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

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EFFECTS OF INTENSIFIED CARE MANAGEMENT ACTIVITIES AND DIABETES MEDICATION COPAYMENT REDUCTION ON MEDICATION ADHERENCE AND HEALTH CARE COSTS

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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.

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PREFACE

The standard format was used in preparation of this thesis.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

FIGURE **PAGE**

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.[10] According to the study, mean hemoglobin A1c of patients decreased from 8.51to 7.41 after 3 months of follow-up.[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.[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.[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.[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.[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.[15-16]Poor medication adherence causes approximately 125,000 deaths due to increase in morbidity in hospitalizations.[17] Furthermore, poor medication adherence costs the U.S. health care system up to $289 billion annually.[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.[18] 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.[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).

CHAPTER 3

RESULTS

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 aged50-64 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 thoseusing1 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 aged65 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 taking8 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.[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.[23] 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.

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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
	N	%	N	%	
Mean [SD] age	54.056 [9.50]		54.585 [8.59]		0.3145
Age group					
18-49	74	26.06	1,433	25.92	0.4396
50-64	176	61.97	3,558	64.36	
65+	34	11.97	537	9.71	
Gender					
Male	174	61.27	3,377	61.09	0.952
Female	110	38.73	2,151	38.91	
Insulin					
No	171	60.21	3,570	64.58	0.1338
Yes	113	39.79	1,958	35.42	
Total Medication Counts					
1-7	71	25.00	1,160	20.98	0.4178
8-13	84	29.58	1,733	31.35	
14-17	48	16.90	926	16.75	
18+	81	28.52	1,709	30.92	
Comorbidity (Respiratory diseases)					
No	264	92.96	4,919	89.11	0.0409
Yes	20	7.04	601	10.89	
Comorbidity (Mental health disorders)					
No	240	84.51	4,728	85.65	0.5920
Yes	44	15.49	792	14.35	
Comorbidity (Cardiovascular diseases)					
No	264	92.96	4,793	86.83	0.0026
Yes	20	7.04	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	35.10	978	64.90	<0.0001
50-64	901	24.13	2,833	75.87	
65+	109	19.09	462	80.91	
Gender					
Male	922	25.96	2,629	74.04	0.2646
Female	617	27.29	1,644	72.71	
Insulin					
No	991	26.49	2,750	73.51	0.9805
Yes	548	26.46	1,523	73.54	
Total Medication Counts					
1-7	485	39.40	746	60.60	<0.0001
8-13	542	29.83	1,275	70.17	
14-17	221	22.69	753	77.31	
18+	291	16.26	1,499	83.74	
Comorbidity (Respiratory diseases)					
No	1,368	26.39	3,815	73.61	0.5423
Yes	171	27.54	450	72.46	
Comorbidity (Mental health disorders)					
No	1,283	25.83	3,685	74.17	0.0037
Yes	256	30.62	580	69.38	
Comorbidity (Cardiovascular diseases)					
No	1,372	27.13	3,685	72.87	0.0058
Yes	167	22.36	580	77.64	
Intervention					
No	1,462	26.45	4,066	73.55	0.8042
Yes	77	27.11	207	72.89	

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

	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

Table5: 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	Ref				
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	Ref				
Yes	-0.1350	0.874	0.769	0.993	0.0379
Total Medication Counts					
1-7	Ref				
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	Ref				
Yes	-0.3526	0.703	0.595	0.831	<0.0001
Intervention					
No	Ref				
Yes	0.00808	1.008	0.765	1.328	0.9542

Table6: 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)

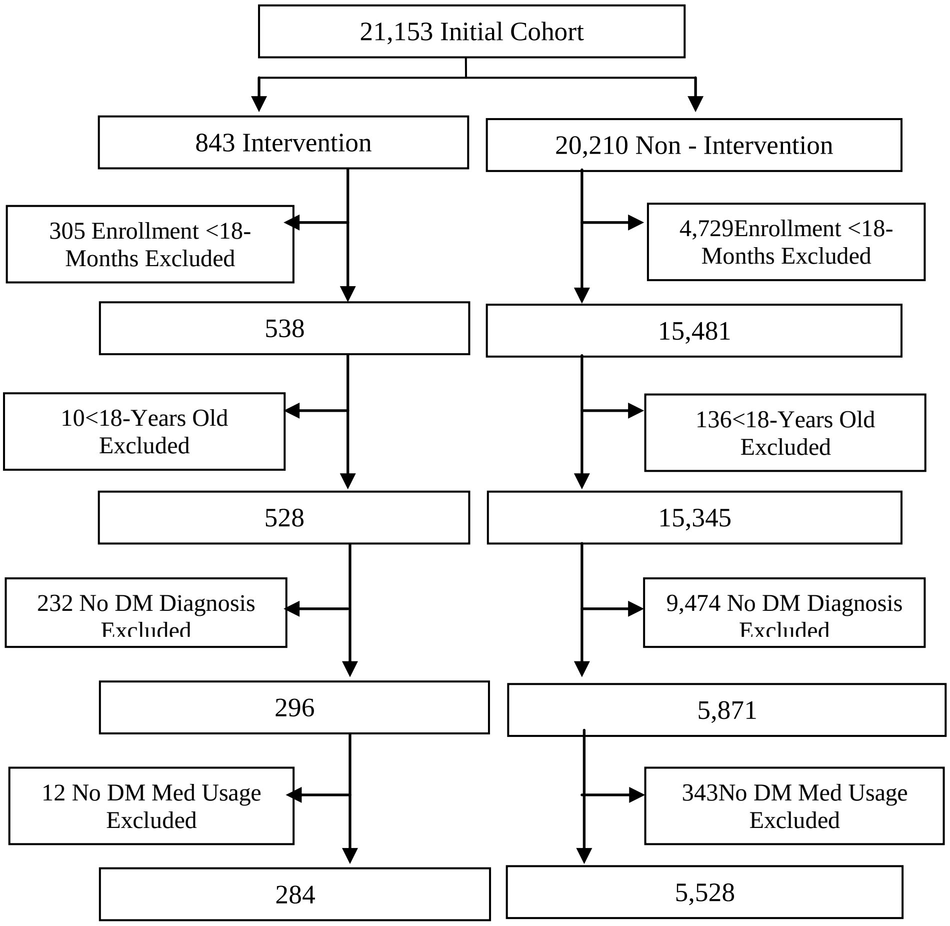
	INTERVENTION		NON-INTERVENTION		
	Mean ($)	Sd	Mean ($)	Sd	P value
Pharmacy	2,904.92	2,890.37	2,655.21	3,265.73	0.2065
PMPM	242.08		221.27		
Medical	5,922.08	13,303.75	7,438.93	16,889.93	0.1363
PMPM	493.51		619.91		
Total	8,827.01	14,246.70	10,096.53	17,628.76	0.2327
PMPM	735.58		841.38		

*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		
	Mean ($)	Sd	Mean ($)	Sd	P value
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



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

491.0 491.1 491.20 491.21 491.22 491.8 491.9 492.0 492.8 493.00 493.01 493.02 493.10 493.11 493.12 493.20 493.21 493.22 493.81 493.82 493.90 493.91 493.92 496 518.1 518.2

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

295.00295.01295.02295.03295.04295.05295.10295.11295.12295.13295.14295152 95.20295.21 295.22295.23295.24295.25295.30295.31 295.32295.33295.34295.35295.40295.41295.42295.43295.44295.45295.50295.51 295.52295.53295.54 295.55295.60295.61295.62295.63295.64295.65295.70295.71295.72295.73295.74 295.75295.80295.81295.82295.83295.84295.85295.90295.91295.92295.93295.94 295.95296.00296.01296.02296.03296.04296.05296.06296.10296.11296.12296.13 296.14296.15296.16296.20296.21296.22296.23296.24296.25296.26296.30296.31 296.32296.33296.34296.35296.36296.40296.41296.42296.43296.44296.45296.46 296.50296.51296.52296.53296.54296.55296.56296.60296.61296.62296.63296.64 296.65296.66296.7296.80296.81296.82296.89296.90296.99297.0297.1297.2297.3 297.8297.9298.0298.1298.2298.3298.4298.8298.9299.00299.01299.10299.11299. 80299.81299.90299.91300.3300.4301.0301.10301.11301.12301.13301.20301.213 01.22301.23301.3301.4301.50301.51301.59301.6301.7301.80301.81301.82301.83 301.84301.89301.9308.0308.1308.2308.3308.4308.9309.0309.1309.21309.22309. 23309.24309.28309.29309.3309.4309.81309.82309.83309.89309.9311312.00312. 01312.02312.03312.10312.11312.12312.13312.20312.21312.22312.23312.30312. 31312.32312.33312.34312.35312.39312.4312.81312.82312.89312.9313.0313.131 3.21313.22313.23313.3313.81313.82313.83313.89313.9314.00314.01314.1314.23 14.8314.9

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

410.00410.01410.02410.10410.11410.12410.20410.21410.22410.30410.31410.32 410.40410.41410.42410.50410.51410.52410.60410.61410.62410.70410.71410.72 410.80410.81410.82410.90410.91410.92411.00411.10411.81411.89412.00413.00 413.10413.90414.00414.01414.02414.03414.04414.05414.06414.07414.10414.11 414.12414.19414.80414.90

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

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