Super Utilization of Healthcare Resources Among Schizophrenia Patients in United States Medicaid System

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ABSTRACT

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Background: It is well documented that a small part of US population (top 5 to 10%) consumes 50% to 70% of the healthcare resources. Multiple emergency and hospitalization visits among schizophrenia patients may point to a poorly managed disease with multiple relapses. There is sparse understanding of the extent and causes of super utilization of emergency and hospitalization among patients with schizophrenia. Innovative population health management strategies targeting the super users with schizophrenia can alleviate the cost and improve the quality of care. This study aims to identify demographics and clinical characteristics associated with super utilizer of healthcare resource utilization among Medicaid schizophrenia patients.

Methods: A systematic literature review was conducted to understand the economic cost and resource utilization in managing schizophrenia across all payer types in the US. The narrative systematic literature review was utilized to identify factors associated with resource utilization among Medicaid schizophrenia patients. The literature was also analysed to define "super utilizer" cohort. Using IBM MDCD Medicaid health insurance claims data (January 2001-Decemeber 2019), adult patients with schizophrenia claims, and ≥12 months of continuous insurance coverage before and ≥12 months after the first schizophrenia diagnosis in the database were included in the analysis.

Abstract

Based on literature review and the emergency and hospital visit distribution in the database, top 10% of resource utilizer were defined as “Super Utilizer”. Bivariate analyses were conducted to identify explanatory variables for a predictive analysis. Logistic regressions were used to identify the demographic and clinical characteristics of being in the top 10% of patients with the highest emergency and hospitalization use. As the database had 11% missing race information, models were tested with data with and without missing race. Single and Two-stage models with varied factors were tested to find the model with strongest predictive power.

Results: Top 10% of Medicaid schizophrenia patients had at least 9 visits to ER and hospitals in a year. In the study population with missing race (n=253,495) and a single model approach, Charlson Comorbidity Index-Romano (CCI), young age (18-34 years), suicide ideation or attempt were strong predictors of high emergency and hospital resource use, with odds ratios (ORs; 95% confidence interval [CI]) of 12.57 (10.6-14.9), 3.29 (3.05-3.55) and 3.04 (2.93-3.14), respectively. In the absence of CCI data, having suicide ideation or attempt (SIA), End Stage Renal Disease (ESRD), and being young age (18-34 years) were the top three factors. All included factors were statistically significant, but the strength of odds ratios were small with race and gender. Given significant zero utilizers, a two-stage model approach was also applied. Being young, CCI, and being middle age emerged as top three predictors with SIA as close fourth. The odds ratios were 1.95 (1.76-2.16), 1.87 (1.39-2.51), 1.80 (1.67-1.94) respectively. In this model, alcohol and substance abuse and missing race data were not statistically significant. Without CCI as a factor, ESRD emerged as third strongest in effect size after young and middle age with SIA as close fourth.

Limitations: Study was limited to data elements found in a payer sourced claims database. Thus, variables such as homelessness, perception of poor health, social isolation and other social determinants of health may be relevant but were not available.

Conclusion: This study suggests that schizophrenia patients with super resource utilization have a high level of comorbidity burden along with being younger in age. Given the model's high predictability in identifying super utilizer based on a claims data analysis, a practical, cost-effective, schizophrenia disease management is possible to improve quality of life among a significantly burdened patient and their caregiver population.

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AUTHOR'S DECLARATION

I declare that this thesis is my own work and has not been submitted for the award of a higher degree elsewhere.

The word count from Chapter One to Chapter 6 is 41773.

CHAPTER 1. SUMMARY OF THE PHD STUDY

1.1 BACKGROUND

Rise of healthcare cost is impacting all key stakeholders in the US economy. Along with the government and employers who bear significant part of insuring cost, patients are also feeling the financial burden as they are being asked to share in the increasing cost in the form of copayments, deductibles, and coinsurances. Despite spending most per capita in healthcare, US key health outcomes, such as infant mortality and life expectancy, are worse than comparable Western Europe countries. Thus, providers, payers and policymakers are all examining strategies to reign in the cost without undermining the quality of care and, if possible, by improving the health outcomes of Americans.

It is well documented that a small part of US population (top 5 to 10%) consumes 50% to 70% of the healthcare resources. (Nunn, Parsons, & Shambaugh, 2020) This small number of individuals are called High Utilizers or Super Utilizers. One of the major factors associated with super utilization is under or unmanaged behavioural health along with other factors such as multi chronic disease burden or elderly age. (Fuller, Sinclair, & Snook, 2017) Studies have been conducted in understanding resource use by Serious Mental Illness group but to develop effective cost containing and quality improving strategies, one must understand the causes of super utilization of specific disease groups within Serious Mental Illnesses. Schizophrenia is one of the most burdensome diseases in comparison to other major chronic diseases such as depression, heart diseases and diabetes and merits further research. (Coultier, et al., 2016) individuals suffering from schizophrenia are most vulnerable. Innovations in the field of medicine have led to effective medications and

medication deliveries, psychological treatments, and rehabilitative care such as housing or caregiver support, but access to these are severely constrained. (MHA, 2024) The increasing deinstitutionalization of patients with mental illness has shifted the burden of caregiving on family members who find it very challenging to care for schizophrenia family member. (Caqueo-Urízar, Caqueo-Urizar, Gutierrez-Maldonado, & Miranda-Castillo, 2009)

Significant cognitive impairment coupled with low caregiver support lead them to seek care in emergency departments (Doran & Rosenhenck, 2013) resulting in hospitalizations (Cahoon, McGinty, Ford, & Daumit, 2013). There is sparse understanding of the extent and causes of super utilization of emergency care and hospitalization among patients with schizophrenia. Given the high cost of managing schizophrenia, innovative population health management strategies targeting the super utilizers with schizophrenia can alleviate the cost and improve quality of care. The identification of factors associated with super utilizers among schizophrenia patients will enable development and application of cost-effective population health interventions to improve the health outcomes for this cohort of vulnerable patient population with significant unmet needs.

Although schizophrenia is a debilitating chronic disease with significant burden for patients and their care givers, given its low prevalence rate of less than 1% (Kessler, et al., 2005), research in its role in super utilization is sparse. Since 67% of patients with schizophrenia are covered by Medicaid in USA (Khaykin, Eaton, Ford, Anthony, & Daumit, 2010), it seems the most logical system to understand resource utilization among

schizophrenia patients and understand the factors associated with high utilization of resources.

1.2 STUDY OBJECTIVES

The main aim of this study was to:

i. Conduct a systematic review of cost and resource utilization in managing schizophrenia in the US health system.

ii. Characterize super utilization among Schizophrenia patients in the US Medicaid System.

iii. Analyse factors associated with super utilization of resources among US Medicaid schizophrenia patients.

1.3 METHODS

A systematics review to synthesize real world evidence on direct cost or resource used in the management of schizophrenia by all payers in the United States of America was conducted first. This research critically appraised peer-reviewed published literature, dissertation, systematic reviews, and registries of observational studies published from January 2000 to August 2021 on schizophrenia cost and resource utilization. A Medline Complete, Cinnahl, APA PsycInfo, and APA PsycArticles search was conducted. Given the heterogeneity in the study designs and outcomes, qualitative narrative synthesis was conducted based on the Popay's guidance. (Popay, et al., 2006). Literature review was also

conducted to understand the existing definition of super utilization among schizophrenia patients as well as the factors that may be associated with utilization of healthcare resources.

Post a systematic literature review, a retrospective descriptive analysis was conducted using existing robust claims database to characterize super utilization among Schizophrenia patients in the US Medicaid System. A retrospective analysis of claims of schizophrenia patients from US Medicaid population from year 2010-2019 was conducted on a nationally represented Medicaid database, MarketScan® Multi-State Medicaid Database V2047, released on 7th March 2022. It is a large database with more than 33 million lives. It contains pooled healthcare experience of Medicaid enrolees who are covered under both fee for service and the managed care plans. The database includes records of inpatient or hospital services, inpatient admissions, outpatient services, and prescription drug claims, as well as information on long-term care along with demographic information such as age, race and gender.

As the current literature lacks a standard definition of “Super Utilization”, the distribution of ER and Inpatient Resources in the IBM Medicaid data was used to define the Super versus Not Super Utilizer cohort. As cost and management of emergency and hospitalization vary by region, plans and over time, picking a definition such a top 10% provided a consistency with super utilizer literature and a more stable and systematic approach that is applicable and comparable across regions, plans, diseases and time.

Finally, a multivariate logistic regression analysis was applied to analyse factors that may predict Super Utilization of resources among the Medicaid schizophrenia patients. The Dahlgren and Whitehead "Rainbow Model" (Dyar OJ, et al., 2022) provided the theoretical framework to identify factors impacting high utilization of resources by severe mentally ill schizophrenia patients. The rationale for using the “Rainbow Model” lies in its ability to provide a powerful framework for understanding how mental health such as schizophrenia is shaped by various layers of social, economic, and environmental factors. This allows the researchers to explore beyond biological factors to other social and environmental issues that impact mental health and may need to be addressed if a policy is to be designed for population health improvement. Factors selected for the data analysis were limited to data available in the Medicaid IBM database and included individual Medicaid member personal characteristics such as age, sex, and co-morbid conditions and member’s lifestyle such as alcohol and substance abuse.

Given significant zero utilizers in the study cohort, a two-stage regressions approach was also applied. The rationale was that there is a possibility of distinct reasons for their zero-utilization compared to any positive utilizers. By treating zero utilizers same as non-zero utilizers in one model, we may overlook critical differences. The first stage of the model estimated whether the subject had zero healthcare expenditure. In the second stage of the model, a regression was conducted to identify factors associated with a patient being a high utilizer.

1.4 RESULT

A systematic narrative synthesis of all the studies confirmed that it is significantly more expensive, at least fifty percent more to manage a patient with schizophrenia than a patient without schizophrenia. It also confirmed that there was variability in resource utilization among the Medicaid schizophrenia patients. Findings pointed to a small proportion of schizophrenia patients who may be relapsing more frequently and leading to disproportionate use of health resources. Thus, confirming the importance of understanding distribution of resource utilization among the patients in order to develop targeted solutions for better disease management.

Data analysis of Medicaid schizophrenia patients showed that the top 10% of the super utilizer experience 9 + emergency visit or hospitalizations in a 12-month period. In the study population with missing race (n=253,495), with singe model approach, Charlson Comorbidity Index-Romano (CCI), young age (18-34 years), Suicide Ideation or Attempt were strong predictors of high emergency and hospital resource use, with odds ratios (ORs; 95% confidence interval [CI]) of 12.57 (10.6-14.9), 3.29 (3.05-3.55) and 3.04 (2.93-3.14), respectively. In the absence of CCI, Suicide Ideation or Attempt, End Stage Renal Disease, and young age comorbidities. All included factors were statistically significant, but the strength of odds ratios was small with race and gender, while being female was positively related to super utilization.

Given 30% of schizophrenia users were zero healthcare utilizer, a two-stage regression was conducted. Being young, CCI, and being middle age emerged as top three

predictors with SIA as close fourth. The odds ratios were 1.95 (1.76-2.16), 1.87 (1.39-2.51), 1.80 (1.67-1.94) respectively. In this model, alcohol and substance abuse and missing race data were not statistically significant in predicting SU. Without CCI as a factor, ESRD emerged as third strongest in effect size after young and middle age with SIA as close fourth. Another key output which was different from Single model approach was the finding that female was negatively associated with high utilization while use of anti-psychotics was positively related. The model had strong predictability with AUC = 0.75.

Despite a lack of variables such as homelessness, perception of poor health, social isolation and other social determinants of health which may be relevant in identifying super utilizers but are not available in claim databases. the model remained robust and provides guidance needed to shape a population management tool to minimize avoidable Emergency Room and hospital stays among schizophrenia patients who are unfortunately experiencing these 9 times or more in a year.

1.5 CONCLUSIONS

Since this study is first of its kind to predict High Utilization of emergency and hospital resources using easily existing Medicaid claims data, its findings will contribute to development of pragmatic population health management tools for better health management of, often forgotten and stigmatized, schizophrenia patients. It will also provide applications in other payer systems as well as other burdensome chronic diseases.

CHAPTER 2. INTRODUCTION & BACKGROUND

2.1 INTRODUCTION

US healthcare spending is significantly high in terms of absolute number and is substantially higher in comparison to other developed nations. Furthermore, US healthcare spending rate of growth in 2022 was 4.1 percent, thus reaching $4.5 trillion or $13,493 per person. (AMA, 2024) As a share of the US Gross Domestic Product, health spending accounted for 17.3 percent (CMS, 2024). In contrast, the US economy grew only 1.7% in 2022. A rising healthcare spending will draw resources away from other economic activities. A disproportionate increase in healthcare will eventually lead to higher tax or reduced spending on other important government function such as public security, infrastructure, investment in research and development and education.

Reinhardt et al had predicted in 2004 that increasing healthcare spending in US will lead to increasing burden which will first affect the lower income households and by 2040s may lead to reduction in non-health related GDP (Reinhardt, Hussey, & Anderson, 2004). In other words, US consumers by 2040 may have less income for their non-household expenditures than what they have today. Not surprisingly, US healthcare expenditure has become a major focus of policy makers and has taken centre stage in election debates. Making the situation worse, unfortunately, the high health spending has not translated to better health outcomes for Americans. Thus, researchers have been focusing in understanding the enormous fiscal challenge faced by the nation to provide solutions to reign in the high cost and to enhance the quality of care for better health outcomes.

In general, healthcare spending depends on the utilization of the number of services of goods and the price of the services or goods used while delivering health care. An increase in either of these factors will result in higher healthcare costs. The factors leading to increase in healthcare spending range from innovations in healthcare treatments to expanded health coverage for Americans, increasing utilization of treatments and services to increasing prices for them along with increasing waste and inefficiencies in the health system. Some of these factors are desirable as they result in better health outcomes such as increased life expectancy and improved quality of life after diagnosis for many diseases (Wamble, 2019) but a significant proportion of increase in the healthcare spending is not positive. A landmark JAMA study by Papanicolas (Papanicolas, Woskie, & Jha, 2018) have shown that higher prices of health services or products is a major cause of high health care spending in US in comparison to ten of the highest-income countries (United Kingdom, Canada, Germany, Australia, Japan, Sweden, France, the Netherlands, Switzerland, and Denmark).

Hospital care accounts for one-third of the US healthcare spending followed by professional services outside hospitals that accounts for roughly one-fourth of the overall cost (Nunn, Parsons, & Shambaugh, 2020). Thus, it is crucially important to understand factors leading to high cost in hospital and professional care in developing solutions to alleviate the increasing cost of healthcare. Another key factor behind the significant increasing healthcare cost is a small proportion of patients to disproportionality utilize very high healthcare resources such as expensive emergency and hospital care (Cohen, 2014). While half spends population accounts for only 3% of the total healthcare spend, the top 10 percent account for 50% of the

healthcare spend (Nunn, Parsons, & Shambaugh, 2020) and 1% of the US population incurs almost 25% of the nation's healthcare expenditures. (Cohen, 2014).

While the US government continues to explore policies to reign in the high cost caused by inefficient administrative costs and monopolistic pricing, researchers are also focusing on the high-cost patients who have higher need for healthcare. Providing better care for these patients not only hold promise of saved resources but may also provide the care they need in an optimal manner thus improving their health outcomes.

The term Super Utilizers (SU) or High Utilizers (HU) are given to the small proportion of US population that consumes a significant part of health care resources. (Nunn, Parsons, & Shambaugh, 2020) (Cohen, 2014) (Knight, 2022). Evaluation of the factors associated with super utilization may be an effective way in designing and implementing health care solutions. These high-cost patients are heterogeneous with diverse and complex needs. Thus, the solutions need to be tailored to the major sub-groups of high-cost patients. Researchers have uncovered the critical role of multiple chronic diseases and behavioural health issues as key characteristics of these patients. (Fuller, Sinclair, & Snook, 2017). Although, it is well studied that Serious Mental Illness (SMI) is a key factor among Super Utilizers, research focusing on the role of individual diseases within SMI definition (schizophrenia, severe major depression, and severe bipolar disorder) is needed for successful targeted health management programs.

2.2 HIGH UNSUSTAINABLE HEALTHCARE SPENDING IN THE UNITED STATES

The United States (US) healthcare spending is the highest in the world both in terms of its total number as well as in terms of per capita spending. In 2022, In US healthcare spending totalled $4.5 trillion (CMS.gov, 2024), which averages to approximately thirteen thousand dollars per capita spending. In general, as seen in Table 2-1, the per capita spend on health care is twice as much as other wealthy countries like France, Canada and United Kingdom. (OECD, 2023)

Table 2. 1: Per Capita Health Expenditure in High Income Countries

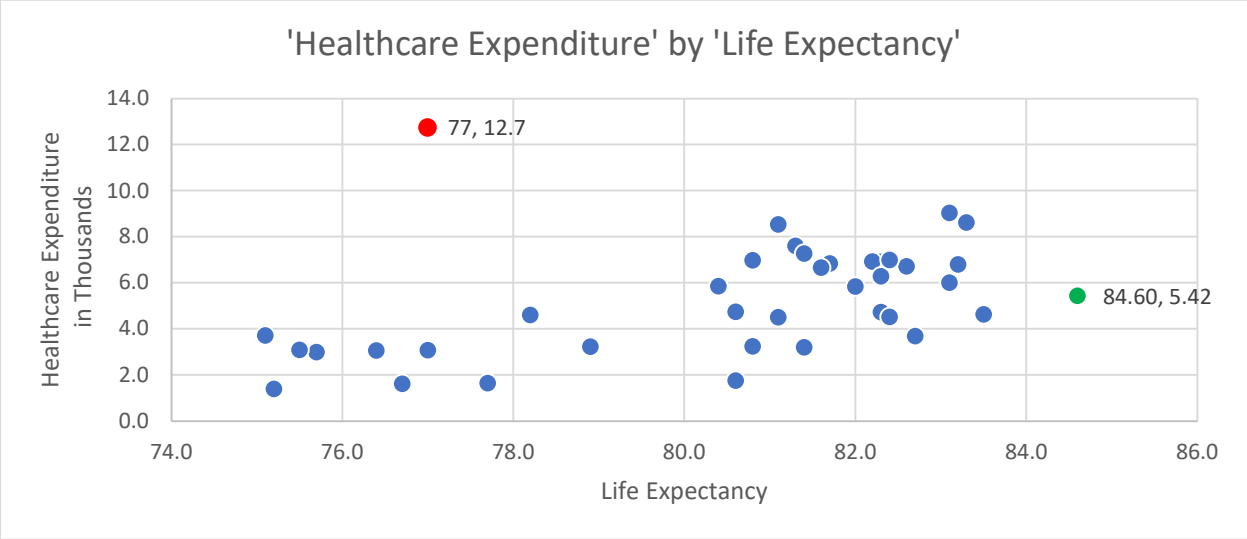
Countries	**Health Expenditure per Capita in 2022**
United States	$12742.10
Germany	$8,541.50
France	$6,923.60
Canada	$6,845.10
United Kingdom	$5,866.80

Source: OECD Health Statistics 2023; WHO Global Health Expenditure Database. In 2022 prices, PPP Converted

In spite of significantly higher spending on healthcare, in comparison to other to economically well-off nation, United States does not have better healthcare outcomes in terms of life expectancy, obesity, overweight rates and infant mortality rates. (OECD, 2023). US data are shown in red dots in the figures below. As seen in Figure 2-1, while US health care spending is highest at nearly thirteen thousand dollars in 2022 dollars, life expectancy is one of the

lowest among OECD countries at 77 years. In contrast, country like Japan, shown in green, that spends half as much in health care ($5,423 annually in 2020 US dollar, PPP adjusted) has a much higher life expectancy of 84 years.

Figure 2. 1: High cost and low life expectancy in the US



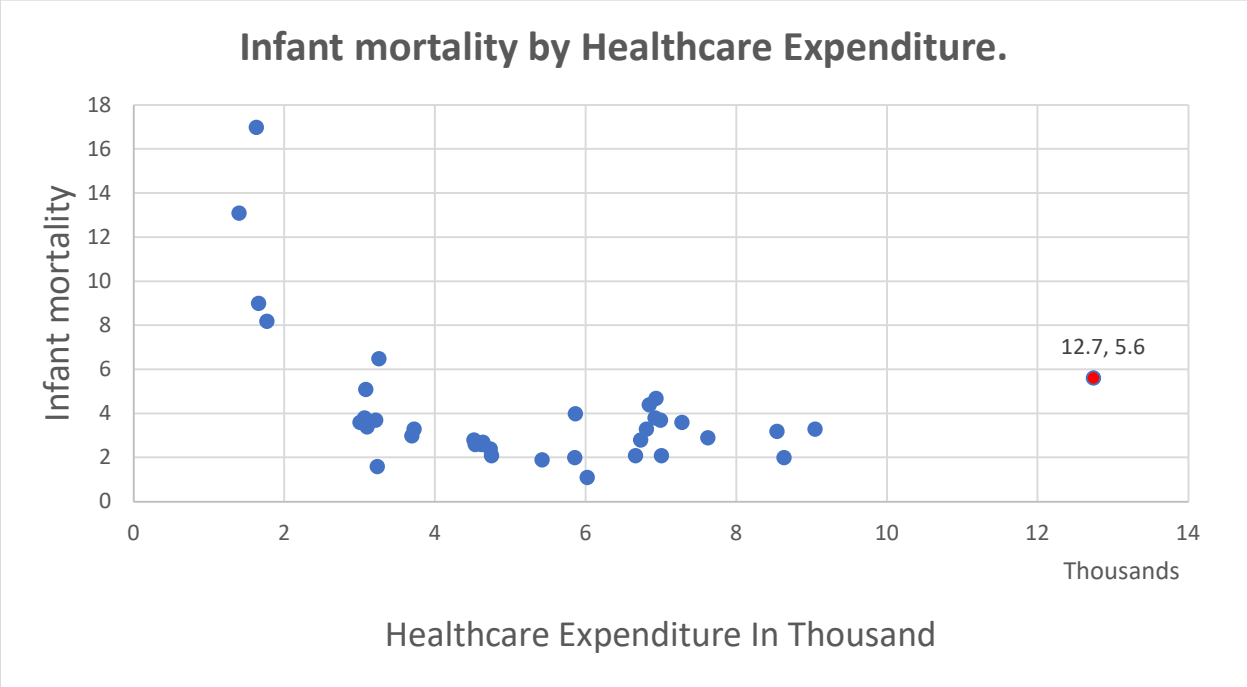
Source: OECD 2020 Data. Healthcare spending in current dollars.

Obesity and overweight are major risk factors for multiple chronic diseases such as heart diseases, cancer and diabetes and hence having a higher rate is a sign of a nation with significant burden of illness. US with highest healthcare spend has the highest obesity and overweight rates at a total of 74 percentage. (OECD, 2023)

A similar disconnect with the healthcare spend is the statistics on infant mortality which is estimated as 5.6 per 1000 infants born. It is the highest among the developed nation. OECD countries with higher infant mortality rates are Chile, Costa Rica, Turkey and Mexico which have

significantly lower healthcare spending compared to that of US with 3,256, 1,769, 1,660, and 1,401 US dollars adjusted PPP respectively.

Figure 2. 2: Infant Mortality by Healthcare Expenditure



Source: https://www.oecd.org/en/data/indicators/infant-mortality-rates (OECD, 2023)

Healthcare costs continue to increase as a part of the overall size of the US economy. It has increased significantly over the past seven decades, from 5 percent of its Gross Domestic Product (GDP) in 1962 to 17 percent in 2022. It has now become a key driver of America's unsustainable national debt. (PGPF, 2024) The recent long-term projections from the Congressional Budget Office (CBO) have shown that the national debt is on an unsustainable path especially with the recent rise in nation's interest rates. The nation's debt is projected to rise from nearly 100 percent of gross domestic product (GDP) in 2024 to 166 percent in 2054. One of the major causes behind the increasing debt is the federal spending on major healthcare

programs, such as Medicare, public program for elderly, Medicaid, public program for needy and indigent and VA & DOD, health coverage for US veterans and armed service men and women. Government health spending is projected to increase by 73 percent over the next 10 years and will exceed other categories of federal spending in 2028. Thus, by 2054 accounting for 30 percent of total federal expenditures, exceeding the total amount spent on discretionary programs, such as defence and education, by 51 percent. (PGPF, 2024) (CBO, 2023)

Given the significant spending and the continued projected increase on healthcare, it is critical to US long-term economic and fiscal well-being to understand the reasons behind them to reign in the cost as well as its growth. Various research has been conducted to understand the causes to develop solutions to improve US health systems so it can deliver better quality care at a lower cost. US has a complex heath care delivery system and the key sources of the $4.5 trillion healthcare expenditure number are hospital care which accounts for 31% of the overall spending, followed by physician services which contributes to 20% , prescription drugs at 10% and nursing care facilities at 5%. (CMS, 2023)

There are many factors behind the increasing trend in healthcare spending ranging from aging population with rising chronic diseases, increasing price of healthcare services due to monopolistic health providers, complex health delivery leading to administrative waste in insurance and provider payment systems, inadequate health insurance causing overuse of emergency care, to the introduction of new, innovative healthcare technology that has led to better, more expensive procedures and products. (Crowley, Daniel, & Cooney, 2020) (Nunn, Parsons, & Shambaugh, 2020)

Researchers have also found that the cost of healthcare is significantly driven by a small minority of high-cost individuals. (Nunn, Parsons, & Shambaugh, 2020) (Cohen, 2014) Thus, there is a strong rationale to target this minority high cost individuals to reign in the cost. Not surprisingly, the high concentration of health care cost in a small proportion of the population has generated various research to understand the extent, the characteristics of these individuals and the associated causes behind their disproportionate use. Research have been conducted in an effort to reduce health care spending and or to improve health care quality or both by targeting high-need, high-cost patients of the health care system.

2.3 SUPER UTILIZERS OF HEALTH RESOURCE

A relatively small numbers of people make significant use of health care services at enormous cost to healthcare system. The term Super Utilizers (SU) or High Utilizers (HU) are given to these people. In health economics literature, SU have been defined in multiple different ways. Most commonly SU definitions have been based on either the number of hospitalizations or ER visits in a 12-month period which could have been perhaps prevented by early less expensive primary care or being part of the top 5% or 10% of the healthcare utilizer in a plan or cohort of patients. Since the trends in hospital or emergency use has been changing in the United States (CDC, 2023), defining high utilization as the top 5% or 10% of the resource users is a more robust approach.

Multiple studies have shown that these SU consume a significant part of health care resources. (Jiang, Weiss, Barrett, & Sheng, 2012) Cohen found that 1% of the US population

incurs almost 25% of the nation's healthcare expenditures and 5% of patients account for 50% of the total healthcare cost. (Cohen, 2014) A 2020 study by Davenport et al found that the most expensive 10% of individuals accounted for 70% of total healthcare costs. (Davenport, Grey, & Melek, 2020) They conducted a large study on 21 million insured lives. In this report, the top 10% users, 2.1 million individuals, were referred to as the "High-cost Group" and their annual total healthcare costs, in 2020 dollars, averaged $41,631. This was estimated to be 21 times higher than the average ($1,965) of the remaining 90% of the population studied.

It is thus not surprisingly that these patients have become focus for cost management and quality improvements and consequently population health management. This disproportionate focus on HU is also referred to as "hot spotting" which targets super-utilizers of emergency departments and hospital services with targeted health and social services with the objective to improve health outcomes while decreasing healthcare costs. (Finkelstein, Zhou, Taubman, & Doyle, 2020)

Evaluation of the extent, the characteristics and the factors associated with super utilization may be an effective way in designing and implementing health care solutions for targeted patient population that would benefit from more intensive levels of care or support. One needs to understand the different predictors of super utilization of healthcare cost to allow population health decision makers to apply strategic high-risk care management by directing resources and services towards patients who are likely to be high utilizers of resources and may experience poor health outcomes. (Powers, Sreekanth, & Chatguru, 2016)

Successful healthcare management programs require health delivery interventions that are tailored to patients' clinical needs. Research by Powers et al suggest that there is variability in characteristics of SU across different health insurance systems in the United States, such as Medicare, Commercial and Medicaid plans, as there are differences in the demographics of the members enrolled in these plans. (Powers, Sreekanth, & Chatguru, 2016) In order to understand the demographic differences, understanding of the US health Insurance system is warranted.

2.31 US HEALTH INSURANCE PLANS

The health expenditure in the US is complex and is mostly financed by public payers, which include Federal, State, and local government, and private insurance, also known as commercial insurance. There is also a segment of uninsured patients in the US. Thus, there is no single nationwide health insurance system. The private health insurance is mostly voluntarily provided by employers to their employees and their dependents. A small segment of private insurance is purchased directly by the insured through insurance exchanges. The government provides health coverage to the elderly, the disabled, and some of the poor. There is variability with respect to benefit coverage, sources of financing, and payments to medical care providers across various public and private health insurances. The complexity of multiple insurance provisions is further amplified by lack of coordination among various private and public programs.

According to US Census bureau, approximately 92% of the US population (304 million) were insured in 2022. The private insurance accounts for nearly two-thirds (65.6%) of the overall coverage while public insurance covered 36.1% of the insured. The total adds up to be more than 100%, as small proportion of individuals have both private and public coverage. Employment-based insurance is the most common insurance covering 54.5% of the US population. There are more than thousand private health insurance companies with different benefit structurers and coverages, premiums, and rules for reimbursing the insured or medical care providers. Among the public insurances, the largest is Medicaid which covers 18.8% of the US insured population and this is followed very closely by Medicare at 18.7%. the other small public insurances are TRICARE (2.4 percent), and Veteran Affairs (VA) and Civilian Health and Medical Program of the Department of Veterans Affairs (CHAMPVA), which accounts for 1.0 percent of all insured. Direct purchased insurance accounts for 9.9% of all insured people in US.

Among the public insurance systems, Medicaid covers about 70 million Americans who are low-income adults, children, pregnant women, and people with disabilities. The Medicaid program is funded jointly by states and the federal government and administered by individual states within federal requirements and guidelines. Federal laws require that states cover low-income families, qualified pregnant women and children, and individual receiving income assistance from government, which is called Supplemental Security Income. Individual state can expand the coverage eligibility to other groups such as children in foster care and individuals who are receiving community and home care. The Affordable Care Act of 2010, also known as Obamacare, created opportunity to expand Medicaid to nearly all low income (income at or below 138% of federal poverty level) under 65 Americans and most states chose to do so.

According to Health Policy Research group, KFF, in 2021, the percentage of the population covered by the Medicaid ranged from 10% to 34% Across the States. (Rudowitz, Burns, Hinton, & Mohamed, 2023) The Medicaid Program covers more than 1 in 5 Americans and most of these Americans have many complex and costly needs for care. This program is also the principal source of long-term care coverage for people in the United States. Combined state and federal Medicaid spending comprised nearly one-fifth of all health care spending in the U.S. Thus, it provides significant financing for hospitals, community health centres, physicians, nursing homes, and community-based long-term services.

Medicaid is an entitlement, which means that individuals who meet eligibility requirements are guaranteed coverage. While Medicaid covers 20 percent of people living in the United States, Medicaid is a particularly more important source of coverage for certain populations. In 2021, Medicaid covered four in ten children, eight in ten children in poverty, one in six adults, and almost half of adults in poverty. Relative to White children and adults, Medicaid covers a higher share of Black, Hispanic, and American Indian American Native (AIAN) children and adults. Medicaid covers 43% of nonelderly, noninstitutionalized adults with disabilities, who are defined as having one or more difficulty related to hearing, vision, cognition, ambulation, self-care, or independent living. (KFF.org, 2019)

Certain US population is mostly dependent of Medicaid coverage. For example, 41% of all births in the United States, nearly half of children with special health care needs, five in eight nursing home residents, 23% of non-elderly adults with any mental illness, and 40% of non-elderly adults with HIV are covered under Medicaid. Along with coverage for Medicare

premiums for low-income elderly, which is one in five Medicare beneficiaries, it often provides wrap around coverage for services not covered by Medicare (like most long-term services and supports). Half of Medicaid beneficiaries are children under age 19, while six in ten are people of colour (35% are blacks and 31% are Hispanics), 57% are female; and seven in ten are in a family with a full or part-time worker. (KFF.org, 2019) A significant proportion of adult Medicaid enrolees are working but they do not have insurance coverage form their employer.

Elderly who are poor, have both Medicare and full Medicaid coverage are called “dual eligible.” Medicare pays first when an individual is dual eligible, and one receives Medicare-covered services. Any remaining need is paid then by Medicaid which may include premium for Medicare programs. 43% of Medicaid beneficiaries are disabled and are the key driver behind high Medicaid cost along with dual eligible elderly. Although the elderly and disabled account for 21% of the overall Medicaid enrolees, they account for 55% of the overall Medicaid expenditure.

Unlike Medicaid, which is social welfare program, Medicare is a social insurance program which is funded by taxes from working people to cover aged beneficiaries. Thus, Medicare is an inter-generational transfer program which provides a uniform national insurance for the aged, disabled, and any age with end stage renal disease or permanent kidney failure needing dialysis or transplant. (HHS, 2022) The Medicare program consists of: Part A and Part B for hospital and medical insurance and Part C and Part D that provide additional coverage such as vision and prescription drugs.

A smaller public insurance, TRICARE, is a uniformed services health care program for active-duty service members (ADSMs), active-duty family members (ADFMs), National Guard and Reserve members and their family members, retirees and retiree family members, survivors, and certain former spouses worldwide. VA health care is a type of medical benefits package for honourably discharged veterans who served in the U.S. military. Civilian Health and Medical Program of the Department of Veterans Affairs (CHAMPVA) provides coverage for the spouse or surviving spouse or a child of a Veteran with disabilities or a Veteran who has died and is not covered under TRICARE.

The largest health insurance segment in the United States is the commercial or the private health insurance. It is a health insurance policy from a commercial entity that is not affiliated with the government. Like public insurance plans, they provide preventive care, diagnosis, treatment, and emergency care. But these plans vary in coverage and cost as some are more comprehensive, and they could cover alternative therapies like acupuncture and experimental and novel treatments, while others cover basic healthcare. They are regulated by the state and hence the insurers plans and thus coverage may vary by state. Some the largest insurers in the U.S. are UnitedHealth Group, Anthem, Aetna, Cigna, Humana and Kaiser. Some are pure insurers while others are payer provider entities and are also referred to as Integrated Delivery Networks. Employers are the major source of commercial insurance benefit. Since the 2010 Affordable Care Act, insurance coverage could also be purchased directly by individuals at Marketplace or directly through an insurance company.

There are significant differences in demographics of people covered by different health plans in the United States. Individuals with commercial coverage are relatively financially well off in comparison to Medicaid members while members of Medicare are older in comparison to both commercial and Medicaid plan members. One may also observe higher level of education among commercially insured in comparison to Medicaid members. According to World Health Organization (WHO), multiple factors affect health of individuals. (WHO, 2024) Factors such as age, income level, education level among other factors such as genetics and gender have significant impact on health status. These factors in fact may play a more significant role than having access and use of health services.

WHO's assessment of Social Determinants of Health shows that income level is positively correlated with better health. The report concludes that higher the income status, the greater the difference in health status. A similar relationship exists between education and health. Low level of education is a strong predictor of poor health. It is also well understood that old age is generally accompanied with multiple chronic ailments.

Given the differences in demographics such as age and income level, and extent of coverage across the health insurance plans, the level and characteristics of SU would differ across all of them along with factors that are associated with SU of healthcare resources. Powers et al showed that SUs in a Medicare Plan that covers elderly have on an average eight co-morbidities (Powers, Sreekanth, & Chatguru, 2016). They typically have cardiovascular risk factors along with of ischemic heart disease, congestive heart failure, or chronic kidney disease.

This would suggest a chronic health management along with care-co-ordination through a nurse care manager.

Different from Medicare, SUs in a commercial plan were mostly patients who had experienced catastrophic injuries, or they were on specialty pharmaceuticals such as expensive biologics for rheumatoid arthritis or cancer. A high-risk health management program would require specially drug utilization program or care models for injuries. On the other hand, SUs in Medicaid plans is different from both commercial and Medicare plans. Created in 1965, SU in Medicaid, which covers significant number of poor, unemployed and disabled individuals, had mental health issues along with multiple chronic diseases. The health care management program in a Medicaid plan would require a holistic physical and mental health management tailored to the different mental health diseases that they have. (Cantor, 2016)

2.4 CHALLENGES IN BEHAVIORAL HEALTHCARE IN THE UNITED STATES

US healthcare has significant challenges. One of the worst among them is behavioural health. According to Mental Health America, one in five Americans are suffering from a mental illness and they face varied and significant healthcare challenges. (MHA, 2024) Key factors creating challenges are widespread shortage of providers, especially in rural areas, fragmented health system, cost of treatment, stigma and disparities in care. American Psychological Association in 2022 conducted a Covid-19 Practitioner Impact Survey which showed that 60% of psychologists reported having no openings for new patients. (APA, 2022). According to American Counselling Association report shortage of providers are caused by lack of funding

from the government for a patient population that disproportionately relies of public funding. (Phillips, 2023) Other key reasons listed in the reports, behind shortage of providers, are poor reimbursement rates leading to low retention rate among providers, lack of mental health facilities in rural areas, stigma and continued increased need for services along with aging workforce. (Phillips, 2023)

The fragmented and a maze-like US health system is extremely difficult for any ill person to navigate, but the negative impact on access is increased when the individual is living with mental illnesses. The delivery of mental health services is fragmented across outpatient healthcare providers, inpatient hospital services, prescription drugs, and other behavioural interventions provided community mental health clinics with each system having a separate billing and electronic medical record system. The intention behind carving out of behavioural health was to provide accessible mental health but it has also contributed to poor care coordination, overuse and duplication of certain services, and ineffective restraints on cost. (Richman, Grossman, & Sloan, 2010) The system fragmentation is further intensified by the fact that physical health is separated from behavioural health. Thus, a patient with both, which is quite common, finds it's very difficult to navigate and receive much needed comprehensive care. Many schizophrenia patients have comorbidities such as diabetes and heart related diseases, (Rosenfeld, et al., 2022) but fragmentation prevents complete care which leads to worsening overall health and further acute episodes leading to hospitalization.

The mental health has been significantly challenged by inadequate public funding thus triggering healthcare crisis as most of the severe mentally ill patients rely on public assistance. A 2022 survey conducted by the Kaiser Family Foundation and CNN, showed that one-third of mentally ill respondents could not get the mental health services they needed. (Lopes, Kirzinger, Sparks, Stokes, & Brodie, 2022) Approximately 80% cited cost as the barrier while about 60% experienced stigma. (Lopes, Kirzinger, Sparks, Stokes, & Brodie, 2022)

Among the mentally ill, individuals suffering from serious mental illnesses, like schizophrenia, are most vulnerable. Innovations in the field of medicine have led to effective medications and medication deliveries such as long-acting drugs, psychological treatments, and rehabilitative care such as housing or caregiver support, access to these are severely constrained. Access to care among this group is a dismal 50 percent. (MHA, 2024) The increasing deinstitutionalization of patients with mental illness has shifted the burden of caregiving on family members who find it very challenging to care for schizophrenia family member. The psychotic behaviour associated with this disease along with the cultural and social negative perception leads to tensions and difficulties in caregiver role. (Caqueo-Urízar, Caqueo-Urizar, Gutierrez-Maldonado, & Miranda-Castillo, 2009) (Caqueo-Urizar, Rus-Calafell, Urzua, Escudero, & Gutierrez-Maldonando, 2015)

Significant cognitive impairment coupled with low caregiver support leads to lack of appropriate disease management and psychotic episodes leading to high emergency use, frequent hospitalization, homelessness and crime. (Doran & Rosenhenck, 2013) (Cahoon, McGinty, Ford, & Daumit, 2013). Impaired global functioning, challenging family, social and

healthcare support systems, lead to homelessness. (Olfson M. M., 1999) Desperation or as a response to their tough environment, schizophrenia patients, also find themselves resorting to crimes (Gottfried & Christopher, 2017).

2.5 RELATIONSHIP BETWEEN BEHAVIORAL HEALTH AND HIGH UTILIZATION OF EMERGENCY AND INPATIENT CARE

Frequent visits to emergency department and resulting hospitalization is a major factor behind research showing that majority of high-cost individuals have behavioural health problems. (Stoddard, Gre, & Melel, 2020) In most cases, costs for behavioural health-specific treatment represented a small fraction of total healthcare costs for these individuals, and many had no or minimal spending on behavioural health-specific services. (Stoddard, Gre, & Melel, 2020) This points to the unmet need in terms of better management in terms of behavioural health. Thus, making a case for a comprehensive strategy to manage the health of patients who have behavioural health problems. Stoddard's 2017 analysis of 21 million commercially or privately insured lives showed that the most expensive 10% of the covered lives, which they referred as the "High-Cost Group" cost as much as 21 times higher than the rest of the 90% of the covered lives ($41,631 versus $1,965 per annum). A significant factor associated with the "High-Cost Group" was the presence of behavioural health problems. A high percentage of the HU had behavioural health (57%) while accounted for only 5.7% of the total 21 million lives studied by Stoddard. These HU group accounted for 44% of the total healthcare cost. Thus, this study concluded that most high-cost individuals had behavioural health problems and there was a significant need to manage their health better. Other studies conducted by Joynt (Joynt,

Gawade, Orav, & Jha, 2013), Powers (Powers, Sreekanth, & Chatguru, 2016) and Figueroa (Figueroa, Frakt, Lyon, Zhou, & Jha, 2017) also confirm higher rate of behavioural health conditions among high-cost individuals among health plans and have arrived at similar conclusions.

Studies suggesting strong association between mental disorders and high utilization have shown significant use of healthcare resources such as emergency care and inpatient services. (Ford, 2004) (Borckardt, 2011) A study by Jiang et al found that mental and behavioural health was the top diagnosis among hospital use by Medicaid patient population. (Jiang, Weiss, Barrett, & Sheng, 2012) Although it is well studied that Serious Mental Illness (SMI) is a key factor among Medicaid's Super Utilizers (Fuller, Sinclair, & Snook, 2017), research focusing on the role of individual diseases within SMI definition is needed for successful targeted health management programs. SMI includes schizophrenia, severe major depression, and severe bipolar disorder. What is needed for a severely major depressed patient will be very different from what will be relevant for a patient suffering from schizophrenia.

One of the major diseases with high economic burden is schizophrenia. It is also a disease which is small in prevalence in comparison to chronic diseases like diabetes or depression but significant in its impact on cost of managing healthcare. Doran's multivariable analyses to understand the key factors associated with high utilization of emergency resources in the VA database showed that the factors that most strongly associated with all levels of Emergency Department use was schizophrenia (odds ratio range 1.44 [95% confidence interval of 1.41 to 1.47] to 6.86 [95% Confidence Interval of 5.55 to 8.48], homelessness, opioid use and

heart failure. (Doran & Rosenhenck, 2013)It is also interesting to note that a significant proportion of schizophrenia patients have addiction, homelessness and crime problems suggesting a better management of schizophrenia may alleviate addiction and homelessness problems as well. Having a small prevalence and high per patient cost, schizophrenia lend itself as a suitable disease area for population health management.

2.6 SCHIZOPHRENIA: HIGH UNMET HEALTH NEED DISEASE

Schizophrenia is a chronic and severe mental disorder that affects a person's perception of reality, social interactions, and thought processes. Schizophrenia patients experience hallucinations which may be visual or auditory, delusions, cognitive impairment which leads to unusual way of thinking or disorganized speech, and difficulty in social relationships. The schizophrenia symptoms significantly impact a patient's ability to work or to take care of themselves and hence, is associated with significant health, social, and economic concerns. Not surprisingly, it is one of the top leading causes of disability worldwide and has an increased risk of premature mortality. (Olfson, Gerhard, Huang, Crystal, & Stroup, 2015) They also suffer from significant comorbidities, alcohol, and substance abuse, and resulting social isolation and personal neglect or significant caregiver burden. (Kennedy, Taylor, Degtiar, & Hornberger, 2014) The overall economic cost of schizophrenia in USA was $155 billion in 2013 (Coultier, et al., 2016) resulting in significant burden on the patient, caregivers, payers and the society.

Schizophrenia patients face inadequate services while presenting challenges in maintaining optimal treatments. (Zipursky, 2014) Factors ranging from poor treatment

response, lack of treatment adherence, treatment side effects, substance abuse, significant comorbidities to loss of functioning and caregiving support makes it a very challenging disease to manage. (Dutta, Spoorthy, Patel, & Agarwala, 2019) There is evidence that treatment for schizophrenia is significantly delayed. Reasons such as lack of education or awareness, stigma and financial constraints, lack of family support play a huge role in resulting a delay between onset of psychosis and treatment. In many cases by the time the patients receive treatment they have loss of functioning. (Dutta, Spoorthy, Patel, & Agarwala, 2019)

There is also, significant empirical work in the last decade that has revealed stark differences between Black and White communities in the schizophrenia diagnoses rate, treatment strategies, and outcomes post-treatment. Blacks have disproportionately higher diagnosis rate, higher use of older technologies and worse outcomes. (Alang, 2019) (Cook, et al.) The challenges in managing schizophrenia as a disease is further exacerbated due significant stigma, prejudice and discrimination against people with mental illness. These can lead to delayed therapies and makes the patient more prone to emergency care. (American Psychiatric Association, 2024)

Given the challenges that schizophrenia patients face due to their disease such as communication difficulties, cognitive impairment, lack of caregiving or social support, they encounter multiple barriers in seeking high quality primary care. The fragmented healthcare delivery in the United States makes it even more difficult to seen optimal timely care. Thus, these patients seek more emergency care and many of those result in hospitalizations which could have been prevented with timely primary care. A study conducted with data on 1000

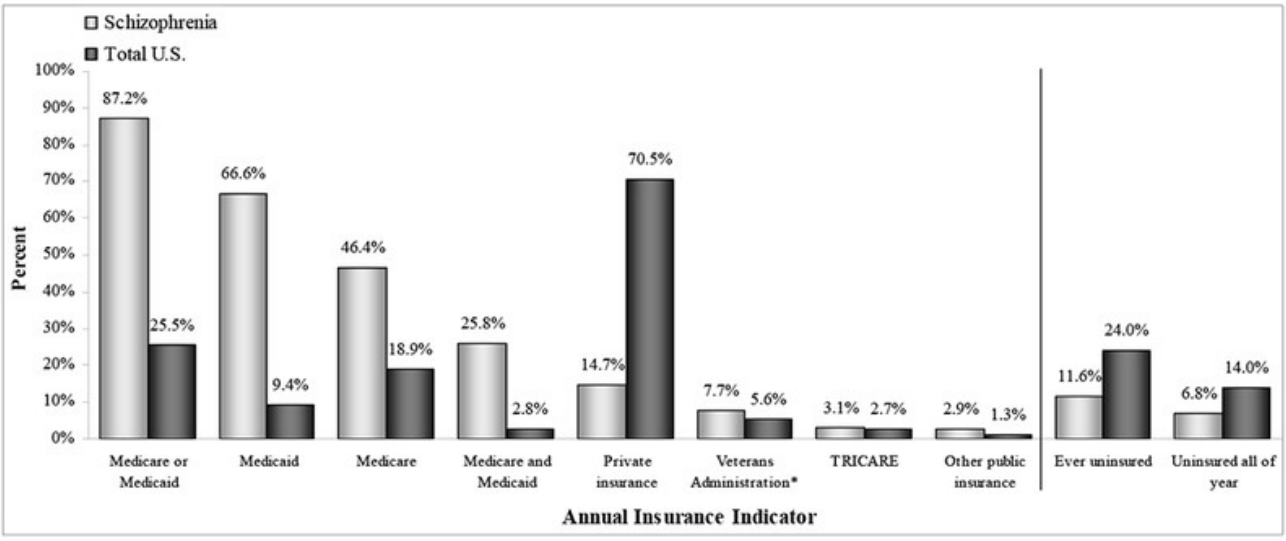
hospitals across 35 states in United states, showed that schizophrenia was associated with increased odds of acute preventable hospitalization (OR 1.34, 95% CI 1.31-1.38). (Cahoon, McGinty, Ford, & Daumit, 2013)

According to National Institute of Mental Illness, 5.3 percent of US adult population has SMI and prevalence estimates range from approximately 0.25% to 0.64% (Kessler, et al., 2005) to approximately 1% (APA, 2024) of US adult population has schizophrenia. Although the incidence of schizophrenia is low (McGrath, Saha, Chant, & Welham, 2008) the chronic nature of the disease with multiple relapses characterized by periods of psychosis lead to multiple ER visits, hospitalizations, and significant economic burden. (Ascher-Svanum, et al., 2010). Schizophrenia and mood disorders were found to be the top 10 diagnosis for high utilizers by Healthcare Cost and Utilization Project (HCUP) researchers. (Jiang, Weiss, Barrett, & Sheng, 2012) SU in this study was defined as patients who had at least four hospital stays during the study period which was year 2012. This research also found that schizophrenia was the second most common diagnosis among the Medicaid and Medicare SU patients. (Jiang, Weiss, Barrett, & Sheng, 2012) Among Medicaid patients, schizophrenia inpatient cost was a significant cost driver. (Jiang, Weiss, Barrett, & Sheng, 2012) (Ascher-Svanum, et al., 2010). High cost of managing schizophrenia is confirmed by a study by Broder (Broder, et al., 2018) which found, in 2016 dollars, cost of managing schizophrenia patients annually to be $34,204 vs. $26,396 for Bipolar patients.

2.61 SCHIZOPHRENIA IN MEDICAID

Although the prevalence of schizophrenia among U.S adults is below 1% (APA, 2024), it a common diagnosis among Medicaid patients. This is expected as Medicaid is a public insurance program that provides health coverage to low-income and disabled individuals and schizophrenia is a disabling disease and thus highly correlated with poverty and unemployment. In US, 67% of insured schizophrenia patients in the United States were covered by Medicaid. (Khaykin, Eaton, Ford, Anthony, & Daumit, 2010) Figure 2.4 below shows the disproportionate coverage of schizophrenia patients in Medicaid followed by Medicare system in US. High prevalence along with the evidence that schizophrenia patients incur significant healthcare cost due to multiple relapse related hospitalizations, makes it important to understand its role in super utilization of Medicaid healthcare resource. (Ascher-Svanum, et al., 2010) Evaluation of the characteristics of schizophrenia patients who are SU may help in designing and implementation of effective health care solutions for schizophrenia patient population who would benefit from more intensive and integrated levels of care or support.

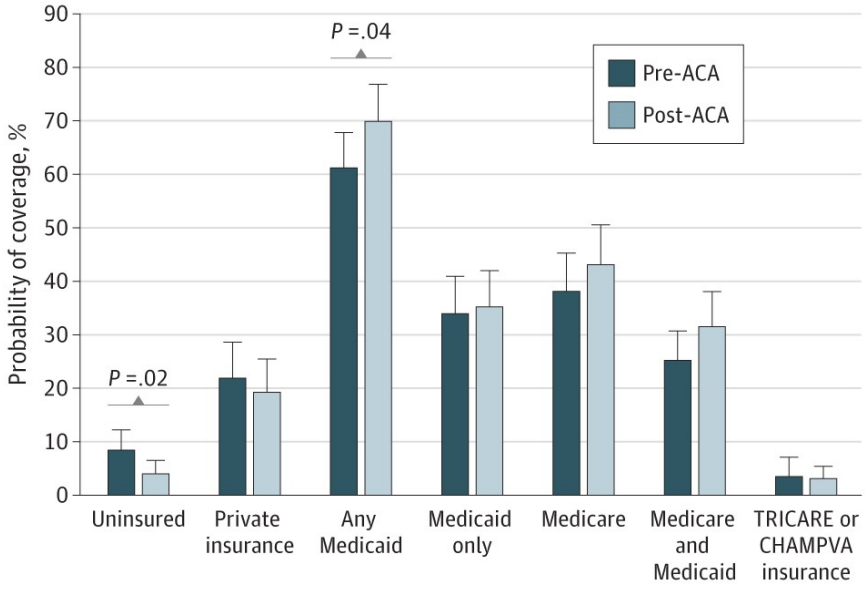
Figure 2. 3: Coverage of schizophrenia in US health systems



Health insurance among U.S. noninstitutionalized civilian adults with schizophrenia and persons in the U.S. general population. Source: (Khaykin, Eaton, Ford, Anthony, & Daumit, 2010). Data were from the Medical Expenditure Panel Survey—Household Component, 2002–2006.

A recent 2023 study by Geissler confirmed that Medicaid is the major insurance source for schizophrenia with a probability of 70% coverage under any Medicaid. It concluded a decrease in uninsured schizophrenia patients due to Obamacare that was enacted in 2010. (Geissler, et al., 2023)

Figure 2. 4: Probability of Insurance Coverage Types for Individuals with Schizophrenia (2008 to 2020)



Source: Geissler 2023 (Geissler, et al., 2023)

2.7 RESEARCH RATIONALE

Given the role schizophrenia plays in high utilization of health resources, it is important to understand the factors associated with SU of resources. Significantly disproportionate proportions of all diagnosed schizophrenia patients, approximately 70%, are covered by the government funded Medicaid insurance plans. Thus, this thesis aims to extend the literature in understanding of High Utilization among patients with schizophrenia in the US Medicaid System as it may provide policy guidance for optimal management of schizophrenia patients who are at risk of multiple acute needs for hospitalizations or emergency services.

The purpose of this research is also timely as the Coronavirus pandemic has expanded the footprints of Medicaid in US. In 2022, 74 million people were enrolled in Medicaid. Thus, the main aim of this research is to characterize super utilization of resources by Schizophrenia patients in US Medicaid system and study the factors associated with the super utilization. The current research

1. Conducted a systematic review of cost of managing schizophrenia in US health system.

2. Characterized high utilization among Schizophrenia patients in the US Medicaid System.

3. Analysed factors associated with Super Utilization of resources among Medicaid schizophrenia patients.

The research will serve the following purposes:

1. Inform researchers on the healthcare utilization among schizophrenia patients.
2. Inform researchers on the factors that may predict high utilizers among schizophrenia patients.
3. Enable development of health management strategies & programs that may prevent expensive schizophrenia relapse and hospitalizations thus reducing cost and enhancing health outcomes and improving patients' quality of life.
4. Further research in area of schizophrenia burden and care management.

2.8 THEORETICAL FRAMEWORK FOR PROPOSED RESEARCH

The Dahlgren and Whitehead "Rainbow Model" (Dyar OJ, et al., 2022) provides the theoretical framework to identify factors impacting high utilization of resources by severe mentally ill schizophrenia patients. The “Rainbow Model” provides a powerful framework for understanding how mental health such as schizophrenia is shaped by various layers of social, economic, and environmental factors. This allows the researchers to explore beyond biological factors to other social and environmental issues that impact mental health and may need to be addressed if a policy is to be designed for population health improvement.

The Rainbow Model organizes determinants of health into five concentric layers with the individual in the centre.

- Core: Individual characteristics such as age, sex, and co-morbid conditions. These factors may not exist in isolation and may be impacted by lifestyle factors.

- Second layer: Individual lifestyle factors such as diet, alcohol & substance abuse. These individual lifestyle factors may be impacted by broader societal influence such absence for good grocery stores close to their residence (Compton & Ku, 2023) or lack of preventative health services. (Mueser, et al., 1990)

- Third layer: This layer includes Social and community network factors such availability of caregivers, which is very important in a severely mentally ill patient with schizophrenia and wider community support. Presence of stigma or discrimination in schizophrenia patients can reduce social support or employability or ability to socially interact. (Corrigan, Druss, & Perlick, 2014)

- Fourth layer: This layer includes living and working conditions such as access to healthcare, housing or education. These factors are very important for schizophrenia patients, to stay in recovery phase. (Mueser, et al., 1990)

- Fifth and Outer layer: General socioeconomic, cultural, and environmental conditions such as mental health funding policies, cultural beliefs and stigma and environmental pollution.

The final structure of the predictive model will rely on the above framework, findings from existing literature and availability of patient level data elements.

2.9 STRUCTURE OF THE THESIS

In addition to the summary, introductory and a final conclusive discussion chapter, this thesis consists of three additional chapters which cover a systematic literature review of the economic burden of schizophrenia in the US across all insurance systems, an empirical description of the high healthcare utilization among schizophrenia patients in US Medicaid system and finally a chapter summarizing the method, data and results of the empirical analysis researching the factors associated with high utilization of resources among schizophrenia patients in the US Medicaid system.

A systematic review of cost of managing schizophrenia, presented in chapter three, will highlight the seriousness of this disease and will provide rationale for further research into the factors that are associated with high utilization among the patients who suffer from this burdensome disease. It will also provide guidance on potential factors that may be behind the high utilization and thus worse disease outcomes.

Characterization of schizophrenia patients and the extent of resource utilization in chapter 4 provides the analysis of a large Medicaid database in terms of demographics and utilization of both ER and hospital services. It provides the foundation for chapter 5 which has the methods and analysis results of the regression model to identify factors that are strongly associated with high utilization of resources among Medicaid patients in the US.

CHAPTER 3. ECONOMIC BURDEN OF SCHIZOPHRENIA IN THE UNITED STATES: A SYSTEMATIC LITERATURE REVIEW

3.1 INTRODUCTION

Schizophrenia is a debilitating chronic disease with significant burden for patients and their care givers. (Awad, Awad, & Voruganti, 2008) It affects approximately 0.25% to 0.64% (Kessler, 2005) to approximately 1% (APA, 2024) of US adult population and has an incidence rate ranging from 10.2 to 22 per 100,000 person years. (Offord, Lin, Mirski, & Wong, 2013). Although the incidence of schizophrenia is low, the chronic nature of the disease with multiple relapses characterized by periods of psychosis leads to ER visits and hospitalization and consequently significant economic burden. (Ascher-Svanum, et al., 2010) It is also one of the top 10 causes of disability with significant negative impact on life expectancy. On an average a schizophrenia patient may live 12-15 years less than general population in US. (Kennedy, Taylor, Degtiar, & Hornberger, 2014) This debilitating disease has its onset during the most formative years of an individual, age 16 to 25, leading to significant impact on their ability to live a productive life. They also suffer from significant comorbidities, alcohol, and substance abuse, and resulting social isolation and personal neglect or significant caregiver burden. (Kennedy, Taylor, Degtiar, & Hornberger, 2014) A meta-analysis of Quality of Life (QOL) standardized measures by Dong et al confirmed that QOL in schizophrenia subjects is significantly lower than healthy controls. (Dong, et al., 2019)

Not surprising the overall economic cost of schizophrenia in USA is significant and continues to increase over the years. It was estimated $155 billion in 2013 (Coultier, et al.,

2016) and it doubled by 2019 to 343 billion as recently estimated by Kadakia et al. (Kadakia, et al., 2022) It results in significant burden on the patient, caregivers, payers and the society. The severity of this disease with psychiatric and physical symptoms and functioning impairments requires, in many cases, substantial family caregiving support. Thus, families of schizophrenia patients spend significant resource and time caring for them as they live in constant fear of relapse. (Patel & Chatterji, 2015). Cloutier study showed that on an average a schizophrenia patient in US can annually cost as high as $44,773 per annum and a significant driver behind the cost was frequent hospitalizations and ER visits due to disease relapse. (Cloutier, et al., 2016) In addition, there is significant incremental cost to the society due to resultant loss in terms of productivity and quality of life of the patient and in many cases of their caregivers. (Caqueo-Urízar, Caqueo-Urizar, Gutierrez-Maldonado, & Miranda-Castillo, 2009) (Gupta, Isherwood, Jones, & Van, 2015)

Given the significant overall economic burden of schizophrenia, it is important to conduct a systematic literature review to characterize the resource utilization by these patients in the United States health care system. A review of cost of managing schizophrenia will highlight the seriousness of this disease and will provide evidence to gather factors that may be behind the high utilization and thus worse disease outcomes. This will enable development of disease management strategies focused on preventing relapses and resulting cost, loss of quality of life and productivity of the patients and their caregivers.

Cost of managing schizophrenia may differ across payers due to differences in age, race and other socio-economic factors in the membership across various key US health plans.

Although there have been systematic literature reviews of schizophrenia cost by some payer types, there has been no systematic literature review of cost of managing schizophrenia in US across all key payers. A comprehensive review by all payers will serve following purposes:

1. Inform researchers on the healthcare utilization among schizophrenia patients by different health systems and allow us to compare and contrast them.
2. Inform researchers on the factors that may be associated with high utilization of resources among schizophrenia patients.
3. Enable development of plan specific health management strategies & programs that may prevent expensive schizophrenia relapse and hospitalizations thus reducing cost and enhancing patient health outcomes.
4. Further research in area of schizophrenia care management.

3.2 OBJECTIVES OF LITERATURE REVIEW:

The main objective of this systematic literature review is to synthesize real world evidence on direct cost or resource used in the management of schizophrenia by all the payers in the United States of America. This will provide the rationale for additional research to understand the distribution of the utilization of resources among this cohort of patients. As a small cohort of schizophrenia patient may be resulting in significant portion of the overall resource utilization and cost, the literature review was conducted with following two secondary objectives:

1. To compile various definitions of high or super utilizers in schizophrenia patients

2. To identify and understand factors that may play a role in high utilization of resources.

3.3 METHOD: SYSTEMATIC LITERATURE REVIEW APPROACH

A systematic approach was taken to thoroughly review relevant evidence from peer-reviewed published literature, dissertation, systematic reviews, and registries of observational studies published from January 2000 to August 2021. Given the multiple approaches, different time-period, and heterogenous outcome variables of the studies, a quantitative meta-analysis was not feasible. Hence, a qualitative narrative synthesis was conducted based on the Popay's guidance. (Popay, et al., 2006)

3.3.1 INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria in the papers or reports of the literature searched were as follows: Schizophrenia or schizophrenic disorder, SMI, Serious Mental Illness, US studies, real world studies, Quantitative study, Longitudinal study, Retrospective study & Prospective study.

Exclusion criteria were as follows: Clinical studies, articles before 2000, adult less than 18 years, non-cost or non-resource use studies, qualitative studies, mixed-methods studies. Table 3-1 below lists the criteria and provides the rationale for them.

Table 3. 1: Literature Review: Inclusion Criteria with Rationale

Inclusion criteria	**Rationale**
Schizophrenia or schizophrenic disorder	Disease of interest
Serious Mental Illness and its acronym SMI	As schizophrenia is included in the definition of Serious Mental Disorder (SMI)
US Studies	As healthcare differs by country the study just focuses on US findings
Real world studies	Resource utilization can be observed best in real world settings
Quantitative	To study the extent of the resource use
Longitudinal	It needs to be studied over a period of time to assess robust resource use
Retrospective & Prospective	Both approaches are relevant
Reviewed publications, dissertation, systematic reviews, and registries	To include all robust sources not found in the primary review
Exclusion criteria	**Rationale**
Clinical studies	A controlled environment of clinical trials will not reflect real world resource use
Studies before 2000	Atypical treatment fundamentally changed schizophrenia care by providing new treatment options with a more favourable side-effect profile compared to older medications. The new drugs offered broader symptom control, better adherence and promised improvements in overall quality of life, which shifted the focus of treatment beyond simply preventing relapses. Although 1990s saw the launches of atypical antipsychotics, it took years for them to become a standard of care for patients with schizophrenia. (Weiden, 2006) Furthermore, adoption of atypical Long-Acting medications, with adherence benefits, changed the health resource use dynamics with lower relapse and subsequent hospitalization. (Pesa, Doshi, Wang, Yuce, & Basur, 2017) (D'Arrigo, 2021) Since the current study objective is to characterize emergency and hospitalization use by schizophrenia patients, it was important to study the time period that included significant use of latest treatment options. Hence, it was decided to include studies

	published after 2000. This does allow for evidence generated in late 1990s which is the period of adoption of atypical medicines.
Adult less than 18 years	Schizophrenia symptoms generally start in the mid- to late 20s. Schizophrenia is considered early onset when it starts before the age of 18. Onset of schizophrenia in children younger than age 13 is extremely rare and presents differently.
Non cost or non-resource use study	Outside the scope as the focus of the study is resource use
Qualitative studies	The rationale to exclude qualitative studies was threefold: i. Qualitative and Mixed-methods research on a vulnerable population, such as individuals with schizophrenia, introduces challenges in ability to remember and describe resource use hence these studies were not included. ii. Qualitative studies on caregivers have multiple challenges such as recruitment, time commitment, fears. iii. The studies required comprehensive measurable evidence on resource use which can be derived from quantitative studies.
Mixed-methods Studies	Similar to rationale for Qualitative studies
Grey Literature	To maintain robustness of findings
Non-English language literature	To include only US studies

3.3.2 A COMPREHENSIVE SEARCH STRATEGY

The literature search strategy is as follows:

Population: Adult patients (18 years and above) with schizophrenia in the US health plans.

Interventions: The review will not consider any intervention. It will review resource utilization by schizophrenia patients.

Context: The study will be limited to United States given the treatment and health management variability among different countries.

Comparator: Patients who do not have schizophrenia

Outcomes:

- Healthcare resources utilization by schizophrenia patients (Cost, Hospitalization, ER use, Outpatient, Prescriptions).
- Definition of high utilization among schizophrenia patients.
- Characteristics of schizophrenia patients who are high utilizers.

Study designs: Real world, retrospective, prospective cohort studies and surveys on cost and resource use.

3.3.3 SEARCH TERMS

The search terms were Schizophrenia, schizophrenia disorder, SMI, Serious Mental Illness, United states, America, USA, US, Unites States of America, cost, utilization, utilisation, utilizer, utiliser, resource use. Details of the search strategy are in Appendix I.

3.3.4 SOURCES

The search includes peer reviewed publications, dissertation, systematic reviews, and registries. It excludes grey literature. The search will be limited to English language as the review focuses is on schizophrenia patients in USA.

3.3.5 TIME PERIOD:

As the treatment for schizophrenia have changed significantly with adoption of atypical anti-psychotics and long-acting medications search period will begin January 1, 2000, and cover till 14th of August 2021.

3.3.6 DATABASE SEARCHED:

A Medline Complete, Cinnahl, APA PsycInfo, and APA PsycArticles search was conducted on August 14, 2021, using the search terms below:

(schizophrenia OR schizophrenic disorder OR "serious mental illness" OR SMI) AND (cost or utili or "resource use") AND (united states or america or usa or u.s or united states of america or u.s.a)*

Given the Medicaid system has disproportionate higher prevalence of schizophrenia patients (Pilon, et al., 2021) and thus higher associated burden of its management, a focus search was conducted on super utilization in Medicaid channel using following terms,

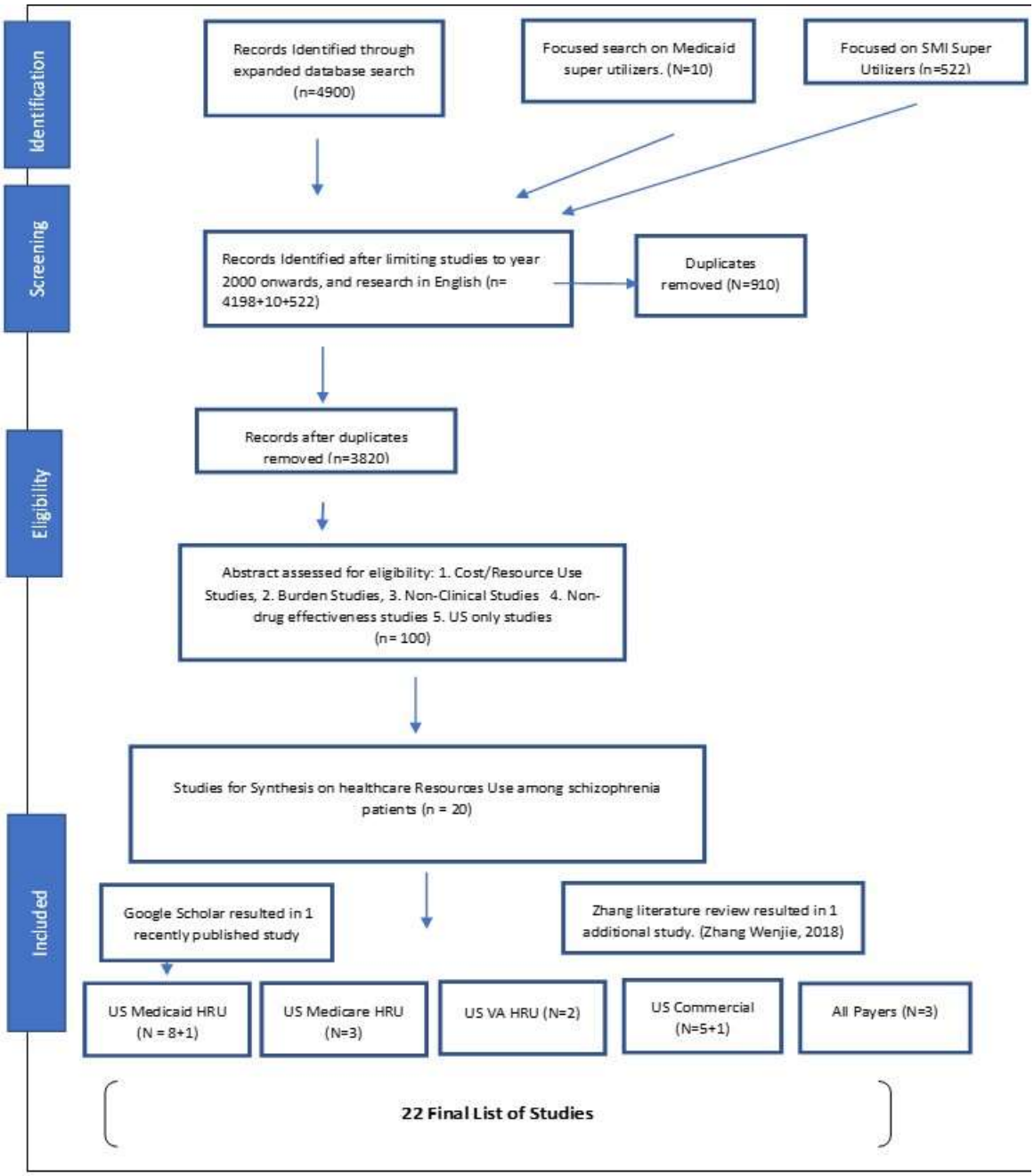
"Medicaid", "super util or "high util*" or superutil**

To confirm inclusion of all high or super utilization studies, a separate focused search was also run on SMI and schizophrenia high and super utilizers using following search terms:

(schizophrenia or SMI) AND ((high utili) or (super utili*)) AND (united states or america or usa or u.s)*

Abstracts of all the studies were reviewed for resource utilization and cost evidence. The Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) flowchart details the main and supplemental strategies along with outcomes (Figure 3-1).

Figure 3. 1: PRISMA



3.3.7 QUALITY APPRAISAL

Critical appraisal tools vary based on intent, components, and construction of the systematic reviews. For the current research, the studies were critically appraised using

adapted Joanna Briggs Institute (JBI) Critical Appraisal (JBI, 2017) to ensure comprehensive, unbiased and valid findings. They were appraised for 9 quality attributes. Each attribute was accounted as a score of one. The scores are additive and the studies with a total score 7 and above were included for final synthesis.

The 9 attributes for study quality were:

1. Is there a well-defined research question?

2. Is there comprehensive description of alternatives?

3. Are all important and relevant costs and outcomes for each alternative identified?

4. Are costs and outcomes measured accurately?

5. Are costs and outcomes valued credibly?

6. Are costs and outcomes adjusted for differential timing?

7. Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?

8. Do study results include all issues of concern to users?

9. Are the results generalizable to the setting of interest in the review?

Given each attribute had a score of 1, a maximum score a study could get was 9. The Quality Appraisal tool is included in Appendix II.

3.3.8 DATA EXTRACTION

Key data elements were manually extracted after careful assessment of the papers. The data elements were Authors, Methodological approach, Study period, Payer Types, Study population, Resource use, Definition of high cost and the Data source. Details of the data extraction is included in Appendix III.

3.4 SYNTHESIS OF RESOURCE UTILIZATION: A THREE STEPS APPROACH

First, the literature reviews on resource utilization were assessed for relevant studies for the final review. Then a critical appraisal was conducted on all remaining studies for final synthesis. Third, to provide understanding of the current body of research and the gaps in this literature, a detailed qualitative review of the remaining 22 studies was conducted on the cost and resource use of managing schizophrenia patients by all insurance types in the United States. The following tools as per Popay et al (Popay, et al., 2006) guidance was applied to synthesize the findings of the final 22 studies.

1. Brief descriptions of studies

2. Groupings and clusters by payers

3. Tabulation of the findings and transformation of data into a common rubric: Methodological approach, Study Period, Study population (all, men only, Women only, other sub-groups), Resource use: cost per patient per annum, Other Resource use, Data source, and Critical Appraisal Score.

4. Counting the frequency of the result

5. Thematic and content analysis.

Two supplementary assessments on the above primary literature review were also conducted. Firstly, a descriptive synthesis was done to understand the key drivers of the cost across all payer types. A second supplementary analysis included a synthesis of evidence on the definition of high utilization of resources by schizophrenia patients was summarized. This assessment would later assist in defining super utilizers and understanding the drivers behind their high utilization of resources.

Microsoft Word was used to manage references.

3.5 PRIMARY SEARCH RESULT

The main search yielded 4900 articles. Once all the articles before year 2000 were removed, 4226 remained. Exclusion of non-English articles led to 4198 articles. A supplemental search on super utilization in Medicaid channel resulted in ten articles. After abstract review, one relevant study on "Characteristics of Hospital and Emergency Care Super-utilizers with Multiple Chronic Conditions" by Harris (Harris, et al., 2016) was included. The second supplemental search focused on high or super utilization among SMI and Schizophrenia resulted in 522 studies. When compared to main search results, no additional studies were added to the list. Once the duplicates were removed, 3820 articles remained. An abstract review with following eligibility criteria: 1. Cost/Resource Use Studies, 2. Burden Studies, 3. Non-Clinical Studies 4. Non- drug effectiveness studies 5. US only studies resulted in 100 studies. A recent study by Pilon (Pilon, et al., 2021) was included through a Google search for

recent studies post August 2021. An evaluation of a literature review by Zhang (Zhang Wenjie, 2018) led to inclusion of an incremental study by Wilson (Wilson, Gitlin, & Lightwood, 2011). This study was not in the original search as it was not listed on PubMed. This brought the total studies to 102.

Post critical appraisal, only 22 studies remained as the other studies did not have robust relevant cost and resource utilization data. Although, most of remaining 22 studies still missed on sensitivity analysis and generalizability attributes, they received a score of 7 out of 9 attributes needed for inclusion. The list of selected studies with their critical appraisal scores along with key data that were manually extracted for systematic narrative synthesis are presented below in Table 3.2 by various payer categories. Out of 22 studies, 9 were on Medicaid, 3 were on Medicare, 2 studies were on US Veteran Affairs (VA) system, 6 on private insurance or Commercial and 3 studies were in All-payer category. There was 1 study by Hendrie that had data for both Medicare and Medicaid and hence was reviewed and included in both categories. (Hendrie, Wanzhu, Rebeka, Ambuehl, & Callahan, 2014)

Table 3. 2: Selected Lit for Review of Schizophrenia cost & resource use in the US by different payers

	Authors	**Methodological approach**	**Study Period**	**Study population (all, men only, Women only, other sub-groups)**	**Resource use: cost per patient per annum**	**Other Resource use**	**Data source**	**Critical Appraisal Score**

Medicaid System

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
1	McCombs J. et al (McCombs, Nichol, Johnstone, & Lizheng, 2000)	Retrospective analysis OLS model	1985-1996	Schizophrenia	$25,940 per patient per year	None	Medi-Cal 5 % file	7/9
2	Bartels et al 2003 (Bartels, Clark, Peacock, Dums, & Pratt, 2003)	Retrospective comparative analysis dual eligible in New Hampshire Compare to other diseases	1999	Schizophrenia Depression Dementia Non-psychiatric	Per annum cost among 65-75 years: $ 39,154 $11,304 higher than depression and $28,256 higher than other medical disorders	None	New Hampshire Dual	7/9
3	Miller L S. (Miller & Bradley, 2004)	Autoregressive integrated moving average time series models to forecast	1990-1997		PMPM: $700 Medicaid With increasing prescription cost trend	Estimated in 1995 dollars: 700 times 12 = $10,800	Medicaid Georgia State-based institutional data: DHR	7/9
4	Lum T. Y. (Lum, et al., 2013)	Retrospective Logistic & Two-part model	2005	Elderly with Mental Disorder	Among the five MHDs, major depression and schizophrenia were associated with the highest percentage increase in total health care expenditures of 73% ($17,607)	None	CMS dual eligible data	7/9

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
					and 72% ($14,356), respectively, followed by anxiety (63% or $15,689)			
5	Shim, R. S. et al (Shim, et al., 2014)	Retrospective cohort analysis of claims data for Medicaid beneficiaries with both schizophrenia and diabetes	2006-2007	Schizophrenia Only, Diabetes only, non-Diabetes & non-Schizophrenia	None	Medicaid patients with comorbid diabetes and schizophrenia had an average number of 7.5 ED visits per year, compared to the sample Medicaid population with neither diabetes nor schizophrenia (1.9 ED visits per year), diabetes only (4.7 ED visits per year), and schizophrenia only (5.3 ED visits per year)	Medicaid data on fourteen Southern states: Medicaid Analytic File	7/9
6	Hendrie et al. (Hendrie, Wanzhu, Rebeka, Ambuehl, & Callahan, 2014)	Observational cohort study Schizophrenia vs. no schizophrenia	1999-2008	31,588 older adults with schizophrenia	Medicare, mean per annum spend $63335.01 vs $49829.53. Medicaid, mean per annum spend. $130954.01 vs. $19996.80	Mean Hospital Days 58.98 vs. 31.10 days	Urban Public Health System	8/9
7	Pesa J. et al (Pesa, Doshi, Wang, Yuce, & Basur, 2017)	Retrospective matched cohort Paleperidone Palmitate Long Acting Injectable (LAI)treatmen	2009-2013	Adult schizophrenia	$25,546 vs. $25,307 Per patient per year	None	MediCal (California Medicaid)	7/9

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
		t vs. Orals anti-psychotic treatment for 12 months						
8	Shah, A. et al (Shah, Xie, Kariburyo, Zhang, & Gore, 2018)	Propensity score matching (PSM) between the LAI cohort and the oral anti-psychotic treatment. Outcomes were assessed over a 12-month period	2011-2014	Adult Schizophrenia	Overall, both cohorts had similar total medical costs (LAI vs. oral: $24,988 vs. $23,887, p = 0.354) during the follow-up period.	Patients prescribed LAIs had lower monthly inpatient ($US4007 vs. 8769, p \0.001) and ER visits costs ($682 vs. 891, p \ 0.001) but higher monthly medication costs ($10,713 vs. $655, p \0.001)	Truven Medicaid Data	9/9
9	Pilon et al (Pilon, et al., 2021)	Retrospective matched cohort design. Data from Six Medicaid states. Compared to non-schizophrenia	1998-2018	All adults and young adults (18-34 years) who have schizophrenia	$28,644 vs. $14,557 (all adults)	Mean 2.0 (vs. 1.12) in ER and 1.3 (0.66 day) inpatient days per annum	Iowa, Kansas, Mississippi, Missouri, New Jersey and Wisconsin Medicaid data	8/9

Medicare System

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
10	Merrick E. et al (Merrick, Perloff, & Tompkins, 2010)	Descriptive	2004	Emergency utilization by Medicare Schizophrenia vs, Depression patients	None	Disabled beneficiaries with a psychiatric ED 9.5% (major depression) 19.8% for schizophrenia. Percentage of aged beneficiaries with any psychiatric ED use ranged from 5.4% major depression to 8.6% for Schizophrenia	Medicare 5%	8/9
6	H (Hendrie, Wanzhu, Rebeka, Ambuehl, & Callahan, 2014)	Observational cohort study Schizophrenia vs. no Schizophrenia	1999-2008	31,588 older adults with schizophrenia	Medicare, mean per annum $63335.01 vs $49829.53 Medicaid, mean per annum $130954.01 vs. $19996.80	Mean Hospital Days 58.98 (vs. 31.10	Urban Public Health System	8/9
11	Feldman, R (Feldman, Bailey, Muller, Le, & Dirani, 2014)	Retrospective Comparison with non Medicare beneficiaries diagnosed with non-schizoaffective schizophrenia	2001-2009	Non schizoaffective Schizophrenia	The cost of care for schizophrenia member in 2009 was, on average, 80% higher than for the average member per patient year (2010 dollars)	None	Medicare 5% file	7/9

VA System

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
12	Zhu B. (Zhu, et al., 2008)	Observation non interventional study	1997-2003	Schizophrenia with recent crisis	Average annual mental health treatment costs who attempted suicide ($46,024), followed by persons with psychiatric hospitalization ($37,329), persons with prior arrests ($31,081), and persons with violent behaviours ($18,778). Total cost was not significantly higher for those with co-occurring substance use disorder ($19,034).	None	U.S. Schizophrenia Care and Assessment Program (US-SCAP), a prospective, non-interventional, non-randomized, 3-year observational study	8/9
13	Doran, K (Doran & Rosenhenck, 2013)	Retrospective	2010	High ED users	None	Patients with schizophrenia were 6.9 times more likely to be in the most frequent ED use group	VA	8/9

US Commercial/Private Insurance System

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
14	D. Nicholl et al. (Nicholl, Kasem, Diels, & Schadrack, 2010)	Recent diagnosed vs. chronic	1998-2007	Within Schizophrenia	The mean annual healthcare costs of recently diagnosed patients were also greater ($20,654 vs $15,489) Chronic	None	Pharmetrics Database	8/9
15	Wilson et al (Wilson, Gitlin, & Lightwood, 2011)	Claims database analysis of a	June 2001– May 2004	Newly diagnosed patients vs. previously	Total: $15,282 vs. $12,029 ($p$ = 0.09)	None	Private Insurer	7/9

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
		private insurer		diagnosed patients Within schizophrenia	Total inpatient services: $7,745 vs. $4,440 ($p$ = 0.03) Total prescriptions: $3,165 vs. $4,548 ($p$ = 0.002)			
16	Offord, S et al (Offord, Lin, Mirski, & Wong, 2013)	Early nonadherence vs. not	2006-2009	13-65 years of age and within schizophrenia	$15,400 (22,149) vs. $17,636 (33,791)	None	Marketscan	9/9
17	Fitch et al (Fitch, Iwasaki, & Villa, 2014)	Retrospective matched cohort	2007-2011	Schizophrenia Vs Non-Schizophrenia	The mean monthly cost for a patient with schizophrenia was $1806, which is more than 4 times the mean monthly cost of $419 for a demographically matched member without schizophrenia	None	Marketscan	8/9
18	Cloutier et al (Cloutier, et al., 2016)	Retrospective matched cohort	2013	Schizophrenia	Medication = $3,500 Outpatient = $2,468 Inpatient = $5,160 ED = $871 Other medical = $281 Total = $12,461	None	Marketscan Commercial	8/9
19	Huang Ahong et al (Huang, Amos, Joshi, Wang, & Nash, 2018)	Longitudinal retrospective 1=18-35 years schizo vs. matched non-schizo	2011-2016	9,889 schizophrenia patients vs. non	23.70% were young adults (aged 18–35), had higher all cause per-patient-per-year (PPPY) costs ($22,338 vs $7,332; p < .0001), higher inpatient costs ($8,857 vs $1,289; p < .0001),	longer inpatient length-of-stay (LOS) (5.0 vs 0.4 days, p < .0001	OptumInsight	9/9

All-Payers

	Authors	Methodologic Approach	Study Period	Study population (all, men only, Women only, other sub-groups)	Resource use: cost per patient per annum	Other Resource Use	Data Source	Critical Appraisal Score
20	Chwastiak et al (Chwastiak, et al., 2009)	Data from antipsychotic trials (CATIE trial): all vs Obese patients	2001-2003	Schizophrenia patients only	$1726 X 12 = $20,712	None	CATIE trial	8/9
21	Desai, Pooja et al (Desai, Lawson, Barner, & Rascati, 2013)	Retrospective	2005-2008	Within schizophrenia	The mean cost per patient-year was $3,656 (SE=$283) for the low-cost group and $27,944 (SE=$4,639) for the high-cost group	None	MEPS	9/9
22	Broder Michael S., (Broder, et al., 2018)	Retrospective claims	January 1, 2012 - June 30, 2016	Schizo vs. Bipolar vs. both	All-cause total health care costs were highest in the cohort having a diagnosis of both SCZ and BD-I (mean [SD]), $51,085 [$62,759]), followed by the SCZ alone cohort ($34,204 [$52,995]), and the BD-I alone cohort ($26,396 [$48,294])	Hospitalization (67.4% vs 39.5% in SCZ alone and 33.7%)	*Truven*	9/9

3.5.1 KEY FINDINGS ON SCHIZOPHRENIA PATIENTS IN MEDICAID

Among the key health insurers in the United States, Medicaid provides disproportionate coverage to schizophrenia patients. The impact schizophrenia disease management on the

Medicaid budget has been considerable. Among the 9 studies, 5 have compared the direct cost or resource use of managing schizophrenia in comparison to similar patients without schizophrenia. These studies are by Bartels, Hendrie, Pilon, Shim and Lum. (Bartels, Clark, Peacock, Dums, & Pratt, 2003) (Hendrie, Wanzhu, Rebeka, Ambuehl, & Callahan, 2014) (Shim, et al., 2014) (Pilon, et al., 2021) (Lum, et al., 2013). Bartels's et al study concluded that annual cost of managing an elderly Medicaid schizophrenia patient, age 65-75 years, was $39,154 which was $11,304 higher than similar patient with depression and $28,256 higher than for patients with other medical disorders. Hendrie study also concluded that elderly Medicaid schizophrenia patients had much higher cost, but its annual cost estimates were significantly higher at $130954.01 versus only $19996.80 for non-schizophrenia patients. It also found that Annual Mean Hospital Days for schizophrenia patients were 58.98 versus 31.1 days for matched cohort of non-schizophrenia patients. Both studies are among elderly, but Hendrie's analysis is more recent and focused on urban health systems that are typically more expensive, which perhaps explains the significantly higher cost estimates.

A third study excluded elderly Medicaid recipients and includes all adult Medicaid patients aged 18-64 from 14 southern states of the United States. (Shim, et al., 2014) It provided estimates on resource use in terms of Emergency Department (ED) use per year instead of overall cost of managing schizophrenia patients. This study provides robust estimate showing much higher annual ED visits by a schizophrenia patient (5.3 visits) in comparison to patients with diabetes only (4.7 visits) and patients with neither schizophrenia nor diabetes (1.9 visits). The fourth Medicaid study in this review is a recent analysis by Pilon (Pilon, et al., 2021). This study was conducted on Medicaid data on all adult members from six US states and it

confirms that Medicaid patients with schizophrenia cost were more than similar patients without this disease in terms of annual cost ($28,644 versus $14,557), in terms of annual Emergency Room (ER) use (2.0 versus 1.12) and in terms of inpatient days per annum (1.3 versus 0.66). There was a difference in estimates observed between Shim and Pilon which may be due to data sourced from different state, different age cohort and the study time period.

Lum's study also compares cost of managing schizophrenia to other diseases but in terms of increase in resource use. (Lum, et al., 2013) It concluded that among five mental health diseases, schizophrenia and depression were associated with highest annual increase in total health expenditures of 72% ($14,356) and 73% ($17,607) respectively, followed by anxiety (63% or $15,689).

Studies by Pesa and Shah made comparisons within groups of schizophrenia patients and provided insights into factors that may lead to high utilization among schizophrenia patients. (Pesa, Doshi, Wang, Yuce, & Basur, 2017) (Shah, Xie, Kariburyo, Zhang, & Gore, 2018) They highlighted sub-adherence to treatment among schizophrenia patients as a major driver behind healthcare resource use. Their study analysed the impact of treating schizophrenia with a Long Acting Injectables to aid in adherence of treatment. They both show that the incremental cost of branded Long-Acting medications are negated by lower hospitalization cost perhaps due to better adherence in comparison to daily oral medications by a seriously mentally ill population resulting in less emergency care and hospitalization. Both provide estimate of approximately $25,000 per year as cost of managing schizophrenia among Medicaid patients. An older study by McCombs is limited to data from only one state, California, also had

a very similar number for annual cost of managing schizophrenia ($25,940 per annum) although the cost estimates are 17 years apart. (McCombs, Nichol, Johnstone, & Lizheng, 2000). These studies point to the importance of adherence as a factor and focusing on ER and Inpatient reduction caused mostly by disease relapse, as a key objective of population health management.

Miller's study has the lowest cost estimate of 700 dollars per member per month which translates to $8400 per year to manage schizophrenia patients in Medicaid. (Miller & Bradley, 2004) The key difference with this study is that the data is very old (1995 dollars). It is also from only one state, Georgia, which does have lower cost of living in comparison to states like California and New York.

Given the multiple approaches, time-period, outcome variables, the review was not conducive to a meta-analysis. A qualitative synthesis does point to the fact that schizophrenia patients in Medicaid are suffering from multiple ER visits and hospitalizations and consequently the system is facing a higher cost in managing its schizophrenia patient population even in comparison to resource intensive disease such as diabetes. It also concludes that adherence to therapies can lead to alleviation in inpatient and ER cost and better patient health outcomes.

3.5.2 KEY FINDINGS ON SCHIZOPHRENIA PATIENTS IN MEDICARE

Three studies were appropriate for synthesis of cost and resource use associated with schizophrenia patients in Medicare. All of them had comparative data to non-schizophrenia

patients. One 2009 study found that the cost of care for non-schizoaffective schizophrenia members, on average, was 80% higher than for the average Medicare beneficiary per year in 2010 dollars and that 50% of the cost of care was due to hospitalization. (Feldman, Bailey, Muller, Le, & Dirani, 2014) Hendrie's study was conducted on urban public health system observational cohort study of 31,588 older adults. Not surprising the estimates were more expensive, $63335.01 for cost of managing schizophrenia patients in comparison to $49829.53 for non-schizophrenia patients. One study based on 129,805 Medicare beneficiaries concluded that the percentage of disabled beneficiaries with a psychiatric emergency department visit ranged from 9.5% (major depression) to nearly twice as high for schizophrenia (19.8%). Additionally, the percentage of aged beneficiaries with any psychiatric ED use ranged from 5.4% for members with major depression to 8.6% for schizophrenia members. (Merrick, Perloff, & Tompkins, 2010) Across all studies patients with schizophrenia was about 50% or more expensive in comparison to various cohorts in the three studies. Two of the studies also showed that hospitalization and Emergency as major factors behind high resource use by schizophrenia patients.

3.5.3 KEY FINDINGS ON SCHIZOPHRENIA PATIENTS IN VETERAN AFFAIRS:

Nearly half of US Veterans suffer from mental health problems (Betancourt JA, 2023) but a comprehensive systematic literature search on economic cost of managing schizophrenia resulted in only 2 VA studies. The outcomes analysed in the two studies were different. While Doran et al focused-on Emergency Department (ED) visits, Zhu et al studied the variability

among the direct cost associated with managing schizophrenia patients. The study by Doran is a retrospective cross-sectional multivariate analysis of national VA database with robust data on 5.5MM VA members. (Doran & Rosenhenck, 2013). It concluded that having a diagnosis of schizophrenia was most strongly associated with ED use. Factors, such as, homelessness, opioid use, and heart failure were also associated with high ED use. The patients were divided into 6 categories of increasing annual ED use: 0, 1, 2-4, 5 10, 11-25 and greater than 25 ED visits. 83.2% of the patients had no ED visit in the fiscal year 2010. Among the remaining 16.8% VA members (N = 930,712) who used ED services, 53% had 1 ED visit, 38.3% had 2-4 ED visits, 7.6% had 5-10 ED visits, 1 % had 11-25% ED visits and 0.07% (n= 617) had more than 25 ED visits in that year. The study makes a case for understanding the needs for emergency resource use by high utilizers better.

The study by Zhu et al is a 3-year non-interventional study called US-SCAP (U.S. Schizophrenia Care and Assessment Program) conducted between 1997 to 2003. (Zhu, et al., 2008) It studied the cost of managing 1550 schizophrenia patients and the impact of crisis on it. The study concluded that all recent crisis events positively impacted the cost of mental health treatment, the biggest being among patients who attempted suicide ($46,024).

The two studies have significant differences in focus although both Zhu and Doran show that there is variability in the cost of managing schizophrenia patients driven by factors such as recent crisis, co-morbidities like heart failure and socioeconomic factors such as homelessness. They also show that schizophrenia patients have high resource utilization in terms of Emergency or hospitalization use. They both also confirm that there is value in researching

factors that may lead to disproportionate use of resources such as ER and hospitals as they may lead to development of tools for better schizophrenia management.

3.5.4 KEY FINDINGS ON SCHIZOPHRENIA PATIENTS IN PRIVATE INSURANCE

Schizophrenia is often characterized by social and economic deprivation and most adults with schizophrenia become dependent on government for their living and health insurance due to their inability to work. With advent of ACA, also known as Obamacare in 2010, which mandated coverage up to 26 years of age, many patients with early-onset schizophrenia now received health coverage under their parents' employer-based health plans. Centres for Medicare & Medicaid Services (CMS) projected that 1.2 million young adults would receive coverage under their parents' health thus making it important to understand the cost of managing schizophrenia in this payer group which is funded by US Employers. Approximately 18% of adult schizophrenia patients are covered by private insurance plans. (Geissler, et al., 2023)

A systematic search of heath care resource and cost of managing schizophrenia in private health system originally resulted in 6 studies including a study by Wilson et al found in a literature review by Zhang et al. It was added to the final literature review list. The first study on private insurance literature list is by Fitch et al. (Fitch, Iwasaki, & Villa, 2014) This analysis showed that on a monthly per patient basis, a schizophrenia patient was four times as expensive as a patient that does not have schizophrenia. Although the second comparative study, which is by Huang et al, was focused on young adults (18-35 years) and was conducted 5

years later, also showed a similar annual per patient direct cost of managing schizophrenia ($22,338). (Huang, Amos, Joshi, Wang, & Nash, 2018) In this study, the cost of managing a schizophrenia patient was seen to be three times to that of a non-schizophrenia patient. (Huang, Amos, Joshi, Wang, & Nash, 2018)

Cloutier estimates on annual per patient direct cost of schizophrenia was one of the lowest in the literature at $12,461. (Cloutier, et al., 2016) The oldest estimate (2001-2004) in the literature list is from an analysis conducted on California private insurer and it compared the difference in per patient annual cost of schizophrenia patients who are newly diagnosed versus schizophrenia patients who were previously diagnosed. (Wilson, Gitlin, & Lightwood, 2011) The study concluded that the cost is higher during the early phase of the disease with an annual cost of $15, 282 versus $12,029 (p=0.09) for previously diagnosed. The difference was mostly due to higher inpatient services ($7,745 vs. $4,440 p=0.03) during earlier phase of the disease. Another analysis with a similar goal was conducted during 1998-2007 on a national commercial database called Pharmetrics. (Nicholl, Kasem, Diels, & Schadrack, 2010) It confirmed that the mean annual healthcare costs of recently diagnosed patients were greater than Chronic ($20,654 vs $15,489). A MarketScan study conducted during 2006-2009 found adherence as a factor in lowering cost of managing schizophrenia: $15,400 (22,149) vs. $17,636 (33,791). (Offord, Lin, Mirski, & Wong, 2013) The higher cost was driven by higher hospitalization (0.57 vs. 0.38; P = 0.0006) with longer length of stay (LOS, 5.0 vs. 3.0 days; P = 0.0013) by the schizophrenia patients

3.5.5 KEY FINDINGS ON SCHIZOPHRENIA PATIENTS IN ALL PAYERS:

A review of studies where data was sourced from multiple payers resulted in three studies. The data sources for these three studies vary from an observational perspective trial (CATIE Trial), a national claims database such as Truven to a national survey called Medical Expenditure Panel Survey. Only one study compares cost of managing schizophrenia to another disease, Bipolar. (Broder, et al., 2018) It found, in 2016 dollars, schizophrenia patients annual cost was $34, 204 ($52,995) vs. $26, 396 ($48,294). It also concluded that a higher proportion of schizophrenia patients were Medicaid patients in comparison to Bipolar patients. Another study estimated the cost of managing schizophrenia patients using Market scan database also known as Truven and showed that in 2001-2003, the average annual cost was $20,712 per patient. (Chwastiak, et al., 2009) A 2005-2008 study by Desai looks at the variability of cost within schizophrenia patient population and showed a range of annual mean cost per patient year as $3,656 (SE=$283) for the low-cost group to $27,944 (SE=$4,639) for the high-cost group. (Desai, Lawson, Barner, & Rascati, 2013)

3.6 OVERALL FINDINGS ON KEY DRIVERS OF UTILIZATION AND DEFINITION OF SUPER UTILIZER

A secondary objective of this literature review was to find key factors associated with super or high utilization of resources. Eleven studies reviewed had findings on key drivers of high utilization among schizophrenia patients. They are listed in Table 3-3. The main drivers of high utilization by schizophrenia patients were higher emergency room admissions and hospitalizations and associated inpatient days. In multiple studies they were estimated as much

as twice as much in terms of frequency or length of hospital stays. Factors that were associated with higher resource cost among schizophrenia patients were identified as sub optimal treatment adherence, use of long-acting therapies, homelessness, early versus late disease, co-morbidities such as suicide and substance abuse, Congestive Heart Failure, demographics such as age, and race (Table 3.3).

It was also observed from the synthesis that the cost of managing schizophrenia was varied and that a small proportion of schizophrenia patients utilized disproportionate amount of health resources. Thus, mean resource use does not represent the full picture of resource use and hence it important to understand the distribution of cost and to characterize the high utilizers in order to develop targeted and impactful population health management tools.

Table 3. 3: Factors affecting High/Super Utilization and High Cost

Variables	Number of Studies
Age	3 (Bartels, Clark, Peacock, Dums, & Pratt, 2003) (Huang, Amos, Joshi, Wang, & Nash, 2018) (Desai, Lawson, Barner, & Rascati, 2013)
Sex	None
Race	1 (Desai, Lawson, Barner, & Rascati, 2013)
Co-morbidities	Diabetes (Shim, et al., 2014), Opioid and CHF (Doran & Rosenhenck, 2013), Early (Cloutier, et al., 2016) (Offord, Lin, Mirski, & Wong, 2013)Suicide ((Zhu, et al., 2008)
Treatment adherence	(Offord S. L., 2013) (Pesa, Doshi, Wang, Yuce, & Basur, 2017) (Shah, Xie, Kariburyo, Zhang, & Gore, 2018), (McCombs, Nichol, Johnstone, & Lizheng, 2000)
Homelessness	(Doran & Rosenhenck, 2013)

Another secondary objective of the research was to extract the definition of high utilization. Two studies by Desai and Doran presented definition for high use but they both

differed in their approach. (Desai, Lawson, Barner, & Rascati, 2013) (Doran & Rosenhenck, 2013) Doran was based on frequencies of Emergency Department use while Desai et al dichotomized into high-cost (expenditures ≥ $16,000) and low-cost category based a natural break concept. The summary of the findings is presented in Table 3.4. The findings confirmed lack of standard definition of Super Utilizer in the literature.

Table 3. 4: Definition of High/Super Resource Utilization and High Cost

Spending category	Number of Studies: 2
Inpatient Care	None
Emergency Room Visit	0, 1, 2-4, 5 10, 11-25, > 25 visits (Doran & Rosenhenck, 2013)
Hospitalization	None
Long term care	None
Physician service	None
Total Cost	The cost variable was dichotomized into high-cost (expenditures ≥ $16,000) and low-cost (expenditures < $16,000) groups based on a natural break in the distribution of costs, while ensuring that there were sufficient patients in each group. (Desai, Lawson, Barner, & Rascati, 2013)

3.7 LIMITATIONS AND STRENGTHS

This is a comprehensive literature review across all payers in US but despite the rigorous methodology employed in this review, it has limitations. The studies differed significantly in population characteristics, geography, final outcomes and time-period thus precluding a quantitative assessment and perhaps an incomplete picture of schizophrenia resource

utilization. From methodological rigor perspective, the review does include studies that have strong regional biases. It also in general lack sensitivity analysis which may create bias in final findings. Another limitation also emanates from common use of cost studies based on administrative claims databases that were structured for reimbursement purposes. Not all claims are reimbursed and hence the final actual cost of the care may be lower in estimates. The findings on healthcare resource are actual and more reliable. Another limitation to note is that in an increasing healthcare cost and innovative treatment environment, studies from different time period have cost or resource use data that are not directly comparable. Furthermore, because our studies were limited to US payers, its findings cannot be extrapolated to populations ex-US as they have very different health systems and hence schizophrenia may be managed very differently. Another limitation to note is that the analysis is limited to direct cost and the overall cost of burden of schizophrenia would be much higher due to the patient's disability leading to reduced productivity and negative monetary and productivity impact on caregivers.

The strength of this review lies in the comprehensive review by all payer types that shows consistent finding in terms of incremental schizophrenia burden and the critical role of emergency and hospitalization in the high cost of managing schizophrenia patients. This is the first review to incorporate all payer types in the United States. Another area of strength is the long-time span covering two decades. Additionally, the search approach that includes all PubMed studies along with google search adds to the robustness of the findings.

3.8 DISCUSSION

This systematic literature review synthesized cost and resource utilization by patients with schizophrenia since year 2000 among all various major payers in USA. This study is the first comprehensive review of schizophrenia cost from all payer perspective and across all payer types and it confirms the fact that patients with schizophrenia experienced a significant economic burden. Although the studies were varied in their approach in estimating the resource use and in comparators, the findings were very consistent across all payer types. The research review spans all payer types, but Medicaid emerged as a major payor in terms of research focus as most of the studies on schizophrenia cost and resource use were based on Medicaid data. This is not surprising as about 70% of US schizophrenia patients are covered by Medicaid.

A systematic narrative synthesis of all the studies confirms that it is significantly more expensive, at least fifty percent more to manage a patient with schizophrenia than a patient without schizophrenia. Various studies across payer types also confirmed that schizophrenia patients utilize more health resources than patients with other well recognized burdensome diseases such as diabetes, bipolar and depression. It was also observed from the synthesis that the mean cost of managing schizophrenia hid the variability in the cost of managing this disease. The incremental cost associated with schizophrenia varied based on the comparator in the studies, but it was confirmed that in all cases schizophrenia was the most resource intensive chronic disease. The review also shows the critical factor behind the high resource use among the schizophrenia patient. These patients have twice as much or even higher use of

emergency services and hospitals in terms of both frequency and the time they spend in inpatient setting.

Another key finding was that the cost associated with management of schizophrenia are varied and that a small proportion of schizophrenia patients may be relapsing more frequently and leading to disproportionate use of health resources. In one study it showed that some schizophrenia patients may be seeking emergency services as much as 25 times a year, in other words, they are going to ED at least twice a month. Thus, it is important to understand the distribution of resource use and to characterize the super utilizers in order to develop targeted population health management tools. Cost of schizophrenia is mostly due to hospitalization and ER visits caused by multiple relapses of the disease. Identifying the factors that may be behind the high utilization of these services will enable development of optimal disease management strategies.

This literature review also points to few factors that may be leading to multiple hospital and ER visits. Studying these factors, such as, treatment adherence, race, homelessness, early versus late disease, co-morbidities, gender and age, along with other socio-economic factors may aid in creating a predictive model to identify patients who are at risk of relapse and thus in need of better care.

Given that Medicaid is the major provider of insurance coverage to schizophrenia patient, the next chapter characterizes schizophrenia patient population according to their resource utilization in a large Medicaid database. This Medicaid focused research will enable development of health management strategies and programs that may prevent expensive

schizophrenia relapse and hospitalizations thus reducing cost in already financially stretched health system. It will also enhance health outcomes and improve Medicaid schizophrenia patients' and their caregiver's quality of life.

SECTION 4: CHARACTERIZATION OF SUPER UTILIZATION AMONG SCHIZOPHRENIA PATIENTS IN THE US MEDICAID SYSTEM

4.1 INTRODUCTION

The patients with schizophrenia face significant health challenges leading to sub optimal healthcare. Unmanaged or sub optimally treated schizophrenia (Ward, Ishak, Proskorovsky, & Caro, 2006) and key comorbidities such as substance abuse (Gupta, Hendricks, Kenkel, Bhatia, & Haffke, 1996), lead to multiple unplanned ER visits and hospitalization which are the key leading factors of high cost of care. Treatment challenges and lack of social support, in these patients, lead to nonadherence to treatment and thus higher risk of relapse, rehospitalization, and self-harm. Patients and their caregivers suffer reduced Quality of Life and increased economic burden. Population health decision makers are interested in improving treatment adherence and outcomes through various strategies ranging from latest long-acting medications, social programs to shared decision making tools.

The high cost of managing schizophrenia is not evenly distributed across all patients. Similar to other chronic diseases, a small proportion of schizophrenia patients result in disproportionate high cost. (Desai, Lawson, Barner, & Rascati, 2013) (Doran & Rosenhenck, 2013) Thus, a cost effective approach to improving schizophrenia patients health outcomes and decreasing associated cost would be to apply a targeted approach towards patients who are disproportionate super utilizers of hospital and emergency services.

Although schizophrenia prevalence is less than 1%, according to a recent study by Finnerty et al, the US Medicaid system has significantly higher, prevalence of Schizophrenia

patients at 2.13%, as it covers patients who typically have low income and/or education level. (Finnerty, et al., 2024) Medicaid members also have disproportionate representation from minority communities with less social support. (CMS, 2020)

A recent 2023 study by Geissler confirmed that Medicaid is the major insurance source for schizophrenia with a probability that 70% of these patients have Medicaid coverage. (Geissler, et al., 2023) Given the high burden of managing schizophrenia patients in the Medicaid system, which has been experiencing increasing cost and state budget constraints (CBPP, 2020), the current research is focused on understanding the resource utilization among schizophrenia Medicaid patients and the factors associated with high utilizers among this cohort of patients. This chapter analyses the utilization of emergency and hospitalization services by these patients to estimate the extent of the use of these services. Also given a lack of standard definition of “high” or “super” utilization of resources among this patient population, this chapter, develops a pragmatic approach to define super utilizers in this cohort and compares the hospitalization and emergency use between the super and the rest or the low utilizers.

4.2 STUDY OBJECTIVE

The main aim of this chapter was to characterize super utilization of resources by Schizophrenia patients in US Medicaid system. Super utilization is defined by high utilization of Emergency Room (ER) and hospitalization. In Chapter 3, the research reviewed literature on the

definition of super utilization and found a lack of standardized approach for schizophrenia studies. Recent literature, including a systematic review by Wammes et al on high utilization have used top 5% to 10% of resource users as a definition for Super Utilizer (SU). (Coughlin & Long, 2009) (Wammes, van der Wees, Tanke, Westert, & Jeurissen, 2018) Thus, this study sourced Medicaid data on schizophrenia patients from IBM® MarketScan® Multi-State Medicaid Database V2047, to characterize super utilization of ER and Inpatient services among Schizophrenia patients in the US Medicaid System and provide a definition of SU for the current research. The findings are presented in this chapter. In the following chapter, the study analyses factors that are associated with super utilization of ER and hospitalization resources among Medicaid schizophrenia patients.

4.3 STUDY DESIGN:

This is a retrospective observational cohort study which characterizes ER and hospitalization resource use by patients in the MarketScan® Multi-State Medicaid Database V2047, released on 7th March 2022. The following section describes the definition of super utilization in literature and for this research. This is followed by data description and methods to characterize and compare the super versus low resource utilization among Medicaid patients with schizophrenia.

4.3.1 DEFINITION OF SUPER UTILIZATION

Rationale for defining High Utilizers among schizophrenia patients, in our current health systems, is provided by the sad fact that there are individuals whose physical, behavioural and social needs are complex, and the current fragmented US health system do not adequately meet their needs, and they typically visit to emergency departments significantly more and experience multiple inpatient hospital admissions, readmissions and institutionalizations. This absence of standardized definitions creates a significant barrier to analysis and data-driven policymaking. The literature review found no common definitions of “high” or “super” utilization. Without common definitions, answering questions such as “What is the impact or total cost of Schizophrenia high utilizers?” is difficult. Studies have used a variety of definitions:

i. Top 5% or 10% of resource utilizers. (Coughlin & Long, 2009) (Wammes, van der Wees, Tanke, Westert, & Jeurissen, 2018)

ii. Persons with three or more hospitalizations in a 12-month period, or with both serious mental health diagnosis and two or more hospitalizations within 12 months. (Johnson, et al., 2015)

iii. People with three or more chronic conditions and two or more hospitalizations in six months, or three or more emergency visits in six months, or two or more emergency visits in 30 days. (Lynch, et al., 2016)

iv. People with three or more hospitalizations, or with two or more hospitalizations and two or more emergency visits within a six-month period. (Harris, et al., 2016)

v. A break in distribution of cost as a cutoff point for high and low utilization. (Desai, Lawson, Barner, & Rascati, 2013)

A common thread across these definitions is that these individuals experience large numbers of emergency visits and hospital admissions which could have been avoided with early targeted care. To develop a definition of Super Utilizer for this research, a systematic approach to categorize the top 10% of ER and hospitalization user was applied. The decision to use the above definition was taken after a distribution of ER and hospitalization burden of schizophrenia patients in the US Medicaid system was analysed. As cost and management of ER and hospitalization vary by region, plans and over time, picking a definition such a top 10% also provides a more stable and systematic approach that is applicable and comparable across regions, plans, and time. It is also comparable across multiple high-cost chronic diseases.

4.3.2 DATA

The IBM Marketscan database captures person-specific clinical utilization and expenditures associated with the clinical utilization across inpatient and outpatient setting. It also includes prescription and carve-out services. The data is pooled from a selection of large employers, health plans, and both government and public organizations. To enable research, this database links paid claims to encounter clinical and patient demographic data across all their providers and site of care over time.

The current research analyses the Multi-state Medicaid part of the IBM Marketscan database. IBM® MarketScan® Multi-State Medicaid Database V2047 was sourced from Johnson

& Johnson internal database acquired from IBM. This Multi-State Medicaid Database reflects the healthcare service use of individuals covered by Medicaid programs in numerous geographically dispersed states in USA. It is a large database with more than 33 million lives. It contains pooled healthcare experience of Medicaid enrolees who are covered under both fee for service and the managed care plans. With fee for service plan, a person can visit any physician's office, including specialists, of their choice while with managed care plans, there is a strong financial incentive to consult with only those physicians who are covered under the managed care plan. Under a managed Medicaid plan, a Medicaid member belongs to a plan that contracts with medical providers to provide facilities at a reduced cost. Thus, by including members from both plan type, it provides a comprehensive view of Medicaid patients resource utilization.

The data elements of the IBM® MarketScan® Multi-State Medicaid Database V2047 include records of inpatient or hospital services, inpatient admissions, outpatient services, and prescription drug claims, as well as information on long-term care. Data on eligibility and type of service and provider type are also included. In addition to standard demographic variables such as age and gender, the database includes variables of value to researchers investigating Medicaid populations, such as federal aid category (income based, disability, Temporary Assistance for Needy Families) and race. Ethnicity information is also collected but sparsely populated in the database. Medicaid recipients are from several states but due to Health Insurance Portability and Accountability Act of 1996, widely known as HIPAA privacy regulations, we do not know the state the member specific data is from. Members maintain

their same identifier even if they leave the system for a brief period and this allows for analysis that require longitudinal depth in data.

The major data elements contained within this database are outpatient pharmacy dispensing claims coded with National Drug Codes, NDC, inpatient and outpatient medical claims with provider procedure codes (coded in CPT-4, HCPCs) and diagnosis codes (coded in ICD-9-CM, ICD-10-CM and SNOMED). The data does not contain laboratory results.

The data include tables with information on:

- Medical/Surgical
    - Inpatient Admissions Table. It contains records that summarizes information about a beneficiary's hospital admission. It includes diagnosis and procedure codes which area assigned chronologically based on the dates of the service provided. It has no duplication. To qualify as an inpatient admission, the services should include certain criteria pertaining to room and board claim otherwise the records are moved to Outpatient Services Table.
    - Facility Header Table: This table includes complete information of the facility where care is provided.
    - Inpatient Services Table: This table includes the individual facility and professional encounters and services included in a patient's inpatient record. There is a case identifier link between Inpatient Admission and Outpatient services table to identify the individual service records.

    - Outpatient Services Table: This part of the dataset contains encounters and claims for services that provided in a doctors' office and/or the hospital outpatient facility.
    - Long-Term Care Table: It contains beneficiary level services that are rendered in a long-term care setting such as room and board claims.
- Outpatient Prescription Drug Claims Table: This includes outpatient pharmaceutical claims data which may be mail-order or card programs prescriptions.
- Enrolment Table: This table contains individual beneficiary level enrolment records which include demographic and plan information. It contains one record per beneficiary per month of enrolment of an individual enrolee.
- Member Days Table: This table provides the information on beneficiary enrolment start and end date. This allows researchers to select the cohort pf patient with pre-specified longitudinal depth.

The IBM database has Medicaid member information from year 2006 to 2022 allowing researchers to study patterns of disease specific resource utilization over a long period of time. Although the database is robust in terms of clinical encounter information thus clinical utilization information, it provides limited financial information thus presenting a challenge when analysing health care cost information. Since the current research is focused on Emergency and Inpatient hospital service utilization, the financial information limitation is not of any consequence.

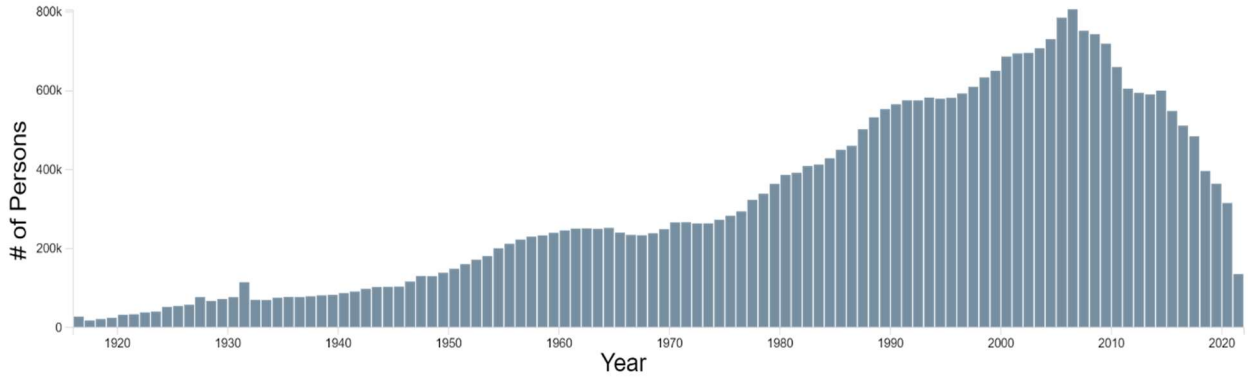
4.3.3 STATISTICAL ANALYTICAL TOOL

The Observational Health Data Sciences and Informatics (or OHDSI, pronounced "Odyssey") is used for some of the analysis. (OHDSI, 2023) This program is a multi-stakeholder, interdisciplinary collaborative to bring out the value of health data through large-scale analytics. The analysis is facilitated through a user-friendly interface, and the solutions are open-sourced. OHDSI has established an international network of researchers and observational health databases with a central coordinating centre housed at Columbia University. Johnson & Johnson uses this for its internal research, and IBM® MarketScan® Multi-State Medicaid Database V2047 was linked to OHDSI to facilitate analysis for this research. The uploaded IBM Medicaid data was a descriptive analysis was conducted for this research using the OHDSI interface. The interface automatically generates the R code for each study descriptive analysis. For analysis that were not conducted using OHDSI, R statistical software was used.

4.4 ANALYTIC APPROACH FOR IBM MDCD (V2047) DATABASE

This research created a cohort of schizophrenia patients from Medicaid IBM database. At first it analysed the key demographics of the entire database to assess the robustness of the database by comparing key data elements with overall Medicaid beneficiary demographics. The figure below shows the number of people in the database and the year they are born. As expected, it shows that most patients in Medicaid are young. This is not surprising as only 10% of recipients of Medicaid system are above 65 years. (KFF.org, 2019)

Figure 4. 1: Medicaid IBM MDCD Data Demographics



Source: IBM MDCD (v2047)

The total number of members in the IBM® MarketScan® Multi-State Medicaid Database V2047 is 33.36 MM. Women are overrepresented in the Medicaid database as the United Census estimates show women make 50.4% of the US population while 56.1% are women in the IBM Medicaid database. (Department of Commerce, 2022) This is also expected as women typically have lower incomes and thus are more likely to qualify for Medicaid than men under one of Medicaid's eligibility categories; low income, low income and pregnant, parent of children under 18, disabled, or over 65.

Three quarters of member data has race information. While White was listed as race for 48% of the members, Blacks made 27% of the entire database, which is significantly higher than the proportion of US population that identifies itself as Black. conversely Whites are much lower in proportion. According to July 1, 2022, United States Census estimates, 13.6% are Blacks while 75.5% are Whites alone in USA. (Department of Commerce, 2022). This conforms to the data from CMS that the Medicaid enrolees are more racially and ethnically diverse than

the overall U.S. population. Center of Medicare and Medicaid Services (CMS) data confirms that Medicaid has a larger share of Black than the U.S. population, and a smaller share are White. (CMS, 2020)

4.4.1 STUDY PERIOD

For the current research, 2010-2019 was selected as the study time-period. The start of the study time-period is January 2010 because a significant legislation impacting healthcare system of US called Accountable Care Act (ACA), also known as Obamacare, was passed in the same year. This had a significant impact on the insurance design of the US healthcare system and especially the Medicaid. The purpose of the ACA was to expand access to insurance, increase consumer protections, emphasize prevention and wellness, improve quality and system performance, expand the health workforce, and curb rising health care costs. The ACA

"provides consumers with subsidies ("premium tax credits") that lower costs for households with incomes between 100% and 400% of the federal poverty level (FPL).

If the income is above 400% FPL, one may still qualify for a premium tax credit.

If the income is at or below 150% FPL, one may qualify to enroll in or change Marketplace coverage through a Special Enrollment Period.

It expanded the Medicaid program to cover all adults with income below 138% of the FPL. (Not all states have expanded their Medicaid programs.) (Healthcare.gov, 2023)*"*

Medicaid grew as a result and by January 2014, most provision was phased into the system. 2019 was chosen as the end of the study time-period because, 2020 is the start of coronavirus pandemic which significantly impacted members' in-person access to healthcare for multiple years.

4.4.2 DEMOGRAPHIC COMPARISON FOR FULL COHORT AND STUDY PERIOD

The study further compared the key demographics such as age, race and gender, of the overall IBM database and the study period, 2010-2019, data. It also confirmed the availability of large and thus robust sample size for analysis.

The time-period, 2010 to 2019, provides robust number of (16,077,945) unique Medicaid members with very similar gender and race distribution as the full data cohort. The average age of the two cohorts was very similar with mean of 24.06 years and 24.62 years respectively. The Table 4-1 below shows the gender, race, and age data for the selected time periods and the complete IBM database time period.

Table 4. 1: Characteristics of Sample Cohort from 2010-2019.

Beneficiaries	2006-2022	Percentage	2010-2019	Percentage
Total	33,362,501	100	16,077,945	100
Male	14,632,498	43.9	6930187	43.1
Female	18,730,003	56.1	9147758	56.9
White	16,047,363	48.1	7910213	49.2
African American	9,018,009	27.0	4235435	26.3
Age (Years)	24.1 (22.6 SD)		24.6 (21.5 SD)	

Source: OHDSI Analysis reference: All Medicaid 2006-2022 Cohort #14047 & All Medicaid 2010-2019 Cohort # 11773 and Characterization #633 and Characterization #632

The gender and race bias in the 2010-2019 cohort is similar to the overall cohort in comparison to overall US Medicaid population. There is slight overrepresentation of Women

(56.9% vs. 56.1%) and under-representation of Blacks (26.3% vs. 27%) by small percentages when comparing the two-time periods in the database.

4.5 IDENTIFICATION OF SCHIZOPHRENIA PATIENT COHORT

The cohort of schizophrenia patients selected for this analysis included all adult schizophrenia patients who had occurrence of schizophrenia diagnosis for the first time and the occurrence was between the time-period 01-01-2010 and 12-31-2019. SNOMED codes were used to identify all schizophrenia patients. SNOMED CT Codes (Systematized Nomenclature of Medicine - Clinical Terms) is a standardized, multilingual vocabulary of clinical terminology that is used by physicians and other health care providers for the electronic exchange of clinical health information. They include clinical findings, symptoms, diagnoses, procedures, body structures, organisms and other etiologies, substances, pharmaceuticals, devices and specimens. The schizophrenia definition included the following SNOMED codes.

Table 4. 2: Schizophrenia SNOMED Codes

Condition name	Code	Vocabulary
Acute exacerbation of chronic latent schizophrenia	191564007	SNOMED
Chronic latent schizophrenia	191562006	SNOMED
Latent schizophrenia	191559008	SNOMED
Schizophrenia	58214004	SNOMED
Sub chronic latent schizophrenia	191561004	SNOMED

4.5.1 CHARACTERISTICS OF SCHIZOPHRENIA PATIENTS IN MEDICAID

There are 471,286 schizophrenia patients in the entire IBM® MarketScan® Multi-State Medicaid Database V2047 representing 1.4% of the total patients in the database. Since significant proportion Medicaid patients are children and schizophrenia onset are mostly among adults, the prevalence of schizophrenia among all adult Medicaid patients in the database would be higher. Among all schizophrenia patients, 452,890 are adult schizophrenia members. As expected during the study time period of 2010-2019, the total number of schizophrenia patients drops to 380,250 with 366,565 adult members. Given schizophrenia is diagnosed in early adult ages, it is not surprising that 96% of schizophrenia members are adult. The percentage of adult schizophrenia is same as the overall cohort schizophrenia data. To assess the base line characteristics of the schizophrenia cohort, data was limited to members who had at least 365 days of continuous data before diagnosis of schizophrenia and to analyse the utilization of ER and inpatients hospitalization, the cohort required at least 365 days of continuous observation post diagnosis. Once this selection criteria were applied, the total remaining cohort is 253,495 which remains a significant large sample size.

The theoretical foundation for this research is the Dahlgren and Whitehead "Rainbow Model" which organizes determinants of health into five concentric layers with the individual in the centre. The core determinant is Individual characteristics such as age, sex, and race. Both age (Bartels, Clark, Peacock, Dums, & Pratt, 2003) (Huang, Amos, Joshi, Wang, & Nash, 2018) and race (Desai, Lawson, Barner, & Rascati, 2013) were also seen as factors that may lead to super utilization of ER and hospitalization. Thus, as a first step, a comparison of the two cohorts, All Adults Schizophrenia – 2010-2019 and Study Cohort Adult Schizophrenia were

conducted in terms of basic demographics. A comparison of the selected study cohort with the all adult 2010-2019 schizophrenia cohort is shown in the table 4.2.

Table 4. 3: Descriptives of Study Cohort in comparison to All Adult Schizophrenia (2010-2019)

	All Adult Schizophrenia- 2010-2019		Study Cohort Adult Schizophrenia		P value (Z-Test)
Total members	366,565		253,495		
Average Time in cohort (in Days)	1422		1741		0.0001
Male	199,230	54.4%	135209	53.3%	0.00001
Female	167,335	45.6%	118286	46.7%	0.00001
Black	138,679	43.7%	102589	45.5%	0.00001
White	178,944	56.3%	122705	54.5%	0.00001
Age	46.32 (Mean)	16.09 SD	47.2 (Mean)	15.67 SD	0.001

Source: OHDSI Analysis reference Atlas Characterization #637 and #638

The data has missing race information. Adult Schizophrenia- 2010-2019 cohort has 13.4% beneficiaries who have missing race data. while the Study cohort has 11.3% missing race data. In comparing the two cohorts, we find a higher proportion of black members (45.5% vs. 43.7%) and a higher longitudinal time depth of 1741 days versus 1422 days for the study cohort. The higher percentage of black members in the study cohort could be explained by a higher proportion of whites who rely on Medicaid for brief amount of time and find it easier to find other support or a job. The second difference can be explained by the cohort requirement of 365 days of continuous observation pre and post diagnosis of schizophrenia in the database.

The IBM® MarketScan® Multi-State Medicaid Database V2047 has age distributed among 15 groups within adult members category. In order to make a meaningful comparison, the age cohorts were further collapsed into three categories. The cohorts chosen were 18-34 years, 35-64 years, and 65+ years. The rationale behind these age categories were two-fold. One, schizophrenia can occur at any age but on an average the age of disease onset is usually late teens to the early 20s for men, and for women it is late 20s to early 30s. (NAMI, 2023) This explains the 18-34 category as it will include schizophrenia patients who are mostly early in their disease cycle. Second, there have been research conducted that have shown that higher age is inversely related to high utilization. (Bartels, Clark, Peacock, Dums, & Pratt, 2003) (Huang, Amos, Joshi, Wang, & Nash, 2018) This explains the third (Desai, Lawson, Barner, & Rascati, 2013) category for 65+. This age cohort may also be doubly covered by Medicaid and Medicare and may have differences in access to care and hence overall health management. Table 4-4 compares the three age groups between the All-Adult Schizophrenia - 2010-2019 and the Study Cohort Adult Schizophrenia.

Table 4. 4: Age Group Comparison between All Adult and Study Cohort

	All Adult Schizophrenia- 2010-2019		Study Cohort Adult Schizophrenia		P-Value (Z-Test)
Total members	366,565		253495		
Age Group	Number	Percentage	Number	Percentage	
18 - 34	101745	28	63309	25	0.00001
35 - 64	217812	59	156994	62	0.00001
65+	46575	13	33192	13	0.00001
Missing	433	0	0	0	

When comparing the age distribution, the study cohort has more middle-aged population and less young-aged population. This difference can be explained due to the passage of the Obamacare in 2010. This act extended the age of children covered under parents' insurance from 21 years to 26 years. This may have led to more schizophrenia young patients to stay on their parents' commercial insurance plans.

In order to describe the Study Cohort in terms of super resource utilization of ER and hospitalization services, a resource utilization distribution was analysed to define super utilization. To test the difference in proportions of super utilization, Z-test were conducted to test the hypothesis that there was no statistical difference within the two genders, race and the three age cohorts. The assessment of the findings is presented in the subsequent section.

4.6 SUPER UTILIZATION AMONG SCHIZOPHRENIA COHORT IN US MEDICAID

A common thread across various Super Utilizers definitions, found in literature, is that these individuals experience large numbers of emergency visits and hospital admissions which could have been avoided with early targeted care. To develop a definition of Super Utilizer for this research, a systematic approach was applied. The distribution of ER and hospitalization burden of schizophrenia patients in the US Medicaid system was analysed. The table below provides the distribution of Medicaid schizophrenia Cohort A population by number of annual ER or inpatient hospital visits.

Table 4. 5: Distribution of Annual ER & Hospital Utilization

Cumulative ER visits & Hospitalization	Cumulative Percentage of Study Cohort	Annual ER Visits & Hospitalizations	Percentage of Study Cohort
0+	100%	0	37%
1+	63%	1	17%
2+	46%	2	11%
3+	35%	3	8%
4+	27%	4	5%
5+	22%	5-8	12%
9+	10%	9+	10%

The analysis shows that 37% of the study cohort had no hospitalization and ER visits in a year, 54% had 1+, 46% had 2+, 35% had 3+, 27% have 4+, 22% have 5+ hospitalization and ER visits annually with 10% percent of the study cohort had 9+ hospitalization and ER visits. It also shows that 17% had only 1 visit annually while 11% had 2, 8% had 3 visits annually and 5% had 4 visits annually. Twelve percent of schizophrenia patients in the study Cohort had 5 to 8 visits annually. Overall, it shows that a significant proportion of the schizophrenia patients are going for repeat ER and hospitalization services in a year with top 10% having 9 such visits. This above analysis also confirms the finding in Chapter 3 on the significant economic burden of managing schizophrenia due to high numbers of Emergency Room visits and hospitalizations.

Taking top 10% percent as the definition of high utilization, the study used 9+ hospitalization and ER visits as the definition for High Utilization. The distribution shows number of hospitalization and Emergency Room visits among schizophrenia patients are very high and the definition here is close to Harris's definition of two or more hospitalizations and two or more emergency visits within a six-month period as it would add up to 8+ hospitalizations and or ER in a 12-month period. (Harris, et al., 2016) This also conforms to Wammes systematic review finding of using top 10% of resource users who used on an average 68% of the overall health care cost in a given year. (Wammes, van der Wees, Tanke, Westert, & Jeurissen, 2018) The 9+ Emergency and hospitalization user cohort has 25,832 schizophrenia patients in the study Cohort which is close to 10% of the cohort of 253,495.

4.7 COMPARISON BETWEEN HIGH AND LOW UTILIZER COHORT

To fully assess the potential factors associated with super utilization, as defined by 9+ ER and hospital services (approximately top 10%), a bivariate descriptive analysis on key demographic data was conducted. Since 11.1% of the study cohort has missing race data, the utilization characterization was also conducted on the cohort that has no missing race data to explore the impact of the missing race information on the research findings. The number of schizophrenia members in the study cohort with no missing race data is 225,294. From here on, the cohort that has missing race data (N=253,495) is referred as Study Cohort A and the cohort with no missing race data is referred to as Study Cohort B (N=225,294). Both cohorts are analysed hereon to assess the sensitivity of missing race data.

4.7.1 SUPER VS LOW UTILIZATION AMONG COHORT A & B BY GENDER, RACE AND AGE

As shown in Table 4-6 below, in Cohort A, 11.3 percent of female schizophrenia patients were super utilizers, defined as 9+ ER or hospitalization in a year. Men on the other hand had lower percentage of 9.2% in super utilization category. The findings were similar for cohort B, presented in Table 4-7, where 11% of the females and 9% of males were SU. The proportion of female high utilizer is statistically different from proportion of male SU for both cohort A & cohort B. (Cohort A: Z statistic: 16.6 with a p-value of 0.00001 & Cohort B: Z statistic of 15.8 and a p-value of 0.00001) Thus, a bivariate analysis shows that Female are more likely to be SU of ER and hospital services. This seems to stand in contrast with the finding by Albert et al that

among adults aged 18-64, the rate for ED visits related to schizophrenia was about twice as high for men as for women. (Albert & McCaig, 2015) This could be explained by the fact that the current analysis is specific to patients with schizophrenia in Medicaid and it analyses SU of both ER and hospitalization versus average ER use as in the Albert's study.

Table 4. 6: Utilization by Gender, Race and Age – Cohort A

	Super Utilizer Number	Super Utilizer %	Low Utilizer Number	Low Utilizer %	Total Number
Male	12512	9.2	122697	90.8	135209
Female	13320	11.3	104966	88.7	118286
p-value Z-statistic					0.00001 16.6
White	13212	10.8	109491	89.2	122705
Black	9279	9	93310	91	102589
p-value z-statistic					0.00001 13.6
18-34 Years	7927	12.5	55382	87.5	63309
35–64 years	16402	10.4	140592	89.6	156994
65-89 years	1503	4.5	31689	95.5	33192
p-values* Z-statistics					0.0001 0.00001 14.05 39.72

*P-values when comparing middle and elderly age groups super utilization to young age group respectively.

With respect to race, the analysis shows that while 10.8% of whites in Cohort A, which is same as Cohort B (due to missing race data in Cohort A) fell in high utilizer category, only 9.2 % of blacks were SU. The data is presented in both Table 4.6 and Table 4.7. The Z-statistic of the bivariate analysis was 13.6 and the p-value was 0.00001. This bivariate analysis does not

conform to the findings of Desai where blacks were positively related to high utilization of resources (Desai, Lawson, Barner, & Rascati, 2013). This could be due to difference in the definition of super utilization. Cost was used as a cutoff in Desai study instead of visits to hospital and ER. Another study exploring the disparities in health care utilization among Black and White Medicaid enrolees by Wallace et al confirms the incremental use of emergency room by blacks. (Wallace, Lollo, Duchowny, Lavallee, & Ndumele, 2022) While this study estimates that adult Black enrolees had 2.53 more emergency room visits per 100 enrolees per year when compared with adult White enrolees (95% CI, 2.00-3.06), it also showed that Blacks had 0.25 less inpatient admissions per 100 enrolees per year. This estimate was derived after adjustment was made for demographic characteristics and health status. One must consider that Wallace study includes all Medicaid patients from three states and is not limited to schizophrenia patients. The lower use among Blacks in the current analysis could be also explained by limitation of access of healthcare for patients with serious mental illnesses and potential presence of provider bias or stigma in reaching out for mental care within black cohort of patients. (NAMICA, 2024)

The proportion of Medicaid schizophrenia patients in Cohort A by their age groups are shown in Table 4-7. The age distribution in Cohorts A, shows that the youngest age group, youngest-aged, which is 18-34 years, have the highest percentage of high utilizers (12.5%). Using the young-aged as reference, a bivariate analysis shows that the middle-aged cohort (35-64 years) is statistically significantly different. The z-score 14.0523 and a p-value of 0.0001. A similar conclusion is made when comparing the old-aged (65-89 years) in cohort A. When

testing statistical significance in the difference in proportion in HU category, the Z-score is 39.7218 with a p-value of 0.00001.

Table 4. 7: Utilization by Gender, Race and Age – Cohort B

	Super Utilizer Number	Super Utilizer %	Low Utilizer Number	Low Utilizer %	Total Number
Male	10790	9.0	108539	11.0	119329
Female	11703	11.0	94262	89.0	105965
p-value z-statistic					0.00001 15.8
White	13212	10.8	109491	89.2	122705
Black	9279	9	93310	91	102589
p-value z-statistic					0.00001 13.6
18-34 Years	6598	12.5	46183	87.5	52781
35–64 years	14495	10.3	126793	89.7	141288
65-89 years	1400	4.5	29825	95.5	31225
p-values* Z-statistics					0.00001 0.00001 14.11 39.72

*P-values and z-statistics when comparing middle and elderly age groups super utilization to young age group respectively.

As seen in Table 4-7 above, Cohort B has similar SU by age distribution with age group 18-34 with highest percentage of schizophrenia patients in SU category in comparison with age cohort 35-64 years and 65+ years. Upon testing statistical significance for the differences in the

proportion of schizophrenia members, one finds that the middle-aged and old-aged are both significantly different from the young aged with p value less than 0.00001 in both comparisons. The z-scores were 14.12and 38.3 respectively. There are studies that confirm higher use of resource among younger schizophrenia patients. (Huang, Amos, Joshi, Wang, & Nash, 2018) (Pesa, et al., 2021)

4.8 THE ZERO UTILIZER

A significant proportion (37%) of schizophrenia patients did not use any ER or hospital services in a year. It is imperative to characterize this cohort of zero utilizer patients. Table 4.8 displays the descriptives by key demographics. It is interesting to note that while Whites make a bigger proportion of super utilizers, they also make a bigger proportion of zero utilizers. Less ER and hospitalization represent better management of schizophrenia disease, and this shows more whites may be receiving optimal care to prevent sudden trips to emergency care. A parallel observation can be drawn from male versus female zero utilization data. Females have a lower zero utilization of ER and hospitalization services in comparison of males (32.5% vs 40.8%), they also have a much higher proportion in super utilization category (11% vs. 9%). This suggests lack or sub optimal care or support among female schizophrenia patients.

Table 4. 8: Zero Utilization by Gender, Race and Age – Cohort A

	Zero Utilizer Number	Zero Utilizer %
Male	55230	40.8
Female	38485	32.5
p-value z-statistic		0.00001 43.25
White	52504	42.8
Black	39483	38.5
p-value z-statistic		0.00001 20.69
18-34 Years	20399	32.2
35–64 years	58609	37.3
65-89 years	14707	44.3
p-values* Z-statistics		0.00001 0.00001 -22.63 37.08

*P-values and z-statistics when comparing middle and elderly age groups zero utilization to young age group respectively.

Super utilization of ER and hospitalization was highest among young cohort of patients which conforms to the lowest proportion in the zero-use category, (32,2%) in comparison to other two age groups. A similar observation is seen for the other two age groups of 35-64 Years and 65-89 years with 37.3% and 44.3% respectively. The elderly group had the lowest proportion of super utilizer and highest among the zero utilizers.

4.9 CONCLUSION

The descriptive analysis on utilization of emergency services and hospitalization shows that a significant proportion of schizophrenia members utilize substantial ER and hospital resources in Medicaid part of the US health care system. It is observed that at least one in ten schizophrenia patients in the Medicaid system are seeking emergency or hospitalization care at least 9 times in a year! This points to the fact that these patients may be receiving sub optimal care leading them to seek emergency services and/or hospitalizations most of the months in a year. The analysis also shows that there is a significant proportion (37%) of schizophrenia patients who do not need any emergency or hospitalization in a year pointing to a disease which is either milder or better managed or patient may have complete lack of access to health care. Complete lack of access is highly unlikely. Although Medicaid mental health care has challenges, and the beneficiaries often have unmet needs and difficulty getting access to appropriate services (MACPAC, 2021) but Medicaid still remains a significant provider of mental healthcare (CMS, 2024).

Overall, based on bivariate analysis of both Cohort A and Cohort B (with and without missing race data), there is larger proportion of high utilization among White vs. Black, younger vs. older, and Female vs Male schizophrenia patients. The higher proportion of female in high utilizer category stand in contrast to findings in literature that men use more ER than women, but the finding can perhaps be explained by the fact that the current analysis is for patients with schizophrenia in Medicaid and it analyses high utilizer of both ER and hospitalization versus average ER use. (Albert & McCaig, 2015)

Lower rates of super utilization among Black were not expected given the findings of earlier studies by Desai. (Desai, Lawson, Barner, & Rascati, 2013) The difference may be due to significant differences in the source of data and the design of the studies including definition of super utilizer. The current research is based on a significantly large dataset with robust sample size of hundreds of thousands of schizophrenia Medicaid patients in comparison of only 317 schizophrenia patients in Desai's study who have various insurance coverages and hence not specific to Medicaid. Another reason for the difference could be because of how the data was collected in Desai's study, which was survey based on personal recollection of medical services uses, while this study analysis is based on actual medical services used and reimbursed by Medicaid. Desai's study data was sourced from the National Medical Expenditure Survey which does have the benefit of a more comprehensive data elements such as access to care, family status and other determinants of health but the accessibility to these incremental data elements should not play a role in the conclusion regarding Blacks being less in comparison to Whites in the Super Utilizer cohort. It is possible that the role of race in high utilization may be different for different health issues. Wallace study is in line with findings in terms of hospital utilization although it also showed that Blacks make a higher proportion of high utilizers of emergency services. A reason for the difference between Wallace and this analysis is that Wallace's analysis included all Medicaid members, not just schizophrenia, and they were from only three US states. The year of Wallace study was also limited to 2016 while the current research includes 10 years of data from 2010 to 2019.

This finding is also confirmed by research conducted by Shim et al which found that the whites had the higher emergency visit rate in comparison to all other minority groups. (Shim, et

al., 2014) The study also found the finding as “strikingly” different when it was compared to patients with diabetes or other emergency visits among patients with other diseases. (Shim, et al., 2014) Confirming this finding is deep research showing lower use of healthcare among Black community with serious mental illness like schizophrenia, due to multitude of reasons such as: negative stigma associated with mental health, lack of cultural competency among healthcare professional preventing effective interactions, lack of diversity of healthcare professional or lack of representation in health system, challenges related to transportations from remote underserved areas, discrimination and distrust in their providers leading them to believe that their care will be compromised. (Tirrell, 2023) (Shim, Compton, Rust, Druss, & Kaslow, 2009)

The finding that young are more represented in SU category is not surprising based on literature. The disease usually strikes patients in their 20s and early 30s and higher utilization by the patients in 20s and 30s are confirmed by prior studies. (Huang, Amos, Joshi, Wang, & Nash, 2018) (Pesa, et al., 2021) (Cloutier, et al., 2016) (Desai, Lawson, Barner, & Rascati, 2013)

Upon a closer look at the zero-utilization category, one finds that there is higher proportion of Male and Whites in comparison to females and blacks. This may point to better managed disease among Males and Whites. This could be due to several reasons such as better access, caregiver impact, less stigma or racial bias. Another key conclusion is that missing race data in Cohort A does not seem to lead to different conclusions for gender and age utilization of Emergency and hospital services.

Thus, the current findings conclude that, based on a bi-variate analysis of nationally represented Medicaid data, black and female schizophrenia patients make a smaller proportion of SU group. A multivariate analysis was conducted next to confirm the findings above.

Furthermore, design of a robust schizophrenia management tool will need to also consider other factors, besides basic demographics, that might affect high utilization such as disease management with antipsychotics and key co-morbid health conditions. The next chapter presents the selection of other social determinants of health that may be associated with super utilization along with additional descriptives of utilization by the new factors beyond key demographics selected here. This is followed by research on the association of the key factors with super utilization of ER and hospital services.

CHAPTER 5. FACTORS ASSOCIATED WITH HIGH UTILIZATION OF RESOURCES

5.1 INTRODUCTION

Schizophrenia is a chronic, debilitating illness in which most patients experience frequent relapse. As a result of the relapses, patients experience significant emergency room visits and hospitalizations. The relapses lead to increased economic burden to the patient, caregivers, and the health care systems. The disease also leads to progressive functional deterioration and worsening of clinical outcomes for the patients. (Almond, Knapp, Francois, Toumi, & Brugha, 2004) Therefore, the prevention of relapse is a primary treatment goal for the successful long-term management of schizophrenia. Research show that preventative strategies such as combination of psychoeducation, active monitoring for prodromal symptoms along with medications, weekly group therapy for patients, and multifamily therapy groups can help in preventing worsening of the disease. (Herz, et al., 2000)

The healthcare resource utilization among schizophrenia patients is not uniformly distributed. A small percentage of patients consume disproportionate resources. With research showing that these small numbers of as colloquially known as “frequent fliers” or “super utilizers” create significant burden in terms of healthcare resource use. Understanding the factors that lead to super utilization may present an opportunity to better the quality of care as well alleviate economic burden to the system and patients. These factors are critical in designing management strategies to prevent relapses in schizophrenia patients and improving their and their caregiver’s quality of life. Hence, the key objective of this thesis is to characterize

super utilization among Schizophrenia patients in the US Medicaid System, as presented in chapter 4, and analyse factors associated with super utilization of resources. This chapter will identify factors that may predict super utilizers among schizophrenia patients for whom a targeted disease management tool can be developed.

This chapter presents multivariate approaches and the subsequent results from the analysis. The model contruct is based on Dahlgren and Whitehead Rainbow Model (Dyar OJ, et al., 2022). This "Rainbow Model" provides a powerful framework for understanding how mental health such as schizophrenia is shaped by various layers of social, economic, and environmental factors. The final list of key factors is dependent on data elements available in the US Medicaid databases. This may limit us in fully understanding all the key factors that may drive high utilization, but it may also give us an analytic approach that is significant in identifying schizophrenia members who are at risk of multiple emergency services and hospitalization with the limitation of data elements available to population health decision makers. Thus, the approach this analysis takes is of pragmatism.

5.2 METHOD

This is a retrospective observational cohort study which analyses the factors associated with high utilization among patients with schizophrenia in the US Medicaid system. The data was drawn from MarketScan® Multi-State Medicaid Database V2047, released on 7th March 2022. Information on the data source and statistical tool is same as the descriptive analysis presented in chapter 4.

5.2.1 MULTIVARIATE APPROACH

With the objective of understanding factors that are associated with a schizophrenia patient being a super utilizer or not, Logistic regression analysis is used. This type of regression technique is applied to examine the association of (categorical or continuous) independent variable(s) with one dichotomous dependent variable which is a “super utilizer” or “not a super utilizer”. Logistic regression provides odds ratio in the presence of more than one explanatory variable. The procedure is quite similar to multiple linear regression, with the exception that the response variable is binomial. The result will provide the impact of each variable on the odds ratio of being in the super utilizer category. This regression not only gives a measure of how relevant an independent variable is (i.e. the coefficient size) but also tells us about the direction of the relationship whether it is positive or negative.

Logistic regression is a statistical model that uses Logistic function to model the conditional probability. For binary regression, which is used here, we calculate the conditional probability of the dependent variable Y, given independent variables or the factors Xi.

It can be written as $P(Y=1|Xi)$ or $P(Y=0|Xi)$

And read as the conditional probability of Y=1, a patient is a “super utilizer” given Xi or conditional probability of Y=0, a patient is “not a super utilizer” given Xi. $P(Y \mid Xi)$ is approximated as a sigmoid (s-shaped) function applied to a linear combination of input features.

The goodness of the fit was assessed using the Area under the curve (AUC) of the ROC curve and the Brier test. ROC curves are graphs that plot a model's false-positive rate against its true-positive. AUC is a summary statistic that ranges between 0.5 and 1. It indicates how good the Logistic Regression Model is correctly predicting positive and negative outcomes (i.e. 0 and 1). The larger the AUC, the better the model is. Brier scores are also calculated by estimating the mean squared error between predicted probabilities and the observed values, in other words the actual value. The value of the Brier score is always between 0.0 and 1.0. A model that is perfect will have a score of 0.0 and the worst will have a score of 1.0. AUC evaluates the rank of the prediction while Brier score calculates the accuracy of probabilistic predictions. Odd Ratios (ORs), 95% confidence intervals, coefficients and Z-statistics were computed for all covariates of the models.

The z value and Pr(>|z|) represent the statistical significance of each coefficient in the model. The z value is the ratio of the estimated coefficient to its standard error. It measures the number of standard deviations that the estimated coefficient is away from zero. A higher absolute value of z value indicates that the estimated coefficient is more statistically significant. The Pr(>|z|) represents the p-value for each coefficient, which is the probability of observing a z value as extreme or more extreme than the observed value, assuming the null hypothesis that the coefficient is zero. A lower p-value indicate that the coefficient is more statistically significant, and a value less than 0.05 is often considered as evidence to reject the null hypothesis.

5.2.2 DATA COHORT

The data includes all adult schizophrenia patients in the nationally represented Marketscan IBM Medicaid database from year 2010 to 2019. The previous chapter discusses the rationale for the time-period chosen for the analysis. During this time-period, there are 366,565 adult schizophrenia members. To assess the base line characteristics of the schizophrenia cohort, data was then further limited to members who had at least 365 days of continuous data before diagnosis of schizophrenia and to analyse the utilization of ER and inpatients hospitalization, the cohort required at least 365 days of continuous observation post diagnosis. Once this selection criteria were applied the total remaining cohort is 253,495 which remains a significant large sample size. Since 11.1% of this cohort has missing race data and race is seen as an important factor that may been associated with utilization (Bartels, Clark, Peacock, Dums, & Pratt, 2003) (Desai, Lawson, Barner, & Rascati, 2013) (Huang, Amos, Joshi, Wang, & Nash, 2018), regression was also conducted on the cohort that has no missing race data. The number of schizophrenia patients in the study cohort with no missing race data is 225,294. The cohort that has missing race data (n = 253,495) is referred from here on as Study Cohort A and the cohort with no missing race data is referred to as Study Cohort B (n = 225,294).

One key finding in the earlier chapter is that 37% of the schizophrenia patients do not have any emergency and hospitalization in a year time period. Given the presence of a significant cohort of “zero utilizers”, regressions were also conducted on a subgroup of dataset which excludes all zero utilizers to see if that changes key findings. A two-stage model was also estimated to separate the factors that are more related to zero utilization from the ones that lead to super utilization.

5.2.3 REGRESSION MODEL CONSTRUCT FOR SUPER UTILIZATION OF RESOURCES

"The Dahlgren and Whitehead "Rainbow Model" provided the rationale for selection of variables impacting high utilization of resources by severe mentally ill schizophrenia patients. This was complemented by findings from the systematic literature review in chapter 3.

Studies by Doran and Shin led to identification of Individual characteristics such as significant comorbidities like diabetes, heart failure and renal disease along with individual lifestyle factors such as alcohol, opioid and substance abuse as drivers of resource utilisation. (Doran & Rosenhenck, 2013) (Shim, et al., 2014) The study by Doran which was conducted among veteran population with data sourced from 5.5MM Veteran Affairs members (Doran & Rosenhenck, 2013) also concluded that, living condition factor, such as, homelessness was associated with high Emergency Department use. Zhu's 2008 study is another source for identification of explanatory variable. (Zhu, et al., 2008) This study is a 3-year non-interventional study called US-SCAP (U.S. Schizophrenia Care and Assessment Program) which was conducted between 1997 to 2003. It studied the cost of managing 1550 schizophrenia patients and the impact of crisis on it. The study concluded that all recent crisis events positively impacted the cost of mental health treatment, the biggest being among patients who attempted suicide. Both Zhu and Doran study show that there is variability in the cost of managing schizophrenia patients driven by factors such as recent crisis, co-morbidities like heart failure and socioeconomic factors such as homelessness. (Doran & Rosenhenck, 2013) (Zhu, et al., 2008).

Cloutier's study showed that schizophrenia patients use more resources in the earlier phase of their disease and Bartels and Huang also concluded the role of age in resource

utilization (Cloutier, et al., 2016) (Bartels, Clark, Peacock, Dums, & Pratt, 2003) (Huang, Amos, Joshi, Wang, & Nash, 2018). Treatment adherence led to better disease management and hence it was not surprising to see Offord, Pesa, Shah and McCombs conclude the negative associating between treatment adherence and resource utilization. (Offord S. L., 2013) (Pesa, Doshi, Wang, Yuce, & Basur, 2017) (Shah, Xie, Kariburyo, Zhang, & Gore, 2018)**,** (McCombs, Nichol, Johnstone, & Lizheng, 2000)**.** Desai's work showed positive association between black race and resource utilization. Her study also showed that younger patients (compared with older patients), patients with private insurance (compared with the uninsured), and those living in the northeastern United States (compared with those living in the southern United States) had higher schizophrenia-related direct medical costs.

Guided by the Rainbow Model, along with the findings from the literature on the factors that may be associated with high use of resources among schizophrenia patients, a list of variables was identified. The list was as follows:

Age, sex, race, ethnicity, comorbidities (Heart Failure, Diabetes, Cancer, Suicide Ideation & Attempt, End Stage Renal Disease) alcohol or substance abuse, homelessness, housing, location of the residence, education, perception of poor health and social isolation, and treatment adherence. The above list of variables was then further refined based on availability of these data elements in the Medicaid Marketscan database. The remaining variables were age, sex, race, ethnicity, comorbidities, alcohol and substance abuse, treatment adherence as measured by availability of antipsychotic prescription. Ethnicity was available but had significant missing data and hence it was removed as an explanatory variable.

Multiple regression analysis was conducted. At first a single logistic model was estimated with four different combinations of explanatory variables. These models were estimated for both Cohort A and Cohort B to understand the impact of 11% missing race data. Secondly, given a significant proportion of schizophrenia patients had zero utilization in a year (37%), a single regression model was estimated with data without zero utilizer. Thirdly, a two-stage logistic regression was estimated to treat differently the non-users, whose zero-healthcare use may have different determinants.

5.3 SINGLE REGRESSION MODEL FOR SUPER UTILIZATION OF RESOURCES: DATA INCLUDES ZERO UTILIZERS

There are four separate single logistic regressions models (Model I, II, III & IV) analysed to research the factors associated with high utilization of emergency and hospital services among Medicaid schizophrenia patients. The primary differences among them are the selection of explanatory variables. The rationale for the selection of explanatory variables and the construct of the four models is presented below.

5.3.1 EXPLANATORY VARIABLES – MODEL I

The following explanatory variables were selected for logistic regression:

Demographics: Age, Sex, Race

Comorbidities: Heart Failure, Diabetes, Cancer, Suicide Ideation & Attempt, End Stage Renal Disease, and Alcohol and/or Substance Abuse

Treatment adherence: Use of antipsychotics in past 30 days

Subsequently, additional explanatory variables were added with a systematic approach. The variables added were Charlson Comorbidity Index (Romano Version), and Obesity. They were added both together as well as one at a time. The rationale for adding both Charlson Comorbidity Index (Romano Version) and Obesity are presented below.

5.3.2 CHARLSON COMOBIDITY INDEX AS AN EXPLANATORY VARIABLE

Charlson Comorbidity Index (CCI) is an algorithm that predicts 10-year survival in patients with multiple comorbidities such as diabetes and heart failure (Charlson, Pompei, Ales, & MacKenzie, 1987). CCI is a method where comorbidities of patients are categorized based on the International Classification of Diseases (ICD) diagnosis codes found in claims databases such as the IBM® MarketScan® Multi-State Medicaid Database V2047 used in the current analysis. Each comorbidity category has an associated weight, which is from 1 to 6, based on the adjusted risk of mortality or resource use. The weights are summed, and the result is defined as a single comorbidity score for a patient. A score of zero indicates that no comorbidities were found. The higher the score, the more likely the patients will experience health outcomes that will result in mortality or higher resource use. (Charlson, et al., 2008)

The original CCI has evolved over time. While the original CCI included 19 categories, modification by Deyo reduced it to 17 categories. (Charlson, Pompei, Ales, & MacKenzie, 1987) (Deyo, 1992). Subsequently the list of specific ICD diagnosis codes that are used to identify different categories of comorbidity were modified (Romano, 1993) and updated from ICD-9-CM to work with ICD-10 coding (Halfon, 2002) (Quan H, 2005). The CCI disease categories along with their ICD codes are included in Appendix IV.

Each comorbid condition is given a score depending on the risk of dying associated with one. The scores are 1, 2, 3, or 6. The clinical conditions and their associated scores are as follows:

Myocardial Infarction, Congestive Heart Failure, Peripheral Vascular Disease, Cerebrovascular Disease, Dementia, Chronic Pulmonary Disease, Rheumatologic Disease, Peptic Ulcer Disease have a score of 1. Mild Live Disease has a score of 1 and 3 if moderate or severe, and Diabetes have a score of 1 if it is controlled and gets a score of 2 if it is uncontrolled. Hemiplegia or Paraplegia, Renal Disease is given a score of 2. Cancer is given a score of 2 when local and a score of 6 when metastatic. AIDs is given a score of 6. Patients who are 50 years old or more get additional 6 points with an additional 7 point if 50-59 years, an additional 8 points if 60-69 years, and additional 9 points if 70-79 years and 10 points if the age is 80 and above. The scores are then summed to provide a total score to predict mortality.

Logistic regression requires that there should be no, or very little, multicollinearity between the predictor variables—in other words, the predictor variables (or the explanatory variables) should be independent of each other. This means that there should not be a high

correlation between the independent variables. In statistics, certain tests can be used to calculate the correlation between the predictor variables. Given the Model I include comorbid diseases such as heart failure, diabetes, cancer, and End Stage Renal Disease (ESRD), the Pearson correlation coefficient was estimated to understand the extent of their correlation with Charlson Comorbidity Index-Romano. The correlations findings are presented in the Table 5-1 below.

Table 5. 1: Correlation among Charlson Comorbidity Index-Romano and Comorbid conditions

	CCI	Heart failure	Suicide Ideation & attempt	Type 2 Diabetes	ESRD	Alcohol & substance abuse
CCI	1	0.48	0.06	0.53	0.23	0.1
Heart failure	**0.48**	1	0.01	0.22	0.17	0.02
Suicide ideation & attempt	0.06	0.01	1	0	0	0.28
Type 2 Diabetes	**0.53**	0.22	0	1	0.09	0
End Stage Renal Diseases	**0.23**	0.17	0	0.09	1	0
Alcohol & substance abuse	0.1	0.02	0.28	0	0	1

The highest correlation coefficient seen is 0.53 between Type 2 diabetes and CCI while the correlation coefficient was below 0.5 at 0.48 and 0.23 between CCI and Heart Failure and End State Renal Disease respectively. Given the correlation between CCI and other comorbidities are moderate to low (Moderate: 0.40 to 0.69 Low: below 0.4), a second logistic regression including CCI was also included in the analysis plan. Thus, Model II includes all explanatory variables from Model I plus CCI.

5.3.3 OBESITY AS AN EXPLANATORY VARIABLE

The utilization of healthcare resources is significantly higher in individuals with obesity. A meta-analysis by Kent et al has shown that there is a corresponding increase in healthcare costs for class I, II and III Obesity. (Kent S, 2017) Norton et al showed that the positive relationship between high utilization of resources and obesity is seen in both United States and United Kingdom (Nørtoft E, 2017) Their study showed that there was "consistency in the impact of obesity on healthcare utilization across two very different healthcare systems". Another key factor that led to inclusion of obesity as an explanatory variable is the fact that the risk of obesity is threefold higher among people diagnosed with schizophrenia. (Annamalai A, 2017) Given the positive relationship between obesity and resource use, coupled with significantly higher prevalence of obesity among schizophrenia patients, obesity was selected as another explanatory factor that was added in a stepwise manner in the logistic regression for the current study and is included in Model III along with all the base explanatory variables in Model I. A fourth model (Model IV) was analysed which include all the base explanatory variable in Model I along with CCI and Obesity.

5.3.4 OTHER KEY EXPLANATORY FACTORS NOT INCLUDED

The literature points to other factors such as homelessness (Doran & Rosenhenck, 2013), perception of poor health and social isolation (Samuel T, 2022) and region of patient residence (Desai, Lawson, Barner, & Rascati, 2013) as significant in identifying super resource utilizers but the current study is unable to include them due to absence of these data elements

in the MarketScan® Multi-State Medicaid Database. The unavailability of these variables is discussed in the limitation sections of this chapter.

5.3.5 EXPLANATORY VARIABLES FOR THE REGRESSION

The final list of all explanatory variables selected are presented in the Table 5-2 along with their count in Super Utilizer and Not Super Utilizer group. The table below shows the data counts from Cohort A which has 253,495 patients. The definition of "Not Super Utilizer" includes zero utilizers. Table 5-3 shows the utilization among Cohort A by all explanatory variables but excludes zero utilizers.

Table 5. 2: Super utilization by explanatory variables in Cohort A

Factors	Super Utilizer (N = 25832)		Not Super Utilizer (N = 227663)		p-values
	Count	Mean/%	Count	Mean/%	
Charlson Comorbidity Index (CCI)		0.12		0.08	0.00001
Male	12512	48%	122697	54%	0.00001
Black	9279	36%	93310	41%	0.00001
White	13214	51%	109491	48%	0.00001
Female	13320	52%	104966	46%	0.00001
Heart Failure	4060	16%	19571	9%	0.00001
Suicide Ideation or Attempt	11660	45%	34968	15%	0.00001
Type 2 Diabetes	9056	35%	61122	27%	0.00001
Obesity	9230	36%	52504	23%	0.00001
End Stage Renal Disease	917	4%	2725	1%	0.00001
Alcohol & Substance Abuse	20208	78%	115508	51%	0.00001
Use of Antipsychotic	10246	40%	83529	37%	0.00001
Age 18-34 Years	7927	31%	55382	24%	0.00001
Age 35-64 Years	16402	63%	140592	62%	0.00001
Age 65+ Years	1503	6%	31689	14%	0.00001

As expected, the differences in the comorbid proportions are substantial when comparing the two categories of utilization. As shown in Table 5.2, Heart Failure is 16% among the super utilizer while only 9% of not super utilizer had heart failure, thus a 78% higher prevalence. Suicide Ideation or Attempt is three times higher in prevalence (45% vs. 15%), 30% higher with Type 2 Diabetes (35% vs. 27%), approximately 50% higher obesity among super utilizers (36% vs. 23%). Interestingly the differences in the proportion of Super Utilizer versus Not Super Utilizer in the categories of "use of antipsychotics", "race" and "gender' do not look as big as with other factors.

Table 5. 3: Super utilization by explanatory variables in Cohort A Without Zero Utilizers

Factors	Super Utilizer (N = 25832)		Not Super Utilizer excl Zero utilizers (N = 133948)		p-values
	Count	Mean/%	Count	Mean/%	
Charleson Comorbidity Index		0.12		0.09	0.00001
Male	12512	48%	67467	50%	0.00001
Black	9279	36%	53827	40%	0.00001
White	13214	51%	64716	48%	0.00001
Female	13320	52%	66481	50%	0.00001
Heart Failure	4060	16%	13737	10%	0.00001
Suicide Ideation or Attempt	11660	45%	27362	20%	0.00001
Type 2 Diabetes	9056	35%	38471	29%	0.00001
Obesity	9230	36%	35319	26%	0.00001
End Stage Renal Disease	917	4%	2012	2%	0.00001
Alcohol & Substance Abuse	20208	78%	79819	60%	0.00001
Use of Antipsychotic	10246	40%	48421	36%	0.00001
Age 18-34 Years	7927	31%	34983	26%	0.00001
Age 35-64 Years	16402	63%	81983	61%	0.00001
Age 65+ Years	1503	6%	16982	13%	0.00001

The differences in the proportion of all the explanatory variables in the super utilizer category versus the not super utilizer are all statistically significant but the differences are narrower with multiple variables when zero utilizers are excluded. For example, End Stage Renal disease is four times higher for super utilizers when comparing the complete data set, but it is only twice as high in the data set which removes zero utilizers. Another data to note is the prevalence of Suicide Ideation or Attempt is 3 times higher in the cohort inclusive of zero utilizer but only 2.25 times higher when zero utilizers are excluded from Not High Utilizer group. This is expected as the second table has only those patients that have ER and or hospital visits in a year. This is also indicated in higher CCI (0.9 versus 0.8) for the cohort that excludes zero utilizers in comparison to the one that does not.

5.4 REGRESSION APPROACHES: SINGLE MODEL

The model was approached in a systematic way where the first model, described as the primary model or Model I, included variables found in the literature review and were present in the IBM Marketscan database that is used in this research. The regression was enhanced with the addition of Charlson Comorbidity Index-Romano version and/or Obesity in subsequent models. Thus, the various model versions are:

1. Primary Model: Model I
2. Primary Model + Charlson Comorbidity Index: Model II
3. Primary Model + Obesity: Model III
4. Primary Model + Charlson Comorbidity Index + Obesity: Model IV

The analysis was conducted on both Cohort A and Cohort B. This was to assess whether missing race data changed our model results. Missing race was also added as a variable to cohort A to assess its association to super utilization.

5.4.1 Primary Regression Models with Zero Utilizers – Model I

The primary logistic regression model, also referred to as Model I, is used to assess the relationship between patient demographic factors, key co-morbidities and treatment use with the super utilization of ER and hospital services among Medicaid schizophrenia patients. The demographic variables included in this regression are age, gender, and race. Age is grouped in three categories. AY is Age Young (18-34 years), AM is Age Middle (35-64 years), and AO is Age old (65+ years). The five comorbidities included were Type 2 Diabetes, End Stage Renal disease, Heart Failure, Suicide Ideation and/or Attempt, Alcohol and/or Substance Abuse. Disease treatment or antipsychotic use variable. This variable is estimated based on presence of 30-day supply of medicine at the time of the outcome. Assumption is made that if the patient has the drug supply that they are also taking the medicine as prescribed by their physician.

The equation of the primary model, Model I, is presented below:

$$Log\ (p/(1-p)) = b_0 + b_1(R) + b_2(G) + b_3(HF) + b_4(SI) + b_5(D) + b_6(ESRD) + b_7(ASA) + b_8(AP) + b_9(AY) + b_{10}(AM)$$

where,

b_0 = Intercept

R = Race is Black

G = Gender is Female

HF = Heart Failure

SI = Suicide Ideation and/or Attempt

D = Type 2 Diabetes

ESRD = End Stage Renal Disease

ASA = Alcohol and/or Substance Abuse

AP = Antipsychotics use

AY = Age 18-34 Years

AM = Age 35-64 Years

In this model, the reference factors are White, Male and AO (Age group 65+) for Blacks, Female, and AY and AM respectively.

5.5 RESULTS OF REGRESSION – SINGLE MODEL APPROACH

The regression was conducted with both Cohort A (missing race data) and Cohort B (No missing race). . Regression results for all four Models are presented in Table 5-4 and Table 5-5 for Cohort A and Table 5-6 and Table 5-7 for Cohort B. Table 5-4, and Table 5-6 displays the Odds Ratios for Cohort A and B respectively while Table 5-5 and Table 5-7 include the model

coefficients and z-scores. Results of are all four models are displayed together to enable comparisons. Table 5-8 presents the goodness of fit of the various models in Cohort A and Cohort B respectively. This table presents the AUROC and Brier scores to determine whether a set of observed values match those expected under the applicable model.

Table 5. 4 : Cohort A Models I II III & IV Regression Results: Odds Ratios

	Model I			Model II			Model III			Model IV		
	Odds Ratio	**2.50%**	**97.50%**	**Odds Ratio**	**2.50%**	**97.50 %**	**Odds Ratio**	**2.50 %**	**97.50%**	**Odds Ratio**	**2.50%**	**97.50%**
Intercept	0.02	0.02	0.02	0.01	0.01	0.01	0.02	0.02	0.02	0.01	0.01	0.01
CCI				13.33	11.25	15.80				12.57	10.60	14.90
Black	0.92	0.89	0.95	0.92	0.89	0.96	0.92	0.89	0.95	0.93	0.90	0.96
Female	1.25	1.22	1.29	1.24	1.20	1.28	1.20	1.16	1.24	1.19	1.15	1.23
Heart Failure	1.87	1.78	1.96	1.37	1.29	1.44	1.80	1.71	1.89	1.33	1.26	1.40
Suicide Ideation or Attempt	3.20	3.09	3.31	3.08	2.98	3.18	3.14	3.04	3.25	3.04	2.93	3.14
Type 2 Diabetes	1.43	1.38	1.49	1.11	1.07	1.16	1.36	1.31	1.41	1.06	1.02	1.11
Obesity							1.28	1.24	1.33	1.24	1.20	1.29
End Stage Renal Disease	2.79	2.54	3.07	2.12	1.92	2.34	2.78	2.53	3.06	2.12	1.93	2.34
Alcohol and/or Substance Abuse	2.41	2.32	2.51	2.26	2.18	2.35	2.41	2.32	2.50	2.26	2.18	2.35
Antipsychotics use	0.91	0.88	0.94	0.91	0.89	0.94	0.90	0.87	0.93	0.91	0.88	0.94
Age 18-34 Years	2.72	2.53	2.93	3.44	3.19	3.71	2.61	2.42	2.81	3.29	3.05	3.55
Age 35-64 Years	2.08	1.94	2.22	2.36	2.21	2.53	2.00	1.87	2.14	2.28	2.13	2.44
Missing race	1.07	1.02	1.13	1.08	1.03	1.14	1.08	1.03	1.13	1.09	1.04	1.14

Table 5. 5: Cohort A Models I, II, III & IV Regression Results: Coefficients & Z-Value

	Model I			Model II			Model III			Model IV		
	Coeff Est.	**Std. Error**	**z value**	**Coeff Est.**	**Std. Error**	**z value**	**Coeff Est.**	**Std. Error**	**z value**	**Coeff Est.**	**Std. Error**	**z value**
Intercept	-4.08	0.04	-109.59	-4.30	0.04	-112.40	-4.06	0.04	-109.21	-4.29	0.04	-111.91
CCI				2.59	0.09	29.94				2.53	0.09	29.17
Black	-0.09	0.02	-5.08	-0.08	0.02	-4.56	-0.08	0.02	-4.81	-0.08	0.02	-4.32
Female	0.23	0.02	14.11	0.21	0.02	13.33	0.18	0.02	10.91	0.17	0.02	10.50
Heart Failure	0.62	0.02	25.11	0.31	0.03	11.45	0.59	0.03	23.38	0.28	0.03	10.42
Suicide Ideation or Attempt	1.16	0.02	67.92	1.12	0.02	65.34	1.15	0.02	66.80	1.11	0.02	64.41
Type 2 Diabetes	0.36	0.02	19.96	0.10	0.02	5.21	0.31	0.02	16.54	0.06	0.02	3.07
Obesity							0.25	0.02	13.75	0.22	0.02	12.03
End Stage Renal Disease	1.03	0.05	20.98	0.75	0.05	14.95	1.02	0.05	20.93	0.75	0.05	15.03
Alcohol and/or Substance Abuse	0.88	0.02	45.72	0.82	0.02	42.07	0.88	0.02	45.56	0.82	0.02	42.05
Antipsychotics use	-0.09	0.02	-5.68	-0.09	0.02	-5.42	-0.10	0.02	-6.17	-0.10	0.02	-5.85
Age 18-34 Years	1.00	0.04	26.70	1.23	0.04	32.06	0.96	0.04	25.47	1.19	0.04	30.82
Age 35-64 Years	0.73	0.03	21.25	0.86	0.03	24.71	0.69	0.03	20.13	0.82	0.03	23.64
Missing race	0.07	0.03	2.83	0.08	0.03	3.17	0.08	0.03	3.07	0.09	0.03	3.38

Note: Pr(>|z|) was 0.0 for all variables in all models.

Table 5. 6: Cohort B Regression Model I, II, III & IV Results: Odds Ratios

	Model I			Model II			Model III			Model IV		
	Odds Ratio	**2.50%**	**97.50%**	**Odds Ratio**	**2.50%**	**97.50 %**	**Odds Ratio**	**2.50 %**	**97.50**	**Odds Ratio**	**2.50%**	**97.50%**
Intercept	0.02	0.02	0.02	0.01	0.01	0.01	0.02	0.02	0.02	0.01	0.01	0.01
CCI				14.04	11.73	16.81				13.22	11.03	15.84
Black	0.92	0.88	0.95	0.92	0.89	0.96	0.92	0.89	0.95	0.93	0.90	0.96
Female	1.26	1.22	1.30	1.25	1.21	1.29	1.20	1.16	1.24	1.19	1.15	1.24
Heart Failure	1.87	1.77	1.97	1.36	1.28	1.44	1.79	1.70	1.89	1.32	1.25	1.40
Suicide Ideation or Attempt	3.21	3.10	3.33	3.10	2.98	3.21	3.16	3.05	3.27	3.05	2.94	3.16
Type 2 Diabetes	1.42	1.37	1.47	1.09	1.05	1.14	1.34	1.29	1.40	1.05	1.00	1.09
Obesity							1.29	1.24	1.34	1.25	1.20	1.30
End Stage Renal Disease	2.88	2.61	3.19	2.18	1.96	2.41	2.87	2.60	3.18	2.18	1.97	2.42
Alcohol and/or Substance Abuse	2.35	2.26	2.45	2.20	2.11	2.29	2.34	2.25	2.44	2.20	2.11	2.29
Antipsychotics use	0.92	0.89	0.95	0.92	0.89	0.95	0.91	0.88	0.94	0.91	0.88	0.95
Age 18-34 Years	2.74	2.54	2.96	3.49	3.22	3.77	2.62	2.43	2.83	3.34	3.08	3.61
Age 35-64 Years	2.07	1.93	2.22	2.36	2.20	2.54	2.00	1.86	2.14	2.28	2.13	2.45
Missing race												

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Table 5. 7: Cohort B Models I, II, III & IV Regression Results: Coefficients & Z-Value

	Model I			Model II			Model III			Model IV		
	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value
Intercept	-4.06	0.04	-105.29	-4.30	0.04	-107.99	-4.05	0.04	-104.93	-4.28	0.04	-107.51
CCI				2.64	0.09	28.74				2.58	0.09	28.00
Black	-0.09	0.02	-5.10	-0.08	0.02	-4.57	-0.08	0.02	-4.83	-0.08	0.02	-4.32
Female	0.23	0.02	13.53	0.22	0.02	12.80	0.18	0.02	10.47	0.18	0.02	10.10
Heart Failure	0.63	0.03	23.84	0.31	0.03	10.67	0.58	0.03	22.13	0.28	0.03	9.64
Suicide Ideation or Attempt	1.17	0.02	63.52	1.13	0.02	61.14	1.15	0.02	62.42	1.12	0.02	60.22
Type 2 Diabetes	0.35	0.02	18.27	0.09	0.02	4.13	0.30	0.02	15.04	0.05	0.02	2.12
Obesity							0.25	0.02	13.19	0.22	0.02	11.54
End Stage Renal Disease	1.06	0.05	20.76	0.78	0.05	14.85	1.06	0.05	20.71	0.78	0.05	14.93
Alcohol and/or Substance Abuse	0.85	0.02	41.60	0.79	0.02	38.07	0.85	0.02	41.46	0.79	0.02	38.07
Antipsychotics use	-0.09	0.02	-4.97	-0.08	0.02	-4.73	-0.10	0.02	-5.44	-0.09	0.02	-5.14
Age 18-34 Years	1.01	0.04	25.74	1.25	0.04	30.98	0.96	0.04	24.52	1.20	0.04	29.76
Age 35-64 Years	0.746	0.036	20.83	0.86	0.04	23.83	0.69	0.04	19.31	0.83	0.04	22.77
Missing race												

Note: Pr(>|z|) was 0.0 for all variables in all models.

Table 5. 8: Cohort A & B Model I, II, III & IV: Goodness of Fit Results

	Model A		Model B	
	AUROC	Brier	AUROC	Brier
Model I	0.74	0.082	0.74	0.082
Model II	0.75	0.084	0.75	0.082
Model III	0.74	0.084	0.74	0.082
Model IV	**0.75**	**0.083**	**0.75**	**0.082**

5.5.1 RESULT OF THE PRIMARY MODEL (MODEL I)

The odds ratios from the logistic regression with Cohort A is presented along with the coefficient from logistic regressions, their z value and Pr(>|z|) in Table 5-4 and Table 5-5

All the explanatory variables, in Model 1, are significant in their association with resource utilization. While most factors are positively associated with Super Utilization of ER and hospitalization among schizophrenia patients in U.S. Medicaid system, being Black and using schizophrenia medication (Antipsychotic use) is negatively related. The odds ratio for blacks and antipsychotic use is below 1 (0.92 and 0.91 respectively). The relationship between being black and being a SU was surprising but expected based on the bivariate analysis findings in chapter 4. A multivariate analysis did not change the relationship, but it also confirmed a relatively small negative effect of being black on being a SU. The negative relationship between antipsychotic treatment and being a SU is expected but the effect size is surprisingly small (OR=0.91) and that could be due to the fact that they have just started the therapy. They might be also non-adherent to the medication but claims data cannot confirm that. There is data to support significant low adherence to antipsychotics among schizophrenia patients (Acosta, Hernández, Pereira, Herrera, & Rodríguez, 2012). Suicide Ideation or Attempt has the highest effect with odds ratio at 3.2, followed by End Stage Renal Disease (ESRD) at 2.79 and being young age (Age 18-34 years) at 2.72. Suicide Ideation or Attempt has the highest z value of 67.92, followed by Alcohol and/or Substance abuse at 45.72 and young age group of 18-34 years with z-value 26.7. The corresponding Pr(>|z|) is 0.00 for all variables, which means that the coefficient for all is statistically significant at the 5% significance level but there is highest effect size with Suicide Ideation or Attempt. The coefficients estimate point to an existence of

Suicide Ideation or Attempt in the patient record, having a diagnosis of ESRD and being young age (Age 18-34 years) will result in an increase in the log-odds of being high utilizer, with other variables remaining same, by 1.16, 1.03, and 1.00 respectively.

Although Black and Antipsychotic use is negatively correlated, the relationship has relatively small negative z values of -5.08 and -5.68 respectively. The smallest z-value of 2.3 was for the variable "missing race". The model results point to positive relationship between missing data and being a super utilizer and the relationship has the odds ratio of 1.07.

The performance of the model was strong with the AUROC of 0.74. The larger the AUC, the better the model is. A model with AUC at 0.74 can be interpreted as the model is better than flipping a coin, which has a 50% chance, in predicting the outcome by 24%. The Brier score is 0.082 which is very close to 0 and thus close to a perfect score.

Cohort A had a total sample of 253,495 but it has 11.1% of race data missing. Thus, a logistic regression was conducted on Cohort B (data set with no missing race data) to see if the relationship between super utilization and black race changes to positive. The regression results are presented in Table 5-6 and Table 5-7. It shows show that an Odd Ratio of being black (0.92) is same as in Cohort A and is less than 1 confirming the negative relationship with smaller effect size compared to variables such Suicide Ideation or Attempt. This can be further displayed with a negative co-efficient of -0.09 for the Black variable in Table 5.7. The missing race data seems to have no impact in terms of model output and Table 5-5 have quite similar results. The odd ratios continue to be highest for Suicide Ideation or Attempt (3.21), followed by End Stage

Renal Disease with a odds ratio of 2.88 and being young age (Age 18-34 years) at 2.74. The odds ratios are slightly higher in effect size for these top three factors in Cohort B.

Model I output for Cohort B in Table 5-7 confirm the findings in Cohort A which is presented in Table 5-5. The highest z-value remained for the variable Suicide Ideation or Attempt at 63.72, followed by Alcohol and/or Substance Abuse (z-value = 41.6) and Age 18-34 with a z-value of 25.74. The corresponding Pr(>|z|) is 0.00, which means that the coefficient for all is statistically significant at the 5% significance level. Although Black and Antipsychotic use is negatively correlated but the relationship is relatively small with odds ratios of only -0.09 for both.

Cohort B included data that had full set of race information. The total sample size was 225,294 schizophrenia patients. Given the outcome of the model, it seems missing race data in cohort A did not have any impact on the strength of the predictive power. The Cohort B Model I also have same AUC of 0.74 and a Brier score of 0.082. Both have strong predictive power. This confirms that the missing 11% of the race data, in this data set, does not play a significant role in understanding the key factors that are associated with SU.

5.5.2 RESULT OF THE REGRESSION MODEL II

Model II includes all the variables in the Primary Model and adds Charlson Comorbidity Index-Romano version as an additional covariate. Charlson Comorbidity Index (CCI) is an algorithm that predicts 10-year survival in patients with multiple comorbidities such as diabetes and heart failure (Charlson, Pompei, Ales, & MacKenzie, 1987). It is included in Model II, as it

has been shown in multiple studies that it not only predicts the mortality risk of the individual patients, but it also strongly predicts healthcare resource utilization. (Ofori-Asenso, et al., 2018) (Charlson, et al., 2008) Given this unique data element is available in the IBM Marketscan claims database, the data source for this analysis, it is incorporated in the Model II to explore as a significant factor associated with Super Utilization of Health resource among Medicaid schizophrenia patients. Since some the elements of the CCI are also included as explanatory variables in the model (Diabetes Type 2, Heart Failure, ESRD), a correlation analysis was run to check for multicollinearity. Given the correlation were not found to be strong, decision was made to include the CCI variable along with all the Model I variables. The results of Model II logistic regression are shown in Table 5-4 and Table 5-5 for Cohort A (with missing race data) and Table 5-6 and Table 5-7 for Cohort B (no missing race data).

5.5.2.1 RESULTS OF MODEL II (COHORT A)

The model output shows CCI with the highest Odds Ratio of 13.33 which is followed by Young Age with OR of 3.44, Suicide Ideation or Attempt with OR of 3.08. It is not surprising to see the odds ratio of Heart Failure, ESRD and diabetes fall in comparison to Model I as CCI index becomes the strongest variable in terms of odds ratio as CCI construct includes co-morbid conditions such as End Stage Renal Disease and Heart Failure. Use of antipsychotic and being Black remain negatively associated with the outcome of being in the super utilizer category but the effect size remains small with odds ratio of 0.92 and 0.91 respectively.

CCI has the highest co-efficient followed by Young Age and Suicide Ideation or Attempt. Looking at z-values, one sees Suicide Ideation or Attempt remain the one with the highest value with a score of 65.34 followed by Alcohol and/or Substance Abuse with a z value of 42.07. Both CCI and being in age category 18-34 years are significant with coefficients of 2.59 and 1.23 respectively. Thus, a unit increase in CCI, will result in an increase in the log-odds of being high utilizer with other variables remain same by 2.59. Similarly, having a diagnosis of Suicide Ideation or Attempt will result in an increase in the log-odds of being high utilizer, with other variables remaining same, by 1.12. The model predictability as measured by AUROC improves to 0.75 with a Brier score of 0.084. Brier score continues to be robust as close to zero. With addition of CCI, there is slight improvement in predictability of the model.

5.5.2.2 RESULTS OF THE MODEL II (COHORT B)

The regression results for the model with CCI as an explanatory variable on the data set with no missing race confirms a negative relationship between Black and Super Utilization of health resources. The odd Ratio (0.92) is same as Cohort A of Model II with a negative co-efficient of -0.08 for the Black variable in Table 5.7. The missing race data seems to have no impact in terms of model output and Table 5-4 and Table 5-6 have quite similar output. The odds ratios continue to be highest for CCI (14.04) followed by being in Young Age Group (18-34 years) with a odds ratio of 3.49, Suicide Ideation or Attempt (3.10), and Age 35-64 year with a odds ratio of 2.36. Inclusion of CCI leads to an increase in association with the outcome of being in super utilizer category and Suicide Ideation or Attempt and Younger age in comparison to

Model I which had no CCI as a covariate. This is expected as CCI is a composite of key major comorbidities such as Heart Failure and Type 2 Diabetes and End Stage Liver Disease.

All covariates have strong association with utilization of resources. A unit increase in CCI, being between age of 18-34 and an existence of Suicide Ideation or Attempt will result in an increase in the log-odds of being high utilizer, with other variables remaining same, by 2.64, 1.25 and 1.13 respectively. The AUROC of the model remains high at 0.75 with a Brier score of 0.082 confirming strong predictive power of the model.

5.5.3 RESULTS OF THE REGRESSION MODEL III

A third regression model includes Obesity and excludes CCI as a covariate. The resulting model outputs are also presented in Table 5-4 to Table 5-7.

5.5.3.1 RESULTS OF MODEL III (COHORT A)

The Model III on the dataset Cohort A (With missing race data) output shows obesity has a positive relationship with Super Utilization but the relation (OR = 1.28), although it significantly falls behind Suicide Ideation or Attempt which has the highest OR of 3.14 followed by End Stage Renal Disease (OR = 2.78) and being Age 18-34 (OR = 2.61) which is similar to Model A outcomes. Use of antipsychotic and being Black remain negatively associated with the outcome of being in the super utilizer category while being Female remain positively associated but relatively smaller effect size.

The highest coefficients are associated with Suicide Ideation or Attempt (1.15) and End Stage Renal Disease (1.02) with respective z value of 66.8 and 20.93. The output shows that having a diagnosis of Suicide Ideation or Attempt, End Stage Renal Disease and being between age of 18-34 will result in an increase in the log-odds of being high utilizer, with other variables remaining same, by 1.15, 1.02 and 0.96 respectively.

The model predictive power remains strong with AUROC at 0.74 and a Brier score very close to zero (0.084). Based on the analysis the missing race variable has very small association with High Utilization. To confirm that association with Black Race is negative, this model was also run on a cohort with no missing Race data. This is presented in the next section.

The outcomes of Model III are very similar to Model I which also did not include CCI but was without Obesity. Addition of Obesity did not improve the model predictability, but it remains a strong model.

5.5.3.2 RESULTS OF MODEL III (COHORT B)

The regression results for the model with Obesity as an explanatory variable on the data set with no missing race confirms a negative relationship between Black and use of Anti-Psychotics and being a SU of health resources. The odd Ratio (0.92) is same as Cohort A of Model III with a negative co-efficient of -0.08 for the Black variable in Table 5.7. The missing race data seems to have no impact in terms of model output as shown in Table 5-5 to Table 5-7. Suicide Ideation or Attempt followed by End Stage Renal Disease and being young in age remain the covariates with highest coefficient (1.15, 1.06 and 0.96). All the variables are significantly associated with being a ER and hospital super resource utilizer. The AUROC of the model

remains high at 0.74 with a Brier score of 0.082 confirming strong predictive power of the model.

5.5.4 RESULTS OF THE REGRESSION MODEL IV

A fourth regression model was run with both CCI and Obesity along with all covariates of Model I. The resulting model output are presented in Table 5-4 to Table 5.7 .

5.5.4.1 RESULTS OF MODEL IV (COHORT A)

Close to Model II Cohort A, the Model IV output shows CCI with the highest Odds Ratio of 12.57 which is followed by Young Age with OR of 3.29, Suicide Ideation or Attempt with OR of 3.04. It is not surprising to see the odds ratio of Heart Failure, ESRD and diabetes fall as CCI index becomes the strongest variable in terms of odds ratio. Use of antipsychotic and being black remain negatively associated with the outcome of being in the Super Utilizer category while being female remain positive. Table 5-5 displays the findings with CCI with highest coefficients followed by being Young Age and having Suicide Ideation and or Attempt diagnosis. The output shows that an incremental unit of CCI, being in young age group of 18-25 years, and having a diagnosis of Suicide Ideation or Attempt, will result in an increase in the log-odds of being high utilizer, with other variables remain same, by 2.53, 1.19 and 1.11 respectively. Black and Antipsychotic use remain negatively associated with being Super Utilizer category although

the relationship remains weak but significant. Females continue to have small but positive relationship.

In terms of model predictability, AUROC is slightly higher, in comparison to Model I and Model III and similar to Model II, at 0.75. Brier score is similar at 0.083.

5.5.4.2 RESULTS OF MODEL IV (COHORT B)

Regression with CCI and Obesity in Cohort B did not change the finding with CCI, Young Age, and Suicide Ideation or Attempt being top 3 factors in terms of association with being High Utilizer with odds ratio of 13.22, 3.34 and 3.05 (table 5.6), 1.12, 1.20.

The model has the best strength in terms of predictive power with Brier Score of 0.082 and AUROC at 0.75 (Table 5.8), albeit the models are extremely close with each in terms association of key factors with Super Utilization of Healthcare resources and overall predictive power.

5.6 MODEL RESULTS WITHOUT ZERO UTILIZER: COHORT A

Approximately one third of the Medicaid schizophrenia patients had zero utilization of emergency and hospital services. This it is important to understand if the factors that are highly associated with high utilizers remain the same if the zero utilizers are removed from the not high utilizer category. This scenario was analysed to see if there was better predictive power

when zero utilizers are removed and whether there were changes in the explanatory variables association with the outcome which is being a SU. Regression results from the data cohort without zero utilizers are presented in Table 5-9. It displays the coefficient estimates, Standard Error and Z Values for all the four models in Cohort A. The relationship with Black race, Antipsychotic use continues to be negative but small. The factors that rose higher in effect size in the cohort that includes all zero utilizers remained as key factors in this current model with no zero utilizers. They are Charlson Comorbidity Index (CCI), being in the younger age category of 18-34 years and having an indication of Suicide Ideation or Attempt. End Stage Renal Disease become more important and was ranked second in effect size after Suicide Ideation or Attempts when Charlson comorbidity Index is not included in the list of explanatory variables. Suicide Ideation or Attempt has the highest Z value across all four models. Overall, conclusions of the model remain same as the model with Zero Utilizer in terms of directional relationships.

Table 5. 9: Cohort A Models I, II, III & IV Regression Coefficients: No Zero Utilizers.

	Model 1			Model 2			Model 3			Model 4		
	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value
Intercept	-3.18	0.04	-84.90	-3.37	0.04	-87.27	-3.17	0.04	-84.67	-3.36	0.04	-86.94
CCI				2.06	0.09	23.03				2.01	0.09	22.41
Black	-0.08	0.02	-4.41	-0.07	0.02	-3.89	-0.07	0.02	-4.17	-0.07	0.02	-3.68
Female	0.11	0.02	6.90	0.11	0.02	6.49	0.07	0.02	4.36	0.07	0.02	4.23
Heart Failure	0.47	0.03	18.61	0.23	0.03	8.19	0.44	0.03	17.19	0.20	0.03	7.32
Suicide Ideation or Attempt	0.96	0.02	54.86	0.93	0.02	53.24	0.94	0.02	53.97	0.92	0.02	52.49
Type 2 Diabetes	0.30	0.02	16.34	0.10	0.02	4.72	0.26	0.02	13.54	0.06	0.02	2.94
Obesity							0.21	0.02	11.29	0.19	0.02	10.00
End Stage Renal Disease	0.80	0.05	15.78	0.58	0.05	11.17	0.80	0.05	15.77	0.59	0.05	11.26
Alcohol and/or Substance Abuse	0.59	0.02	30.19	0.55	0.02	27.69	0.60	0.02	30.22	0.55	0.02	27.80
Antipsychotics use	-0.03	0.02	-1.80	-0.03	0.02	-1.72	-0.04	0.02	-2.23	-0.04	0.02	-2.09
Age 18-34 Years	0.80	0.04	21.35	0.99	0.04	25.65	0.77	0.04	20.32	0.96	0.04	24.61
Age 35-64 Years	0.62	0.03	17.90	0.72	0.03	20.68	0.59	0.03	16.93	0.69	0.04	19.74
Missing race	0.06	0.03	2.22	0.07	0.03	2.65	0.06	0.03	2.51	0.07	0.03	2.90

Note: Pr(>|z|) was 0.0 for all variables in all models.

Although there is similarity on the association of variables with the outcomes, the overall predictive power diminishes significantly in the analysis that removes zero utilizers. As seen in table 5-10, the AUROC drops to 0.69-0.70 in comparison to the model with zero utilizer where the score ranges from 0.74-0.75. Model with no zero-utilizer data has about 5-6% lower predictive power. The Brier score, presented in the third column of Table 5-10, points in the same direction in terms of reduced strength of predictive power of this model. The brier scores rise to 0.13 pointing to increased mean square error between the predicted probabilities and the observed values.

Table 5. 10: Cohort A Models I, II, III, & IV: Goodness of Fit: No Zero Utilizers

Model	AUROC	Brier
Model I	0.69	0.13
Model II	0.70	0.13
Model III	0.70	0.13
Model IV	0.70	0.13

5.7 TWO-STAGE REGRESSION MODEL

Given a significant proportion, 37%, of schizophrenia patients in Medicaid have zero utilization of healthcare resources, a two-stage regression was also conducted. The rationale is that there is a possibility of distinct reasons for their zero-utilization compared to any positive utilizers. By treating zero utilizers same as non-zero utilizers in one model, we may overlook critical differences. This was noted by Deb & Norton (Deb & Norton, 2018) who highlighted the challenges in modelling Healthcare expenditures and their use because these dependent variables may have a large proportion at zero as seen in the above analysis. Thus, a two-stage model was estimated. The first stage of the model estimated whether the subject had zero healthcare expenditure. In the second stage of the model, a regression was conducted to identify factors associated with a patient being high utilizer.

The equation of the first stage of the model is presented below:

$$Log\ (u/(1-u)) + b_0 + b_1(CCI) + b_2(R) + b_3(G) + b_4(HF) + b_5(SIA) + b_6(D) + b_7(O) + b_8(ESRD) + b_9(ASA) + b_{10}(AP) + b_{11}(AY) + b_{12}(AM) + b_{13}(RM)$$

where,

probability of u=1, if a patient is a zero-utilizer. This model allows us to understand factors associated with zero utilization.

b_0 = Intercept coefficient

CCI = Charlson Comorbidity Index

R = Race is Black (i.e. Black has value of 1)

G = Gender is Female

HF = Heart Failure

SIA = Suicide Ideation and/or Attempt

D = Type 2 Diabetes

O = Obesity

ESRD = End Stage Renal Disease

ASA = Alcohol and/or Substance Abuse

AP = Antipsychotics use

AY = Age 18-34 Years

AM = Age 35-64 Years

RM = Race Missing

Two models were estimated. Model I without CCI and Obesity and Model II with both. The regression was analysed on dataset with missing race (Cohort A) with RM as a variable and without Missing race (Cohort B)

In the second stage of the model, a logistic regression to identify factors associated with a patient being a SU is conducted on both Cohort A (missing race) and Cohort B (No missing race). The key difference in this analysis, unlike the model in section 5.4, also includes the probability of being a zero utilizer (M1p) as an input.

$$Log\ (u/(1-u)) + b_0 + b_1(CCI) + b_2(R) + b_3(G) + b_4(HF) + b_5(SIA) + b_6(D) + b_7(O) + b_8(ESRD) + b_9(ASA) + b_{10}(AP) + b_{11}(AY) + b_{12}(AM) + b_{13}(RM) + b_{14}(M1p)$$

for Cohort A.

And

$$Log\ (u/(1-u)) + b_0 + b_1(CCI) + b_2(R) + b_3(G) + b_4(HF) + b_5(SIA) + b_6(D) + b_7(O) + b_8(ESRD) + b_9(ASA) + b_{10}(AP) + b_{11}(AY) + b_{12}(AM) + b_{13}(M1p)$$

for Cohort B.

where,

M1p is the probability of being a zero utilizer as estimated from Stage 1 model.

5.71 RESULTS OF TWO-STAGE REGRESSION

Regression results for Stage 1, shows the factors associated with a patient being a zero utilizer, are presented in Table 5-11 and Table 5-12 for both Cohort A and Cohort B. Table 5-13 - Table 5-15 presents the regression results of the second stage to identify predictors of being a Super Utilizer. Model 1 is without CCI and Obesity as explanatory variable while Model 2 includes both.

Table 5. 11: Stage 1 Cohort A & Cohort B Regression Results: Odds Ratios for Zero Use

	Cohort A						Cohort B					
	Model 1			Model 2			Model 1			Model 2		
	Odds Ratio	CI 2.50	CI 97.50	Odds Ratio	CI 2.50	CI 97.50	Odds Ratio	CI 2.50	CI 97.50	Odds Ratio	CI 2.50	CI 97.50
Intercept	1.70	1.64	1.75	2.07	2.00	2.14	1.68	1.63	1.74	2.05	1.98	2.13
CCI				0.07	0.06	0.08				0.07	0.06	0.08
Black	1.05	1.02	1.07	1.03	1.01	1.05	1.05	1.02	1.07	1.03	1.01	1.05
Female	0.66	0.64	0.67	0.69	0.67	0.70	0.66	0.64	0.67	0.69	0.67	0.7
Heart Failure	0.58	0.56	0.60	0.81	0.77	0.84	0.59	0.56	0.61	0.82	0.78	0.85
Suicide Ideation or Attempt	0.40	0.39	0.41	0.42	0.41	0.43	0.40	0.39	0.41	0.42	0.41	0.43
Type 2 Diabetes	0.78	0.76	0.79	1.04	1.01	1.07	0.78	0.76	0.80	1.04	1.01	1.07
Obesity				0.80	0.78	0.82				0.79	0.77	0.82
End Stage Renal Disease	0.51	0.46	0.57	0.68	0.62	0.76	0.51	0.46	0.56	0.67	0.61	0.75
Alcohol and/or Substance Abuse	0.44	0.43	0.44	0.46	0.45	0.47	0.44	0.43	0.45	0.47	0.46	0.48
Antipsychotics use	**1.22**	1.19	1.24	**1.23**	1.20	1.25	**1.20**	1.18	1.23	**1.22**	1.19	1.24
Age 18-34 Years	0.61	0.59	0.63	0.51	0.49	0.53	0.60	0.58	0.63	0.51	0.49	0.53
Age 35-64 Years	0.83	0.80	0.86	0.75	0.73	0.78	0.84	0.81	0.86	0.76	0.73	0.78
Missing race	0.90	0.87	0.93	0.88	0.85	0.91						

Note: Pr(>|z|) was less than or equal to 0.01 for all variables in all models.

Table 5. 12: Stage 1 Cohort A & Cohort B Regression Results: Coefficients and Z Values for Zero Use

	Cohort A						Cohort B					
	Model 1			Model 2			Model 1			Model 2		
	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value	Coeff Est.	Std. Error	z value
Intercept	0.53	0.02	31.39	0.73	0.02	40.55	0.52	0.02	29.98	0.72	0.02	38.77
CCI				-2.65	0.07	-36.46				-2.64	0.08	-34.71
Black	0.04	0.01	4.09	0.03	0.01	2.77	0.04	0.01	4.12	0.03	0.01	2.81
Female	-0.42	0.01	-40.35	-0.38	0.01	-35.61	-0.42	0.01	-38.20	-0.38	0.01	-33.66
Heart Failure	-0.55	0.02	-27.38	-0.21	0.02	-9.87	-0.53	0.02	-25.94	-0.2	0.02	-9.07
Suicide Ideation or Attempt	-0.92	0.02	-56.60	-0.87	0.02	-53.33	-0.92	0.02	-52.89	-0.87	0.02	-49.77
Type 2 Diabetes	-0.25	0.01	-21.11	0.04	0.01	2.58	-0.25	0.01	-19.97	0.04	0.01	2.67
Obesity				-0.22	0.01	-17.26				-0.23	0.01	-16.79
End Stage Renal Disease	-0.67	0.05	-13.06	-0.38	0.05	-7.30	-0.68	0.05	-12.82	-0.4	0.05	-7.32
Alcohol and/or Substance Abuse	-0.83	0.01	-79.05	-0.77	0.01	-72.62	-0.82	0.01	-73.73	-0.76	0.01	-67.6
Antipsychotics use	0.20	0.01	18.38	0.20	0.01	19.08	0.19	0.01	16.50	0.2	0.01	17.18
Age 18-34 Years	-0.50	0.02	-26.85	-0.67	0.02	-33.99	-0.50	0.02	-25.85	-0.67	0.02	-32.63
Age 35-64 Years	-0.19	0.02	-11.93	-0.29	0.02	-17.55	-0.18	0.02	-10.95	-0.28	0.02	-16.35
Missing race	-0.11	0.02	-6.23	-0.13	0.02	-7.28						

Note: Pr(>|z|) was less than or equal to 0.01 for all variables in all models.

Use of antipsychotics and being black are the only two factors positively associated with being a zero utilizer with positive coefficient of 0.2 and 0.04 in Model 1, although both the coefficient estimate is significant the effect size of being a black is relatively small (Odds ratio of 1.05). The result is similar for Cohort B. This result shows very strong inverse relationship between having a diagnosis of Suicide Ideation or Attempt and Alcohol and/or Substance Abuse with odds ratios of 0.4 and 0.44 in model 1. When CCI and Obesity is included in the model, CCI becomes the most negatively related with odds ratio of 0.07 followed by having a diagnosis of Suicide Ideation or Attempt and Alcohol and/or Substance Abuse.

Table 5. 13: Stage 2 Cohort A & Cohort B Regression Results: Odds ratios for SU

	Cohort A						Cohort B					
	Model 1			Model 2			Model 1			Model 2		
	Odds Ratio	CI 2.50	CI 97.50	Odds Ratio	2.50	97.50	Odds Ratio	CI 2.50	CI 97.50	Odds Ratio	CI 2.50	CI 97.50
Intercept	0.31	0.20	0.46	0.20	0.14	0.29	0.32	0.21	0.50	0.20	0.14	0.29
CCI				1.87	1.39	2.51				1.97	1.43	2.72
Black	0.94	0.91	0.98	0.94	0.91	0.97	0.94	0.91	0.98	0.94	0.91	0.97
Female	0.88	0.83	0.93	0.90	0.86	0.95	0.87	0.82	0.93	0.90	0.86	0.95
Heart Failure	1.17	1.08	1.27	1.14	1.07	1.20	1.16	1.07	1.27	1.13	1.06	1.20
Suicide Ideation or Attempt	1.42	1.26	1.60	1.56	1.42	1.71	1.39	1.23	1.58	1.56	1.41	1.72
Type 2 Diabetes	1.16	1.11	1.22	1.10	1.05	1.14	1.15	1.09	1.21	1.08	1.04	1.13
Obesity				1.08	1.03	1.12				1.08	1.03	1.13
End Stage Renal Disease	1.48	1.31	1.67	1.50	1.35	1.66	1.50	1.32	1.72	1.54	1.38	1.71
Alcohol and/or Substance Abuse	0.97	0.86	1.11	1.07	0.97	1.18	0.95	0.83	1.09	1.06	0.96	1.18
Antipsychotics use	1.09	1.05	1.14	1.07	1.03	1.11	1.10	1.05	1.15	1.07	1.03	1.12
Age 18-34 Years	1.72	1.56	1.89	1.95	1.76	2.16	1.71	1.55	1.90	1.97	1.77	2.20
Age 35-64 Years	1.71	1.59	1.84	1.80	1.67	1.94	1.72	1.60	1.86	1.82	1.69	1.96
Missing race	0.98	0.93	1.03	0.99	0.95	1.05						
Probability of being a Zero Utilizer	0.01	0.00	0.01	0.01	0.01	0.02	0.01	0.00	0.01	0.01	0.01	0.02

Table 5. 14: Stage 2 Cohort A Regression Results: Coefficients and Z Values for SU

	Cohort A							
	Model 1				Model 2			
	Coeff Est.	Std. Error	z value		Coeff Est.	Std. Error	z value	Pr(>|z|)
Intercept	-1.19	0.21	-5.71	0.00	-1.60	0.18	-9.01	0.00
CCI					0.62	0.15	4.11	0.00
Black	-0.06	0.02	-3.32	0.00	-0.06	0.02	-3.43	0.00
Female	-0.13	0.03	-4.17	0.00	-0.10	0.02	-4.20	0.00
Heart Failure	0.16	0.04	3.84	0.00	0.13	0.03	4.46	0.00
Suicide Ideation or Attempt	0.35	0.06	5.83	0.00	0.44	0.05	9.49	0.00
Type 2 Diabetes	0.15	0.02	6.33	0.00	0.09	0.02	4.51	0.00
Obesity					0.07	0.02	3.49	0.00
End Stage Renal Disease	0.39	0.06	6.26	0.00	0.40	0.05	7.67	0.00
Alcohol and/or Substance Abuse	-0.03	0.07	-0.43	**0.67**	0.07	0.05	1.31	**0.19**
Antipsychotics use	0.09	0.02	4.34	0.00	0.07	0.02	3.54	0.00
Age 18-34 Years	0.54	0.05	10.96	0.00	0.67	0.05	13.08	0.00
Age 35-64 Years	0.54	0.04	14.75	0.00	0.59	0.04	15.68	0.00
Missing race	-0.02	0.03	-0.86	**0.39**	-0.01	0.03	-0.22	**0.82**
Probability of being a Zero Utilizer	-4.98	0.35	-14.05	0.00	-4.43	0.29	-15.30	0.00

Note: Pr(>|z|) was 0.0 for all variables in all models except Alcohol and/or Substance Abuse and missing race. AUC =0.75 for both models

Table 5. 15: Stage 2 Cohort B Regression Results: Coefficients and Z Values for SU

	Cohort B							
	Model 1				Model 2			
	Coeff Est.	Std. Error	z value	Pr(>|z|)	Coeff Est.	Std. Error	z value	Pr(>|z|)
Intercept	-1.13	0.22	-5.04	0.00	-1.62	0.19	-8.40	0.00
CCI					0.68	0.16	4.11	0.68
Black	-0.06	0.02	-3.37	0.00	-0.06	0.02	-3.53	-0.06
Female	-0.14	0.03	-4.05	0.00	-0.10	0.03	-3.82	-0.10
Heart Failure	0.15	0.04	3.40	0.00	0.12	0.03	4.03	0.12
Suicide Ideation or Attempt	0.33	0.07	5.06	0.00	0.44	0.05	8.70	0.44
Type 2 Diabetes	0.14	0.03	5.40	0.00	0.08	0.02	3.68	0.08
Obesity					0.08	0.02	3.32	0.08
End Stage Renal Disease	0.41	0.07	6.07	0.00	0.43	0.06	7.75	0.43
Alcohol and/or Substance Abuse	-0.05	0.07	-0.73	0.47	0.06	0.05	1.13	0.06
Antipsychotics use	0.09	0.02	4.27	0.00	0.07	0.02	3.38	0.07
Age 18-34 Years	0.54	0.05	10.19	0.00	0.68	0.05	12.40	0.68
Age 35-64 Years	0.54	0.04	14.35	0.00	0.60	0.04	15.28	0.60
Probability of being a Zero Utilizer	-5.05	0.38	-13.15	0.00	-4.39	0.31	-13.95	0.00

Note: Pr(>|z|) was 0.0 for all variables in all models except Alcohol and/or Substance Abuse. AUC =0.75 for both models

In comparison to Single model approach, this model result shows that being female is negatively associated with being a SU and being on antipsychotics is positively related to being a SU with Odds Ratios of 0.88 and 1.09 respectively. It is a different significant conclusion from Single Regression Model. Another difference is having an Alcohol and/or Substance Abuse diagnosis is not statistically significant as an explanatory variable for being a high utilizer. The factors that emerge to the top in terms of effect size are, being Age 18-34 and Age 35-64, ESRD

and having Suicide Ideation or Attempt as a diagnosis. The effect size of these variables is smaller compared to Single Regression Model. The relationship between being SU and being a zero utilizer is rightly zero or very close to zero. When CCI and Obesity are added to the model, CCI rises to the top in effect size, along with being young (Age 18-34). AUC remains a strong 0.75 across all four two-stage models.

Although Alcohol and/or Substance Abuse is not a significant factor, Suicide Ideation or Attempt is still a significant factor with one of the larger effects in this model. The effect size of Suicide Ideation or Attempt is lower in comparison to single model approach. Having comorbidities like ESRD or a comorbidity index like CCI remain key predictors in both modelling approaches.

5.8 LIMITATIONS, STRENGTHS, AND CONCLUSIONS

Multiple models were tested to find the list of explanatory variables that can provide the highest predictive power. All models showed strong predictive power. Since study database is large and the explanatory variables were mostly selected based on learnings from past studies, all the explanatory variables are statistically significant except Alcohol and/or Substance Abuse in a two-stage modelling approach is applied. This is expected given hundreds of thousands of data points. In this case, focus is on the size of the odds ratio to understand the key factors that are important in predicting whether a patient is going to be high utilizer of emergency or hospital resources or not.

Overall, in the single regression model, inclusion of obesity and Charlson comorbidity scores minimally improves the model. There is slight benefit of excluding missing race data, but the difference is minimal. CCI and Obesity as explanatory variable in the data cohort without missing race and including zero utilizers (Model 4, Cohort B), has the best strength in terms of predictive power with Brier Score of 0.082 and AUROC at 0.75, but all the models are very close in predicting power. CCI emerges as one of the strongly associated factors with being in high utilizer category, followed by having a diagnosis of Suicide Ideation or Intent and being young in age. The primary model without CCI and Obesity remain strong with a Brier score as low as 0.82 and AUC of 0.74. The model continues to remain strong in the scenario where the data source does not have Charlson Comorbidity Index. Thus, a dataset with information on Suicide Ideation or Intent, age, End Stage Renal Disease and Heart Failure can strongly predict a patient to be a "Super Utilizer". Without information on CCI, comorbid conditions such as End Stage Renal Diseases and Heart Failure become very important as these rises in association significantly with the outcome variable.

The strength of the predictive power of the Single model in Cohort A, which includes missing race, is very close to the best model, which is Model 4 in Cohort B which excludes missing data, lending significant confidence in using data even when one out of 10 schizophrenia patients have missing race data. This makes the model quite applicable to real world where data sources generally have missing information.

Since the zero utilizers of emergency and hospital services were a robust one third of the Medicaid schizophrenia patients, a separate regression was run in a cohort excluding that

population. This scenario analysis further strengthens the findings as it did not change the factors that are highly associated with being a SU. The relationship with being Black race and Antipsychotic use continued to be negative, but the overall predictive power did drop down by 5-6%. The strength of the predictability of the model, as measured by the Brier score, was reduced as well.

A two-stage model approach was also applied to account for 37% Zero utilizers. This produced a model with strong predictive power and some new findings. Unlike the Single model approach, this approach showed Alcohol and/or Substance Abuse as not being a predictor of SU but a big predictor of not being zero utilizer. It also showed that being a female is more positively associated with being a non-zero utilizer but is not a positive predictor of being a high utilizer. While being female is not a positive predictor of SU is corroborated with past research findings (Albert & McCaig, 2015), being on an antipsychotic treatment is surprising. The first stage of the two-step model showed antipsychotics use as the strongest positive predictor of being a zero utilizer, but it surprisingly remained a positive predictor of being a SU as well. The low but significant positive relationship with antipsychotic use is maybe due to the use of drug is measured by 30-day drug supply period in this research and schizophrenia patients need compliant use of antipsychotic drugs for more than few weeks to prevent relapses. It is also a well-researched finding that compliant use of antipsychotics is very low and a major cause of relapse. (Fenton, Blyler, & Heinssen, 1997) Fenton et al studied the non-adherence for oral antipsychotics among schizophrenia and found non-adherence to be as high at 55%. (Fenton, Blyler, & Heinssen, 1997) The positive relationship could also be because it could be representative of sicker patients.

The regression results also confirm the significant but smaller negative effect size of being black on being a SU. The negative relationship with black race is different from the findings of Desai et al (Desai, Lawson, Barner, & Rascati, 2013) but can be attributed to different definition of SU and patient population in this study. It also points to perhaps healthcare access challenges, provider bias, distrust and stigma for black schizophrenia patients in Medicaid. Two-stage model is a better approach when a significant proportion of individuals have zero utilization as it allows the researcher to separate factors that are predictive of SU from any use.

One of the strengths of all the model is that the regression was run on very large sample size of schizophrenia patients, but it was limited to data elements found in a payer sourced claims database. Based on "Rainbow Model" framework and earlier research findings, other social determinants of health variables such as homelessness, perception of poor health, social isolation and other factors may be relevant but are not available in claim databases. Inclusion of these factors may provide a stronger predictive power. Even with the absence of other key data elements, the model remains robust and provides guidance needed to shape a population management tool to minimize avoidable Emergency Room and hospital stays among schizophrenia patients who are unfortunately experiencing these 9 times or more in a year. This finding has the potential to better manage health of schizophrenia patients who are leading a very poor quality of life and suffering work impairment with severe negative impact on their caregivers as well.

Another limitation that this model may have is the choice of logistic regression to study association. Logistic regression fails to predict a continuous outcome. Since the outcomes in this research is Super Utilizer or Non-Super Utilizer, this is not a limitation of the research. Second, logistic regression assumes linearity between the predicted (dependent) variable and the predictor (independent) variables. In the real world, it is highly unlikely that the observations are linearly separable. This can be seen as a limitation here. Logistic regression may not be accurate if the sample size is too small. If the sample size is on the small side, there is not enough input data available for the model to find patterns in it. In this case, the model cannot accurately predict the outcomes of a new or future dataset. Given the robust sample size of the current model, in terms of number of schizophrenia patient data, this may not be a limitation for this research.

CHAPTER 6: DISCUSSION AND CONCLUSIONS

6.1 KEY GOALS

This thesis characterizes the utilization of emergency and hospital services, estimates its super utilization and investigates the factors associated with the super utilizers among Medicaid patients with Schizophrenia in the United States. This chapter presents the key conclusions and the discussion of the main findings from the literature review and empirical studies presented in previous chapters that fulfil the objectives of the main thesis. The objectives of the main thesis were to

1. Conduct a systematic review of cost and resource utilization in managing schizophrenia in US health system.

2. Characterize Super Utilization among Schizophrenia patients in the US Medicaid System.

3. Analyse factors associated with Super Utilization of resources among Medicaid schizophrenia patients.

6.2 MAIN FINDINGS & INTERPRETATIONS

The findings of the current research are presented in Chapter 2 to Chapter 5. This section presents a summary of key findings with their interpretations.

The aim of Chapter 2 was to present the challenging task faced by United States policymakers to reign in rising healthcare cost. US spends significantly more in healthcare that any other developed nation but has worse health outcomes compared to many other

developed countries. It is well documented that a small part of US population (top 5 to 10%) consumes 50% to 70% of the healthcare resources. (Davenport, Grey, & Melek, 2020) This small number of individuals are called HU or SU or "Hot Spotters". (Finkelstein, Zhou, Taubman, & Doyle, 2020) Rationale for focusing on Super Utilizers in our current health systems is provided by the sad fact that there are individuals who have complex physical, behavioural and social needs which are not adequately met given the complex, disjointed and expensive US health system. These SU avail significant emergency services which also lead to multiple hospital admissions, readmissions, and institutionalizations. (Cohen, 2014) Thus, creating an opportunity to focus on a small segment of healthcare recipients, the Super Utilizers (SU), to significantly impact healthcare utilization.

To successfully manage healthcare, one must design health delivery interventions that are tailored to patients' clinical needs. The fragmented healthcare system in the US lends to variability in characteristics of Super Utilizers across different health insurance systems, such as Medicare, Commercial and Medicaid plans, due to differences in the demographics of the members enrolled in these plans. (Powers, Sreekanth, & Chatguru, 2016) The variability is further exacerbated by diseases suffered by these members who have different clinical needs. In other words, the SU among diabetes patients are expected to have different characteristics and clinical needs than SU among patients who have depression. This presents a unique challenge to policy makers to design polices that are specific for an insurance system as well as tailored for specific clinical condition.

One of the major factors associated with high utilization of healthcare resources is under or unmanaged behavioural health. (Stoddard, Gre, & Melel, 2020) There is significant unmet need for better delivery of behavioural healthcare. Stoddard's 2017 analysis of 21 million commercially or privately insured lives showed that the most expensive 10% of the covered lives, which they referred as the "High-Cost Group" cost as much as 21 times higher than the rest of the 90% of the covered lives ($41,631 versus $1,965 per annum). (Stoddard, Gre, & Melel, 2020) Although small in prevalence number, a serious behavioural health diagnosis, schizophrenia is one of most burdensome disease due to its chronic nature filled with multiple relapses leading to repeat utilization of emergency or hospital services. (Coultier, et al., 2016) (Dutta, Spoorthy, Patel, & Agarwala, 2019) It is also a disease which is characterized by extremely variability in resource use and is a significant driver of high utilization of health resources such as emergency care. (Doran & Rosenhenck, 2013) A study conducted with data on 1000 hospitals across 35 states in United States showed that schizophrenia was associated with increased odds of acute preventable hospitalization (OR 1.34, 95% CI 1.31-1.38). (Cahoon, McGinty, Ford, & Daumit, 2013) Studies have also shown strong association between mental disorder such as schizophrenia and high utilization of healthcare resources spend in emergency care and inpatient services. (Ford, 2004) (Borckardt, 2011)

According to Mental Health America, one in five Americans are suffering from a mental illness and they face varied and significant healthcare challenges. (MHA, 2024) Key factors creating challenges are lack of providers, especially in rural areas, fragmented health system, high cost of treatment, stigma and disparities in care. American Psychological Association in 2022 conducted a Covid-19 Practitioner Impact Survey which showed that 60% of psychologists

reported having no openings for new patients. (APA, 2022). This problem is further exacerbated by lack of funding from the government for a patient population that disproportionately relies of public funding. (Phillips, 2023) Other key reasons listed in the report is lack of mental health facilities in rural areas, stigma and continued increased need for services along with aging workforce. (Phillips, 2023) To make matters worse, the fragmented and a maze-like US health system is extremely onerous for seriously ill schizophrenia person to navigate. Carving out of behavioural health was intended to provide accessible mental health, but it has also contributed to poor coordinated care, overprovision and duplication of certain services, and ineffective restraints on cost. (Richman, Grossman, & Sloan, 2010)

The increasing deinstitutionalization of patients with mental illness has shifted the burden of caregiving on family members who find it very challenging to care for schizophrenia family member. (Caqueo-Urizar, Rus-Calafell, Urzua, Escudero, & Gutierrez-Maldonando, 2015) Unmanaged severe mental illness presents dire situation for schizophrenia patients, leading them to seek care in emergency departments (Doran & Rosenhenck, 2013) resulting frequent hospitalizations (Cahoon, McGinty, Ford, & Daumit, 2013). There is also, significant empirical work in the last decade that has revealed stark differences between Black and White communities in the schizophrenia diagnoses rate, treatment strategies, and outcomes post-treatment. (Alang, 2019) (Cook, et al.) The challenges in managing schizophrenia as a diseases is further exacerbated due to significant stigma, prejudice and discrimination against people with mental illness. These can lead to delayed therapies and makes the patient more prone to emergency care. (American Psychiatric Association, 2024)

Given that schizophrenia has a small prevalence and high per patient cost, it lends itself as a suitable disease area for population health management. Better management of this disease could lead to substantial savings in emergency and hospital care while making QOL better for a cohort of Medicaid members with or at risk of significant disability.

Low in prevalence with estimates ranging from approximately 0.25% to 0.64% (Kessler, et al., 2005) to approximately 1% (APA, 2024) of US adult population has schizophrenia, it makes 2.30% and 2.71% of US Medicaid population and Medicaid covers two thirds of US schizophrenia patients. (Pilon, et al., 2021) (Khaykin, Eaton, Ford, Anthony, & Daumit, 2010) This is not surprising as Medicaid is a public insurance program that provides health coverage to low-income and disabled individuals and schizophrenia is a disabling disease and thus highly correlated with poverty and unemployment. Given Medicaid covers a significant proportion of US population (about 70 million) who are low-income adults, children, pregnant women, and people with disabilities and schizophrenia patients are mostly insured by Medicaid, this thesis's aim was to characterize resource utilization, specifically "Super Utilization" and the factors associated with it among patients with schizophrenia, in the US Medicaid System.

The Dahlgren and Whitehead "Rainbow Model" (Dyar OJ, et al., 2022) provided the theoretical framework to identify factors impacting high utilization of resources by severe mentally ill schizophrenia patients. The rationale for using the "Rainbow Model" lay in its ability to provide a powerful framework for understanding how mental health such as schizophrenia is shaped by various layers of social, economic, and environmental factors. This allowed this research to explore beyond biological factors to individual lifestyle factors, such substance

abuse, and social and environmental issues, such as homelessness and racism, that impact mental health and may need to be addressed if a policy is to be designed for population health improvement.

The next step of this research was to conduct a systematic literature review to demonstrate the high resource use among schizophrenia patients. A secondary literature search was conducted to understand the definition of Super Utilizer among schizophrenia patients which could be applied in the current research. Another secondary literature search was to identify any factors that may be associated with high utilization of resources among schizophrenia patients. The findings from the literature review are captured in Chapter 3.

A systematic approach was taken to thoroughly review relevant evidence from peer-reviewed published literature, dissertation, systematic reviews, and registries of observational studies published from January 2000 to August 2021. Given the multiple approaches, different time-period, and heterogenous outcome variables of the studies, a quantitative meta-analysis was not feasible. Hence, a qualitative narrative synthesis of 22 studies was conducted based on the Popay's guidance. (Popay, et al., 2006)

An in-depth review of 22 studies found that schizophrenia was significantly burdensome across all payers. Most of the 9 Medicaid studies reviewed confirmed that schizophrenia cost more than other chronic diseases with one showing the annual cost difference can be 1.5 to 6 times as much in comparison to cohort of patients with no schizophrenia. (Pilon, et al., 2021) (Hendrie, Wanzhu, Rebeka, Ambuehl, & Callahan, 2014) Hendrie and Shim also confirmed the

high prevalence of emergency and hospitalization among schizophrenia patients. (Hendrie, Wanzhu, Rebeka, Ambuehl, & Callahan, 2014) (Shim, et al., 2014)

A qualitative synthesis of resource utilization by schizophrenia patients in Medicaid confirms that they are suffering from multiple ER visits and hospitalizations and consequently the system is facing a higher cost in managing its schizophrenia patient population even in comparison to resource intensive disease such as diabetes. These findings were confirmed with reviews among Medicare, Commercial, Veteran Affairs and All-payers group.

This systematic literature review shows that patients with schizophrenia face significant healthcare resource use in comparison to patients with other major diseases such as diabetes, bipolar disease, or depression. The findings are consistent across all payer types showing that it is more expensive to manage a patient with schizophrenia than a patient who does not. Although there is cost variability across studies due to payer reimbursement rates and differences in time periods of the studies, the average cost of managing a schizophrenia patient consistently more in comparison to other matched cohorts with no schizophrenia.

Another key finding from the literature review is that the cost of schizophrenia is mostly driven by hospitalization and ER visits due to relapse of the disease which may happen if the disease is not well managed. Findings suggest, small proportions of patients are resulting in high cost of managing schizophrenia. (Desai, Lawson, Barner, & Rascati, 2013) (Doran & Rosenhenck, 2013) Identifying the factors that may be behind the high utilization will enable development of disease management strategies focused on preventing relapses and resulting high cost and disabilities. This literature review also points to few factors that may be leading to

multiple hospital and ER visits. Studying these along with other socio-economic factors may aid in creating a predictive model to identify patients who need better care.

A secondary objective of this literature review was to find key factors associated with super or high utilization of resources. Eleven studies reviewed are listed in Table 3-3. Higher emergency room admissions and hospitalizations and associated inpatient days emerged as key reasons behind high resource use. In multiple studies they were estimated as much as twice as much in terms of frequency or length of hospital stays. Treatment adherence, use of long-acting therapies, homelessness, early versus late disease, co-morbidities, age, and race were identified as factors associated with resource use. The syntheses also confirmed that schizophrenia patients' management costs are varied, and a small proportion of schizophrenia patients utilized disproportionate amount of health resources.

The review to identify definition of high utilization returned only two studies leading to no standard definition of a High Utilizer. (Desai, Lawson, Barner, & Rascati, 2013)) (Doran & Rosenhenck, 2013) Doran was based on frequencies of Emergency Department use while Desai et al dichotomized into high-cost (expenditures ≥ $16,000) and low-cost category based a natural break concept. The research had to lean on definition of high utilizer in non-schizophrenia studies.

Lack of reliable studies on high utilization among schizophrenia patients was a major impetus behind the current study which conducts a comprehensive estimation of emergency and hospital services use by this patient cohort in a large database Medicaid database. The resulting analysis, with a focus on SU, along with the analysis methodology is included in

Chapter 4. The IBM® MarketScan® Multi-State Medicaid Database V2047 with more than 33 million lives was the main source of data for the current research. Included in the third chapter is the research approach towards a SU definition. SU was defined as schizophrenia patients who are the top 10% of Emergency room and Inpatient services utilizer. The distribution of utilization of emergency and hospitalization in the IBM® MarketScan® Multi-State Medicaid database further strengthened the decision to select top 10% of schizophrenia patients as a SU as the number of emergency and hospital visits among the top 10% matched to other definitions of high utilizers in the literature. (Harris, et al., 2016) (Lynch, et al., 2016)

A retrospective analysis of the IBM® MarketScan® Multi-State Medicaid Database of schizophrenia patients from year 2010-2019, showed that the top 10% of the Super Utilizer experienced 9 + emergency visits or hospitalizations in a 12-month period. Nearly one per month! Post selection of a Super Utilizer definition, this chapter confirmed the literature findings on significantly high and variable use of emergency services and hospitalization among schizophrenia patients in Medicaid system. While top 10% experienced 9+ visits to emergency or hospitalizations, about 37% did not have any visits in a year, 17% had only 1 and another 11% had 2 visits in a year! This furthered the thesis to focus on patients with significant unmet needs who are frequently visiting emergency and hospitals.

Thereafter, the chapter explored bivariate relationship being a Super Utilizer with key demographic factors such as Gender, Race and Age. The analysis showed that being Female, White and in age group 18-34 years were disproportionately over-represented in High Utilizer category. Since the IBM Marketscan database had 11% missing race (Cohort A). The analysis

was also conducted on a cohort of data with no missing race (Cohort B). Both cohorts of data had similar bivariate results. Lower rates of super utilization among Black were not expected given the findings of earlier studies by Desai and Wallace. (Desai, Lawson, Barner, & Rascati, 2013) (Wallace, Lollo, Duchowny, Lavallee, & Ndumele, 2022) Perhaps Blacks who have schizophrenia have more access challenges than blacks with other burdensome chronic diseases that what is understood in the current literature. The only schizophrenia study found in the literature suggesting Black as a factor for high utilization is Desai. (Desai, Lawson, Barner, & Rascati, 2013) Her study is survey based on personal recollection, which may have methodological challenges when understanding resource use among schizophrenia patients. Furthermore, her work is based on a much smaller sample of 317 schizophrenia patients, and her definition of High cost is based on natural break in cost data which is different than this study. The findings of this research do conform to Shim's research which also found that White schizophrenia patients had higher emergency visits which was "strikingly" different than White diabetes or other disease patients. (Shim, Compton, Rust, Druss, & Kaslow, 2009)

The research also found that the cohort of schizophrenia patients who were young (18-34 years) were more represented in super utilizer category. This was not surprising as the disease usually strikes patients in their 20s and early 30s and higher utilization is seen when their providers are trying to find the right treatment strategies. This is also confirmed by prior studies. (Huang, Amos, Joshi, Wang, & Nash, 2018) (Pesa, et al., 2021) (Cloutier, et al., 2016) (Desai, Lawson, Barner, & Rascati, 2013) But the higher proportion of female in super utilizer category stands in contrast to findings in literature that men use more emergency than women but there is lack of literature specific to schizophrenia Medicaid women. Given low-income

status and behavioural health challenges of this cohort of Medicaid women, their ability to seek care may be significantly disadvantaged and hence they may be more prone to emergency help.

The analysis also found a higher proportion of Male and Whites in comparison to Females and Blacks in the zero-utilization category. This may point to better managed disease among Males and Whites. This could be due to several reasons such as better access, caregiver impact, stigma or racial bias. Another key conclusion from the descriptive analysis on resource utilization is that missing race data does not seem to have an impact on bivariate descriptive findings.

In chapter 5, descriptive analyses were conducted on additional factors that have shown relationship between schizophrenia and resource use. These factors included were Charlson Comorbidity Index, Type 2 Diabetes, Suicide Ideation or Attempt, Heart Failure, Obesity, End Stage Renal Disease, Alcohol and/or Substance Abuse and Use of antipsychotic medications. Comparison was made between the “Super Utilizer” and “Not Super Utilizer” groups and “Super Utilizer” and “Not Super excluding Zero Utilizer” groups.

The differences in the comorbid proportions are substantial when comparing the two categories of utilization. For example, Heart Failure is 16% among the super utilizer while only 9% of not super utilizer had heart failure, thus a 77% higher prevalence. Suicide Ideation or Attempt is three times higher in prevalence (45% vs. 15%), 30% higher with Type 2 Diabetes (35% vs. 27%), approximately 50% higher obesity among super utilizers (36% vs. 23%). The differences in the proportion of all the explanatory variables in the super utilizer category

versus the not super utilizer are all statistically significant but the differences are narrower with multiple variables when zero utilizers are excluded.

The bi-variate analysis was followed by a multivariate logistic regression with all the explanatory variables discussed above to understand the factors that are associated with being a Super Utilizer. Given that one of the main goals of this research was to identify factors that may be highly associated with being a Super Utilizer, logistic regression on multiple variables was selected as the appropriate statistical methodology. This type of regression technique is applied to examine the association of (categorical or continuous) independent variable(s) with one dichotomous dependent variable which in this study is being a Super Utilizer or Not Super Utilizer. Given that there are 11% missing race data, all the regression analysis was run on both complete data set (Cohort A) and the dataset excluding missing race data elements (Cohort B). This approach was taken to analyse whether a typical Medicaid database with missing race information can be used to develop population health management strategies.

Dahlgren and Whitehead "Rainbow Model" provided the theoretical framework to identify factors impacting high utilization of resources by schizophrenia patients. This theoretical framework provided a powerful framework for understanding how mental health such as schizophrenia is shaped by various layers of social, economic, and environmental factors. The explanatory variables selection was based on “Rainbow Model” framework (Deyo, 1992) and complemented by the systematic literature review findings in Chapter 3. The final selection was dependent on availability of data elements in the Marketscan Medicaid database which allowed for unique data elements such as Charlson Comorbidity Index (CCI) but no social

and environmental factors such stigma, homelessness and lack of access to care. Although not studied in past literature, Obesity was included in the analysis given its unique high prevalence in this patient population.

Three different regression approaches were applied. First, a Single logistic regression approach included four different regression models on both Cohort A & B and the base model included variables demographics such as Age, Sex, Race, comorbidities such as Heart Failure, Diabetes, Cancer, Suicide Ideation & Attempt, End Stage Renal Disease, and Alcohol and/or Substance Abuse and a variable to reflect adherence to schizophrenia treatment with "Use of antipsychotics in past 30 days". The goodness of the fit was assessed using Area under the curve (AUC) of the ROC curve and Brier test. 0.0 and 1.0. A model that is perfect will have a score of 0.0 and the worst will have a score of 1.0. AUC evaluates the rank of the prediction while Brier score calculates the accuracy of probabilistic predictions. Odd Ratios (ORs), 95% confidence intervals, coefficients and Z-statistics were computed for all covariates of the models. Subsequent models II to IV included CCI and Obesity and both respectively.

All models had strong predictive power with minor improvements with the addition of CCI and Obesity to the base model. There is a slight benefit of excluding missing race data, but the difference is minimal. The strength of the model ranged from Brier Score of 0.082 to 0.084, this all very close to zero and AUROC ranged from 0.74 to 0.75. Given CCI is a composite score that reflects the health of an individual, it was not surprising to see it emerge as the most strongly associated factor with being in Super Utilizer category. The other factors that rose to top were having a diagnosis of Suicide Ideation or Intent, and being young in age. Without CCI,

the model remained strong with Suicide Ideation or Intent, ESRD and being young in age emerging as top there in effect size. Since study database is large and the explanatory variables were mostly selected based on learnings from past studies, all the explanatory variables were found to be statistically significant. Thus, the focus is on the size of the odds ratio to understand the key factors that are important in predicting whether a patient is going to be High Utilizer of emergency or hospital resources.

Given a significant cohort of schizophrenia patients, 37%, in Medicaid database had zero use of emergency room or hospitals, a Second approach excluding zero utilizer cohort was also analysed. The model output was similar with weaker predictability power.

Furthermore, since schizophrenia patients with zero utilization of healthcare services may have different reasons for zero use than resource users, the application of Single logistic regression approach may ignore critical differences. Hence, a Third model approach of a Two-stage model was estimated to identify if determinants of being a non-user was different from those influencing the frequency of use.

In comparison to Single model approach, two-stage model result showed that being female is negatively associated with being a SU and being on antipsychotics is positively related to being a SU with Odds Ratios of 0.88 and 1.09 respectively. Another difference was that having an Alcohol and/or Substance Abuse diagnosis is not statistically significant as an explanatory variable for being a high utilizer but a significant factor in being a user of any resources. The factors that emerge to the top in terms of effect size were, being Age 18-34 and Age 35-64, ESRD and having Suicide Ideation or Attempt as a diagnosis. The effect size of these

variables was found to be smaller compared to Single Regression Model. When CCI and Obesity are added to the model, CCI rises to the top in effect size, along with being young (Age 18-34). AUC remains a strong 0.75 across all four two-stage models. Having comorbidities like ESRD or a comorbidity index like CCI remain key predictors in both modelling approaches.

Across all models, a key finding in chapter 5 is that missing race data of about 11% is not a limitation. This makes the learnings very applicable in the real world where missing race data will be present as one always has the choice of withholding that information from the health systems. As Blacks were expected to be bigger use of emergency and hospitalization, this study presents unexpected outcome that shows negative relationship between black and SU. This new data suggest perhaps blacks in Medicaid with serious mental health problems may have higher barrier to care, provider bias, distrust and stigma. (Shim, et al., 2014) (Tirrell, 2023)

6.3 OVERALL THESIS

This thesis contributes to the understanding of high burden faced by schizophrenia patients in the Medicaid Health System in the United States. It also characterizes the depth and variability in the resource utilization for services associated with emergency and hospital care which mostly represents unmanaged or sub optimally managed health of this highly vulnerable cohort of Medicaid members. Schizophrenia poses a significant economic impact on a health system that is facing increasing unsustainable cost increase. It is also a disease where patients are costing 50% to 300% more than other burdensome diseases like bipolar and diabetes.

In first of its kind, this study finds that top 10% of resource utilizers among Medicaid schizophrenia patients are seeking emergency or hospital care 9 or more times a year. This amounts to close to monthly or more interaction with acute care for a chronic disease and points to high degree of disability and low quality of life. Thus, it is worthy of deeper study of reasons behind the unmanaged care for Medicaid schizophrenia members. Although this research is focused on Medicaid patients, as the prevalence of this disease is highest in this insurance system, the unmet need and burden that schizophrenia patients and their caregivers face is of concern across all payer types. This is confirmed with first of its kind systematic literature review of the resource used by schizophrenia patients across all payer types. This sheds light on a small patient population, hence generally ignored, could be a significant catalyst behind high utilization of health care resources in the US thus worthy of policy makers attention.

This study confirms that there is significant variability of resource use and that small percentages of the overall population are consuming disproportionate amount of care. (Jiang, Weiss, Barrett, & Sheng, 2012) (Cohen, 2014) (Davenport, Grey, & Melek, 2020) (Finkelstein, Zhou, Taubman, & Doyle, 2020) In this study, top 10% were experiencing 9+ visits to emergency and hospitalization while 37% had none in a year. This is new data in understanding the schizophrenia population in the Medicaid system which is a significant provider of care for patients with behavioural health challenges.

The current study's approach on finding key factors associated with high emergency and hospital use is also unique in terms of its size, focus and applicability. There have been studies

with similar objectives in other diseases like depression (Robinson, 2016) or multiple chronic diseases (Harris, et al., 2016) or with focus on schizophrenia patients across all health systems (Desai, Lawson, Barner, & Rascati, 2013) or in high utilizers in other health system such Veteran Affairs but across all diseases (Doran & Rosenhenck, 2013). Being young in age, having higher Charlson Comorbidity Index, having comorbid conditions like Suicide Ideation or Attempts, End Stage Liver disease, Heart Failure were expected factors in identifying patients who are at high risk of being in emergency or hospital care but findings the negative relationship between high use of resources and being Black, and use of current antipsychotic prescription came as a surprise. This research provides a closer look at how schizophrenia patients might be different from patients with other burdensome chronic diseases. The surprising result of positive association between female and SU was overturned by two stage approach which conforms to literature findings.

The predictability score across all models in this research shows that an approach based on existing claims database can lead to identification of nearly 75% of patients at risk of significant emergency and hospital resource use as well as resulting disability. Missing race data in one out of ten patients was not a limitation thus making the method applied very practical and applicable. Since the zero utilizers of emergency and hospital services were a significant 37% of the Medicaid schizophrenia patients, a separate regression was run excluding that population along with a two-stage model approach. A scenario analysis excluding zero utilizers of resources weakened the overall predictive strength of the model but the factors that rose to the top in terms of association remained the same.

In the two-stage approach, the relationship with Black race, continued to be negative in all models but relationship with Antipsychotic use measured over 30 days and being Female became negative. Across all models having ESRD and being young in age had highest effect size. In models with CCI data, CCI emerged with highest Odds Ratios. Although all included factors were statistically significant in predicting SU in Single Model approach, having Alcohol and/or substance abuse dropped as a significant factor for being a SU in a two-stage approach. Application of two-stage model provided a methodology to separate the factors that determine SU use from not being a zero utilizer.

Frequent utilization of emergency and hospital care is an indicator of high disease burden as well as unmet health management need. Without appropriate preventative care, these patients present themselves in emergency or hospital due to acute relapses in schizophrenia symptoms thus making them one of the most vulnerable populations. This research exploring the top 10% of emergency and hospital services user among a very disabling and costly disease like schizophrenia in a resource constrained health system like Medicaid will provide useful data to US policy makers who aim to reduce unnecessary resource use while improving the health outcomes of Americans.

6.4 STRENGTHS AND LIMITATIONS

6.4.1 STRENGTHS

One of the key strengths of this research is a systematic literature review of the burden of schizophrenia in the US across all its major payer types. A significant source of the high

resource use among schizophrenia patients was found to be emergency visits and hospitalization stays across all payer types. Another main strength of this research is that it is conducted on a very large Medicaid database representing approximately half of Medicaid population. This provides robust characterization of High Utilizers among schizophrenia patients. The analytical approach also provides a framework that can be applied in other payer databases as economic and clinical burden among schizophrenia patients is not unique to Medicaid but cuts across all payer types.

There is only one prior research by Desai et al that is based on National Health Expenditure Survey which a more robust set of data elements such as homelessness, social support which are known to impact schizophrenia disease management. (Desai, Lawson, Barner, & Rascati, 2013) The analysis was however not focused on just Medicaid and was based on just 136 patients. This study is based on an easily accessed claims database which has more than 200,000 schizophrenia members for analysis and a longer time frame of 10 years. High predictability scores of the current thesis model on easily available payor specific claims data add to usefulness and thus applicability of this research.

Given a lack of standardized approach in defining Super Utilizer, this research selects and conforms to most of earlier definitions in the literature. (Wammes, van der Wees, Tanke, Westert, & Jeurissen, 2018) (Johnson, et al., 2015) (Lynch, et al., 2016) A common thread across the definitions in the literature is that these individuals experience large numbers of emergency visits and hospital admissions which could have been avoided with early targeted care. To

develop a definition of Super Utilizer for this research, a systematic approach to categorize the top 10% of ER and hospitalization user was applied.

The multiple logistic regression models with different combinations of explanatory variable producing equally strong results point to a rigorous approach to selecting explanatory variables. The finding conformed to earlier research showing the significant role played by comorbid conditions in creating high need patients but also added new insights on Black, Male and Female schizophrenia patients. The strength of the predictive power of logistic regression shows that a large easily available claims database, with its limitations, may still become a strong source for population management efforts A two-step approach was useful in separating factors that were associated with zero utilization versus those who were utilizers. Analysis accounting for missing race information confirmed that the limitations presented in data collections due to HIPAA laws may not handicap our ability to find better ways of providing care.

An additional strength of this model is that the methodological approach can be applied to understand the develop population health management tools for other highly burdensome diseases like bipolar or diabetes or congestive heart failure.

6.4.2 LIMITATIONS

This absence of standardized definition of High Utilizer, in the literature, creates a significant barrier to analysis and data-driven policymaking targeting this group of patients. The literature review found no common definitions of “high” or “super” utilization. Studies have

used a variety of definitions, and this research chose to use top 10% of resource utilizers as the High Utilizer group. Although this definition conforms to most of the other definitions, a limitation of this research is whether the study results remain the same with a different definition. Desai's study uses a natural break in cost approach toward a High Utilizer definition, making it difficult to compare and contrast the only other study with similar objective. (Desai, Lawson, Barner, & Rascati, 2013)

Although one of the strengths of the model is that the regression was run on very large sample size of schizophrenia patients, it was limited to data elements found in a payer sourced claims database. Based on earlier research, variables such as homelessness, perception of poor health, social isolation and other social determinants of health may be relevant but are not available in claim databases. Inclusion of these factors may provide a stronger predictive power. With the absence of other key data elements, the model still remains robust and provides guidance needed to shape a population management tool to minimize avoidable Emergency Room and hospital stays among schizophrenia patients who are unfortunately experiencing these 9 times or more in a year.

Another limitation was lack of a good measure of adherence to antipsychotic as an explanatory variable. A positive relationship between being a Super Utilizer and being on an antipsychotic, in two-stage model results, is surprising and should not be conclusive because of the data limitation. There are multiple studies showing the positive relationship between lack of treatment adherence and high rate of relapses and hence hospitalization. Expanding data element with actual adherence to treatment would have enhanced the model although that

would have also created a problem of autocorrelation with other explanatory variables such as suicide ideation or attempt, alcohol or substance abuse and adherence to medication. (Semahegn, 2020) Overall, lack of adherence data still remains a limitation. Missing race information in 11% of dataset can be seen as a limitation as well since race was seen as an important explanatory variable in Desai's study. (Desai, Lawson, Barner, & Rascati, 2013) This research applies various methodologies to study the sensitivity to missing race and thus alleviates the limitation of missing race data.

Another key limitation of this research is that the study is limited to Medicaid patients and hence may not be applicable to other payer types. Similarly, the study is also limited to schizophrenia patients in the United States and hence the findings may not be appliable to similar patients in other countries.

6.5 POLICY IMPLICATION

This study strives to provide policy guidance for optimal management of schizophrenia patients who are at risk of multiple acute needs for hospitalizations or emergency services. Research findings presented in this thesis have several health policy implications. The health system of the United States is saddled with significantly high health care cost which continues to disproportionally consume its GDP. Given the high cost has not translated to better health outcomes, focusing on high unmet need area seems to be a logical place to look for solutions to not only curtail runaway cost of care but also enhance quality of care and productivity. One of

the areas of high unmet need is among patients suffering from schizophrenia, especially among the Medicaid population. Frequent emergency and hospital care are an indicator of unmet health and social needs, especially among patients with serious mental health problem like schizophrenia.

Fragmentation in behavioural and physical health care in the US prevents comprehensive care which leads to worsening overall health and further acute episodes leading to hospitalization. Inadequate public funding has worsened mental health crisis as most of the severe mentally ill patients rely on public assistance. A 2022 survey conducted by the Kaiser Family Foundation and CNN, showed that one-third of mentally ill respondents could not get the mental health services they needed. 80% cited cost as the barrier while about 60% experienced stigma. (Lopes, Kirzinger, Sparks, Stokes, & Brodie, 2022)

Among the mentally ill, individuals suffering from serious mental illnesses like schizophrenia, are most vulnerable. Innovations in the field of medicine have led to effective medications, psychological treatments, and housing or caregiver support, and access to these are severely constrained. The increasing deinstitutionalization of patients with mental illness has shifted the burden of caregiving on family members who find it very challenging to care for schizophrenia family member.

This study proves robust evidence on the extent of these patients' unmet needs and especially among the Super Utilizer group. The finding that SU schizophrenia patients are making 9+ visits for emergency or hospital care will bring much needed attention to this extremely high need and often ignored group. In addition to societal recognition of the

resource use impact of schizophrenia, it will also make a case for better treatment, better identification of patients who are at risk for relapses, along with tools to better manage the key co-morbid conditions like Suicide Ideation or Attempt, Heart Failure, End Sage Liver Diseases and Diabetes. The evidence from this research is also important for Patient Advocacy groups who are trying hard to bring attention to an often-neglected disease due to stigma and low prevalence rate. This study confirms that regardless of low prevalence in comparison to other chronic diseases, this disease cost is much more burdensome and more suited for focused preventative care.

Finding the reasons behind the Medicaid schizophrenia patients' recurrent disease relapses and consequently emergency and hospital care will enable policy makers to shape health management strategies to prevent these costly and debilitating trips to emergency and hospitals. This research enables policy makers to identify and focus on schizophrenia patients with better and less expensive timely outpatient treatments. The regression outputs form the current research can be used to identifying patients who are risk of avoidable emergency visits and hospitalizations. The policy makers can then develop a customized disease management strategy for the patients who are at risk of repeat emergency and hospitalization.

Research by Herz et al show that preventative strategies such as combination of psychoeducation, active monitoring for prodromal symptoms along with medications, weekly group therapy for patients, and multifamily therapy groups can help in preventing worsening of the disease. (Herz, et al., 2000) Another study by Prince confirms the value of symptom education, outpatient service continuity and daily structure in maintaining treatment and care

in preventing inpatient stay or hospitalization. The study does bring up the challenge of providing continuous outpatient care to all schizophrenia patients, given how resource poor in general the system is. A finding that allows identification of super utilizers, patients that are young in age and have substance abuse, Suicide ideation & attempt, Heart Failure, ESLD allows for targeted and much less resource intensive outpatient care & symptom education while having the most impact in preventing hospitalization or need for emergency care. (Prince, 2006)

A recent publication by Ben-Zeev et al study showed that a health technology program with individualized schizophrenia health management when delivered in-person or via smartphones, computers along with web based prescriber decision support program can nearly cut hospitalization by half during the 6 months after discharge (43% of control and 24% of intervention participants). (Ben-Zeev, 2023) Ben-Zeev health technology program, when applied to Super Utilizers could have significant impact in preventing hospitalizations among a group that is at risk of experiencing 9+ hospitalization and emergency care.

The US Department of Veteran Affairs has taken a proactive approach in providing integrated and coordinated care to schizophrenia patients. (VA, 2021) All Veterans with schizophrenia have mental health treatment coordinators who help navigate the health specialty clinics, primary care clinics, nursing homes, and residential care facilities. VA integrates mental health staff into Patient Aligned Care Teams (PACTs) and the members with serious mental health problems like schizophrenia may participate in specialized programs such as mental health intensive case management, day centres, work programs, and psychosocial rehabilitation.

A disease management programs for all schizophrenia patients, such as provided by the VA, can be expensive as well as wasteful. 37% of Medicaid schizophrenia patients had no emergency or hospital visits. But a disease management program when focused on super utilizers, can provide better access to continuous care in identifying, understanding and controlling symptoms whether in-person or web-based, in a cost-effective manner. This way the policy makers can achieve the two-fold objective of alleviating the cost for an economically burdened health system like Medicaid and improving the quality of care of schizophrenia patients. In terms of improvement in quality of care, studies have shown that targeted schizophrenia management can effectively even reduce substance abuse, homelessness and criminal activity in the community they live in. (Gowda, 2022)

6.6 METHODOLOGICAL IMPLICATIONS

The systematic approach of this research to assess the economic burden across all payer types can be a useful resource for other researchers. The “Rainbow Model” provided a powerful framework for understanding how mental health such as schizophrenia is shaped by various layers of social, economic, and environmental factors. This study subsequently employed a pragmatic approach to use readily available albeit limited claims databases to test models to explore and understand the factors associated with the health and economic burden associated with mostly preventable emergency and hospitalizations among a high need patient cohort. This will also serve as a useful resource to population health managers who are seeking to reign in cost of healthcare while improving the quality of care for patients with high unmet needs.

Application of Two-stage modelling in a case where a significant proportion of population had zero use of resources provides a robust way of identifying factors that predict super utilization. This approach also allows for a better understanding of the cohort that is utilizing no emergency or hospital resource.

6.7 FUTURE RESEARCH

This research raises a lot of questions that may become the foundation for future research. Although the literature points to higher use of emergency care by Black and Male, the current study shows the opposite. There is need to understand the challenges that Blacks Medicaid schizophrenia patents face in seeking care or perhaps, although highly unlikely, the findings of this research are pointing towards better management of schizophrenia disease among Black Medicaid patients. Although schizophrenia is found burdensome across all payer types in the US, this research to characterize Super Utilizer and understand this population is specific to Medicaid population only. A similar research approach in other payer types can build on evidence needed to alleviate the high burden and cost of schizophrenia. There are social factors that impact schizophrenia care, such as homelessness, lack of caregivers, prior criminal activity and incarceration. These have been out of scope for this study due to data limitation. Applying the findings of this study to another database that includes these social determinants of health along with incarceration data, can enhance the predictability of the approach in identifying schizophrenia patients who need health management the most. Additionally, as this study is US specific, similar research in other countries can provide insights into any differences and perhaps solutions to alleviating the economic and clinical burden of schizophrenia.

6.8 CONCLUSION

Literature has robust evidence confirming the high resource utilization of emergency and hospitalization among schizophrenia patients in the United States. Past studies also point to cost variability and suggest that small proportions of patients are resulting in significantly high cost of healthcare. This research conducts a systematic literature review of resource use by schizophrenia patients across all payers in the US and concludes that this disease is more burdensome in comparison to other known burdensome chronic conditions.

Given the high prevalence of schizophrenia patients in the Medicaid system, this thesis characterizes the extent of their high utilization of emergency and hospitalization in his payer segment. The study found that top 10 percent of resource users, characterized as Super Utilizers, visited emergency or hospitals 9 or more times a year!

This current research also identifies the key factors associated with super utilization of resources and measures the extent of the association. It uncovers the critical role played by being young and of key comorbid conditions, Suicide Ideation or Attempt, Heart failure, End Stage Renal Disease and diabetes, in being a SU. The findings in this thesis deepens our understanding of high resource drain among a very burdened Medicaid health system. This research may benefit the development of targeted interventions aimed at improving patient outcomes and health care spending efficiency.

The current research is based on a large data sample of hundreds of thousands of Medicaid schizophrenia members, making it first of its kind in terms of highly predictable

models based on readily available claims database. The findings have the potential to better manage health of Medicaid schizophrenia patients who are leading a very poor quality of life and suffering work impairment with severe negative impact on cost of care. Little attention has been given to a mental illness like schizophrenia due to its low prevalence and stigma attached to it. As a result, local, state and federal government funding has been sparse to understand the causes behind the recurrent emergency and hospital use among this patient population. This study aims to provide evidence for development of better schizophrenia population health management strategies and draw attention to conduct more research in an often-neglected disease area.

RESEARCH ETHICS

The research contained in this thesis was approved by the Faculty of Health and Medicine Research Ethics Committee of Lancaster University. It was also approved by Johnson & Johnson Research Approval Process.

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APPENDIX I: SEARCH IN MEDLINE

Completed on August, 2021

Inclusion: Year 2000 onwards, Adult only (18year +) and publication is English only

Search 1:

(schizophrenia or schizophrenic disorder OR "serious mental illness" OR SMI) AND (cost or utili or "resource use") AND (united states or america or usa or u.s or united states of america or u.s.a)*

Search 2:

(schizophrenia or SMI) AND ((high utili) or (super utili*)) AND (united states or america or usa or u.s)*

Abstract were assessed to include: Cost/Resource Use Studies, Burden Studies, Non-Clinical Studies, Non- drug effectiveness studies and US only studies.

APPENDIX II: JBI CRITICAL APPRAISAL CHECKLIST FOR ECONOMIC EVALUATIONS (JBI, 2017)

Reviewer_ _ _ _ _ _____Date_____

Author_____Year_____ Record Number_____

		Yes	No	Unclear	Not applicable
1.	Is there a well-defined question?	☐	☐	☐	☐
2.	Is there comprehensive description of alternatives?	☐	☐	☐	☐
3.	Are all important and relevant costs and outcomes for each alternative identified?	☐	☐	☐	☐
4.	Are costs and outcomes measured accurately?	☐	☐	☐	☐
5.	Are costs and outcomes valued credibly?	☐	☐	☐	☐
6.	Are costs and outcomes adjusted for differential timing?	☐	☐	☐	☐
7.	Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?	☐	☐	☐	☐
8.	Do study results include all issues of concern to users?	☐	☐	☐	☐
9.	Are the results generalizable to the setting of interest in the review?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐

Comments (Including reason for exclusion)

APPENDIX III: DATA EXTRACTION FORM

Authors	Methodological approach	Study period	Payer: Medicaid, Medicare, VA, Commercial, others	Study population (all, men only, Women only, other sub-groups)	Resource use: per patient per annum	Resource use: Per patient per month	Definition of high cost	Data source

APPENDIX IV: CHARLSON COMORBIDITY CONDITIONS

Comorbid Condition	ICD-9-CM Diagnosis Codes	ICD-10-CA Diagnosis Codes	Weight
Myocardial Infarction	410, 412	I21, I22, I25.2	1
Congestive Heart Failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428 (hosp), 398, 402, 425, 428 (med)	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9,I43, I50, P29.0	1
Peripheral Vascular Disease	093.0, 437.3, 440, 441, 443.1–443.9, 447.1, 557.1, 557.9, V43.3 (hosp) 440, 441, 443, 447, 557 (med)	I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9	1
Cerebrovascular Disease	362.34, 430–438 (hosp) 430–438 (med)	G45, G46, H34.0, I60–I69	1
Dementia	290, 294.1, 331.2 (hosp) 290, 294, 331 (med)	F00–F03, F05.1, G30, G31.1	1
Chronic Pulmonary Disease	416.8, 416.9, 490–505, 506.4, 508.1, 508.8 (hosp) 416, 490–496, 500–505 (med)	I27.8, I27.9,J40–J47, J60–J67 J68.4, J70.1, J70.3	1
Connective Tissue Disease-Rheumatic Disease	446.5, 710.0–710.4, 714.0–714.2, 714.8, 725 (hosp) 446, 710, 714, 725 (med)	M05, M06, M31.5, M32–M34, M35.1, M35.3, M36.0	1
Peptic Ulcer Disease	531–534	K25–K28	1
Mild Liver Disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570, 571, 573.3, 573.4, 573.8, 573.9, V42.7 (hosp) 070, 570, 571, 573 (med)	B18, K70.0–K70.3, K70.9, K71.3–K71.5, K71.7, K73, K74, K76.0, K76.2–K76.4, K76.8, K76.9, Z94.4	1
Diabetes without Chronic Complications	250.0–250.3, 250.8, 250.9 (hosp) 250 (med)	E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9	1
Diabetes with Chronic Complications	250.4–250.7 (med n/a)	E10.2–E10.5, E10.7, E11.2–E11.5, E11.7, E12.2–E12.5, E12.7, E13.2–E13.5, E13.7, E14.2–E14.5, E14.7	2
Paraplegia and Hemiplegia	334.1, 342, 343, 344.0–344.6, 344.9 (hosp), 334, 342–344 (med)	G04.1, G11.4, G80.1, G80.2, G81, G82, G83.0–G83.4, G83.9	2
Renal Disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582, 583.0–583.7, 585, 586, 588.0. V42.0, V45.1, V56 (hosp), 403, 582, 583, 585, 586, 588, V56 (med)	I12.0, I13.1, N03.2–N03.7, N052–N05.7, N18, N19, N25.0, Z49.0–Z49.2, Z94.0, Z99.2	2
Cancer	140–172, 174–195.8, 200–208, 238.6 (hosp), 140–172, 174–195, 200–208, 238 (med)	C00–C26, C30–C34, C37–C41, C43, C45–C58, C60–C76, C81–C85, C88, C90–C97	2
Moderate or Severe Liver Disease	456.0–456.2, 572.2–572.4, 572.8 (hosp), 456, 572 (med)	I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5–K76.7,	3
Metastatic Carcinoma	196–199	C77–C80	6
HIV/AIDS	042–044	B20–B22, B24	6

APPENDIX V: ETHICS APPROVAL

From: donotreply@infonetica.net <donotreply@infonetica.net>
Sent: Monday, August 8, 2022 8:47 AM
To: Tandon, Neeta (Postgraduate Researcher) <n.tandon@lancaster.ac.uk>
Cc: Mateus, Ceu <c.mateus@lancaster.ac.uk>; Ahmed, Faraz <faraz.ahmed@lancaster.ac.uk>
Subject: [External] FHM-2022-0902-RECR-2 Ethics Approval from FREC

This email originated outside the University. Check before clicking links or attachments.

Name: Neeta Tandon

Supervisor: Ceu Mateus

Department: Health Economics & Policy

FHM **REC Reference:** FHM-2022-0902-RECR-2

Title: Super Utilization of Healthcare Resources Among Schizophrenia Patients in the United States Medicaid System

Dear Neeta Tandon,

Thank you for submitting your ethics application in REAMS, Lancaster University's online ethics review system for research. The application was recommended for approval by the FHM Research Ethics Committee, and on behalf of the Committee, I can confirm that approval has been granted for this application.

As Principal Investigator/Co-Investigator your responsibilities include:

- ensuring that (where applicable) all the necessary legal and regulatory requirements in order to conduct the research are met, and the necessary licences and approvals have been obtained.

- reporting any ethics-related issues that occur during the course of the research or arising from the research to the Research Ethics Officer at the email address below (e.g. unforeseen ethical issues, complaints about the conduct of the research, adverse reactions such as extreme distress).

- submitting any changes to your application, including in your participant facing materials (see attached amendment guidance).

1

Please keep a copy of this email for your records. Please contact me if you have any queries or require further information.

Yours sincerely,

Dr Laura Machin
Chair of the Faculty of Health and Medicine Research Ethics Committee
fhmresearchsupport@lancaster.ac.uk

Lancaster University