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Patient adherence to chronic disease medications in a medication therapy management program in Lucas County, Ohio

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The University of Toledo

A Thesis

Entitled

Patient Adherence to Chronic Disease Medications in a Medication Therapy Management Program in Lucas County, Ohio

By

Abhilasha Ramasamy

Submitted as partial fulfillment of the requirements for

The Master of Science Degree in Pharmaceutical Sciences,

Administrative Pharmacy Option

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Advisor: Dr. Sharrel Pinto

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College of Graduate Studies

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An Abstract of

Patient Adherence to Chronic Disease Medications in a Medication Therapy Management Program in Lucas County, Ohio

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Medical expenditures can be controlled by improving patient adherence to medications. Various interventions, such as disease state management programs and medication therapy management (MTM) programs, have been initiated in an attempt to improve adherence to medications. One such program, Lucas County MTM program is sponsored by an employer group and provides services to Lucas County employees diagnosed with diabetes, hypertension, and hyperlipidemia.

The purpose of this study was to evaluate patient adherence to chronic disease medications and to determine the effect of adherence on the clinical outcomes of patients enrolled in Toledo Lucas County MTM program.

This was a retrospective, longitudinal study. Data was obtained for 272 patients from The Pharmacy Counter prescription database. Medication adherence was measured using Medication Possession Ratio (MPR). Pearson correlation was used to determine the relationship between medication adherence and desired clinical outcomes. Multiple linear regression was used to determine if medication adherence is a predictor of clinical outcomes. Data analysis was performed using SPSS version16.0 and Microsoft Excel.

Pearson correlation results indicated that MPR to diabetic medications was significantly correlated with age (r=0.387, p=0.000) and gender (r=-0.167, p=0.021). Further, age was significantly correlated with gender (r=-0.148, p=.042) and number of diseases (r=0.278, p=0.000) among diabetic patients. However, there were no significant predictors of change in A1c among diabetic patients.

Among hypertension patients, change in systolic blood pressure was significantly correlated with change in diastolic blood pressure (r=0.553, p=0.000), gender (r=0.134 p=0.024), co-pay (r=0.118, p=0.048), and number of diseases (r=-0.132, p=0.026). Further, change in diastolic blood pressure was significantly correlated with MPR (r=-0.178, p=0.003). MPR was also found to be significantly correlated with gender (r=-0.138, p=0.020, co-pay (r=0.141, p=0.018), and number of diseases (r=0.139, p=0.019).

Regression model for hypertension patients indicated that number of diseases (β = -0.130, p = 0.01), and change in diastolic blood pressure (β = 0.550, p = 0.000) were significant predictors of change in systolic blood pressure. Further, MPR (β = -0.151, p = 0.003) and change in systolic blood pressure (β = 0.552, p = 0.000) were found to be significant predictors of change in diastolic blood pressure.

Thus, patients enrolled in the Lucas County MTM program showed high average adherence to hypertension medications. This study also identified predictors of clinical outcomes associated with diabetes and hypertension.

I dedicate this thesis to

My parents – Ramasamy and Uma Ramasamy,

My husband – Vignesh

My brother – Ajay Kumar

My parents-in-law – Balaji and Geetha

My brother-in-law-Vikram

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Chapter-1

Introduction

Background

Nearly 63 million Americans have two or more chronic diseases.[1] Chronic conditions, such as diabetes, hypertension, hyperlipidemia, and cardiovascular conditions place a significant financial burden on the economy.[2] Each year, seventy-five percent of health care costs are attributed to chronic conditions.[3] Medical expenditures can be controlled by improving patient adherence to medications.[4] As the costs of treatment for chronic conditions continue to rise, it is important to ensure that the quality of care can be improved and expenditures controlled.[5]

In total, the costs associated with poor medication adherence are estimated to approach $100 billion per year.[6] Poor adherence has been found to be associated with development of complications, disease progression, premature disability and death.[7] For diabetes, hypertension, and hyperlipidemia medications, non-adherence has been associated with worsened medical outcomes, higher hospitalization rates, and/or increased health care costs.[8, 9] Studies have shown that poor adherence to medication causes an estimated 125,000 deaths annually, and accounts for 10% of hospital admissions.[10, 11]

Medication adherence not only reduces overall medical expenditures, but also improves clinical outcomes. Previous studies on diabetes have found a strong association between medication adherence and achieving desired Hemoglobin A1c levels.[12, 13] Similarly, compliance with anti-hypertensive medications is associated with better blood pressure control and the potential for improved long-term outcomes.[8] While drug costs increase with improved adherence to medications, overall cost savings occur in the form of fewer physician and emergency room visits, fewer hospitalizations, and reduced morbidity and mortality.[14]

Adherence to medication is one of the most important factors for successfully managing a chronic disease. Non-adherence is a common problem among patients with chronic diseases, especially diabetes, hypertension, and hyperlipidemia.[15-17] Management of these chronic diseases requires taking several medications, making it difficult for patients to adhere to their medications. Various interventions, such as disease state management programs and medication therapy management programs, have been initiated in an attempt to improve adherence to medications. With the launch of the Medicare Part D drug benefit program on January 1, 2006, the focus of the pharmacy industry shifted from the mere distribution of medications to programs that ensure patients are taking medications properly and that desired outcomes are being achieved. These programs are commonly referred to as Medication Therapy Management Programs to recognize the broader scope of their purpose.[18] Medication Therapy Management (MTM) is a distinct service or group of services that optimize therapeutic outcomes for individual patients.[19] MTM programs, as defined by the Center for Medicare and Medicaid services (CMS), improve adherence to therapy, and reduce adverse events with the goal to improve the overall quality of medication use.[19]

Statement of problem

Typical adherence rates among chronic disease patients are approximately 50%.[20] A previous study showed that the average adherence with prescribed therapy for patients with diabetes is 67.5% lower than that found in many other conditions.[21] Yet another study, which measured average adherence to oral diabetes medication regimens, indicated an adherence range from 36% to 93%.[22] For hypertension, the adherence rate is often better (50-70%), but still not ideal.[23] The importance of adherence with blood pressure medications lies in the finding that uncontrolled blood pressure is 27 times more likely in non-adherent individuals.[24] A similar trend of non-adherence is also observed in lipid lowering therapy. Observational studies have reported that the discontinuation rate of lipid lowering therapy after one year of treatment is 15-60%, depending on the patient population.[25-27] The concomitant presence of hypertension and hyperlipidemia increases the risk of cardiovascular diseases, compared to having either condition alone.[28] Poor adherence also leads to increased complications for untreated diseases, additional medical therapies, as well as the tendency for physicians to prescribe higher doses than necessary to achieve desired results, only to increase the likelihood of drug side effects.[5, 29] Thus, poor adherence is a common problem in chronic diseases such as diabetes, hypertension, and hyperlipidemia.

In an attempt to improve patient adherence to medications and to decrease overall healthcare expenditures, MTM programs have been initiated. The main purpose of MTM programs is to optimize therapeutic outcomes on an individual patient basis. A critical review of MTM services, provided by Lewin Group, suggests that cost reduction and improved health outcomes can occur if MTM programs are provided, especially to elderly patients.[30] MTM programs can also reduce expensive emergency room and hospital services by reducing adverse health events. The Lewin report also suggests that MTM programs can reduce per-member per-month total health costs.[30] Thus, MTM programs not only help to achieve the desired therapeutic outcomes, but also reduce the overall healthcare expenditure.

Rationale

One such employer-sponsored MTM program is provided in Lucas County, Ohio. This program is provided to Lucas County employees diagnosed with diabetes, hypertension, and hyperlipidemia, by a coalition of independent community pharmacies in Toledo, Ohio. These services are of great importance. However, there are currently no quantified results to illustrate if patients are being adherent to their chronic disease medications in the MTM program.

In an employer-sponsored medication therapy management program, it is important to determine if patients are being adherent to their medications in order to prevent long-term complications associated with the disease, reduce healthcare expenditures, and also to ensure that the employees are more productive, indicated by reduced absenteeism, and reduced number of sick days. Furthermore, in the Lucas

County MTM program, all the employees continue to receive health care benefits from their employer group, even after retirement. Hence, from the Lucas County employer group perspective, it is important to avoid long-term complications, thereby reducing the overall health care expenditures.

The costs associated with diabetes create a considerable economic burden for patients, families, and society.[31,32] In 2002, productivity losses from diabetes were estimated to be almost half ($40 billion) of the medical costs ($92 billion) associated with diabetes.[33] The increased prevalence of diabetes among younger individuals suggests that diabetes will become more common in the working-age population. [33] Consequently, employment and work productivity of individuals with diabetes are important issues for patients, families, employers, and policy makers. Several studies have found negative associations between diabetes and employment outcomes, such as absenteeism, productivity, sick days, retirement, and mortality.[34-38] In a longitudinal study, Vijan et al. found that diabetes had a profound negative effect on economic productivity due to early retirement, increased sick days, disability, and mortality.[39]

Poor adherence to antihypertensive medications has been associated with a mean loss of three and a half workdays per year, and increased annual health care costs for patients with hypertension.[40-42] Similarly, in another study, adherent patients with hyperlipidemia had total health care costs of $3,924 compared to $6,888 for non-adherent patients.[43] Thus, it is important to ensure that patients are adherent to medications for chronic diseases in order to reduce the total health care costs, and also to improve employment outcomes mentioned above.

Currently, adherence to chronic disease medications is not being measured in the Lucas County MTM program. This study will bridge this gap by measuring the adherence of patients diagnosed with diabetes, hypertension, and hyperlipidemia, enrolled in the Lucas County MTM program. The purpose of this study, then, is to measure the effectiveness of the Lucas County MTM program, in terms of improving patients' adherence to chronic disease medications, which, in turn, should result in improved clinical outcomes.

Significance

Non-adherence to prescription medications may result in worsened clinical outcomes, which may lead to the addition of a more complex medication regimen to the therapy. Thus, not only may non-adherence increase due to the more complex regimen, but overall healthcare expenditures would also increase. Thus, results from this study will help to identify non-adherence to prescription medications. Since the County is a self-insured employer; higher adherence will help avert long-term complications associated with these chronic diseases, thus reducing the premium and overall healthcare expenditures.

Goals: The goals of the present study were to:

1. Determine patient adherence to diabetes, hypertension, and hyperlipidemia medications in a Medication Therapy Management Program for Lucas County employees.

2. Determine the effect of adherence on the clinical outcomes of patients with diabetes, hypertension, and/or hyperlipidemia.

Objectives: The specific study objectives were to:

1. Determine patients' adherence to chronic disease medications, as determined by medication possession ratios.
2. Determine the relationship between medication adherence and selected clinical outcomes * among chronic disease patients.

   *- Change in A1c, change in systolic blood pressure, and change in diastolic blood pressure in a sample of patients with Diabetes and Hypertension.

3. Determine the factors* affecting clinical outcomes.

   *- Change in A1c, change in systolic blood pressure, change in diastolic blood pressure, age, gender, co-pay, and number of diseases.

Research Questions

RQ 1: What is the adherence rate of patients taking medications for chronic diseases?

RQ 2: Is there a relationship between medication adherence and clinical outcomes* among patients with chronic diseases?

RQ 3: What factors* affect clinical outcomes?

Research Hypothesis

RH 2: There is a statistically significant relationship between medication adherence and clinical outcomes among patients with chronic disease conditions.

Chapter-2

Literature Review

Overview

This chapter gives a brief overview of the topics relevant to this study and covers a review of the literature.

Adherence

A medication's success in producing the desired benefit depends on a person's compliance with the therapeutic regimen. Adherence is defined by the World Health Organization as "the extent to which a person's behavior-taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider".[44] Persistence has been defined as the continuation over time with long-term drug therapy prescribed for the management of chronic conditions.[45] Adherence to medications is also important to reduce the overall healthcare expenditures. Literature has demonstrated that decreased medication adherence is associated with increased hospitalization rates and total costs of care.[5, 45] Assessment of adherence is important to identify patients with low adherence in order to provide appropriate interventions and also to evaluate the outcomes associated with adherence.

Adherence to chronic medications

The prevalence of chronic diseases is growing, with many people having more than one chronic condition. Adherence to chronic disease medications has been found to be a common problem. Adherent patients incur lower total healthcare costs compared to non-adherent patients.[37] On average, patients with chronic medical conditions take 30% to 70% of the prescribed medication doses and on average 50% discontinue medications in the first months of therapy.[44] Care for chronic diseases, such as diabetes, hypertension, and hyperlipidemia, accounts for 75% of the total health care expenditures. [3]

Diabetes

Diabetes affects people throughout the world and is one of the oldest diseases known. According to the National Diabetes Information Clearinghouse (NDIC), as of 2007, 23.6 million people in the United States have diabetes.[46] 17.9 million people were diagnosed with diabetes in 2007.[46] There are two common types of this disease: type 1 and type 2 diabetes. Type-1 diabetes accounts for 5-10% of all diagnosed diabetes. This type of diabetes is developed when the body's immune system destroys the beta cells in the pancreas. Beta cells are responsible for making insulin, which regulates blood glucose.[46] It is a serious disease and it requires insulin injections to control the disease.

Type-2 diabetes is the most common form of diabetes. It accounts for 90-95% of diagnosed diabetes. This type of diabetes occurs when the body does not produce enough insulin or the cells in the body ignore the insulin. It can be controlled with the help of a healthy diet and exercise. Oral medications are also used to treat the disease.

There are several co-morbidities associated with diabetes. Co-morbidities include obesity, high blood pressure, elevated triglycerides, high-density lipoprotein or good cholesterol, and low-density lipoprotein or bad cholesterol. If diagnosed early and provided with appropriate treatment, the risk of these complications can be greatly reduced.

For 2007, the total cost of treating diabetes in the United States was $174 billion.[4] The direct medical costs of treating diabetes accounted for $116 billion.[4] Direct medical costs include medical care, pharmaceutical drugs, insulin and other diabetes supplies, and costs to the healthcare sector, such as physician and hospital visits. The costs of treating diabetes continue to grow each year. Hence, it is important to ensure that patients are adherent to their diabetes medications in order to reduce the overall healthcare expenditures.

Adherence to diabetes medications

A systematic review on adherence to diabetic medications has indicated that the adherence ranged from 36%-93%.[22] A study conducted by Pladevall et al indicated that non-adherent patients with diabetes had clinically worse outcomes compared to adherent patients. Non-adherence was found to be significantly associated with low HbA_{1c} and LDL cholesterol levels.[7] Thus, it is important to improve the adherence of patients with diabetic medications in order to improve their clinical outcomes.

Hypertension

Another commonly occurring chronic disease is hypertension. High blood pressure increases the risk of heart disease and stroke. Randomized controlled trials conducted in the past have provided evidence that lowering blood pressure reduces the risk of cardiovascular disease.[47] Control of blood pressure was defined by the Joint National Committee (JNC 7) guidelines as <140/90 mm Hg, and 130/80 mm Hg for patients with diabetes.[48] Some of the risk factors of hypertension include obesity, alcohol, family history, and smoking. There are two types of hypertension, namely primary hypertension and secondary hypertension. Primary hypertension is more common, occurring in 90-95% of the hypertension population. There is no identifiable cause and it develops gradually over many years. Secondary hypertension occurs in 5-10% of the hypertension population.[49] The total health care costs of treating hypertension is estimated to be around $15.0 billion to $60 billion.[50] Adherence to anti-hypertensive medications has been found to be a common problem.

Adherence to hypertension medications

A study conducted to measure adherence to antihypertensive medications indicated that during the first year of the treatment, patients filled their prescriptions less than 50% of the time and only 1 in 5 patients were found to be adherent to the treatment.[51] Another study found that the annual percentage of patients adherent with antihypertensive medications dropped steadily from 58% in the second year of treatment to 39% in the tenth year.[52] Thus, it is evident from literature that adherence is a significant issue for hypertensive patients.

Hyperlipidemia

Hyperlipidemia is another chronic disease where there is an elevation of lipids (fats) in the bloodstream. Hyperlipidemia can be classified into two categories, namely hypercholesterolemia, in which there is a high level of cholesterol, and hypertriglyceridemia, in which there is a high level of triglycerides, the most common form of fat. Hyperlipidemia, along with diabetes, hypertension (high blood pressure), family history, and smoking are all major risk factors for coronary heart disease.[53] Treatment of hyperlipidemia itself includes dietary changes, weight reduction and exercise. If lifestyle modifications cannot bring about optimal lipid levels, then medications may be necessary.[53] Current national guidelines suggest a LDL cholesterol goal of <100 mg/dl for individuals already with heart disease or diabetes, <130 mg/dl for those with moderate risk of heart disease, and <160 mg/dl for the rest.[53] Similar to diabetes and hypertension, adherence to lipid-lowering medications is also not ideal.

Adherence to hyperlipidemia medications

Previous studies measuring adherence to lipid-lowering medications have reported a discontinuation rate of 15%-60% after the first year of treatment.[25-27] Another study, which measured adherence to statin therapy, indicated that among low income people, only 26% were adherent to the therapy even after 5 years of initiating the therapy.[42] Simons et al have found that only 50% of the patients are adherent to their hyperlipidemia medications after 6 months of treatment and only 30-40% take their hyperlipidemia medications after one year of the treatment.[54]

Reasons for non-adherence

Non-adherence to chronic medications occurs for many different reasons. Patients often fail to either fill their prescription for chronic medications or discontinue therapy early or take their medication less often than indicated.[55] Some of the reasons for poor medication adherence include low socioeconomic status, higher number of medications taken, higher medication costs, amount of co-pay, lack of prescription drug coverage, side effects of medications, poor patient-provider relationship, complex treatment regimens, and financial issues.[56-58] Thus, knowing the reasons for non-adherence to chronic disease medications, appropriate steps need to be taken to improve adherence.

Methods of measuring non-adherence

Medication adherence can be measured in various ways, including direct and indirect techniques. Direct methods include biological assays and involve observable data, such as blood and urine testing. Direct methods are more accurate in measuring adherence. Indirect methods are less accurate and include pill counts, electronic monitoring, pharmacy refill records, and the use of an administrative claims database.[44] Despite the limitations of being less reliable, indirect methods, such as pharmacy refill records, are convenient and inexpensive to obtain.

In recent years, the use of administrative claims data to measure medication adherence has gained importance. A systematic review conducted by Andrade et al identified 136 studies on medication adherence using administrative claims databases.[59] There are several ways to measure medication adherence. About 57% of the studies have used medication possession ratio to measure adherence.[59] 10% of the studies used medication gaps and 43% used switching and discontinuation in calculating medication adherence.[59]

Medication possession ratio (MPR) is defined as the number of day's supply of medications in an index period excluding the last refill divided by the number of days in the study period.[60] Gap is defined as the number of days between the calculated end date of a prescription and the start date of the following prescription. To determine the adherence rate, the gap is divided by 366 days, expressed as percentage, and then subtracted from 100%.[61] MPR relies on the assumption that patients consume their medications throughout their measurement period. While an MPR of 100% is considered ideal, patients are considered adherent if they have an MPR of at least 80%.[45] A systematic review conducted in the past indicated that 75% of the studies conducted on adherence have considered a MPR value of 80% or higher as adherent.[59] MPR is useful in assessing adherence to medications intended for long-term use, such as chronic medications.[45]

In response to the issues surrounding non-adherence, management strategies have been implemented.[55] These management strategies, such as medication therapy management (MTM) programs have resulted in reduced overall health expenditure by optimizing therapeutic outcomes.[55]

Medication Therapy Management Programs

The profession of pharmacy has been integral to providing drug therapy to patients.[62] However, pharmacists were dissociated from the use, monitoring, and evaluation of drug therapy. The IOM report increased the awareness of lack of continuity of care. [63-66] There has been an increase in adverse drug reactions and drug costs. This has prompted an enhanced role for pharmacists in ensuring effective drug use and patient safety.[62] The U.S Government decided to bring this change in the role of pharmacists when the Medicare Modernization Act (MMA) of 2003 established Part D, Medicare Prescription Drug Benefit Plan in 2006. Medicare Part D offers beneficiaries the opportunity to remain in traditional Medicare, while the drug benefit comes through a prescription drug plan (PDP).[67] This helped Medicare beneficiaries afford the increasing costs of prescription drugs.[67] One of the ways MMA made this possible is by making Part D prescription drug plans operate Medication Therapy Management (MTM) programs.

These programs provide counseling and other services to beneficiaries with multiple chronic conditions (such as diabetes, hypertension, hyperlipidemia, and asthma) and who use multiple medications and incur high drug costs.[39] MTM programs are designed to promote better understanding of medication use, improve adherence to therapy, and reduce adverse effects with the goal of improving the overall quality of medication use.[39] The majority of programs in 2008 require either a minimum of two or three chronic diseases as part of the program's targeting criteria.[20] While MTM programs focus on managing a patient's medications, disease management programs are developed to manage a patient's chronic disease condition.

Disease Management Programs

Disease management programs were widely adopted in 1990s due to the establishment of health maintenance organizations.[62] The Disease Management Association of America defines disease management as a system of coordinated health care interventions and communications for populations with conditions in which patient self-care efforts are significant.[68] Disease management can be provided by a wide variety of health care professionals such as physicians, nurses, nutritionists, and pharmacists.[62] Disease management focuses on a specific disease and helps patients successfully manage their disease condition. Disease management goes beyond patient counseling by addressing the patient’s drug and nondrug therapy as well as lifestyle modifications associated with a particular disease.[62]

Successful MTM/DSM Programs

Many successful MTM/DSM programs have been implemented. One such MTM programs is the Asheville project which began in 1996 in the City of Asheville, North Carolina by a self-insured employer to provide education and personal oversight to patients with chronic diseases such as asthma, diabetes, hypertension, high cholesterol.[69] Interventions included one-on-one education on the disease condition by certified educators, follow-up with community pharmacists using scheduled consultations, clinical assessment, goal setting, monitoring, and collaborative drug therapy management with physicians. Employees, dependants, and retirees with diabetes soon began showing improved A1c levels, lower total healthcare costs, fewer sick days, and increased satisfaction with pharmacy services.[69] Similarly for patients with hypertension/hyperlipidemia, there was an improvement in mean systolic, diastolic blood pressure, and low-density lipoprotein (LDL). Further, the percentage of patients at blood pressure and LDL cholesterol goal also increased. Thus, Asheville project proved that patients with chronic conditions such as diabetes, Hypertension, and Hyperlipidemia showed significant improvements in their clinical, economic, and humanistic outcomes as a result of the MTM program.[69]

Another successful MTM program is the Project ImPACT for patients with hyperlidemia, depression, and osteoporosis. After the initial visit with the pharmacist, patients were scheduled for follow-up visits every month for the first three months and quarterly thereafter. Pharmacists' interventions included coordination of care, monitoring of adverse drug reactions, drug interactions, drug dosing, drug selection, and side effects. As a result of the interventions, persistence and compliance with medication therapy were 93.6% and 90.1% respectively. Further, more than 62.5% of the patients had reached and were maintained at their NCEP goals at the end of the study period. [70] Thus, project ImPACT showed significantly better clinical and humanistic outcomes as a result of collaborative care provided to patients by pharmacists, physicians, and other healthcare providers.[70]

The Diabetes Ten City Challenge is another successful MTM program which demonstrated how employers and pharmacists can work together to help people with diabetes manage their disease and reduce healthcare costs. As a result of the pharmacist's interventions, there was a reduction in the average total healthcare costs. Further, there were also improvements in key clinical outcomes including A1c, cholesterol, and blood pressure, and increased number of people with current influenza vaccinations, eye exams, and foot exams. [71]

The results from the successful MTM programs mentioned above indicate that pharmacist interventions results in improved clinical, economic, and humanistic outcomes of patients with chronic disease conditions.

Summary

Adherence to chronic medications is a major problem. Various strategies, such as Medication Therapy Management Programs, have been implemented in order to improve the clinical outcomes and also to reduce health care expenditures. The Lucas County MTM program is one such program providing services to patients diagnosed with diabetes, hypertension, and hyperlipidemia. Currently, no study has measured patient adherence to chronic disease medications in the Lucas County MTM program. This study will bridge this gap in literature.

Chapter-3

Methodology

This chapter will describe the methodology used in the study. It will focus on the study design, study subjects and settings, data collection, sampling, and data analysis. The methodology is based on the research objectives of the study.

The Lucas County MTM Program

The Lucas County MTM program is sponsored by the Lucas County employer group in Ohio. This program is provided by a coalition of independent community pharmacies in Toledo, Ohio. The participating pharmacies include The Pharmacy Counter, Kahler Pharmacy, Glenbyrne Pharmacy, Erie Drug, and Ryan Pharmacy. The Lucas County MTM program is offered to any employees of Lucas County who are enrolled in the program. Patients can enroll in the program for any condition such as chronic diseases, allergy etc. The interventions provided by pharmacists in the Lucas County MTM program are based on the previously successful MTM programs mentioned above.

The patients enrolled in the Lucas County MTM program are required to visit the pharmacy on six occasions during the one year time-period following enrollment. The initial visit is followed by five counseling sessions with the pharmacist. Individual timelines vary for each patient depending on their disease state and expert advice of the clinical pharmacist. A brief description of each visit is provided below:

Initial Visit (Baseline or Pre-Intervention)

At the initial visit, the patient is given an informed consent form to participate in the program. Also, the clinical outcomes, social history, and process measures of the patient is collected using intake forms. At the end of this visit, the patient's first visit with the pharmacist is scheduled.

Visit 1 (1st month)

Prior to the patient's first visit with the pharmacist, the pharmacist assesses the patient's demographic information, clinical markers, and social history. Also, at each visit the importance of process measures associated with clinical indicators are discussed on a patient specific basis.

As per national guidelines, interventions for diabetes and hypertension are typically scheduled every three months. However, for hyperlipidemia, interventions are scheduled based on risk assessment. Therefore, for patients with hyperlipidemia, the pharmacist uses a Hyperlipidemia risk assessment tool to identify their level of risk and frequency of visits. Their future appointments are based on their risk level. Also, at this visit the pharmacists discuss the patients' disease state, their therapy and management, and they also work with the patient to identify and establish their personal goals of therapy.

Visit 2 (3rd month)

The pharmacist provides patient counseling tailored specifically to the patient's disease state. During this follow-up visit, pharmacist re-evaluates disease state specific clinical markers and the treatment goals. The importance of diet and exercise is also reaffirmed during this visit. A follow-up drug therapy review is also conducted which includes, addressing any new medications/diagnoses since the last visit, answering any follow-up questions patients might have had since their last visit, determining if the current plan is working and if goals are being met.

Visit 3 (6th month)

The pharmacist evaluates the patient's clinical markers and provides follow-up information from the previous visit. Any new medications or changes to therapy are addressed. Along with the intervention the pharmacist also focuses on educating the patient about the importance of medication adherence and compliance with therapy.

Visit 4 (9th month)

The pharmacist provides follow-up patient counseling to ensure optimal pharmaceutical care. The importance of meeting goals, maintaining a consistent diet and exercise regimen, and discussing patient's success with therapy, if applicable, is the focus of this visit.

Visit 5 (12th month)

During this final visit, a final reassessment of drug therapy is conducted. New patient goals are established, if needed, or if the patient has not met his prior established goals a new plan is devised. The importance of medication adherence and compliance is discussed. Finally, the pharmacist provides a summary of the disease state and medications to the patient. Patients are encouraged to continue with the program if needed. Thus, the services provided by the independent pharmacy coalition participating in Lucas County MTM program are of great value; however there are no quantified results to illustrate if patients are being adherent to their medications in the Lucas County MTM program.

Study design

This was a longitudinal, retrospective study design. Prescription refill records of patients with diabetes, hypertension, and/or hyperlipidemia, participating in the Lucas County MTM program, were obtained from The Pharmacy Counter, an independent pharmacy located in Toledo, Ohio. Though, four other pharmacy sites participated in the MTM program, pharmacy refill records were obtained only from one site, The Pharmacy Counter, as less than 20 patients visit the other pharmacies to get their prescriptions filled.

Study subjects and settings

Lucas County MTM program is provided by the Toledo area network of independent pharmacies. One of the pharmacies where the MTM program is provided is the Pharmacy Counter in Toledo. The Pharmacy Counter is an independent pharmacy and has three sites in Toledo. The study subjects may visit any one of the three Pharmacy Counter locations. The Pharmacy Counter maintains a central database of all their patients visiting any of the three centers. The subjects used for this study were Lucas County employees and their dependants enrolled in the MTM program at the Pharmacy

Counter in Toledo. For the purpose of this study, these patients had either one or more of the following chronic diseases: Diabetes, Hypertension, and Hyperlipidemia.

Data Collection

Database

Adherence data was obtained from the Pharmacy Counter in the form of prescription refill records. The database consisted of prescription refill records of Toledo Lucas County employees with chronic diseases such as diabetes, hypertension, and/or hyperlipidemia. The database contained the patient ID of the Lucas County employee and their dependant, date of birth, gender, date of prescription refill, name of the medication, number of days supply of medications, and amount of co-pay.

Chart Reviews

The database provided by the Pharmacy Counter did not include clinical outcomes of patients; therefore, patient chart reviews were conducted to track the desired clinical outcomes of each patient and their diagnosis was determined. The Pharmacy Counter maintains patient charts and records the clinical outcomes (A1c, blood pressure, height, weight, cholesterol values) for all the patients. Patient charts were kept in house at the three sites of The Pharmacy Counter. Chart reviews were conducted for a period of one month from March-April, 2009 by the authors for all the patients whose prescription refill records were provided. Clinical outcomes such as A1c and blood pressure values were recorded on the data collection form (Appendix B).

Inclusion Criteria

Patients were eligible for the study if they were enrolled in the Lucas County MTM program for at least one year at one of the Pharmacy Counter sites. Other criteria included Lucas County employees and their dependants who were diagnosed with Diabetes, Hypertension, and/or Hyperlipidemia, and who had filled at least one prescription for a diabetes, hypertension, and/or hyperlipidemia medication since their enrollment in the MTM program.

Sampling

The total number of patients who were enrolled in the MTM program at the time of the study was 476. However, based on the inclusion criteria stated above, 272 patients were included in the analysis. It is possible that the remaining 204 (476-272) patients may have been enrolled in the MTM program for a different disease other than diabetes, hypertension, and hyperlipidemia, or may have less than one year refill data.

Data Analysis

SPSS v.16 and Microsoft Excel was used for performing data analysis. Adherence rates of patients were determined using Medication Possession Ratio (MPR). Patients with a MPR value of greater than 80% were considered adherent. Adherence of patients was considered medium if their MPR ranged from 50%-79% and low if their MPR was less than 50%. These cut off values are considered in adherence research and several studies in the past used these values to categorize adherence. [2, 7, 26, 44] The Wilcoxon signed rank test was conducted to measure the difference in adherence from year 1 to year 2.

Pearson correlation was conducted to address the second objective which was to measure the relationship between medication adherence (MPR) and the clinical outcomes such as change in A1c, change in systolic and diastolic blood pressure in a sample of patients with diabetes and hypertension. MPR was treated as a continuous variable, and the outcomes were calculated as a change and hence, change in A1c, change in systolic, and diastolic blood pressure were treated as continuous variables. Change in A1c was calculated as a difference in the A1c from baseline value to the last A1c value. Similarly, change in systolic and change in diastolic blood pressure were also calculated.

Multiple linear regression analyses were conducted to address the third objective, which was to determine if medication adherence affects clinical outcomes such as change in A1c, change in systolic, and change in diastolic blood pressure. MPR, age, gender, co-pay, and number of diseases were also included in all the three regression analysis.

Chapter-4

Results

This chapter describes the analyses performed on the data and presents the results of the study. Demographic characteristics of the study subjects will be presented, followed by their adherence to diabetes, hypertension, and hyperlipidemia medications. Association between clinical outcomes and the study variables will then be presented separately for diabetes and hypertension patients, followed by the predictors of clinical outcomes.

Table 1 shows the demographic characteristics of the study subjects. A majority of the study subjects were female (61%). Further, a majority of the study population was between the ages of 51 and 60 (46%).

Table 1: Demographic characteristics of study population

Characteristics		Frequency N (%) ***ΣN=272***
Gender	Male	106 (39)
	Female	166 (61)
Age (Years)	10-20	2 (0.7)
	21-30	3 (1.1)
	31-40	10 (3.7)
	41-50	59 (21.7)
	51-60	125 (46)
	61-70	67 (24.6)
	>70	6 (2.2)

Table 2 shows the distribution of the study population per disease state. A majority of the study subjects had hypertension (N=172)

Table 2: Number of patients per disease state

Disease State	Frequency (N)
Diabetes	104
Hypertension	172
Hyperlipidemia	156

*** ΣN>272 since some patients may appear more than once due to co-existing conditions.**

Adherence to Diabetic Medications

The following section presents the results of adherence to different classes of diabetic medications. Adherence was calculated separately for patients who were in the program for one year, two years, and three years. An average adherence was then calculated for each of these years. The Wilcoxon signed rank test was then conducted to measure whether there is a significant change in adherence from year 1 to year 2 for oral diabetic medications. Due to the limited sample size in insulin (N=3) and non-insulin injectable medication classes (N=6), an appropriate statistical test could not be conducted for these patients to check for the significant change in adherence from year 1 to year 2. Five patients were omitted from the adherence calculation as they had less than six months refill data for diabetic medications.

Table 3 shows the average adherence of patients taking oral diabetic medications. As seen from the table, patients who were in the program for only 1 year had high average adherence to oral diabetic medications (0.84). Further, patients who were in the program for two years had shown improved adherence from year 1 to year 2. This can be seen from their average adherence in year 1 (0.81) and year 2 (0.83). However, patients who were in the program for three years had shown decreased adherence as they stayed longer in the program. The adherence of these patients in year 1 was high (0.86). However, there was a steady decline in their average adherence from year 2 (0.74) to year 3 (0.69).

Table 3: Average Adherence to Non-Insulin Oral Diabetic Medications (ΣN=65)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=65	0.84	-	-
Patients with 2 years data N=36	0.81	0.83	-
Patients with 3 years data N=6	0.86	0.74	0.69

Due to the non-parametric distribution of the data for patients in the program for two years, the Wilcoxon signed rank test was conducted to measure the change in patient's adherence to oral diabetic medications from Year 1 to Year 2. There was no statistically significant change in patient's adherence from year 1 (mean=0.81, SD=0.21) to Year 2 (mean=0.83, SD=0.18); p=0.617. This indicated that there was no significant change in adherence to oral diabetic medications as a patient stayed in the program for a longer period of time.

Table 4 shows the average adherence to insulin. As seen from the table, patients who were in the program for only one year had a medium average adherence to insulin medications (0.57). Further, patients who were in the program for two years also had a medium average adherence both in year 1 (0.57) and in year 2 (0.53). In addition, there was a decrease in average adherence from year 1 to year 2 in these patients.

Table 4: Average Adherence to Insulin (ΣN=15)

	Year 1 average	**Year 2 average**
Patients with 1 year data N=15	0.57	-
Patients with 2 years data N=3	0.57	0.53

An appropriate statistical test could not be conducted to measure if the change in adherence from year 1 to year 2 was statistically significant due to the limited sample size of patients taking insulin medications in year 1 and year 2 (N=3).

Table 5 shows the average adherence to non-insulin injectable medications. As seen from the table, patients who were in the program for only one year and taking non-insulin injectable medications had a medium average adherence of 0.72. Patients who were in the program for two years still had medium adherence both in year 1 (0.69) and year 2 (0.71). Further, patients who were in the program for three years had improved average adherence in year 2 (0.61) from year 1 (0.53), however, their average adherence declined in year 3 (0.4).

Table 5: Average Adherence to Non-Insulin Injectable Medications (ΣN=19)

	Year 1 average	Year 2 average	Year 3 average
Patients with 1 year data N=19	0.72	-	-
Patients with 2 years data N=6	0.69	0.71	-
Patients with 3 years data N=1	0.53	0.61	0.4

An appropriate statistical test to measure the significant change in adherence from year 1 to year 2 could not be conducted for these patients because of the limited sample size of patients with one- and two- year data (N=6).

Adherence to Hypertension Medications

This section presents the results of adherence to different classes of hypertension medications. Similar to diabetic medications, adherence to hypertension medications was measured separately for each year that patients were in the program. An average adherence was then calculated for each year. The Wilcoxon signed rank test was then conducted to check if there was a significant change in adherence from year 1 to year 2.

Table 6 shows the average adherence to ACE inhibitors. From the table, patients who were in the program for only one year had a high average adherence (0.89) to ACE inhibitors. Also, patients who were in the Lucas County MTM program for two years had high average adherence in both year 1 (0.88) and year 2 (0.87). These patients maintained almost similar adherence for the two years they were enrolled in the program. Further, patients who were enrolled in the program for three years showed improved adherence as they stayed in the program for a longer period of time. These patients had an average adherence of 0.88 in the first year, which improved to 0.94 in the second year, and they had their highest average adherence in the third year (0.99). This indicated that for patients on ACE inhibitors, adherence improved the longer they stayed in the Lucas County MTM program.

Table 6: Average Adherence to ACE inhibitors (ΣN=61)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=61	0.89	-	-
Patients with 2 years data N=37	0.88	0.87	-
Patients with 3 years data N=7	0.88	0.94	0.99

Due to the non-parametric distribution of the sample, the Wilcoxon signed rank test was conducted to measure if there is a significant change in adherence from year 1 to year 2. There was no statistically significant change in adherence to ACE inhibitors from year 1 (mean=0.881, SD=0.18) to year 2 (mean=0.872, SD=0.19), p=0.474. This indicated that there was no positive or negative trend in adherence to ACE inhibitors from year 1 to year 2.

Table 7 shows the average adherence to beta blockers. As seen from the table, for patients who were in the program for only one year and taking beta blockers, their average adherence was 0.91, which indicated that they were highly adherent to their beta blocker medications. Further, patients who were in the program for two years also had high average adherence in both year 1 (0.91) and year 2 (0.86). However, there was a decline in their average adherence in year 2 from year 1. Patients who were in the program for three years had high average adherence in year 1 (0.96) which then reduced to a high average adherence of 0.84 in year 2, and in year 3 there was an increase in their average adherence to 0.96. This indicated that adherence of patients taking beta blockers increased as they stayed for a longer time in the Lucas County MTM program.

Table 7: Average Adherence to Beta Blockers (ΣN=62)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=62	0.91	-	-
Patients with 2 years data N=34	0.91	0.86	-
Patients with 3 years data N=10	0.96	0.84	0.96

Due to the non-parametric distribution of the sample, the Wilcoxon signed rank test was conducted to measure the change in adherence between year 1 and year 2. The results indicated that there was no statistically significant change in adherence to beta blockers between year 1 (mean=0.91, SD=0.169) and year 2 (mean=0.86, SD=0.25); p=0.189. This indicated that there was no positive or negative trend in adherence to beta blockers from year 1 to year 2.

Table 8 shows the average adherence to calcium channel blockers. From the table, the average adherence to calcium channel blockers among patients who were in the program for only one year was high (0.83). However, patients who were in the Lucas County MTM program for two years had high average adherence to calcium channel blockers for both year 1 (0.93) and year 2 (0.92). Further, there was an increase in average adherence from year 1 to year 2 in these patients. Only one patient was in the program for three years and this patient's adherence was high in year 1 (0.96), medium in year 2 (0.5), and high in year 3 (0.98). However, based on the results of patients who were in the program for two years, it can be said that the longer the patient stayed in the MTM program, the higher was their adherence to calcium channel blockers.

Table 8: Average Adherence to Calcium Channel Blockers (ΣN=29)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=29	0.83	-	-
Patients with 2 years data N=11	0.93	0.92	-
Patients with 3 years data N=1	0.96	0.5	0.98

Due to the low sample size of patients who were in the program for two years (N=11), an appropriate statistical test could not be conducted to measure if there was a significant change in adherence to calcium channel blockers from year 1 to year 2.

Table 9 shows the average adherence to angiotensin II receptor antagonist. The average adherence to angiotensin II receptor antagonist among patients who were in the program for a year was high (0.91). However, among patients who were in the program for two years, their average adherence decreased in year 2 (0.89) from year 1 (0.97). A different trend was observed among patients who were in the program for three years. Their average adherence to angiotensin II receptor antagonist was high in year 1 (0.99), followed by a decline in their average adherence in year 2 (0.93), followed by an increase to 0.99 in year 3.

Table 9: Average Adherence to Angiotensin II Receptor Antagonist (ΣN=30)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=21	0.91	**-**	**-**
Patients with 2 years data N=10	0.97	0.89	-
Patients with 3 years data N=1	0.99	0.93	0.99

Due to the limited number of patients with two-year data (N=10), it cannot be determined if the change in adherence from year 1 to year 2 was significant.

Table 10 shows the average adherence to thiazide diuretics. Patients who were in the program for one year had a high average adherence of 0.91. Further, patients who were in the program for two years also had a high average adherence in their first year (0.96), but had a slight decrease in their average adherence in year 2 (0.94). Patients who were in the program for three years had a high average adherence in year 1 (0.94), followed by an increase in average adherence in year 2 (0.96), followed by a decrease in average adherence in year 3 (0.93).

Table 10: Average Adherence to Thiazide Diuretics (ΣN=26)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=26	0.91	-	-
Patients with 2 years data N=16	0.96	0.94	-
Patients with 3 years data N=3	0.94	0.96	0.93

Due to the small sample size of patients with two- year data (N=16), the significance of their change in adherence from year 1 to year 2 could not be determined.

Adherence to Hyperlipidemia Medications

This section presents the results of the adherence to different classes of hyperlipidemia medications. Similar to diabetes and hypertension medications, adherence to hyperlipidemia medications was calculated separately for each year the patient was enrolled in the program. Average adherence was then calculated separately for each year. The Wilcoxon signed rank test was then conducted to measure if there is a significant change in adherence from year 1 to year 2 for statins.

Table 11 shows the results of average adherence to statin therapy. Patients who were in the program for one year had a high average adherence to statins (0.84). Further, patients who were in the program for two years had almost the same average adherence to statins in year 1 (0.86) and year 2 (0.85). However, patients who were in the program for a longer period of time showed decreased adherence across the years. They had a high average adherence in year 1 (0.84), which declined to 0.78 in year 2, and which further declined to 0.74 in year 3.

Table 11: Average Adherence to Statins (ΣN=83)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=83	0.84	**-**	**-**
Patients with 2 years data N=55	0.86	0.85	-
Patients with 3 years data N=9	0.84	0.78	0.74

Due to the non-parametric nature of the data, the Wilcoxon signed rank test was conducted to check if there was a significant change in adherence to statins from year 1 to year 2. The results indicated that there was no significant difference in adherence from year 1 (mean=0.86, SD=0.19) to year 2 (mean=0.85, SD=0.24), p=0.691. Thus, no trend was observed in adherence to statins if patients stayed in the Lucas County MTM program for a longer period of time.

Table 12 shows the average adherence to cholesterol absorption inhibitors. The average adherence of patients who were taking cholesterol absorption inhibitors and who were in the program for one year was high (0.84). However, for patients who were in the program for two years, average adherence was high in year 1 (0.86) but declined to a medium adherence in year 2 (0.73). Further for patients who were in the program for three years, average adherence was high in year 1 (0.88) and year 2 (0.91) but medium in year 3 (0.74).

Table 12: Average Adherence to Cholesterol Absorption Inhibitors (ΣN=21)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=21	0.84	**-**	**-**
Patients with 2 years data N=12	0.86	0.73	-
Patients with 3 years data N=2	0.88	0.91	0.74

An appropriate statistical test could not be conducted to check if there is a statistically significant change in adherence to cholesterol absorption inhibitors from year 1 to year 2 due to the low sample size of patients with two-year data (N=12).

Table 13 shows the average adherence to fibrates. Patients who were in the program for one year had high average adherence to fibrates (0.92). Similarly, patients who were in the program for two years also had high average adherence in year 1 (0.93) but their average adherence declined to 0.87 in year 2. However, patients who were in the program for three years had high average adherence in year 1 (0.98) with a decline in average adherence to 0.85 in year 2, followed by an increase in average adherence to 0.97 in year

3. This indicated that as patients stayed longer in the program, their adherence to fibrates increased.

Table 13: Average Adherence to Fibrates (ΣN=18)

	Year 1 average	**Year 2 average**	**Year 3 average**
Patients with 1 year data N=21	0.92	**-**	**-**
Patients with 2 years data N=12	0.93	0.87	-
Patients with 3 years data N=2	0.98	0.85	0.97

Due to the small sample size of patients with two- year data (N=12), appropriate statistical analysis could not be conducted to check whether the change in adherence from year 1 to year 2 is statistically significant.

Change in A1c among Diabetes Patients

Table 14 shows the number of patients who were at goal A1c (<=7.0) and not at goal A1c (>7) at the start and end of the study period. The number of patients who had A1c of greater than 7 (not at goal) increased by one patient from the start of the study period to the end of the study period. Correspondingly, the number of patients with A1c <=7 (goal) decreased by one patient from the start to the end of the study period.

Table 14: Goal Attainment among Diabetic Patients

A1c	Number of patients (start of the program) ΣN=104	Number of patients (end of the program) ΣN=104
A1c >7	44	45
A1c<=7	60	59

Table 15 shows the change in A1c among diabetic patients. At the end of the study period, 35 patients showed an improvement in their A1c and this improvement was towards goal. Further, 14 patients showed an improvement in their A1c but this improvement was not at goal. Only three patients had no change in their A1c but they were within goal A1c of <=7. Also, only one patient showed no change in A1c but the A1c was not at goal. Similarly, the number of patients who had worse A1c but were still within goal was 21. However, the number of patients who had worse A1c but were not at goal was 30.

Table 15: Change in A1c among Diabetic Patients

Change in A1c	Number of patients ΣN=104
Improvement (Decrease: A1c<=7)	35
Improvement (Decrease: A1c>7)	14
No Change (A1c<=7)	3
No Change (A1c>7)	1
Worse (Increase: A1c**<=7**)	21
Worse (Increase: A1c>7)	30

Change in Systolic and Diastolic Blood Pressure among Hypertension Patients

Table 16 shows the number of hypertensive diabetic patients in different stages of hypertension at the start and the end of the study period. According to JNC-7 guidelines, patients with hypertension and diabetes have a different goal blood pressure (systolic goal blood pressure <130 mm Hg, diastolic goal blood pressure <80 mm Hg) compared to patients with only hypertension whose goals are 140/90 mm Hg. Hence, change in systolic and diastolic blood pressure was calculated separately for both these groups due to the difference in their goal blood pressure.

The number of patients who had normal blood pressure remained the same from the start to the end of the study period. Further, the number of patients in pre-hypertension stage decreased from 35 at the start of the study period to 31 by the end of the study period. These patients moved to stage-1 hypertension. Further, four patients moved from stage-2 hypertension to stage-1 hypertension by the end of the study period resulting in a total increase of 8 patients in stage-1 hypertension by the end of the study period.

Table 16: Stages of Hypertension among Hypertensive Diabetic Patients

Stages of Hypertension	Number of patients (start of the study period) ΣN=92	Number of patients (end of the study period) ΣN=92
Normal (systolic <120, diastolic < 70)	24	24
Pre-hypertension (systolic 120-129, diastolic 70-79)	35	31
Stage-1 Hypertension (systolic 130-149, diastolic 80-89)	24	32
Stage-2 Hypertension (systolic >=150, diastolic >=90)	9	5

Table 17 shows the change in systolic blood pressure among hypertensive diabetic patients. At the end of the study period, 33 patients showed improvement in their systolic blood pressure to goal. Further, 20 patients showed improvement in their systolic blood pressure but their improvement was not at goal. Only one patient had no change in their systolic blood pressure but within goal. Twelve patients had worse systolic blood pressure but they were still within goal. Further, 26 patients had worse systolic blood pressure but they were not at goal.

Table 17: Change in Systolic Blood Pressure among Hypertensive Diabetic Patients

Change in Systolic Blood Pressure	**Number of patients** **ΣN=92**
Improvement (Decrease: Systolic BP<130)	33
Improvement (Decrease: Systolic BP>=130)	20
No Change (Systolic BP<130)	1
No Change (Systolic BP>=130)	0
Worse (Increase: Systolic BP<130)	12
Worse (Increase: Systolic BP>=130)	26

Table 18 shows the change in diastolic blood pressure among hypertensive diabetic patients. Twenty-two patients showed improvement in diastolic blood pressure and this improvement was towards goal at the end of the study period. Only one patient had no change in diastolic blood pressure but was still within goal. Six patients had no change in diastolic blood pressure but were not at goal. Eighteen patients had worse diastolic blood pressure but were still within goal compared to 45 patients who had worse diastolic blood pressure but were not at goal

Table 18: Change in Diastolic Blood Pressure among Hypertensive Diabetic Patients

Change in Diastolic Blood Pressure	Number of patients ΣN=92
Improvement (Decrease: Diastolic BP<80)	22
Improvement (Decrease: Diastolic BP>=80)	0
No Change (Diastolic BP<80)	1
No Change (Diastolic BP>=80)	6
Worse (Increase: Diastolic BP<80)	18
Worse (Increase: Diastolic BP>=80)	45

Table 19 shows the different stages of hypertension among patients with hypertension. The number of patients who had normal blood pressure decreased from the start of the study period (36) to the end of the study period (33). Further, patients in the pre-hypertension stage increased from 35 at the start of the study period to 40 at the end of the study period. The number of patients in stage-1 hypertension also decreased from 9 to 6 by the end of the study period. Also, 1 patient moved to stage-II hypertension by the end of the study period.

Table 19: Stages of Hypertension among Hypertensive Patients

Stages of Hypertension	Number of patients (start of the study period) ΣN=80	Number of patients (end of the study period) ΣN=80
Normal (systolic <120, diastolic < 80)	36	33
Pre-hypertension (systolic 120-139, diastolic 80-89)	35	40
Stage-1 Hypertension (systolic 140-159, diastolic 90-99)	9	6
Stage-2 Hypertension (systolic >=160, diastolic >=100)	0	1

Table 20 shows the change in systolic blood pressure among hypertensive patients. For 39 patients, systolic blood pressure improved by the end of the study period and this improvement was towards goal. Four patients showed improvement in their systolic blood pressure but they were not at goal. Only one patient had no change in the systolic blood pressure but was still at goal by the end of the study period. One patient showed improvement in the systolic blood pressure but was not at goal. Nineteen patients had worse systolic blood pressure but were still at goal whereas 16 patients had worse systolic blood pressure but were not at goal by the end of the study period.

Table 20: Change in Systolic Blood Pressure among Hypertensive Patients

Change in Systolic Blood Pressure	**Number of patients** **ΣN=80**
Improvement (Decrease: Systolic BP<140)	39
Improvement (Decrease: Systolic BP>=140)	4
No Change (Systolic BP<140)	1
No Change (Systolic BP>=140)	1
Worse (Increase: Systolic BP<140)	19
Worse (Increase: Systolic BP>=140)	16

Table 21 shows the change in diastolic blood pressure among patients with hypertension. Thirty patients showed improvement in diastolic blood pressure and were at goal by the end of the study period. Two patients had no change in the diastolic blood pressure but were still at goal. Further, 36 patients had worse diastolic blood pressure but were goal whereas 12 patients had worse diastolic blood pressure but were not at goal by the end of the study period.

Table 21: Change in Diastolic Blood Pressure among Hypertensive Patients

Change in Diastolic Blood Pressure	Number of patients ΣN=80
Improvement (Decrease: Diastolic BP<90)	30
Improvement (Decrease: Diastolic BP>=90)	0
No Change (Diastolic BP<90)	2
No Change (Diastolic BP>=90)	0
Worse (Increase: Diastolic BP<90)	36
Worse (Increase: Diastolic BP>=90)	12

Correlation between Change in A1c and MPR among Diabetic Patients

This section presents the results of the correlation analysis to test the relationship between the dependant variable, change in A1c, and the independent variables MPR, age, gender, co-pay, and number of diseases. Change in A1c for each patient was calculated by taking a difference between the baseline A1c and the last A1c recorded for that patient. For some patients, MPR was calculated even before the patient's baseline A1c was recorded. Hence, for the purpose of the correlation and regression analysis, MPR for each patient was re-calculated only for the same period during which their A1c was recorded. Descriptive statistics indicated that the data for MPR and co-pay was negatively skewed affecting the normal distribution of the sample. The Grubb's test indicated the MPR of five patients to be significantly skewed and co-pay of four patients to be significantly skewed. Hence, these nine patients' records were removed to make the data normally distributed. Pearson correlation was then conducted to determine the relationship between change in A1c and the other independent variables mentioned above.

Table 22 shows the results of the correlation analysis. There was a statistically significant positive relationship between adherence (MPR) and age (r=0.387, p=0.000). This indicated that as age increased, patients were more adherent to their diabetic medications. MPR was also found to have a significant negative relationship with gender (r=-0.167, p=0.021). This indicated that males had higher adherence to their diabetic medications. Further, there was a significant negative relationship between age and gender (r=-0.148, p=.042). This indicated that among diabetic patients enrolled in the Lucas County MTM program, the older population was predominantly male. There was also a significant positive relationship between age and number of diseases (r=0.278, p=0.000). This indicated that as age increased, the number of diseases also increased.

Table 22: Correlation Results for Diabetic Patients (ΣN=190)

	Change in A1c	**MPR**	**Age**	**Gender**	**Co-pay**	**Number of diseases**
Change in A1c	1	0.009	-0.082	0.027	0.104	-0.014
MPR	0.009	1	**0.287****	**-0.167***	0.012	0.124
Age	-0.082	0.287**	1	**-0.148***	0.110	**0.278** **
Gender	0.027	-0.167*	-0.148*	1	-0.109	-0.142
Co-pay	0.104	0.012	0.110	-0.109	1	0.057

** Significant at 0.01 level * Significant at 0.05 level; ΣN>104 since some patients may have filled more than one medication.

Predictors of Change in A1c among Diabetic Patients

A multiple linear regression was conducted to determine the predictors of change in A1c among diabetic patients. Table 23 shows the results of the regression analysis. None of the independent variables namely MPR, age, gender, co-pay, and number of diseases were found to be significant predictors of change in A1c. The overall model R^2 was 0.022 indicating that 2.2 % of the variance in the change in A1c can be accounted for by the independent variables.

Table 23: Results of Multiple Linear Regression Predicting Change in A1c (ΣN=190)

Variables	Standardized Regression Coefficients	Standard error	p-value
MPR	0.042	0.688	0.583
Age	-0.104	0.019	0.190
Gender	0.032	0.340	0.668
Co-pay	0.118	0.004	0.112
Number of diseases	0.008	0.293	0.918

Correlation between Change in Systolic Blood Pressure; Change in Diastolic Blood Pressure, and MPR among Hypertension Patients

This section shows the results of the correlation analysis. A Pearson correlation was conducted to determine the relationship between the dependant variables, change in systolic blood pressure and change in diastolic blood pressure, and the independent variables, MPR, age, gender, co-pay and number of diseases. Change in systolic and diastolic blood pressure were calculated based on the difference between the baseline to the last blood pressure reading. Similar to the change in A1c calculation, for some patients, MPR was calculated even before the patient's baseline blood pressure was recorded. Hence, for the purpose of the correlation and regression analysis, MPR for each patient was re-calculated only for the same period during which their blood pressure was recorded.

Table 24 shows the results of the correlation analysis. Change in systolic blood pressure was found to have a significant positive correlation with change in diastolic blood pressure (r=0.553, p=0.000). This indicated that an increase in diastolic blood pressure resulted in an increase in systolic blood pressure. Further, change in systolic blood pressure was also found to have a significant positive correlation with gender (r=0.134 p=0.024). Since gender was coded as "1-Male" and "2-Female", a positive correlation indicated, females had worse systolic blood pressure compared to males. Also, change in systolic blood pressure had a significant positive correlation with co-pay (r=0.118, p=0.048). Thus, as co-pay increased, patients had worse systolic blood pressure. Change in systolic blood pressure was also found to have a significant negative correlation with number of diseases (r=-0.132, p=0.026). This indicated that as the number of diseases increased, systolic blood pressure increased.

MPR was found to have a significant negative relationship with diastolic blood pressure (r=-0.178, p=0.003). This indicated that as adherence to hypertension medications increases, diastolic blood pressure decreases and it improves. Further, MPR had a significant negative relationship with gender (r=-0.138, p=0.020). This indicated that males are more adherent to their medications than females. MPR was also found to have a significant positive correlation with co-pay ($r=0.141$, $p=0.018$). This indicated that as co-pay increased, patients were more adherent to their medications. MPR was also found to have a significant positive correlation with the number of diseases ($r=0.139$, $p=0.019$). Thus, as the number of diseases increased, patients were more likely to be adherent to their medications.

Age was found to have a significant negative correlation with gender ($r=-0.146$, $p=0.014$). Thus, among hypertension patients who were enrolled in the Lucas County MTM program, older patients were predominantly males. Age was also found to have a significant positive relationship with the number of diseases ($r=0.119$, $p=0.045$). Thus, older patients had a higher number of diseases compared to the younger patients. Gender was found to have a significant negative relationship with the number of diseases ($r=-0.131$, $p=0.027$) indicating that males had a higher number of diseases than females.

Table 24: Correlation Results for Hypertension Patients (ΣN=283)

	Change in Systolic BP	Change in Diastolic BP	MPR	Age	Gender	Co-pay	Number of Diseases
Change in Systolic BP	1	**0.553****	-0.063	-0.056	**0.134***	**0.118***	**-0.132***
Change in Diastolic BP	0.553**	1	**-0.178****	-0.081	0.095	0.042	-0.017
MPR	-0.063	-0.178**	1	0.055	**-0.138***	**0.141***	**0.139***
Age	-0.056	-0.081	0.055	1	**-0.146***	-0.052	**0.119***
Gender	0.134*	0.095	-0.138*	-0.146*	1	0.040	**-0.131***
Co-pay	0.118*	0.042	0.141*	-0.052	0.040	1	0.083
MPR*Number of Diseases	**-0.142***						

** Significant at 0.01 level * Significant at 0.05 level; ΣN>172 since some patients may have filled more than one hypertension medication

Predictors of Change in Systolic Blood Pressure and Diastolic Blood Pressure among Hypertension Patients

This section presents the results of multiple linear regression to determine the predictors of change in systolic blood pressure and diastolic blood pressure.

Table 25 shows the results of multiple linear regression predicting the change in systolic blood pressure. The R^2 for the overall model was 0.338 indicating that 33.8% of the variance in change in systolic blood pressure was accounted for by the independent variables. The ANOVA table further indicated that the overall model was significant at p=0.000. Change in diastolic blood pressure (β = 0.550, p = 0.000) was found to be a significant predictor of change in systolic blood pressure. This indicated that on average for every one unit increase in the change in diastolic blood pressure, the change in systolic blood pressure increased by 0.55 units. In other words, as systolic blood pressure increased, diastolic blood pressure also increased correspondingly.

Also, number of diseases (β = -0.130, p = 0.01) was found to be a significant predictor of change in systolic blood pressure. This indicated that on an average for every one unit increase in the number of diseases, the change in systolic blood pressure decreased by 0.13 units. In other words, as the number of diseases increased, systolic blood pressure decreased.

Table 25: Results of Multiple Linear Regression Model Predicting Change in Systolic Blood Pressure (ΣN=283)

Variables	Standardized Regression Coefficients	Standard error	p-value
MPR	0.049	4.659	0.340
Age	0.016	0.122	0.744
Gender	0.070	1.949	0.166
Co-pay	0.097	0.024	0.054
Number of diseases	-0.130	1.229	**0.010**
Change in Diastolic Blood Pressure	0.550	0.083	**0.000**

** Significant at 0.01 level * Significant at 0.05 level; ΣN>172 since some patients may have filled more than one hypertension medication.

Table 26 shows the results of the multiple linear regression predicting the change in diastolic blood pressure. The R^2 for the overall model was 0.335 indicating that 33.5% of the variance in change in diastolic blood pressure was accounted for by the independent variables. The ANOVA table further indicated that the overall model was significant at p=0.000. Change in systolic blood pressure ($\beta = 0.55$, $p = 0.000$) was found to be a significant predictor of change in diastolic blood pressure. This indicated that on an average for every one unit increase in the change in systolic blood pressure, the change in diastolic blood pressure increased by 0.552 units. In other words, as systolic blood pressure increased, diastolic blood pressure also increased correspondingly.

Also, MPR ($\beta = -0.151$, $p = 0.003$) was found to be a significant predictor of change in diastolic blood pressure. This indicated that on an average for every one unit increase in MPR, the change in diastolic blood pressure decreased by 0.15 units. In other words, as MPR increased, there was a decrease in diastolic blood pressure.

Table 26: Results of Multiple Linear Regression Model Predicting Change in Diastolic Blood Pressure (ΣN=283)

Variables	Standardized Regression Coefficients	Standard error	p-value
MPR	-0.151	2.775	**0.003**
Age	-0.051	0.074	0.305
Gender	0.004	1.182	0.934
Co-pay	-0.012	0.015	0.814
Number of diseases	0.085	0.748	0.096
Change in Systolic Blood Pressure	0.552	0.030	**0.000**

** Significant at 0.01 level * Significant at 0.05 level; ΣN>172 since some patients may have filled more than one hypertension medication.

Summary

The trend analysis of the adherence to diabetes, hypertension, and hyperlipidemia medications indicated that there was no significant difference in adherence to any class of diabetes, hypertension, and hyperlipidemia medications from year 1 to year 2. This indicated that no positive or negative trend was observed in adherence to these medications.

Among patients with diabetes, adherence to diabetic medications had significant correlation with age and gender of the patients. No significant predictors were found for change in A1c among diabetic patients.

Among patients with hypertension, change in systolic blood pressure was found to be significantly correlated with change in diastolic blood pressure, gender, co-pay, and number of diseases. Also, change in diastolic blood pressure was found to be significantly correlated with adherence (MPR) to anti-hypertension medications. MPR was also found to be significantly correlated with gender, co-pay, and the number of diseases.

In the regression models, change in diastolic blood pressure and number of diseases were found to be significant predictors of change in systolic blood pressure. Further, change in systolic blood pressure and MPR were found to be significant predictors of change in diastolic blood pressure.

Chapter-5

Discussion

This chapter presents a discussion of the results obtained in the study and the conclusions drawn from the results. The limitations of the study and recommendations for future research are also presented in this section. The discussion is based on the objectives of the study.

Demographic Results

A majority of the patients (46%) in the Lucas County MTM program were between 51 and 60 years of age followed by 24.6% of the patients who were between 61 and 70 years old. According to the American Diabetes Association, about 23.1% of all people above age 60 have diabetes.[72] Further, national demographics of hypertension indicates that hypertension is highly prevalent among patients 55 years and older.[73] Thus, the subjects included in this study are a good representation of the national population.

Also, other employer sponsored MTM programs such as the Asheville project [74], and the Diabetes Ten City Challenge[75] have shown a similar age range for their study sample.

Since, this study is also an employer-sponsored MTM program, the study sample is a good representation of employees with chronic disease conditions. Further, this study had more females (61%) than males. Literature has shown that females take a more active part in their own healthcare compared to males.[76]

Adherence to Diabetic Medications

The average adherence to oral diabetic medications increased for patients who were in the program for two years, indicating that the pharmacist interventions were effective in improving the adherence to oral diabetic medications. However, this change was not significant due to the low sample size. Contrary to the above finding, the average adherence to oral diabetic medications decreased as patients were in the program for all three years. A systematic literature review conducted on adherence to diabetic medications indicated that on an average, adherence to oral diabetic medications range from 36-93%.[23] Further, it also indicated that adherence to oral diabetic medications decreased over a period of time.[23] Although shown in the literature, since there were only six patients in our study with all three years data, this trend cannot be generalized to the entire diabetic population of the Lucas County MTM program. There might be other factors contributing to the low adherence for these six patients such as number of medications, medication changes, side effects, complex medication regimen, and income which are not considered in this study.

The average adherence to insulin therapy was medium (0.57). Further, there was a decrease in average adherence from year 1 to year 2. Several side effects are associated with insulin therapy such as weight gain, which might contribute to the low adherence observed. Hypoglycemia can also occur due to insulin therapy, resulting in confusion, nausea, hunger, and tiredness. Patients may also experience blurred vision due to the sudden drop in their glycemic level.[77] All the above mentioned side effects together might impact adherence to insulin therapy. Literature has shown that adherence to insulin therapy is lower than oral diabetic medications which is similar to our study findings.[78]

Patients had medium adherence to non-insulin injectable medications (0.72). A majority of the patients in the Lucas County MTM program used Exenatide which is an injectable form of non-insulin medication. Similar to insulin therapy, several side effect are associated with Exenatide, the most prominent being gastrointestinal tract upset. Other side effects include hypoglycemia, diarrhea, dizziness, headache, and heartburn.[79] A previous study which measured adherence patterns for Exenatide, indicated that over a period of 12 months, the average MPR was 0.68, which is slightly lower than our study average MPR (0.72) for a 12 month period.[80] The higher average MPR in our study could be because Exenatide is also known to be associated with weight loss. A majority of the patients enrolled in the Lucas County MTM program were overweight or obese. Hence, despite side effects, patients may have still taken Exenatide for weight loss.

Adherence to Hypertension Medications

This study found a high average adherence (0.89) to ACE inhibitors throughout enrollment period. Further, adherence to ACE inhibitors also increased the longer the patient stayed in the program, indicating that pharmacist interventions may have been effective in improving adherence for these patients. One possible reason for the high adherence could be because ACE inhibitors are inexpensive and also well tolerated by patients. A previous study which measured adherence to medications and clinical outcomes of patients with diabetes showed that only 23% of the patients taking ACE inhibitors were non-adherent.[80] Another study which measured adherence to ACE inhibitor therapy for heart failure indicated an average adherence of 85-100%. [81]

Similar to ACE inhibitors, beta blockers also showed high average adherence (0.91) for all years. However, adherence to beta blockers decreased for patients in the second year of their treatment. Adherence then improved for patients who continued in the program for 3 years. A potential reason for this trend could be because beta blockers are known to cause rebound hypertension when patients abruptly stop taking them. Successful pharmacist interventions might have helped the patients to increase their adherence from year 2 to year 3. Further, the reduced adherence in year 2 could be because, as per JNC-7 guidelines, therapy begins with thiazide diuretics followed by ACE inhibitors or angiotensin II receptor antagonists followed by beta blockers.[82] Hence, by the time, a patient starts on beta blockers, he/she might be taking several other hypertension medications, thus leading to a complex medication regimen. Hence, their adherence in year 1 is high as they begin the beta blocker therapy. However, as time proceeds, their adherence declines.

A similar trend was also seen with calcium channel blockers. Overall, patients taking calcium channel blockers were highly adherent in all the years of therapy. Patients with only 1 and 2 year refill data had almost similar adherence in the two years. Since, there was only one patient record for all three years, it cannot be concluded whether staying in the program for a longer period of time showed improved adherence. However, a previous study which measured the long term patient adherence with prescribed regimens of calcium channel blockers indicated a decline in adherence as the length of the therapy increased, although this change was not found to be significant.[83]

Average adherence was high for thiazide diuretics across all years. One potential reason could be because, according to JNC-7 guidelines, for most patients diagnosed with hypertension, treatment begins with thiazide diuretic alone or in combination with other anti-hypertensive medications. A previous study which measured adherence to anti-hypertensive medications such as thiazide diuretics, beta blockers, calcium channel blockers, angiotensin II receptor blockers, also indicated high adherence to thiazide diuretics.[84] Further in this study, high average adherence was also observed for other classes of anti-hypertensive medication such as beta blockers (0.94), calcium channel blocker (0.96), and angiotensin receptor blockers (0.95). The results of this study are comparative to our study as high average adherence was seen for all the above classes of hypertension medications. Even though patients were found to be highly adherent to hypertension medications, there was a decrease in adherence as the number of years in the program increases. Hence, pharmacists could target the patients who are in the program for a longer period of time to improve their adherence.

Adherence to Hyperlipidemia Medications

Adherence to statin therapy was high in the first year that the patients were enrolled in the program. However, a steady decline in average adherence was seen as patients stayed in the program for a longer period of time. This is consistent with literature where studies have shown that about 40-75% of the patients discontinue statin therapy after 1 year of the treatment. [85-87] Another study which measured adherence with statin therapy in elderly patients indicated a two year adherence rate of 36%. [88] Literature has shown that some of the predictors of poor statin adherence are toxic effects of medication, treatment duration, and socio-economic factors.[89] However, in spite of the low adherence shown in the literature, our study still showed high adherence in the second year of treatment, indicating that pharmacist interventions, may have helped the patients to maintain high adherence in the second year of their treatment.

Adherence results have clearly indicated that patients enrolled in the Lucas County MTM program showed high adherence to most classes of diabetic, hypertension, and hyperlipidemia medications.

Change in A1c Among Diabetic Patients

Approximately 47% of patients with diabetes showed improvement in A1c, with 34% within goal and 13.5% not at goal. Other successful employer-sponsored MTM programs such as the Asheville project [74] also had 50% of their patients show an improvement in A1c at every visit. Despite being employed, under the care of a physician, and having a health plan that included good prescription and medical benefits, 43% of the patients still did not reach the goal A1c of <=7. Usually, patients with diabetes require multiple medications in order to see any significant improvement in their A1c. Hence, it is possible that those patients whose A1c was not at goal were on one or two medications which might not have affected their A1c much to bring it to goal. Further, other additional factors such as severity of the disease, co-morbid conditions, income, race/ethnicity, lifestyle modifications, and side effects could also affect A1c for these patients.

In summary, 59 out of 104 patients were at goal A1c at the end of the study period, whereas 30 out of 104 patients had increased A1c and were not at goal at the end of the study period. Thus, future interventions by the pharmacists should be directed towards these 30 patients who had worse outcomes and who were not at goal A1c.

Change in Systolic and Diastolic Blood Pressure Among Hypertension Patients

Among patients who had hypertension and diabetes, 50% of the patients were within the goal for systolic blood pressure while 45% of the patients were at goal for diastolic blood pressure at the end of the study period. Our results are similar to the INVEST trial where nearly 50% of the patients achieved the blood pressure goal as per the JNC-7 guidelines.[90] In addition, our results are better than the results obtained in the two studies conducted in real-world setting.[91-92] One of the studies measured the control of cardiovascular risk factors in patients with diabetes and hypertension. In this study, only 26.7% of the patients reached the systolic and diastolic blood pressure goals. [91] Another study, which evaluated the Health Employer Data Information Set (HEDIS) measures for 2000 to assess goal achievement in a practice-based setting indicated that only 22% of the patients met the more stringent systolic and diastolic blood pressure goals among patients with diabetes and hypertension.[92] Compared to other studies, our study has a higher number of patients with diabetes and hypertension reaching systolic and diastolic goal.

Further, among patients with only hypertension, 74% of them reached the systolic blood pressure goal and 85% of them reached the diastolic blood pressure goal. One possible explanation to the higher number of patients reaching the diastolic blood pressure goal than the systolic blood pressure goal could be because, in our study, most of the patients had controlled diastolic blood pressure when they enrolled in the program. Hence, it is possible that they continued to be at goal at the end of the study period.

This study also determined the association between adherence and clinical outcomes. Further, predictors of change in clinical outcomes were also determined for patients with diabetes and hypertension.

Correlation between Change in A1c and MPR Among Diabetic Patients

Adherence to diabetic medications was found to be significantly correlated with age and gender. This indicates that in the Lucas County MTM program, older patients were more adherent to their diabetic medications. Further, among the study subjects, males were found to be more adherent to diabetic medications than females. The findings of this study are similar to a previous study by Rozenfeld et al which measured the adherence to antidiabetic medications and glycemic control in a managed care population. In the Rozenfeld study, age was significantly correlated with adherence indicating that older patients are more adherent to their medications. However, Rozenfeld study did not find any significant correlation between gender and adherence.[93] A study by Walker et al which measured the predictors and outcomes of adherence in a diabetes prevention program also indicated that older patients were more adherent to diabetic medications compared to the younger population. [94] A study by Hellman et al which measured the effect of ethnicity on adherence to diabetic medications indicated that gender had a significant relationship with adherence.[95] A study by Polluzi et al which measured adherence to oral diabetic medications showed that males were more adherent to oral diabetic medications compared to females. The Polluzi study also indicated that older patients were more adherent to oral diabetic medications compared to the younger population.[96]

Hence, it was not surprising that we found a significant positive correlation between age, gender, and MPR as is evident from the literature.

Predictors of Change in A1c among Diabetic Patients

There were no predictors of change in A1c among diabetic patients. Due to the retrospective nature of the study, several other factors could not be considered which might have significantly predicted change in A1c. Previous MTM programs such as Asheville, and Diabetes Ten City Challenge, showed improvement in clinical outcomes, however, they were non-significant. However, other variables such as reduced number of sick days, reduced number of hospitalizations and ER visits, improved patient satisfaction, increased return on investment to employers, and increased employer satisfaction were found to be significant in these studies.[74,75] Thus, literature has shown that there are other significant predictors of A1c which were not considered in this study. Had the factors mentioned above been included in the model, there might have been significant predictors to change in A1c.

Association and Predictors of Change in Systolic Blood Pressure; Change in Diastolic Blood Pressure, and MPR among Hypertension Patients

Change in systolic blood pressure was significantly correlated with change in diastolic blood pressure. Thus, as systolic blood pressure increases, diastolic blood pressure also increases. There is a linear relationship between systolic and diastolic blood pressure and this is indicated in a previous study which measured the linear relationship between systolic and diastolic blood pressure in an ambulatory data.[97] Further, in our study, change in systolic blood pressure was also a predictor of change in diastolic blood pressure and vice versa. Change in systolic blood pressure was also found to have a significant correlation with gender indicating that females have increased systolic blood pressure compared to males. A previous study which measured if males and females differ on their systolic and diastolic blood pressure indicated that systolic blood pressure is higher in females than males.[98]

Change in systolic blood pressure was also found to be correlated with co-pay indicating higher the co-pay, higher the systolic blood pressure. One possible explanation to this finding could be linked to the nature of the study population. Majority of the study population consisted of blue-collar workers employed with Lucas County. Though not considered in this study, majority of the patients might have had low annual household income and therefore were not able to afford the higher co-pay associated with some of the hypertension medications. Hence, as co-pay goes higher, these patients may not have got their prescription filled resulting in higher systolic blood pressure.

Further, systolic blood pressure was also found to be correlated with the number of diseases indicating that as the number of diseases goes higher, there is a better control of systolic blood pressure. One possible reason to this could be based on another finding in our study where a significant positive correlation was seen between MPR and number of diseases indicating that as number of diseases goes high, MPR increases. Hence, as a patient begins to develop more chronic diseases, he/she may need a greater number of medications, and therefore, they may begin to take their health more seriously.

Ultimately, this leads to greater adherence findings. Further, in our study, the interaction of adherence and number of diseases had a significant relationship with systolic blood pressure change. Hence, for patients with higher number of diseases, due to their high adherence to hypertension medications, there is a better control on their systolic blood pressure. Further, in our study, number of diseases was also found to be a significant predictor of change in systolic blood pressure. Our study findings corroborates with a previous study conducted by Fung et al., which measured the effect of adherence on systolic blood pressure. In this study, it was found that higher the number of drugs, patients are more likely to be adherent. Also, patients who were more adherent had better controlled systolic blood pressure.[99]

A significant correlation was also found between change in diastolic blood pressure and MPR indicating that higher adherence to hypertension medications resulted in lower diastolic blood pressure. Our findings are similar to a previous study which assessed the role of medication adherence as a determinant of blood pressure control. In this study, higher adherence to anti-hypertensive medications was associated with a better controlled diastolic blood pressure than systolic blood pressure. Further, higher adherence was also found to be a significant predictor of diastolic blood pressure and not systolic blood pressure [100] which is also similar to the findings of our study where higher MPR was significantly predicting diastolic blood pressure change.

A significant correlation also existed between MPR and gender indicating that males in the Lucas County MTM program were found to be more adherent to anti-hypertensive medications than females. This finding corroborates with a previous study which measured the adherence to anti-hypertensive medications. In this study gender was significantly associated with adherence to hypertension medications with males being more adherent than females.[101]

Further, based on the correlation results, patients with higher co-pay had a high adherence to hypertension medications. The study population consisted of employees ranging from maintenance workers to lawyers and judges. Looking at the income of these patients might actually reveal that those patients who pay a higher co-pay and are adherent to their medications might be having a higher income. In order to explain this finding better, future research should involve including income as an important determinant for medication adherence.

In addition, similar to diabetic patients, age was found to be significantly correlated with higher number of diseases among hypertension patients indicating that older patients in the Lucas County MTM program had more number of diseases than the younger population.

Study Limitations

Similar to other retrospective studies, our study too has several limitations. Due to the retrospective nature of the study, some important variables such as race/ethnicity, income, severity of the disease, number of sick days, number of hospitalizations and ER visits, and patient satisfaction could not be obtained which might have resulted in non-significant predictors for change in A1c. Also, MPR is not an accurate method to determine the actual adherence to medications. Patients might not be taking their pills but still come for their refills as there are added benefits in participating in the Lucas County MTM program such as free coupons, and reduced cost of medications. Also, the yearly time period for calculating adherence was different for each patient. For example, for one patient, the one year time period had refill records available for only nine months while for another patient, it was available for 11 months. Due, to the longitudinal nature of the study, this limitation could not be controlled. Further, generalizability of the results to all patients with diabetes, hypertension, and hyperlipidemia might not be possible due to the unique nature of the study population (employees). However, the results can still be generalized to employees with similar characteristics as our study population and who are diagnosed with diabetes, hypertension, and hyperlipidemia.

Conclusion

This study determined the adherence to chronic disease medications among enrollees of the Lucas County MTM program. From the results, patients enrolled in the Lucas County MTM program had high adherence to their hypertension medications. This study also identified associations and predictors of clinical outcomes among diabetes and hypertension patients. Future pharmacist interventions should be directed towards females and younger population with diabetes and hypertension in order to improve their clinical outcomes.

Recommendations for Future Research

Future research should involve measuring adherence to diabetes, hypertension, and hyperlipidemia medications in an MTM program provided to Medicare beneficiaries. Older patients are diagnosed with more chronic diseases. Hence, it is important to evaluate the impact of MTM programs among this patient population. This study could also be replicated in a different working population and those receiving services from the

Lucas County MTM program to add external validity to the study. Also, future studies could measure the impact of economic and humanistic outcomes associated with Lucas County MTM program such as number of sick days, number of hospitalization and emergency room visits, patient satisfaction, return on investment to employer, and employer satisfaction on the clinical outcomes of patients.

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Appendix A

Operational Definitions

Adherence to chronic medications: A patient is termed as being highly adherent to the medications if he or she had a medication possession ratio of 80% or higher.

Medium adherence to chronic medications: A patient is termed as having medium adherence to the medications if he or she had a medication possession ratio between 50%-79%.

Low adherence to chronic medications: A patient is termed as having low adherence to the medications if he or she had a medication possession ratio of less than 50%.

Improvement in clinical outcomes: A patient is said to have shown improvement in clinical outcomes if there is a reduction in the value of any of the following outcomes compared to the first visit: HbA_{1c}, blood pressure and BMI

Based on the American Diabetes Association guidelines ideal values of the clinical outcomes: HbA_{1c} (6.5% - 7%), blood pressure (<130/80 mm Hg for patients with diabetes), and BMI (18.5 – 24.9 for adults).

Appendix B

Data Collection form

ID	Diagnosis	HbA$_{1c}$						Blood pressure						BMI					
		Visits						Visits						Visits					
		Baseline	1	2	3	4	5	Baseline	1	2	3	4	5	Baseline	1	2	3	4	5