Effects of intensified care management activities and diabetes medication copayment reduction on medication adherence and health care costs

Kyungwan Hong

University of Rhode Island, hong.kyungwan@gmail.com

Follow this and additional works at: https://digitalcommons.uri.edu/theses

Recommended Citation
Hong, Kyungwan, "Effects of intensified care management activities and diabetes medication copayment reduction on medication adherence and health care costs" (2015). Open Access Master's Theses. Paper 628.
https://digitalcommons.uri.edu/theses/628

This Thesis is brought to you for free and open access by DigitalCommons@URI. It has been accepted for inclusion in Open Access Master's Theses by an authorized administrator of DigitalCommons@URI. For more information, please contact digitalcommons@etal.uri.edu.
EFFECTS OF INTENSIFIED CARE MANAGEMENT ACTIVITIES AND DIABETES MEDICATION COPAYMENT REDUCTION ON MEDICATION ADHERENCE AND HEALTH CARE COSTS

BY

KYUNGWAN HONG

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN PHARMACEUTICAL SCIENCES

UNIVERSITY OF RHODE ISLAND

2015
MASTER OF SCIENCE THESIS

OF

KYUNGWAN HONG

APPROVED:

Thesis Committee:

Major Professor:  Stephen Kogut

Rita Marcoux

Mary Greaney

Nasser H. Zawia

DEAN OF THE GRADUATE SCHOOL

UNIVERSITY OF RHODE ISLAND
2015
ABSTRACT

Diabetes mellitus (hereinafter referred to as diabetes) is a serious health concern affecting the daily lives of many Americans in both clinical and financial aspects. Diabetes affects approximately 26 million people of all ages in the United States, and the total estimated medical costs of diagnosed diabetes in the U.S. in 2012 exceeded $200 billion. To obtain better health outcomes, prevent complications, and reduce unnecessary costs, some health insurance plans encourage patients to enroll in diabetes management programs that monitor patient's health status more closely and assist in the adoption of healthy behaviors and habits. The aims of this study are to compare medication adherence rates and total healthcare cost among patients participating in a Diabetes Care Management Incentive Program offered by a commercial health insurer with usual care.

This study was performed using a retrospective cohort study design; subjects were insurance plan members with diabetes using metformin-containing medications. Logistic regression analyses were performed to measure the degree of association between intervention status (i.e. participation in the diabetes incentive program) and adherence rates. The adjusted odds ratio with 95% confidence intervals were reported as the measure of effect. For the total healthcare cost analysis, the Mann-Whitney U test was utilized to evaluate differences between the median intervention and non-intervention cost values.

Odds ratios for rates of achieving medication possession ratio (MPR) of 0.80 or greater among the intervention group as compared with the non-intervention groups were 0.966 (95% CI: 0.739 - 1.264) in the bivariate logistic regression model, 0.995 (95% CI: 0.755 - 1.312) in the full logistic regression
model, and 1.008 (95% CI: 0.765 - 1.328) in the fitted logistic regression model. Additionally, the mean annual total healthcare cost was $8,827.01 ($735.58 per month) in the intervention group and $10,096.53 ($841.38 per month) in the non-intervention group), yet the difference was not statistically significant (p = 0.2327).

Study results indicate that the medication adherence rates among patients using metformin-containing medications were similar between members who were enrolled in the diabetes management program and members who were not enrolled in the program. However, members participating in the program incurred approximately $2,200 less in annual total healthcare cost.
ACKNOWLEDGEMENT

I would like to acknowledge and express my sincerest gratitude to my master professor, Dr. Stephen Kogut, for his passionate support, enduring guidance, and endless encouragement that I have been received. I cannot express how fortunate I am to have an opportunity to cooperate and work with him. Also, I offer my sincere appreciation for the learning opportunities provided by my committee members, Professor Rita Marcoux, and Dr. Mary Greaney.

I was very fortunate to be a part of the University of Rhode Island's Program in Pharmacoepidemiology and Pharmacoeconomics. My completion of this project could not have been accomplished without educational guidance and encouragement from Dr. Paul Larrat, Dr. Brian Quilliam, Dr. Cynthia Willey, Dr. Aisling Caffrey, and Chuck Wentworth.

Lastly, I want to express my heartfelt gratitude to my parents Jongweon Hong and Eunsook Choi for their unlimited support.
PREFACE

The standard format was used in preparation of this thesis.
# TABLE OF CONTENTS

ABSTRACT ....................................................................................................... ii

ACKNOWLEDGEMENT ................................................................................. iv

PREFACE ....................................................................................................... v

TABLE OF CONTENTS .................................................................................. vi

LIST OF TABLES ........................................................................................... vii

LIST OF FIGURES ....................................................................................... viii

CHAPTER 1 ..................................................................................................... 1
  BACKGROUND ............................................................................................ 1

CHAPTER 2 ..................................................................................................... 5
  METHODS .................................................................................................... 5

CHAPTER 3 ..................................................................................................... 9
  RESULTS ...................................................................................................... 9

CHAPTER 4 .................................................................................................... 15
  DISCUSSION .............................................................................................. 15

CHAPTER 5 .................................................................................................... 22
  CONCLUSION ............................................................................................ 22

LIST OF REFERENCES .................................................................................. 23

APPENDICES ............................................................................................... 35

BIBLIOGRAPHY ........................................................................................... 39
# LIST OF TABLES

| TABLE | PAGE |
|-------|------|
| Table 1. Selected Characteristics of Patients Participating in the Diabetes Incentive Program and Patients in the Comparison Group (Intervention vs. Nonintervention) | 27 |
| Table 2. Association between Selected Characteristics of Study Patients and Diabetes Medication Adherence | 28 |
| Table 3. Bivariate Logistic Regression Analysis Assessing the Likelihood of Diabetes Medication Adherence According to Selected Patient Characteristics | 29 |
| Table 4. Saturated Model Logistic Regression Analysis: Likelihood of Adherence (Medication Possession Ratio $\geq 80\%$) among Selected Patient Characteristics | 30 |
| Table 5. Fitted Logistic Regression Model with Adjusted Odds Ratio for Intervention versus Non-Intervention Status as a Predictor of Medication Adherence (MPR $\geq 80\%$), Controlling for Patient Age, Insulin Use, Number of Rx Utilized, and Presence of a Mental Health Disorder | 31 |
| Table 6. Mean Annual Pharmacy, Medical, and Total Health Care Cost among Patients Participating in the Diabetes Incentive Program and Patients in the Comparison Group | 32 |
| Table 7. Mean Total Yearly Cost for Selected Characteristics of Patients Participating in the Diabetes Incentive Program and Patients in the Comparison Group | 33 |
## LIST OF FIGURES

| FIGURE | PAGE |
|--------|------|
| Figure 1. Population Selection Flowchart | 34 |

viii
CHAPTER 1

BACKGROUND

Diabetes mellitus (hereinafter referred to as diabetes) is a serious health concern affecting the daily lives of many Americans. Diabetes affects approximately 25.8 million people of all ages in the United States, and the affected number is projected to increase due to an increase in the number of older Americans and increase in the prevalence of obesity due to westernized diets and sedentary lifestyles.1,2

Diabetes is an acute and chronic disease caused by high blood glucose level requiring continuous monitoring and management. There are two major types of diabetes: Type 1 and Type 2. Type 1 diabetes, which accounts for approximately 5 to 10% of all diabetes cases, is caused by absolute insulin deficiency and is treated by exogenous insulin.3 Type 2 diabetes, the most common type of diabetes, accounting for approximately 90 to 95% of all cases, is characterized by insulin sensitivity and insulin secretion defects.4 People with type 2 diabetes have various treatment options including oral hypoglycemic agents and insulin. Among patients with type 2 diabetes, approximately 24% do not recognize they have diabetes.4

The total estimated medical costs of diagnosed diabetes in the U.S. in 2012 was $245 billion, a 40% increase from $174 billion in 2007, and the cost will continue to increase due to an increasing number of patients having diabetes.5 This expenditure includes both direct medical costs such as hospital inpatient care, prescription medications, physician office visits, and residential/nursing facility
stays, and indirect medical costs such as reduced productivity and inability to work.⁵

To obtain better health outcomes, prevent complications, and reduce unnecessary costs, some health insurance plans encourage patients to enroll in diabetes management programs. Typical components of diabetes management programs, include periodic physical examinations, appointment reminders by health care personnel, patient education to enhance self-management skills and encourage healthful behaviors such as daily exercises and eating more fresh fruits and vegetables, and laboratory examinations including cholesterol levels, liver function tests, and blood glucose levels.

Research evaluating the effectiveness of diabetes management programs have assessed clinical outcomes such as decrease in hemoglobin A1c level, cardiovascular risks, and foot infection risks to determine effectiveness.⁶⁻⁷ For example, the Asheville Project, a disease management program, started in 1996 by the city of Asheville, North Carolina.⁸ The program enrolled patients with asthma, hypertension, hypercholesterolemia and diabetes and provided educational and personal disease management services for employees of the city of Asheville.⁸ Participants with diabetes experienced improved hemoglobin A1C levels, lower total health care costs, and fewer sick days.⁸ A long term follow-up study determined that approximately 50% of participants experienced decreases in mean hemoglobin A1c and lipid level at each follow-ups.⁹ Another study evaluated the association between a health maintenance organization (HMO) sponsored diabetes management program and hemoglobin A1c level and determined that individuals participating in the diabetes management program improved short-term glycemic
control significantly.\textsuperscript{10} According to the study, mean hemoglobin A1c of patients decreased from 8.51 to 7.41 after 3 months of follow-up.\textsuperscript{10}

However, there is a lack of study of the cost effectiveness of diabetes management programs, due to the difficulty and complexity in describing economic outcomes.\textsuperscript{11} It is often difficult to gather all of the diabetes-related direct and indirect costs, and as a result, less is known about the disease management programs' impact on medical expenditure for patients with diabetes.\textsuperscript{11-12} Nonetheless, results of one study suggested that intensified diabetes care management activities increased diabetes medication adherence by 4\%, and another study determined that patients with diabetes that participated in the Asheville Project experienced a decrease in total mean direct medical costs of $1,200 to $1,872 per year compared to patients with diabetes who did not participate in the intervention. Additionally, the Asheville Project saved an employer group approximately $18,000 per year.\textsuperscript{9,13} However, not all diabetes management programs have a favorable impact on financial outcomes with incremental medical costs ranging from -$16,996 to $3,305 per patient per year.\textsuperscript{14}

This current study will assess the associations between enrollment in a diabetes management program provided by a commercial insurance plan and health expenditure and diabetes medication adherence rate. Diabetes management programs are known for assisting participants to achieve better diabetes medication adherence and, eventually, better health outcomes, thus insurance plans can possibly reduce spending through better diabetes medication adherence and better health outcomes: less hospitalization, less diabetes complications and increase in work productivity.\textsuperscript{15-16} Poor medication adherence causes approximately 125,000 deaths due to increase in morbidity in hospitalizations.\textsuperscript{17} Furthermore, poor
medication adherence costs the U.S. health care system up to $289 billion annually.\textsuperscript{17} In addition, cost burdens of diabetes are large with medication costs, frequent hospital visits, and possible hospitalizations, as noted above.

The diabetes incentive program evaluated in our study aims to improve diabetes-related care and decrease medical expenses due to diabetes and diabetes-related complications. The program provides participants' diabetes medications free of charge if they agree to participate in an annual physical examination, complete a hemoglobin A1c blood test at least twice a year, have an annual low density lipoprotein cholesterol test, participate in case coordination led by case managers, and personalized support and educational sessions provided by a registered nurses and dieticians.

This study will help in fulfilling pharmacoeconomic-research demands about diabetes management programs and contribute to the development of more economically efficient diabetes management programs. The study's hypothesis is that the members enrolled in the diabetes management program will achieve higher medication adherence rate than those who are not enrolled in the diabetes management program. A secondary hypothesis is that the members enrolled in the diabetes management program will experience reduced total healthcare expenditure compared to the members nor enrolled in the diabetes management program.
CHAPTER 2

METHOD

This study was a retrospective cohort study, assessing the association between a diabetes management program and its effects on participants' medication adherence and medical costs. The data were provided by a commercial health insurer, and included members' medical diagnoses, basic demographics, medical and pharmacy spending information, and health care procedures. The dataset includes members who enrolled in the Diabetes Incentive Program (intervention) and who did not enroll (non-intervention) between January 1st of 2008 and May 31st of 2010. Through the participation of the Diabetes Incentive Program, members were able to obtain the following health management services: (a) participate in care coordination with a case manager, (b) have an annual physical examination, (c) have a hemoglobin A1c blood test at least twice annually, (d) have a low density lipoprotein cholesterol (LDL-C) test at least once annually, and (e) attend dietary, lifestyle, and diabetes management educational sessions led by registered nurses and dieticians. If members participated in all of these services, they received a substantial to full price discounts on their hypoglycemic prescriptions.

In order to be included in the study population, patients had to be aged 18 years or above and have at least 1 ICD-9-CM (The International Classification of Diseases, Ninth Revision, Clinical Modification) for diabetes, and at least 1 claim for an anti-diabetic medication during the last 12-month period of continuous enrollment (365 days). In this study, only metformin and metformin-containing combination medications were considered as metformin is the first line oral
hypoglycemic agent. In addition, patients with diabetes generally utilize metformin continuously, whereas other diabetes medications such as sulfonylurea and dipeptidyl peptidase-4 (DPP-4) inhibitors are used as add-on therapies. All possible metformin-containing combination medications on the market were included in this study (see Appendix A). To assist in identifying all metformin-containing medications, drug information databases Clinical Pharmarmacology® and Micromedex® were used.

Patient gender, comorbidities, insulin usage, the total number of medications used (diabetes and non-diabetes), and age group were defined as categorical variables. Cardiovascular diseases, pulmonary diseases, and mental health disorders were the examined comorbidities, and were determined based on published ICD 9 code sets (see Appendix B,C,D,E,F,G). The total number of dispensed medications represented the number of different prescription medications dispensed to these patients for 12 months. Quartiles of frequency distribution were used to categorize the total number of dispensed medications: group 1 (1-7 total medications), group 2 (8-13 total medications), group 3 (14-17 total medications) and group 4 (18 and more total medications). Age was described as a continuous variable; and then categorized according to groupings that generally reflected older (age of 65 and above), middle aged (age of 50 to 64), and young adult patients (age of 18 to 49).

Statistical analysis (Medication adherence)

The first analysis assessed the relationship between enrollment in the Diabetes Incentive Program and the diabetes medication adherence rate. To measure the medication adherence rate, the study utilized MPR (Medication
Possession Ratio), calculated as the sum of the days supply for all relevant medication dispensing during the measurement period, divided by the number of days elapsed during the period.\textsuperscript{19-21} This study evaluated MPR based on 12-month elapsed period of enrollment in the diabetes management program. If a patient had an MPR of equal to or higher than 0.80 (80%), the patient was classified as being adherent to the diabetes medication. For these analyses, we focused on dispensings of metformin-containing medications, regardless of different strengths, dosage forms, and releasing forms.

Chi-square tests were performed to determine if there were differences in the percentage of patients classified as adherent and those enrolled and not enrolled in the Diabetes Incentive program. Multivariate logistic regression analyses were performed to determine the association between the enrollment in the Diabetes Incentive Program and the MPR (dependent variable), controlling for other independent variables including patient age group, gender, comorbidities, insulin usage, and the total number of medications dispensed. Independent variables were assessed for co-linearity, and the Hosmer-Lemeshow goodness of fit test was performed to assess the calibration of the final model. The adjusted odds ratio with 95% confidence intervals were reported as the measure of effect.

Statistical analysis (Healthcare cost)

The second analysis assessed differences in health care cost among patients with diagnosed diabetes participating in the Diabetes Incentive Program and those receiving usual care. We determined health expenditures for the range of utilized health services, including hospitalization costs and diabetes medication costs of participants who were enrolled in the Diabetes Incentive Program and for
those who were not enrolled in the Diabetes Incentive Program. Costs were defined as the amount paid by the health insurance plan, which does not include copayments made by patients. Costs included both diabetes-related and non-diabetes related physician visits, hospitalizations, laboratory tests, and prescription drug costs. Total healthcare expenditures during the 12 month timeframe was compared between intervention and non-intervention groups.

The distribution of costs was analyzed prior to determining the appropriate statistical test for evaluating group differences in healthcare spending. Mean costs by group were reported, and where data were skewed, a log transformation was performed. The student's t-test was used to assess mean differences in cost, and given the skewed nature of the data, median-based tests were also performed to assess the statistical significance of these cost differences.

These costs analyses included the same independent variables from the adherence analysis: age, gender, comorbidities, insulin usage, and total number of medications dispensed. To evaluate the statistical significance of differences in these baseline characteristics and health expenditure, the students t-test was utilized. The Mann-Whitney U test was also utilized to evaluate differences between the median intervention and non-intervention cost values.

Data analysis was performed using SAS (version 9.3).
A total of 284 intervention members and 5,528 non-intervention members met all the cohort selection criteria (see Figure A). The intervention group had a mean age of 54.06 years (SD=9.50) and the non-intervention group had a mean age of 54.59 years (SD=8.59) (see Table 1). About one-quarter in the intervention group (26.06%, n=74) and the non-intervention group (25.92%, n=1,433) were between 18-49 years of age. The frequency of the population aged 50-64 years was 61.97% in the intervention group and 64.36%, while the frequency of population who is 65 years and above was 11.97% in the intervention group and 9.71% in the non-intervention group. Percent differences across age groups were not statistically significant (p=0.4396).

The frequency of males was 61.27% in the intervention group and 61.09% in the non-intervention group, and the frequency of females was 38.73% in the intervention group and 38.91% in the non-intervention group. Although it was not a statistically significant difference, the frequency of insulin use was 39.79% in the intervention group and 35.42% in the non-intervention group (p=0.952).

Differences in the prevalence of the comorbidities of respiratory disease and cardiovascular disease were statistically significant between the two groups (p=0.0409 Respiratory disease, p=0.0026 Cardiovascular disease); 7.04% of the intervention group and 10.89% of the non-intervention group had a respiratory disease, while 7.04% of the intervention group and 13.17% of the non-intervention group had a documentation of cardiovascular disease, respectively. Additionally,
15.49% of the intervention group and 14.35% of the non-intervention group had a mental health disorder, although this difference was not statistically significant (p=0.5920). The frequency of those using 1 to 7 total medications was 25.00% in the intervention group and 20.98% in the non-intervention group, and the frequency of those using 8 to 13 total medications was 29.58% in the intervention group and 31.35% in the non-intervention group. The frequency of those using 14 to 17 total medications was 16.90% in the intervention group and 16.75% in the non-intervention group, and the frequency of those using more than 18 total medications was 28.52% in the intervention group and 30.92% in the non-intervention group. The frequency based on the number of total medications was not statistically significant, and both intervention and non-intervention patients appeared to utilize a similar number of medications during the measurement period.

Results (Medication adherence)

Result assessing medication adherence revealed that 72.89% of the intervention group and 73.55% of the non-intervention group achieved MPR of 0.80 or greater, although this difference was not statistically significant (p=0.8042). Mean ages of the subgroups who achieved MPR greater than or equal to 0.80 and who did not achieve MPR of 0.80 or higher were 55.24 and 52.64, respectively (p=<0.0001, SD=8.34 and 9.15) (see Table 2). Adherence rates increased with age: 64.90% of the subgroup aged 18-49 years, 75.87% of the subgroup aged 50-64 years old, and 80.91% of the subgroup aged 65 years old and above achieved MPR greater than or equal to 0.80 (p=<0.0001). Although this finding was not statistically significant (p=0.2646), 74.04% of male and 72.71% of female achieved MPR greater than or equal to 0.80. Patients utilizing higher numbers of
medications were more frequently classified as adherent to the diabetes medications: 60.60% of the subgroup using 1 to 7 total medications, 70.17% of the subgroup using 8 to 13 total medications, 77.31% of the subgroup using 14 to 17 total medications, and 83.74% of the subgroup using more than 18 total medications achieved MPR greater than or equal to 0.80 (p=<0.0001). Among patients with documented mental health disorders, 74.17% of the subgroup without mental health disorders and 69.38% of subgroup with mental health disorders achieved MPR greater than or equal to 0.80 (p=0.0037). For cardiovascular disease, 72.87% of the subgroup without cardiovascular disease and 77.64% of the subgroup with cardiovascular disease achieved MPR greater than or equal to 0.80 (p=0.0058).

Being enrolled in the intervention was not associated with higher medication adherence rate in the bivariate logistic regression analysis (see Table 3). Both the intervention group and the non-intervention group had a similar likelihood of achieving MPR of 0.80 (OR= 0.966; 95% CI: 0.739 - 1.264). Increasing age was associated with increased likelihood of achieving MPR of 0.80 or greater. The subgroup aged 50 to 64 years was 39% more likely to have been adherent (OR 1.393; 95% CI: 1.236 - 1.570), while the subgroup aged 65 years and above was 59% more likely to have been adherent (OR 1.590; 95% CI: 1.279 - 1.975). Female members had similar likelihood of achieving MPR of 0.80 or greater as the male members, with an odds ratio of 0.934 (95% CI: 0.830 - 1.053). If members were taking more medications, they were more likely to achieve MPR of 0.80 or greater. The subgroup taking 8 to 13 total medications was 22% less likely to have been adherent (OR 0.782; 95% CI: 0.691 - 0.885). The subgroup taking 14 to 17 total medications was 27% more likely to have been adherent (OR
1.276; 95% CI: 1.084 - 1.501) while the subgroup taking 18 or more medications was 131\% more likely to have been adherent (OR 2.317; 95% CI: 2.010 - 2.672).

Based on the saturated logistic regression model, the impact of intervention group status was also not significantly associated with medication adherence (see Table 4). The intervention group had similar likelihood of achieving MPR of 0.80 or greater as the non-intervention group, with an adjusted odds ratio of 0.995 (95% CI: 0.755 - 1.312). Similar to results from the bivariate logistic regression analysis, if members were older, they were more likely to achieve MPR of 0.80 or greater.

The patient subgroup aged 50 to 64 years was 46\% more likely to have been adherent (OR 1.467; 95% CI: 1.283 - 1.679), while the subgroup aged 65 years and above was 89\% more likely to have been adherent (OR 1.897; 95% CI: 1.488 - 2.418), (p=<0.0001). Female members had similar likelihood of achieving MPR of 0.80 or greater as the male members, with an adjusted odds ratio of 0.909 (95% CI: 0.802 - 1.030). Also, similar to results from the bivariate logistic regression analysis, if members were taking more medications, they were more likely to achieve MPR of 0.80 or greater. The subgroup taking 8 to 13 total medications was 49\% more likely to be adherent (OR1.493; 95% CI:1.279 - 1.744). The subgroup taking 14 to 17 total medications was 119\% more likely to have been adherent (OR 2.194; 95% CI: 1.810 - 2.659), while the subgroup taking 18 or more medications was 248\% more likely to have been adherent (OR 3.480; 95% CI:2.905 - 4.170),(p=<0.0001).

In the fitted multiple logistic regression model, the impact of intervention group status was not statistically significant (see Table 5). The intervention group had similar likelihood of achieving MPR of 0.80 or greater as the non-intervention
group, with an adjusted odds ratio of 1.008 (95% CI: 0.765 - 1.328). Older members were more likely to achieve MPR of 0.80 or greater. Those aged 50 to 64 years were 45% more likely to have been adherent (OR 1.458; 95% CI: 1.276 - 1.667), and individuals aged 65 years and above were 86% more likely to be adherent (OR 1.861; 95% CI: 1.464 - 2.365), (p=<0.0001). If members were taking more medications, they were more likely to achieve MPR of 0.80 or greater. The subgroup taking 8 to 13 total medications was 49% more likely to have been adherent (OR 1.492; 95% CI: 1.279 - 1.742). The subgroup taking 14 to 17 total medications was more than twice as likely to have been adherent (OR 2.161; 95% CI: 1.784 - 2.618), while the subgroup taking 18 or more total medications was more than 3 times as likely to have been adherent (OR 3.354; 95% CI: 2.809 - 4.005), (p=<0.0001). Good model calibration was shown by the Hosmer-Lemeshow goodness of fit test with a p-value of 0.3768, implying good matching between expected and observed event rates in population's subgroup.

Results (Healthcare cost)

Although it was not statistically significant (p=0.2327), The mean annual per patient total healthcare cost, including both pharmacy-related cost and medical cost, was $8,827.01 ($735.58 per month) in the intervention group and $10,096.53 ($841.38 per month) in the non-intervention group (see Table 6). The mean annual per patient pharmacy-related cost was $2,904.92 ($242.08 per month) in the intervention group and $2,655.21 ($221.27 per month) in the non-intervention group (p=0.2065), and the mean medical cost was $5,922.08 ($493.51) in the intervention group and $7,438.93 ($619.91 per month) in the non-intervention group (p=0.1363).
The mean total healthcare costs of male and female patients in the intervention group were $7,761.1 and $10,513.0 respectively, and the mean total healthcare costs of males and females in the non-intervention group were $9,785.9 and $10,583.1, respectively (see Table 7). Analysis of age groups revealed a mean total healthcare cost of intervention and non-intervention population aged 18 to 49 years to be $7,015.2 and $8,244.1, respectively. For those who were 50 to 64 years old, intervention group had the mean total healthcare costs of $9,117.0, and non-intervention group had the mean total healthcare costs of $10,551.7. The mean total healthcare costs of intervention and non-intervention population who are 65 years old and above were $11,269.4 and $12,028.0, respectively. All the mean total healthcare cost results based on different age groups were not statistically significant. For the total medication counts, the mean total healthcare costs of intervention and non-intervention members who are taking 1 to 7 total medications were $4,495.2 and $6,261.6, respectively. For those who are taking 8 to 13 total medications, intervention group had the mean total healthcare costs of $6,836.4, and non-intervention group had the mean total healthcare costs of $7,661.0. The mean total healthcare costs of intervention and non-intervention members who are taking 14 to 17 total medications were $7,689.9 and $9,380.5, respectively. The mean total healthcare costs of intervention and non-intervention members who are taking 18 or more total medications were $15,362.3 and $15,548.9, respectively.
CHAPTER 4

DISCUSSION

Diabetes mellitus is a serious obstacle for the United States health care system in both clinical and financial terms. Affecting approximately 8.3% of the U.S. population, it is the seventh leading cause of death, and is a major cause of cardiovascular diseases, the first leading cause of death in the U.S.\textsuperscript{1,22}

Discussion (Medication adherence)

The first goal of this study was to determine whether the participation in a Diabetes Incentive Program provided by a commercial insurer affects the diabetes medication adherence rate. Contrary to the study hypothesis, members who were enrolled in the diabetes management program did not achieve higher MPR of 0.80 or greater than members who were not enrolled in the diabetes management program. Odds ratios for rates of achieving MPR of 0.80 or greater among the intervention group as compared with the non-intervention groups were 0.966 (95% CI: 0.739 - 1.264) in the bivariate logistic regression model, 0.995 (95% CI: 0.755 - 1.312) in the full logistic regression model, and 1.008 (95% CI: 0.765 - 1.328) in fitted logistic regression model. All three logistic regression analyses provided consistent results and demonstrated that the medication adherence rates with metformin-containing medications between members who were enrolled in the diabetes management program and members who were not enrolled in the diabetes management program were similar.

Medication adherence rates, however, were associated with age, total medication dispensings, and presence of mental health disorders. Older patients
were more likely to achieve MPR of 0.80 or greater than younger patients. The subgroup who were 50 to 64 years old had odds ratio of 1.458 (95% CI: 1.276 - 1.667) in the fitted logistic regression model. The subgroup who were 65 years old and above had odds ratio of 1.861 (95% CI: 1.464 - 2.365) in the fitted logistic regression model. Based on these consistent results, those older than 65 years old and above had approximately twice the likelihood of achieving MPR of 0.80 or greater than group that were 18 to 49 years old, indicating that older patients may manage their health conditions more diligently due to the possibility of having more comorbidities and health issues.

Those using more medications were more likely to achieve MPR of 0.80 or greater than those using less medications. All three logistic regression analyses provided consistent results of increasing likelihood of achieving MPR of 0.80 or greater if total medication counts increase. The subgroup using 18 or more medications had an odds ratio of 3.354 (95% CI: 2.809 - 4.005) in the fitted logistic regression model. Based on these results, subgroup using more 18 or more medications had approximately three times the likelihood of achieving MPR of 0.80 or greater than population using 1 to 7 medications. These results reveal that members taking more medications were more adherent to their medications, which maybe indicating that members taking more medications regard the activity of medication intake more seriously due to their possibly less healthy status. Therefore, the diabetes management program should specifically target younger members taking less medications to improve their suboptimal medication adherence and enhance the program's performance.

Among the three comorbidities evaluated, the subgroup having a diagnosis of a mental health disorder was less likely to achieve MPR of 0.80 or greater than
population without a mental health disorder. The population with mental health disorders had odds ratio of 0.703 (95% CI: 0.595 - 0.831) in the fitted logistic regression model. All three logistic regression analyses provided consistent results of decreasing likelihood of achieving MPR of 0.80 or greater if one has a documented mental health disorder. The presence of respiratory diseases or cardiovascular diseases did not affect the likelihood of achieving MPR of 0.80 or greater. The state of depression affects one's medication adherence due to decreased motivation and willingness. A meta analysis by Grenard et al (2011) found that depressed patients are 1.76 times more likely to be non-adherent to their medications compared to patients without depression. Therefore, the diabetes management program should specifically target depressed patients to prevent patients' disengagement and improve program's performance.

Other independent characteristics including gender were not associated with medication adherence. The subgroup that used insulin was less likely to achieve MPR of 0.80 or greater, although this association was not consistent across the three logistic regression models. In the fitted logistic regression model, the odds ratio for insulin use was 0.874 (95% CI: 0.769 - 0.993), (p=0.0379). This result is maybe due to the relationship between diabetes severity and insulin usage. If diabetes worsens, patients tend to switch to insulin therapy from oral diabetes medications including metformin.

The results of this study indicate that an incentive-based diabetes management program did not yield increased rates of medication adherence among participants when compared with rates among members with diabetes not participating in the diabetes management program. Medication adherence rates were similar between the two groups in all three logistic regression statistical tests.
which indicates that the program likely did not yield clinical benefits as a consequence of more consistent medication taking. However, medication adherence rates were already fairly high among all patients included in this study, suggesting that the opportunity for improvement was limited.

Discussion (Healthcare cost)

The second aim of this study was to determine whether the participation of a Diabetes Incentive Program provided decreased health expenditures including both medical and pharmacy-related costs. Although the cost analyses performed did not reveal statistically significant differences in cost, members who were enrolled in the diabetes management program had lower total health expenditures than members who were not enrolled in the diabetes management program. The mean total healthcare cost, including both pharmacy-related cost and medical cost, was $8,827.01 ($735.58 per month) in the intervention group and $10,096.53 ($841.38 per month) in the non-intervention group. While patients in the diabetes management program incurred approximately $2,200 less in annual healthcare cost, cardiovascular and respiratory comorbidities were less prevalent among program participants.

Total healthcare costs varied across several of the independent variables evaluated. As expected, older patients were more likely to have higher mean total healthcare cost than younger patients in both the intervention group and non-intervention group. Female patients were more likely to have higher mean total healthcare cost than male patients in both the intervention group and non-intervention group. Patients using insulin were more likely to have higher mean total healthcare cost than population not using any insulin in both intervention
group and non-intervention group, reflecting the progressed disease status among these patients. Patients using more medications were more likely to have higher mean total healthcare cost than population using less numbers of medications in both intervention group and non-intervention group. Analysis of the relationship between patient age and total medication dispensings suggested that these two continuous variables were not highly correlated (Spearman r = 0.179), suggesting that both increasing age and a greater number of medications used were independently associated with higher health care expenditure.

As expected, patients with comorbidities (respiratory disease, mental health disorder, and cardiovascular disease) were more likely to have a higher mean total healthcare cost than population without comorbidities. When examining costs across comorbidity categories, the mean total healthcare costs of intervention and non-intervention population with respiratory diseases were $23,337.4 and $17,937.7, respectively; the mean total healthcare costs of intervention and non-intervention population with cardiovascular diseases were $24,627.6 and $19,503.9, respectively. These results reveal that older members with more comorbidities and more medications prescribed incurred greater total healthcare costs. Based on this finding, diabetes management program should consider focusing on older members with comorbidities and use of a greater number of medications to reduce total healthcare costs through the programs components.

Discussion (Limitations)

There were several limitations in this study. First, intervention and non-intervention groups were fundamentally different, and this difference prevented us to confirm that the diabetes management program solely contributed to
intervention group's lower total healthcare costs. In the intervention group, subgroups with respiratory diseases and cardiovascular diseases were 7.04% and 7.04%, and in non-intervention group, subgroups with respiratory diseases and cardiovascular diseases were 10.89% and 13.17% (p=0.0409 and 0.0026). The intervention group was generally healthier than the non-intervention group.

Additionally, there were no comparisons to medication adherence rates or cost in prior months. Without having access to previous data, the study was unable to determine if the intervention was progressively improving members' medication adherence and costs. It is possible that the intervention may have provided greater gains or losses in medication adherence and costs from the previous year than the non-intervention group, yet we were not able to evaluate the progressive impacts on the diabetes management program. Moreover, the study's 12-month evaluation period may have been too limited to measure the intervention's impact on medication adherence and total healthcare costs.

Furthermore, the study was unable to determine the temporal relationships between examined variables due to the short time period for follow up. In this case, there is a possibility that some members could have been diagnosed with a cardiovascular disease on the last day of their enrollment periods of 12 months and would have been labeled as cardiovascular patients for the entire study period. This limitation could falsely increase cost burdens of participants with some comorbidities. An additional limitation is that the study only considered metformin and metformin-containing medications for adherence to diabetes medication. As metformin is usually the first line oral therapy agent for diabetes mellitus and non-metformin medications are add-on therapies. Users of other oral diabetes medications such as sulfonylureas, DPP-4 inhibitors, or thiazolidinediones were
excluded in this study. The medication adherence rates of this study, therefore, could over-represent healthier populations, and overall oral diabetes medication adherence rates may be different from the result.

Additionally, another study limitation is that the administrative data source only included information about paid claims and excluded any procedure or medication that were paid out-of-pocket. The study, also, assumed that members consumed the dispensed medications, but compliance to dispensed medications was not measured or assessed. There is a possibility that the study misclassified members that did not take medications that had been dispensed as adherent to their medications. Also, the data source did not include information about patient race, ethnicity, and socioeconomic factors, which may have been associated with both the independent variables studied and the outcomes of medication adherence, and total healthcare cost.

There were cost outliers, affecting average medical, pharmacy, and total healthcare cost values. The highest cost for the non-intervention group was $345,862.33 and for the intervention group was $166,091.36. To evaluate the two groups not affected by the outliers, a median-based test was performed in the statistical analysis. Due to these outliers in the cost analysis, standard deviations became higher than mean values, and analysis results turned out to be statistically not significant.

In addition, the lack of randomization may not avoid impacts from unidentified or unseen biases or confounders. Also, members deciding to enter the diabetes management program could have been more careful about their own health, and this may have possibly led to a selection bias.
CHAPTER 5

CONCLUSION

Results of this study found that a Diabetes Incentive Program did not improve participants' medication adherence rates. Although not statistically significant, participation was associated with reduced total healthcare costs. Older participants and those taking more medications were associated with greater adherence to diabetes medications but incurred greater total healthcare costs. Certain comorbidities such as mental health disorders also affected medication adherence and total healthcare costs adversely. Further studies about the Diabetes Incentive Program should be performed to evaluate changes in rates of medication adherence and total healthcare costs over time.
1. National Diabetes Fact Sheet: national estimates and general information on Diabetes and prediabetes in the United States, 2011. Atlanta, GA: Centers for Disease Control and Prevention; 2011. Available at http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed November 20, 2013.

2. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, et al. Prevalence of diabetes, impaired fasting glucose and impaired glucose tolerance in US adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care. 1998;21(4):518-524.

3. Daneman D. Type 1 diabetes. Lancet. 2006;367(9513):847-858.

4. Nyenwe EA, Jerkins TW, Umpierrez GE, Kitabchi AE. Management of type 2 diabetes: evolving strategies for the treatment of patients with type 2 diabetes. Metabolism. 2011;60(1):1-23.

5. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013;35:1033-1046.

6. Ilag LL, Martin CL, Tabaei BP, Isaman DJ, Burke R, Greene DA, et al. Improving diabetes processes of care in managed care. Diabetes Care. 2003;26(10):2722-2727.
7. Lavery LA Wunderlich RP, Tredwell JL. Disease management for the diabetic foot: effectiveness of a diabetic foot prevention program to reduce amputations and hospitalizations. Diabetes Res Clin Pract. 2005;70(1):31–37.

8. Kepple SR. Pharmacists in Asheville, North Carolina, pick up city paychecks for diabetes services. Am J Health Syst Pharm. 1998;55:10-13.

9. Cranor CW, Bunting BA, Christensen DB. The Asheville Project: long-term clinical and economic outcomes of a community pharmacy diabetes care program. J Am Pharm Assoc (Wash) 2003;43(2):173–184.

10. Sidorov J, Gabbay R, Harris R, Shull RD, Girolami S, Tomcavage J, et al. Disease management for Diabetes mellitus: Impact on Hemoglobin A1C. Am J Manag Care. 2000;6(11):1217–1226.

11. Sidorov J, Shull R, Tomcavage J, Girolami S, Lawton N, Harris R. Does diabetes disease management save money and improve outcomes? A report of simultaneous short-term savings and quality improvement associated with a health maintenance organization-sponsored disease management program among patients fulfilling health employer data and information set criteria. Diabetes Care. 2002;25:684–689.

12. Gibson, TB, Wang S, Kelly E, Brown C, Turner C, Frech-Tamas F et al. A
value-based insurance design program at a large company boosted medication adherence for employees with chronic illnesses. Health Aff (Millwood). 2011;30(1):109-117.

13. Chernew ME, Shah MR, Wegh A, Rosenberg SN, Juster IA, Rosen AB, et al. Impact of decreasing copayments on medication adherence within a disease management environment. Health Affairs.2008;27(1):103–112.

14. De Bruin SR, Heijink R, Lemmens LC, Struijs JN, Baan CA. Impact of disease management programs on healthcare expenditures for patients with diabetes, depression, heart failure or chronic obstructive pulmonary disease: a systematic review of the literature. Health Policy.2011;101(2):105-121.

15. Thiebaud P, Demand M, Wolf SA, Alipuria LL, Ye Q, Gutierrez PR. Impact of disease management on utilization and adherence with drugs and tests: the case of diabetes treatment in the Florida: a Healthy State (FAHS) program. Diabetes Care. 2008;31(9):1717-1722.

16. Berg GD, Wadhwa S. Health services outcomes for a diabetes disease management program for the elderly. Dis Manag. 2007;10(4):226-234.

17. Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RC et al. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. Ann Intern
Med. 2012;157(11):785-795.

18. American Diabetes Association. Standards of medical care in diabetes - 2014. Diabetes Care. 2013;37(Suppl 1):S14-S80. doi: 10.2337/dc14-S014.

19. Sclar DA, Robison LM, Skaer TL, Legg RF, Nemec NL, Galin RS, et al. Antidepressant pharmacotherapy: economic outcomes in a health maintenance organization. Clin Ther. 1994;16(4):715-730.

20. Okano GJ, Rascati KL, Wilson JP, Remund DD, Grabenstein JD, Brixner DI. Patterns of antihypertensive use among patients in the US Department of Defense database initially prescribed an angiotensin-converting enzyme inhibitor or calcium channel blocker. Clin Ther. 1997;19(6):1433-1445.

21. Blandford L, Dans PE, Ober JD, Wheelock C. Analyzing variations in medication compliance related to individual drug, drug class, and prescribing physician. J Manag Care Pharm. 1999;5(1):47-51.

22. Hoyert DL, Xu J. Deaths: preliminary data for 2011. Natl Vital Stat Rep. 2012; 61(6):1-51.

23. Grenard JL, Munjas BA, Adams JL, Suuorp M, McGlynn EA, Gellad WF. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Intern Med.2011;26(10):1175–1182.
Table 1: Selected Characteristics of Patients Participating in the Diabetes Incentive Program and Patients in the Comparison Group (Intervention vs. Nonintervention)

| Variable                        | Intervention (N=284) | Non-intervention (N=5,528) | P value |
|---------------------------------|----------------------|-----------------------------|---------|
| Mean [SD] age                   | 54.056 [9.50]        | 54.585 [8.59]               | 0.3145  |
| Age group                       |                      |                             |         |
| 18-49                           | 74                   | 1,433                       | 25.92   | 0.4396  |
| 50-64                           | 176                  | 3,558                       | 64.36   |
| 65+                             | 34                   | 537                         | 9.71    |
| Gender                          |                      |                             |         |
| Male                            | 174                  | 3,377                       | 61.09   | 0.952   |
| Female                          | 110                  | 2,151                       | 38.91   |
| Insulin                         |                      |                             |         |
| No                              | 171                  | 3,570                       | 64.58   | 0.1338  |
| Yes                             | 113                  | 1,958                       | 35.42   |
| Total Medication Counts         |                      |                             |         |
| 1-7                             | 71                   | 1,160                       | 20.98   | 0.4178  |
| 8-13                            | 84                   | 1,733                       | 31.35   |
| 14-17                           | 48                   | 926                         | 16.75   |
| 18+                             | 81                   | 1,709                       | 30.92   |
| Comorbidity (Respiratory diseases) |                    |                             |         |
| No                              | 264                  | 4,919                       | 89.11   | 0.0409  |
| Yes                             | 20                   | 601                         | 10.89   |
| Comorbidity (Mental health disorders) |                  |                             |         |
| No                              | 240                  | 4,728                       | 85.65   | 0.5920  |
| Yes                             | 44                   | 792                         | 14.35   |
| Comorbidity (Cardiovascular diseases) |                |                             |         |
| No                              | 264                  | 4,793                       | 86.83   | 0.0026  |
| Yes                             | 20                   | 727                         | 13.17   |
Table 2: Association Between Selected Characteristics of Study Patients and Diabetes Medication Adherence (Medication Possession Ratio (MPR) < 80 vs. MPR >= 80)

| Variable                        | MPR < 80 | MPR >= 80 | P value |
|--------------------------------|----------|-----------|---------|
|                                | N        | N         |         |
|                                | %        | %         |         |
| Mean [SD] age                  | 52.64 [9.15] | 55.24 [8.34] | <0.0001 |
| Age group                      |          |           |         |
| 18-49                          | 529      | 978       | <0.0001 |
| 50-64                          | 901      | 2,833     |         |
| 65+                            | 109      | 462       |         |
| Gender                         |          |           |         |
| Male                           | 922      | 2,629     | 0.2646  |
| Female                         | 617      | 1,644     |         |
| Insulin                        |          |           |         |
| No                             | 991      | 2,750     | 0.9805  |
| Yes                            | 548      | 1,523     |         |
| Total Medication Counts        |          |           |         |
| 1-7                            | 485      | 746       | <0.0001 |
| 8-13                           | 542      | 1,275     |         |
| 14-17                          | 221      | 753       |         |
| 18+                            | 291      | 1,499     |         |
| Comorbidity (Respiratory diseases) |        |           |         |
| No                             | 1,368    | 3,815     | 0.5423  |
| Yes                            | 171      | 450       |         |
| Comorbidity (Mental health disorders) |       |           |         |
| No                             | 1,283    | 3,685     | 0.0037  |
| Yes                            | 256      | 580       |         |
| Comorbidity (Cardiovascular diseases) |       |           |         |
| No                             | 1,372    | 3,685     | 0.0058  |
| Yes                            | 167      | 580       |         |
| Intervention                   |          |           |         |
| No                             | 1,462    | 4,066     | 0.8042  |
| Yes                            | 77       | 207       |         |
Table 3: Bivariate Logistic Regression Analysis Assessing the Likelihood of Diabetes Medication Adherence According to Selected Patient Characteristics

|                      | Beta | OR   | 95% CI Low | 95% CI High | P value |
|----------------------|------|------|------------|-------------|---------|
| **Age group**        |      |      |            |             |         |
| 18-49                | Ref  |      |            |             |         |
| 50-64                | 0.3315 | 1.393 | 1.236      | 1.570       | <0.0001 |
| 65+                  | 0.4634 | 1.590 | 1.279      | 1.975       | <0.0001 |
| **Gender**           |      |      |            |             |         |
| Male                 | Ref  |      |            |             |         |
| Female               | -0.0678 | 0.934 | 0.830      | 1.053       | 0.2647  |
| **Insulin**          |      |      |            |             |         |
| No                   | Ref  |      |            |             |         |
| Yes                  | 0.00152 | 1.002 | 0.887      | 1.131       | 0.9805  |
| **Total Medication Counts** |      |      |            |             |         |
| 1-7                  | Ref  |      |            |             |         |
| 8-13                 | -0.2455 | 0.782 | 0.691      | 0.885       | <0.0001 |
| 14-17                | 0.2435 | 1.276 | 1.084      | 1.501       | 0.0034  |
| 18+                  | 0.8405 | 2.317 | 2.010      | 2.672       | <0.0001 |
| **Comorbidity (Respiratory diseases)** |      |      |            |             |         |
| No                   | Ref  |      |            |             |         |
| Yes                  | -0.0580 | 0.944 | 0.783      | 1.137       | 0.5423  |
| **Comorbidity (Mental health disorders)** |      |      |            |             |         |
| No                   | ref  |      |            |             |         |
| Yes                  | -0.2372 | 0.789 | 0.672      | 0.926       | 0.0037  |
| **Comorbidity (Cardiovascular diseases)** |      |      |            |             |         |
| No                   | ref  |      |            |             |         |
| Yes                  | 0.2570 | 1.293 | 1.077      | 1.553       | 0.0059  |
| **Intervention**     |      |      |            |             |         |
| No                   | ref  |      |            |             |         |
| Yes                  | -0.0342 | 0.966 | 0.739      | 1.264       | 0.8028  |
Table 4: Saturated Model Logistic Regression Analysis: Likelihood of Adherence (Medication Possession Ratio>= 80%) among Selected Patient Characteristics

| Characteristic                  | Beta    | OR     | 95% CI% low | 95% CI% High | P value |
|--------------------------------|---------|--------|-------------|--------------|---------|
| **Age group**                  |         |        |             |              |         |
| 18-49                          | ref     |        |             |              |         |
| 50-64                          | 0.3835  | 1.467  | 1.283       | 1.679        | <0.0001 |
| 65+                            | 0.6401  | 1.897  | 1.488       | 2.418        | <0.0001 |
| **Gender**                     |         |        |             |              |         |
| Male                           | ref     |        |             |              |         |
| Female                         | -0.0959 | 0.909  | 0.802       | 1.030        | 0.1329  |
| **Insulin**                    |         |        |             |              |         |
| No                             | ref     |        |             |              |         |
| Yes                            | -0.1323 | 0.876  | 0.771       | 0.995        | 0.0421  |
| **Total Medication Counts**    |         |        |             |              |         |
| 1-7                            | Ref     |        |             |              |         |
| 8-13                           | 0.4011  | 1.493  | 1.279       | 1.744        | <0.0001 |
| 14-17                          | 0.7855  | 2.194  | 1.810       | 2.659        | <0.0001 |
| 18+                            | 1.2471  | 3.480  | 2.905       | 4.170        | <0.0001 |
| **Comorbidity (Respiratory diseases)** |         |        |             |              |         |
| No                             | ref     |        |             |              |         |
| Yes                            | -0.1919 | 0.825  | 0.678       | 1.004        | 0.0552  |
| **Comorbidity (Mental health disorders)** |         |        |             |              |         |
| No                             | ref     |        |             |              |         |
| Yes                            | -0.3248 | 0.723  | 0.611       | 0.855        | 0.0002  |
| **Comorbidity (Cardiovascular diseases)** |         |        |             |              |         |
| No                             | ref     |        |             |              |         |
| Yes                            | -0.0946 | 0.910  | 0.748       | 1.106        | 0.3435  |
| **Intervention**               |         |        |             |              |         |
| No                             | ref     |        |             |              |         |
| Yes                            | -0.00516| 0.995  | 0.755       | 1.312        | 0.9708  |
Table 5: Fitted Logistic Regression Model with Adjusted Odds Ratio for Intervention versus Non-Intervention Status as a Predictor of Medication Adherence (MPR >= 80%), Controlling for Patient Age, Insulin Use, Number of Rx Utilized, and Presence of a Mental Health Disorder

|                      | Beta | OR  | 95% CI Low | 95% CI High | P value   |
|----------------------|------|-----|------------|-------------|-----------|
| **Age group**        |      |     |            |             |           |
| 18-49                |      |     |            |             |           |
| 50-64                | 0.3772 | 1.458 | 1.276 | 1.667 | <0.0001 |
| 65+                  | 0.6211 | 1.861 | 1.464 | 2.365 | <0.0001 |
| **Insulin**          |      |     |            |             |           |
| No                   |      |     |            |             |           |
| Yes                  | -0.1350 | 0.874 | 0.769 | 0.993 | 0.0379 |
| **Total Medication Counts** |      |     |            |             |           |
| 1-7                  |      |     |            |             |           |
| 8-13                 | 0.4004 | 1.492 | 1.279 | 1.742 | <0.0001 |
| 14-17                | 0.7705 | 2.161 | 1.784 | 2.618 | <0.0001 |
| 18+                  | 1.2102 | 3.354 | 2.809 | 4.005 | <0.0001 |
| **Comorbidity (Mental health disorders)** |      |     |            |             |           |
| No                   |      |     |            |             |           |
| Yes                  | -0.3526 | 0.703 | 0.595 | 0.831 | <0.0001 |
| **Intervention**     |      |     |            |             |           |
| No                   |      |     |            |             |           |
| Yes                  | 0.00808 | 1.008 | 0.765 | 1.328 | 0.9542 |
Table 6: Mean Annual Pharmacy, Medical, and Total Health Care Cost among Patients Participating in the Diabetes Incentive Program and Patients in the Comparison Group (Intervention vs. Nonintervention; N=5,812)

|             | INTERVENTION | NON-INTERVENTION | P value |
|-------------|--------------|------------------|---------|
|             | Mean ($)     | Sd ($/PMPM)    | Mean ($) | Sd ($/PMPM) |         |
| Pharmacy    | 2,904.92     | 2,890.37        | 2,655.21 | 3,265.73    | 0.2065  |
| PMPM        | 242.08       |                 | 221.27   |             |         |
| Medical     | 5,922.08     | 13,303.75       | 7,438.93 | 16,889.93   | 0.1363  |
| PMPM        | 493.51       |                 | 619.91   |             |         |
| Total       | 8,827.01     | 14,246.70       | 10,096.53| 17,628.76   | 0.2327  |
| PMPM        | 735.58       |                 | 841.38   |             |         |

*PMPM = Per Member Per Month
Table 7: Mean Total Yearly Cost for Selected Characteristics of Patients Participating in the Diabetes Incentive Program and Patients in the Comparison Group (Intervention vs. Nonintervention).

|                  | INTERVENTION |               | NON-INTERVENTION |               | P value |
|------------------|--------------|---------------|------------------|---------------|---------|
|                  | Mean ($)     | Sd            | Mean ($)         | Sd            |         |
| Age group        |              |               |                  |               |         |
| 0 (18-49)        | 7,015.2      | 8,664.0       | 8,244.1          | 13,869.2      | 0.4507  |
| 1 (50-64)        | 9,117.0      | 16,310.2      | 10,551.7         | 18,436.3      | 0.3112  |
| 2 (65+)          | 11,269.4     | 12,242.1      | 12,028.0         | 20,517.6      | 0.8314  |
| Gender           |              |               |                  |               |         |
| Male             | 7,761.1      | 10,070.4      | 9,785.9          | 18,450.7      | 0.1510  |
| Female           | 10,513.0     | 19,008.7      | 10,583.1         | 16,250.3      | 0.9651  |
| Insulin          |              |               |                  |               |         |
| No               | 7,521.2      | 11,343.2      | 8,818.1          | 15,866.6      | 0.2911  |
| Yes              | 10,803.1     | 17,635.6      | 12,422.3         | 20,247.1      | 0.4055  |
| Rx number        |              |               |                  |               |         |
| 1-7              | 4,495.2      | 4,717.4       | 6,261.6          | 12,887.4      | 0.2504  |
| 8-13             | 6,836.4      | 7,214.9       | 7,661.0          | 13,806.1      | 0.5867  |
| 14-17            | 7,689.9      | 9,152.6       | 9,380.5          | 14,393.5      | 0.4209  |
| 18+              | 15,362.3     | 23,032.0      | 15,548.9         | 23,261.4      | 0.9437  |
| Comorbidity (Respiratory diseases) |              |               |                  |               |         |
| No               | 7,727.7      | 9,563.4       | 9,138.5          | 15,834.6      | 0.1518  |
| Yes              | 23,337.4     | 38,971.4      | 17,937.7         | 27,097.8      | 0.3887  |
| Comorbidity (Mental health disorders) |              |               |                  |               |         |
| No               | 8,302.2      | 14,837.1      | 8,827.1          | 15,617.6      | 0.6106  |
| Yes              | 11,689.8     | 10,115.7      | 17,674.5         | 25,369.5      | 0.1198  |
| Comorbidity (Cardiovascular diseases) |              |               |                  |               |         |
| No               | 7630.0       | 9920.0        | 8669.6           | 15239.4       | 0.2733  |
| Yes              | 24627.6      | 37125.5       | 19503.9          | 26972.4       | 0.4076  |
Figure 1: Population Selection Flowchart

21,153 Initial Cohort

843 Intervention

305 Enrollment <18-Months Excluded

538

10<18-Years Old Excluded

528

232 No DM Diagnosis Excluded

296

12 No DM Med Usage Excluded

284

20,210 Non-Intervention

4,729 Enrollment <18-Months Excluded

15,481

136<18-Years Old Excluded

15,345

9,474 No DM Diagnosis Excluded

5,871

343 No DM Med Usage Excluded

5,528
Appendix A: Metformin-Containing Combination Medications

Actoplus met
Avandamet
Fortamet
Glipizide/Metformin
Glucophage
Glucophage XR
Glumetza
Glyburide/Metformin
Metaglip
Metformin
Metformin ER
Riomet
Appendix B: ICD-9 Codes to Identify Respiratory Disease

| Code  | Description                        |
|-------|------------------------------------|
| 491.0 | Chronic bronchitis                 |
| 491.1 |                                    |
| 491.2 |                                    |
| 491.5 |                                    |
| 491.8 |                                    |
| 491.9 |                                    |
| 492.0 |                                    |
| 492.1 |                                    |
| 492.2 |                                    |
| 492.3 |                                    |
| 492.4 |                                    |
| 492.5 |                                    |
| 492.6 |                                    |
| 492.7 |                                    |
| 492.8 |                                    |
| 493.0 |                                    |
| 493.1 |                                    |
| 493.2 |                                    |
| 493.3 |                                    |
| 493.4 |                                    |
| 493.5 |                                    |
| 493.6 |                                    |
| 493.7 |                                    |
| 493.8 |                                    |
| 493.9 |                                    |
| 518.1 |                                    |
| 518.2 |                                    |

Appendix C: Descriptions of Used ICD-9 Codes to Identify Respiratory Disease

| Code  | Description                        |
|-------|------------------------------------|
| 491   | Chronic bronchitis                 |
| 492   | Emphysema                          |
| 493   | Asthma                             |
| 496   | Chronic airway obstruction         |
| 518   | Other diseases of lung             |
Appendix D: ICD-9 Codes to Identify Mental Health Disorder

| Code               | Description                                                                 |
|--------------------|-----------------------------------------------------------------------------|
| 295                | Schizophrenia                                                               |
| 296                | Episodic mood disorders including manic disorder, depression, and bipolar disorder |
| 297                | Paranoia                                                                    |
| 298                | Other nonorganic psychoses                                                  |
| 299                | Other psychoses specific to childhood                                        |
| 300                | Neurotic disorder                                                           |
| 301                | Personality disorders                                                       |
| 308                | Acute reaction of stress                                                    |
| 309                | Adjustment reaction                                                         |
| 311                | Depressive disorder                                                         |
| 312                | Disturbance of conduct (specifically to childhood)                          |
| 313                | Disturbance of emotions (specifically to childhood)                         |
| 314                | Hyperkinetic syndrome (specifically to childhood)                           |

Appendix E: Descriptions of Used ICD-9 Codes to Identify Mental Health Disorder

| Code | Description                                                                 |
|------|-----------------------------------------------------------------------------|
| 295  | Schizophrenia                                                               |
| 296  | Episodic mood disorders including manic disorder, depression, and bipolar disorder |
| 297  | Paranoia                                                                    |
| 298  | Other nonorganic psychoses                                                  |
| 299  | Other psychoses specific to childhood                                        |
| 300  | Neurotic disorder                                                           |
| 301  | Personality disorders                                                       |
| 308  | Acute reaction of stress                                                    |
| 309  | Adjustment reaction                                                         |
| 311  | Depressive disorder                                                         |
| 312  | Disturbance of conduct (specifically to childhood)                          |
| 313  | Disturbance of emotions (specifically to childhood)                         |
| 314  | Hyperkinetic syndrome (specifically to childhood)                           |
### Appendix F: ICD-9 Codes to Identify Cardiovascular Disease

| Code | Description |
|------|-------------|
| 410  | Acute myocardial infarction |
| 412  | Old myocardial infarction |
| 413  | Angina |
| 414  | Other forms of chronic ischemic heart disease |

### Appendix G: Descriptions of Used ICD-9 Codes to Identify Cardiovascular Disease

| Code | Description |
|------|-------------|
| 410  | Acute myocardial infarction |
| 412  | Old myocardial infarction |
| 413  | Angina |
| 414  | Other forms of chronic ischemic heart disease |
Afifi AA, Morisky DE, Kominski GF, Kotlerman JB. Impact of disease management on health care utilization: evidence from the "Florida: A Health State (FAHS)" Medicaid program. Prev Med. 2007;44(6):547-553.

Albisser AM, Harris RI, Albisser JB, Sperlich M. The impact of initiatives in education, self-management training, and computer-assisted self-care on outcomes in diabetes disease management. Diabetes Technol Ther. 2001;3(4):571-579.

American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013;35:1033-1046.

American Diabetes Association. Standards of medical care in diabetes - 2014. Diabetes Care. 2013;37(Suppl 1):S14-S80. doi: 10.2337/dc14-s014.

Beich J, Scanlon DP, Ulbrecht J, Ford EW, Ibrahim IA. The role of disease management in pay-for-performance programs for improving the care of chronically ill patients. Med Care Res Rev. 2006;63(1 Suppl):96S-116S.

Benedetti R, Flock B, Pedersen S, Ahern M. Improved clinical outcomes for fee-for-service physician practices participating in a diabetes care collaborative. Jt Comm J Qual Saf. 2004;30(4):187-194.
Berg GD, Wadhwa S. Health services outcomes for a diabetes disease management program for the elderly. Dis Manag. 2007;10(4):226-234.

Berringer R, Shibley MC, Cary CC, Pugh CB, Powers PA, Rafi JA. Outcomes of a community pharmacy-based diabetes monitoring program. J Am Pharm Assoc (Wash). 1999;39(6):791-797.

Blandford L, Dans PE, Ober JD, Wheelock C. Analyzing variations in medication compliance related to individual drug, drug class, and prescribing physician. J Manag Care Pharm. 1999;5(1):47-51.

Bullano MF, Fisher MD, Grochulski WD, Menditto L, Willey VJ. Hypoglycemic events and glycosylated hemoglobin values in patients with type 2 diabetes mellitus newly initiated on insulin glargine or premixed insulin combination products. Am J Health Syst Pharm. 2006;63(24):2473-2482.

Bunting BA, Cranor CW. The Asheville Project: long-term clinical, humanistic, and economic outcomes of a community-based medication therapy management program for asthma. J Am Pharm Assoc (2003). 2006;46(2):133-147.

Bunting BA, Smith BH, Sutherland SE. The Asheville Project: Clinical and economic outcomes of a community-based long-term medication therapy management program for hypertension and dyslipidemia. J Am Pharm Assoc (2003). 2008;48(1):23-31.
Chernew ME, Shah MR, Wegh A, Rosenberg SN, Juster IA, Rosen AB, et al. Impact of decreasing copayments on medication adherence within a disease management environment. Health Affairs. 2008;27(1):103–112.

Chin MH, Drum ML, Guillen M, Rimington A, Levie JR, Kirchhoff AC, et al. Improving and sustaining diabetes care in community health centers with the health disparities collaboratives. Med Care. 2007;45(12):1135-1145.

Clouse JC, Zitter M, Herman ME. Health economic considerations in the management of type 2 diabetes. Manag Care Interface. 2002;15(1):66-71.

Coberley CR, McGinnis M, Orr PM, Coberley SS, Hobgood A, Hamar B, et al. Association between frequency of telephonic contact and clinical testing for a large, geographically diverse diabetes disease management population. Dis Manag. 2007;10(2):101-109.

Cranor CW, Christensen DB. The Asheville Project: factors associated with outcomes of a community pharmacy diabetes care program. J Am Pharm Assoc (Wash). 2003;43(2):160-172.

Cranor CW, Christensen DB. The Asheville Project: short-term outcomes of a community pharmacy diabetes care program. J Am Pharm Assoc (Wash). 2003;43(2):149-159.
Cranor CW. Bunting BA, Christensen DB. The Asheville Project: long-term clinical and economic outcomes of a community pharmacy diabetes care program. J Am Pharm Assoc (Wash) 2003;43(2):173–184.

Cutler TW, Palmieri J, Khalsa M, Stebbins M. Evaluation of the relationship between a chronic disease care management program and california pay-for-performance diabetes care cholesterol measures in one medical group. J Manag Care Pharm. 2007;13(7):578–588.

Daneman D. Type 1 diabetes. Lancet. 2006;367(9513):847-858.

De Bruin SR, Heijink R, Lemmens LC, Struijs JN, Baan CA. Impact of disease management programs on healthcare expenditures for patients with diabetes, depression, heart failure or chronic obstructive pulmonary disease: a systematic review of the literature. Health Policy. 2011;101(2):105-121.

Dore DD, Trivedi AN, Mor V, Lapane KL. Association between extent of thiazolidinedione exposure and risk of acute myocardial infarction. Pharmacotherapy. 2009;29(7):775-783.

Fera T, Bluml BM, Ellis WM, Schaller CW, Garret DG. The Diabetes Ten City Challenge: interim clinical and humanistic outcomes of a multisite community pharmacy diabetes care program. J Am Pharm Assoc (2003). 2008;48(2):181-190.
Garrett DG, Martin LA. The Asheville Project: participants' perceptions of factors contributing to the success of a patient self-management diabetes program. J Am Pharm Assoc (Wash). 2003;43(2):185-190.

Gibson, TB, Wang S, Kelly E, Brown C, Turner C, Frech-Tamas F et al. A value-based insurance design program at a large company boosted medication adherence for employees with chronic illnesses. Health Aff (Millwood). 2011;30(1):109-117.

Grenard JL, Munjas BA, Adams JL, Suuorp M, McGlynn EA, Gellad WF. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Intern Med.2011;26(10):1175–1182.

Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, et al. Prevalence of diabetes, impaired fasting glucose and impaired glucose tolerance in US adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care. 1998;21(4):518-524.

Herrin J, Nicewander DA, Hollander PA, Couch CE, Winter FD, Haydar ZR, et al. Effectiveness of diabetes resource nurse case management and physician profiling in a fee-for-service setting: a cluster randomized trial. Proc (Bayl Univ Med Cent). 2006;19(2):95-102.

Home PD, Pocock SJ, Beck-Nielsen H, Curtis PS, Gomis R, Hanefeld M, et al. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination
therapy for type 2 diabetes (RECORD): a multicentre, randomised, open-label trial. Lancet. 2009;373(9681):2125-2135.

Hoyert DL, Xu J. Deaths: preliminary data for 2011. Natl Vital Stat Rep. 2012; 61(6):1-51.

Ibrahim IA, Beich J, Sidorov J, Gabbay R, Yu L. Measuring outcomes of type 2 diabetes disease management program in an HMO setting. South Med J. 2002;95(1):78-87.

ICD-9-CM Official Guidelines for Coding and Reporting. Centers for Medicare & Medicaid Services; 2011. Available at http://www.cdc.gov/nchs/data/icd/icd9cm_guidelines_2011.pdf. Accessed July 17, 2015.

ICD-9 Code Lookup. Centers for Medicare & Medicaid Services; 2014. Available at http://www.cms.gov/medicare-coverage-database/staticpages/icd-9-code-lookup.aspx. Accessed July 17, 2015.

Ilag LL, Martin CL, Tabaei BP, Isaman DJ, Burke R, Greene DA, et al. Improving diabetes processes of care in managed care. Diabetes Care. 2003;26(10):2722-2727.

Kepple SR. Pharmacists in Asheville, North Carolina, pick up city paychecks for diabetes services. Am J Health Syst Pharm. 1998;55:10-13.
Kogut SJ, Johnson S, Higgins T, Quilliam B. Evaluation of a program to improve diabetes care through intensified care management activities and diabetes medication copayment reduction. J Manag Care Pharm. 2012;18(4):297-310.

Lamanna C, Monami M, Marchionni N, Mannucci E. Effect of metformin on cardiovascular events and mortality: a meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2011;13(3):221-228.

Lavery LA Wunderlich RP, Tredwell JL. Disease management for the diabetic foot: effectiveness of a diabetic foot prevention program to reduce amputations and hospitalizations. Diabetes Res Clin Pract. 2005;70(1):31–37.

Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. Diabetes Care. 2006;29(6):1288-1293.

Lee GC, Mick T, Lam T. The Hickory Project builds on the Asheville Project-an example of community-based diabetes care management. J Manag Care Pharm. 2007;13(6):531-533.

Love TE, Cebul RD, Einstadter D, Jain AK, Miller H, Harris CM, et al. Electronic medical record-assisted design of a cluster-randomized trial to improve diabetes care and outcomes. J Gen Intern Med. 2008;23(4):383-391.
Machado M, Bajcar J, Guzzo FC, Einarson TR. Sensitivity of patient outcomes to pharmacist interventions. Part I: systematic review and meta-analysis in diabetes management. Ann Pharmacother. 2007;41(10):1569-1582.

Mangione CM, Gerzoff RB, Williamson DF, Steers WN, Kerr EA, Brown AF, et al. The association between quality of care and the intensity of diabetes disease management programs. Ann Intern Med. 2006;145(2):107-116.

McCord AD. Clinical impact of a pharmacist-managed diabetes mellitus drug therapy management service. Pharmacotherapy. 2006;26(2):248-253.

National Diabetes Fact Sheet: national estimates and general information on Diabetes and prediabetes in the United States, 2011. Atlanta, GA: Centers for Disease Control and Prevention; 2011. Available at http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed November 20, 2013.

Nau DP, Pacholski AM. Impact of pharmacy care services on patients' perceptions of health care quality for diabetes. J Am Pharm Assoc (2003). 2007;47(3):358-365.

Norris SL, Engelgau MM, Naravan KM. Effectiveness of self-management training in type 2 diabetes: a systematic review of randomized controlled trials. Diabetes Care. 2001;24(3):561-587.
Norris SL, Nichols PJ, Caspersen CJ, Glasgow RE, Engelgau MM, Jack L, et al. The effectiveness of disease and case management for people with diabetes. A systemic review. Am J Prev Med. 2002;22(4 Suppl):15-38.

Nyenwe EA, Jerkins TW, Umpierrez GE, Kitabchi AE. Management of type 2 diabetes: evolving strategies for the treatment of patients with type 2 diabetes. Metabolism. 2011;60(1):1-23.

Okano GJ, Rascati KL, Wilson JP, Remund DD, Grabenstein JD, Brixner DI. Patterns of antihypertensive use among patients in the US Department of Defense database initially prescribed an angiotensin-converting enzyme inhibitor or calcium channel blocker. Clin Ther. 1997;19(6):1433-1445.

Patrick K, Stickles JD, Turpin RS, Simmons JB, Jackson J, Bridges E, et al. Diabetes disease management in Medicaid managed care: a program evaluation. Dis Manag. 2006;9(3):144-156.

Pearson SA, Ross-Degnan D, Payson A, Soumerai SB. Changing medication use in managed care: a critical review of the available evidence. Am J Manag Care. 2003;9(11):715-731.

Recommendations for healthcare system and self-management education interventions to reduce morbidity and mortality from diabetes. Am J Prev Med. 2002;22(4 Suppl):10-14.
Renders CM, Valk GD, Griffin SJ, Wagner EH, Eijk Van JT, Assendelft WJ. Interventions to improve the management of diabetes in primary care, outpatients, and community settings: a systematic review. Diabetes Care. 2001;24(10):1821-1833.

Rubin RJ, Dietrich KA, Hawk AD. Clinical and economic impact of implementing a comprehensive diabetes management program in managed care. J Clin Endocrinol Metab. 1998;83(8):2635-2642.

Sclar DA, Robison LM, Skaer TL, Legg RF, Nemec NL, Galin RS, et al. Antidepressant pharmacotherapy: economic outcomes in a health maintenance organization. Clin Ther. 1994;16(4):715-730.

Shepherd M. Unprecedented opportunities for managed care organizations and community pharmacies to work together. J Manag Care Pharm. 2007;13(5):426-428.

Sidorov J, Gabbay R, Harris R, Shull RD, Girolami S, Tomcavage J, et al. Disease management for Diabetes mellitus: Impact on Hemoglobin A1C. Am J Manag Care. 2000;6(11):1217–1226.

Sidorov J, Shull R, Tomcavage J, Girolami S, Lawton N, Harris R. Does diabetes disease management save money and improve outcomes? A report of simultaneous short-term savings and quality improvement associated with a health maintenance
organization-sponsored disease management program among patients fulfilling health employer data and information set criteria. Diabetes Care. 2002;25:684–689.

Smith SA, Shah ND, Bryant SC, Christianson TJ, Bjornsen SS, Giesler PD, et al. Chronic care model and shared care in diabetes: randomized trial of an electronic decision support system. Mayo Clin Proc. 2008;83(7):747-757.

Stroebel RJ, Scheitel SM, Fitz JS, Herman RA, Naessens JM, Scott CG, et al. A randomized trial of three diabetes registry implementation strategies in a community internal medicine practice. Jt Comm J Qual Improv. 2003;28(8):441-450.

Thiebaud P, Demand M, Wolf SA, Alipuria LL, Ye Q, Gutierrez PR. Impact of disease management on utilization and adherence with drugs and tests: the case of diabetes treatment in the Florida: a Healthy State (FAHS) program. Diabetes Care. 2008;31(9):1717-1722.

Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RC et al. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. Ann Intern Med. 2012;157(11):785-795.

Weber V, Bloom F, Pierdon S, Wood C. Employing the electronic health record to improve diabetes care: a multifaceted intervention in an integrated delivery system. J Gen Intern Med. 2008;23(4):379-382.
Wubben DP, Vivian EM. Effects of pharmacist outpatients interventions on adults with diabetes mellitus: a systematic review. Pharmacotherapy. 2008;28(4):421-436.

Zhang X, Norris SL, Chowdhury FM, Gregg EW, Zhang P. The effects of interventions on health-related quality of life among persons with diabetes: a systematic review. Med Care. 2007;45(9):820-834.