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Empirical Study: Exploring Medication Adherence for Medicaid Insured Asthma Patients in Louisiana

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EMPIRICAL STUDY: EXPLORING MEDICATION ADHERENCE FOR MEDICAID INSURED ASTHMA PATIENTS IN LOUISIANA

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ABSTRACT

Asthma is a chronic disease whose effects are controlled/ prevented using appropriate medication. Although benefits of asthma medication is well known, poor medication adherence among asthma patients has been reported. Medication non-adherence is associated to increased healthcare costs, unnecessary hospital utilization, readmissions and even death in few cases. The overarching goal of this research was to evaluate the impact of medication non-adherence on hospital admissions, and identify key factors that result in medication non-adherence for Medicaid insured asthma patients.

To achieve these objectives, Correlation analysis, T-tests, Multivariate logistic analysis and odds ratios were performed. Based on results of the study, the present study did not find significant relationships between control medication adherence and the different types of hospital visits (i.e. emergency department visits, inpatient admits, and readmissions). However, patients with high rescue medication adherence had fewer emergency department visits (p-value=0.0004) and inpatient admissions (p-value=0.0303). Patients with more than 4 office visits had better rescue medication adherence, older and low-income patients had higher 30-day readmissions rate. While, male and low-income patients had emergency visits

Additionally, The two types of insurance coverages (Temporary Assistance for Needy Families and Supplemental Security Income-Non Dual) were the only significant predictors of control medication adherence among the factors analyzed (with p-values =0.0001). Asthma patients with TANF and SSI- Non Dual coverages are less adherent to control medication adherence compared to other coverages. Also, control and rescue medication adherence was not significantly different among case managed and non-case managed asthma patients.

CHAPTER 1: INTRODUCTION

1.1 Introduction

In recent times, the healthcare industry has made great strides in the prevention and curing of disease through science. Prescription medicines and advances in medical treatment are available to manage chronic and acute conditions. Even though the healthcare industry has been vouching for proper use of medication, evidence is available on the prevalence of medication non-adherence. Multiple studies have suggested that patients with poor medication adherence experience poorer health outcomes and often are the most costly members for their insurance companies. Although asthma medications can not cure asthma they help reduce symptoms and prevent asthma attacks. Health outcomes of asthma patients can be improved through pharmacologic interventions by patient or their family and provider (Pedersen, 2011). Subpar or irregular medication use has been associated with hospitalizations, hospital readmissions, emergency department visits, office visits and unnecessary utilization of medical resources (Miller, 1997). Taking the right medicine at the right time in a proper way, as prescribed by the doctor, is very important for many chronic illnesses, such as asthma.

According to an Asthma fact report published by Centers for disease control (CDC) in 2013, 3,404 deaths, 439,400 hospitalizations, 1.8 million ED visits and 14.2 million office visits were reported for the year 2010 (Asthma facts, 2013). Hospital admissions, especially readmissions are costly. Medicare estimated the cost of hospital readmissions to be $17.4 billion annually (Jencks et al., 2009) and most of these readmissions are preventable. In an attempt to reduce healthcare costs and readmission rates, the hospital readmission reduction program (HRRP) under the Affordable Care Act penalizes hospitals with excessive readmission rates within 30-days of initial discharge. Therefore under this policy, hospitals and care providers are forced to improve patient care and reduce unplanned 30-day readmissions (Greenwald, 2007). This readmission program greatly impacts hospital's financial performance and makes patient with chronic illnesses, such as asthma, a high risk.

Understanding factors resulting in medication non-adherence is valuable to improve medication adherence behavior in patients and in turn reduce non-adherence related hospital readmission of asthma patients. In the literature, research concerning barriers for medication adherence among asthma is well documented. However, it mainly focuses on identifying risk factors, and very few studies attempted to look at the bigger picture i.e. determining the influence of medication adherence on 30-day readmission rates as well as identifying factors affecting medication non-adherence and appropriate intervention strategies.

The asthma data needed for this study was collected from a healthcare insurance provider in Louisiana from active members with an insurance enrollment gap of 45 days or less during January 2015 through December 2016. Medication Possession Ratio (MPR) with variable duration (first and last medication fill date for each individual patient) was used to measure medication adherence for this study. MPR was calculated for each class of asthma medication i.e. Control medication adherence, Rescue medication adherence and overall MPR for both classes of medication for each individual patient. Variable MPR was calculated as summation of all days supply divided by the time between the last and first fill date plus the last days supply of medication MPR. Days supply of the last fill is added to estimate the expiration of supply.

This study is divided into two parts. The objective of the first part was to evaluate the impact of medication adherence on 30 day & 90 day hospital readmissions for asthma among Medicaid patients in Louisiana. Further, the effect of age, gender, and discontinuation of certain medications on medication adherence and readmissions will also be evaluated. The next part of the study focuses on exploring factors influencing medication adherence among asthma patients and proposing interventions to improve medication adherence behavior**.**

1.2 Problem Statement

Recent policy changes in healthcare, requires healthcare businesses to have a better understanding of factors that can reduce their cost and improve health outcomes for their patients. Research shows that 75% of total healthcare spending is accounted by chronic conditions such as heart failure, COPD, diabetes, hypertension, asthma and depression (Jack Meyer, 2013). Patients with chronic conditions avail more healthcare resources such as emergency visits, hospital admissions, special assistance and multiple expensive medications. Although most of the chronic conditions can be managed via proper medication regimen and life style changes, there is a definite gap between physician orders and patients' compliance. Previous studies have shown that 10 to 50% of hospital readmissions are considered to be avoidable (Jencks, 2009). Therefore, in order to reduce avoidable healthcare costs, the focus needs to be shifted to improve patient health and reduce unnecessary utilization of resources. Understanding major contributors of medication non-adherence will be a useful resource in quality improvement and cost reduction efforts (Anika et al., 2014) and in turn reduce expensive hospitalizations and readmissions.

1.3 Research Objectives

The overarching goal of this research was to evaluate the impact of medication non-adherence on hospital readmission, and identify key factors that result in medication non-adherence for asthma patients. This thesis document comprises two journal papers directed toward medication non-adherence and hospital readmission trends for asthma patients.

Paper 1: Empirical Study on Medication Adherence and Hospital Readmission for Medicaid Insured Asthma Patients- this paper focuses on evaluating the effects of medication non-adherence on patient readmission rates for asthmatic patients. Furthermore, it identifies trends among asthmatic patient's medication adherence behaviors with respect to scheduled doctor visits versus emergency visits (e.g. emergency department, hospitalization and readmission). This paper will be submitted for publication in the Journal of Allergy and Clinical Immunology.

Paper 2: Selection Criteria for Intervention to Improve Medication Adherence for Asthma Patients - this paper focuses on identifying key factors and barriers of medication non-adherence among Medicaid insured asthma patients, evaluating the effectiveness of case management services and recommending effective patient selection criteria for intervention that will improve medication adherence rates. This paper will be submitted for publication in the International Journal of Health Care Quality Assurance.

1.4 Outline of the thesis

This thesis follows the paper style, and entails an introduction, two journal papers, conclusion, future work and reference section.

CHAPTER 2: PAPER #1

"Asthma study on medication adherence and hospital utilization among Medicaid insured asthma patients", proposed submission to the Journal of Allergy and Clinical Immunology

2.1 Abstract

Medication adherence is an important indicator of quality in healthcare and non-adherence is associated with increased healthcare costs, hospitalizations, readmissions and decline in health outcomes. Despite the availability of medication to control and avoid adverse health situations, adherence to these medications among asthma patients varies between 40% and 60%, with 80% and above being the threshold of good medication adherence (Menckeberg et al., 2008). The aim of this study is to evaluate the effects of medication non-adherence on patient hospital readmission rates for asthmatic patients in Louisiana, according to their pharmacy records from their insurance company during the study period of January 2015- December 2016. Furthermore, the study identifies trends among asthmatic patient's medication adherence behaviors with respect to scheduled doctor visits versus emergency visits (e.g. emergency department, hospitalization and readmission). The present study did not find significant relationships between control medication adherence and the different types of hospital visits (i.e. emergency department visits, inpatient admits, and readmissions). However, patients with high rescue medication adherence had fewer emergency department visits (p-value=0.0004) and inpatient admissions (p-value=0.0303). Patients with more than 4 office visits had better rescue medication adherence. Older and low-income patients had higher 30-day readmissions rates. Similarly, male and low-income patients had emergency visits.

2.2 Introduction

Non-adherence to medications is a persistent problem, in particular for patients with chronic conditions. Taking medications as prescribed is associated with lower healthcare expenditure, decline in number of hospitalizations, readmissions and deaths (Claxton, 2012). Medication adherence is critical for the success of pay-for-performance approach recently adopted by the U.S. healthcare system. This approach provides financial incentives to hospitals, physicians, and other health care providers for achieving optimal outcomes for patients, making readmission within 30 days for the same condition a main concern. Pay-for-performance has become popular among policy makers and private and public payers, including Medicare and Medicaid. One in five Medicare patients discharged from hospitals are readmitted to a hospital within 30 days of initial discharge (Nehi, 2012). Asthma is a common chronic disease affecting 300 million people across the world (Jindal, 2012) that could result in hospitalizations and readmissions. Most asthma hospitalizations are considered avoidable, as the symptoms can be prevented and controlled with the appropriate use of medications, proper asthma management at home and outpatient care (Mackinon, Flagstad, Peterson, & Mesch-Beatty, 1996). The objective of this study is to investigate the association between medication adherence and hospital readmissions among Medicaid insured asthma patients in Louisiana. The study evaluates the medication adherence and readmission rates (30 day and 90 day) among asthma patients for a 2 years period (January 2015- December 2016) using pharmacy and healthcare claims data provided by an insurance company serving Medicaid beneficiaries.

2.3 Literature review

2.3.1 Asthma Medication and Current Treatment

Medication is the primary choice for medical interventions in all chronic conditions since these conditions cannot be cured, but exacerbations can be prevented and controlled. This study focuses on one chronic condition, asthma. Asthma management focuses on avoiding triggers, controlling the symptoms and reducing exacerbations- the latter two can be achieved by using proper medications. Asthma medicines minimize the risk of severe flare-ups and help asthma patients in leading an active life. Medicines are prescribed depending on age, severity of asthma, symptoms and side effects. According to National Asthma Education and Prevention Program (NAEPP), asthma medications are classified as "rescue" or quick relief or short-term medications, and "control" or preventive or long-term medications (NAEPP, 2007).

Rescue medications are often referred to as "bronchodilators" and are used in case of acute asthma attacks for quick relief. The effect of rescue medications lasts up to 4 to 6 hours (Adkinson, 2014). These medications are not recommended to be used very often due to their reported side effects such as muscle tremor, rapid heartbeat and restlessness (O'Byrne, 2001). Rescue medications are available in forms of liquids, tablets, capsules, and injections but inhalers are most commonly prescribed and preferred. There are three classes of rescue medications:

- Short-acting beta- agonists (SABA): Bronchodilator used to relieve symptoms quickly (e.g. Albuterol)
- Anticholinergics: Bronchodilators used with or instead of SABA (e.g. Ipratropium)
- Systemic corticosteroids: Drugs used to manage flare-ups and acute asthma attacks (e.g. Cortisone)

Rescue medications helps stop asthma attacks after they have started; whereas control medications are used to prevent asthma attacks from starting. Control medications reduce the swelling and mucus production in airways. They are used on daily basis for patients with persistent asthma to prevent exacerbations and inflammations. Effects of these medications last up to 12 hours or more (Adkinson, 2014; (Watts, 2009), and there are different classes:

- Inhaled corticosteroids (ICS): Anti-inflammatory drugs (e.g. Budesonide)
- Long-acting beta-agonists (LABA): Bronchodilator used to open airways (e.g. Severent)
- Combination inhalers (ICS/LABA): Combination of ICS and LABA (e.g. Advair and Symbicort)
- Cromolyn sodium and nedocromil: Add on controller medications or alternatives for inhaled steroids.
- Leukotriene receptor antagonists (LTRAs): Anti-inflammatory drugs (e.g. Singulair and Zyflo)
- Immunomodulators: Injection used for moderate to severe asthma related to allergies
- Methylxanthines: Bronchodilator used to prevent symptoms in the night (e.g. theophylline).

Additional treatments also include bronchial thermoplasty and immunotherapy (Dhar & Goshal, 2013).

(a) Bronchial thermoplasty: The U.S. Food and drug Administration (FDA) approved procedure involving direct application of thermal energy to mass of smooth muscle in managing severe asthma (Cox et al., 2006).
(b) Immunotherapy: Small doses of substances (to which a person is allergic to) are injected under the skin of an asthma patient to reduce their response to the allergens and symptoms overtime (Joint Task force, 2011).

A wide majority of asthma patients are not be able to use bronchial thermoplasty as it is an expensive procedure and is not covered under government insurance. In addition, there is a lot of controversy surrounding immunotherapy and using medication to manage exacerbations and prevent attacks is unanimously agreed upon in the literature.

Asthma medications prescribed vary across ages. Adults are treated with independent medication (monotherapy), while combination medications (adjunctive medication) are often prescribed for children and adolescents (NAEPP, 2007). Although, monotherapy with control medications is most effective in reducing airway inflammations and improving lung function, LABA monotherapy is not recommended for long-term control of asthma due to increased risk of asthma deaths (Nelson, 2006). There is conflicting research over which controller medication should be preferred. The National Asthma Education and Prevention Program (NAEPP) recommends ICS over other control medication due to reduced exacerbations, fewer hospitalizations and its superior anti-inflammatory quality compared to other controller medication, including leukotriene receptor antagonists (LTRAs) (NAEPP, 2007; Strunk, 2006; O'Byrne, 2006). Although ICS is referred to as the cornerstone for controlling asthma symptoms, concerns have been raised due to perceived adverse effects experienced by few people. A retrospective data analysis on outcomes associated with initiation of different controller therapies among Medicaid asthma population found that LTRAs are more effective in controlling asthma over ICS (Balakrishnan, 2005). As a part of treatment, asthma patients that cannot be controlled by using only one control medication are often prescribed combination medication, also known as adjunctive therapy. Three of the most common choices of combination medication with ICS are ICS + long-acting beta-agonists (LABA), ICS + LTRA, and ICS + theophylline. ICS + LABA combination is widely preferred over other combinations among older people and additional research is required on its effects on children 5-11 years (Watts, 2009). The British Thoracic Society/ Scottish Intercollegiate Guideline Network (BTS/SIGN) recommended prescribing ICS in combination with LABA in a single inhaler, to avoid adverse effects with LABA monotherapy (SIGN, 2012). Complete treatment for asthma includes combination of long-term medications such as inhaled corticosteroids (ICS) and use of short-acting beta-agonists in case of sudden attacks (Mayo Clinic, 2012). In order to find association between medications and related chances of readmissions, all the drug classes of rescue and controller medication taken by asthma patients (with an inpatient admission) during the study period are considered in this study.

2.3.2 Asthma Management Guidelines

Certain guidelines have been published in order to improve patient health outcomes and encourage involvement of patients through education and demonstration of the benefits on following a plan. The National Heart, Lung and Blood Institute (NHLBI) established strategies through the National Asthma Education and Prevention Program (NAEPP) for diagnosis and management of asthma in 1991. The practice of these clinical guidelines resulted in fewer hospitalizations and deaths associated to asthma, as reported on the 2007 Expert Panel Report 3 (EPR-3) (NAEPP, 2007). EPR-3 is a complete report of the best clinical practices in asthma care focusing on reducing impairment and likelihood of future asthma attacks. The report focuses on four components of care: a) Assessment and monitoring, b) Patient education, c) Control environmental factors and comorbid conditions, and d) Medications. Importance of using an asthma action plan was highlighted in this report. An asthma action plan is developed by the doctor and helps patient get involved in taking responsibility and self-managing their or their children's illness. It is a plan for how and when a medication needs to be taken.
Another asthma treatment strategy that was the basis for many national guidelines is the Global Initiative for Asthma (GINA). GINA was initiated with a goal of providing information about asthma management and translating scientific evidence research into improved care. GINA has published and annually updated its global strategy for asthma management and prevention for the past 20 years. This strategy emphasizes the patient and doctor partnership as being crucial for satisfactory health outcomes. While the issue of 2012 placed significant importance on having a written asthma action plan for self-management of asthma, the 2015 issue recommended targeted treatment and evidence-based approach to implement interventions effectively. A retrospective research containing data from three clinical studies, based on parameters derived from GINA guidelines, showed a positive relationship between the guidelines and improved quality of life (Bateman, Frith, & Braunstein, 2002).

Both NAEPP and GINA guidelines are a step-wise approach to control asthma. NAEPP has a 6-step approach and GINA has 5-Step approach of medications to be used, asthma education and management of comorbidities. According to both guidelines, low-dose ICS are considered first for controlling asthma across adults and older people. SABAs are prescribed across all age groups and severities for quick relief to bronchospasm or exercise induced asthma. Frequent need for SABA or LABA is an indication for need of increased care, medical attention and therapy (NAEPP, 2007).

2.3.3 Medication Adherence

Approximately 117 million people in the United States live with at least one of the 10 common chronic conditions (i.e. hypertension, coronary heart disease, stroke, diabetes, cancer, arthritis, hepatitis, weak or failing kidneys, current asthma, or chronic obstructive pulmonary disease). Nearly half of all the adults have at least one illness that requires prescribed medication (Ward at el., 2012) and 1 in 12 people were reported to have asthma in the year 2009 (CDC, 2011).

A person is said to be 'adherent' when they take correct doses of medication at times prescribed by a physician (Osterberg & Blaschke, 2005). Medication adherence is an umbrella term for compliance and persistence. It is often defined as "the extent to which a patient's behavior corresponds with recommendations from a health care provider" (WHO, 2003). In terms of medication fills, adherence refers to filling out a medication prescription at the prescribed

frequency. Importance of medication adherence and its positive association with improved healthcare outcomes has been well documented in the literature. A study on patients with cardiovascular diseases found that high adherence to antihypertensive medications were associated with higher control of blood pressure compared to low or medium adherence (Krousel-Wood et al., 2015). One asthma study conducted in Canada looked at the effect of regular use of inhaled corticosteroids on hospitalizations, and found an overall reduction in hospitalization rate due to regular use of asthma medication (Suissa, 2002). Medication adherence is alarmingly lower among chronically ill patients compared to patients with acute conditions (Cramer, 2003; Jackevicius, 2002). Therefore, different measures are being taken by health care providers to increase medication adherence and avoid adverse situations, including: using electronic devices set up with reminders, follow-up telephone calls, case management and other healthcare services provided for educating patients on positive effects of medication adherence, robust discharge instructions and primary care provider's (PCP) emphasis on medication (Bradley et al., 2012).

2.3.4 Medication Non-adherence

The practice of delaying or entirely failing to fill prescriptions, and taking them as per the recommendations of a physician is called non-adherence. Approximately one-half of patients in the United States do not take their medications as prescribed (WHO, 2003). Non-adherence could be intentional or unintentional and might occur during different stages of their treatment (Vriijens, 2012). Typically, physician prescribes the minimum doses of medication required to control asthma based on patient's condition. Inconsistency in adhering to these medications might cause exacerbations and mislead physicians from identifying the actual reasons for the loss of treatment effects. This often results in unnecessary increase of dosage strength or change of medications (Creer & Bender, 1995). Thus, it's critical to have a good understanding of the reasons and magnitude of medication non-adherence, in particular for patients with chronic diseases such as asthma.

Recent estimation shows that medication non-adherence is attributed to $100-$300 billions of avoidable costs in the U.S. annually (IMS, 2013). The cost per non-adherent asthma patient per year ranged from $321 for those who were prescribed ICS monotherapy to $741 for those who were prescribed a combination of ICS and leukotriene receptor antagonists (Tan et al., 2009). Medication non-adherence not only affects the patient, it also has severe economic impact and is a major cause of concern for healthcare providers, organizations and payers alike (Hugtenburg J. G., Timmers L., Elders P. J., Vervloet M., & L, 2013). Non-adherence to medication has been related to reemergence of tuberculosis (Bloomm & Murray, 1992), higher viral loads in children with HIV/ AIDS (Martin et al., 2007), lower quality of life among adolescents receiving liver transplant (Fredericks et al., 2008), and higher disease-related costs and hospitalizations among patients with diabetes, hypertension, congestive heart failure and hypercholesterolemia (Sokol, McGuigan, Verbrugge, & Epstein, 2005). In particular for asthma patients, medication non-adherence has become an area of active interest and poor adherence has been associated to mortality, increased direct and indirect costs, additional healthcare resource utilization, reduced quality of life and increased asthma symptoms (Bender, 2004; Harrison, 2003; Horne, 2006; (Engelkes, Janssens, de Jongste, Sturkenboom, & Verhamme, 2015).

2.3.5 Non-Adherence to Asthma Medications

Despite of the known benefits of using control medications on a daily basis, low adherence rates have repeatedly been reported across studies, with ICS adherence ranging from 40% to 60% (Rand et al., 1995; Breekveldt, 2004). A study on asthma medication adherence and beliefs conducted in Sweden showed that the mean adherence value for filled prescriptions of general asthma medications was about 68% and although adherence to combination inhalers was higher compared to single inhaled corticosteroids; overall adherence to asthma medication was low (Axelsson, 2015). A study found that filling oral steroids prescriptions among children within 7 days of discharge was 56% (Cooper & Hickson, 2001), and a children's study in Canada evaluated the effect of filling inhaled corticosteroids within 3 months of discharge (Blais et al., 1998). Another observational study of 56,168 in U.S., measured asthma controller medication adherence using pharmacy refill data and found that non-adherence was associated with higher asthma medical costs (Tan, 2009). The variable nature of symptoms in asthma (with periods of no attacks) often encourage non-adherent behavior and overtime leads to unexpected asthma attacks. Non-adherence to asthma medications among children can cause excessive wheezing and variability in pulmonary function, limiting daily activities (Bauman, Sallis, Dzewaltowski, & Owen, 2002), results in exacerbations, deterioration of health, need for excessive urgent care, hospitalizations and death in some cases.

2.3.6 Medication Adherence Measurement

In order to control their illnesses, patients with chronic conditions take necessary medications throughout their life. Therefore tracking or measuring medication adherence among chronically ill yields better results compared to patients with acute illnesses. Currently, there is no gold standard for measuring medication adherence. Selection of an appropriate method depends on various factors such as the definition of adherence used, resources available, characteristics being evaluated, patient population, time assessment, and ethical/ legal considerations in contacting or interviewing the patient (Banfield, 2015). Medication adherence measures can be divided into two categories: subjective and objective measures.

2.3.6.1 Subjective Measures of Medication Adherence:

Self-reporting and self-assessment of medication adherence with surveys, questionnaires, and patient diaries, where patients or their family members (on behalf of children) record daily medication intake patterns are subjective measures of adherence (Elliott, 2006; Rand & Wise, 1994). Many measurement scales and questionnaires, such as Morisky's medication adherence scale (MMAS), Medication adherence rating scale (MARS), and Beliefs about medicines questionnaire (BMQ) have been developed and validated in the literature. In addition, some scales are developed to measure medication adherence among specific conditions. Medication adherence rating scale for asthma (MARSA), is a scale used in clinical practice setting to evaluate medication taking behaviors and attitudes among asthma patients and ASK20 is a self-reporting tool used to measure and identify barriers for medication adherence among asthma and COPD patients. Although, subjective methods are cost-effective, they are unreliable and increase the complexity of research, Patient recall bias issues and possible "Hawthorne effect" i.e. increase in patient's medication adherence because of their knowledge of being observed might produce dubious results.

2.3.6.2 Objective measures of medication adherence:

Objective measures documented in the literature includes:

- Biological assays: Bodily fluids such as serum, urine, blood or saliva is tested to detect traces of medication. Positive results for the test/ finding traces of medication is not an indication of adherence, it only confirms that medication was taken before the test. This method is invasive and gives consistent results only for certain drugs (e.g. theophylline and cycloporism).
- Electronic monitoring devices: Electronic devices equipped with chips are installed in with inhalers or oral medications to record the time, frequency and doses of medication taken by the patient. Although this method is widely used, it has been equally criticized as the devices are expensive, need training to use and patients were found to deliberately use the device several times shortly before their doctor visits.
- Pill counts and canister weights: Pill counts is a simple method where medication adherence is calculated by counting number of remaining medication and comparing it with units of medication issued. Weighing the canister or device and calculating the change in weight is another similar method. These methods are cost effective and simple, but might overestimate patient's medication use; since pills can be disposed and inhalers could be emptied prior to doctor visit.
- Pharmacy records: Pharmacy records provide patient's medication and refill information. It is a simpler way of collecting medication related information such as drug name, dose, how many days' worth of medication was filled by the patient, prescribing doctor and filling patterns of patient's (by identifying if the patient was/ was not in possession of medication or if there were gaps in filling medications over the study period) for target population or large number of patients at once. Pharmacy information can be obtained from pharmacy claims data maintained by pharmacies, Insurance and healthcare providers. Reliability and validity of prescription claims data has been examined by numerous researchers in the United States This method is cost effective, noninvasive, simpler and proven to be efficient. However, refill behaviors do not guarantee that patients are actually taking the medication as prescribed. Various methods of calculating medication adherence using pharmacy claims records are available. This method requires data set to be valid, complete and accurate, patients continuous eligibility during the study is required along with information on changes in insurance plans and any additional treatment services available to the patients. A number of calculations are available in literature to report the rate of medication adherence among chronically ill patients. Some of the most commonly used calculations include Medication possession ratio (MPR), Cumulative medication gap (CMG) and Proportion of days covered (PDC).

2.3.7 Medication Possession Ratio (MPR)

MPR is calculated as the sum of the days' supply obtained during the study period divided by the total number of days in this time period plus the last fills days supply. It has been a go-to method to calculate medication adherence using claims data in the past. MPR measures adherence by assessing medication availability and determining skipped or discontinued medications (Md Redzuan, Lee, & Mohamed Shah, 2014). MPR is used in the literature to measured variable or fixed periods and they are called variable MPR (VMPR) and Fixed MPR

(FMPR), respectively. The main difference in the measurement of MPR is in calculating the denominator. The denominator of VMPR varies for each individual depending on their first and last fill date while the denominator of FMR is fixed for all study subjects i.e., the number of days in the study period (e.g. 1 year study period =365 days). Both methods of measurements are quite popular but the difference in calculating them complicates comparisons across studies (Kozma, Dickson, Phillips, & Meletiche, 2013).

$$\text{FMPR} = \frac{\text{Sum of the days supply for all claims during the study period}}{\text{No. of days in study period}} \text{ x } 100$$

Equation 1. Fixed Medication Possession Ratio formula

$$\text{VMPR} = \frac{\text{Sum of the days supply for all claims during the study period}}{\text{Elasped days (inclusive of last prescription)}} \text{ x } 100$$

Equation 2. Variable Medication Possession Ratio formula

MPR approach to adherence measurement has a few drawbacks, such overestimating medication adherence as it does not address overuse that occurs when patients buy early refills of their medication causing an overlap and also inflation in the resulting value (Martin et al., 2009). However, MPR is a widely used and accepted method to measure medication adherence in the literature and in practice for various illnesses (Patel et al., 2010; Duncan, 2016). Several asthma studies evaluated medication adherence using MPR. MPR with variable denominator is the selected method for calculating medication adherence of asthma patients in this study. Various researchers have considered patients with MPR lower than 80% as non-adherent and more than 80% are to be adherent to medication (Briesacher, 2009).

2.3.8 Hospital Readmissions

Hospital readmissions are defined as multiple hospital stays by the same patient within a specified time for reason same as related or unrelated to the index admission. Readmissions may occur due to multiple unexplainable reasons and can be separated by days, weeks, months or years (Stone &Hoffman, 2010). American Hospital Association (AHA) created a framework dividing readmissions into 4 types: "(a) planned readmission related to the original admission, such as placement of ventricular assist device following a heart attack; (b) planned readmission unrelated to the original admission, such as readmission for a removal of lung tumor discovered during an admission for heart attack; (c) an unplanned readmission unrelated to the original admission, such as readmission for a fracture caused by accident following an initial stay of pneumonia; (d) an unplanned readmission related to the initial admission, such as a surgical site infection or adverse reaction to a medication" (AHA, 2009). Planned readmissions are not a cause of concern, they are a part of treatment such as surgery follow up or rehabilitation and agreed upon by the provider and the patient. Unplanned readmissions related to index admission, on the other hand accounts to preventable costs, unnecessary resource utilization, patient dissatisfaction and stress to the family (Jencks, 2009). All hospital readmissions might not be preventable, many of them could be avoided by providing better care during treatment, and while transitioning from inpatient stay.

According to a study by University HealthSystem Consortium, most readmissions occur within 7 days of discharge (Arnold, Buys, & Fullas, 2015). Readmissions occurring shortly after hospital discharge are crucial. They might be a sign of insufficient discharge instructions,

miscommunication, physician's inexperience, or patient's non-adherence to discharge instructions. There is no a single timeframe for defining hospital readmissions in the literature. Studies examined readmissions within 15, 30, 60, 90 days or even a year following the discharge from a hospital (Stone &Hoffman, 2010). This study will focus on the 30 day readmission, given its criticality in regards to the pay-for-performance approach recently adopted by the U.S. healthcare system (MedPAC, 2007; CMS, 2012).

In 2007, 17.6% percent of hospital admissions resulted in 30-day readmissions, accounting to $15 billion in Medicare spending. Medicare Payment Advisory Committee (MedPAC) reported that 76% of the readmission could have been avoided. Preventable inpatient spending costs owing to readmissions increased from $15 billion (in 2007) to $17.5 billion by 2010 Medicare claims (MedPAC, 2007; CMS, 2012). To address this issue and hold hospitals accountable for high readmissions, Congress and the Centers for Medicare and Medicaid Services (CMS) established the Affordable Care Act and created a Readmission Reduction Program in the year 2012. Hospitals with excessive readmissions were penalized with one percent reduction in payments for heart attack, heart failure and pneumonia and the penalty was supposed to increase to three percent reductions extending to COPD, asthma and select cardiovascular procedures by the year 2015 (Axon, 2011). As a result, hospitals and care providers were forced to improve inpatient care, discharge planning coordination, and transitional care from hospital to home (Greenwald, 2007). Although direct cost of asthma was reported to be $2.2 billion annually with about 347,000 hospital admissions in the year 2013, limited studies examined 30-day readmissions among asthma patients, especially among adults (Hasegawa, Gibo, Tsugawa, Shimada, & Camargo Jr, 2016). Hospital readmissions, especially 30-day readmissions are considered as indicator of quality. It is used as a pay per performance measure by affordable care act. Therefore, 30-day readmission of asthma patients across all ages will be evaluated in this study. Asthma studies in the literature also look at 90-day readmission rates while formulating interventions. A childhood asthma study, which analyzed inpatient hospitalization, outpatient and prescription claims records to identify patients who filled asthma discharge medication (short acting agonist, oral corticosteroid, or inhaled corticosteroid), within 3 days of discharge from a facility found that filling beta agonists and inhaled steroids was associated with lesser hospital readmissions (i.e. 90-days) (Kenyon et al., 2015). In addition, the 90-day readmission will also be analyzed.

2.3.9 Factors Affecting Readmission

Chronic conditions account for many hospitalizations and readmissions due to their persistent illness. Chronic illnesses require more resources, budget, attention and specialized services (such as disease management, case management, etc.) for an extended period (WHO, 2002a). Therefore, readmission's role as a quality measure has increased during the past decade and recent studies all over the world examined factors that contribute to patient's readmission.

A study on childhood asthma based in Auckland, New Zealand found that patient's age, gender, number of previous admissions, and severity of the condition were related to readmission during a 6 month period after discharge (Mitchell, Bland, & Thompson, 1994). Few other studies found comorbidity, length of stay, lack of documented patient or family education, insurance status, and marital status are patient-level factors affecting 30-day readmissions (Holloway, Medendorp, & Bromberg, 1990; Marcantonio et al., 1999). Gender, race, insufficient discharge planning, drug management and polypharmacy (e.g. use of five or more drugs), have been identified as

contributory factors with the highest risk of readmission (Kansagara et al., 2011, Viktil et al., 2007;Wong et al., 2011). This goes to show that reasons for readmission are varied and hence not all the cases of readmission can be avoided in one specific way.

2.3.10 Link between Readmission and Non-Adherence

Hospital readmissions are known for being indicators of inadequate quality and key contributors to healthcare costs in the U.S. and around the world. Although many programs have been implemented to address increasing readmissions and their concurrent healthcare costs, more than 1,400 hospitals were penalized for high readmissions rates in 2012, resulting to costs more than $280 million (Krauskopf et al., 2013). CMS uses data from three full years to calculate each hospital's readmission rate. Therefore, data from the three years, June 2008 to July 2011 was used for 2013 calculations penalizing 64% of hospitals for diagnosis of heart attack, heart failure and pneumonia. Similarly, June 2009-July 2012 hospital data was used for calculations in 2014 with 66% of hospitals being penalized for diagnosis of heart attack, heart failure and pneumonia. COPD, Hip or knee replacement were added to the list in 2015 for data from the years 2010 to July 2013. 78% of hospitals were penalized in the year. June 2012-July 2015 data were used to calculate penalties for the year 2016 owing to similar penalty as the year before i.e. 78% (Boccuti, 2015).

CMS estimated that 11% of hospital readmissions occur due to medication non-adherence and the resulting costs are estimated to be $100-$289 billion annually (Osterberg & Blaschke, 2005). A study reported that hospitalizations, readmissions and even death rate were low among patients that are medication adherent and the risk of these hospitalizations and readmissions among non-adherent patients was 5.4 times high among hypertension patients, 2.8 times high among dyslipidemia and 1.5 times high among patients with heart diseases (Gwadry-Sridhar et al. 2009). A pediatric asthma study aimed at evaluating factors associated with readmission conducted a survey regarding asthma knowledge, beliefs, and medication adherence. The study demonstrated the need to target medication adherence in order to reduce inpatient readmissions (Auger, Kahn, Davis, & Simmons, 2015). Another study at a university hospital during an 11 month period found that one-third of hospital admissions due to adverse drug events were medication non-adherence related (McDonnell & Jacobs, 2002). A retrospective cohort analysis from 12 geographically diverse states on relationship between asthma prescription filling patterns and hospital readmission rates among patients discharged from an inpatient facility found that filling of all of three recommended mediations (beta agonists, oral steroids and inhaled steroids) following discharge was associated with lowest risk of hospital readmission within 14 days and a statistically significant reduction in readmissions between 15 and 90 days (Kenyon et al., 2015). One study based in Brazil, assessing the effect of free asthma medications on hospital admissions showed that the free asthma medications provided by the Brazilian health system significantly decreased asthma hospitalization rates over a three year period (Comaru, Pitrez, Friedrich, Silveira, & Pinto, 2016). Among few studies that examined association between readmissions and specific asthma medications, Saratsafavi et al evaluated controller medication, reliever medications associated with different inhaled controller treatments as an add on to systemic corticosteroids, and readmission rate over a period of one year following discharge among asthma patients (ages 12-25). Taking inhaler medication early after discharge was associated with reduced readmissions and combination therapy seems to be as effective as inhaler medication in reducing readmissions and increasing long-term adherence (Sadatsafavi,

Lynd, De Vera, Zafari, & FitzGerald, 2015). A similar study regarding recurrence risk after an ED visit or hospitalization and delay in filling asthma controller medication reported increase in asthma related- ED visits or IP stay when there was a delay in initiation of controller medication (Sadatsafavi et al., 2015). Treatment with Budesonide inhalation suspension during the first 30 days after inpatient stay and emergency department (ED) visits reduced asthma readmissions or ED visits. Asthma medication adherence has been associated with reduced exacerbations and hospitalizations (Camargo, Ramachandran, Ryskina, Lewis, & Legorreta, 2007). Thus, there is plenty of evidence in the literature on the association between medication adherence and hospital readmissions. This paper aims at finding the relationship between medication adherence and 30 day readmissions among asthma patients under Medicaid. All classes of asthma medication will be examined to map the medication taking behavior among asthma patients.

2.3.11 Current Practices Aimed At Reducing Readmissions

A systematic review and meta-analysis aimed at examining the difference in medication adherence and readmissions between patients who received usual care and an intervention group found that, the intervention group (patients who received education, self-management and medication adherence strategies from trained nurses) had lower likelihood of readmission compared to control subjects (Hyrkas & Wiggins, 2014). Therefore, a number of programs have been designed to address transitional care needs for patients. Some of the current practices for readmissions and care transitions include "Project RED", "Care Transitions Program", "Project BOOST", and "Medicare Demonstrations: Details For Community-Based Care Transition Program". Project RED, is short for Project Re-Engineered Discharge developed by a research group at Boston University Medical Center. The group develops and tests strategies that improve hospital discharge process, promote safety and reduce readmission rates. RED, consists of 11 components that have been successful in reducing readmissions. This project has demonstrated reduction in ED visits and readmissions within 30 days of discharge by approximately 30% (Jack et al., 2009). Care Transition Program is a four week program aimed to improve patient's transition from hospital to home. As a part of this program, a Transition Coach educates patients on self-management using specific tools to reduce readmissions among high-risk Medicare beneficiaries (CMS, 2007). Project BOOST, stands for Project "Better Outcomes for Older Adults through Safe Transitions". This is a care initiate by Society of Hospital Medicine to improve transitional care among patients. A study to determine the effect of project BOOST on rehospitalizations and length of stay found that participation in the project appeared to be associated with decrease in readmission rates. The Community- Based Care Transitions Program (CCTP) is a program by U.S. Department of Health & Human Services, Centers for Medicare & Medicaid Services. It aims at reducing hospital readmissions, improving quality of care and document measurable savings to the Medicare program (CMS fact sheet).

2.4 Research Methodology

The general purpose of this study is to evaluate the effects of medication non-adherence on patient readmission rates for asthmatic patients. Furthermore, identifies trends among asthmatic patient's medication adherence behaviors with respect to scheduled doctor visits versus emergency visits (e.g. emergency department, hospitalization and readmission).

2.4.1 Study setting

Data for this study was sourced from a healthcare insurance provider based in Baton Rouge. The company provides health coverage to Medicaid or LaCHIP qualified people through state's Healthy Louisiana program and links Medicaid recipients to primary care providers, pharmacies and case managers. Institutional Review Board at Louisiana State University reviewed and approved the study.

2.4.2 Study population

The study population consists of Medicaid patients of all ages with primary or secondary diagnosis of asthma and insured (with 0 or maximum 45 day enrollment gap from insurance) during January 1, 2015 to December 31, 2016. International Classification of Diseases, ninth revision code (ICD 9 codes) 493.XX and tenth revision code (ICD 10 codes) J45.XX, and the list of asthma medications with 9-digit National Drug Codes (NDC) within each asthma drug class (Control and rescue medications) were used to identify members with asthma. Patients were eligible for study inclusion if they met the following criteria: asthma patients admitted at least once to a hospitals (e.g. inpatient facility) in Louisiana for reason related to asthma; if they had two or more pharmacy claim for asthma control medication; if they were continuously eligible and enrolled in health coverage during the study period. Patients who died during the study period or were discharged to other facility from the hospital during their initial admission, had missing or invalid claims data, and medical or pharmacy claims for reasons other than or not related to asthma were excluded from the study. In order to compare the readmission rates an inpatient admissions data set was collected from a random sample of 1000 non-asthmatic members to be used as the non-asthmatic group.

2.4.3 Data Source

The insurance company's databases, MicroStrategy and data warehouse (EDW), were used to gather the required data for the years 2015 and 2016. These databases capture patient level clinical utilization, expenditures, and admissions across inpatient, outpatient, and emergency department, prescription drugs filled, and enrollment into healthcare services (i.e. case management, disease management or other care services from within the plan). The databases include present and past members, and dependents insured under them. Data was available separately for each admits/ visits. Therefore, separate CSV files were gathered from different reports and linked to the patient through their Medicaid ID, initially. Health Insurance Portability and Accountability Act of 1996 (HIPPA) policies and guidelines were followed, and all the data was de-identified before data analysis.

2.4.4 Data collection

Data was collected from different databases called MicroStrategy and data warehouse (EDW) used by the insurance company. Separate reports on member data, emergency department data, inpatient stay and prescription medication data was collected. All the reports are linked to one another through member ID numbers. Figure 1 shows a schematic representation of the data points available in each of the reports retrieved from the database.

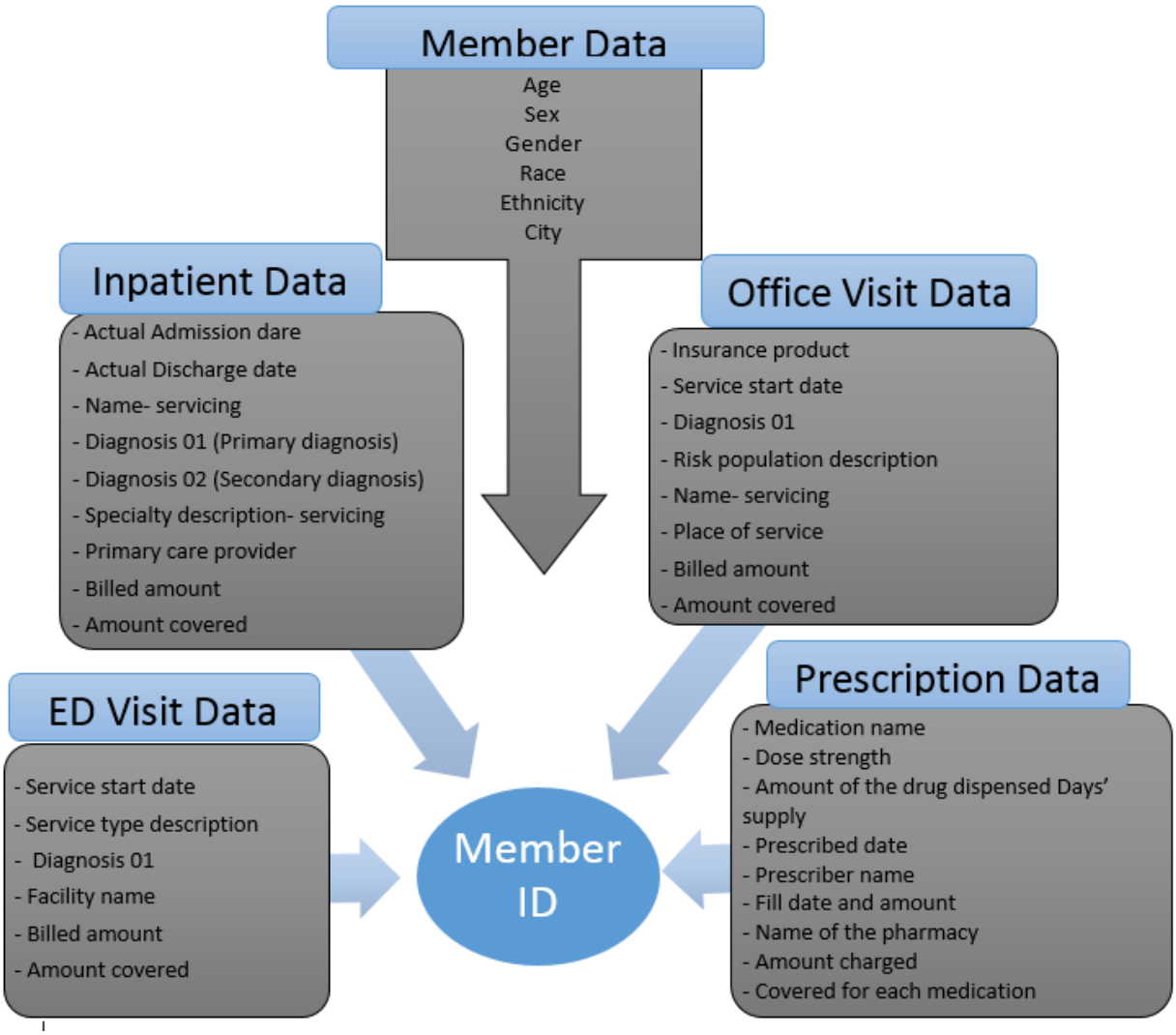

Figure 1. Schematic of data files provided by the healthcare provider

2.4.5 Measurement of Hospital Readmissions

30-day and 90-day readmissions were calculated from data available in the insurance claims' records. Readmissions were calculated by counting days between index discharge and subsequent admission into the hospital and if this value fell between within 30 days and 90 days, it was considered as 30 or 90-day readmission. Transfer from one facility to other facility is not considered as hospital readmission. If the patient is discharged from the transferred facility to home and is admitted back into a hospital within 30 or 90 days, then it is considered as a readmission.

2.4.6 Measurement of medication fills

Pharmacy claims for the following asthma medications during the study period will be used to calculate the medication adherence of patients for the two types of medications- Type I- Rescue Medication: (1) short-acting beta agonists; (2) oral corticosteroids/ systemic corticosteroids; and Type II- Control Medication: (1) inhaled corticosteroids or a combination inhaled steroid and

long acting beta agonist; (2) Long-acting beta-agonists; (3) Leukotriene receptor antagonists; (4) Immunomodulators; (5) Cromolyn sodium and nedocromil; (6) and Methylxanthines.

Medication Possession ratio (MPR)

Control medications are the preferred medication for long-term management of asthma symptoms, while rescue medications are only used as per need during an asthma attack event. Studying Control medication adherence on patients with chronic disease like asthma is critical for better healthcare outcomes. MPR was calculated for control medication and rescue medications separately for each patient.

$$\text{MPR} = \frac{\text{Total number of days covered}}{\text{Last fill date} - \text{first fill date} + \text{days supply of last fill}} \text{ x } 100$$

The above equation, was used to calculate medication adherence in this study. First, a data file containing the variables such as patient ID number, National Drug Code (NDC) for drugs, date of prescription claim, days of supply for prescription claim, and region identifier needed to calculate MPR for all patients in the study was created and then the equation for calculating MPR, was followed. Numerator of the formula is the sum of all the days supply for the study period (2 years for this study) divided by the number of days elapsed (last fill date- first fill date for each individual) plus days supply of last fill .
SAS 9.4 version and excel were be used to calculate MPR.

2.4.7 Statistical Analysis

The overarching purpose of this study is to evaluate the effects of medication non-adherence on hospital visit rates for asthma patients. Some of the research questions explored in this study include:

1. What is the impact of asthma patients' prescription non-adherence (fail to refill in this context) on their 30-day and 90-day hospital readmission rate?
2. Are the readmission rates for asthma patients the same as readmissions for patients without asthma illness (non-asthmatic group)?
3. At the beginning of an asthma treatment, patients are scheduled to visit their doctors every 2 to 6 weeks and a comprehensive asthma action plan is developed to manage care. Once the asthma is controlled they can be scheduled to meet the doctors monthly to twice a year depending on their health and signs of symptoms (NHLBI, 2014). Therefore one of the questions was: Are 4 visits for the 2 year study period associated to higher levels of adherence?
4. What is the effect of patients' demographics on medication adherence and readmission?

The proposition of this study is that prescription non-adherence negatively impacts the readmission rates on hospitals. In order to better understand the relationship between medication adherence and different types of patient-doctor interaction including office visits and emergency visits (i.e. emergency department visits, inpatient stay and hospital readmission rates), the following hypothesis will be tested:

- H1: Asthmatic patients with lower level of medication adherence, as measured by Medication Possession Ratio (MPR), have more emergency visits, including (emergency department visits, inpatient stay and hospital readmission at various intervals i.e. 30-day and 90-day).
- H2: Asthmatic patients that attend at least 4 scheduled office visits have higher levels of medication adherence.
- H3: Patients prescription adherence and emergency visit rates will differ by demographic groups (age, gender and income level).
- H4: Readmission rates of asthma patients will be significantly different from readmission rates of non-asthmatic group.

2.4.8 Data Analysis

SAS 9.4 was used for data analysis

1. Descriptive analysis was conducted on the sample to summarize the data collected for the study. This includes age, gender, income level, and insurance distribution of the study sample.
2. In order to address H1, a correlation analysis was performed to discover the relationship and direction of relationship between office visits, emergency visits and prescription non-adherence of asthma patients (control medication and overall medication).
3. In order to address H2, a t-test was performed to see if patients with at least 4 scheduled office visits have higher levels of medication adherence.
4. In order to address H3, a multiple regression analysis was performed to explore the relationship between prescription adherence and emergency visits with demographics (age, gender and income level).
5. In order to address H4, a t-test as well as odds ratio was performed to assess whether the means of the two groups are statistically different from each other. This analysis was conducted to understand if readmissions characteristics are similar among asthma patients and the non-asthmatic group. Lessons learned from this evaluation are discussed and used to propose effective asthma management guidelines to increase medication adherence.

2.5 Results:

2.5.1 Descriptive Analysis

(a). Sample description of asthma patients (n=687)

Out of the 2085 asthma patients with continuous insurance eligibility for the two-year study period (January 2015 to December 2016), 687 patients fulfilled the inclusion criteria. A summary of descriptive statistics for the study population (687 patients) is shown in the tables (2.1- 2.4) below. The average age was found to be 20 years, with the youngest patient being 1 year old and the oldest being 65 years old. Most patients (65%, 449) are considered minors, under the age of 18. Approximately 56% of the patients are females (n=384) and 44% are male (n=303), as shown in Table 2.2. Table 2.3 is related to income distribution shows that 70% of the patients received median household income of $25,000 to $50,000. From Table 2.4, it is noted that asthma population for this study are covered under 6 insurance coverages: Temporary assistance for needy families (TANF) covers 60% of the patients, Medicaid Expansion covers 22% of the patients, Supplemental security income Non-dual (SSI Non-Dual) covers approximately 12%,

Foster care covers 2%, Behavioral health covers 1% and Children's Health Insurance Program (CHIP) covers 0.29% of the patients. Eligibility criteria for each of the coverages is different and all of them provide low-cost healthcare coverage to Americans falling under one or more of the following criteria: people with low income, children, foster care, families, pregnant women, mental health and substance use disorder, elderly or people with disabilities.

Table 2. 1. Age distribution of asthma patients (n=687)

Age Groups	Number (n)	Percent (%)	Cumulative Frequency	Cumulative Percent
1-18 years	449	65.36	449	65.36
18-29 years	49	7.13	498	72.49
30-39 years	64	9.32	562	81.8
40-49 years	52	7.57	614	89.37
50-59 years	58	8.44	672	97.82
60-65 years	15	2.18	687	100

Table 2. 2. Gender distribution of asthma patients (n=687)

Gender	Number (n)	Percent (%)	Cumulative Frequency	Cumulative Percent
Female	384	55.9	384	55.9
Male	303	44.1	687	100

Table 2. 3. Income distribution of asthma patients (n=687)

Income Level	Number (n)	Percent (%)	Cumulative Frequency	Cumulative Percent
Less than 25K	35	5.09	35	5.09
Between 25K and 50K	482	70.16	517	75.25
Between 51K and 75K	165	24.02	682	99.27
Between 76K and 100K	5	0.73	687	100

Table 2. 4. Insurance distribution of asthma patients (n=687)

Insurance coverage	Number (n)	Percent (%)	Cumulative Frequency	Cumulative Percent
Behavioral Health	7	1.02	7	1.02
CHIP	2	0.29	9	1.31
Foster Care	17	2.47	26	3.78
Medicaid Expansion	153	22.27	179	26.06
SSI Non-Dual	87	12.66	266	38.72
TANF	421	61.28	687	100

(b). Hospital admissions and medication adherence of asthma patients (n=687)

Table 2. 5 summarizes inpatient admissions, Emergency department visits, office visits, 30 day readmissions and 90 day readmissions for the asthma population. Of 687 asthma patients, 148 patients had inpatient admissions, 263 had emergency visits, 489 had office visits, 25 had 30 day

readmissions and 24 had 90 day readmissions. During the 2-year period on an average, asthma patients attended 3 (SD=4.25) office visits, had 2.3 (SD=2.4) emergency department visits, and 2 (SD=1.8) were admitted into the hospital (Inpatient admission). Also, these patients had an average rate of 1.68 (SD= 1.14) 30-day readmissions and 1.9 (SD=1.8) 90-day readmissions into the hospital.

Table 2. 5. Description of inpatient, emergency department, office visits, 30 day and 90 day readmissions for asthmatic population.

Variables	Inpatient admits (n=148)	Emergency Department (n=263)	Office Visits (n=489)	30 day Readmissions (n=25)	90 day Readmissions (n=24)
Mean	1.91	2.35	3.25	1.68	1.96
Standard Error	0.15	0.15	0.19	0.23	0.37
Standard Deviation	1.82	2.42	4.25	1.14	1.81
Sample Variance	3.31	5.86	18.08	1.31	3.26
Minimum	1	1	1	1	1
Maximum	14	18	65	5	9
Total admissions/visits	283	618	1587	42	47
Number of patients	148	263	489	25	24
Female	84 (57%)	133 (51%)	255 (52%)	15 (60%)	15(63%)
Male	64 (43%)	130 (49%)	235 (48%)	10(40%)	9(38%)

Medication adherence was measured using variable Medication Possession Ratio (MPR) for control and rescue medication separately. The inclusion criteria for this study focused on patients with two or more fills of control medication. Table 2. 6 shows the number and percentage of asthma patients with control medication adherence, as calculated by their MPR, greater and less than the threshold of 80% (Briesacher, 2009) across age groups. By inspection, it appears that younger asthma patients are more adherent to control medication than older patients. The grand total at the end of the table for the two columns show that 213 (31% are adherent) have control medication adherence less than 80 and 474 (69% are non-adherent) have MPR more than 80.

Table 2. 6. Control medication adherence for asthma patients across age groups (n=687)

	Control medication adherence	
Age groups	**Less than or equal 80 (non – adherent) #(%)**	**More than 80 (adherent) #(%)**
0 to 9	90 (13%)	173 (25%)
10 to 18	63 (9%)	123 (18%)
19 to 29	7 (1%)	42 (6%)
30 to 39	12 (2%)	51 (7%)
40 to 49	12 (2%)	40 (6%)
50 to 59	22 (3%)	36 (5%)
60 to 69	6 (1%)	9 (5%)
Grand Total	213 (31%)	474 (69%)

(c). Sample description of non-asthmatic group

A group of 972 non-asthmatic members were randomly selected i.e., none of these members had a primary or secondary diagnosis of asthma. These 972 members had continuous Medicaid eligibility with the same insurance company from January 2015 to December 2016. Of the 972 members only 90 members had 180 inpatient visits for the study period. Therefore 90 non-asthmatic patients were selected to be compared against asthma patients with inpatient admissions for this study. Reasons for inpatient admissions ranged from general health checkups, acute illnesses, chronic illnesses, and behavioral health related disorders. Diagnosis description and count of inpatient admissions for each diagnosis are attached in the Appendix B. 24% of the members (i.e. 22 members) had 30-day readmissions and 12% of the members (i.e. 11 members) had 90-day readmissions with minimum number of readmissions being 1 and maximum being 4 readmissions. 8% of the non-asthmatic group members (i.e. 7 members) had both 30 day and 90-day readmissions to the hospital.

A cluster analysis was conducted on the non-asthmatic group in order to determine if all the individuals have the same behavior or to find groups, which are acting differently from the rest. This analysis was done to determine if was diverse enough to test the non-asthmatic group against the asthmatic group. Dividing the patients into 4 clusters is associated with an R square of 82.8 %, which means that the variation of the 4 clusters can explain 82.8% of the entire variation. Cluster analysis is done to identify homogenous groups that have similar behaviors but are distinctively different from the other groups. 90 members in the non-asthmatic group are therefore divided into 4 similar groups. At 4 clusters, the Pseudo F is very high with a value of 138, which confirms the number of clusters found. In addition, the cluster history shows the components of each cluster (Appendix B)

2.5.2 Correlational analysis for hypothesis #1

A correlation analysis was performed to determine the relation between emergency department visits, inpatient admits, hospital readmissions (30 day and 90 day) with Control and Rescue medication adherence, as measured by their MPR.

2.5.2.1 Correlation matrix with control medication:

From table 2. 7., it can be noted that no variable is significantly correlated with Control medication adherence (MPR), as p-values are all greater than 0.05, but control medication adherence has a weak negative relationship with emergency department visits (r= -0.03886), inpatient admits (r= -0.00463) and 90-day readmissions (r= -0.00363). I.e. patient's adherent to control medication will have less emergency visits and inpatients admits. Also, there is a weak positive relationship between control medication adherence and 30-day readmissions (r= 0.03787), i.e. 30 day readmissions increase with increase in control medication adherence.

Table 2. 7. Correlation Matrix for Emergency, inpatient admits, 30 and 90 day readmissions and Control medication adherence for asthma patients (n=687)

Pearson Correlation Coefficients, N=687 Prob> |r| under H0:Rho=0					
	Emergency Department	Inpatient Admits	30 day readmissions	90 day readmissions	Control medication MPR
Control medication MPR	r= -0.03886 p-value= 0.3091	r= -0.00463 p-value= 0.9037	r= 0.03787 p-value= 0.3216	r= -0.00363 p-value= 0.9244	r= 1

In addition, results (attached in Appendix C) showed that there's a strong correlation between the number of emergency visits and the inpatient admits, between the number of Emergency visits and the 90 day readmissions, between inpatient admits and the 30 day readmissions, between inpatient admits and the 90 day readmissions, and between 30 day readmissions and the 90 day readmissions (p values < 0.05). Which means that any type of hospital utilization results in a subsequent admission ore readmission to the hospital. We can observe these correlations clearly in the scatter plots in Appendix B.

2.5.2.2 Correlation matrix with Rescue medication:

Table 2. 8. Correlation Matrix for Emergency, inpatient admits, 30 and 90 day readmissions and Rescue medication adherence for asthma patients (n=546)

Pearson Correlation Coefficients, N=687 Prob> |r| under H0:Rho=0					
	Emergency Department	Inpatient Admits	30 day readmissions	90 day readmissions	Rescue medication MPR
Rescue medication MPR	r= -0.14970 p-value= 0.0004	r= -0.09271 p-value= 0.0303	r= -0.03454 p-value= 0.4206	r= -0.03059 p-value= 0.4756	r= 1

Rescue medication adherence refers to patients that took rescue medications at some point during the 2 years. Out of 687 asthma patients that took control medications, 546 patients also took rescue medications as needed. The correlation matrix in table 2. 8., evaluates the relation between all the hospital visit types and Rescue medication adherence. From table 2.2 it can be noted that a significant negative relationship exists between emergency department visits (r = -0.14970, p value=0.0004) and inpatient admits (r = -0.09271, p value=0.0303) with Rescue medication adherence i.e. patients with rescue medication adherence have less number of emergency department and inpatient admits.

In addition, results (attached in Appendix C) show that there's a significant strong correlation between the number of emergency department visits and the inpatient admits, between the number of Emergency visits and the 90 day readmissions, between inpatient admits and the 30 day readmissions, between inpatient admits and the 90 day readmissions, and between 30 day readmissions and the 90 day readmissions (p values <0.05). Which means that any type of hospital utilization results in a subsequent admission ore readmission to the hospital. We can observe these correlations in scatterplot attached in Appendix C.

2.5.3 T-test for hypothesis #2

In order to test hypothesis #2, evaluating if patients with more than 4 scheduled office visits for 2 years had higher levels of medication adherence, a t-test was run between the two groups (coded as 0= patients with 0 to 3 office visits, 1= patients with office visits greater than or equal to 4) with control medication adherence and Rescue medication adherence. From table 2. 9., it can be noted that variances are equal (p-value is greater than 0.05), therefore we look at the p-value for "pooled" section. Since the p-value (0.6853) for the pooled section in the table 2. 9., is greater than 0.05, there is no significant difference. Patients with more than 4 office visits do not have higher level of control adherence as measured by their MPR.

Table 2. 9. T- Test for Control medication of patients with/without more than 4 office visits.

Variable: Control medication MPR						
Office_visits	N	Method	Mean	95% CL Mean		Std Dev
0	552		82.5574	80.358	84.7569	26.3083
1	135		81.5364	77.128	85.945	25.8984
Diff (1-2)		Pooled	1.02	-39236	5.9657	26.2287
Diff (1-2)		Satterthwaite	1.021	-3.8967	5.9388	

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	685	0.41	0.6853
Satterthwaite	Unequal	206.96	0.41	0.6827
Cochran	Unequal	.	41	0.6829

Equality of Variances				
Method	Num DF	Den DF	F Value	Pr > F
Folded F	551	134	1.03	0.8399

Table 2. 10. T- Test for Rescue medication adherence for patients with and without more than 4 office visits.

Variable: Rescue medication MPR						
Office_visits	N	Method	Mean	95% CL Mean		Std Dev
0	430		61.911	58.628	65.1944	34.6405
1	116		52.0574	45.923	58.1922	33.357
Diff (1-2)		Pooled	9.8536	2.7893	16.9179	34.3732
Diff (1-2)		Satterthwaite	9.8536	2.9118	16.7954	

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	544	2.74	0.0063
Satterthwaite	Unequal	187.39	2.8	0.0056
Cochran	Unequal	.	2.8	0.0058

Equality of Variances				
Method	Num DF	Den DF	F Value	Pr > F
Folded F	429	115	1.08	0.6344

From table 2. 10, It can be noted that p-value for pooled section is 0.0063 (less than 0.05). Therefore patients with more than 4 office visits have higher levels of rescue medication adherence compared to patients with less than 4 office visits.

2.5.4 Regression analysis for hypothesis #3

Regression analysis was used in order to explore the relationship between control medication adherence, type of medical visits (including, inpatient admits, emergency department visits, 30 and 90-day readmissions), and demographics (age, gender, income). The scale of control medication adherence is if MPR is greater than 80%, patient is considered adherent; and if MPR is less than 80% patient is considered non-adherent First, the collinearity between the independent variables age, gender (coded as male=1, female=0) and income level are examined. No collinearity was found between any of the independent variables (age vs male, age vs income, and male vs income) (Attached in Appendix D).

Table 2. 11. Regression analysis results for control medication adherence, emergency visits, inpatient admits, 30 day readmissions and 90 day readmissions vs Age, gender, income.

Analysis	Regression Model	Model after backward elimination
Control adherence	control adherence=beta0+beta1*Age+beta2*Male+beta3*income+ Error	control adherence=beta0 + error
Emergency visits	Emergency Visits=beta0+beta1*Age+beta2*Male+beta3*income+ Error	Emergency visits=1.25365+0.29872*Male-0.0000116*income+ Error
Inpatient admits	InpatientAdmits=beta0+beta1*Age+beta2*Male+beta3*income+ Error	Inpatient admits=beta0+error
30 day readmissions	30dayreads=beta0+beta1*Age+beta2*Male+beta3*income+ Error	30dayreads=beta0+ Error
90 day readmissions	90dayreads=beta0+beta1*Age+beta2*Male+beta3*income+ Error	90dayreads=beta0+ error

Regression models were run for control medication adherence, emergency visits, inpatients admits, and 30 day readmissions and 90 day readmissions vs Age, gender, income. Backward elimination method was used. The table 2. 11, shows the equation for regression model before and after backward elimination. Also, from the results of regression analysis (Attached in Appendix D), it can be concluded that:

- Control medication adherence has no relationship with age, gender, and income.

  Since the p-values for age (0.5342), gender (0.2785) and median household income (0.4134) are greater than 0.05 and after backward elimination, no variable is left in the model. Therefore no relation exists between the dependent and independent variables.

- Emergency visits are influenced by gender and income.

  P-values for gender (0.0387) and median household income (0.0430) are less than 0.05, therefore emergency department visits are explained by gender and income. Therefore men and lower income patients have more emergency visits. All assumptions for residuals were satisfied.

- Inpatient admits have no relationship with age, gender, and income.

  Since the p-values for age (0.2008), gender (0.8378) and median household income (0.5305) are greater than 0.05 and after backward elimination, no variable is left in the model. Therefore no relation exists between the dependent and independent variables.

- 30 day readmissions are influenced by age and median household income.

P-values for age (0.0616), and median household income (0.0662) are closer to 0.05. Therefore older patients and lower income patients tend to have more 30 day readmissions.

- 90 day readmissions have no relationship with age, gender, and income.

  Since the p-values for age (0.7033), gender (0.1488) and median household income (0.5773) are greater than 0.05 and after backward elimination, no variable is left in the model. Therefore no relation exists between the dependent and independent variables.

2.5.5 T-test for hypothesis# 4

A T-test was performed in order to test for hypothesis #4, readmission rates of asthma patients will be significantly different from readmission rates of non-asthmatic group. Asthma patients and non-asthmatic group patients with readmissions were included in this test and labeled as asthma patient=1 and non-asthmatic group=0.

For 30 day readmissions:

Table 2. 12., shows that in all cases, the null hypothesis of equal .means and equal variances are rejected. The p-value (0.0005) <0.05 for Satterthwaite method. Therefore we can conclude that 30-day readmissions among asthma patients and non-asthmatic group are significantly different.

For 90 day readmissions:

Similarly, from table 2. 13., we note that the equality of variances (p value <0.05) is rejected. Since the equality of variances is rejected, Cochran and Satterthwaite approximations for the p-value are used here. The p-value is almost equal to 0.05. Therefore, the 90 day readmissions for the two groups are significantly different.

Table 2. 12. T-test results for 30 day readmissions among asthma patients and non-asthmatic group

Variable: 30 day readmissions					
Asthma patient	**Method**	**Mean**	**95% CL Mean**		**Std Dev**
0		0.4111	0.2204	0.6018	0.9105
1		0.0611	0.0326	0.0897	0.3807
Diff(1-2)	Pooled	0.35	0.2459	0.454	0.4728
Diff(1-2)	Satterhwaite	0.35	0.1572	0.5427	

Method	**Variances**	**DF**	**t Value**	**Pr>|t|**
Pooled	Equal	775	0.93	<.0001
Satterhwaite	Unequal	93.117	3.61	0.0005
Cochran	Unequal		3.61	0.0005

Equality of Variances				
Method	Num DF	Den DF	F Value	Pr> F
Folded F	89	686	5.72	<.0001

Table 2. 13. T-test results for 90 day readmissions among asthma patients and non-asthmatic group

Variable: 90 day readmissions					
Asthma patient	**Method**	**Mean**	**95% CL Mean**		**Std Dev**
0		0.2111	0.0725	0.3479	0.6619
1		0.0684	0.0318	0.105	0.4886
Diff(1-2)	Pooled	0.1427	0.0301	0.2553	0.4873
Diff(1-2)	Satterhwaite	0.1427	-0.00054	0.2859	

Method	**Variances**	**DF**	**t Value**	**Pr>|t|**
Pooled	Equal	775	2.49	0.013
Satterhwaite	Unequal	102.09	1.98	0.0509
Cochran	Unequal		1.98	0.0511

Equality of Variances				
Method	**Num DF**	**Den DF**	**F Value**	**Pr> F**
Folded F	89	686	1.83	<.0001

Odds ratios:

From table 2. 14 and 2. 15 it can be noted that asthma patients have lower chances of 30 day and 90 day readmissions compared to non-asthmatic group (odds of 30 day readmission is 0.117 times non-asthmatic group [OR 0.117, 95% CI (0.062, 0.218)], odds of 90 day readmissions is 0.260 times the non-asthmatic group [OR 0.260, 95% CI (0.123,0.551)]).

Table 2. 14. Odds ratio of asthma patient and non-asthmatic group for 30 day readmissions

Analysis of Maximum Likelihood Estimates					
Parameter	**DF**	**Estimate**	**Std Err**	**Wald Chi-Square**	**Pr>Chisq**
Intercept	1	-1.1285	0.2453	21.1673	<.0001
Asthma patients	1	-2.1479	0.3189	45.3776	<.0002

Odds Ratio Estimates		
Effect	**Point Estimate**	**95% Wald CL**
Asthma patients	0.117	0.218

Table 2. 15. Odds ratio of asthma patient and non-asthmatic group for 30 and 90 day readmissions

Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	Std Err	Wald Chi-Square	Pr>Chisq
Intercept	1	-1.9751	0.3218	37.5312	<.0001
Asthma patients	1	-1.3472	0.3831	12.3681	0.0004

Odds Ratio Estimates		
Effect	Point Estimate	95% Wald CL
Asthma patients	0.26	0.551

2.6 Conclusion and Discussion

The current study explored the relationship between medication adherence and hospital utilization (inpatient visit, office visit, emergency department visit, 30 day hospital readmission and 90 day readmission) among Medicaid insured asthma patients. After conducting a statistical analysis, inpatient admits (p-value= 0.0004) and visits to the emergency department rates (p-value=0.0303) of asthmatic patients were found to be significantly correlated to rescue medication adherence. Thus, patients that take their rescue medication tend to have less number of emergency visits and inpatient admits. Instinctively, this relation seems right. Asthma patients that understand their medication and use rescue medication in the event of an asthma attack tend to have lesser emergency department visits, and therefore fewer admissions to the hospital.

In addition, results showed there was a strong positive correlation between the inpatient visits and 30 day readmissions (r=0.7634, p value <0.05), between inpatient visits and 90 day readmissions (r=0.7474, p value<0.05) as the r value is closer is to 1. Moderate positive correlation between 30 day readmissions and 90 day readmissions (r=0.4633, p value<0.05). Further, from the scatterplots (attached in Appendix b) and p values (Tables 7 and 8) it was found that emergency department visits were correlated to inpatient admits and 90 day readmissions. Although lower level of control medication adherence was expected to affect all types of visits to the hospital, the results showed otherwise. The correlations between the types of hospital visits were quite expected. As the number of inpatient admits increase the number of 30 and 90 day readmissions also increase and as the number of 30 day readmissions increase, 90 day readmissions increase. This is intuitive, as patients admitted to the hospital often end up being readmitted. Previous studies reported that one in five Medicare patients discharged from an inpatient facility end up in the hospital within 30 days (Nehi, 2012). Also, a study to assess factors that increase 30 day readmissions among asthma patients found that higher frequency of previous hospital utilizations like emergency department visits and inpatient admissions have higher likelihood to 30 day readmissions (Gonzalez-Barcala et.al, 2017).

It is a known fact that patients with chronic conditions are often managed at their primary care physician's (PCP) office. However, patients might see multiple PCP for their chronic conditions (Nehi, 2012). This study hypothesized that having more than 4 office visits per year, would benefit the patient and increase their medication adherence. This number of visits was derived from the standard of care for asthma patients. The results however showed that patients with more than 4 office visits do not have higher levels of control medication adherence, a possible reason for this result, could be the patient's medical reason for the office visits (i.e., if the visit

was scheduled or unscheduled because of worsened conditions). This is a limitation of this study, since the reason for the office visit was not reflected in the insurance data. Knowing the reason for office visit would help better understand better the relationship among regular scheduled office visits and patients adherence to their prescribed control medication. Also, in case of sudden/ seasonal asthma attacks, the trip to the doctor's office would often result in rescue medication being prescribed to control asthma. This is in lieu with the result of another t-test for patients taking rescue medications which showed that patients with more than 4 office visits tend to have higher levels of rescue medication adherence.

Control medication adherence, emergency visits, inpatient admits, and 30 and 90 day readmission were checked against age, gender and income, to understand their relationship. Control medication adherence, inpatient admissions, and 90 day readmissions had r square values nearly equal to 0 and showed no relationship with age, gender or income level. Emergency visits were influenced by gender and income level i.e. men and low-income asthma patients tend to have more Emergency Department visits. Similarly, 30 day readmissions are influenced by age and median household income, i.e. older and low income patients tend to have 30 day readmissions.

Lastly, 30 day readmissions and 90 day readmissions among asthma patients and non-asthmatic group were significantly different at 5% significance level. Non-asthmatic group for this study was a mix of Medicaid insured members without asthma (might or might not have other illnesses). Although this test does not tell us much, it is interesting to see that 30 day readmissions among the two groups was significantly different. The chances of 30 day and 90 day readmissions is lower among asthma patients compare to non-asthmatic group.

Previous studies reported that adherence to control medications among asthma patients varies between 40% and 60%, with 80% and above being the threshold of good medication adherence (Menckeberg et al., 2008). Average control medication adherence for our population is 82%, with 474 out of 687 (i.e., 69%) of the patients adhering to their control medications. 283 patients (41%) had inpatient admissions and 7% of these patients were readmitted into the hospital within 30 and 90 days. The present study did not find any relationship among control medication adherence and any type of hospital visits (emergency department visits, inpatient admits, office visits, 30 and 90 day readmissions), while rescue medication adherence was related to emergency department visits and inpatient admits. Office visits did not seem to improve control medication adherence but they increased rescue medication adherence among our study population. Male and low income patients tend to have more emergency visits and older and low income patients have more 30 day readmissions.

2.6.1 Ethical considerations

IRB committee approval was taken prior to beginning the study and efforts were taken to protect confidentiality of subjects. Data have been appropriately cleaned and de-identified. Evidence for reliability and accuracy of data was validated by the data analytics team at the insurance company.

2.6.2 Study Limitations and Assumptions

Some of the limitations encountered in the study include possible human error as claims and other data used in the study is entered and handled by designated person. Demographic information such as race, ethnicity, marital status etc. and also reasons for office visits were not available. Discharge instructions given by the doctor after an inpatient admission were not available and hence it would be hard to track if a medication was discontinued or the strength of the medication was reduced due to the doctor's orders or the patient's negligence. The current study may not have external validity or generalizability for asthma patients as the study sample was small and only consisted of patients from one insurance company in the state of Louisiana. Assumptions made in the study are prescriptions filled are assumed to be prescriptions consumed and it might not actually be the case.

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CHAPTER 3: PAPER #2

"Selection Criteria for Intervention to Improve Medication Adherence for Medicaid insured Asthma Patients", proposed submission to the International Journal of Health Care Quality Assurance.

3.1 Abstract

The benefits of asthma medications have been well documented, yet poor medication adherence is often reported among asthma patients. Uncontrolled asthma is associated with a long list of events such as missed school days; reduced productivity; quality of life; social functioning; family distress; inflated healthcare costs; hospitalizations; and hospital readmissions (Baena-Cagnani et al., 2001). Medication adherence rates are as low as 50% in children and 30%-70% among adults (Bateman et al., 2008; Milgrom et al., 1996). Asthma results in hundreds of millions of dollars in healthcare costs – costs that are largely preventable. Medication non-adherence varies across diseases, individuals and across time (Sewitch, 2004), but is prevalent among asthmatic patients. Poor medication adherence leaves a larger percentage of patients vulnerable to sudden asthma attacks, hospitalizations and might even result in potential emergency department visits or hospital readmissions. In order to develop interventions and improve medication adherence, understanding reasons for non-adherence is important. This paper focuses on identifying key factors and barriers of medication non-adherence among Medicaid insured asthma patients in Louisiana and recommends potential interventions. The two types of insurance coverages (Temporary Assistance for Needy Families and Supplemental Security Income-Non Dual) were the only significant predictors of control medication adherence among the factors analyzed (with p-values =0.0001). Asthma patients with TANF and SSI- Non Dual coverages are less adherent to control medication adherence compared to other coverages. Also, control and rescue medication adherence was not significantly different among case managed and non-case managed asthma patients.

3.2 Introduction:

According to the National Health Interview Survey conducted in 2014, there are as many as 24 million people diagnosed with asthma in the United States (CDC). Asthma is a chronic illness that causes variable degrees of airflow obstruction due to inflammation of airways, increased mucus secretions, constriction of smooth muscles of bronchi and airway remodeling in the lungs. Asthma is classified into four-severity levels namely intermittent, mild persistent, moderate persistent and severe persistent asthma (NAEPP, 1997; Taitel, Allen, & Creer, 1998). Certain triggers such as irritants, allergens, viral or bacterial infections, exercise or strenuous work, seasonal changes, and a few others cause sudden asthma attacks or exacerbations among patients. Triggers for asthma symptoms vary among individuals and they often cause episodes of wheezing, breathlessness, chest tightness, low oxygen levels, shortness of breath and coughing (NAEPP, 1997). Therefore there are multiple reasons for an asthma patient to appear at emergency departments and asthma management is a priority as it results in costly hospitalizations and even death in some cases.

Although there is unanimous agreement on medications being primary tools to prevent complications and manage chronic conditions, numerous studies show that medication adherence

among chronically ill patients is only 50-60 %. Patients need to follow their medication and get refills on time to lessen the occurrence of adverse events and to increase their quality of life**.** Education/knowledge about illness, targeting high-risk populations, evaluating interventions in the home environment, and preventive treatment and relief (through medication) from the attacks are some of the known interventions to effectively keep asthma control in check (CDC, 1996). This study focuses on finding barriers/ factors affecting medication adherence among asthma patients, identifying gaps in providing care (such as case management services) and proposing effective patient selection criteria for intervention to assist in reducing healthcare costs associated with medication non-adherence**.**

3.3 Literature Review

3.3.1 Asthma in Louisiana

In Louisiana, an estimated 7.7% (270,261) adults, 18 years of age and older, suffer with asthma (CDC, 2014). Louisiana Department of Health (DHH) reported that 33 parishes have average adult asthma prevalence rate higher than 6.7% (2010 asthma prevalence rate) and 11 parishes (De Soto, E. Feliciana, Richland, Sabine, St. Bernard, St. John the Baptist, Tensas, Vernon, Washington, W. Baton Rouge, and W. Carroll) have average adult prevalence rates (2006-2010) that are higher than the 2010 asthma prevalence for the United States (8.8%). Reports indicate that one in ten (10.7%) Louisiana households with children had at least one child who was asthmatic (DHH, 2011). According to the factsheet by DHH in 2011, 22.7% of high school students have reportedly missed more than one school days due to asthma. Due to increasing prevalence of asthma among children and subsequent missed school days, a law called Louisiana ACT 145 came into effect in the year 2009, making Louisiana the 49th state in the U.S. to allow students to carry asthma medications in school. The bill was passed to eliminate the need to retrieve medications from nurse or offices at school at first signs of asthma attacks.

3.3.2 Asthma Treatment and Care

Expert Panel Reports (EPR) serving as guidelines for diagnosis and management of asthma, are developed under the National Asthma Education and Prevention Program by National Heart, Lung, and Blood Institute. Since the nature of asthma symptoms is erratic, it needs continuous assessment and changes to the patient's treatment plan. According to the latest Expert Panel Report (EPR- 3) developed in the year 2007, every person with asthma should have a written asthma action plan. Typically, an action plan is developed by the doctor and tailored for each individual patient depending upon the severity and other details of their illness. An asthma action plan is a daily treatment plan containing measures to be taken in case of asthma attacks or exacerbations, identifying need to seek doctor/emergency department visit, detailed description of long-term control treatment, and information on what medication is to be taken at what time (NAEPP, 2007). Schools, day cares, guardians, family and friends need to know of a child's asthma action plan and should be ready in case of emergencies (CDC, 2011).

Treatment goals for asthma are to control symptoms, prevent asthma attacks and reduce exacerbations. At the beginning of an asthma treatment, patients are scheduled to visit their doctors every 2 to 6 weeks and a comprehensive asthma action plan is developed to manage care. Once the asthma is controlled they can be scheduled to meet the doctors once a month to twice a

year depending on their health and signs of symptoms (NHLBI, 2014). Pulmonary function is monitored regularly among asthma patients (especially among older patients) using peak flow meters in order to avoid severe obstruction of airflow (NAEPP, 2007). Peak flow meters are small hand held devices used to determine the degree of obstruction in the airways and severity of asthma symptoms (Elana, 2011). Peak flow number shows how well a patient's lungs are working while the patient is resting. They are used in emergency departments and clinics to quickly assess patient's condition. Patients and their families are educated on usage of Peak flow meters to be used at home for efficient treatment (Self, 2005).

3.3.3 Asthma Medication

Doctors prescribe asthma medication depending on the type of symptoms some medications are used to reduce inflammations and swelling in the airways, while others are used to relax the airways, some medicines are prescribed to be taken even in the absence of symptoms to prevent any sudden deadly attacks (DHH, 2011). According to the National Asthma Education and Prevention Program, rescue and control medications are two main categories of asthma medications. (i) Rescue medication/short-term medication: Acute exacerbations of symptoms such as coughing, wheezing, chest pain etc. are treated using rescue or short acting medications. These come in three classes, short-acting beta-agonists, anticholinergics, and systemic corticosteroids. They are used for instant relief in case of sudden asthma attacks. They are also called as short-term medication. (ii)Control medication/ long-term medication: Persistent symptoms such as inflammation or bronchospasms are controlled using control medications. All asthma control medications were developed to reduce symptoms, improve asthma control, improve quality of life, prevent exacerbations, and reduce the need for emergency department usage, hospitalizations and death due to asthma attacks (NAEPP, 2007). There are 8 classes of control medications: (a) inhaled corticosteroids (ICS), (b) cromolyn sodium and nedocromil, (c) immunomodulators, (d) systemic corticosteroids, (e) leukotriene receptor antagonists (LTRAs), (f) 5-liopxygenase inhibitor, (g) long-acting beta-agonists, and (h) methylxanthines. They are also called long-term medication.

Asthma medications are available in either pill or liquid form to be taken by mouth, injections or inhalers. Inhalers are most effective and widely used hand held devices used to deliver asthma medications directly into lungs. Different types of inhalers are available for use. Some of the inhalers dispense one medication while others are used for combination therapy, meaning they contain two different medications. Metered dose inhalers (MDI), dry powder inhalers (DPI) and nebulizers are different types of inhalers used to deliver asthma medication in different ways. Metered dose inhalers are canisters containing asthma medication. When the inhaler is pushed, medication is sprayed through it and needs to be breathed in by the patient. Dry powder inhalers deliver medications in the form of dry powder. These type of medications are hard to breathe in during an asthma attack. Nebulizers are simple devices where medications are delivered through a mouthpiece or a mask. They are easier to use and are recommended in case of severe asthma, as patients can breathe normally while taking the medication (WebMD medical reference, 2015). In order to lead a normal active life, asthma patients are advised to always have their medication available and adhere to them as per their prescription.

3.3.4 Medication adherence and non-adherence:

Chronic illnesses are highly prevalent as about half of all adults in the U.S. (117 million) and approximately 40% (133 million) of the total population have one or more chronic conditions. This number is projected to increase to 157 million by the year 2020 (Lancet, 2009). 75% of healthcare costs are incurred by chronic conditions and four of the most expensive healthcare conditions are namely: heart diseases, cancer, mental disorders, and pulmonary conditions (Stanton, 2006). Majority of the patients with chronic diseases are prescribed to follow lifelong medication in order to control their conditions and avoid complications. Medication adherence is a key component. It is defined as 'the extent to which patients follow the instructions given in their prescribed treatments' (Haynes et al. 2005). Medication adherence is often studied in terms of non-adherence, as non-adherence to medication leads to health complications, financial crisis and poor disease management (Haynes, 2008; Munger et al. 2007). Absence of treatment results even after prescribing effective medications, led physicians to look into the concept of non-adherence (Rapoff, 1997). Medication non-adherence is taking less medication than prescribed, or patients not refilling their prescription after the initial fill. About 33% to 69% of medication related readmissions are due to non-adherence (Osterberg, 2005). Medication adherence is alarmingly low among patients with chronic conditions and approximately one half of these patients do not take medications as prescribed by their providers. Poor medication adherence lead to approximately 125,000 and $100-$300 billion direct and indirect costs every year in the U.S. (McCarthy, 1998; Mahoney, 2008).

In spite of a detailed asthma action plan, many patients take asthma medications only when they experience asthma symptoms or attacks and reduce or completely stop using medications during long symptomless periods. Patients can be completely adherent, completely non-adherent or have sporadic pattern of adherence. Poor medication adherence is of great concern for physicians when it comes to medication or dosage selection (Creer & Bender, 1995). A study on asthmatic patients reported a range from 30% to 70% for adherence to medication, and that adherence to regular preventive drugs are even lower, about 28% in developing countries (Bender et al., 1997; Reid et al., 2000; Pearson et al., 1999).

Non-adherence results in increased use of expensive healthcare services which end up costing more time, money and efforts (such as, emergency care, special care, primary care provider visits, more medications, hospital services etc.) than treating the original condition. It is also associated with poor health outcomes, premature deaths and hospital readmissions (Braithwaite et al., 2013). Research shows that medication non-adherence is related to more than one-third of medication related hospital visits and 40% of nursing home visits (PhRMA, 2012; APha, 2004). Therefore, it is important to assess the level of medication adherence among chronically ill patients to introduce interventions, if needed, to increase medication adherence and health outcomes. Medication adherence can be measured by:

- Subjective measurements include maintaining medication dairies, self-reporting tools, questionnaires and surveys (Elliott, 2006). Morisky's scale, is an example for widely used self-reported measure of adherence, the scale consisted of four questions, and a negative answer to any of those four questions was considered as non-adherence (George, 2007). Many such self-reported adherence scales have been developed and validated.
- Objective measures include pharmacy data, electronic measurement devices, biologic assays; measurement of testing serum, urine, saliva, and tablet counts, canister weights,

etc. Biological assays are invasive and do not give long term results, technology based measurements are ineffective if patients do not use the inhalers properly and pharmacy data assists in evaluating medication behavior of the patients and insufficient filling of prescriptions are an indicator of patients who are likely non-adherent but this data could have discrepancies (Hess, 2006).

In summary, in order to measure medication adherence, an ideal study would include both objective and subjective methods but in case of time constraints or cost related issues, objective measure alone can be calculated with consistent pharmacy claims data. This study will conduct both objective and subjective techniques to measure and understand medication non-adherence among the studied population.

3.3.5 Factors Affecting Non-adherence

Treatments are only effective when patients adhere to them. Despite the availability, proven significance in preventing complications, improving health outcomes and reducing asthma related deaths, non-adherence to medication remains a significant problem. Though numerous studies on medication non-adherence and factors affecting adherence exists in literature, there is no consistency in the reported results. A study on adherence and healthcare costs summarized literature on medication non-adherence by categorizing factors. Categories specified in previous studies are patient related factors such as demographic (age, gender, income, family size, marital status), sociocultural (medication beliefs, health literacy, side effects or threats, social standing and network) and behavioral data (mental illness, stress, substance abuse, cognitive function). Healthcare provider related factors include communication and provider-patient relations (Iuga, 2014).

A study in Korea on identifying factors that can predict medication adherence among elderly people found that education level, health-related problems, dosing frequency, satisfaction with patient counseling and explanation of medication were the main contributors to medication non-adherence (Jin et al., 2016). According to the Harris Interactive 10,000 patient's survey conducted in 2002, Among 9,412 patients that participated in the survey, 24% reported forgetfulness was the main reason for non-adherence followed by 20 % patients reported side effects, 17 % patients as high drug costs and 14% of respondents reported patient's perception of medication effectiveness (Boston Consulting Group, 2003). Number of medications were recognized as a factor for lower levels of adherence, as requirement of taking multiple medications at variable intervals in a day is associated with non-adherence among older patients (Ickovics & Meisier, 1997; Bedell, 2000; Claxton, Cramer, & Pierce, 2001). A cross-sectional survey of 24,017 adults with asthma, hypertension, diabetes, hyperlipidemia, osteoporosis, or depression found that 67% agreed that they forget to take medications, 37% of respondents ran out of medications and 23% reported they were careless about taking medications sometimes (Gadkari & McHorney, 2010). Adherence to pulmonary medication was found to be as low as 30% among adolescents. (Dekker, 1993).

Evidence shows that reasons for medication non-adherence among asthma patients are complex and multifold. Factors found in the literature are listed below.

3.3.6 Patient Related Factors

Age and gender: Many studies have found that age is risk factor for medication non-adherence and most of them agreed that older age is associated to non-adherent behavior (Jonasson, 1999; Strunk, 2002). Although some papers found that females were more non-adherent to medication than males, Jonasson and Strunk found no such difference in their research.

Race and ethnicity: A study on examining differences between white patients and African-American patients with asthma found that African-American patients showed poorer medication adherence compared to white patients. Additionally, white females were found to be non-adherent compared to white males (Willliams, 2007).

Socioeconomic: A study on factors affecting adherence in asthmatic children evaluated preventive medication use among fifty one children for 1 month using electronic monitoring device and found that child's age, family income and parent's level of education did not affect medication adherence, but parental stress, forgetting medication or child's reaction to medication were reported by parents as the main factors. By comparing the actual usage of medication and parent's perspective from a questionnaire, parents were found to report overestimated medication use (Burgess, Sly et al. 2008).

Sociocultural: A cohort study of elderly asthma patients found that negative attitude towards inhaled controller medications, family dysfunction, psychological adjustment, and depression are risk factors for poorer adherence (Krauskopf, 2013). An 18-month study on fill patterns of underserved children with asthma revealed that filling of controller medication was lower than prescribed, while rescue medications were filled abundantly. Side effects from medication, low asthma and medication knowledge was found to be the barrier in this study (Bollinger, 2013).

Disease related**:** A study found that adherence to asthma medication was affected by comorbidity, adverse reactions to medications disease severity (Charach, 2008), and long symptom free period.

Medication related: According to a study on patient preferences for enhancing adherence, too many pills, side effects, lack of information on the benefits of medication, physician and patient relationship were reported as a few factors to be tackled (Cascade, 2010). Other factors include children's understanding of taking medication (Charach, 2008), regimen complexity, and frequent doses (Viswanathan, 2012; Morisky, 2008; Battistella, 2016).

Other factors include: lack of transportation, physician and patient relationship (Martin, 2005), healthcare locations, and disruptions in lifestyle.

The literature on asthma studies shows that the factors influencing medication adherence are broad and a more thorough understanding is necessary to address this issue. Most studies in the past have used correlation or regression analysis to find associations between medication adherence and a variety of factors or predictors appropriate to the population being examined (Rapoff, 2010). This paper also used correlation and multiple logistic regression analysis to examine factors affecting medication non-adherence among asthma patients.

3.3.7 Current Methods to Improve Medication Adherence

Numerous interventions were developed over the years to improve patient's adherence to medication such as dosage modification, reminder systems, adherence packaging, drug education, side effect management, self-monitoring (Chen, 2010), and intervention through pharmacists, physicians or nurses etc. Some of the current interventions methods are discussed below:

1. Educating patients to promote medication adherence by healthcare providers: Explaining the importance and discussing any reluctance to take medications has been considered as an educational intervention and it is quite successful in most chronic illnesses (Ratanawongsa, 2013). Attempts to improve adherence through written education alone turned out to be unfruitful therefore, Nicholoas-English, DiMatteo and Cascade E, in their respective studies suggested to embrace patient centered activities that empower them (Nicholas-Green, 2000; DiMatteo,M.R, 2004; Cascade, 2009). These patient-centered activities could be a combination of written, verbal and other approaches that educate patients on their overall adherence.
2. Intervention through monitoring patient activity: A randomized clinical study on Internet-based monitoring of asthma among 300 patients was conducted in the year 2005. Patients were randomly assigned to three groups monitoring by specialist, monitoring by general practitioner, and home telemonitoring through Internet (Intervention group). A 6 month long study concluded that intervention group of home telemonitoring through internet reported lesser asthma symptoms during the study period than the other two groups and were found to have better pulmonary function and quality of life (Rasmussen et al., 2005). Few other studies reported similar results for Internet based interactive methods among asthma patients (Jan et al., 2007; Guendelman et al., 2002).
3. Health coaching: Heath coaches are being used in primary care settings to help patients cope with one or multiple chronic diseases. Medication adherence counselling and collaborative communication are facilitated by these trained professionals in clinical settings to improve health outcomes (Thom et al., 2015). A study on impact of health coaching on medication adherence among patients with three poorly controlled illnesses, type 2 diabetes, hypertension and or hyperlipidemia for 12 months found that health coaching significantly increased medication adherence (10%).
4. Packaging interventions: Blister packs, unit-packaging, pill boxes, unit of dose packaging and monitored dosage systems are some of the examples of packaging interventions currently in use to improve medication adherence. Single use packaging of medications by a professional is called a blister pack, these are generally recommended for adults with multiple chronic conditions (Mahtani, 2011).
5. Case or illness management for chronic illnesses: Case management services emerged in 1990s as a strategy to manage and coordinate care using nurses and other resources to impart knowledge on self-management skills, reduce readmissions, improve quality, discharge planning, consistency and administer cost effective care for chronic illnesses (Rosenthal, 2008; Joo, 2014; Berg, 2015).

Although the definition of case management is ambiguous, the goal for all the case management services stand the same. Licensed professionals are appointed as case managers to high risk or patients in need to assistance. Generally, physician visit reminders, follow up phone calls, health assessment, and planning depending upon the requirements of the client. These services are designed to provide safety, efficiency and patient centeredness.

A study by Boyd showed significant reduction in hospitalization rates after 1 year of case management intervention compared to usual care group of patients (Boyd, 1996). Woohyun et al, focused on using mobile computing, medical sensors and communication technology for supportive communication between adolescents with asthma and case managers, the findings of this study were consistent with literature and has identified the usefulness of interaction between clinician and patient, successful information exchange and patient centeredness of case management services (Yoo, 2015).

3.3.8 Strategies to improve medication adherence

Medication adherence is a particularly important health-related behavior for many people faced with complex therapeutic regimens and/or chronic illnesses. A combination of several simple strategies, such as more thorough patient instructions, reminders, pill containers, self-management plans and phone follow-up, have been found to improve adherence and treatment outcomes (De Geest et al. 2006, Haynes et al. 2008). Patient education alone has not been found to be sufficient to change and sustain adherence to medication (Sabate 2003). Interventions that focus on the whole person and the therapeutic relationship are needed to improve health outcomes (Sabate 2003, Maizes et al. 2009).

Many of the interventions though effective are undesirable in many cases as they are expensive, have low external validity, labor intensive, complicated to carry out, not extremely effective and can be carried out for small durations only (Bender, 2015). Interventions should be tailor made for the target population and disease condition as a single intervention cannot be expected to play an effective role across all patients, establishments and conditions (Burkhart & Sabate, 2003). Improving medication adherence might be the best investment for tackling chronic conditions, enhances patient safety and health system effectiveness, reduces poor outcomes and associated health care costs (Burkhart & Sabate, 2003).

3.3.9 Research gaps

Failure to take asthma medication as prescribed has many consequences, few of which include poor health, increased healthcare costs, and increased service utilizations. Even though there are established guidelines for management of asthma such as EPR-3, GINA etc. adherence to asthma medications have not significantly improved over the years. Services and interventions such as telemonitoring, asthma health education, self –management education, and case management services etc. have been set up for improved healthcare outcomes. Case management services have been established in the 1990s and reduce the gap between patient and healthcare services. A physician might not be able to dedicate more than his scheduled time for the doubts and concerns of every patient, due to their busy schedule. Therefore, nurses, healthcare officials and other trained resources as case managers help bridge the gap between patient and healthcare services,

encourages self-management of their illnesses, address their concerns and be a continual member in their healthcare journey.

Understanding factors resulting in medication non-adherence is important to improve medication adherence behavior in patients and in turn reduce the readmission rates of asthma patients. Large body of investigations on this topic are available but very few studies attempted to determine the influence of case management services on medication adherence. Most studies focus on its effect on reducing hospitalizations and readmissions. Most of the research concerning medication adherence in asthma is covered in healthcare journals and revolves around finding the factors only. Therefore, there is a clear gap in the knowledge of the role of case management services in improving medication adherence behavior for asthma patients.

3.4 Materials and methodology

3.4.1 Objective of the study

In order to develop interventions and improve medication adherence, understanding reasons for non-adherence is important. The objective of this study is to identify key factors and barriers of medication non-adherence among Medicaid insured asthma patients and recommends potential interventions. An additional objective is to propose effective patient selection criteria for intervention that will improve medication adherence rates.

3.4.2 Subjects

The study population includes Medicaid asthma patients, insured by Insurance company from January 2015 to December 2016 with maximum of 45 days of enrollment gap from the insurance, have had taken prescribed asthma controller medication during the study period (January 2015 to December 2016), and have had one or more hospital claims (Inpatient stay) with primary or secondary diagnosis of asthma are the subjects in the study.

3.4.2.1 Participant inclusion criteria

- Patients with at least one refill of asthma medication and at least one or more hospital claims of primary or secondary diagnosis of asthma during the study period will be included.
- Patients with a maximum of 45-day enrollment gap with the insurance are considered.

3.4.2.2 Participant exclusion criteria

- Patients with interrupted claims data history (<6 months) during the study period.
- Medical claim that is not related to asthma treatment (such as an accident, sprain etc.).
- Pharmacy claim during the study period for any reason other than asthma medication.
- Patient that discontinued insurance with the insurance company during the study period.
- Missing invalid data on claims and demographics.

3.4.3 Dependent variables

The dependent variable for this study is Medication adherence and the Medication Possession ratio (MPR) will be used to measure medication adherence in this paper. Following is the formula of MPR.

$$\text{MPR} = \frac{\text{Total number of days covered}}{(\text{Number of days in measurement period}) + \text{last fills supply}} \text{ x } 100$$

1. To calculate the numerator, the study period was determined (2 years for this study) and all the days supply of asthma medication obtained from claims data was summed to get total number of days covered.
2. The total number of days covered were then divided by the number of days in the study period plus the last fills days supply and multiplied by 100 to obtain MPR for one patient.
3. If the number was greater than 80% Patient was considered adherent and lesser than 80% was considered non-adherent.

3.4.4 Independent variables

The independent variables include patients' age, gender, income level(socioeconomic indicator by zip codes), number of inpatient visits, number of ED visits, number of 30 day and 90 day readmissions to a facility, type of insurance, and enrollment in case management services.

3.4.5 Selection Criteria for Case management

Effect of case management on medication adherence behavior is an integral part of this study. Information on the selection criteria for patients to be case managed, procedure that follows, the role and interaction of case managers with members was documented. Risk utilization reports consisting of details on frequency of resource utilization, unit cost, and time to event are the main triggers for selecting potential patients that need case management. Once the patients are identified they are referred for case management and are contacted by the company for approval on being case managed.

3.4.6 Data Source:

Data for this study was obtained from software databases namely Microstrategy and EDW data warehouse used by the insurance provider company. The data comprises of patient information, medical claims, outpatient claims, and pharmacy claims. Since the study population only consists of asthma patient's asthma ICD, procedure and medication codes were used to identify asthma patients from all the members in the insurance plan.

1. ICD 9 (493.XX) and ICD 10 (J45.XX) codes for asthma. Codes used in the study are attached as Appendix A.

2. Procedure codes (Attached in Appendix F) of most commonly used resources by asthma patients. E.g.: Code 94010 for spirometry, including graphic record, expiratory flow rate measurements. This procedure is commonly used to determine the pulmonary function among asthma patients. A list of such most common procedures for asthma patients were created to identify population that used asthma services.

3. Complete list of asthma medication available in the HEDIS 2015 asthma medication list is the third component used in obtaining asthma population. Each drug in the HEDIS medication list has a NDC (National Drug Identifier) number. NDC code is a 10 digit, 3 segment unique identifier for each medication. Labeler, product and trade package are the 3 segments of the identifier number. Medications of drug categories namely short-acting beta agonists, oral corticosteroids/systemic corticosteroids, inhaled corticosteroids, combination medications, long-acting beta agonists, leukotriene receptor agonists, immunomodulators, cromolyn sodium, nedocromil, and methylxanthines were part of the list and were used to determine the population taking asthma medications. Asthma medication list by HEDIS is attached as APPENDIX G of this paper.

The combination of all the above three steps that is ICD codes, procedure codes and asthma medication list are used to identify asthma patients/members in the insurance plan or have undergone any special procedures or taken medication related to asthma.

3.4.7 Data collection:

(i). Hospital data was collected for demographic information such as age, gender, Zip codes (indicator of socioeconomic standing of the member), office visits, ED visits, inpatient stay, and primary care physician. (ii). Economic data such as median household income was not available for the study. However, this study used the economic indicator data by zip codes provided by the United States Census Bureau to report median household income. (iii). Medical claims data was collected to obtain information such as date, place, and type of service, procedure performed, cost charged and covered per service. (iv). Pharmacy records helped understand the medication history. It included the following: Name of the medication, day of prescription fills, number of refill, dosages, medication counts and, duration of medication/ day's supply. (v). Insurance information: patients enrolled in case management or any other disease management services, insurance eligibility for the study period etc. (vi). Interviews with insurance professionals were conducted to get an idea of types of insurances offered, eligibility criteria for it, and eligibility criteria to enroll in case management services. (vii). Group interviews were conducted with the Chief medical affairs director, case managers, and pharmacy officials for clear understanding on the working techniques in the insurance company. (viii). Telephone interviews were to be conducted for a random sample of 30-case managed members and 30-non case managed members originally, but only 12 case managed and 15 non case managed patients participated in the interviews. The Interview consists of 20 questions related to the member, illness (asthma), physician, and medication related. The interview procedure and questions are attached in the appendix A. Each typical phone call lasted 10 minutes.

3.4.8 Hypothesis testing

- H1: Levels of control medication adherence for asthma patients will differ by
    - Age, gender, number of inpatient visits, number of ED visits, number of 30 day readmissions to a facility, type of insurance eligibility, and number of medications will affect prescription adherence.

  H2: The insurance company offers several services to help asthmatic patients manage their illness at their home, such as case management services. Patients who receive these services will have higher levels of prescription adherence. Levels of prescription

adherence for asthma patients will differ among Case Management and non-asthmatic group.

3.4.9 Data Analysis:

Descriptive statistics was conducted on the sample to analyze characteristics of the data. (i) To address H1a Multivariate logistic regression model was built by backward elimination method to determine the association of variables of interest such as age, gender, income level, type of insurance, enrollment in case management services, number of ED visits, number of inpatient visits, number of 30 day readmissions to a facility with control medication adherence for the asthma population. (ii) To address H2 a t-test was performed to see if case managed patients have higher levels of prescription adherence. (iii) Telephone interview results were analyzed to identify objective measure of medication adherence and point out barriers to medication adherence with respect to the study population. All the analysis required in the study was conducted using SAS.

3.5 Results

3.5.1 Sample description

Patient population for this study consists of 687 asthma patients that fulfilled the inclusion criteria. Of these 687 patients 41 (6%) patients are case managed by the insurance company. A summary of the descriptive statistics of the study population is shown in the table 2. 16., below. The average age was 20 years, with the youngest patient being 1 year old and the oldest being 65 years old. Most patients (65%, 449) are considered minors, under the age of 18. 384 (56%) of the patients were females, while 303 (44%) were male. According to the 2016 U.S Census bureau income statistics, 75% (517) of the households received $25,000 to $50,000 approximately, per year.

Table 2. 16. Patient demographics of asthma patients (n=687).

Variable	Number (n)	Percent (%)	Cumulative Frequency	Cumulative Percent
Age				
0-18 years	449	65.36	449	65.36
18-29 years	49	7.13	498	72.49
30-39 years	64	9.32	562	81.8
40-49 years	52	7.57	614	89.37
50-59 years	58	8.44	672	97.82
60-69 years	15	2.18	687	100
Gender				
Female	384	55.9	384	55.9
Male	303	44.1	687	100
Income Level				
Less than 25K	35	5.09	35	5.09
Between 25K and 50K	482	70.16	517	75.25

Variable (Cont'd)	Number (n) (Cont'd)	Percent (%) (Cont'd)	Cumulative Frequency (Cont'd)	Cumulative Percent (Cont'd)
Between 51K and 75K	165	24.02	682	99.27
Between 76K and 100K	5	0.73	687	100
Insurance coverage				
Behavioral Health	7	1.02	7	1.02
CHIP	2	0.29	9	1.31
Foster Care	17	2.47	26	3.78
Medicaid Expansion	153	22.27	179	26.06
SSI Non-Dual	87	12.66	266	38.72
TANF	421	61.28	687	100

3.5.2 Medication adherence:

Medication adherence was measured using variable Medication possession ratio for control medication and rescue medications separately. MPR for rescue adherence and control adherence are shown in the table 2. 17. below. All MPR values were truncated and do not exceed 100 %. On an average, asthma patients (n=687) showed 82.3% (SD=26.2) control medication adherence. 546 out of 687 patients took rescue medication during the study period and showed 60% (SD=34.6) rescue medication adherence.

Table 2. 17. MPR for Control and Rescue medications.

Variables	MPR for control adherence (n=687)	Rescue medication MPR (n=546)
Mean	82.36	59.82
Standard Error	1	1.48
Median	100	60.06
Standard Deviation	26.21	34.58
Range	91.26	97.42
Minimum	8.74	2.58
Maximum	100	100
Total number of claims	56579	32660
Number of patients	687	546
Largest	100	100
Smallest	8.74	2.58
Confidence Level(95.0%)	1.96	2.91

The study population were covered with one of the following type of coverages during the study period: Temporary assistance for needy families (TANF), Medicaid Expansion, Supplemental security income Non-dual (SSI Non-Dual), Foster care. Eligibility criteria for each of the coverages is different and all of them provide low-cost healthcare coverage to Americans falling

under one or more of the following criteria: people with low income, children, foster care, families, pregnant women, mental health and substance use disorder, elderly or people with disabilities. Table 2. 18., shows that 279 members out of the total asthma patients were covered under TANF are control medication adherent and 142 members do not take their medication as prescribed. Out of 87 SSI non dual covered patients, 47 are control medication adherent and 40 are non-adherent to control medication.

Table 2. 18. MPR for Control and Rescue medication depending on the type of insurance.

Coverage	Control medication MPR(less than 80)	Control Medication MPR (greater than 80)
TANF	142	279
SSI non-dual	40	47
Medicaid expansion	28	125
Foster care	2	15
CHIP	0	2
Behavioral Health	1	6
Total	213	474

3.5.3 Multivariate logistic regression for hypothesis #1

Factors associated with control medication adherence were analyzed using backward selection in multivariate logistic regression. In step 0: age, gender, income level, number of inpatient admits, number of emergency department visits, number of 30 and 90 day readmissions, case management status, and type of insurance coverage (i.e., Temporary assistance for needy families (TANF), Medicaid Expansion, Supplemental security income Non-dual (SSI Non-Dual), Foster care) were entered into the model. After performing multivariate logistic regression the following variables were removed from the model (Table 2. 19.).

Table 2. 19. Summary of effects removed in backward elimination

Summary of Backward Elimination					
Step	**Effect Removed**	**DF**	**Number In**	**Wald Chi-Square**	**Pr>ChiSq**
1	Emergency Department	1	11	0.0002	0.9901
1	Case managed	1	10	0.0029	0.9568
1	Inpatient admits	1	9	0.0063	0.9368
1	Foster Care	1	8	0.2284	0.6327
1	Medicaid Expansion	1	7	0.1698	0.6803
1	90 day readmissions	1	6	0.3788	0.5382
1	Median Household Income	1	5	0.4516	0.5016

From table 2. 20, it is clear that two types of insurance coverage TANF and SSI-nondual (p-values=<0.0001) are significant at 0.05 level. Also even though age, male and 30-day readmissions were not significant at 0.05 level, they were still allowed into the model since their

coefficients' directions are consistent with literature (i.e. females are more adherent to medication than males, older people are less adherent than younger population). Model fit statistics for the final model is shown in Table 2. 21.

Table 2. 20. Analysis of maximum likelihood.

Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr>ChiSq
Intercept	1	2.0672	0.3426	36.4064	<.0001
Age	1	-0.0121	0.00678	3.1699	<.0001
Male	1	-0.2456	0.1813	1.8351	0.075
30 day readmissions	1	0.3888	0.287	1.8352	0.1755
TANF	1	-1.1399	0.2869	15.7895	<.0001
SSI-Non Dual	1	-1.5228	0.3026	25.3192	<.0001

Table 2. 21. Model fit statistics

Model Fit Statistics		
Criterion	Intercept Only	Intercept and Covariates
AIC	852.692	829.264
SC	857.225	856.478
(-2 Log L)	850.692	817.284

The equation for the final model is:

Log (odds of control medication adherence) = 2.0672-0.0121*age-0.2456*male+0.3888*30 day readmissions-1.1399*TANF-1.5228*SSI-nondual

Table 2. 22. Odds ratio for multivariate logistic regression for asthma patients (n=687).

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
Age	0.988	0.975	1.001
Male	0.782	0.548	1.116
30 day readmissions	1.475	0.841	2.589
TANF	0.32	0.182	0.561
SSI-Non Dual	0.218	0.121	0.395

From Table 2. 22.

(i) It can be seen that patients with TANF and SSI Non-dual coverages tend to be less adherent to control medication adherence than other coverages (odds of TANF being adherent is 0.320 times and SSI non dual is 0.218 times lesser than other insurance types and they are both significant at 0.05 level).

(ii) Older patients are less adherent to medication than younger patients (Odds for an older patient being adherent is 0.988 times less the odds of younger patient [OR 0.988, 95% CI (0.975-1.001)]) this result is not significant at 0.05 level.

(iii) Men are less adherent to control medication (Odds of male being adherent is 0.782 times less than female being adherent) this result is not significant at 0.05 level.

(iv) Patients with 30-day readmissions have higher control medication adherence compared to patients without readmissions (Odds for patients with 30-day readmissions being adherent are 1.475 times higher than the odds of patients without 30-day readmissions) this result is not significant at 0.05 level.

Table 2. 22. Testing of global null hypothesis for the multivariate logistic regression analysis.

Testing Global Null Hypothesis: BETA=0			
Test	**Chi-Square**	**DF**	**Pr>ChiSq**
Likelihood	33.4084	5	<.0001
Score	31.6526	5	<.0001
Wald	29.7308	5	<.0001

The overall logistic regression model was highly significant at the 5% significance level as indicated by the likelihood ratio, Wald and score tests of the global null hypothesis i.e., the model parameters are significant (Table 2. 22).

Following is a table of Summary for the factors that were retained in the regression model after backward elimination.

Table 2. 23. Summary for multiple logistic regression.

Factors	Control Medication	Odds Ratio Results
Age	Not significant	[OR=0.988, 95% CI (0.975,1.001)]
Gender	Not significant	[OR=0.782, 95% CI (0.548,1.116)]
30 day Readmissions	Not significant	[OR=1.475, 95% CI (0.841, 2.589)]
TANF	Significant	[OR=0.320, 95% CI (0.182,0.561)]
SSI-Non Dual	Significant	[OR=0.218, 95% CI (0.121, 0.395)]

3.5.4 T- Test case managed and non-case managed adherence for hypothesis #2

In order to address H2, exploring if both control and rescue medication, will differ among case managed and non-cased managed patients, a t test was performed.

First part in table 2. 24, displays the mean and the standard deviation, and confidence interval of the means of control medication adherence depending on whether the patient is a case managed or not. Table 2. 24, shows that the null hypothesis of equal means and equal variance is not rejected since the p-value is greater than 0.05 (p=0.1655). It can be concluded that control medication adherence will not differ among case managed and non-case managed patients (p-value=0.1310, is greater than 0.05 significance level for pooled).

Table 2. 24. T-test for control medication adherence among (1=case managed and 0= non-case managed asthma patients)

Variable: Control medication MPR						
Case managed	N	Method	Mean	95% CL Mean		Std Dev
0	68		81.6244	75.5699	87.6789	25.0131
1	41		88.6634	82.2274	95.0995	20.3905
Diff(1-2)		Pooled	-7.039	-16.2081	2.1301	23.3922
Diff(1-2)		Satterhwaite	-7.039	-15.767	1.689	

Method	Variances	DF	t Value	Pr>|t|
Pooled	Equal	107	-1.52	0.131
Satterhwaite	Unequal	97.564	-1.6	0.1127
Cochran	Unequal	.	-1.6	0.1159

Equality of Variances				
Method	Num DF	Den DF	F Value	Pr> F
Folded F	67	40	1.5	0.1655

From table 2. 25. below, since p-value for the test of equality of variances (p-value=0.8936) is greater than 0.05, the variances are equal and therefore we look at the p-value for pooled section. It is 0.5424 (greater than 0.05). Therefore, adherence to rescue medication does not seem to differ among case managed and non-case managed patients.

Table 2. 25. T-test for Rescue medication adherence (1=case managed and 0= non-case managed asthma patients)

Variable: Rescue medication MPR						
Case managed	N	Method	Mean	95% CL Mean		Std Dev
0	41		64.6391	54.3862	74.892	32.4831
1	35		60.0193	48.6274	71.4112	33.1631
Diff(1-2)		Pooled	4.6198	-10.4195	19.6591	32.7973
Diff(1-2)		Satterhwaite	4.6198	-10.4526	19.6922	

Method	Variances	DF	t Value	Pr>|t|
Pooled	Equal	74	0.61	0.5424
Satterhwaite	Unequal	71.648	0.61	0.5431
Cochran	Unequal	.	0.61	0.545

Equality of Variances				
Method	Num DF	Den DF	F Value	Pr> F
Folded F	34	40	1.04	0.8936

3.5.5 Telephone interview:

Out of the entire asthma population for the study (n=687), 41 patients are case managed. When contacted, only 4 of 41 case managed patients participated in the interview. Therefore, case managed asthma patients outside our main study population (n=687) were also contacted for the telephone interview. A total of 27 asthma patients (15 non-case managed and 12 case managed patients) participated in the telephone interview. Demographic, socioeconomic and clinical data of these patients, obtained from the interview questions are displayed in the table 2. 26. below. Mean age of this population was 22 years. There were equal number of African American and Caucasian patients in both case managed (6 Caucasian, 6 African American) and non-case managed groups (7 Caucasian, 7 African American and 1 not specified). Students were in majority among the two groups. About 75% patients in both groups were single and had comorbidities (chronic illnesses other than asthma). More than 80% patients had a primary care physician (PCP).

Table 2. 26. Interview population (15 non case managed and 12 case managed)

Variables	**Non case managed (n=15)**	**Case managed (n=12)**
Age (Mean)	24 years	22 years
Gender		
Male	3 (20%)	7 (58%)
Female	12 (80%)	5 (42%)
Asthma severity		
Mild	7 (46.6%)	5 (41.6%)
Intermittent	3 (20%)	4 (33.3%)
Severe	5 (33.3%)	3 (25%)
Ethnicity		
African American	7 (46.6%)	6 (50%)
Caucasian	7 (46.6%)	6 (50%)
Will not specify	1 (6.6%)	0
Employment status		
Unemployed	4 (26.6%)	4 (33.3%)
Employed	3 (20%)	0
Student	6 (40%)	7 (58%)
Retired	1 (6.6%)	1 (8.3%)
Does not apply	1 (6.6%)	0
Education		
Elementary School	4 (26.6%)	4 (33.3%)
Middle school	2 (13.3%)	2 (16.6%)
High School Graduate	3 (20%)	2 (16.6%)
College Graduate	3 (20%)	2 (16.6%)
Drop out	2 (13.3%)	0
Does not apply	1 (6.6%)	0

Variables (Cont'd)	Non case managed (n=15) (Cont'd)	Case managed (n=12) (Cont'd)
No answer	0	2 (16.6%)
Marital status		
Single	12 (80%)	9 (75%)
Married	2 (13.3%)	1 (8.3%)
Separated	0	1 (8.3%)
Divorced	1 (6.6%)	0
Widowed	0	1 (8.3%)
Members in the house		
4 or less	9 (60%)	8 (66.6%)
5 or more	6 (40%)	4 (33.3%)
Comorbidities		
Yes	11 (73.3%)	9 (75%)
No	4 (26.6%)	2 (16.6%)
PCP		
Yes	13 (86.6%)	10 (83.3%)
No	2 (13.3%)	2 (16.6%)

Following table 2. 27. Shows the yes and no responses of case managed and non-case managed asthma patients for questions regarding their medications, physician and themselves.

Table 2. 27. Interview questions and responses among non-case managed and case managed asthma patients (n=27).

Interview questions	Non case managed (n=15)		Case managed (n=12)	
	Yes	No	Yes	No
Currently taking medications	11 (73.3%)	4 (26.6%)	10 (83.3%)	2 (16.6%)
Control medication even without symptoms	6 (40%)	9 (60%)	5 (41.6%)	7 (58%)
Physician related questions				
Taught you to recognize early signs of symptoms	12 (80%)	3 (20%)	10 (83.3%)	2 (16.6%)
Have an asthma action plan	7 (46.6%)	8 (53.3%)	9 (75%)	3 (25%)
Showed you how to use an inhaler	14 (93.3%)	1 (6.6%)	12 (100%)	0
Patient related questions				
Take medications even during symptomless period	10 (66.6%)	5 (33.3%)	6 (50%)	6 (50%)
Well informed about asthma medication	12 (80%)	3 (20%)	11 (91.6%)	1 (8.3%)
Side effects with medication	2 (13.3%)	13 (86.6%)	2 (16.6%)	10 (83.3%)
Medications not working	5 (33.3%)	10 (66.6%)	1 (8.3%)	11 (91.6%)
Do not need preventive treatment	6 (40%)	9 (60%)	4 (33.3%)	8 (66.6%)

Forgot to refill	3 (20%)	12 (80%)	5 (41.6%)	7 (58%)
See different PCP every visit	5 (33.3%)	10 (66.6%)	1 (8.3%)	11 (91.6%)
Too many medicines	2 (13.3%)	13 (86.6%)	2 (16.6%)	10 (83.3%)
Skipped medication due to cost	4 (26.6%)	11 (73.3%)	3 (25%)	9 (75%)
Lack of transportation	2 (13.3%)	13 (86.6%)	1 (8.3%)	11 (91.6%)
Anybody in the house smoke or drink	1 (6.6%)	14 (93.3%)	5 (41.6%)	7 (58%)
Family support	14 (93.3%)	1 (6.6%)	12 (100%)	0

Although responses for most of the questions in table 2. 27, above look similar among the two groups. By inspection, from table 2. 28. below, the average MPR for control and rescue medication adherence seem a little higher among non-case managed compared to case managed asthma patients of the interview population.

Table 2. 28. Average control and rescue medication adherence (15 non case managed and 12 case managed)

Variable	**Non case managed**	**Case managed**
Average Control medication adherence	30.4	22.83
Average Rescue medication adherence	57.73	16.92

A t-test was performed for three questions from the phone interview list, including 1) Do you have an asthma action plan?, 2) Do you forget to refill your control medication?, and 3) Do you see different Primary care physician every visit?. The purpose of this test was to find any significant difference among the two groups (case managed and non-case managed). Significant difference was found for the third question- do you see different PCP every visit. Results showed a significant difference among the responses of case managed and non-case managed asthma patients (p-value 0.053). Results of the t-test are attached in Appendix E.

3.6 Discussion

From the literature review, it can be concluded that medication adherence is of utmost importance among patients with chronic illness. Although several guidelines have been laid out, patients with chronic illnesses tend to derail from taking medications as prescribed. Average adherence to control medication (measured by electronic devices) was reported to be 50% to 77% by previous studies (Coutts et.al, 1992; Milgrom et.al, 1996; Burgess, 2011). This study found an average control medication adherence of 82.3% (SD=26.2), while rescue medication adherence was only 59% (SD=34.6). Rescue medications are only used as needed i.e., in case of asthma attacks for quick relief. Therefore, focus was placed on control medication adherence. This study identified five variables that may help explain control medication adherence among

asthma patients. Two demographic variables, age and gender, one clinical variable, 30 day readmissions to the hospital, and two types of Medicaid insurance (TANF and SSI Non dual) remained in the model. Furthermore, only the two types of insurance coverage, TANF (p-value =<0.0001) and SSI- non dual (p-value =<0.0001) were significant at 0.05 level.

Age and gender are the two demographic factors that have been studied widely in the literature in association with medication adherence. Age has been found to affect adherence by some researchers (Jonasson, 1999; Strunk, 2002). Strunk et al. found that for every 2 year increase in age a child was more likely to be non-adherent to asthma medication. Similar results were found by another study, adolescents might be at increased risk of non-adherence (Kyngas, 1999). Conversely, some studies reported that older adults showed better adherence than younger adults (Tebbi, 1993). In the present study, adherence among older patients although not significant, found to be less than younger patients [OR=0.988, 95% CI (0.975-1.001)]. The difference in age might be a risk factor for several reasons such as forgetfulness, unwillingness to take medication daily, and comorbidities, etc. Number of female asthma patients (n=384) were slightly higher than males (n=303) in the present study females were more adherent than males. A study by Lindberg et. al., on medication compliance among asthma patients found similar results i.e., age and female gender were associated with medication taking behavior (Lindberg, Ekstrom, Moller, & Ahlner, 2001).

Medication adherence has been reported as a predictor of 30-day hospital readmissions in many studies (Rosen et al., 2017). Therefore, even though non-significant, 30 day readmissions was considered in the study since it was consistent with the literature with odds ratio [OR=1.475, 95% CI (0.841-2.589)]. Patients can be admitted or readmitted to the hospital for multiple reasons ranging from asthma attack, exacerbation or decline in health. These patients are most definitely given asthma medications upon discharge from the hospital facility. This could be the reason behind association between patients with 30-day readmissions and medication adherence.

Insurance coverage: TANF and SSI non dual were two types of coverage found to be significant predictors of control medication adherence. People with TANF and SSI non dual are less adherent to control medication compared to other types of insurance coverages. TANF stands for temporary assistance for needy families and SSI non dual stands for supplemental security income (SSI) non dual. Although TANF supports families with one or more members with disability, eligibility for TANF is determined by income (Nadel, 2003; Ziliak, 2004). Majority of the asthma study population was covered under TANF (n=421) and SSI non dual coverages (n=87). A study to predict risk factors for cost-related medication non-adherence among older diabetes reported that factors such as out-of-pocket payments for medications and insurance status contribute to higher risk of medication non-adherence (Zhang et. al, 2014).

Comparing the medication adherence for case and non-case managed patient, results showed that there was 95% chances that control medication adherence for non-case managed patient would fall between 80.18 and 84.26. Similarly, there was 95% chances that control medication adherence for case managed patient would fall between 77.28 and 84.51(Tables 8.1 and 8.2). Since the upper bound for both groups could be greater than or equal to 80 (the threshold for medication adherence), these patients will be considered adherent. The t-test concluded that control medication adherence does not significantly differ among case managed and non- case managed patients. Similar results for rescue medication adherence were documented from this study. Although the study hypothesized that case managed population would have better

medication adherence than non-case managed asthma patients, the results looked otherwise. One possible reason could be a small sample size and proportion of patient's case managed versus non case managed. The difference in number of case managed (n=41) and number of non-case managed patients for control medication (n=646), and difference in the number of case managed (n=35) and non-case managed asthma patients (n=511) for patients taking rescue medications.

The telephone interviews were conducted to collect responses on various questions related to demographics, socioeconomic status, medications, physicians and specific questions pointing at factors for non-adherence to asthma medications. For the question, "Did you take asthma medication without suffering an attack?" 6 out of 15 (40%) of the non-case managed and 5 out of 12 (41.6%) of the non-case managed patients reported yes and a similar question (take control medications even during symptomless period) later on in the interview yielded different responses i.e. 66.6% non-case managed and 50% of case managed patients said yes. When claims data was used to calculate average control and rescue medication adherence among these patients. The average MPR values were very low (in table 9.3). 4 out of the 5 non case managed patients that responded yes for "skipped or stopped taking medication because they were not working" were African Americans and one was Caucasian. 33% of non-case managed and 8% of case managed patients reported that they see different physician every time even though they had primary care physician's assigned to them. About 25% of both groups reported that they skipped medications due to cost of medication, While 20 % of non-case managed and 41% of case managed patients reported that they forgot to refill their medications on time. Since the sample size of the telephone interview respondents is small, it is hard to conclude strongly about the factors that might affect medication adherence, even though some kind of trend is seen in the responses. To rectify this, a larger sample group with a face-to-face or a questionnaire to be filled via email might get better details and more number of respondents.

3.6.1 Ethical considerations

Data will be de-identified and necessary steps such as HIPAA training will be taken to honor the privacy of patients and their data. Protection of participants will be ensured by taking approval from Institutional Review Board and submitting needed consent documents. Patients were free to decline participation in the survey methods. The principles of ethical research practices such as confidentiality and anonymity will be followed.

3.6.2 Limitations

Limitations of using pharmacy claims data is assumption that a prescription filled is a prescription consumed. Pharmacy claims data may not reflect stopping medication due to physician's orders or change in patient schedules. Sample was not be divided upon the drug class. Medication possession ratio used to calculate medication adherence for this population has a few short comings as it only helps calculate consistency and not persistency.

3.6.3 Summary and Conclusion

In conclusion, the two types of insurance coverage (TANF and SSI-non dual) were the only significant predictors of control medication adherence among the factors considered in this study. Also, the t-test of the asthma population (n=687) results showed that control and rescue medication adherence is not significantly different among case managed and non-case managed

asthma patients. The sample of 687 asthma patients and also the respondents (n=27) of telephone interview for this study did not provide enough basis to propose an effective selection criteria for interventions (i.e. case management type of intervention) in order to improve control medication adherence.

FINAL CONCLUSION

The asthma population for this study consisted of patients with Medicaid insurance coverage. Medicaid insurance in principal covers members with low income conditions. Results found that control medication adherence has no relationship with any type of hospital visit, patients with rescue medication adherence tend to have lower emergency visits and inpatient admissions. Patients with more than 4 office visits had better rescue medication adherence but not control medication adherence. This goes to explain that people might not follow their doctor's orders on control medication but are knowledgeable in the use of rescue medication. Even though this seems like a good practice, it is not since use of rescue medication should be limited and control medications should be taken as prescribed by the doctor to avoid exacerbations. Further, patients with TANF and SSI-non dual coverages tend to be less adherent to control medication compared to other coverages. Also, males and low income patients were found to have emergency department visits and older lower income patients have more 30 day-readmissions. Even though the results from the analysis and responses for the interview questions was not enough information to propose a selection criteria to improve control medication adherence, they provided clear picture on what needs to be done. Asthma patients need to be educated on the use of control medication, rather than wait until they have an asthma attack and take rescue medication for quick relief. Male, older and low income patients should be further studied to reduce hospital visits and improve medication adherence. It was also found that control and rescue medication adherence was not significantly different among case managed and non-case managed patients.

Future Research

In order to identify hospital utilizations in connection with medication adherence, it would be advisable for future researchers to consider a larger sample with more variables such as patient's race/ ethnicity, individual income, medication cost for each claim, employment status, education, hospital discharge instructions, physician and patient relation, classification of office visits (scheduled or unscheduled) and detailed analysis of medications (classification, drug classes, etc.). Above mentioned variables when analyzed similar to this study might lead to predicting and improving medication adherence for asthmatic patients.

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APPENDIX A: ICD 9 & ICD 10 CODES

ICD 9 codes

493	Asthma
493	Extrinsic Asthma
493.1	Intrinsic Asthma
493.2	Chronic Obstructive Asthma
493.8	Other Forms of Asthma
493.81	Exercise Induced Bronchospasm
493.82	Cough Variant Asthma
493.9	Unspecified Asthma

ICD 10 codes

J45	Asthma
J45.2	Mild Intermittent Asthma
J45.20	Mild Intermittent Asthma, Uncomplicated
J45.21	Mild Intermittent Asthma with (Acute) Exacerbation
J45.22	Mild Intermittent Asthma with Status Asthmaticus
J45.3	Mild Persistent Asthma
J45.30	Mild Persistent Asthma, Uncomplicated
J45.31	Mild Persistent Asthma with (Acute) Exacerbation
J45.32	Mild Persistent Asthma with Status Asthmaticus
J45.4	Moderate Persistent Asthma
J45.40	Moderate Persistent Asthma, Uncomplicated
J45.41	Moderate Persistent Asthma with (Acute) Exacerbation
J45.42	Moderate Persistent Asthma with Status Asthmaticus
J45.5	Servere Persistent Asthma
J45.50	Servere Persistent Asthma, Uncomplicated
J45.51	Servere Persistent Asthma with (Acute) Exacerbation
J45.52	Servere Persistent Asthma with Status Asthmaticus
J45.9	Other and Unspecified Asthma
J45.90	Unspecified Asthma
J45.901	Unspecified Asthma with (Acute) Exacerbation
J45.902	Unspecified Asthma with Status Asthmaticus
J45.909	Unspecified Asthma, Uncomplicated
J45.99	Other Asthma
J45.990	Exercise Induced Bronchospasm
J45.991	Cough Variant Asthma
J45.998	Other Asthma

APPENDIX B: NON-ASTHMATIC GROUP TABLES

Non-asthmatic group diagnosis

Diagnosis	Count of Member ID	Count of Actual Admission Date
ABDOMINAL PAIN, UNSPECIFIED SITE	1	1
AC CHRN COMB SYSTOLIC AND DIASTOL CHF	1	1
ACUT MI OTH INF WALL INIT EPIS CARE	1	1
ACUT MI SUBNDOCRDL INFARCT INIT EOC	1	1
ACUTE CHRON SYSTOLIC HEART FAILURE	1	1
ACUTE CHRONIC RESP FAIL W/HYPOXIA	1	1
ACUTE EMBO THROMBOS RT FEMORAL VEIN	1	1
ACUTE KIDNEY FAILURE UNSPECIFIED	2	2
AGRANULOCYTOSIS SEC TO CANCER CHEMO	1	1
ALCOHOL USE UNS W/UNS ALC-INDUC D/O	1	1
ALCOHOLIC GASTRITIS WITH HEMORRHAGE	1	1
ALCOHOLIC HEPATIC FAILURE W/O COMA	2	2
ALTERED MENTAL STATUS UNSPECIFIED	2	2
ASPERGILLOSIS	2	2
ASPERGILLOSIS UNSPECIFIED	1	1
ATHSC NATV ART EXT REST PAIN BIL	1	1
ATHSC NATV ART EXT W/GANGREN LT LEG	1	1
BENIGN NEOPLASM COLON UNSPECIFIED	1	1
BENIGN NEOPLASM OF RIGHT OVARY	1	1
BILIARY ACUTE PANCREATITIS	1	1
BIPOLAR CURR DEPRESS SEV W/O PSYCH	1	1
BIPOLAR CURR DEPRESS SEV W/PSYCH	1	1
BIPOLAR CURR DEPRESSED MILD/MOD UNS	2	2
BIPOLAR DISORDER UNSPECIFIED	1	1
BIPOLAR II DISORDER	1	1
CELLULITIS AND ABSCESS OF MOUTH	1	1
CELLULITIS&ABSC UPPER ARM&FOREARM	1	1
CELLULITIS&ABSCESS LEG EXCEPT FOOT	1	1
CELLULITIS&ABSCESS OTHER SPEC SITE	1	1
CEREB INFARCT EMBO RT ANT CEREB ART	1	1
CEREBRAL INFARCTION UNSPECIFIED	1	1
CHF UNSPECIFIED	1	1
CLOSED FRACTURE OF SHAFT OF HUMERUS	1	1
COPD WITH ACUTE EXACERBATION	2	2
CORD AROUND NECK-COMPRS DEL	1	1
CRITICAL ILLNESS MYOPATHY	1	1
CUTANEOUS ABSCESS LEFT UPPER LIMB	1	1

CUTANEOUS ABSCESS OF NECK	1	1
DECR FETAL MOVEMENTS UNS TRI NA/UNS	1	1
DISORDER OF BRAIN UNSPECIFIED	1	1
DISPLACEMENT INSULIN PUMP INITIAL	1	1
DISPLCMT LUMBAR DISC W/O MYELOPATHY	1	1
DVTRCLI LG INT NO PERF/ABSC W/O BL	1	1
EMBOLISM THROMBOSIS ART UP EXTREM	1	1
EPILEPSY UNS NOT INTRACT W/O SE	1	1
ESOPHAGEAL REFLUX	1	1
FIRST DEG PERINEAL LAC DUR DELIV	1	1
FX UNS PRT NCK RT FEM INIT CLOS	1	1
HB-SS DISEASE WITH CRISIS	7	7
HB-SS DISEASE WITH CRISIS UNS	12	12
HEMIPLG FLW CEREB INFARCT LT N-DOM	1	1
HEMPLG OTH NTRM INTRCRN HEM L N-DOM	1	1
IMMUNE THROMBOCYTOPENIC PURPURA	2	2
INF&INFLAM REACT INT ORTH DEVICE	1	1
INTEST ADHES W/OBST POSTPROC-INFECT	1	1
INTESTINAL INF DUE OTH ORGANISM NEC	1	1
LABOR AND DEL COMP FETAL STRESS UNS	1	1
LAC NO FB LT F WALL THOR NO PEN INT	1	1
MAJ DEPRESS D/O RECURRENT MOD	1	1
MAJ DEPRESS D/O SINGLE EPIS UNS	4	4
MAJ DEPRESS RECURR SEV W/O PSYCH	4	4
MAJ DEPRESS RECURR SEV W/PSYCH SX	1	1
MAJOR DEPRESSIVE D/O RECURRENT UNS	2	2
MISSED ABORTION	1	1
MORBID SEV OBESITY ALVEOLR HYPOVENT	1	1
MULTIPLE SCLEROSIS	1	1
MYCOPLASMA INFECTION UNSPECIFIED	1	1
NONINFECTIVE GE AND COLITIS UNS	1	1
NON-ST ELEVATION MYOCARDIAL INFARCT	1	1
NONTRAUM IC HEMORR HEMISPH SUBCORT	1	1
NORMAL DELIVERY	2	2
OPEN WND FOREHEAD W/O MENTION COMP	1	1
OPIOID DEPENDENCE WITH WITHDRAWAL	1	1
OTH COMPS DUE INTRL JOINT PROSTH	1	1
OTH CURRENT MATERNAL CCE ANTEPARTUM	1	1
OTH CURRENT MATERNAL CCE W/DELIVERY	2	2
OTH MECH COMP INSULIN PUMP INITIAL	1	1
OTH SPEC ABNORMAL UTERINE VAG BLEED	1	1
OTH SPEC DIAB KETOACIDOSIS NO COMA	1	1
OTHER CHEST PAIN	1	1

OTHER CONVULSIONS	1	1
OTHER GRAM-NEGATIVE SEPSIS	2	2
OTHER NEUTROPENIA	1	1
OTHER POSTOPERATIVE INFECTION NEC	1	1
OTHER SPEC REHABILITATION PROCEDURE	1	1
OTHER SPECIFIED SEPSIS	1	1
PARALYTIC ILEUS	1	1
PARANOID SCHIZOPHRENIA	6	6
PERIAPICAL ABSCESS WITHOUT SINUS	1	1
PERIPHERAL VASCULAR DISEASE UNS	1	1
PNEUMOCOCCAL PNEUMONIA	1	1
PNEUMONIA UNSPECIFIED ORGANISM	5	5
PNEUMONIA, ORGANISM UNSPECIFIED	1	1
POISN OTH RX MEDS BIO SUBS ACC INIT	1	1
POISON OTH OPIOIDS ACC INITIAL ENC	1	1
POISONING BY OPIUM , UNSPECIFIED	1	1
POST-TERM PREGNANCY	1	1
PRE-EXISTING DM TYPE 2 PREG 3RD TRI	1	1
PREMATURE RUPTURE MEMB PG DELIV	1	1
PREV C/S DEL DEL W/WO ANTPRTM COND	3	3
RADICULOPATHY LUMBAR REGION	1	1
SALPINGITIS AND OOPHORITIS UNS	1	1
SCHIZOAFFECTIVE D/O BIPOLAR TYPE	2	2
SCHIZOPHRENIA UNSPECIFIED	2	2
SEPSIS UNSPECIFIED ORGANISM	1	1
SEVERE PRE-ECLAMPSIA, WITH DELIVERY	1	1
SLTR-HARIS II FX LW LT FEM CLO	1	1
STREP B CARR STATE COMP CHILDBIRTH	1	1
SYNOVIAL CYST OF POPLITEAL SPACE	1	1
SYSTEMIC LUPUS ERYTHEMATOSUS	1	1
THROMB VASC PROSTH DEVC GRAFT INIT	1	1
TYPE 2 DM W/FOOT ULCER	2	2
UNS DISLOC RT ULNOHUMERAL JNT INIT	1	1
UNS FX SHFT LT RADIUS INIT OPN I/II	1	1
UNS NONINF GASTROENTERIT&COLITIS	1	1
UNSPEC HEMORRHAGE GI TRACT	1	1
UNSPEC HTN HEART DISEASE W/HF	2	2
UNSPECIFIED ABDOMINAL PAIN	1	1
UNSPECIFIED ACUTE APPENDICITIS	1	1
UNSPECIFIED ANEMIA	1	1
UNSPECIFIED CONSTIPATION	1	1
UNSPECIFIED ESSENTIAL HYPERTENSION	1	1
UNSPECIFIED INTESTINAL OBSTRUCTION	1	1

UNSPECIFIED SEPTICEMIA	2	2
UNSPECIFIED URETHRAL STRICTURE	1	1
UTI SITE NOT SPECIFIED	3	3
VENTRICULAR FIBRILLATION	1	1
Grand Total	**179**	**179**

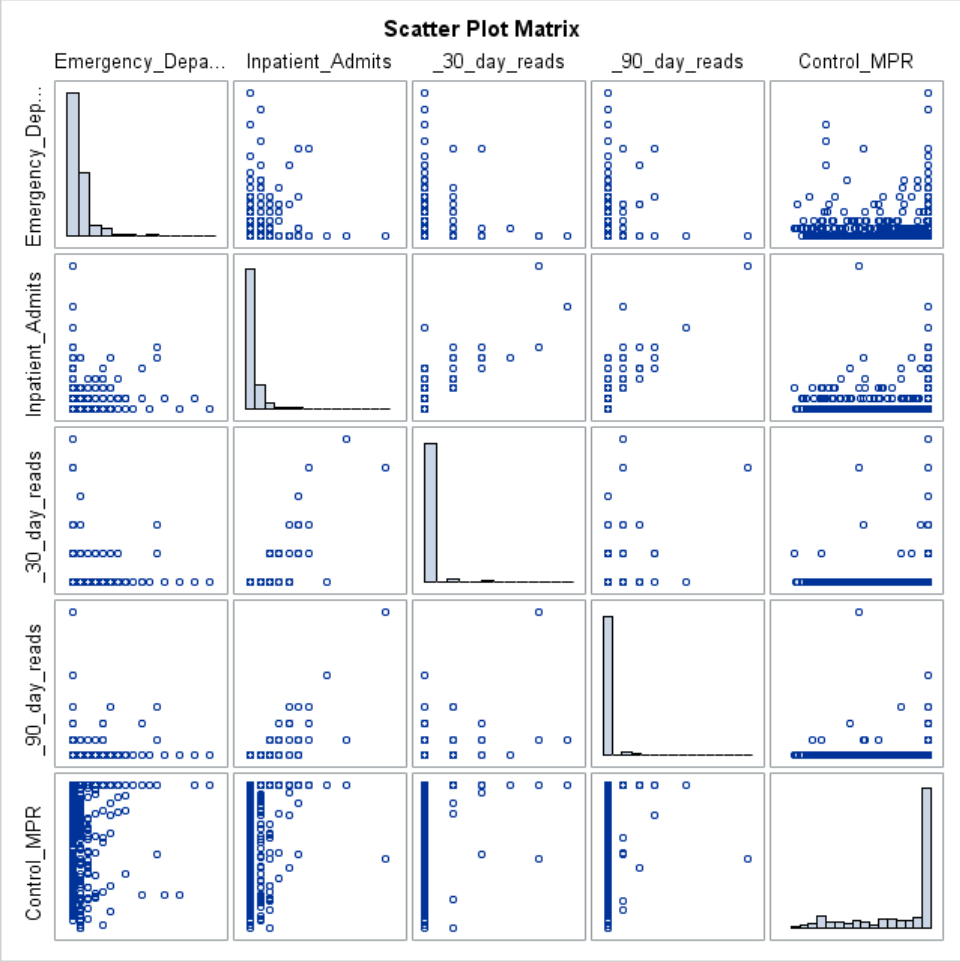
Cluster history of non-asthmatic group

Cluster History

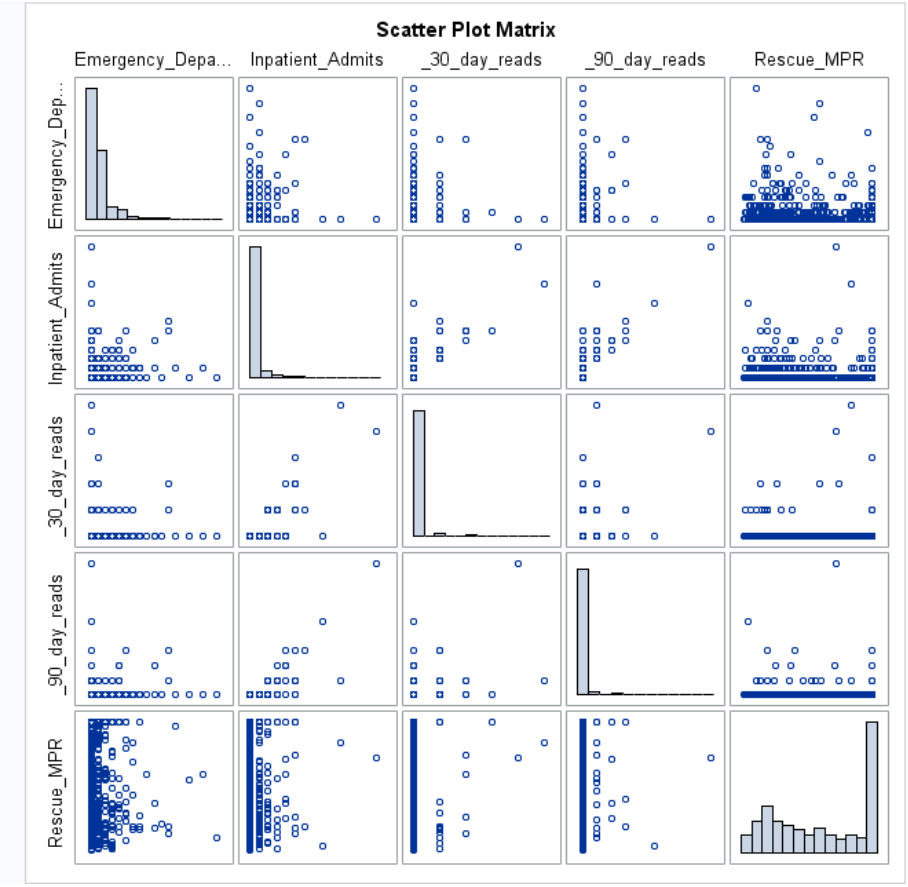
Number of Clusters	Clusters Joined		Freq	Semipartial R-Square	R-Square	Approximate Expected R-Square	Cubic Clustering Criterion	Pseudo F Statistic	Pseudo t-Squared	Tie
15	Samplepatient269	Samplepatient910	2	0.0000	1.00	.960	.	.	.	T
14	Samplepatient871	Samplepatient925	2	0.0000	1.00	.956	.	.	.	T
13	CL35	Samplepatient926	3	0.0000	1.00	.952	.	.	.	T
12	CL37	CL14	46	0.0000	1.00	.946	.	.	.	T
11	CL54	CL16	11	0.0000	1.00	.940	.	.	.	T
10	CL12	CL17	64	0.0000	1.00	.932	.	.	.	
9	CL15	CL62	4	0.0089	.991	.922	22.7	1132	.	T
8	CL13	Samplepatient836	4	0.0133	.978	.910	14.9	517	.	
7	CL9	CL36	6	0.0148	.963	.894	11.4	361	6.7	
6	CL10	CL73	67	0.0254	.938	.874	7.88	253	.	
5	Samplepatient363	Samplepatient760	2	0.0443	.893	.844	4.39	178	.	
4	CL11	CL7	17	0.0650	.828	.800	1.88	138	41.3	
3	CL4	CL8	21	0.1455	.683	.726	-2.1	93.6	27.1	
2	CL3	CL5	23	0.2256	.457	.576	-3.2	74.1	16.2	
1	CL6	CL2	90	0.4572	.000	.000	0.00	.	74.1	

Appendix C: SCATETRPLOT FOR CORRELATION ANALYSIS

Scatterplot for correlation between emergency department visits, inpatient admissions, 30 day readmissions, 90 day readmissions and control medication adherence



Scatterplot for correlation between emergency department visits, inpatient admissions, 30 day readmissions, 90 day readmissions and rescue medication adherence

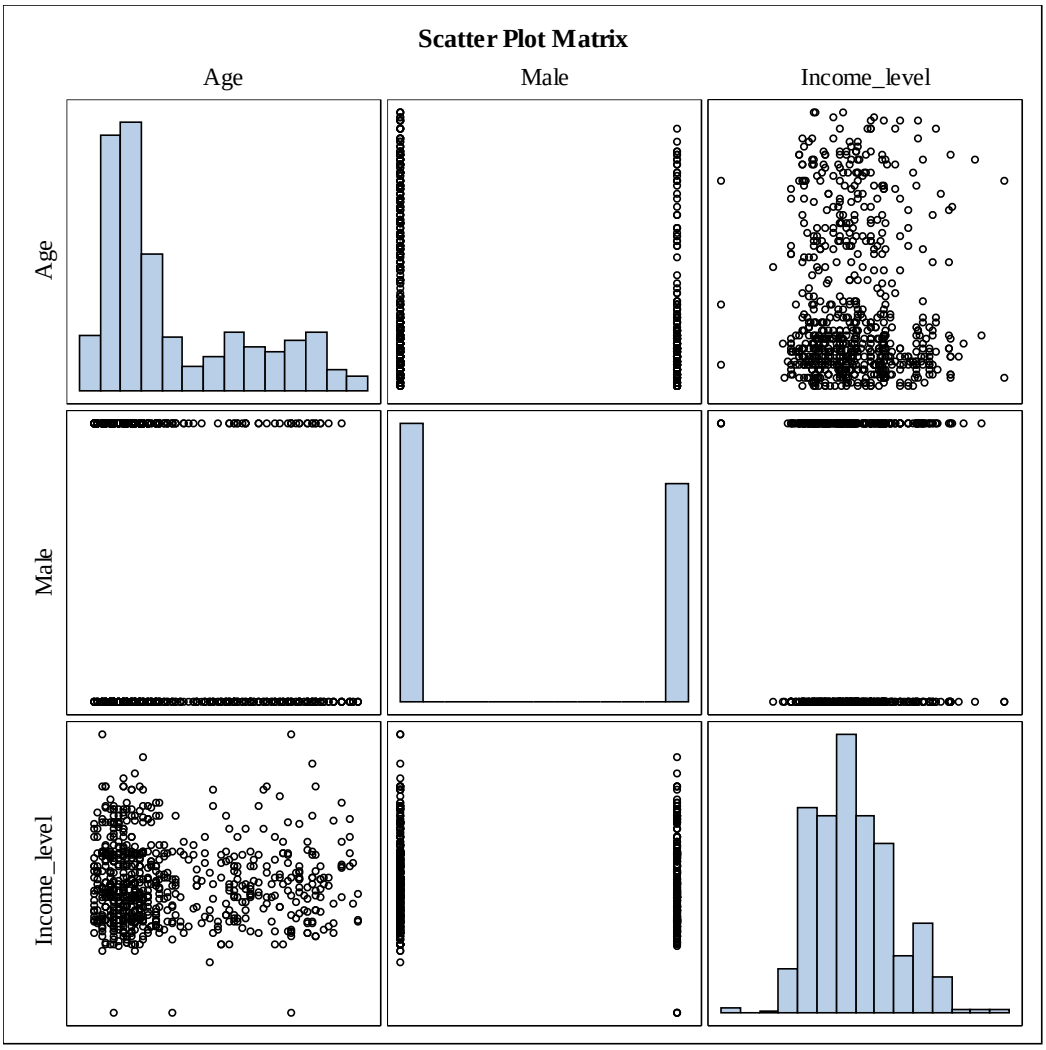


APPENDIX D: REGRESSION ANALYSIS

Correlation matrix between the independent variable

Pearson Correlation Coefficients, N = 687 Prob > |r| under H0: Rho=0			
	Age	Male	_Income_level
Age	1.00000	-0.34524 <.0001	-0.03689 0.3343
Male	-0.34524 <.0001	1.00000	-0.05735 0.1332
_Income_level	-0.03689 0.3343	-0.05735 0.1332	1.00000

Scatterplot of the correlation matrix



Control medication with age, gender and income.

Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	79.88454	4.05158	19.72	<.0001
Age	1	0.03786	0.06087	0.62	0.5342
Male	1	-2.33385	2.15208	-1.08	0.2785
_Income_level	1	0.00006596	0.00008060	0.82	0.4134

Emergency visits with age, gender and income

Variable	Parameter Estimate	Standard Error	Type II SS	F Value	Pr > F
Intercept	1.25365	0.26137	80.74789	23.01	<.0001
Male	0.29872	0.14420	15.06350	4.29	0.0387
_Income_level	-0.00001166	0.00000575	14.42977	4.11	0.0430

Inpatient Admits with age, gender and income

Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	0.44498	0.17813	2.50	0.0127
Age	1	0.00343	0.00268	1.28	0.2008
Male	1	-0.01937	0.09462	-0.20	0.8378
_Income_level	1	-0.00000222	0.00000354	-0.63	0.5305

30 day readmission with age, gender and income

Variable	Parameter Estimate	Standard Error	Type II SS	F Value	Pr > F
Intercept	0.11956	0.05373	0.71238	4.95	0.0264
Age	0.00155	0.00082566	0.50432	3.51	0.0616
_Income_level	-0.00000214	0.00000116	0.48706	3.39	0.0662

90 day readmission with age, gender and income

Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	0.13754	0.07557	1.82	0.0692
Age	1	-0.00043258	0.00114	-0.38	0.7033
Male	1	-0.05802	0.04014	-1.45	0.1488
_Income_level	1	-8.38267E-7	0.00000150	-0.56	0.5773

APPENDIX E: TELEPHONE INTERVIEW

Telephone interview Procedure and Questions

Plan:

- 2 pilot Interviews to track duration
- Reduce or rephrase questions depending on this
- Sample size for interviews: 60 (30 case managed/ 30 without it)

Case manager randomly picks members from asthma population. Introduces herself.

1. Are you (the person we intended to call)? May I confirm your/ your child's age and gender?
2. Have you ever been diagnosed for asthma? Yes, continue. If not end the call
3. What category of asthma do you have? (mild/intermittent/severe)
4. Race/ ethnicity
5. Employment status/ education
6. Marital status/ family members
7. Comorbidities?
8. Do you have a PCP?
9. Are you case managed or do you take any such services provided by the insurance company?
10. (IF YES for q.9) Rate case management or disease management services provided to you by the insurance company
11. Do you know about the transportation facility provided by the insurance company?
12. During the past three months how many asthma attacks have you had? And how long did they last (dash minutes, dash hours, dash days, dash weeks)?

Medication related

13. Are you currently taking any medications? What are they? How often?
14. In the past 3 months have you taken prescription asthma medicine?
15. In the past 3 months did you take asthma medication when you did not have an asthma attack? Or on regular schedule as by the doctor

Physician related

16. Has a doctor ever taught you to recognize early signs of symptoms of an asthma episode? What to do during an asthma episode or prevent an attack?
17. Do you have an asthma action plan? How long ago did you get it?
18. Did a health professional show you how to use an inhaler?

Patient related

19. Let me know if the following are reasons for non-adherence?
    - Take control medication even during symptomless period?

- How well informed do you feel about your health and medication (asthma education/ Uncertain how to use medication/ Uncertain when to use medication)
- Side effects with asthma medication
- Rx wasn't working/ Skipped or stopped taking a medicine because you didn't think it was working?
- Don't need the ICS/ Does not need preventive treatment
- Forgetting to take medication/ did not refill on time/ ran out of medication/ not had medicine with you when it was time to take it?
- Stopped taking medication
- See different provider each visit (PCP)
- Number of prescription medications (Complicated regimen/ Taking medicines more than once a day is inconvenient.)
- Skipped, stopped, not refilled, or taken less medicine because of the cost? / coverage for prescription medication
- Lack of transportation
- Do you or anybody in your home smoke/ drink alcohol?
- Family support

t-test results for:

Asthma action plan

Method	**Variances**	**DF**	**t Value**	**Pr > |t|**
Pooled	Equal	25	1.5	0.1473
Satterthwaite	Unequal	24.754	1.52	0.1416
Cochran	Unequal	.	1.52	0.1541

Equality of Variances				
Method	**Num DF**	**Den DF**	**F Value**	**Pr > F**
Folded F	14	11	1.3	0.6671

Forgot to refill medication

Method	**Variances**	**DF**	**t Value**	**Pr > |t|**
Pooled	Equal	25	1.21	0.2364
Satterthwaite	Unequal	20.924	1.18	0.2499
Cochran	Unequal	.	1.18	0.2599

Equality of Variances				
Method	**Num DF**	**Den DF**	**F Value**	**Pr > F**
Folded F	11	14	1.55	0.4373

Primary casre phyician

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	25	1.92	0.0659
Satterthwaite	Unequal	22.865	2.04	0.053
Cochran	Unequal	.	2.04	0.0622

Equality of Variances				
Method	**Num DF**	**Den DF**	**F Value**	**Pr > F**
Folded F	14	11	3.09	0.0672

APPENDIX F: ASTHMA PROCEDURES & CODES

Asthma procedure codes and description

Codes	Asthma procedure code description
94010	Spirometry: FVC, VC with or without MVV
94011	Up to 2 years old Spirometry
94012	2 years Spirometry w/dilator
94013	2 years lung volumes
94014	Patient recoded spirometry
94015	Patient recorded spirometry
94016	Review patient spirometry
94060	Evaluation of wheezing
94070	Evaluation of wheezing
94150	Vital capacity requires hook up spirometry
94375	Respiratory flow volume loop
94620	Pulmonary stress testing
94640	Pressurized or non-pressurized inhalation treatment
94664	Demonstration and/or evaluation of patient utilization of nebulizer, metered dose
94760	Noninvasive ear or pulse oximetry for oxygen saturation; single determination
94761	Noninvasive ear or pulse oximetry for oxygen saturation; multiple determination
94762	Noninvasive ear or pulse oximetry by continuous overnight monitoring
A4614	Peak expiratory flow rate meter handheld
J7611	Albuterol, inhalation solutions, administered through DME, concentrated form, 1mg
J7612	Levalbuterol, inhalation solution, administered through DME, concentrated form, 0.5mg
J7613	Albuterol, inhalation solution, administered through DME, unit dose, 1mg
J7614	Xopenex: Levalbuterol, inhalation solution, administered through DME
J7626	Budesonide inhalation solution non compounded up to 0.5 mg
J7627	Budesonide inhalation solution compounded up to 0.5 mg
J7644	Atrovent: Ipratropium bromide, inhalation solution administered through DME
J7645	Ipratropium bromide inhalation solution
S8096	Portable peak flow meter
S8097	Asthma Kit
S8110	Peak expiratory flow rate (physician services)
S9441	Asthma education
J7620	Albuterol all formulations inhalation
J2357	Omalizunab
J2810	Theophilline
J7609	Albuterol all formulations inhalation
J7610	Albuterol all formulations inhalation

APPENDIX G: IRB APPROVAL

IRB Approval letter

ACTION ON PROTOCOL APPROVAL REQUEST

TO: Isabelina Nahmens

Mechanical and Industrial Engineering

FROM: Dennis Landin

Chair, Institutional Review Board

DATE: November 29, 2016

RE: IRB# 3722

Institutional Review Board Dr. Dennis Landin, Chair 130 David Boyd Hall Baton Rouge, LA 70803 P: 225.578.8692

F: 225.578.5983

irb@lsu.edu | lsu.edu/irb

TITLE: Evaluating Asthma Care from Hospital to Home to prevent Hospital Readmissions

New Protocol/Modification/Continuation: New Protocol

Review type: Full____Expedited X **Review date:** 6/15/2016

Risk Factor: Minimal__X____Uncertain_____Greater Than Minimal__

Approved_____X_____Disapproved___

Approval Date: 11/29/2016 **Approval Expiration Date:** 11/28/2017

Re-review frequency: (annual unless otherwise stated)

Number of subjects approved: N/A

LSU Proposal Number (if applicable)**:**

Protocol Matches Scope of Work in Grant proposal: (if applicable)

By: Dennis Landin, Chairman

PRINCIPAL INVESTIGATOR: PLEASE READ THE FOLLOWING –

Continuing approval is CONDITIONAL on:

Adherence to the approved protocol, familiarity with, and adherence to the ethical standards of the Belmont Report, and LSU's Assurance of Compliance with DHHS regulations for the protection of human subjects*

Prior approval of a change in protocol, including revision of the consent documents or an increase in the number of subjects over that approved.

Obtaining renewed approval (or submittal of a termination report), prior to the approval expiration date, upon request by the IRB office (irrespective of when the project actually begins); notification of project termination.

1. Retention of documentation of informed consent and study records for at least 3 years after the study ends.
2. Continuing attention to the physical and psychological well-being and informed consent of the individual participants, including notification of new information that might affect consent.
3. A prompt report to the IRB of any adverse event affecting a participant potentially arising from the study.
4. Notification of the IRB of a serious compliance failure.
5. **SPECIAL NOTE: When emailing more than one recipient, make sure you use bcc.**

**All investigators and support staff have access to copies of the Belmont Report, LSU's Assurance with DHHS, DHHS (45 CFR 46) and FDA regulations governing use of human subjects, and other relevant documents in print in this office or on our World Wide Web site at http://www.lsu.edu/irb*

VITA

Archana Nittala was born in December 1991 in Telangana (formerly part of Andhra Pradesh), India. Ms. Nittala received her Bachelor of Technology in Mechatronics (Mechanical Engineering) in May 2013 from Mahatma Gandhi Institute of Technology, Hyderabad, India. In spring 2014, she was admitted to Louisiana State University, Baton Rouge, Louisiana, USA, to pursue her master's degree in Industrial Engineering. She was employed by Mr. Terry Grier as Graduate Assistant for Facility Services and started working towards her degree under the guidance of Dr. Isabelina Nahmens. Ms. Nittala expects to receive the degree of Master of Science in Industrial Engineering (MSIE) in December 2017.