This, in turn, raises the issue of limited generalizability, as study results may potentially incorporate local patient characteristics. Thus, the results of this study are not considered generalizable. There are also differences in the admission process and treatment plans between hospitals. Meanwhile it is important to gather and analyze data from multiple acute psychiatric hospitals. Second, the original sample size (400 patients) was relatively large in terms of the care provided. In this study, 346 patients and 2140 episodes (days of total hospitalization) crossing all main diagnosis groups were included in the regression models. However, the small sample size (one or two patients) for the specific groups under every variable was a concern. However, this issue can be addressed in future studies. Increasing the number of participating research hospitals could help resolve the issue of small sample size, thereby increasing the validity of the regression models.

Despite these limitations, this study analyzed the inpatient mediation costs and LOS based on data including all patients who had enrolled from the data collection period, as opposed to some specific patients restricted to specific diagnostic groups. Importantly, this study analyzed possible factors correlating with increasing inpatient medication costs and longer LOS. LOS may be an important contributor to increased hospital expenditures. Reduced number of inpatient days has been shown to be associated with increased hospital profits, improved treatment quality, and decreased risk of infection and medication side effects [211]. Additionally, a longer LOS may increase the possiblitiy of a hospital-acquired condition (HAC), which, in turn, may harm patients and lead to an even longer and costlier stay [212].

Viewed collectively, considering the high cost of medications in hospitals among populations with MBDs, this study aimed to make a significant contribution to the existing knowledge of cost management and inpatient medication budget in acute psychiatric hospitals.

This study would be helpful for the various relevant stakeholders, including mental and behavioral health hospitals, MBDs patients, payers (Medicare, Medicaid, insurance companies), and policymakers on identifying the leading factors of increased medication costs in acute psychiatric hospitals, as well as costs containment strategies and the future trend in medication spending in psychiatric hospital-based pharmacies.

CHAPTER 4: CONCLUSION AND INNOVATION

Prices for both commonly and infrequently used medications are spiraling up much faster than bundled reimbursements can keep pace with under the existing Medicare reimbursement system. For this reason, hospital medication expenditures are rising at a rapid pace. In addition, medication cost is threatening to inflate hospital operating budgets. Under these circumstances, it is important to control and accurately predict hospital medication budgets. Against this backdrop, the present study is the first one to examine both inpatient medication usage patterns and costs, including the medications prescribed for the treatment of mental and behavioral disorders, as well as the treatment of chronic diseases in an acute psychiatric hospital.

In medical hospitals, many studies revealed the starting point for lowering future drug spending, such as prescribing generic drugs to lower cost, reducing expenditures for an expensive drug class by consolidating to a preferred therapeutic drug, as well as reducing the unit cost of drugs via the pharmacy's drug wholesaler or group-purchasing organization (GPO) [5, 21, 213-218]. An inpatient medication report showed that average inpatient drug expenditures increased approximately 40% on a per admission basis from 2013 to 2015 [1]. However, other factors that may contribute to increased costs need to be taken into consideration. For instance, the Centers for Medicare and Medicaid Services (CMS) only update the prices paid by them every five to seven years for existing medications. Costs may rise faster than revisions are made.

With ever-increasing pharmaceutical costs and decreasing hospital drug reimbursement rates [137], pinpointing the most expensive medications and diagnoses will allow hospitals to develop an optimized budget plan that in turn may enable them to mitigate escalating hospital medication costs. This dissertation research comprises two parts: drug formulary management study (Chapter 2); and the leading drivers regression study (Chapter 3), which was conducted

based on extensive and comprehensive literature review. In chapter 2, we demonstrated that combined ABC and VEN analysis may enable policymakers in acute psychiatric hospitals to focus on the MUC (Medications under control) as one cost-control strategy. To that end, 51of the most expensive medications were explored by the modified ABC-VEN matrix analysis. Findings of this study suggest that a study of drug formulary management will help provide accurate cost-related statistics to identify and prioritize medications. A high-priority list (MUC) was developed, and this list comprised approximately 90% of four-month inpatient medication expenditures, which implies 90% of total medication expenditures for the following quarter could likely to be budgeted for.

The research conducted in chapter 3 can potentially fill the existing gap in understanding medication usage and expenses for patients with mental and behavioral disorders (MBD) in acute psychiatric hospitals. However, more importantly, it may have an impact on the reasonable development of hospital pharmacy budgets by analyzing a variety of contributing factors including patient demographics, diagnostic category, length of stay (LOS), medications under control (MUC), insurance type, as well as month admitted.

Our results indicate that patients with a principal diagnosis code F10 (alcohol related disorders) had a significant impact on the inpatient medication cost, but not LOS. F25 (schizoaffective disorders), and F29 (unspecified nonorganic psychosis) are strongly associated with longer LOS, but not inpatient medication cost. Additionally, no principal diagnosis code is associated with both longer LOS and higher inpatient medication cost. Even though there were no differences by psych diagnoses, these were high volume and thus in total a high cost class of agents. If pharmacy managers can look within that group to possibly narrow the medications included on a formulary to one focusing on medications with the best price and efficacy, then

medication costs may be reduced. Also, exploring the potential to limit the use of high-cost non-formulary agents particularly new agents that offer no known advantage over existing ones may be useful.

Secondary DRGs under the respiratory system include DRG 203 (bronchitis & asthma w/o cc/mcc), DRG 192 (chronic obstructive pulmonary disease w/o cc/mcc), DRG 201 (pneumothorax without cc/mcc); as well as under endocrine, nutritional and metabolic system include DRG 639 (it is also inclusive of diabetes w/o cc/mcc), DRG 642 (inborn and other disorders of metabolism), DRG 645 (endocrine disorders w/o cc/mcc), DRG 638 (diabetes w cc), DRG 641(nutritional & miscellaneous metabolic disorders w/o mcc), and DRG 690 (kidney and urinary tract). Meanwhile other kidney and urinary tract infections in the following DRGs: DRG 675 (other kidney & urinary tract procedures w/o cc/mcc), DRG 699 (other kidney and urinary tract diagnoses w cc), DRG 700 (other kidney and urinary tract diagnoses without cc/mcc) are the most expensive DRGs that have a significant impact on the inpatient drug cost. Among these, DRG 639 (diabetes w/o cc/mcc) and DRG 690 (kidney & urinary tract infections w/o mcc) are the two secondary DRGs that associated with higher inpatient medication cost and longer LOS. Therefore, policymakers and administrators should consider the impact of patients with these secondary DRGs being admitted when developing medication budgets. In this regard, strategies to reduce medication costs for these conditions (diabetes, kidney diseases, asthma, COPD, hypertension) include formulary review to select/consolidate the number of agents within classes (e.g. ACEIs, inhalers), leverage the policy on therapeutic substitution to preferred agents, or leverage the ability to use home medications.

Patients with comorbid psychiatric disorders (psych-psych) may lead to a longer LOS. In this study, patients admitted in April stayed in the hospital for a longer time in comparison to

July indicating that there may be seasonal variations in LOS. This would require further study to determine its importance. No LOS difference was found between patients with various insurance types. We found that the number of secondary ICD-10-CM codes varied between patients with private insurance and Medicare. However, medication costs did not differ. Patient in age groups between 18-35 and 56-75 potentially have a longer LOS as compared to other age groups. Among the many influencing factors, MUC merits the most attention. It affects both inpatient drug cost and LOS within the acute psychiatric hospital. Thus, more efforts should put to control and manage medications on this list.

Hospital pharmacy data are powerful tools that can help regulate and lower medication expenditures. In addition to drug cost, measuring all feasible healthcare data is an important method in studying the reasons for increasing medication expenditures. Rather than merely investigating drug cost per patient, focusing on drug cost per DRGs (diagnosis-related groups) allows the alignment of expense analysis by reimbursement groups. It is important to consider the LOS and other similar measures that reflect the overall drug costs [10]. For this reason, identifying drug cost saving through utilization-based data is imperative.

Using a systemic analysis of drug costs and usage patterns in an acute psychiatric hospital, one can determine whether medication costs are related more to psychiatric conditions or other medical conditions, or a combination of them. This, in turn, could be important information for administrators when negotiating contracts to care for patients if the characteristics of the patient population are known. Notably, this was a study in a unique environment (acute psychiatric hospital) where very little is known about the cost drivers of all medications prescribed in that setting. This study demonstrates the need for exploration of cost

drivers for a particular acute psychiatric hospital as a means of better forecasting medication expenditures within that setting, so as to develop a more accurate pharmacy budget.

This study entailed several innovative aspects. One of the major strengths is that we measured and examined the inpatient medication usage patterns as well as costs, including the drugs prescribed for MBDs treatment and chronic disease treatments within a mental and behavior inpatient setting. It is among the few studies to implement ABC-VEN matrix analysis to MBDs patients, specifically in a psychiatric hospital. Second, one of the strengths of this research is that we generated the secondary DRGs for admitted patients by reprogramming the ICD-10 codes. Additionally, we make use of prediction models to identify the most important factors associated with high inpatient drug cost and longer LOS.

The findings of this study will allow the executives of an acute psychiatric hospital to identify the most important factors associated with high inpatient medication costs by applying the cost prediction model. This implies that the management of hospital pharmacy budget could be improved by an approach rooted in scientific research. Future studies should be focused on patient data collected from multiple psychiatric hospitals. Overcoming the challenge of relatively a small patients sample size will help better target drivers of increasing inpatient medication cost.

REFERENCES

1. McDermott, K.W., A. Elixhauser, and R.J.S.b. Sun, Trends in hospital inpatient stays in the United States, 2005–2014. 2017. 225.
2. Duckworth, K., Mental Illness Facts and Numbers. National Alliance of Mental Illness. 2013.
3. Moore, T.J. and D.R.J.J.i.m. Mattison, Adult utilization of psychiatric drugs and differences by sex, age, and race. 2017. 177(2): p. 274-275.
4. Final report: Trends in Hospital Inpatient Drug Costs: Issues and Challenges. National Opinion Research Center at the University of Chicago. National Opinion Research Center at the University of Chicago. . 2016.
5. Keehan, S.P., et al., National health expenditure projections, 2016–25: price increases, aging push sector to 20 percent of economy. 2017. 36(3): p. 553-563.
6. Schumock, G.T., L.C.J.P.T.J.o.H.P. Vermeulen, and D. Therapy, The rising cost of prescription drugs: causes and solutions. 2017. 37(1): p. 9-11.
7. Vaughn, T., et al., Governing board, C-suite, and clinical management perceptions of quality and safety structures, processes, and priorities in US hospitals. 2014. 59(2): p. 111-128.
8. Larson, L.J.T.t.j.f.h.g.b., Getting to the "C suite". What will it take to see diversity across health care leadership? 2006. 59(3): p. 12-4, 19, 1.
9. Survey: Premier's roadmap for a healthier drug market. 2017.
10. Vieira, J., Data-Driven Change Management: Controlling Hospital Drug Costs Through Data Analysis, in Pharmacy times. 2016.
11. The overview of Mental Health Treatment. National Institution of Mental Health 2016.
12. Mayes, R., J.S.J.A.h.e. Lee, and h. policy, Medicare payment policy and the controversy over hospital cost shifting. 2004. 3(3): p. 153-159.
13. Miller, H.D.J.H.A., From volume to value: better ways to pay for health care. 2009. 28(5): p. 1418-1428.
14. Altman, S.H.J.H.A., The lessons of Medicare's prospective payment system show that the bundled payment program faces challenges. 2012. 31(9): p. 1923-1930.
15. Press, M.J., R. Rajkumar, and P.H.J.J. Conway, Medicare's new bundled payments: design, strategy, and evolution. 2016. 315(2): p. 131-132.
16. Fetter, R.B. and D.A. Brand, DRGs: Their design and development. 1991: Health Administration Pr.
17. Elixhauser, A., Most frequent diagnoses and procedures for DRGs, by insurance status. 1996: US Department Health and Human Services, Public Health Service, Agency for ….
18. Kirschenbaum, B.J.O.I., Quirks in the Reimbursement System: It's Hard to Get Paid if You Don't Know the Rules. 2010. 25(4): p. 38-46.
19. Kamarudin, G., et al., Educational interventions to improve prescribing competency: a systematic review. 2013. 3(8): p. e003291.
20. Vogenberg, F.R., J.J.A.h. Santilli, and d. benefits, Healthcare trends for 2018. 2018. 11(1): p. 48.
21. Schumock, G.T., et al., National trends in prescription drug expenditures and projections for 2017. 2017. 74(15): p. 1158-1173.

22. Ventola, C.L.J.P. and Therapeutics, The drug shortage crisis in the United States: causes, impact, and management strategies. 2011. 36(11): p. 740.
23. Stein, R., Shortages of key drugs endanger patients, in The Washington Post. 2011.
24. Fox, E.R., et al., ASHP guidelines on managing drug product shortages in hospitals and health systems. 2009. 66(15): p. 1399-1406.
25. Johnson, T.J.S.D.m.t.j.o.t.S.D.S.M.A., Drug shortages: an increasing problem for patients and clinicians. 2011. 64(1): p. 14.
26. Report on drug shortages in 2017. 2017.
27. Drug shortage statistics, 2001-2019. 2019.
28. Hoffman, S. Drug shortages pose a public health crisis in the US. 2018.
29. Kesselheim, A.S., J. Avorn, and A.J.J. Sarpatwari, The high cost of prescription drugs in the United States: origins and prospects for reform. 2016. 316(8): p. 858-871.
30. Avorn, J., The $2.6 billion pill—methodologic and policy considerations. J New England Journal of Medicine, 2015. 372(20): p. 1877-1879.
31. DiMasi, J.A., H.G. Grabowski, and R.W.J.J.o.h.e. Hansen, Innovation in the pharmaceutical industry: new estimates of R&D costs. 2016. 47: p. 20-33.
32. Carbon, M., et al., Tardive dyskinesia prevalence in the period of second-generation antipsychotic use: a meta-analysis. 2017.
33. Carroll, B., et al. Healthcare utilization and costs for patients with tardive dyskinesia. in MOVEMENT DISORDERS. 2017. WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.
34. Antos, J., J.C.J.A.P. Capretta, and Studies, Prescription Drug Pricing: An Overview of the Legal, Regulatory, and Market Environment. 2018: p. 1.
35. Gupta, R., et al., Generic Drugs in the United States: Policies to Address Pricing and Competition. 2018.
36. Stefanacci, R.G., Understanding the "American Patients First," Blueprint: Implications for Clinical Pathways. J Clin Pathways, 2018(4(5)): p. 34-36.
37. Walker, E.R., R.E. McGee, and B.G.J.J.p. Druss, Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. 2015. 72(4): p. 334-341.
38. Verhaak, P.F., et al., Chronic disease and mental disorder. 2005. 60(4): p. 789-797.
39. Scott, K.M., et al., Association of mental disorders with subsequent chronic physical conditions: world mental health surveys from 17 countries. 2016. 73(2): p. 150-158.
40. Kaiser Family Foundation analysis of data in National Survey on Drug Use and Health. 2017.
41. Olfson, M., M. King, and M.J.T.J.o.c.p. Schoenbaum, Antipsychotic treatment of adults in the United States. 2015. 76(10): p. 1346-1353.
42. Behavioral Health. 2013, Substance Abuse and Mental Health Services Administration: Rockville, MD.
43. Zito, J.M., et al., A three-country comparison of psychotropic medication prevalence in youth. 2008. 2(1): p. 26.
44. Paulose-Ram, R., et al., Trends in psychotropic medication use among US adults. 2007. 16(5): p. 560-570.
45. Cherry, D.K., E.A. Rechsteiner, and D.A. Woodwell, National ambulatory medical care survey: 2005 summary. 2006: US Department of Health and Human Services, Centers for Disease Control.

46. Middleton, K., E. Hing, and J.J.A.d. Xu, National Hospital Ambulatory Medical Care Survey: 2005 outpatient department summary. 2007(389): p. 1-34.
47. Longitudinal prescription database. IMS Life Link Information 2008.
48. Sahota, S., et al., Women admitted to medium secure care: Their admission characteristics and outcome as compared with men. 2010. 9(2): p. 110-117.
49. Nicholls, T.L., et al., Forensic psychiatric inpatients and aggression: An exploration of incidence, prevalence, severity, and interventions by gender. 2009. 32(1): p. 23-30.
50. Lart, R., et al., Women and secure psychiatric services: A literature review. 1999.
51. McLean, C.P., et al., Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. 2011. 45(8): p. 1027-1035.
52. Coid, J., et al., Women admitted to secure forensic psychiatry services: I. Comparison of women and men. 2000. 11(2): p. 275-295.
53. National Center for Health Statistics (NCHS) Data brief, No. 76. 2011.
54. Elixhauser, A., Most frequent diagnoses and procedures for DRGs, by insurance status. 1996, US Department Health and Human Services, Public Health Service, Agency for ….
55. Cascade, E.F., A.H. Kalali, and L.J.P. Citrome, Antipsychotic use varies by patient age. 2007. 4(7): p. 20.
56. Torio, C. and B. Moore, National inpatient hospital costs: the most expensive conditions by payer, 2013: statistical brief# 204. 2006.
57. Stensland, M., P.R. Watson, and K.L.J.P.S. Grazier, An examination of costs, charges, and payments for inpatient psychiatric treatment in community hospitals. 2012. 63(7): p. 666-671.
58. Stuart, H.J.C.O.i.P., Mental illness and employment discrimination. 2006. 19(5): p. 522-526.
59. Kessler, R.C., et al., Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. 2005. 62(6): p. 617-627.
60. Gerard Anderson, J.H., Chronic Conditions: Making the Case for Ongoing Care. 2002, Robert Wood Johnson Foundation.
61. Chronic disease in America, in National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP). Jan 16. 2019.
62. Dowson, C., et al., The use of the Hospital Anxiety and Depression Scale (HADS) in patients with chronic obstructive pulmonary disease: a pilot study. 2001. 114(1141): p. 447.
63. Harris, L.J., et al., Characteristics of hospital and emergency care super-utilizers with multiple chronic conditions. 2016. 50(4): p. e203-e214.
64. De Hert, M., et al., Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. 2011. 10(2): p. 138-151.
65. Alexander, G.C., et al., Increasing off-label use of antipsychotic medications in the United States, 1995–2008. 2011. 20(2): p. 177-184.
66. Hollingworth, S.A., et al., Affective and anxiety disorders: prevalence, treatment and antidepressant medication use. 2010. 44(6): p. 513-519.
67. Holt, R.I. and A.J.J.N.R.E. Mitchell, Diabetes mellitus and severe mental illness: mechanisms and clinical implications. 2015. 11(2): p. 79.
68. Mangurian, C., et al., Diabetes and cardiovascular care among people with severe mental illness: a literature review. 2016. 31(9): p. 1083-1091.

69. Taylor, V.H., et al., Beyond pharmacotherapy: understanding the links between obesity and chronic mental illness. 2012. 57(1): p. 5-12.
70. Megna, J.L., et al., Obesity in adults with serious and persistent mental illness: a review of postulated mechanisms and current interventions. 2011.
71. Cazzola, M., et al., Asthma and comorbid medical illness. 2011. 38(1): p. 42-49.
72. Oraka, E., M.E. King, and D.B.J.C. Callahan, Asthma and serious psychological distress: prevalence and risk factors among US adults, 2001-2007. 2010. 137(3): p. 609-616.
73. Fernandes, L., et al., Association of anxiety with asthma: subjective and objective outcome measures. 2010. 51(1): p. 39-46.
74. Chapman, D.P., G.S. Perry, and T.W.J.P.c.d. Strine, Peer Reviewed: The vital link between chronic disease and depressive disorders. 2005. 2(1).
75. Rasul, F., et al., Psychological distress, physical illness, and risk of coronary heart disease. 2005. 59(2): p. 140-145.
76. Kotsis, K., et al., Anxiety and depressive symptoms and illness perceptions in psoriatic arthritis and associations with physical health-related quality of life. 2012. 64(10): p. 1593-1601.
77. Geryk, L., et al., The impact of co-morbidity on health-related quality of life in rheumatoid arthritis and osteoarthritis patients. 2015. 33(3): p. 366-374.
78. Carney, R.M. and K.E.J.N.R.C. Freedland, Depression and coronary heart disease. 2017. 14(3): p. 145.
79. Linden, W., et al., Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. 2012. 141(2-3): p. 343-351.
80. Stein, D.J., et al., Associations between mental disorders and subsequent onset of hypertension. 2014. 36(2): p. 142-149.
81. Pan, Y., et al., Association between anxiety and hypertension: a systematic review and meta-analysis of epidemiological studies. 2015. 11: p. 1121.
82. Dickens, C., et al., Depression in rheumatoid arthritis: a systematic review of the literature with meta-analysis. 2002. 64(1): p. 52-60.
83. Ringen, P.A., et al., Increased mortality in schizophrenia due to cardiovascular disease–a non-systematic review of epidemiology, possible causes, and interventions. 2014. 5: p. 137.
84. Drew, N., et al., Mental health and development: targeting people with mental health conditions as a vulnerable group. 2010: World Health Organization.
85. Frank, R.G. and S.A. Glied, Better but not well: Mental health policy in the United States since 1950. 2006: JHU Press.
86. Grob, G.N., From asylum to community: Mental health policy in modern America. Vol. 1217. 2014: Princeton University Press.
87. Pamela L. Owens, P.D., Kathryn R. Fingar, Ph.D., M.P.H., Kimberly W. McDermott, Ph.D., Pradip K. Muhuri, Ph.D., and Kevin C. Heslin, Ph.D. , Inpatient stays involving mental and substance use disorders , 2016: statistical brief# 249. 2019.
88. Karg, R.S., et al., Past year mental disorders among adults in the United States: results from the 2008–2012 Mental Health Surveillance Study. 2014: p. 1-94.
89. Moore, B., K. Levit, and A. Elixhauser, Costs for hospital stays in the united states, 2012: Statistical brief# 181. 2006.
90. Roehrig, C.J.H.A., Mental disorders top the list of the most costly conditions in the United States: $201 billion. 2016. 35(6): p. 1130-1135.

91. Patel, V., et al., Addressing the burden of mental, neurological, and substance use disorders: key messages from Disease Control Priorities. 2016. 387(10028): p. 1672-1685.
92. Babalola, O., et al., Length of hospitalisation for people with severe mental illness. 2014(1).
93. Baumeister, H., et al., Inpatient and outpatient costs in patients with coronary artery disease and mental disorders: a systematic review. 2015. 9(1): p. 11.
94. Cai, X. and Y.J.P.O. Li, Are AMI patients with comorbid mental illness more likely to be admitted to hospitals with lower quality of AMI care? 2013. 8(4): p. e60258.
95. Edmondson, D., et al., Depression is associated with longer emergency department length of stay in acute coronary syndrome patients. 2012. 12(1): p. 14.
96. Versteeg, H., et al., Depression, not anxiety, is independently associated with 5-year hospitalizations and mortality in patients with ischemic heart disease. 2013. 75(6): p. 518-525.
97. Fornaro, M., et al., Predictors of hospitalization length of stay among re-admitted treatment-resistant bipolar disorder inpatients. 2018. 228: p. 118-124.
98. Dalton, K., S.J.I.p.r. Byrne, and practice, Role of the pharmacist in reducing healthcare costs: current insights. 2017. 6: p. 37.
99. HOFFMAN, J.M., L.J. KOESTERER, and R.G.J.A.J.H.-S.P. SWENDRZYNSKI, ASHP guidelines on medication cost management strategies for hospitals and health systems. 2008. 65: p. 1368-84.
100. Young, D., Hospitals take action after theft of expensive drugs. 2003, Oxford University Press.
101. Wilson, A.L., Financial management for health-system pharmacists. 2008: ASHP.
102. Nigah, R., M. Devnani, and A.J.J.o.y.p. Gupta, ABC and VED analysis of the pharmacy store of a tertiary care teaching, research and referral healthcare institute of India. 2010. 2(2): p. 201-205.
103. Sharma, S., Tools for Assessing and Monitoring Medicine Use, in Pharmaceutical Medicine and Translational Clinical Research. 2018, Elsevier. p. 445-463.
104. Antonoglou, D., C. Kastanioti, and D.J.J.o.H.M. Niakas, ABC and VED Analysis of Medical Materials of a General Military Hospital in Greece. 2017. 19(1): p. 170-179.
105. Mousnad, M.A., et al., Medicine expenditures in Sudan National Health Insurance Fund: an ABC-VEN analysis of 5-year medicine consumption. 2016. 7(3): p. 165-171.
106. Ferreri, S.P., et al., Academic Pharmacy: Where is Our Influence? 2017. 81(4): p. 63.
107. Kokane, J.V. and P.S.J.T.J.o.C.H.M. Avhad, Role of pharmacist in health care system. 2016. 3(1): p. 37-40.
108. Informatics, I.I.f.H., Medicines use and spending in the US: a review of 2015 and outlook to 2020. 2016, Institute for Healthcare Informatics Parsippany, NJ.
109. Aitken, M., et al., Medicines use and spending in the US: a review of 2016 and outlook to 2021. 2016.
110. Health, U.D.o., H.S.J.C.f. Medicare, and h.w.c.g.N.N.F.S.a.T. Medicaid Services, National health expenditure fact sheet. 2011.
111. MACINTYRE, C.R., D. SINDHUSAKE, and G.J.I.J.f.Q.i.H.C. RUBIN, Modelling strategies for reducing pharmaceutical costs in hospital. 2001. 13(1): p. 63-69.
112. Samalin, L., et al., Clinical decision-making in the treatment of schizophrenia: focus on long-acting injectable antipsychotics. 2016. 17(11): p. 1935.

113. Reichert, S., T. Simon, and E.A.J.A.o.I.M. Halm, Physicians' attitudes about prescribing and knowledge of the costs of common medications. 2000. 160(18): p. 2799-2803.
114. Tyler, L.S., et al., ASHP guidelines on the pharmacy and therapeutics committee and the formulary system. 2008. 65(13): p. 1272-1283.
115. Leonard, M.C., et al., Strategies for success in creating an effective multihospital health-system pharmacy and therapeutics committee. 2018. 75(7): p. 451-455.
116. Savelli, A., et al., Manual for the development and maintenance of hospital drug formularies. 1996.
117. Singh, S., A.K. Gupta, and M.J.J.o.y.p. Devnani, ABC and VED analysis of the pharmacy store of a tertiary care, Academic Institute of the Northern India to identify the categories of drugs needing strict management control. 2015. 7(2): p. 76.
118. Anand, T., et al., ABC-VED analysis of a drug store in the department of community medicine of a medical college in Delhi. 2013. 75(1): p. 113.
119. Kumar, S. and A.J.m.j.a.f.i. Chakravarty, ABC–VED analysis of expendable medical stores at a tertiary care hospital. 2015. 71(1): p. 24-27.
120. Carbon, M. and C.U.J.C.d. Correll, Rational use of generic psychotropic drugs. 2013. 27(5): p. 353-365.
121. Lessing, C., et al., Do users of risperidone who switch brands because of generic reference pricing fare better or worse than non-switchers? A New Zealand natural experiment. 2015. 42(6): p. 695-703.
122. FDA Approved Drugs for Psychiatry/Psychology. Therapeutic areas. CenterWatch; Available from: https://www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/17/psychiatry-psychology.
123. FDA Approved Drug. 2019; Available from: https://www.centerwatch.com/drug-information/fda-approved-drugs/.
124. Migbaru, S., et al., ABC-VEN matrix analysis of pharmaceutical inventory management in Tikur Anbessa Specialized Hospital for the years 2009 to 2013, Addis Ababa, Ethiopia. 2009. 5: p. 734-743.
125. Organization., W.H. Drug and therapeutic comittees: a practical guide (No.WHO/EDM/PAR/2014.1). 2013.
126. World Health Organization %J Geneva, S.W., The selection and use of essential medicines: report of the 21st WHO Expert Committee. 2017.
127. Kumar, N., et al., Inventory Management using Matrix Analysis and Inventory Index in an Oncology Pharmacy of a Tertiary Care Teaching Hospital. 2018. 10(1).
128. Vaz, F.S., et al., A study of drug expenditure at a tertiary care hospital: An ABC-VED analysis. 2008. 10(1): p. 119-127.
129. Alexander, K., Dosage Forms and Their Routes of Administration, in Pharmacology. 2009, Elsevier. p. 9-29.
130. Yılmaz, F., The drug inventories evaluation of healthcare facilities using ABC and VED analyzes. J Istanbul Journal of Pharmacy, 2018. 48(2): p. 43-48.
131. Pund, S.B., et al., ABC-VED matrix analysis of Government Medical College, Aurangabad drug store. 2017. 3(2): p. 469-472.
132. Khurana, S., N. Chhillar, and V.K.S.J.H. Gautam, Inventory control techniques in medical stores of a tertiary care neuropsychiatry hospital in Delhi. 2013. 5(1): p. 8.
133. Kruger, J., R. Vaidya, and E. Sokn, Pharmacy Management, in Clinical Pharmacy Education, Practice and Research. 2019, Elsevier. p. 41-58.

134. Yang, H., et al., Purified protein derivatives of tuberculin—past, present, and future. 2012. 66(3): p. 273-280.
135. Papanicolas, I., L.R. Woskie, and A.K.J.J. Jha, Health care spending in the United States and other high-income countries. 2018. 319(10): p. 1024-1039.
136. Medicare, C.f. and M. Services, National health expenditures 2017 highlights. 2018.
137. McGinnis, J.M., et al., Best care at lower cost: the path to continuously learning health care in America. 2013: National Academies Press.
138. Durvasula, R., et al., Standardized review and approval process for high-cost medication use promotes value-based care in a large academic medical system. 2018. 11(2): p. 65.
139. Inpatient Psychiatric Facility Prospective Payment Systems. 2018.
140. Croft, H. Inpatient Mental Health Treatment Facilities: Who Needs One? Healthy Place 2018; Available from: https://www.healthyplace.com/other-info/mental-illness-overview/inpatient-mental-health-treatment-facilities-who-needs-one.
141. Strunk, B.C., P.B. Ginsburg, and J.R.J.H.A. Gabel, Tracking Health Care Costs: Hospital care surpasses drugs as the key cost driver. 2001. 20(Suppl1): p. W39-W50.
142. Strunk, B.C. and P.B.J.H.A. Ginsburg, Tracking Health Care Costs: Trends Stabilize But Remain High In 2002: Hospital spending continues to drive overall health care spending trends, fueled by rising hospital price inflation. 2003. 22(Suppl1): p. W3-266-W3-274.
143. Baggs, J., et al., Estimating national trends in inpatient antibiotic use among US hospitals from 2006 to 2012. 2016. 176(11): p. 1639-1648.
144. Flannery, A.H., et al., Managing the rising costs and high drug expenditures in critical care pharmacy practice. 2017. 37(1): p. 54-64.
145. Edwards, R., In struggle to cut expenses, hospitals eye the pharmacy. Hospitals & health networks, 2011. 85(11): p. 28.
146. Bluth, R., Can Someone Tell Me What A PBM Does? 2019: Kaiser family Foundation.
147. Shepherd, J.J.-C.L.R.O., Is More Information always Better; Mandatory Disclosure Regulations in the Prescription Drug Market. 2013. 99: p. 1.
148. Feldman, B.S.J.Q., March, Big pharmacies are dismantling the industry that keeps US drug costs even sort-of under control. 2016. 16.
149. Westerhof, G.J. and C.L.J.J.o.a.d. Keyes, Mental illness and mental health: The two continua model across the lifespan. 2010. 17(2): p. 110-119.
150. Health, N.I.o.M. 2017.
151. Older adults' health and age-relted changes. Reality Versus Myth. 2017, American Psychological Association.
152. Rosenfield, S. and D. Mouzon, Gender and mental health, in Handbook of the sociology of mental health. 2013, Springer. p. 277-296.
153. Mental health. Kaiser Family Foundation analysis of data. 2015.
154. Moussavi, S., et al., Depression, chronic diseases, and decrements in health: results from the World Health Surveys. 2007. 370(9590): p. 851-858.
155. Naylor, C., et al., Long-term conditions and mental health: the cost of co-morbidities. 2012.
156. DeJean, D., et al., Patient experiences of depression and anxiety with chronic disease: a systematic review and qualitative meta-synthesis. 2013. 13(16): p. 1.
157. Egede, L.E., C.J.D.r. Ellis, and c. practice, Diabetes and depression: global perspectives. 2010. 87(3): p. 302-312.

158. Chronic Illness & Mental Health. 2018, National Institute of Mental Health. National Institutes of Health. NIH Publication No. 15-MH-8015.
159. Depression, in Nationl Institute of Mental Health. 2018, National Institute of Health.
160. Brown, A.S.J.P.i.n., The environment and susceptibility to schizophrenia. 2011. 93(1): p. 23-58.
161. Patel, K.R., et al., Schizophrenia: overview and treatment options. 2014. 39(9): p. 638.
162. Bipolar Disorder. 2018, National Institute of Mental Health. National Institute of Health.
163. Whiteford, H.A., et al., Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. 2013. 382(9904): p. 1575-1586.
164. Carlsson, S., et al., Alcohol consumption and the incidence of type 2 diabetes: a 20-year follow-up of the Finnish twin cohort study. 2003. 26(10): p. 2785-2790.
165. Lee, P., J.R. Greenfield, and L.V.J.D.C. Campbell, "Mind the gap" when managing ketoacidosis in type 1 diabetes. 2008. 31(7): p. e58-e58.
166. Rodrigue, J.R., D.W. Hanto, and M.P.J.L.t. Curry, Substance abuse treatment and its association with relapse to alcohol use after liver transplantation. 2013. 19(12): p. 1387-1395.
167. O'Connor, A.D., D.E. Rusyniak, and A.J.M.C. Bruno, Cerebrovascular and cardiovascular complications of alcohol and sympathomimetic drug abuse. 2005. 89(6): p. 1343-1358.
168. Bachs, L. and H.J.F.S.I. Mørland, Acute cardiovascular fatalities following cannabis use. 2001. 124(2-3): p. 200-203.
169. Lange, R.A. and L.D.J.N.E.j.o.m. Hillis, Cardiovascular complications of cocaine use. 2001. 345(5): p. 351-358.
170. Smith, E., Substance abuse and asthma. Journal of Lung, Pulmonary & Respiratory Research, 2015. 2(4): p. 75.
171. Goodell, S., et al., Mental disorders and medical comorbidity. 2011.
172. Organization, W.H., International statistical classification of diseases and related health problems. Vol. 1. 2004: World Health Organization.
173. Medicare, C.f. and M. Services, ICD-10-CM Official Guidelines for Coding and Reporting. 2018, 2018 ICD-10-CM and GEMs.
174. Association, A.M., 2018 ICD-10-CM: The Complete Official Codebook. 2018: American Medical Association.
175. Byrne, S.L., G.R. Hooke, and A.C.J.J.o.a.d. Page, Readmission: a useful indicator of the quality of inpatient psychiatric care. 2010. 126(1-2): p. 206-213.
176. Rachoin, J.-S., et al., The impact of hospitalists on length of stay and costs: systematic review and meta-analysis, in Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. 2012, Centre for Reviews and Dissemination (UK).
177. Shulan, M. and K.J.T.A.j.o.m.c. Gao, Revisiting hospital length of stay: what matters? 2015. 21(1): p. e71-7.
178. Bueno, H., et al., Trends in length of stay and short-term outcomes among Medicare patients hospitalized for heart failure, 1993-2006. 2010. 303(21): p. 2141-2147.
179. Markovich, P.J.H.A., A global budget pilot project among provider partners and Blue Shield of California led to savings in first two years. 2012. 31(9): p. 1969-1976.
180. Freitas, A., et al., Factors influencing hospital high length of stay outliers. 2012. 12(1): p. 265.

181. Kuo, Y.F. and J.S.J.J.o.t.A.G.S. Goodwin, Effect of Hospitalists on Length of Stay in the Medicare Population: Variation According to Hospital and Patient Characteristics: [See editorial comments by Drs. Susan E. Merel and Wayne McCormick, pp 1803-1805]. 2010. 58(9): p. 1649-1657.
182. Carek, P.J., et al., Inpatient care in a community hospital: comparing length of stay and costs among teaching, hospitalist, and community services. 2008. 40(2): p. 119.
183. Wen, C.K., et al., Length of stay and hospital costs among patients admitted to hospital by family physicians. 2012. 58(3): p. 290-296.
184. Goodney, P.P., et al., Hospital volume, length of stay, and readmission rates in high-risk surgery. 2003. 238(2): p. 161.
185. Tulloch, A.D., P. Fearon, and A.S.J.A.P.M.H. David, Length of stay of general psychiatric inpatients in the United States: systematic review. 2011. 38.
186. Newman, L., et al., Factors associated with length of stay in psychiatric inpatient services in London, UK. 2018. 89(1): p. 33-43.
187. Masters, G.A., et al., Factors associated with length of psychiatric hospitalization. 2014. 55(3): p. 681-687.
188. Hendryx, M.S., et al., Psychiatric hospitalization characteristics associated with insurance type. 1998. 25(4): p. 437-448.
189. Fisher, W.H., et al., Insurance status and length of stay for involuntarily hospitalized patients. 2001. 28(3): p. 334-346.
190. Sarel, A., I.J.T.I.j.o.p. Iancu, and r. sciences, The relationship between type of insurance, time period and length of stay in psychiatric hospitals: the Israeli case. 2010. 47(4): p. 284.
191. Eastwood, M.R. and S.J.A.o.G.P. Stiasny, Psychiatric disorder, hospital admission, and season. 1978.
192. Caroline S. Zeind, M.G.C., Applied Therapeutics: The Clinical Use of Drugs. Eleventh, North American edition ed. Koda Kimble and Youngs Applied Therapeutics. December 27, 2017: LWW.
193. Drugs. FDA: FDA Approved Drug Products. [cited 2018; Available from: https://www.accessdata.fda.gov/scripts/cder/daf/.
194. Dr Gily's ICD 10 to MDC to MS-DRG Tracking Tool. Based on CMS' ICD-10 MS-DRG Conversion Project 2014; Available from: http://icd10cmcode.com/icd10-mdc-drg-codes.php?convtype=icd10todrg&code=f250.
195. ICD10 CM codes.Medical coding resource tool. 2018; Available from: https://icd.codes.
196. Benoit, K.J.L.S.o.E., London, Linear regression models with logarithmic transformations. 2011. 22(1): p. 23-36.
197. Bor, J.S., Among the elderly, many mental illnesses go undiagnosed. 2015.
198. Cameron, A.C. and P.K. Trivedi, Regression analysis of count data. Vol. 53. 2013: Cambridge university press.
199. Weaver, C.G., et al., Analyzing hospitalization data: potential limitations of Poisson regression. 2015. 30(8): p. 1244-1249.
200. Best, N.G., K. Ickstadt, and R.L.J.J.o.t.A.s.a. Wolpert, Spatial Poisson regression for health and exposure data measured at disparate resolutions. 2000. 95(452): p. 1076-1088.
201. Herrin, W.E., M.M. Amaral, and A.M. Balihuta, The relationships between housing quality and occupant health in Uganda. Soc Sci Med, 2013. 81: p. 115-22.

202. Gardner, W., E.P. Mulvey, and E.C. Shaw, Regression analyses of counts and rates: Poisson, overdispersed Poisson, and negative binomial models. Psychol Bull, 1995. 118(3): p. 392-404.
203. Long, S.J., Long, J. S., & Fresse, J., Regression models for categorical dependent variables using Stata. 2006: Stata press.
204. Coxe, S., S.G. West, and L.S. Aiken, The analysis of count data: a gentle introduction to poisson regression and its alternatives. J Pers Assess, 2009. 91(2): p. 121-36.
205. Coxe, S., S.G. West, and L.S.J.J.o.p.a. Aiken, The analysis of count data: A gentle introduction to Poisson regression and its alternatives. 2009. 91(2): p. 121-136.
206. Cameron, A.C. and P.K.J.J.o.e. Trivedi, Regression-based tests for overdispersion in the Poisson model. 1990. 46(3): p. 347-364.
207. Herrin, W.E., et al., The relationships between housing quality and occupant health in Uganda. 2013. 81: p. 115-122.
208. Kay, D.W., et al., Mental illness and hospital usage in the elderly: a random sample followed up. 1970. 11(1): p. 26-35.
209. Gulliver, A., K.M. Griffiths, and H.J.B.p. Christensen, Perceived barriers and facilitators to mental health help-seeking in young people: a systematic review. 2010. 10(1): p. 113.
210. Wilson, A.L., Forecasting pharmaceutical expenditures. Financial management for health-system pharmacists. 2008: ASHP.
211. Baek, H., et al., Analysis of length of hospital stay using electronic health records: A statistical and data mining approach. 2018. 13(4): p. e0195901.
212. Agency for Healthcare Research and Quality. (2015). Interim Update on 2013 Annual Hospital-Acquired Condition Rate and Estimates of Cost Savings and Deaths Averted From 2010 to 2013.
213. Hoffman, J.M., et al., Projecting future drug expenditures—2012. 2012. 69(5): p. 405-421.
214. Hoffman, J.M., et al., Projecting future drug expenditures in US nonfederal hospitals and clinics—2013. 2013. 70(6): p. 525-539.
215. Schumock, G.T., et al., National trends in prescription drug expenditures and projections for 2014. 2014. 71(6): p. 482-499.
216. Schumock, G.T., et al., National trends in prescription drug expenditures and projections for 2015. 2015. 72(9): p. 717-736.
217. Schumock, G.T., et al., National trends in prescription drug expenditures and projections for 2016. 2016. 73(14): p. 1058-1075.
218. Keehan, S.P., et al., National health expenditure projections, 2014–24: spending growth faster than recent trends. 2015. 34(8): p. 1407-1417.